American Board of Artificial Intelligence in Medicine (ABAIM)

Study Guide
with
Questions
and
Answers/Explanations

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I. Introduction to Artificial Intelligence

Chapter 1: Basic Concepts of Artificial Intelligence

Questions 1.1/Data-to-Intelligence Continuum

1. What statement is *false* about the data-to-intelligence continuum?
a. Data is the foundational layer of signals and words that have little meaning without context
b. Knowledge is contextual and can be explicit or tacit
c. Data is defined as information in a more structured as well as more meaningful context
d. When information becomes more contextual, this becomes knowledge
[ ]

2. In the data-to-intelligence continuum, when data is more structured as well as in a more meaningful context and in a much better organized format, it is termed:
a. Information
b. Knowledge
c. Intelligence
d. Wisdom
[ ]

3. In the data-to-intelligence continuum, list the correct order that this continuum occurs from bottom to the top:
a. Data-Information-Knowledge-Intelligence
b. Data-Knowledge-Information-Intelligence
c. Data-Information-Wisdom-Intelligence
d. Data-Knowledge-Wisdom-Intelligence
[ ]

4. In the context of the data-to-intelligence continuum, a voxel in a cardiac MRI is an example of:
a. Wisdom
b. Knowledge
c. Data
d. Intelligence
[ ]

5. If data are "atoms", then what are "molecules" in the data-to-intelligence continuum?
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b. Information
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a. Knowledge
b. Information
c. Wisdom
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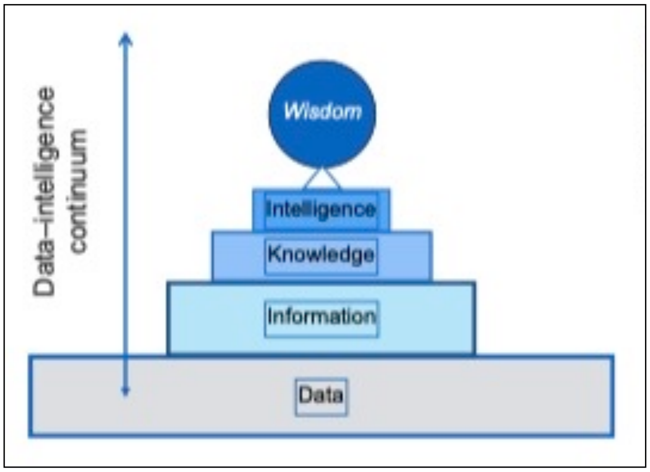
Module 1.1/Data-to-Intelligence Continuum

Data-to-Intelligence Continuum. Intelligence is usually bundled with an interesting list of words like data, information, knowledge, intelligence, and wisdom; these words form an **information hierarchy** but are often misunderstood (see Figure).



Data is the foundational layer of signals and facts that have little or no meaning without context. **Information,** then, is data in a more structured as well as more meaningful context and is often much better organized. If data are atoms of information, then information could be considered a molecule. When information becomes more contextual, this becomes knowledge. **Knowledge** can be explicit or tacit, and involves understanding patterns and is also used to achieve goals. **Intelligence** is the ability to acquire and apply knowledge to achieve goals.

Wisdom is an understanding of principles derived from intelligence and has embedded within it, values and beliefs with self-reflection and futuristic vision. The difference between intelligence and wisdom is that the latter is informed decision powered by good intelligence using values and ethics, so it is more difficult to attain. There is a continuum from data to intelligence and with good intelligence, one can have wisdom; in health care, there should eventually be a bidirectional continuity from wisdom and intelligence directing how data, information, and knowledge be gathered, stored, and shared.

Questions 1.2/Types of Artificial Intelligence

1. IBM Watson defeated the human champions in the game Jeopardy! in 2011. This feat can be described as an example of:
a. Superintelligence
b. Weak artificial intelligence
c. Strong artificial intelligence
d. General artificial intelligence
[ ]

2. An AI agent which acts as a colleague reviewing cases with the clinician is an example of:
a. General artificial intelligence
b. Weak artificial intelligence
c. Narrow artificial intelligence
d. Machine learning
[ ]

3. Which statement *best* describes the state of artificial intelligence today?
a. Artificial intelligence has reached artificial superintelligence as described by philosopher Nick Bostrom
b. Artificial intelligence has reached technological singularity as predicted by futurist Ray Kurzweil
c. Artificial intelligence can perform some narrow tasks as well as or even better than humans
d. Artificial intelligence cannot perform any specific tasks as good as humans
[ ]

4. Which of the following is *not* considered to be an example of narrow artificial intelligence:
a. Playing the game *Go*
b. Reading brain MRI for detecting brain tumor
c. Driving autonomously
d. Reasoning abstractly
[ ]

5. AI in the form of deep learning is now capable of classifying skin cancer. This is an example of:
a. Weak artificial intelligence
b. General artificial intelligence
c. Strong artificial intelligence
d. Artificial general intelligence
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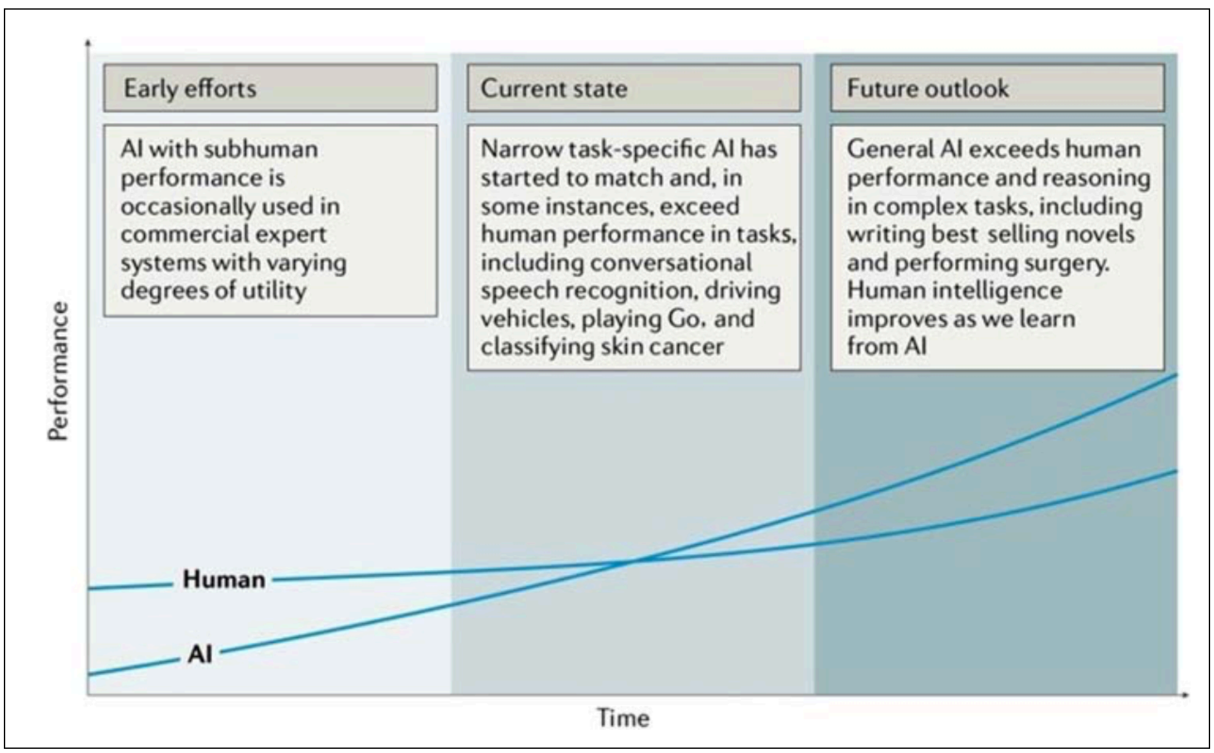
Module 1.2/Types of Artificial Intelligence

Types of Artificial Intelligence. Artificial intelligence can be categorized as weak or strong: **weak AI** (also termed “specific” or “narrow” AI) pertains to AI technologies that are capable of performing specific tasks (like playing chess or Jeopardy!) and **strong AI** (also termed “broad” or “general” AI) is much more difficult to attain; it is also called **artificial general intelligence** (or AGI) or general artificial intelligence (see Figure). AGI relates to machines that are capable of performing intellectual tasks that involve human elements of senses and reason. The public’s inaccurate perception of artificial intelligence, however, continues to be that of the menacing robots that threaten mankind (such as HAL in 2001: A Space Odyssey or the Terminator). Recently, this perception is modified to that of the more sophisticated and complex AI-inspired but still anthropomorphic robots or cyborgs seen in movies like Her (2013) and Ex Machina (2015). The Swedish philosopher Nick Bostrom, in his enlightening book, cautioned the advent of a **superintelligence** that is essentially an intelligent agent that is superior to humans in intelligence (“an intellect that is much smarter than the best human brains in practically every field, including scientific creativity, general wisdom, and social skills”). The futurist Ray Kurzweil similarly described a **technological singularity**, a phenomenon in which the exponential increase in machine intelligence will supersede the human intelligence near the year 2045. In short, these AI intellects are concomitantly optimistic and cautious about the evolution of AI in the coming decades.



Questions 1.3/Human-Machine Intelligence Continuum

1. The type of artificial intelligence that involves machines performing repetitive tasks that are automated and therefore do not require an interaction with a human is called:
a. Assisted
b. Augmented
c. Autonomous
d. Analytical
[ ]

2. Which of the following statements is *true* about augmented type of artificial intelligence:
a. Augmented artificial intelligence involves humans and machines making decisions together
b. Augmented artificial intelligence has little or no human involvement
c. The IDx-DR deep learning AI tool used for screening eye disease is an example of this type of artificial intelligence
d. Augmented artificial intelligence is used for systems that automate repetitive tasks
[ ]

3. Of the following, which is an example of an autonomous artificial intelligence tool in clinical practice:
a. Robot for blood work in the laboratory
b. Watson for Oncology for generating treatment recommendations
c. Chatbot for interacting with patients in the clinic
d. Deep learning screening tool (IDx-DR) for diabetic retinopathy
[ ]

4. The type of artificial intelligence used for the cognitive computing system Watson for Oncology is most accurately called:
a. Amplified
b. Augmented
c. Assisted
d. Autonomous
[ ]

5. Of these types of artificial intelligence, which has the least presence at the current time in medicine and healthcare:
a. Assisted
b. Augmented
c. Autonomous
d. Amplified
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Module 1.3/Human-Machine Intelligence Continuum

The Human-Machine Intelligence Continuum. Artificial intelligence can be described in the context of a human-machine intelligence continuum with three types of artificial intelligence: assisted, augmented, and autonomous (see Table). The table illustrates these three types of artificial intelligence as well as examples in the real and medical worlds. **Assisted intelligence** is when the machines perform tasks that are automated as the tasks do not change and do not require an interaction with humans (such as certain automation tasks in a factory or the robot vacuum cleaner that are now ubiquitous). **Augmented intelligence,** on the other hand, implies that there is an active and ongoing interaction between the human and machine so that both humans and machines are informed and learn (such as machine learning). Some like to use this term in the context of avoiding the term "artificial" all together in hopes to raise the level of acceptance of AI in medicine and health care. **Autonomous intelligence,** as exemplified by the autonomously driven vehicle, involves an automated decision making by the machine with the machine learning continuously.

There is an increasing number of examples of all types of intelligence but the number of autonomously intelligent machines (such as autonomous vehicles and drones) has risen substantially in the last few years. The autonomous intelligence has already started in biomedicine: the recent FDA approval of the first autonomously functioning diagnostic tool, a deep learning screening tool for diabetic retinopathy, does not require a physician's input and can return one of two results: more than mild diabetic retinopathy (referral to eye care professional) or negative for more than mild diabetic retinopathy (repeat screening in 12 months).

Table 1. The Human-Machine Intelligence Continuum

Type of Intelligence	Definition	Level of Human Involvement	Example	Example in Health care
Assisted	System providing and automating repetitive tasks	Little or none	Industrial robots	UR robots for blood work (Copenhagen Hospital)
Augmented	Humans and machines collaboratively make decisions	Some or high	Business analytics	Watson for Oncology (Memorial Sloan Kettering)
Autonomous	Decisions made by adaptive intelligent systems autonomously	Little or none	Autonomous vehicle	IDx-DR for retinal images (University of Iowa)

Questions 1.4/Artificial Intelligence and Data Science

1. Which of the following *least* accurately describes the differences between data analytics and data science:

a. Statistics vs Data modeling
b. Processed vs Raw data
c. Data mining vs Machine learning
d. Python vs R
[ ]

2. Cognitive computing (like IBM Watson) involves a set of AI tools that includes all of the following *except*:

a. Natural language processing
b. Knowledge representation
c. Machine learning
d. Robotics
[ ]

3. Which of the following pairings that describes data analyst vs data scientist is correct?

a. Perspective: looking forward vs looking backward
b. Predictive: causation vs correlation
c. Task: business intelligence vs new algorithm
d. Tools: Pytorch (Python) vs Tableau
[ ]

4. All of the following are related to use of natural language processing (NLP) *except*:

a. Drones
b. Chatbot
c. Virtual assistant
d. IBM Watson
[ ]

5. Natural language processing and machine learning combined as an AI tool can be most likely seen in all of the following *except*:

a. Cognitive computing
b. Robotic process automation
c. Chatbots
d. Computer vision
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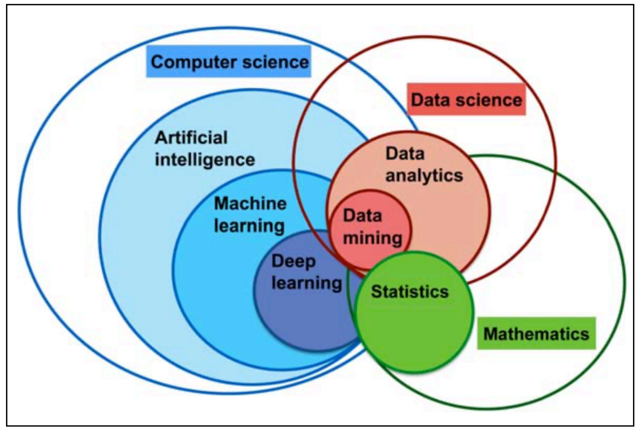
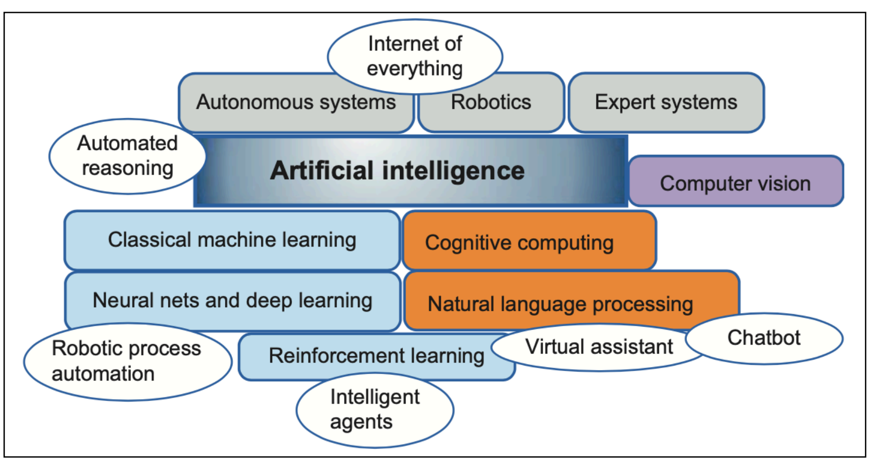
Module 1.4/Artificial Intelligence and Data Science

Artificial Intelligence and Data Science.
The figure and circles show the spheres of computer science and AI, data science, and mathematics. Data science is at the intersection of computer science and mathematics. Deep learning and machine learning are within the domain of AI whereas data analytics and data mining are inside the data science realm.



Other AI methodologies include cognitive computing and natural language processing as well as computer vision, robotics, and autonomous systems (see Figure). **Cognitive computing** (as exemplified by IBM's Watson cognitive computing platform) can involve a myriad of AI tools that simulates human thinking processes while **natural language processing (NLP)** involves connecting human language with computer programmed processing, understanding, and generation. **Computer vision** will not be separately discussed other than under deep learning and convolutional neural networks (CNN). **Robotics** in its impressive panoply of forms is considered part of AI as well as its related **autonomous systems** (in the context of AI not IT). It is perhaps reasonable to think about AI as a "symphony" of musical instruments, and you being the composer and/or conductor can put various music instruments together to realize the music you composed and envisioned. For example, there are many AI tools that are combinations of these elements, such as machine learning and NLP combining for robotic process automation (RPA) or chatbots, or NLP aligning with machine learning for cognitive computing.



The many domains of AI are shown with major ones shown in color. The figure shows one of many ways AI and its portfolio can be illustrated and is not at all meant to be inclusive of all the tools and methodologies. In addition, most of these domains have overlap and are not mutually exclusive. For example, cognitive computing is a portfolio of tools that includes natural language processing and machine learning.

Questions 1.5/Analytics Continuum

1. In the analytics continuum, which of the following types of analytic answers the question "What happened"?
a. Predictive
b. Prescriptive
c. Cognitive
d. Descriptive
[ ]

2. What is the main focus of prescriptive type of analytics in a healthcare system?
a. Forecasting
b. Reporting
c. Optimization
d. Intelligence
[ ]

3. Of the following, which type of analytics optimizes human decision-making by making recommendations utilizing machine and even deep learning by data scientists?
a. Prescriptive
b. Descriptive
c. Predictive
d. Diagnostic
[ ]

4. In healthcare systems, which is the most common type of analytics used in administration?
a. Predictive
b. Cognitive
c. Prescriptive
d. Descriptive
[ ]

5. What will be the most advanced type of analytics in healthcare?
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b. Cognitive
c. Predictive
d. Diagnostic
[b]

Module 1.5/Analytics Continuum

The Analytics Continuum. In addition to the man-machine intelligence continuum, there is also an AI-inspired analytics continuum (descriptive, diagnostic, predictive, prescriptive, and cognitive analytics) that increases in intelligence and autonomous behavior from a data science perspective (see Table).

Descriptive analytics (traditional business intelligence) is commonplace even in health care and uses well-established statistical methodologies and software packages for fulfilling mostly a reporting function. Methodologies used here include data visualization and data mining. **Diagnostic analytics** creates more value but is more difficult to achieve. Methodologies used here include queries and root cause analysis. **Predictive analytics** is less common than the two former types of analytics but provides insights by detecting patterns in data with the use of statistical methods (such as classification, regression, and clustering) that usually falls just short of machine learning. **Prescriptive analytics** is an even higher level of analytics that optimize human decision-making by prescribing recommendations with the utilization of machine and deep learning. This area is usually covered by data scientists more than data analysts. **Cognitive analytics** is the highest level of analytics (and therefore by far the most difficult to achieve) that is present when a project or an enterprise deploys AI methodologies (like reinforcement learning, deep learning, and cognitive computing) to achieve a human-like cognition characterized by self-learning behavior with intelligence.

Table. Analytic Continuum

Type of Analytic	Focus	Tools	Question
Descriptive	Reporting	Statistical software Data visualization	What happened?
Diagnostic	Insight	Statistical software Data visualization	Why did it happen?
Predictive	Forecasting	Statistical models Predictive modeling	What will happen?
Prescriptive	Optimization	Predictive modeling Machine learning	What should I do?
Cognitive	Intelligence	Reinforcement learning Cognitive computing	What is the best that could happen?

Chapter 2: History of Artificial Intelligence

Questions 2.1/History of Artificial Intelligence

1. The British mathematician/computer scientist who helped to decipher the German Enigma machine during the Second World War with his work with theory of computation was:
a. John McCarthy
b. Alan Turing
c. Marvin Minsky
d. Thomas Bayes
[ ]

2. A test of a machine AI ability to pass itself as a human, as judged by humans blinded to the machine or human is called:
a. Bayes' theorem
b. The Antikythera mechanism
c. The Turing test
d. The Analytic Engine
[ ]

3. What was the significance of the perceptron that was conceptualized by Frank Rosenblatt around 1957?
a. This machine subunit inspired by the biological neuron lead to artificial neural network
b. This was the beginning of the concept of the expert system
c. This was a model for cognitive computing
d. This was the first demonstration of natural language processing
[ ]

4. Who was the first to coin the phrase "artificial intelligence"?
a. Alan Turing
b. John McCarthy
c. Frank Rosenblatt
d. Garry Kasparov
[ ]

5. Which of the following events had the *least* significant impact on AI as a field:
a. IBM Watson (cognitive computing) and defeat of human champions in *Jeopardy!* in 2011
b. AlphaGo of DeepMind (deep reinforcement learning) winning the Go tournament in 2016
c. IBM Deep Blue (expert system) and defeat of Garry Kasparov in chess in 1997
d. Billy Beane's statistical approach (analytics) in baseball in 2002
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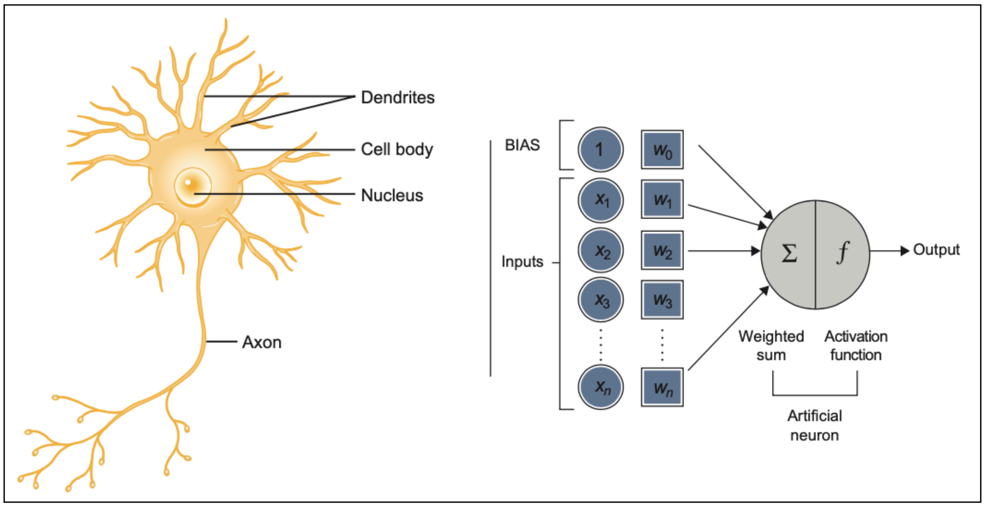
Module 2.1/History of Artificial Intelligence

Key People and Events. The history of artificial intelligence can be traced back to the study of logic delineated by the Greek philosopher Aristotle as he formulated a system of **syllogisms** for proper reasoning as well as the ancient Greek Antikythera Mechanism, the oldest known analog computer in the world. The statistician Thomas Bayes and his framework for **probability and Bayesian inference**, the mathematician George Boole and his Boolean **algebra**, and the polymath Charles Babbage and his early digital programmable **computer** (the Analytic Engine) all contributed to the underpinnings of present day artificial intelligence (see Table).

Alan Turing and the Turing Machine. It is the brilliant British mathematician and computer scientist Alan Turing, however, who would be considered the absolute **progenitor** of artificial intelligence with his pioneering works that included his theory of computation and his work on computing machines. His most valuable contribution was his deciphering of the German Enigma machine during the second World War at Bletchley Park using **machine intelligence** (portrayed in the recent film *The Imitation Game*). The eponymous **Turing Test** is a test of machine AI's ability to pass itself as a human, as judged by humans blinded to the machine or human.

The Dartmouth Conference. In 1956, mathematicians and scientists gathered at the august seminal Dartmouth Conference (organized by John McCarthy and others) and it is the proposal for this august gathering that the term **"artificial intelligence"** was coined by the Stanford computer scientist John McCarthy. This summer conference and its discussions is widely thought to be the birth of AI as an interdisciplinary field. McCarthy was also instrumental in designing the first AI programming language called LISP, which was the precursor to several important concepts such as tree data structure and object-oriented programming.

Rosenblatt's Perceptron. Around this time, a significant contribution was made by the American psychologist Frank Rosenblatt in 1958 in the form of the **perceptron** (see Figure), a biologically-inspired, three-layer structure (with input, transfer function, and output) that was a simple but elegant supervised linear binary classifier (see section on machine learning). The perceptron became the early precursor of the artificial neural network and present day deep learning architecture that we are so familiar with today.



Biological Neuron and Computational Perceptron. On the left, the biological neuron and its anatomy illustrates dendrites carry impulses toward the cell body and nucleus, and these impulses are processed and move from the cell body via an axon and its connections and terminals.

On the right is a schematic diagram of a **perceptron**. The **Inputs** *x* are multiplied by their **weights** *w* and the resultant weighted **sum** then is all the multiplied values added together (not illustrated is an extra weight that helps to neutralize bias in the classifier). These inputs are equivalent to the dendrites carrying impulses toward the neuronal body. The **activation function** (or step function) is placed in the node and is linear or non-linear depending on the data. The activation functions can be sigmoid, tanH (similar to a sigmoid), or ReLU (Rectified Linear Unit) which has a slope of 1. After this function processes the sum, the **output** is delivered.

Table. A Brief History of Artificial Intelligence

Year	AI Events	Key People
384-322 BC	**Syllogism** - Methods of logical argument and analytics	Aristotle Greek philosopher
250-60 BC	**Antikythera Mechanism** - Oldest computer used to predict astronomical positions	Greek scientists and sailors
1763	**Bayesian inference** - Framework for reasoning about the probability of events	Thomas Bayes English statistician
1854	**Logical reasoning** - Framework for representation of logic in equations	George Boole English mathematician
1837	**Analytical Engine** - First computer with general purpose computation	Charles Babbage/Ada Lovelace English mathematician/programmer
1943	**A Logical Calculus of the Ideas Immanent in Nervous Activity** - Concept of artificial neurons and logical functions	Warren McCulloch and Walter Pitts American neuroscientist and logician
1945	**Electronic Numerical Integrator and Computer (ENIAC)** - First electronic general-purpose computer	Gladeon Barnes Chief of research and engineering
1949	**Programming a Computer for Playing Chess** - First reference on chess-playing computer program	Claude Shannon American mathematician
1950	**Computing Machinery and Intelligence** - The "imitation game" that became the Turing test	Alan Turing English mathematician
1951	**Stochastic Neural Analog Reinforcement Calculator (SNARC)** - First artificial neural network	Marvin Minsky American cognitive scientist
1952	**First computer checkers program** - Early demonstration of machine learning	Arthur Samuel American AI researcher
1955	**The Logical Theorists** - First AI program to mimic human problem solving	Allen Newell American computer scientist
1956	**Dartmouth Summer Research Project on AI** - Term "artificial intelligence" coined and AI seminal event	John McCarthy American computer scientist
1957	**The Perceptron algorithm and machine** - Precursor to neural network and deep learning	Frank Rosenblatt American psychologist
1958	**LISt Processing (LISP)** - Programming language for AI research	John McCarthy American computer scientist
1965	**ELIZA** - Interactive NLP program with human-machine communication	Joseph Weizenbaum German American computer scientist
1968	**2001: A Space Odyssey** - HAL, the sentient computer	Arthur C. Clarke English novelist and futurist

Year	AI Events	Key People
1989	**Backpropagation algorithm** - Application in multi-layer neural network	Yann LeCun (AT&T Bell Labs)
	MODERN AI ERA	
1997	**Deep Blue (IBM)** - Chess-playing program defeating world champion	Garry Kasparov Russian chess grandmaster
2011	**Watson (IBM)** - DeepQA project defeating Jeopardy! champions	David Ferrucci Principal scientist
2012	**ImageNet** - CNN with 650,000 neurons reduced error rate to 15.3%	Geoff Hinton English-Canadian computer scientist
2016	**AlphaGo (DeepMind)** - Reinforcement learning defeating Go champion Lee Sedol	Demis Hassabis English AI researcher and neuroscientist
2017	**AlphaZero (DeepMind)** - Superhuman play in multiple games and trained by self-play	Demis Hassabis English AI researcher and neuroscientist
2019	**AlphaStar (DeepMind)** - Deep reinforcement learning defeating StarCraft player	Demis Hassabis English AI researcher and neuroscientist

Chapter 3: History of Artificial Intelligence in Medicine

Questions 3.1/History of Artificial Intelligence in Medicine

1. The expert system has these components listed below *except*:
a. Rules engine
b. User interface
c. Knowledge base
d. Convolutional layer
[ ]

2. The initial effort in application of artificial intelligence in medicine began with a domain-specific rule-based system called:
a. Expert system
b. Deep learning system
c. Machine learning system
d. Artificial neural network
[ ]

The major shortcomings of the early era of AI adoption in medicine include the following *except*:
a. Lack of theory-to-use coupling
b. Inadequate integration into workflow
c. Lack of human champions
d. Slow speed of computation
[ ]

A type of artificial intelligence that deals with degrees or continuum of truth and is therefore particularly well suited for biological systems with continuous data is:
a. Expert systems
b. Fuzzy logic
c. Case-based reasoning
d. Neural network
[ ]

What disease was the first FDA-cleared autonomous artificial intelligence device used for?
a. Congestive heart failure
b. Diabetic retinopathy
c. Asthma
d. Septic shock
[ ]

Answers 3.1/History of Artificial Intelligence in Medicine

1. The expert system has these components listed below *except*:
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c. Knowledge base
d. Convolutional layer
[d]

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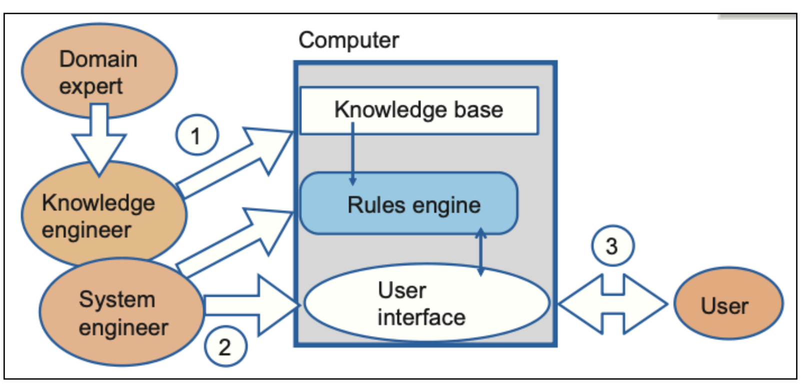
b. Diabetic retinopathy
c. Asthma
d. Septic shock
[b]

Module 3.1/History of Artificial Intelligence in Medicine

Rule-based Expert Systems. Initial efforts in artificial intelligence and its application in medicine began in the 1960's with ruled-based domain specific expert systems and focused mainly on diagnosis and therapy. Among the best known early works on AI in medicine was the Stanford physician and biomedical informatician Edward Shortliffe's innovative heuristic programming project **MYCIN**. This pioneering work was a rule-based expert system (written in the Lisp programming language) that had if-then rules; these rules yielded certainty values that mimicked a human's expertise (such as recommended selection of antibiotics for various infectious diseases).

The **expert system** worked as follows (see Figure): Knowledge is a repository of both factual and heuristic knowledge, and this knowledge from a human domain expert was entered into a **knowledge base** via a knowledge engineer (step 1). The knowledge base is organized and the effectiveness of this knowledge base is proportional to the quality and accuracy of the knowledge entered. This knowledge base was in turn connected to a **rules engine** with its many if-then rules stored within it. A system engineer overlooks the rules engine (as well as the user interface)(step 2). The user then queries a **user interface** (step 3) that was coupled to the inference engine. The final reconciled advice was then given to the user via this user interface. In essence, the expert system is a set of programmed rules that the computer can follow and output an answer based on these rules.

Overall, the main shortcomings during these early decades of AI tools in biomedicine included not only a lack of theory-to-use coupling but also an inadequate integration of the existing AI techniques into workflows to achieve user support (due to slowness of the tools and lack of adequate data or knowledge).



Other AI Methodologies. In addition to the above expert systems, some other AI methodologies were used in medicine included fuzzy logic and neural networks. **Fuzzy logic,** as discussed earlier, deals with degrees or continuum of truth (vs the dichotomous Boolean logic of true or false) and is therefore particularly well suited for biological systems with objective physiological parameters of continuous data (such as heart rate and blood pressure). A recent review concluded that fuzzy logic will need to be an essential part of AI in medicine in the near future as algorithms alone are not feasible for solving enigmas and conundrums in biomedicine. **Neural network** is a processing paradigm that is inspired by the brain; this methodology was applied to various clinical situations such as clinical diagnosis and medical images as well as the critical care setting.

Table. A Brief History of Artificial Intelligence in Medicine

Year	AI in Medicine Events	Key People
1972	**MYCIN** - Expert system for identifying bacteria for infection	Ted Shortliffe American physician-computer scientist
1974	**INTERNIST-1** - Computer-assisted diagnostic tool for medicine	Jack Myers American internist
1982	**Artificial Intelligence in Medicine** - First book on AI in medicine	Peter Szolovits American computer scientist
1985	**Artificial Intelligence in Medicine (AIME)** - First AI in medicine meeting	Mario Stefanelli Italian biomedical engineer
1986	**DXplain** - Clinical decision support system with probabilistic algorithm	EP Hoffer Massachusetts General Hospital
	MODERN AI ERA	
1998	**Artificial Intelligence in Medicine (AIME) Journal** - First AI in medicine journal	Mario Stefanelli Italian biomedical engineer
2002	**ISABEL (Isabel Healthcare)** - Clinical decision support system for pediatrics	Jason Maude Founder
2017	**CheXNet (Stanford)** - CNN algorithm for pneumonia detection at high level	Andrew Ng American AI expert
	Cardio DL (Arterys) - First FDA-approved AI-assisted cardiac imaging in cloud	Fabien Beckers CEO
2018	**ContaCT (Viz.AI)** - First FDA-cleared AI-powered CDSS platform (stroke)	Chris Mansi/ David Golan CEO/CTO
	IDx-DR (IDx) - First FDA-cleared autonomous AI device (diabetic retinopathy)	Michael Abramoff American ophthalmologist-scientist
2019	**AI in Health Care Regulation (FDA)** - FDA proposal for innovations in AI in health care regulation	Scott Gottlieb Chief, FDA

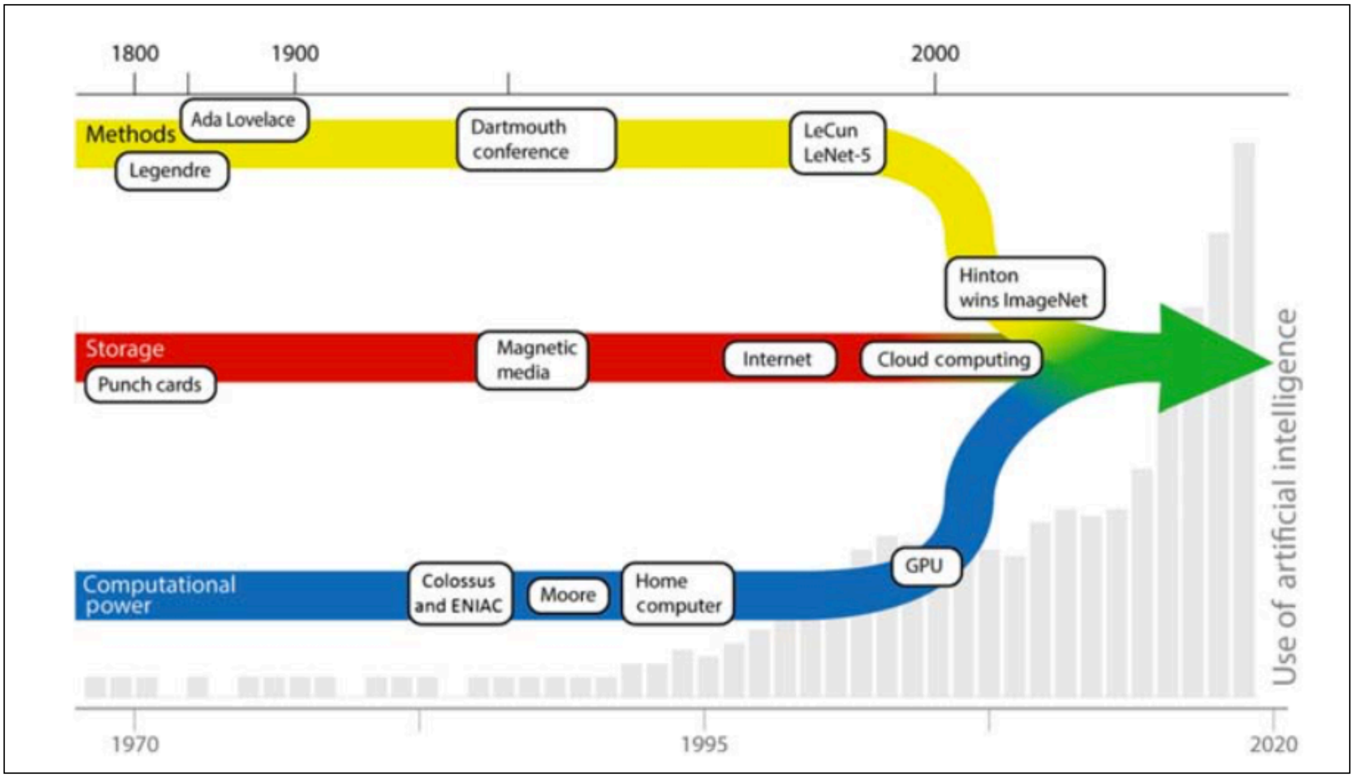
Key Concepts in Section I

- The recent impressive gains in sophistication of deep learning (DL) technology and utilization especially since 2012 have lead to an escalating momentum for AI awareness and adoption.
- Even though the advent of data science and machine and deep learning has advanced information and analyses and promoted innovations, health care and medicine remain very much behind these other domains in leveraging this new AI paradigm.
- There is a continuum from data to intelligence and with good intelligence, one can have wisdom; in health care, there should eventually be a bidirectional continuity from wisdom and intelligence directing how data, information, and knowledge be gathered, stored, and shared.
- Perhaps the best definition of artificial intelligence (AI) is the one conjured by the American cognitive scientist Marvin Minsky: the science of making machines do things that would require intelligence if done by human.
- Artificial intelligence can be categorized as weak or strong: weak (also termed "specific" or "narrow") AI pertains to AI technologies that are capable of performing specific tasks (like playing chess or *Jeopardy!*) and strong (also termed "broad" or "general") AI is much more difficult to attain; it is also called artificial general intelligence (or AGI) or general artificial intelligence.
- Machine learning (ML)(and its more robust and specific type, deep learning) are not synonymous with artificial intelligence but are often used interchangeably; ML as well as DL are AI methodologies.
- Other AI methodologies include cognitive computing and natural language processing as well as computer vision, robotics, and autonomous systems.
- Artificial intelligence can be described in the context of a human-machine intelligence continuum with three types of artificial intelligence: assisted, augmented, and autonomous.
- In addition to the man-machine intelligence continuum, there is also an AI-inspired analytics continuum (descriptive, diagnostic, predictive, prescriptive, and cognitive analytics) that increases in intelligence and autonomous behavior from a data science perspective.
- Innovative AI systems can be partly inspired by the brain just as the brain can be augmented by the machine.
- The "doctor's brain" for day-to-day clinical work can be conveniently deconstructed by its myriad of functions and matched to machine-equivalent capabilities.
- It is the brilliant British mathematician and computer scientist Alan Turing, however, who would be considered the absolute progenitor of artificial intelligence with his pioneering works that included his theory of computation and his work on computing machines.
- The symbolic AI in the 1950s to the late 1980s, also known as good old-fashioned AI (GOFAI) and the "neat" in neat vs scruffy AI, was mainly rooted in symbolic representations of problems and was considered the main school of thought during this epoch.

- An alternative to GOFAI during this earlier period of AI was computational intelligence (the "scruffy" half of neat vs scruffy), which relied on heuristic algorithms such as ones seen in fuzzy systems, evolutionary computation, and neural networks.
- Initial efforts in artificial intelligence and its application in medicine began in the 1960's with ruled-based domain specific expert systems and focused mainly on diagnosis and therapy.
- Artificial intelligence and its failed adoption in medicine during this early period was due to not only lack of favorable work flow logistics and slow speed of computation, but also due to expectations that were unrealistically high.

II. Data Science and Artificial Intelligence in the Current Era

Chapter 4: Healthcare Data and Databases



Questions 4.1/Healthcare Data

1. The recent renaissance of AI in medicine is a convergence of all of the following *except*:
a. Improved algorithms and technology
b. Adoption of AI curriculum in medical schools
c. Increased computational power with increased storage
d. Increased availability of data
[ ]

2. Which of the following is an example of *structured* data in healthcare?
a. An echocardiogram from a year ago
b. A doctor's assessment note from the prior visit
c. A table of serum creatinine levels over a two-year period
d. An MRI of the brain performed last week
[ ]

3. Which of the following is an example of *unstructured* data in healthcare?
a. An ultrasound examination of the renal artery
b. Blood pressure measurements for the last 5 visits
c. List of medications and respective dosages
d. Clinic visit type and time of visit
[ ]

4. The medical classification list put forth by the World Health Organization for hospitals is called:
a. Current Procedural Terminology (CPT) code (93303 and 93304)
b. Diagnosis Related Group (DRG) code (458)
c. International Statistical Classification of Diseases (ICD-10) (H91.21)
d. SNOMED Clinical Terms (CT) (49436004)
[ ]

5. The major differences between ICD and CPT codes listed below are correct *except*:
a. ICD identifies medical services and procedures vs CPT that describes diseases
b. ICD is used mainly by physicians vs CPT that is used by insurance companies and hospitals
c. 3-7 alphanumeric code for ICD vs 5 digit number for CPT
d. ICD published by WHO vs CPT owned by AMA
[ ]

Answers 4.1/Healthcare Data

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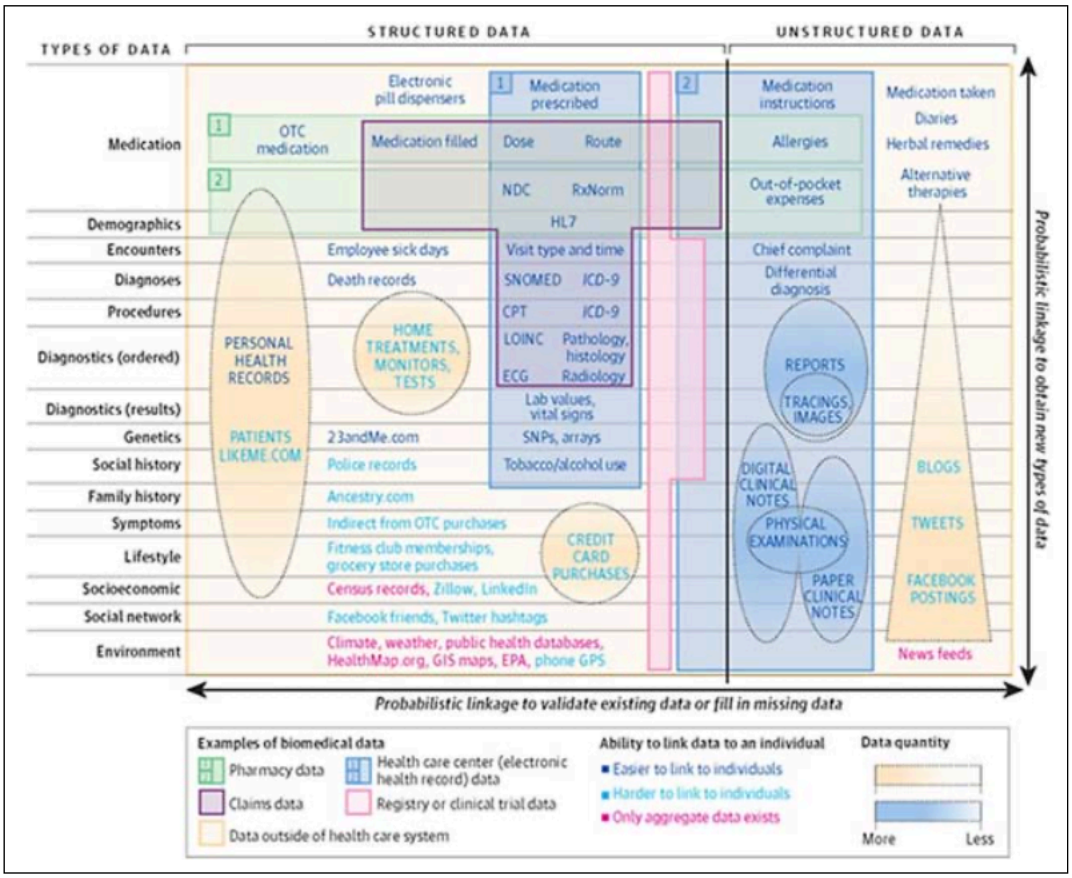
Module 4.1/Healthcare Data

Use of Artificial Intelligence. Among the significant forces that have increased the use of artificial intelligence (see Figure): First, methods improved with more sophisticated algorithms and deep learning. In addition, there is increased storage capacity with cloud computing. Third, computational power has also escalated with the advent of graphic processing units (GPUs). Lastly, the availability of data in large amounts also rendered AI methodologies much more relevant.



Health Care Data. Structured data is usually presented in an organized table or relational database format (integers, strings, etc in a spread sheet for example) and requires less storage while **unstructured data** is without this table format (text, medical image, audio file, video, etc) and requires more storage. It is estimated that about 80% of health care data is unstructured (see Figure).

Biomedical Data. This complicated schema illustrates the very challenging data landscape in health care. The types of data are listed in the left column. As complicated as this diagram is, it is still not complete (wearable technology data not included) nor realistic (as most of health care data is unstructured). In addition, most of the health care data is actually outside the health care system.

International Statistical Classification of Diseases and Related Health Problems (ICD) is a medical classification list put forth by the World Health Organization (WHO). The current **ICD-10** is the 10th version of this list and has codes for diseases (including signs and symptoms of these disease) as well as abnormal findings, injuries, and social situations in great detail (with over 69,000 billable codes, many more than its previous version ICD-9). The 3-7 digits alphanumeric diagnosis characters and procedure codes (e.g. H91.21 for sudden idiopathic hearing loss of the right ear) support interoperability and HIE exchange internationally. Another important aspect of medical records is the **Current Procedural Terminology (CPT) code** that is a list of medical, surgical, and diagnostic services organized by the American Medical Association (AMA). The 5-digits CPT codes (e.g. 93303 or 93306 for transthoracic echocardiogram, the latter code with Medi-Cal insurance) relate to services rendered (rather than diagnoses as in ICD-10).

SNOMED Clinical Terms (CT) is an ontological collection of medical terminologies used in clinical documentation that includes clinical findings, symptoms, diagnoses, procedures, anatomical structures, etc. The four main core components of SNOMED CT are: concept codes, descriptions, relationships, and reference sets. In addition, the **Unified Medical Language System (UMLS)** from the NIH National Library of Medicine integrates and distributes key terminology and standards to provide interoperable biomedical information systems, including EHR. A common "dictionary" is very useful since there can be many ways to describe the exact same medical condition. **Logical Observation Identifiers Names and Codes (LOINC)** is a database specific for medical laboratory observations. The full LOINC name has several components-component: property: timing: specimen:scale (e.g. 2951-2 SOIDUM:SCNC:PT:SER/PLAS:QN). Lastly, **Digital Imaging and Communications in Medicine (DICOM)** for medical imaging is an accepted standard for both communication and management of this image data while **Picture Archive and Communication System (PACS)** is the computer network for digitized medical images and reports. PACS include: imaging data, secure network for transmitting information, workstations for reviewing the images, and archives for storing the images.

Questions 4.2/Big Data in Healthcare

1. Big data and the 4 "V"s include the following *except*:
a. Velocity
b. Variety
c. Vector
d. Volume
[ ]

2. Of the following types of medical data, which has the *largest* quantity of data?
a. Echocardiogram
b. MRI of the brain
c. Electronic medical record for a one week stay
d. Genomic sequencing data
[ ]

3. Approximately what percent (%) of healthcare data is considered *unstructured*?
a. 20%
b. 40%
c. 60%
d. 80%
[ ]

4. The process of replacing missing data with substituted values is called:
a. Imputation
b. Curation
c. Substitution
d. Integration
[ ]

5. The total amount of healthcare data in 2020 is closest to:
a. 10-25 exabytes
b. 10-25 zettabytes
c. 10-25 gigabytes
d. 10-25 terabytes
[ ]

Answers 4.2/Big Data in Healthcare

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Module 4.2/Big Data in Healthcare

Big Data. Data that have escalated in a myriad of ways to the point that traditional data processing applications are no longer adequate is termed **"Big Data".** The four "V"s of big data often mentioned are: 1) **volume** (over 40 zettabytes, or the equivalent of 40 trillion gigabytes, are expected to be in existence by 2020 with internet of things accelerating this growth), 2) **variety** (videos, wearable technology, images, and structured vs unstructured types of data created a digital "tsunami'), 3) **velocity** (speed data is accessed such as with streaming data and over 20 billion network connections in the near future powered by 5G), and 4) **veracity** (uncertainty of data is not only costly but leads to inaccurate conclusions). Additional "V"s in big data can include: value, visualization, and variability. The current imbroglio in health care data is highlighted by an escalating volume of unstructured, heterogeneous medical data with little embedded predictive analytics or machine learning. In regards to the size of biomedical data, while electronic medical records are in the range of 5-10 megabytes, radiological and cardiac imaging studies can be 10-100 fold more at 50-100 megabytes; these data still are not nearly as big as clinical genomic data (which can be in the range of 20 gigabytes or more). Lastly, current estimate of the entire health care data volume is above 150 exabytes in volume and escalating rapidly.

Despite the large volume, variety, velocity, and veracity of big data in biomedicine, there is little dividend in the form of information from this health care big data. Yet, there are sizable opportunities for utilizing health care big data to reduce costs, reduce readmissions, improve triage, predict decompensation, prevent adverse events, and introduce treatment optimization. The current situation will soon be far more complex and daunting with the advent of data "tsunamis": genomic data (as a result of the high throughput next generation sequencing) and physiologic data (from home monitoring and wearable physiologic devices).

Health Care Data Conundrum. Health care data is unique in several ways that renders the data challenging for AI applications: 1) **Data size-** the size of health care data, especially genomic data and some imaging data as well as future wearable technology data, are getting larger and more difficult to manage and store, 2) **Data location**- the data is in various formats (clinical data vs. claims data) and is often stored in several repositories like clinics, hospitals, and other departments (radiology, laboratories, etc); 3) **Data structure**- most (over 80%) of health care data, from handwritten doctors' notes to echocardiograms, remains unstructured and therefore it is difficult to handle as a data bundle; 4) **Data integrity-** it is not uncommon to have some or most of the data in health care missing and/or inaccurate but this aspect can be partly neutralized with data mining and data analytics strategies; 5) **Data consistency**- data is often inconsistently recorded as diagnoses and conditions are frequently defined differently by clinicians as there is often no universal definition for even the simplest of medical terms.

Questions 4.3/Healthcare Data Management

1. Which of the following statements about the transform part of ETL (extract, transform, load) process is *incorrect*?
a. Addition
b. Imputation
c. Normalization
d. Data Integrity
[ ]

2. Differences between a data warehouse and a data lake include:
a. Data scientist for data warehouse and business analysts for data lake
b. Data warehouse has structured and processed data whereas data lake has all types of data including unstructured data
c. Data warehouse is more agile compared to a data lake
d. The transformation part of the ETL process occurs in both data warehouse and data lake
[ ]

3. A business intelligence analyst is working with a data repository. He is most likely working with a:
a. Data warehouse
b. Data lake
c. Data registry
d. None of the above
[ ]

4. According to HIMSS, the three key ancillary department systems to be considered first for EMR adoption include the following *except*:
a. Cardiac catheterization laboratory
b. Radiology
c. Pharmacy
d. Laboratory
[ ]

5. Components of the highest stage (stage 7) in the HIMSS EMR adoption system include all of the following *except*:
a. Data warehousing for data analytics to improve quality of care
b. Clinical information can be shared with a health information exchange
c. Summary data continuity for all hospital services
d. Real-time analytics in the acute care settings in the hospital
[ ]

Answers 4.3/Healthcare Data Management

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d. Real-time analytics in the acute care settings in the hospital
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Module 4.3/Healthcare Data Management

Health Care Data Management

Data Processing and Storage. An **ETL (extract, transform, and load) process** is employed in order to extract data out of the system and configure the data for the **data warehouse** that is favored by business professionals as the data is usually structured (but storage usually more costly). A **data lake** is a lower-cost data storage repository preferred by data scientists and can hold large amounts of raw data, including unstructured data, for later analytic use. The data in the data lake is also somewhat more agile for flexible configuration whereas the data in the **data warehouse** is usually less agile. There are important distinctions between data warehouse and data lake but perhaps a hybrid "**data reservoir**" would be the best data repository to take advantage of both types of data storage. Health care data can be stored in a database management system either on a server or a distributed computing storage platform for both access and analysis (Hadoop is such a system). Vendors such as Amazon, Google, and IBM now have data storage and analytics available in the cloud.

EMR Adoption and Interoperability. In order to facilitate clinical and administrative data being transferred between software applications, especially with AI-related work, **health level-7 (HL7)** denotes the seventh (application) level of the International Organization for Standardization (ISO) seven-layer communications model for **open systems interconnection (OSI).** The HL7 vision is "a world in which everyone can securely access and use the right health data when and where they need it", so AI work in a health care organization mandates HL7 as it promotes interoperability of electronic health records. **Interoperability,** according to HIMSS, is "the ability of different information systems, devices, or applications to connect, in a coordinated manner, within and across organizational boundaries to access, exchange, and cooperatively use data amongst stakeholders with the goal of optimizing the health of individuals and populations". This interoperability can be foundational, structural, semantic, or organizational. This aspect of health care data is vital to multi-institutional collaborations in AI projects. The **Fast Health care Interoperability Resources (FHIR),** developed by Health Level 7 (HL7), is an application programming interface that functions as a standard for data formats for exchanging EHR to promote interoperability. HL7 is sometimes confused with the **Healthcare Information and Management Systems Society (HIMSS) EMR Adoption Model (EMRAM)** and its stage designations (see Table): **Stage 7** is an environment where paper charts are no longer used (complete EHR) whereas stage 6 is its precursor when health care organizations are at the forefront of EHR adoption with interpretable EHR and just prior to stage 7.

Table 1. HIMSS EMR Adoption Model (EMRAM)

Stage		
7	Complete EMR, data analytics to improve care	
6	Physician documentation (templates), full CDSS, closed loop medication administratoin	
5	Full R-PACS	
4	CPOE; Clinical decision support (clinical protocols)	
3	Clinical documentation, CDSS (error checking)	
2	CDR, controlled medical vocabulary, CDS, HIE capable	
1	All three ancillaries installed- lab, radiology, pharmacy	
0	All three ancillaries not installed	

Questions 4.4/Healthcare Databases

1. The most common type of healthcare database is:
a. Graph database
b. Relational database
c. Object-oriented database
d. Hypergraph database
[ ]

2. Comparing relational vs graph databases reveal all of the following *except*:
a. Table in relational database and graph in graph database
b. Relationship is any-to-any in relational database and row and column for graph database
c. Data is structured in relational database but can include unstructured in graph database
d. Relational database is static whereas graph database is dynamic
[ ]

3. A nurse practitioner is interested in looking at chronic heart failure management as a clinical research project. What is an ideal database for this data:
a. Graph database
b. Relational database
c. Object-oriented database
d. Flat files
[ ]

4. What is the major limitation of a graph database in healthcare?
a. The database management system is relatively large and complex
b. It has less number of relationships than a relational database
c. The quality of the relationship is low and sparse compared to relational database
d. The data has to be structured
[ ]

5. Most of healthcare data are in which two forms of data and/or databases:
a. Graph and hyper graph databases
b. Relational and graph databases
c. Flat files and relational databases
d. Relational and hypergraph databases
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Answers 4.4/Healthcare Databases

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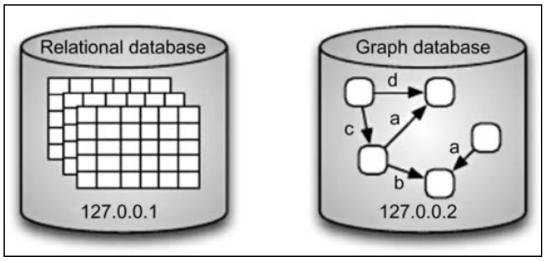
Module 4.4/Healthcare Databases

Database Management Systems. The types of **database management systems (DBMS)** includes: hierarchical, network, relational, and object-oriented DBMS. Medical databases have traditionally been primitive **flat files** with little or no database management and have not advanced far due to electronic medical records only having been recently implemented. The health care data have therefore been static with indirect sharing mostly through hyperlinks. In short, most of the present health care data remain embedded in flat files or at best, in relatively simplistic hierarchical or relational DBMS with most of the data centralized and locked into local operating systems that reside in hospitals or offices. There is a paucity of literature on object-oriented approaches in the biomedical area.

Relational database. As the most common health care database is a relational database, its management system is called a **relational database management system** (**Relational DBMS** or simply RDBMS). Oracle and Structured Query Language (SQL) Server are examples of relational DBMS while NoSQL databases such as MongoDB are non-relational DBMS. An **online transaction processing (OLTP) database** is the predominant use case for RDBMS. A major disadvantage of such a database is that the data is often sequestered. Often, an **online analytical processing database (OLAP)** is used as an **enterprise data warehouse (EDW)** solution to solve the problem. There are limitations to relational DBMS for health care data: these lack sufficient infrastructural support for the larger health care data (such as time-series data, large text documents, and image/videos). In addition, queries are difficult due to the structure of relational DBMS.

Object-oriented database. While this type of database management system is more efficient and flexible, it lacks the practical functionalities of a relational DBMS especially for search and query functions. A hybrid **object-relational DBMS**, therefore, can take advantage of strengths from both relational and object-oriented DBMS; it can therefore accommodate the larger, more complex health care data elements while retaining the relational table structure for query purposes (using Hadoop, Oracle, or SQL). This object-relational DBMS does, however, require more expertise to use, as it is more complex to configure. The **Not Only SQL (NoSQL)** or **next generation databases** represent databases that are characterized by large data volumes, scalable replication and distribution, and efficient queries; these databases are exemplified by document based systems (such as Mongo DB) or graph databases and are the future of health care databases.

Graph database. A **graph DBMS** (used in LinkedIn and Twitter as well as Zephyr Health and Doximity and visualized by Neo4j) can store data in the **non-linear form** of **graph elements** (nodes and edges): A **node** (also called a vertex) is an entity and an **edge** is the relationship between the nodes (see Figure). This type of database is more "three-dimensional" and has distinct advantages over the traditional relational database (see Table). This central tenet of delineating connectedness and relationships in a rapid-changing world is often very much needed in biomedicine as quality of care, overall efficiency, and innovation direction become the new paradigm in health care.



The figure on the left shows the traditional relational database in table format whereas the figure on the right shows nodes (rounded squares) and edges (arrows).
In a graph DBMS, each data element in the graph will need to be described in the universal language. Resource Description Framework (RDF) as a "triple" (<Subject><Predicate> <Object>) is then stored in a semantic database that can be queried using the semantic version of SQL, SPARQL (Simple Protocol and RDF Query Language). Ontologies and accompanying inference rules can then be embedded in the data to enrich the database.

Table. Comparing Relational vs Graph Databases

	Relational Database	Graph Database
Format	Table	Graph
Relationship	Row and column	Any-to-any relationship
Data	Structured	Structured and unstructured
Data Type	Simple to moderate	Complex
Number of Relationships	Hundreds	Thousands to billions
Quality of Relationship	Low and sparse	High and rich
Data Model Type	Collection of interlinked tables	Multi-relational graph
Data Model	Infrequently changed	Constantly changing
Agility	Static	Dynamic
Schema	Rigid	Flexible
Deep Analytic Performance	Poor	Good
Human and Machine	Labor intensive	Machine assisted

In short, if relationships are a high priority and data is constantly evolving (such as medicine and health care), a graph DBMS is much more accommodating than traditional relational databases. The graph DBMS with these search algorithms is especially well designed for complex queries in health care such as chronic disease management, acute epidemiological crises, and health care resource allocation. The location of a similar patient to an index patient can also be performed using this strategy. The major limitation of graph DBMS is that it is relatively large and complex, but this limitation can now be partly neutralized with large storage capacity, semantic storage improvements, and superior search algorithms. A graph or even it more advanced version, hyper graph, are perhaps essential elements for AI in medicine and health care to advance to the next level.

Chapter 5: Machine and Deep Learning

Questions 5.1/Introduction to Machine Learning

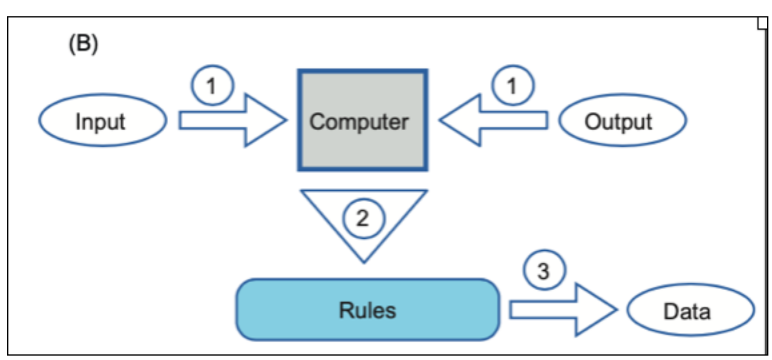
1. A technique developed in the 1930's that uses databases and statistical methodologies to draw information from data (such as emerging patterns), also known as knowledge discovery, is called:
a. Data mining
b. Cognitive computing
c. Deep learning
d. Generative Pre-trained Transformer (GPT-3)
[ ]

2. According to Pedro Domingos in his book *The Master Algorithm*, neural network has its origin in:
a. Philosophy
b. Neurosciences
c. Statistics
d. Evolution
[ ]

3. How is traditional programming *most* different from machine learning?
a. Type of data used
b. Top-down vs bottom-up approach
c. Number of personnel needed
d. Type of computer used
[ ]

4. According to Pedro Domingos in his book *The Master Algorithm*, neurosciences gave rise to all of the following *except*:
a. Deep learning
b. Decision trees
c. Deep reinforcement learning
d. Neural networks
[ ]

5. The diagram to the right is *most* consistent with:
a. Traditional programming
b. Machine learning
c. Conventional statistics
d. Expert system
[ ]



Answers 5.1/Introduction to Machine Learning

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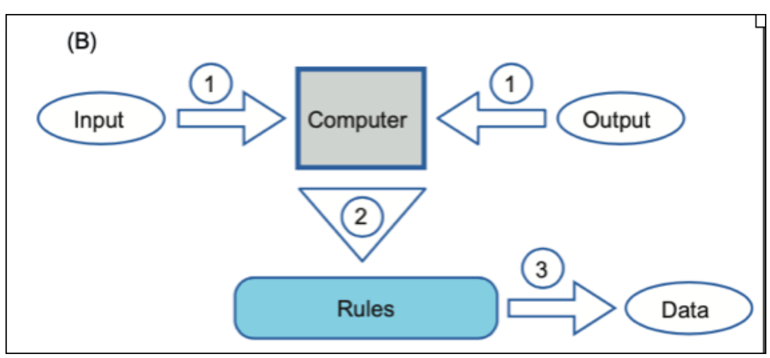


Module 5.1/Introduction to Machine Learning

History and Current State of Machine Learning. Machine learning, defined as the ability of the machine to learn from its experience going through tasks, is widely used in our society (from search engines to spam filtering). Machine learning, a term initially coined by Arthur Samuel in 1959, is an increasingly popular sub-discipline of AI and is the art of computer programming that enables the computer to learn and improve its performance without an external program instructing it to do so. In other words, in machine learning, the algorithms self-improve and “learn” from trial and error just as humans do from experience.

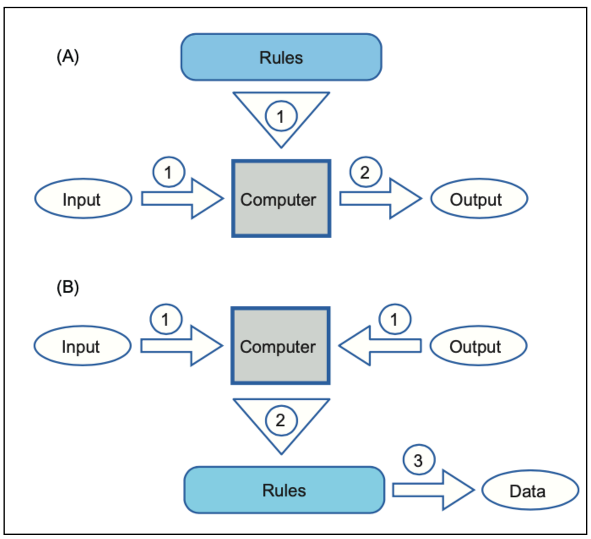
Pedro Domingos, in his book *The Master Algorithm*, described the five schools or “tribes” of machine learning that share one paradigm in common: discovery of the knowledge hidden in the data. He proposed that a master algorithm would need to elements form each of the five schools described below (see Table):

Schools in Machine Learning

School	Representation	Origin and Influence	Methodologies	Key Algorithm
Symbolists	Logic	Philosophy Computer science	Production rule system Inverse deduction Decision trees	Inverse deduction
Connectionists	Neural networks	Neurosciences	Backpropagation Deep learning Deep reinforcement learning	Backpropagation
Evolutionaries	Genetic programs	Evolutionary biology	Genetic algorithms Evolutionary programming Evolutionary game theory	Genetic programming
Bayesians	Graphical models	Statistics	HMM Graphical model Causal inference	Probabilistic inference
Analogizers	Support vectors	Psychology	*k*-NN SVM	Kernel machines

(HMM- Hidden Markov model; *k*-NN- *k*-nearest neighbor; SVM- support vector machines)
(Adapted from *The Master Algorithm*)

Machine Learning vs Conventional Programming. In **traditional programming** (see Figure), data ("Input") along with a computer program ("Rules") (step 1) are entered into the computer and then the answers ("Output") are derived (step 2). In **machine learning**, however, a computer uses both the data ("Input") and the corresponding answers ("Output") (step 1) to derive the "Rules" by examining the patterns in the data (step 2)(and thus "learns" from data). These new rules are then applied to new data to get answers (predictions)(step 3). This latter "bottom up" approach is distinctly different than the traditional programming (such as the aforementioned rule-based expert system) in which the human is imprinting instructions to the computer to follow (therefor a "top down" approach). Machine learning is also different than traditional **statistical analysis** (which is also "top down" like programming in that the data is analyzed by statistical rules to yield output, or answers). In short, machine learning "learns" from both the input and the output data and then finds the patterns that relate the input data to the output data; these patterns (in the form of a model) learned from machine learning are then applied to new data to see how this model would fit the data.



a) Traditional Programming and b) Machine Learning. The diagrams illustrate the major difference between traditional programming and machine learning. In traditional programming (and statistical analysis), a top-down approach provides rules for the input data and output is derived. In machine learning, both the input data as well as output data (labeled by humans) are entered into the computer and the rules are derived from the data. The new rules are then applied to the new set of data (see text for more details).

The advent of complex and efficient **algorithms** (sets of steps to accomplish certain tasks) that are available for not only calculations and data processing but also automated reasoning has advanced the capabilities of machine intelligence. Examples of complex algorithms that are in current use include Pixar's coloring of 3D characters in virtual space (**rendering algorithm**) and NASA's operations of the solar panels on the international space station (**optimization algorithm**). Even the recent first ever picture of the black hole of the galaxy Messier 87 was helped by data scientists and a new algorithm (called Continuous High-Resolution Image Reconstruction using Patch Priors, or CHIRP) that put together data from a virtual consortium of telescopes that rendered this into an Earth-sized giant telescope.

Questions 5.2/Machine Learning Workflow

1. The data sets used in machine learning include the following *except*:
a. Training set
b. Test set
c. Validation set
d. Intermediate set
[ ]

2. Which of the following is the correct order in the machine learning workflow?
a. Data collection>Data processing>Feature extraction>Learning algorithm>Model deployment
b. Data collection>Data processing>Learning algorithm>Model deployment>Feature extraction
c. Learning algorithm>Data collection>Data processing>Learning algorithm>Model deployment
d. Data collection>Data processing>Model deployment>Feature extraction>Learning algorithm
[ ]

3. Of the various data sets in the machine learning workflow, which is usually the largest?
a. Training set
b. Test set
c. Validation set
d. Intermediate set
[ ]

4. Of the following sequential steps of the machine learning workflow, which is usually the most time-consuming:
a. Data collection and processing
b. Feature extraction
c. Learning algorithm
d. Model deployment
[ ]

5. Choose the correct location of Feature extraction [Here] in the following sequences:
a. Data collection>Data processing>Learning algorithm>Model deployment>[Here]
b. Data collection>Data processing>Learning algorithm>[Here]>Model deployment
c. [Here]>Data collection>Data processing>Learning algorithm>Model deployment
d. Data collection>Data processing>[Here]>Learning algorithm>Model deployment
[ ]

Answers 5.2/Machine Learning Workflow

1. The data sets used in machine learning include the following *except*:
a. Training set
b. Test set
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2. Which of the following is the correct order in the machine learning workflow?
a. Data collection>Data processing>Feature extraction>Learning algorithm>Model deployment
b. Data collection>Data processing>Learning algorithm>Model deployment>Feature extraction
c. Learning algorithm>Data collection>Data processing>Learning algorithm>Model deployment
d. Data collection>Data processing>Model deployment>Feature extraction>Learning algorithm
[a]

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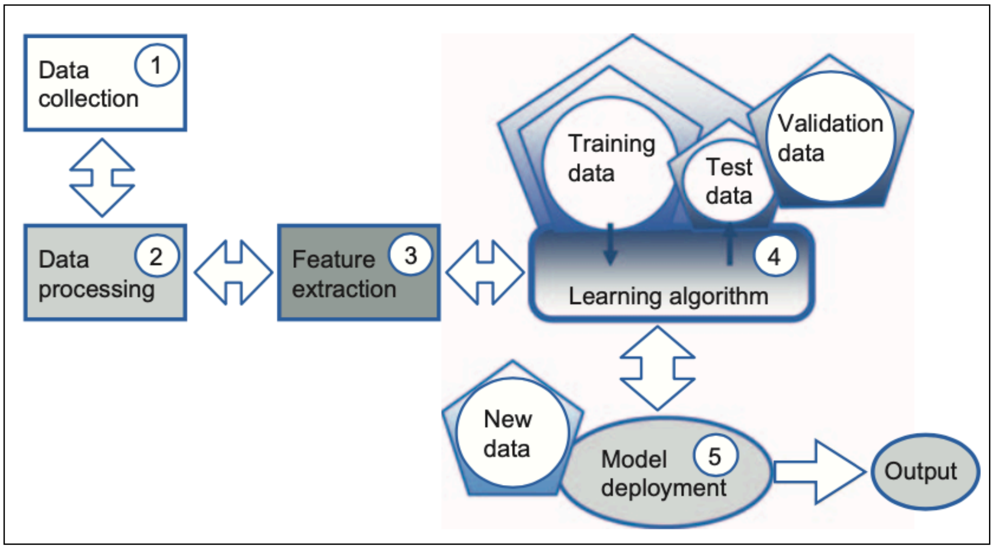
a. Data collection>Data processing>Learning algorithm>Model deployment>[Here]
b. Data collection>Data processing>Learning algorithm>[Here]>Model deployment
c. [Here]>Data collection>Data processing>Learning algorithm>Model deployment
d. Data collection>Data processing>[Here]>Learning algorithm>Model deployment
[d]

Module 5.2/Machine Learning Workflow

Machine Learning Workflow. The following is a brief description of the steps of the machine learning workflow for supervised learning (but can also be applied to unsupervised learning with a small alteration)(see Figure):



Machine Learning Workflow. The entire machine learning workflow is illustrated, from data collection all the way to deployment of the model to real world data at the very end. Most of the workflow has feedback to the prior step(s) and also the model is evaluated and reassessed even during the initial deployment phase so that needed adjustments can be made. The double arrows in the diagram signify the fluidity of these steps so that one can return to previous steps to add/refine/change the data, features, or even model. This is not possible for deep learning as the intermediate steps are "compressed" so that once labelled samples go in, the feature extraction and classification steps are combined in deep learning (machines are performing the feature extraction instead of humans). In other words, steps 3 and 4 are combined in deep learning. For unsupervised learning, the algorithm yields grouping of objects instead of the predictive model in the aforementioned machine learning workflow.

Data Collection (step 1): Prior to data collection, the team as a group should discuss the expected goals of the project as to have a clear direction for what data to collect. When consensus is reached, then members can help to gather the relevant data for the important next step, which prepares the data. Data collection is sometimes challenging depending on the data acquisition and storage capabilities of the institution. In health care, data is mostly unstructured and stored in many different formats (CPT and ICD-10 codes, encounter information, demographics, medications, nurses and doctors' notes, vital signs, etc) as well as venues (hospital, clinic, and now wearable devices), and this makes the process of data collection particularly tedious (see previous section for details).

Data Processing (step 2): This step after collection of data involves utilizing data processing tools to have the data cleaned, readied, and organized into a more structured format for machine learning methodologies to follow. The data preparation involves measures such as missing value imputation, imbalanced data processing, outlier detection, and normalization. There is also **data wrangling,** or **data munging,** which are terms describing the process of converting as well as mapping data from the raw form from step 1 to another format that would be more friendly to the ensuing steps. This step can entail both data transformation (to tables, CSV, etc) and data platform (using Hadoop, MapReduce, Cassandra, etc). Data curation involves grouping of data (procedures, complications, comorbidity, etc).

The steps of collecting and processing the data can easily make up the majority of the effort and time needed to do a project for the data scientist, especially in a clinical setting. It is hoped that these two steps will be much more efficient in the future as projects in AI in medicine become more commonplace and at a more sophisticated level.

Feature Extraction (step 3): Features, also known as variables or parameters, are the "column names" of the data (such as blood pressure, patient names, medications, etc) whereas examples are the actual numbers or data. This step of feature extraction first involves feature selection, which is strategic selection of only relevant features that will create a good predictive model. Feature selection is then followed by feature extraction, which takes the existing features and transforms this into a new set of features that will most likely lead to a good model. Feature engineering is the sophistication of feature extraction using domain expertise. Of note, representation learning, a type of machine learning in which no feature engineering is involved, is a methodology that renders data easier to extract useful information when building the classifier.

Learning Algorithm (step 4): This step involves the algorithm learning to come up with the best **predictive model** to yield good to excellent predictions of future new data. The sub-steps involve using a dataset and dividing it into two smaller datasets: the **training data** (usually larger of the two and around 70%) is used to train (or "fit") the model or algorithm and the smaller subset of **test data** is sequestered and then used for assessing the generalization error of the final chosen model in an unbiased way at the end. Depending on the availability and size of the labeled dataset, a third smaller dataset can be allocated as **validation data** (also smaller than the training dataset and similar in size to the test dataset) which is used to estimate prediction error for model selection. **Overfitting** (see below under Fitting for detailed discussion) occurs when the data fits the training data too closely but ends up not generalizing well for other sets of data.

Model Deployment (step 5): this final step is to deploy and refine the predictive model for real-life applications with new data. The model's performance is evaluated (see section below) and its algorithm refined if necessary for new data or projects. The machine learning "learns" and self-improves by being able to improve its prediction capability or performance via measures such as **optimization** or **loss function** built into the machine learning algorithm (these concepts will be discussed later in this section).

Questions 5.3/Biomedical Data Science

1. Data science is considered the intersection of the following disciplines *except* (choose least fit):
a. Computer science
b. Mathematics
c. Statistics
d. Hardware design
[ ]

2. Data science usually includes the following domains *except*:
a. Extended reality
b. Statistical research
c. Data processing
d. Machine learning
[ ]

3. The study and practice of data and information approach to health care is:
a. Clinical informatics
b. Health strategy
c. Health administration
d. Medical research
[ ]

4. A person who is *least* likely focused on processing and managing of large datasets with software engineering and routinely uses tools like Hadoop and NoSQL is:
a. Data engineer
b. Data scientist
c. Database administrator
d. Data architect
[ ]

5. The person who is more business-focused and utilizes tools such as Excel, Tableau, and SQL for data visual presentation and communication for the enterprise is called:
a. Data analyst
b. Data architect
c. Database administrator
d. Chief technology officer
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Module 5.3/Biomedical Data Science

Data Science in Biomedicine. As we discussed earlier, **data science** is considered to be the intersection of **mathematics** and **statistics** (including modeling and biostatistics) and **computer science** (programming, data concepts, and data mining). The current paradigm of AI in medicine for **biomedical data science** is adding another domain of knowledge to computer science and mathematics: the domain knowledge of **biomedicine** (bioinformatics and clinical informatics as well as biology, genetics and genomics, medicine, and health sciences). **Bioinformatics** is a field that focuses on collecting and analyzing complex biological data (especially genetic information), whereas **clinical informatics** (or **biomedical informatics**) is the study and practice of data and information approach to health care. Both are germane to not only biomedical data science but artificial intelligence in medicine and health care.

Some programs and hospitals offer a **fellowship** in biomedical informatics and there is now a board certification in clinical informatics. At Children's Hospital of Orange County, there is a pilot program to have a senior fellow in data science and AI in medicine and health care. In the near future, there will be many such positions for specialized training and education as a subarea for most subspecialties.

The data science team for biomedicine consists of the following members:

A **data scientist** is very well-rounded and is someone who can usually take a data science project starting from data collection through machine learning and then finishing with data visualization. The data scientist has a skill sets from mathematics and statistical analysis, database warehousing and engineering as well as programming skills (particularly with R, Python, and SQL). A **data engineer** (also known as database administrators or data architects) are mainly focused on processing and managing large datasets with software engineering so that the data scientists can work on these datasets. A data engineer works mainly with Hadoop, NoSQL, and Python (but not usually R as machine learning is usually not in his/her skill set). Finally, a **data analyst** is typically someone who is more business-focused and utilizes tools such as Excel, Tableau, and SQL for data visual presentation and communication for the enterprise. Data analysts are usually not working directly with data science projects (so machine and deep learning are usually not in their portfolio of skills) but are focusing on data warehousing, Hadoop-based analytics, and are familiar with data architecture and ETL tools. These personnel may report to the same person in the C-suite or different leaders depending on the institution. There is considerable overlap with these job descriptions based on the individual's skills and experiences as well as preferences.

This data science team usually works with a leadership team in the health care organization or the chief executives in a company. The **chief information officer (CIO)**(or information technology director) is usually the most senior executive in the information technology sector of the organization. The **chief medical information (or informatics) officer (CMIO)**(or chief health information officer)(CHIO) is usually a physician executive in charge of the health informatics sector of the organization and is the liaison between the clinical and the IT domains. A **chief technology officer (CTO)**(more common in companies rather than health care organizations) is usually someone who knows how to monetize software and deals with software engineering issues. Finally, **chief intelligence officer** or **chief AI officer** (very few at present especially in a health care organization) is someone who has a comprehensive knowledge about AI and the know-how about evaluation and deployment of AI projects.

Questions 5.4/The Data Science Tools

1. The following are common programming languages used in healthcare data science today *except*:
a. R
b. Python
c. MATLAB
d. FORTRAN
[ ]

2. Which of the following is particularly good for statistics and is open source?
a. R
b. Python
c. MATLAB
d. SAS
[ ]

3. The following are deep learning libraries *except*:
a. TensorFlow
b. Hadoop
c. Keras
d. Caffe
[ ]

4. An open-source framework with a set of tools to store and process large volumes of data on a cluster of commodity hardware is which of the following:
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b. Hadoop
c. Keras
d. Caffe
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5. Of the following, which is the most popular programming language in data science in healthcare?
a. Java
b. Ruby
c. Python
d. C#
[ ]

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Module 5.4/The Data Science Tools

Programming Languages in Biomedical Data Science. There are several programming languages that are particularly useful for anyone interested in AI and data science in biomedicine:

Python (named after the comedy series *Monty Python's Flying Circus*) is a very flexible and relatively simple programming language and can be used for a myriad of purposes; it is arguably the most popular language in data science. In addition, Python has numerous special libraries (including NumPy and Pybrain for scientific computations and machine learning, respectively).

R is a common programming language for statistical learning, data analytics, and is particularly strong in visual presentation of data in plots. R tends to be more popular in academic institutions. Like Python, R is also open source and has many libraries for machine learning (like Gmodels, Class, and Tm) in Comprehensive R Archive Network (CRAN).

MATLAB is a high-level programming language by MathWorks that has an interactive environment for numerical computation as well as visualization and programming. It is widely used in science and engineering.

SAS is a relatively expensive commercial analytics software that offers a large portfolio of statistical functions.

Most of the ongoing debate in biomedical data science, however, is between Python and R as the preferred language. Here is a table to help illustrate the strengths and weaknesses of each:

Programming Languages in Data Science and AI: Python vs R

	python	R
Purpose (Year of Inception)	General purpose (1991)	Statistical analysis (1993)
Users	Programmers and developers	Researchers and scholars
Popularity	+++	++
Ease of Learning	+++	++
Usage and Application	+++	+++
Data Handling	++	+
Speed	++	+
Community Support	++	+++
Presentation	++	+++
Advantages	Jupyter notebook for sharing Code readability and syntax simplicity Agile development	Superior data visualization Large data analysis library (CRAN)
Disadvantages	Not as many libraries (as R) Visualization less flexible (as R)	Slow learning curve for especially novices Losing popularity Less deep learning support

For those working in predictive analytics as a domain, R is more popular than Python (with SAS close to R as a programming preference). For data scientists, Python has a slight edge over R in terms of popularity (and this difference seems to be widening). Overall, if one is more interested in efficient deployment, Python would have an edge; if one is more focused on statistical analysis, especially graphical presentations of the data, R would be a slightly better choice.

Both programming languages are excellent for machine learning and AI. One data scientist astutely draws the analogy that R is more like Batman, who is intelligent and more brain than brawn whereas Python is more like Superman, who is strong and more muscle than brain (compared to Batman). The author similarly draws the analogy that Python is more like the every day car that you take to work (functional and gets the job done), but R is your fancy weekend sports car (good for showing off). Perhaps one can have a combined visual: Superman in a Prius (for Python) and Batman in a Porsche (for R).

There are also several frameworks and libraries frequently used in AI projects:
Hadoop (Apache Software Foundation) is not a programming language but an open source framework (usually written in Java but not always) with a set of tools (such as its distributed file system and Map Reduce programming model) to store and processes large volumes of data on a cluster of commodity hardware.

TensorFlow (Google Brain) is perhaps the best known AI library (written in C++, Python, or CUDA) used for deep learning. The flexible architecture accommodates a variety of platforms (not only CPU and GPU but also TPU, Google's Tensor Processing Unit).

Keras is an open source library (written in Python) that can run on top of TensorFlow, but is more of a high-level API for training deep learning models. Other deep learning libraries and frameworks include: Caffe (BAIR), Theano, and MXNet.

Git is an open source project while GitHub consists of a Git repository hosting service in the form of a Web-based graphical interface. **GitHub** is the world largest open source community of developers (over 40 million) designed to discover, share, and build better software and is essentially a code sharing and publishing service.

Questions 5.5/Machine vs Deep Learning

1. Which of the following is *not* considered a type of classical machine learning?
a. Supervised learning
b. Unsupervised learning
c. Convolutional neural network
d. Semisupervised learning
[ ]

2. Which of the following is *not* considered a type of deep learning?
a. Recurrent neural network
b. Convolutional neural network
c. Supervised learning
d. Deep reinforcement learning
[ ]

3. Types of ensemble learning include the following *except*:
a. Boosting
b. Bagging
c. Stacking
d. Compiling
[ ]

4. Clustering is considered a type of:
a. Supervised learning
b. Unsupervised learning
c. Deep learning
d. Ensemble learning
[ ]

5. Classification is considered a type of:
a. Supervised learning
b. Unsupervised learning
c. Deep learning
d. Deep reinforcement learning
[ ]

Answers 5.5/Machine vs Deep Learning

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a. Supervised learning
b. Unsupervised learning
c. Deep learning
d. Ensemble learning
[b]

5. Classification is considered a type of:
a. Supervised learning
b. Unsupervised learning
c. Deep learning
d. Deep reinforcement learning
[a]

Module 5.5/Machine vs Deep Learning

Classical Machine Learning

Machine learning, or more accurately, classical machine learning, is better suited for smaller and less complicated datasets and clinical scenarios with less features. Classical machine learning is categorized into two types of learning: 1) supervised learning and 2) unsupervised learning **(see Figure)**. Additional discussions on semi-supervised and ensemble learning as well as deep learning will follow.

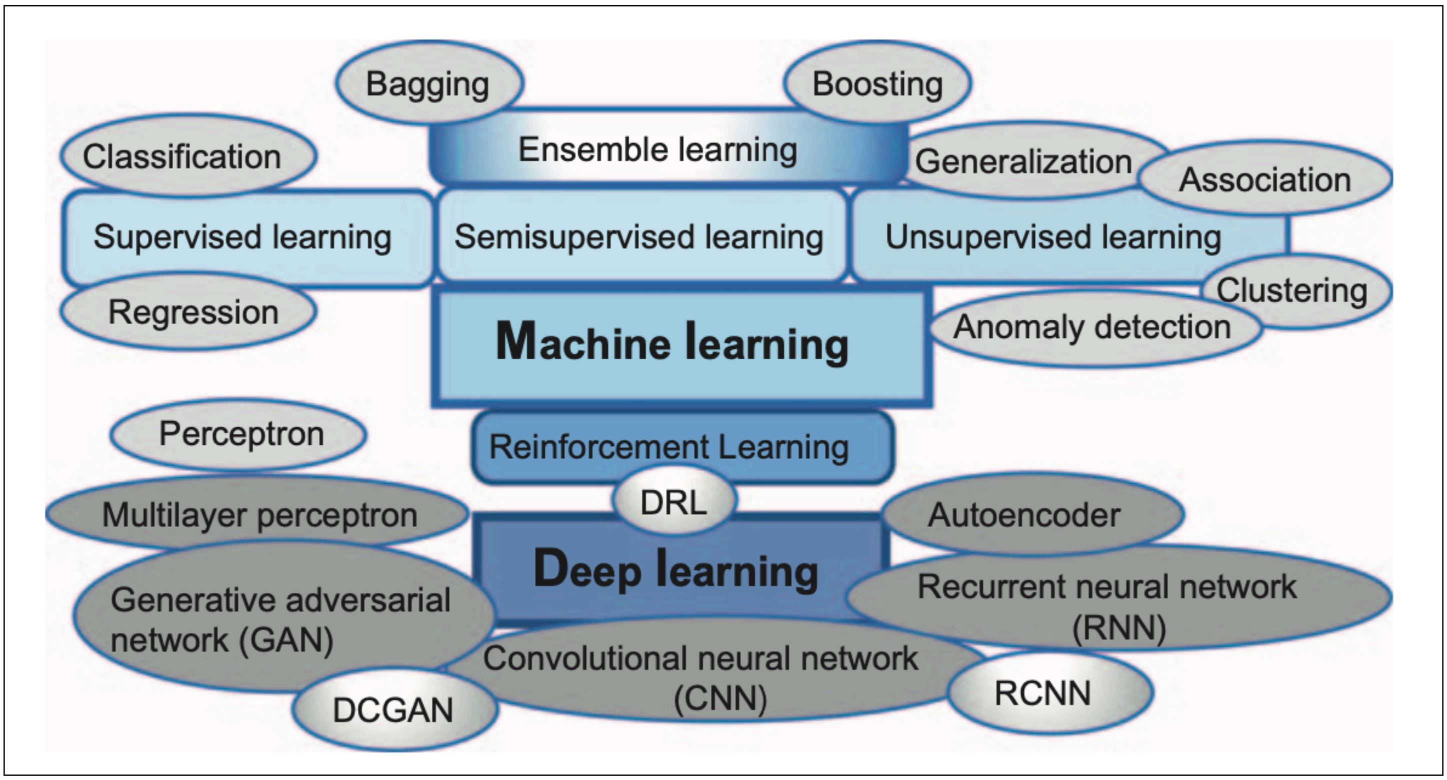
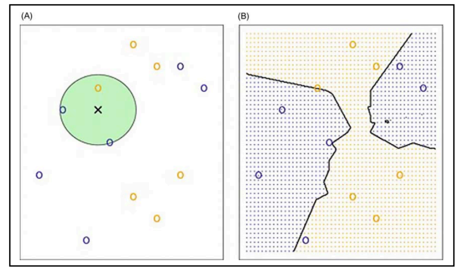


Figure 6. Machine (Classical) and Deep Learning. Classical machine learning is divided into supervised and unsupervised learning. Ensemble learning as well as semi-supervised learning are also variations of machine learning. Deep learning is divided into the various types of deep learning, and reinforcement learning is considered a different type of learning (although deep reinforcement learning, or DRL, combines aspects of both). Other types of deep learning also have similar hybridizations: GAN and CNN (DCGAN) and CNN and RNN (RCNN)(see text for details).

Questions 5.6/Supervised Learning I: Classification

1. The diagram to the right depicts which type of supervised learning?
a. *k*-nearest neighbor
b. Support vector machine
c. Naive Bayes classifier
d. Decision trees
[ ]



2. Classification methodologies in supervised learning include all of the following *except*:
a. Support vector machine
b. Naive Bayes classifier
c. Logistic regression
d. *k*-Means clustering
[ ]

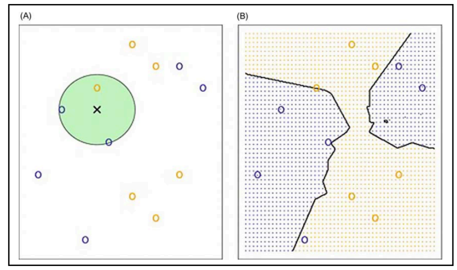
3. Of the following, which is a supervised learning used for classification:
a. Decision trees
b. k-Means clustering
c. Linear regression
d. Deep reinforcement learning
[ ]

4. The supervised learning methodology that utilizes a mathematical trick called a kernel in order to delineate a boundary in a nonlinear fashion is called:
a. Logistic regression
b. Support vector machine
c. Naive Bayes classifier
d. Decision trees
[ ]

5. A supervised learning methodology that uses probability to divide or categorize the data is:
a. Naive Bayes classifier
b. Support vector machine
c. Linear regression
d. *k*-Means clustering
[ ]

Answers 5.6/Supervised Learning I: Classification

1. The diagram to the right depicts which type of supervised learning?
a. *k*-nearest neighbor
b. Support vector machine
c. Naive Bayes classifier
d. Decision trees
[a]



2. Classification methodologies in supervised learning include all of the following *except*:
a. Support vector machine
b. Naive Bayes classifier
c. Logistic regression
d. *k*-Means clustering
[d]

3. Of the following, which is a supervised learning used for classification:
a. Decision trees
b. k-Means clustering
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4. The supervised learning methodology that utilizes a mathematical trick called a kernel in order to delineate a boundary in a nonlinear fashion is called:
a. Logistic regression
b. Support vector machine
c. Naive Bayes classifier
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5. A supervised learning methodology that uses probability to divide or categorize the data is:
a. Naive Bayes classifier
b. Support vector machine
c. Linear regression
d. *k*-Means clustering
[a]

Module 5.5/Supervised Learning I: Classification

Supervised Learning. Supervised learning takes refined raw data and uses an algorithm to predict the outcome (with the algorithm having derived from previously studying the labelled data in a training set of data in the process describe earlier). In other words, the training data help to guide the machine to the right prediction or output via an algorithm so that the model can be used to make predictions of the new data. **Active learning** is a supervised learning that involves a learning algorithm that can query the user for labels to avoid manually labeling a large number of samples.

In short, supervised learning develops a **predictive model** from both input and output data (the later labelled by humans) and this model is then used to make predictions on a new set of data. These supervised learning methodologies lead to classification (dichotomous or categorical) or regression (to a continuous variable)**.** For **classification**, the popular methodologies are support vector machines, naive Bayes classifier, *k*-nearest neighbor, and decision trees (with boosting or bagging); logistic regression is a misnomer and is in fact a classification methodology. For **regression**, linear and polynomial regression methods are most commonly used, but other types (such as ridge and lasso regression) may become more popular in the future.

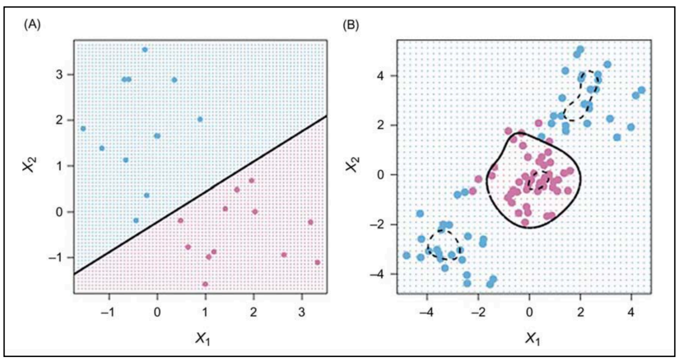
Classification. This methodology leads to predicting or assigning a label or category for an unlabeled sample (for example, “tumor” vs “not tumor” on MRI). Classifi cation strategy is good for fraud detection and facial recognition. In medicine and health care, classifi cation is good for medical images, phenotyping, and cohort identifi cation.

The supervised classification methodologies are listed below but only the more popular methods will be described in more detail **(see Table)**. Logistic regression (which is a misnomer as it is not a true regression but rather a classification methodology) is included in this classification section.

Table 5. Supervised Learning: Classification Methodologies

Classification Methodologies	Key Features
Decision trees	Nodes and branches
***k*-nearest neighbor (*k*-NN)**	Distance between neighbors
Logistic regression	Separating two variables
Naive Bayes classifier	Independent probabilities
Support vector machines (SVM)	Hyperplane and kernels

Support Vector Machine (SVM). This "maximum-distance" classification methodology is achieved by creating a line or an optimal **hyperplane** (a decision surface) in a high-dimensional space that represents the largest separation between the two classes (**see Figure).** In general, the larger this separation, the better the SVM performance. The points that are closest to the border are termed "support vectors". SVM can be in two forms: 1) **linear SVM**: use of **linear optimization** for linear separation (if possible) and this methodology is relatively fast (and resembles logistic regression) and 2) **kernel SVM**: use of many different kinds of dividing structures called **kernels** (Note. The so-called "kernel trick" is a mathematical trick that adds an extra dimension so that what is not possible in certain number of dimensions can now be possible with more dimensions.) In short, kernels delineate the boundary in a non-linear fashion (either curved line or an optimal plane). Common usages are spam filtering, sentiment analysis, image classification and segmentation, recognition of handwritten characters, and fraud detection.

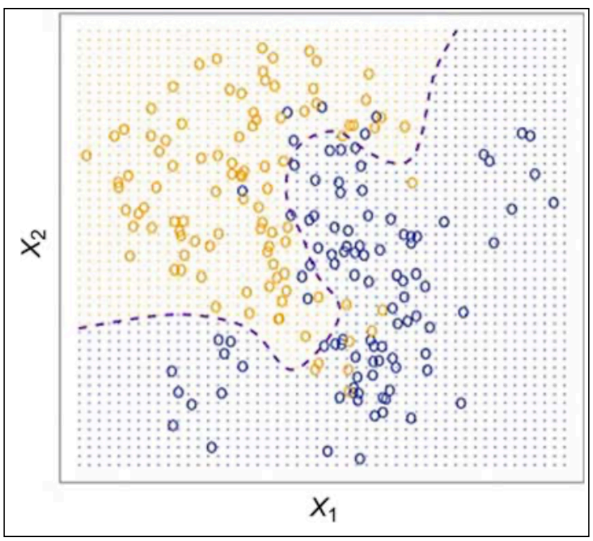


Support Vector Machines. a) Linear SVM. A line is separating the two variables seen in blue and in red with the maximal distance (best separation of all the possible lines) seen in the line drawn. **b) Kernal SVM.** An SVM with radial type of kernel captures the decision boundary as a near circle.

Advantages and Disadvantages. This popular but relatively complex machine learning methodology can be good for **complex nonlinear relationships** between input features and output. This methodology is often considered one of the most **accurate** algorithms for classification, especially when there is high number of features (compared to the number of data points) and is therefore effective in **high-dimensional data.** SVM is also robust and thus can avoid noise as well as **minimize overfitting**. SVM is frequently used when one has a small training dataset as it does not scale well to larger datasets (larger training sets may be better suited for other classification methodologies or even deep learning). While linear SVM is considered **relatively fast** (but less accurate), kernel SVM is perhaps more accurate (but slower) for classification. Disadvantages include SVM needing high levels of both memory and processing power and difficulty in interpreting the precise relationship between input features and output.

An example in the recent biomedical literature is the usage of SVM in CT-based radiomic features to effectively identify high and low grades of clear cell renal cell carcinoma in only 227 patients with area under the curve (AUC) values of 0.88-0.91 ([1]).

Naive Bayes Classifiers. This supervised learning methodology uses **probability** to divide or categorize the data and is based on Bayes' theorem (with its concept of prior probability which selects the outcome with the highest probability). The presumption is that the predictors are independent of each other (hence the term "naive") so the model becomes essentially a probability table where the presence of a certain feature is not dependent on any other feature. In short, the probability of a certain outcome is the product of probabilities given by the features. The dividing line, or **Bayes' decision boundary** (**see Figure)**, is used to separate the samples into the two populations.
This methodology is well suited for real time prediction, text classification/spam filtering, and recommendation system.



Naive Bayes' Classifier. The orange and blue background designate the two regions divided by the Bayes decision boundary (dashed line).

Advantages and Disadvantages. This supervised learning methodology utilizes statistical modeling and has relatively **fast speed** (given parallel process) and is also good when there is **high dimensionality** of the inputs. Another advantage for the Bayesian probabilistic approach is that it does not require large training sets and is relatively **simple** to implement as well as to interpret. For its relatively fast speed, however, there is compromise in terms of accuracy (compared to kernel-type SVM that was just discussed).
Disadvantages include the underlying principle that there is total independence of features (uncommon situation) and relatively lower level of performance in lower-dimensional data.

An example in the recent biomedical literature is the application of Bayesian network modeling to pathology informatics by constructing several Bayesian network models to assess individual patient-specific risk for subsequent specific histopathologic diagnoses and their related prognosis in gynecological cytopathology and breast pathology ([2]).

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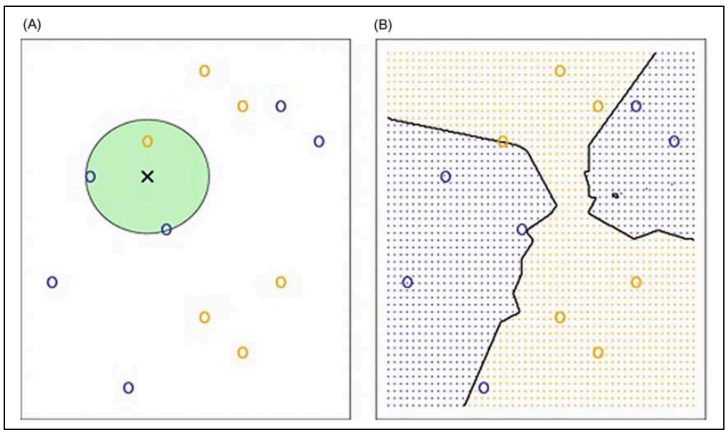
[1] Sun X, Liu L, Xu K et al. Prediction of ISUP Grading of Clear Cell Renal Cell Carcinoma Using Support Vector Machine Model Based on CT Images. *Medicine* 2019; 98:1-6.

[2] Onisko A, Druzdzel MJ, and Austin RM. Application of Bayesian Network Modeling to Pathology Informatics. *Diagnostic Cytopathology* 2019; 47:41-47.

k*-Nearest Neighbor (*k*-NN).** This supervised learning algorithm is used for both classification as well as regression and identifies the number of **nearest neighbors** of any element, hence the appropriate name (**see Figure)**. ***k is the integer of neighbors that is in the feature space closest to a designated point and the class is determined by majority observed in that space (e.g. if *k* is 3 and 2 out of 3 neighbors is a certain class, this class "wins"). Similar to the Bayes' classifier just discussed, there is a decision boundary called the ***k*-NN decision boundary**.
k-NN is well suited for text mining or categorization as well as stock market trends and forecasting.



***k*-nearest neighbor (*k*-NN). a) The *k*-NN process.** Test observation (designated with a cross) is shown with its *k*=3 nearest neighbors showing 2 blue and 1 red. Since the test observation location belongs to the more common class (blue vs red), this area belongs to the blue class.
b) The *k*NN decision boundary. The black lines delineate the decision boundary and the blue and orange background designate each respective blue and orange regions.

Advantages and Disadvantages. This methodology is relatively **simple** to interpret and is therefore considered a "lazy" learning that is instance-based (vs model-based). *k*-NN is well suited for datasets in which there is **no prior knowledge** about the distribution of the data. Like some of the aforementioned supervised methodologies, it is relatively **robust** to noisy training data. Disadvantages include *k*-NN not performing well with either high-dimensional data or massive amounts of data that may contain noise and nuances such as missing data, but this algorithm itself can be utilized to perform missing values imputation, noise filtering, and data reduction. *k*-NN is also susceptible to overfitting from the curse of dimensionality. Lastly, the *k* value can have a large effect on the performance of this model.

An example in the recent biomedical literature is the application of a modified *k*-NN algorithm (enhanced with instance weights) to patients with diabetic retinopathy for more accurate diagnosis ([3]).

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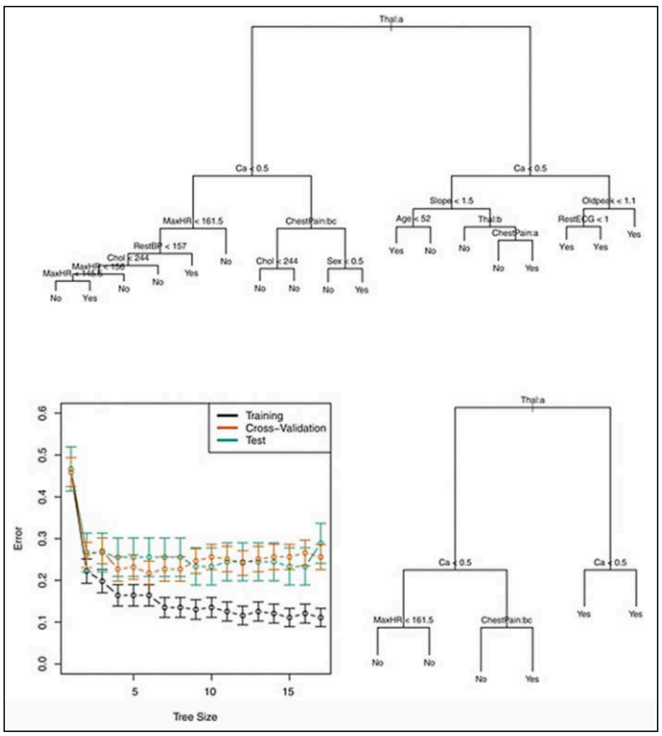
[3] Sarkar RP and Maiti A. Investigation of Dataset from Diabetic Retinopathy Through Discernibility-Based k-NN Algorithm in *Contemporary Advances in Innovative and Applicable Information Technology* pp.93-100, Springer, New York, 2019.

Decision Trees. The decision tree methodology is the most straight forward (also known as classifi cation and regression trees, or CART) with the trees drawn upside down; the decision points are termed **nodes** and the segments of the tree that interconnect the nodes are called **branches (see Figure)**. The leaves are therefore outcomes. To continue the tree terminology, a computational "pruning" process can reduce the size of the tree without sacrifi cing the accuracy of the model. This supervised methodology uses branches in decisions to achieve classifi cation (but can also be used for regression); decision trees, however, are not considered as accurate as the other aforementioned methodologies. Three strategies, therefore, are necessary to build more powerful prediction models with decision trees: bagging, boosting, and stacking (see below under Ensemble Learning).



Decision Trees. a) Unpruned tree and b) Pruned tree. The pruned tree is a result of decreasing the total number of nodes in the decisions without decreasing accuracy.

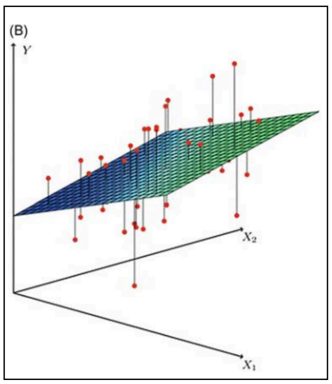
Advantages and Disadvantages. This methodology has **higher explainability** as it is much more relatable (compared to the other classification methodologies discussed earlier) and can be easily visualized as it has a **good graphical representation.** Decision trees are relatively **robust** to noise and incomplete data. Decision trees are also very accommodating for **non-linear relationships** as well as outliers. Lastly, it is also relatively **fast** compared to other methodologies. Disadvantages of decision trees include that these are not as accurate as other methods amongst supervised learning methods (but are relatively fast and efficient like logistic regression). These trees would usually need to be in an ensemble format, however, to be more accurate and be less prone to overfitting. Lastly, decision trees tend not to work well with small training data sets.

An example in the recent biomedical literature is the application of decision trees (vs risk scores) for predicting drug-resistant infections that revealed the decision tree (with 5 predictors) was more user-friendly with fewer variables for the end user in a study of over 1,200 patients ([4]).

[4] Goodman KE, Lessler J, Harris AD et al. A Methodological Comparison of Risk Scores vs Decision Trees for Predicting Drug-Resistant Infections: A Case Study Using Extended-Spectrum Beta-Lactamase (ESBL) Bacteremia. *Infection Control and Hospital Epidemiology* 2019; 40:400-407.

Questions 5.7/Supervised Learning II: Regression

1. In supervised learning, regression is a methodology for predicting a number. The following are regression methodologies *except*:
a. Logistic regression
b. Linear regression
c. Polynomial regression
d. LASSO regression
[ ]



2. The figure on the left is best described as:
a. Multiple linear regression showing least squares plane
b. Simple linear regression with population regression line
c. Logistic regression with a plane
d. Polynomial regression showing a nonlinear relationship
[ ]

3. Linear regression is known as a methodology for:
a. Numeric prediction and speed
b. Numeric prediction and flexibility
c. Non-numeric prediction and speed
d. Non-numeric prediction and flexibility
[ ]

4. For higher capacity in regression, which of the following will be *least* capable of this?
a. Neural network
b. Gradient boosting tree
c. Random forest
d. Linear regression
[ ]

5. Logistic regression is a methodology *best* suited for:
a. Regression
b. Classification
c. Unsupervised learning for clustering
d. Unsupervised learning for dimension reduction
[ ]

Answers 5.7/Supervised Learning II: Regression

1. In supervised learning, regression is a methodology for predicting a number. The following are regression methodologies *except*:
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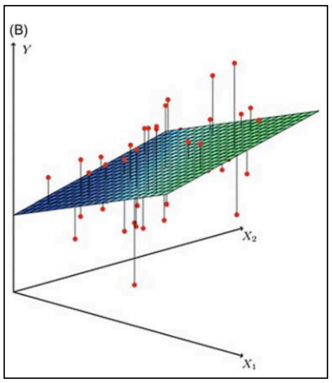
d. LASSO regression
[a]



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c. Random forest
d. Linear regression
[d]

5. Logistic regression is a methodology *best* suited for:
a. Regression
b. Classification
c. Unsupervised learning for clustering
d. Unsupervised learning for dimension reduction
[b]

Module 5.7/Supervised Learning II: Regression

Regression. The supervised regression methodologies lead to numerical representation of output variables in order to predict a number. Regression is good for market forecasting, growth prediction, and life expectancy calculation. In medicine and health care, regression is good for risk prediction and outcome prediction.
Regression methodologies are listed below **(see Table)** but only linear and polynomial regression will be discussed in detail.

Table 6. Supervised Learning: Regression Methodologies

Regression Methodologies	
Least absolute shrinkage and selection operator (LASSO) regression	Model is based on shrinkage and simple sparse models
Linear regression	(see text)
Polynomial regression	(see text)
Ridge regression	Model is a regularized linear regression
Support vector regression	Model is based on maximum margin but output is a number

Linear Regression. This regression is probably the methodology that is most familiar to clinicians. This machine learning method (derived from statistics) delineates the strength of the relationship between two continuous **variables** ("x" being the independent variable whereas "y" is the dependent variable). The method for fitting a regression line in linear regression is the method of least squares with a **correlation coefficient *r***. This regression is termed "**simple**" when there is a single input variable and "**multiple**" when there are multiple input variables **(see Figure)**. There is also **polynomial** (or non-linear) **regression** in which the relationship is not linear. In addition, **generalized linear model (GLM)** is an ordinary linear regression with a generalization that accommodates variables that do not have a normal distribution. Finally, **least absolute shrinkage and selection operator (lasso) regression** increases its prediction accuracy by performing both regularization (a process that decreases overfitting) and variable selection.

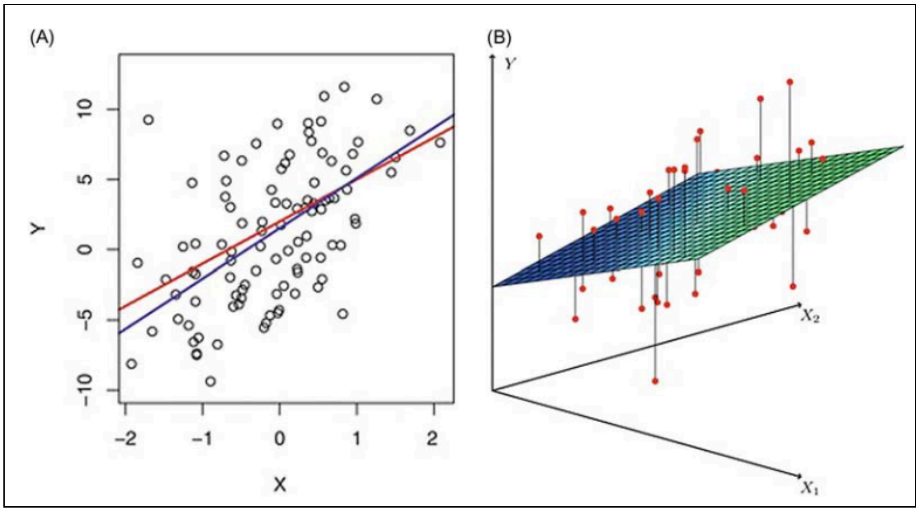

Figure. Linear Regression. a) Simple linear regression shows the population regression line (in red) and the least squares line (in blue). **b) Multiple linear regression** shows that the least squares line becomes a plane, which minimizes the sum of the squared vertical distances between the observations (in red dots) to the plane.

Advantages and Disadvantages. Linear regression is perhaps the **most familiar** regression methodology to all those who are not formally educated in data science. Linear regression is considered **fast** but not perhaps as accurate compared to other methodologies that perform regression. Linear regression performs poorly when the relationship is non-linear. Simple linear regression is usually not as accurate also given that LASSO and Ridge regressions are regularized (penalizing large coefficients) and therefore observed to exhibit less overfitting.

An example in the recent biomedical literature is the use of a hierarchical linear regression analysis of patients with chronic nonspecific low back pain and how this condition correlated with emotional distress ([5]).

[5] Du S, Hu Y, Bai Y et al. Emotional Distress Correlates Among Patients with Chronic Nonspecific Low Back Pain: A Hierarchical Linear Regression Analysis. Pain Practice 2019; [ePub]

Logistic Regression. This is the adaptation of the aforementioned linear regression to a binary classification (via a logistic function to yield maximum likelihood); it is not, therefore, a true regression like linear regression. **Multiple logistic regression** utilizes multiple predictors and is commonly used as a statistical tool for patient studies. A closely related classifier to logistic regression is **linear discriminant analysis (LDA)**, which is more stable than logistic regression in certain situations.

Advantages and Disadvantages. Logistic regression is relatively **fast** compared to other supervised classification techniques such as kernel SVM or ensemble methods (see later in the book) but suffers to some degree in its accuracy. It also has the same problems as linear regression as both techniques are far too simplistic for complex relationships between variables. Finally, logistic regression tends to underperform when the decision boundary is non-linear.

An example in the recent biomedical literature is the use of logistic regression (compared with three other ML methodologies) in a 2-year mortality prognostication study of a small number of patients (76 patients) with heterogenous glioma with highly dimensional datasets ([6]).

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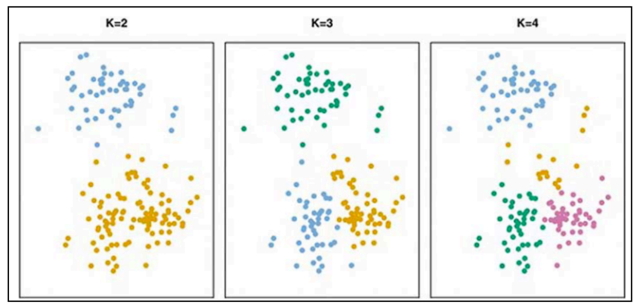
[6] Panesar SS, D'Souza RN, Yeh FC et al. Machine Learning vs Logistic Regression Methods for 2-Year Mortality Prognostication in a Small, Heterogenous Glioma Database. *World Neurosurgery* 2019; 2:100012.

Questions 5.8/UnSupervised Learning

1. A type of learning that takes unlabelled data and uses algorithms to predict patterns or groupings in the data set without any human intervention is called:
a. Supervised learning
b. Unsupervised learning
c. Reinforcement learning
d. Ensemble learning
[ ]

2. The graphs at right shows different colors for different patient groups in an unsupervised methodology called:
a. *k*-means cluster analysis
b. Support vector machine
c. Naive Bayes classifier
d. Decision trees
[ ]



3. A hybrid technique of supervised and unsupervised learning that uses a small amount of labeled data and then a relatively large amount of unlabeled data is called:
a. Semisupervised learning
b. Ensemble learning
c. Generative adversarial network (GAN)
d. Convolutional neural network (CNN)
[ ]

4. An unsupervised methodology that reduces the dimensionality of the data usually by merging features is called:
a. Principal component analysis
b. Support vector machine
c. Decision trees
d. Logistic regression
[ ]

5. Cluster analysis in biomedicine is good for:
a. Correlation between therapy and survival
b. Novel patient subgroups
c. Classification of tumor on MRI
d. Risk prediction of a cohort
[ ]

Answers 5.8/UnSupervised Learning

1. A type of learning that takes unlabelled data and uses algorithms to predict patterns or groupings in the data set without any human intervention is called:
a. Supervised learning
b. Unsupervised learning
c. Reinforcement learning
d. Ensemble learning
[b]

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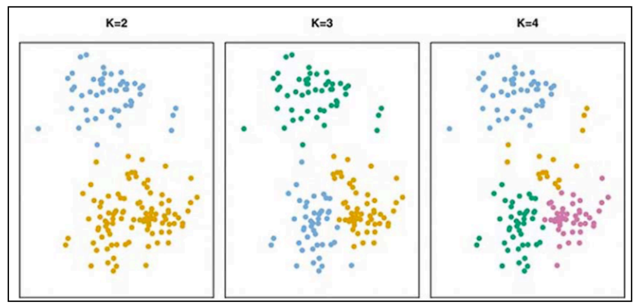

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d. Convolutional neural network (CNN)
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4. An unsupervised methodology that reduces the dimensionality of the data usually by merging features is called:
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[a]

5. Cluster analysis in biomedicine is good for:
a. Correlation between therapy and survival
b. Novel patient subgroups
c. Classification of tumor on MRI
d. Risk prediction of a cohort
[b]

Module 5.8/UnSupervised Learning

Unsupervised Learning. Unsupervised learning takes unlabeled data and uses algorithms to predict patterns or groupings in the data set without any human intervention. It is more challenging than supervised learning as there are no "answers" but can be coupled with supervised learning. This type of learning is more for exploratory purposes (such as to discover market segmentation) or to analyze and label new data. In medicine and health care, there is use for this unsupervised learning in subgroups of various cancers based on their gene expressions.

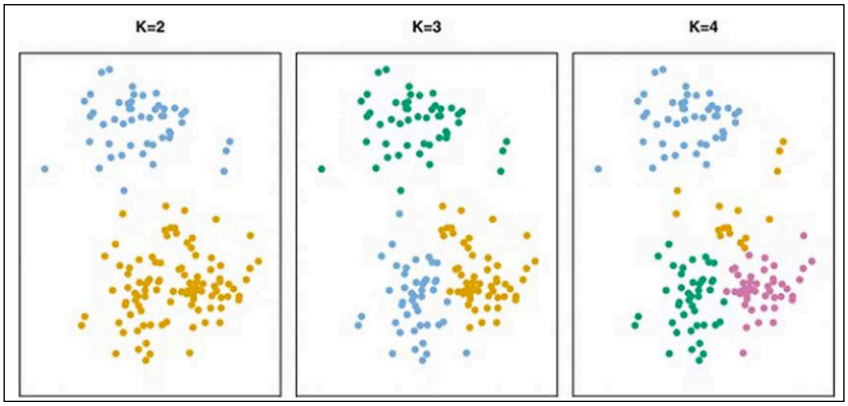
These unsupervised learning methodologies lead to **clustering, generalization, association,** or **anomaly detection**.

Clustering. These methodologies group data by similar characteristics without any human intervention. Clustering can be used for customer segmentation and recommender systems. In medicine and health care, clustering is good for biological hypothesis generation, identifying new populations or therapies, and novel phenotype identifi cation.
Clustering methodologies are listed below with a brief description **(see Table)** but only *k*-means clustering will be described in detail.

Unsupervised Learning: Clustering Methodologies

Affinity propagation	Clusters based on graph distances between points
Density-based spatial clustering of applications with noise (DBSCAN)	Density-based algorithm for clusters of dense regions
Fuzzy C-means clustering	Model based on each data can belong to >1 cluster
Gaussian mixture models	Probabilistic model based on Gaussian distributions
Hidden Markov model (HMM)	Probabilistic model-based approach to sequences
Hierarchical or agglomerative clustering	Model based on a hierarchy of clusters
***k*-means clustering**	(see text)
Mean-shift clustering	Model based on kernel density estimation

***k*-Means Clustering.** This is a commonly used simple unsupervised learning that has an algorithm used to find **clusters** or groups in the data with *k* number of groups that form organically based on similarity (**see Figure**). The end result of the process of using distance formulas yields *k* feature vectors called **centroids** of clusters. When *k* is not designated, the classifier will determine the best *k* based on two techniques, reconstruction error (sum of the mean squared error between all the points and their centroid) or peakedness (best *k* is where the largest cluster is the one with the highest peak in comparison with others).



***k*-Means Clustering.** The panel shows 150 observations with results of different values of *k* (*k*=2, 3, and 4) with different colors designating the groups for the clustering methodology.

Advantages and Disadvantages. One advantage of *k*-means clustering is that it is relatively **easy** and **simple** to implement. It is also **faster** than the other clustering methodologies especially with larger number of variables. Lastly, this methodology also produces relatively **tight clusters**. The weakness of this methodology is that sometimes it is difficult to predict the *k* value. In addition, the clusters may lack the hierarchical significance and consistency that other clustering methodologies may yield.

An example in the recent biomedical literature is the effective use of *k*-means clustering for a cluster-based classification strategy (based on severity) of the heterogenous disorder of bipolar disorder in 224 subjects ([7]).

[7] de la Fuente-Tomas L, Arranz B, Safont G et al. Classification of Patients with Bipolar Disorder Using k-means Clustering. *PLOS ONE* 14(1): e0210314.

Generalization (or **Dimension Reduction**). Generalization is a methodology that reduces the dimensionality of the data, usually by merging features. The advantages of having such abstracted models is that these models can then be more efficient and use less features. This methodology is also used for data visualization and compression of data. In medicine and health care, generalization is good for data visualization, data compression, and variable selection. These methodologies include the popular principal components analysis (PCA) and other generalization methodologies that are listed below with a brief description **(see Table).**

Unsupervised Learning: Generalization Methodologies

Generalization Methodologies	
Laplacian eigenmaps	Technique for nonlinear dimensionality reduction that is computationally efficient
Latent semantic analysis (LSA)	Technique for creating a vector representation of a document in NLP
Power-law stochastic neighbor embedding (p-SNE)	Model designed for visualization of high-dimensional datasets
Principal components analysis	(see text)
Random projection	Model for representing high-dimensional data in Euclidean space to a low-dimensional feature space
Singular value decomposition (SVD)	Model for decomposing or factorizing a matrix into its constituent elements
t-Distributed stochastic neighbor embedding (t-SNE)	Model designed for visualization of high-dimensional datasets

Principal Components Analysis. PCA identifies the features that are most significant in classification and therefore these selected features are then chosen to be used for computation; it is considered a **dimension reduction** method as it reduces a large set of variables into a low-dimensional representation of the dataset with this feature extraction. Each **principal component** is a linear combination of variables that are compressed. PCA can also be used as a dimension reduction technique for the purpose of regression. PCA is often used for data visualization or data pre-processing prior to supervised methodologies are used.

Advantages and Disadvantages. The advantages are several: low noise sensitivity, decreased requirement for capacity and memory, and increased efficiency. The disadvantages of this methodology are centered around its assumptions: linearity and principal components being orthogonal. In addition, the new principals are not interpretable.

An example in the recent biomedical literature is a study that used PCA to eliminate unwanted low frequency signal drift as well as spontaneous high frequency global signal fluctuations in 4D functional MRI so that the these artifacts as part of a more sophisticated preprocessing step in the study acquisition ([8]).

Other categories under unsupervised learning include association rules, or pattern search or recognition, and identifies sequences or relationships in data. The associative unsupervised methodologies include Apriori, FP-Growth, and Equivalence CLAss Transformation (ECLAT) algorithms and are used in sales and marketing strategies as these algorithms can predict buyer behavior.

In addition, there is **anomaly detection** (also called **outlier detection**) that can be performed from unsupervised learning, although supervised as well as semi-supervised techniques can also be applied to anomaly detection. In addition to fraud detection in finance and structural defects in industry, this last category of unsupervised learning can also be very useful in biomedicine for detecting medical problems or errors. It is precisely this population of anomalies or outliers in biomedicine that can be an important source of new knowledge.

An example in the recent biomedical literature is the use of outlier detection in preventing medication errors using an unsupervised methodology named density-distance-centrality (DDC) to detect potential outlier prescriptions in a dataset of over 560,000 prescribed medications ([9]).

---

[8] Parmar HS, Nutter B, Long R et al. Automated Signal Drift and Global Fluctuation Removal from 4D fMRI Data Based on Principal Component Analysis as a Major Preprocessing Step for fMRI Data Analysis. *Proc SPIE 10953, Medical Imaging* 2019: *Biomedical Applications in Molecular, Structural, and Functional Imaging, 109531E.*

[9] dos Santos HDP, Ulbrich AH, Woloszyn V et al. DDC-Outlier: Preventing Medication Errors Using Unsupervised Learning. *IEEE journal of Biomedical and Health Informatics* 2019; 23(2): 874-881.

Finally, a **Boltzmann machine,** a network of symmetrically connected nodes (each node is connected to every other node), is an unsupervised machine learning algorithm that can discover latent features in the dataset. Restricted Boltzmann machine will be discussed below.

Semi-Supervised Learning. A hybrid technique of supervised and unsupervised learning is **semi-supervised learning,** which uses a small amount of labeled data and then a relatively large amount of unlabeled data. Semi-supervised learning can also produce proxy labels on unlabelled data.

Advantages and Disadvantages. These methodologies can therefore be trained on a mixture of small amount of labeled and larger amount of unlabeled data, which will be more **efficient** as it saves human time and effort. The introduction of unlabeled data may actually **reduce human bias** and improve accuracy of the final model.

An example in the recent biomedical literature is a report on the semi-supervised learning approach (combined with generative adversarial networks) in providing a small number of labeled medical data to build a platform for IoT-based medical data and interpretation as part of decision support for this new source of medical data ([10]).

[10] Yang Y, Nan F, Yang P et al. GAN-Based Semi-Supervised Learning Approach for Clinical Decision Support in Health IoT Platform. *IEEE Access* 2019; 7:8048-8057.

Questions 5.9/Ensemble Learning

1. A methodology that involves training of a large number of models that together will surpass the performance of a single model is called:
a. Recurrent neural network
b. Ensemble learning
c. Cognitive computing
d. Supervised learning
[ ]

2. A parallel building of models with equal weights to improve accuracy of the collective group is:
a. Bagging
b. Boosting
c. Tuning
d. None of the above
[ ]

3. A sequential building of models to correct the errors of a preceding algorithm is called:
a. Bagging
b. Boosting
c. Tuning
d. None of the above
[ ]

4. A popular supervised learning algorithm that consists of a bagging ensemble of many decision trees is:
a. AdaBoost
b. Random forest
c. CatBoost
d. None of the above
[ ]

5. Which of the following statements about random forest is *true*?
a. Random forest cannot be used for both classification and regression
b. A major limitation of random forest is its inference or evaluation speed
c. Overfitting is a major problem with random forest
d. Random forest is ideally suited for real-time predictions
[ ]

Answers 5.9/Ensemble Learning

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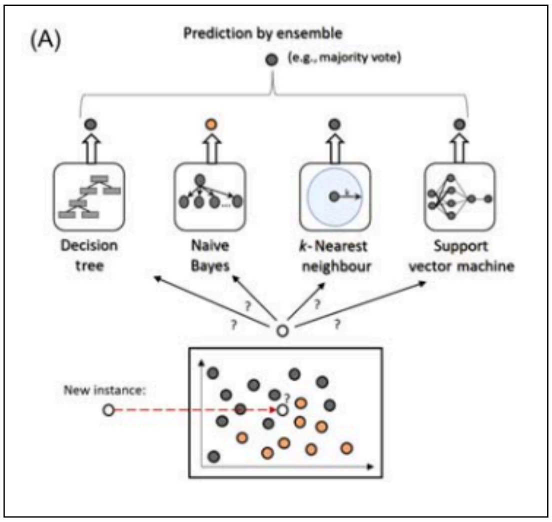
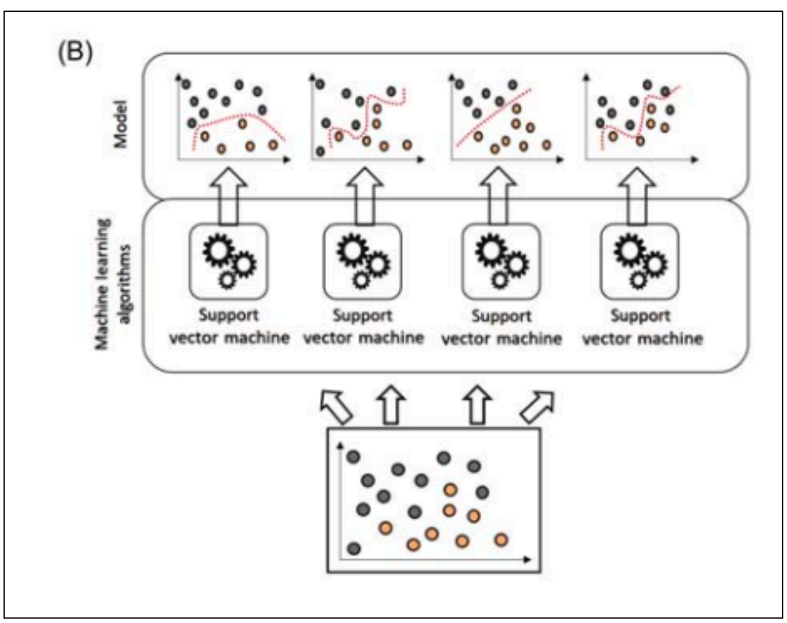
Module 5.9/Ensemble Learning

Ensemble Learning. This ensemble learning strategy (bagging, boosting, and stacking) involves training a large number of models that together will surpass the performance of a single model; in short, it is the creation of a **meta-model** that has better prediction and more stability. This ensemble of models reduces noise, bias, and variance. A common scenario is the utilization of decision tree algorithms to achieve this ensemble to improve accuracy (although generally these ensemble learning methodologies can be slower than others).

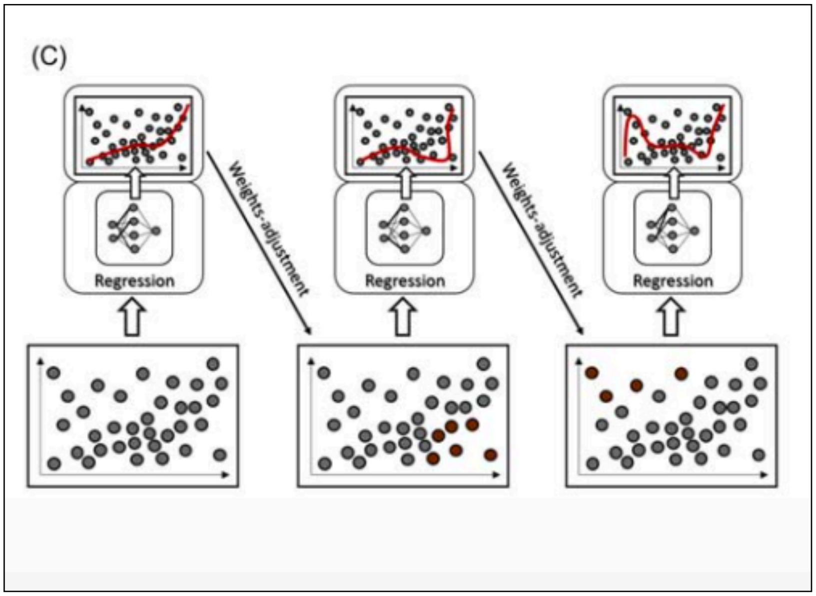


There are three ensemble learning strategies that can improve performance **(see Figure)**.
In a, the general concept of ensemble learning is illustrated with several models assembled to surpass the performance of a single model.

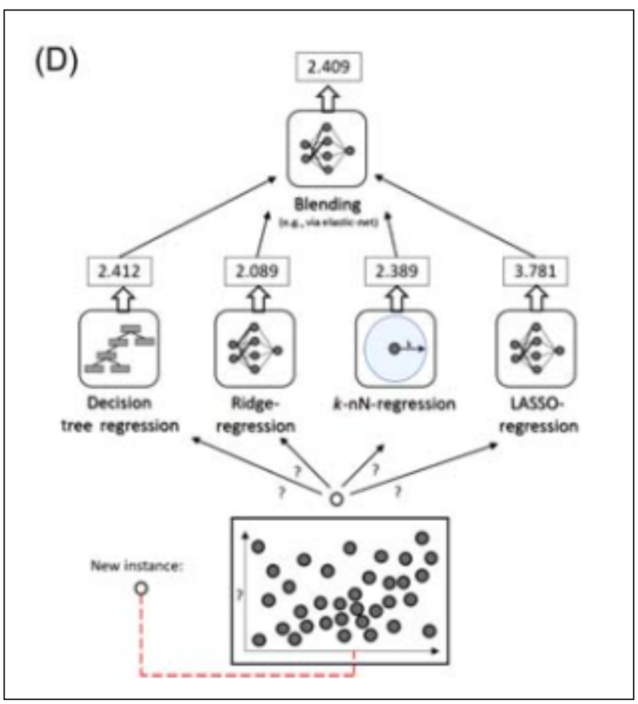


First, **bagging** (also called **bootstrap aggregating**) involves creation of many duplicates or different sets of the training data followed by training with the same model or algorithm and yielding eventually the average of all the models; the variance is reduced. This process of building models is done in **parallel**. **Random forest** is a popular supervised learning algorithm that consists of an ensemble of many decision trees that collectively yield an accurate prediction and minimizes overfitting. One major limitation of random forest is its slow nature (with its large number of trees) so it is not ideally suited for real-time predictions. Random forest is a methodology that is used for detecting fraud and stock projections.

In b, bagging with several SVM models are seen to reduce the model's variance.



Second, **boosting** involves creation of many models with the training data to enable each new algorithm to correct the errors of the previous algorithm, and therefore enable the weak models into a stronger one; the bias is reduced. This process of building models is done in **sequence.** While equal weight is given to all models in bagging, the performance of a model determines the weight of the model in boosting. **Gradient boosting** is one such ensemble algorithm that typically uses decision trees, and another one is **adaptive boosting** (or AdaBoost). Other tools for this boosting function include XGBoost, Light GBM, and CatBoost. In c, boosting (Adaboost) with several models to enable the weaker models into a stronger one by giving more weight to the models with better performance; bias is also reduced.



Third, **stacking** involves having several different algorithms to deliver output to one last algorithm as an arbitrating algorithm for a final decision; the predictive accuracy is increased as a result. Lastly, in d, stacking is seen with several different regression algorithms collectively involved in increasing the predictive force of the classifier.

Advantages and Disadvantages. This strategy of combining algorithms is that the **collective strengths** of several or many models is a good improvement on individual models, particularly decision trees. In addition, less stable or more fragile algorithms can actually (paradoxically) add a **higher quality** to the ensemble of models. Finally, while bagging reduces variance and thus overfitting, boosting reduces bias (but may increase overfitting) so both ensemble methods have its own advantage.

An example in the recent biomedical literature of ensemble methods is the recent study of an ensemble machine learning model for trauma risk prediction that proved to be superior to three established risk prediction models (including one that used Bayesian logic) ([11]).

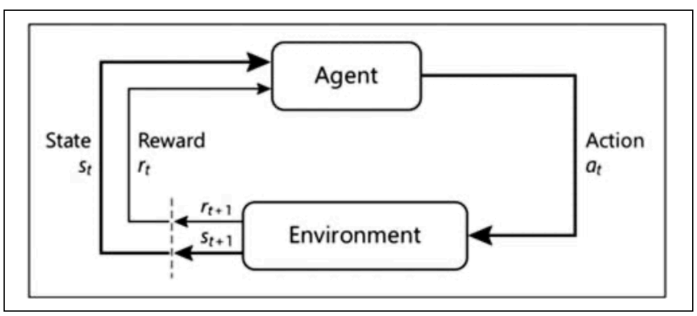
[11] Gorczyca MT, Toscano NC, and Cheng JD. The Trauma Severity Model: An Ensemble Machine Learning Approach to Risk Prediction. *Computers in Biology and Medicine* 2019; 108:9-19.

Questions 5.10/Reinforcement Learning

1. Reinforcement learning with deep learning was demonstrated at which of the following game:
a. Chess
b. Poker
c. Go
d. Jeopardy!
[ ]

2. In reinforcement learning, a function that maximizes the reward in a long term setting is called:
a. Policy
b. Reward
c. State
d. Goal
[ ]

3. Reinforcement learning is ideally suited for which of the following situations?
a. Image recognition
b. Sequential decision process
c. Classification
d. Regression
[ ]



4. The diagram on the left shows:
a. Machine learning- supervised type
b. Machine learning- unsupervised type
c. Reinforcement learning
d. Convolutional neural network
[ ]

5. An autonomous entity that can perform a task based on an input (perceptions) and intelligent processing to lead to an output (action) is called a(n):
a. Agent
b. Node
c. Algorithm
d. Neural network
[ ]

Answers 5.10/Reinforcement Learning

1. Reinforcement learning with deep learning was demonstrated at which of the following game:
a. Chess
b. Poker
c. Go
d. Jeopardy!
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2. In reinforcement learning, a function that maximizes the reward in a long term setting is called:
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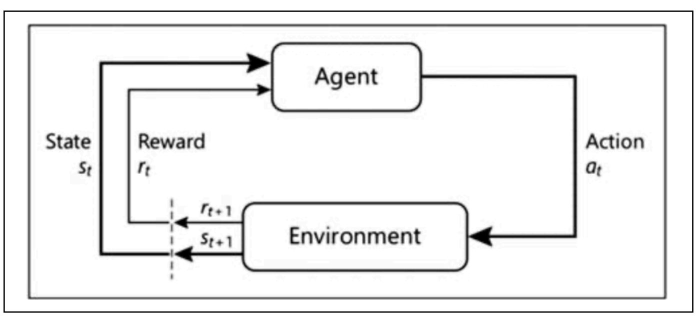

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d. Convolutional neural network
[c]

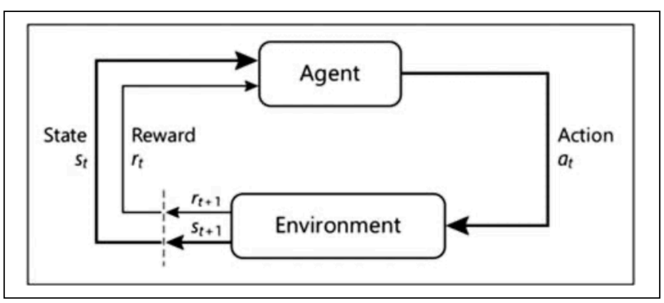
5. An autonomous entity that can perform a task based on an input (perceptions) and intelligent processing to lead to an output (action) is called a(n):
a. Agent
b. Node
c. Algorithm
d. Neural network
[a]

Module 5.10/Reinforcement Learning

Reinforcement Learning. In addition to the aforementioned supervised (task-driven with classifi cation or regression) and unsupervised (data-driven with clustering) learning, another type of learning is **reinforcement learning.** Although reinforcement learning is often described as a third or additional type of machine learning along with supervised and unsupervised learning, it is distinctly different from the former two types of machine learning.

Reinforcement learning and its wondrous capability (along with a Monte Carlo tree search algorithm) was best demonstrated in the Google DeepMind's *AlphaGo* program and its recent successful defeat of the Go champion Lee Sedol. **DeepMind** (based in London and founded in 2010) and its founder Demis Hassabis aim to be the Apollo program of the AI domain with a large number of highly trained AI and ML scientists and with a singular focus on achieving **general-purpose, self-learning AI** with deep reinforcement learning. With an innovative form of reinforcement learning, *AlphaGo Zero* was able to teach itself the game Go entirely on its own and was able to soundly defeat its precursor *AlphaGo* in just 40 days. DeepMind was acquired by Google in 2014 for $500 million and DeepMind Health focuses on AI applications in health care.

In reinforcement learning, the model is not relating itself to data but rather finding the **optimal method** via exploration to achieve the most **desirable outcome** while receiving input data in a dynamic environment (analogous to humans attempting to attain the highest score in a game). In other words, there is a positive and negative feedback to the solution of the algorithm so the goal of reinforcement learning is to learn a **policy** (defined as a function that maximizes the reward in a long term setting, or reward maximization). Reinforcement learning is therefore is well suited for a **sequential decision process** needed for video games, automated trading, and robotic navigation.



An **agent** (which represents the algorithm) interacts with the environment via an **action** and has knowledge of the **state** of the environment. With the action, the agent receives a **reward** (or a penalty). Reinforcement learning enables the agent to maximize the reward via learning from its experience with all the interactions with the environment.

An **intelligent agent,** or simply "agent" in AI parlance, is an autonomous entity that can perform a task based on an input (perceptions) and intelligent processing to lead to an output (action). These agents are different from traditional software programs in that these agents have characteristics of perception, autonomy, learning, and communication. It is essentially a self-contained software program with goal orientation embodied with knowledge and overall represents someone.

Reinforcement learning methodologies are listed below and briefly described **(see Table)** with DQN being the first large-scale application of reinforcement learning with deep neural network ([12]). In DQN, the synergistic combination of reinforcement learning with a novel artificial agent named deep Q-network can learn successful policies directly from high-dimensional sensory inputs using end-to-end reinforcement learning.

Reinforcement Learning Methodologies	
Asynchronous advantage actor critic (A3C)	Algorithm obsoleting DQN and leverages deep learning for continuous action spaces
Deep deterministic policy gradient (DDPG)	Model relies on actor-critic architecture with experience replay and separate target network
Deep Q-network (DQN)	Model that leverages neural network to estimate the Q-value function
Genetic algorithm	Use mutations and crossovers to converge to local optima
Q (Quality)-learning	An off-policy algorithm that aims to maximize the Q-value
State-action-reward-state-action (SARSA)	An on-policy algorithm that learns the Q-value based on the action by current policy
Temporal difference	Model-free methodology in which learning is by bootstrapping from current value function
	Note. Q value is the reward for performing an action a in state s.

Advantages and Disadvantages. The advantage of reinforcement learning is the type of learning is considered more **human learning**. In addition, reinforcement learning is not task nor data driven like supervised and unsupervised learning. Reinforcement learning is also capable of functioning in a **changing environment**. A limitation with reinforcement learning, however, is that some biomedical problems have multiple simultaneous interactions and are real-time without time delay (continuous and not discrete). In addition, reinforcement learning is data hungry and relatively opaque as well as narrow and brittle. Finally, reinforcement learning has to balance exploration and exploitation.

A brief review on not only RL but also DRL is useful (but relatively esoteric on the mathematics) to appreciate basic principles of RL and DRL and their applications in medicine ([13]). An example in the

[12] Mnih V, Kavukcuoglu K, Silver D et al. Human-Level Control Through Deep Reinforcement Learning. *Nature* 2015; 518:529-533.

[13] Jonsson A. Deep Reinforcement Learning in Medicine. *Kidney Dis* 2019; 5:18-22.

recent biomedical literature is the use of deep reinforcement learning (in the form of double Deep Q networks) for optimal pain management in the intensive care setting that is more effective than conventional methodologies ([14]).

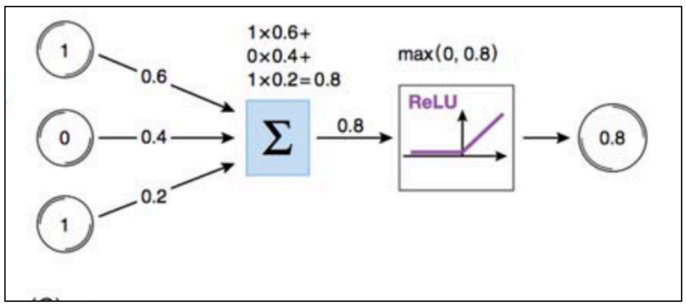
[14] Lopez-Martinez D, Eschenfeldt P, Ostvar S et al. Deep Reinforcement Learning for Optimal Critical Care Pain Management with Morphine Using Dueling Double Deep Q Networks. *arXiv*:1904.11115.

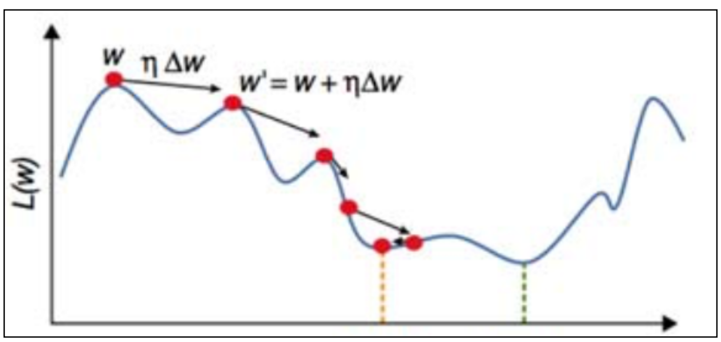
Questions 5.11/Neural Network

1. The following are examples of neural networks *except*:
a. Convolutional neural network
b. Autoencoder
c. Recurrent neural network
d. Support vector machine
[ ]

2. Which of the following pairs is *correct*:
a. Convolutional neural network- sequential data
b. Recurrent neural network- computer vision
c. Generative adversarial network- data generation
d. Autoencoder- supervised learning
[ ]

3. In the diagram on the right, the blue signifies:
a. Input
b. Output
c. Weighted sum
d. Activation function
[ ]





4. An assessment of all the weights and biases of the network provides one number as a performance "grade" of the network is:
a.Loss function
b.Activation function
c.Forward propagation
d.Backward propagation
[ ]

5. The green dotted line shows the lowest cost function and this point is called:
a. Local minimum
b. Global minimum
c. Neural nadir
d. Global nadir
e. [ ]

Answers 5.11/Neural Network

1. The following are examples of neural networks *except*:
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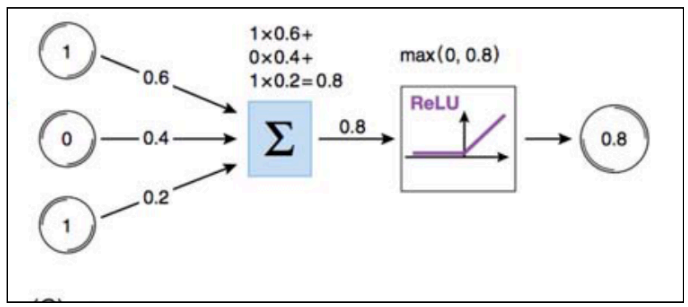

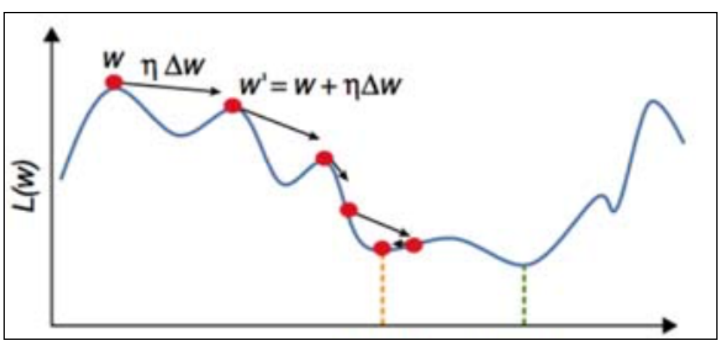

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b. Global minimum
c. Neural nadir
d. Global nadir [b]

Module 5.11/Neural Network

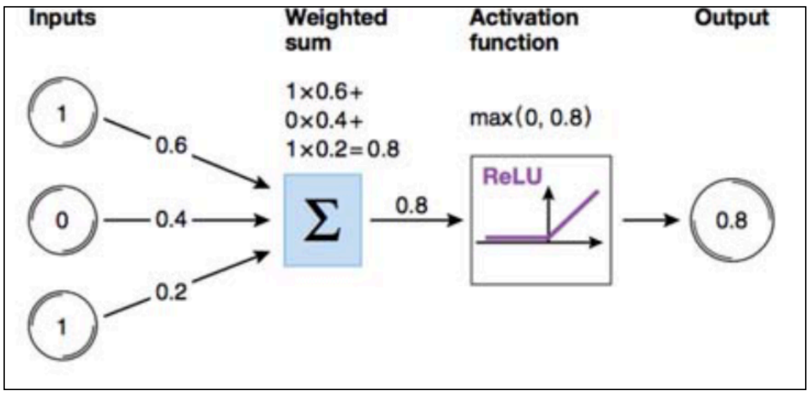
Neural Networks and Deep Learning
A type of machine learning that was inspired (perhaps in a slightly exaggerated manner) by the brain with its neurons and intricate synaptic interconnections is termed **artificial neural network (ANN),** or **neural networks** (also **neural nets** for short). The aforementioned **perceptron,** also called a **node,** is a computational model of a biological neuron.

Compared to the machine learning techniques just discussed, the more sophisticated neural networks and deep learning techniques (with sometimes hundreds of layers of neurons) are particularly well suited for **non-linear** and **complex** relationships, which are not uncommon in biomedicine and health care. This category of neural networks includes: perceptrons (including both the simple perceptron as well as perceptrons in multiple layers called multilayer perceptrons, or MLP), autoencoders, generative adversarial network (GAN), convolutional neural network (CNN), and recurrent neural network (RNN)**(see Table)**.

Table 10. Neural Networks

Type of Neural Network	Features	Function
Multilayer perceptron (MLP)	Hidden layer	Adaptive learning
Antoencoder network	Encoder-decoder	Dimension transformation
Generative adversarial network (GAN)	Generator-discriminator	New data generation
Convolutional neural network (CNN)	Convolutional layer	Computer vision
Recurrent neural network (RNN)	Memory state	Sequential data

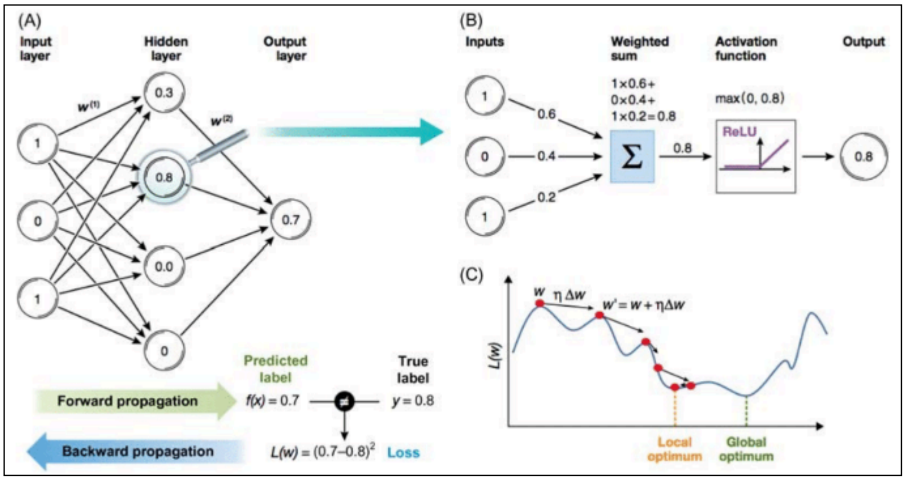
Perceptron and Multilayer Perceptrons (MLP). A **perceptron** is essentially a single layer neural network and is the simplest of all the neural computational models. It is essentially a **binary linear classifier**. This **node** or **neuron** model, with its biologically inspired structure, takes in **inputs** in the form of data, performs designated computational **function(s)**(also termed **activation function,** see below), and then gives out an **output**. In short, the node or neuron is where computational function(s) occur . Even though the neuron and the perceptron have similarities in their architectures (dendrites and axons are equivalent to inputs and outputs respectively), a major difference between these two models is the number of connections: while the perceptrons can be connected to a few other perceptrons, biological neurons can be connected to as many as 10,000 other neurons.



These nodes are connected via their **connections**, which are respectively modulated by parameters called **weights.** These weights determine the relative strength of the transmitted signal for each connection and can be positive or negative. In other words, this weight influences the effect that the input will have on the neuron and is adjusted in order for the neural network to "learn". There is also a **bias**, which is a number that tells one how high the weighted sum needs to be before the neuron is activated. In summary, the sum of the inputs is multiplied by the weights and then the bias is considered. In addition, there is an **activation function** of the neural network that learns via connection between the input and the output (and can limit the breadth of the neuron's output). The activation function determines the value of the perceptron's output. The activation function can therefore improve the performance of the neural network; the activation function of a neuron is usually in a sigmoid shape as it is the balance between linear and non-linear behavior.

Training of the neural network occurs in two different stages: forward and back propagations. **Forward propagation** is essentially the weighted sum of the inputs and the predicted label (compared to the true label). **Backward propagation** (short for backward propagation of errors) then, is a mechanism in which the neural network can learn (or fine tune). The difference between the actual output and the desired output is used to calculate a modification called the **loss** or **cost function** (see also below) to achieve the desired outcome.

The **multilayer perceptron**, or MLP, is therefor a multilayer feedforward network with one or more hidden layers. Each of these neural networks have an **input layer**, a **hidden layer**, and an **output layer**. The hidden layer performs computations received from the input layer and pass the results to the output layer. Learning, therefore, is for the network to find not just the right weights but also the best biases (usually many more the former than the latter) to perform correctly.



Artificial Neural Network. The ANN is seen in A, with the input layer pushing data though the hidden layers and then end up in the output layer. Weights, $w^{(1)}$, are parameters that learn from input and output comparisons. Learning occurs by minimizing the loss function *L(w)* that measures the fit of the output from the model to the actual sample. In B, data and mathematical functions of the neuron is seen. Each neuron computes the inputs with a weighted summation (seen in blue) and then applies an activation function (rectified linear unit, or ReLU in this case) so that an output is calculated. The loss is backward propagated through the network in order to generate the gradients of the of *L(w)*, which is optimized using the gradient descent approach for a global optimum (seen in C).

Loss or **cost function** is an assessment of all the weights and biases of the network and provides one number as a performance "grade" of the network; the lower the number the better the network's performance. (Note. Some authors do differentiate loss function (or error) as an element for a single training example whereas cost function is for the entire training set). In essence, "learning" in a network is refl ected by minimizing this loss or cost function in an iterative fashion.

A **gradient descent** is an **optimization algorithm** to improve the parameter of the machine learning model (the coefficients in linear regression and the weights in neural networks) so that these models can be at the lowest cost function (or at the highest accuracy). This strategy is performed by iteratively decreasing the gradient until a **global minimum** is reached (as a local minimum is usually not the lowest) of the cost function **(see Figure)**. Optimization with gradient descent to a global minimum point (global minima). A local minima is seen but it is not the lowest point. The complicated nature of the image reflects the non-linear nature of neural networks.

Advantages and Disadvantages. The advantages of multilayer perceptrons include its **adaptive learning capability** and its back propagation algorithm can perform mapping between input and output well. Among the disadvantages are its relatively slow speed of learning and that it requires labeled data. In addition, there is also its possibility of overfitting with MLP.

An example in the recent biomedical literature is a recent report using radiomic features and multilayer perception network classifier for a relatively robust MRI classification strategy (compared to GLM or even CNN) for distinguishing glioblastoma from primary central nervous system lymphoma ([15]).

[15] Yun J, Park JE, Lee H et al.Radiomic Features and Multilayer Perceptron Network Classifier for a More Robust MRI Classification Strategy for Distinguishing Glioblastoma from Primary Central Nervous System Lymphoma. *Scientific Reports* 2019; 9:5746.

Questions 5.12/Deep Learning

1. Deep learning promulgated from the following elements *except*:
a. Methods and algorithms
b. Cloud computing
c. Feature engineering
d. Computational power
[ ]

2. Current applications of deep learning includes all of the following *except*:
a. Computer vision
b. Autonomous driving vehicle
c. Causal inference
d. Speech recognition
[ ]

3. Which statement about the differences between machine and deep learning is *true*:
a. Deep learning usually requires a bigger dataset whereas machine learning performs well with a small or medium dataset
b. The training time is longer with machine learning
c. Both require computational power of GPUs
d. Both require feature engineering
[ ]

4. Which of the following statements is *not* true?
a. An auto encoder is a relatively simple neural network
b. Generative adversarial network has a generator and a discriminator network
c. Generative adversarial network is good at generating synthetic text but not image data
d. Both variational auto encoder and generative adversarial network can generate synthetic data
[ ]

5. The diagram on the right is an example of:
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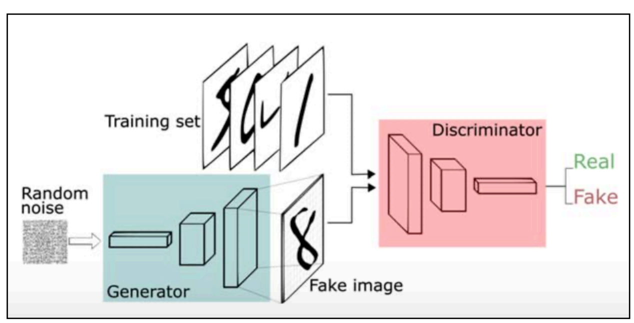
b. Generative adversarial network (GAN)
c. Convolutional neural network (CNN)
d. Support vector machine
[ ]



Answers 5.12/Deep Learning

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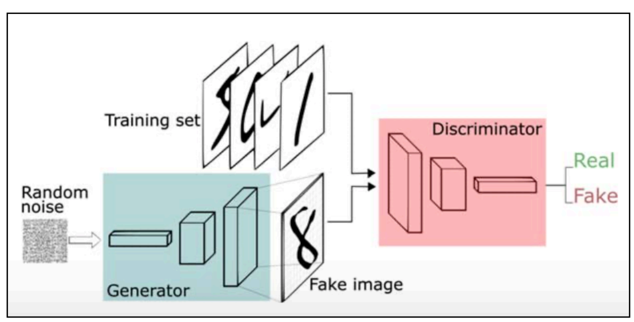
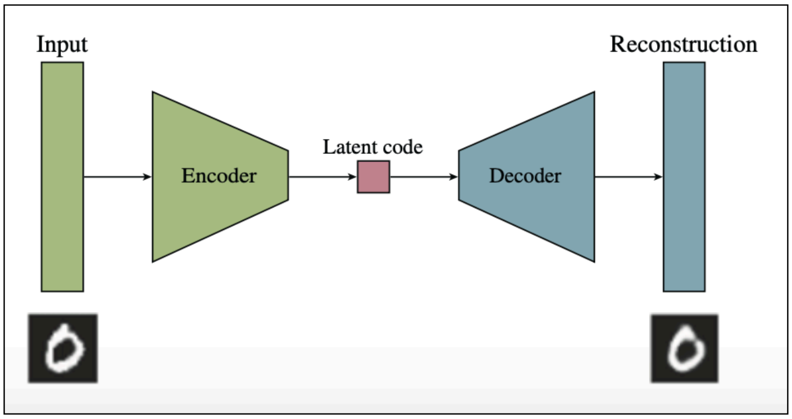
d. Support vector machine
[b]



Module 5.12/Deep Learning

Deep Learning. Deep learning promulgated from three separate influences. First, the evolution of **methods** from early mathematicians to LeCun's convolutional neural network in 1989 and culminating in Hinton's work later on with ImageNet in 2012. Second, **storage** capacity of computers increased dramatically from punch cards in earlier periods to internet and finally the current cloud form of storage. Finally, **computational power** also increased from its origin in the form of the ENIAC computer to the present day graphical processing units (GPUs), which are specialized type of microprocessors with memory that are parts of the graphics cards and have more processing cores than CPUs (see previous Figure). Current applications of deep learning include speech recognition and natural language processing, computer vision with visual object recognition and detection, speech recognition, and autonomous vehicle driving.

An excellent review on deep learning in medicine discusses deep learning in computer vision, natural language processing, reinforcement learning, and generalized methods. The following types of deep learning will now be discussed: auto encoder neural network, generative adversarial networks (GANs), convolutional and recurrent neural networks (CNN and RNN), and others.



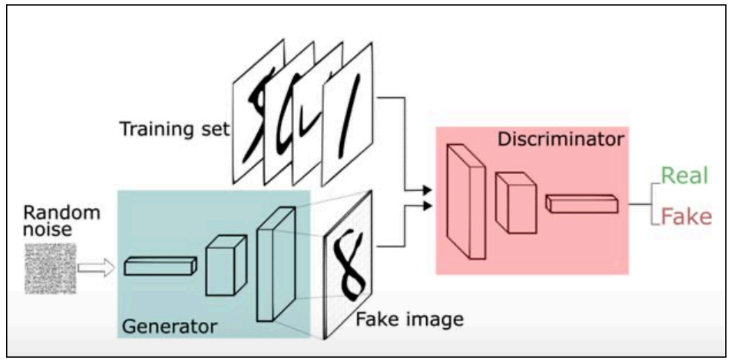
Autoencoder neural network. This is a relatively simple 3-layer (or more) neural network that is an unsupervised learning tool that "encodes" input data (as a vector) into a more compressed representation **(see Figure)**; it is a therefore a form of **dimension reduction.**
An autoencoder has an intentional "bottleneck" in the network so that this area forces a compressed knowledge representation (or exact copy) of the original input; a decoder is usually paired with this encoder in order to reconstruct the input data that was compressed. An autoencoder is also used for **data denoising**. Unlike PCA and its capability for dimension reduction, autoencoder performs dimension reduction in a non-linear fashion. An interesting application of autoencoders is the **variational autoencoder (VAE),** which not only compresses input data but is also generative- it synthesizes new, similar data of the type that the autoencoder has observed (essentially new images from old images).
An autoencoder can be applied to computer vision, anomaly detection, and information retrieval.

Advantages and Disadvantages. An autoencoder is easier to use for dimension reduction than PCA, and is considered to be more accurate as well. In addition, as autoencoder is a neural network, it is well suited for image and audio data. One drawback of an autoencoder is that one can miss theoretical insights and information about the input data, especially with VAEs. Another potential weakness is that it requires relatively high volume of data to train.

An example in the recent biomedical literature of an autoencoder is the use of a novel prediction method for Parkinson's disease gene prediction using a three-part strategy: extracting features of genes based on network, reducing the dimension using deep neural network in the form of an autoencoder, and predicting Parkinson's disease genes using a machine learning method (SVM) ([16]).

[16] Peng J, Guan J, and Shang X. Predicting Parkinson's Disease Genes Based on Node2vec and Autoencoder. *Front Genet* 2019; 10;226.

Generative adversarial network (GAN). Introduced by Ian Goodfellow in 2014, GANs are deep neural network architectures that consist of two networks that are competing against each other but can generate data from scratch. In addition, according to Yann LeCun, director of Facebook AI, GAN is "the most interesting idea in the last ten years in machine learning." In GANs, two adversarial models (called "generator" and "discriminator") can co-train through back propagation as a form of unsupervised learning (thus giving the computer the capability of "imagination"). There has been many applications of GANs in computer vision and images with training semi-supervised classifi ers and generating higher resolution images from originals with lower resolution.



The deep learning concept is the following **(see Figure):** the **generator**, a neural network that is generating new data instances, is a dyad with another neural network called the **discriminator,** which is assessing the created data instances from the generator for authenticity. In essence, the discriminator acts as a "judge" to force the generator to produce more authentic images so these two neural nets are simultaneously being trained. GANs have been coupled with CNN to create an unsupervised learning **deep convolutional generative adversarial network, or DCGAN**. DCGAN differs from CNN in that it has only the convolutional layers but not the pooling nor the fully connected layers.

Advantages and Disadvantages. GANs are good at training classifiers in a semi-supervised way as it does not require labeled data; it is relatively easy to for this deep learning methodology to **generate new** (artificial but good) **data**. While GANs are good at generating image data, it is not easy for these neural networks to generate text data. In addition, some experts feel that it is not easy to train GANs as these are relatively huge computations. Lastly, "mode collapse" occurs in GANs when the generator produces samples of extremely little variety and is considered a weakness of GANs.

An example in the recent biomedical literature of GANs is the recent work by Guan on using both generative adversarial networks and transfer learning for breast cancer detection by CNN as innovative dual solutions for lack of training images ([17]). In short, the authors applied GANs for image augmentation and transfer learning in CNN for breast cancer detection.

[17] Guan S and Loew M. Using Generative Adversarial Networks and Transfer Learning for Breast Cancer Detection by Convolutional Neural Networks. *Proceedings Medical Imaging 2019: Imaging Informatics for Health care, Research, and Applications* 2019; 109541C.

A **restricted Boltzmann machine (RBM)** is a shallow (two-layer) ANN that is essentially an unsupervised generative deep learning algorithm; the first layer is called the visible or input layer and the other layer is the hidden layer. The “restricted” term is from no two nodes in the same layer have a connection. An RBM can also be considered the building blocks of deep belief networks (DBM) and can be used for classification and dimensionality reduction. Overall, RBM is not used as frequently now as most users have changed to GANs or VAEs (see above).

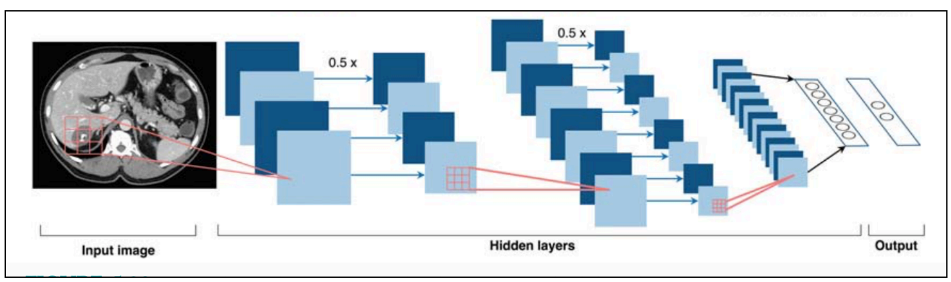
Questions 5.13/Convolutional Neural Network

1. The deep neural network that is inspired by the human visual cortex for image interpretation is:
a. Convolutional neural network
b. Recurrent neural network
c. Variational autoencoder
d. Generative adversarial network
[ ]

2. Convolutional neural network can be applied to medical images in the following ways *except*:
a. Segmentation
b. Classification
c. Detection
d. Prognostication
[ ]

3. Which of the following descriptions of the convolutional neural network is *not* correct?
a. Fully connected layer and classification
b. Convolutional layer and feature extraction
c. Pooling layer and feature aggregation
d. Focusing layer and feature visualization
[ ]

4. The figure at right is a:
a. Support vector machine
b. Convolutional neural network
c. Generative adversarial network
d. Auto encoder
[ ]



5. Which is *true* of deep convolutional neural network (CNN) as compared to machine learning:
a. CNN tends to require more data as compared to machine learning
b. CNN needs human labeling but machine learning does not require this process
c. CNN is more easily explained as compared to machine learning
d. Machine learning usually yields higher accuracy than CNN
[ ]

Answers 5.13/Convolutional Neural Network

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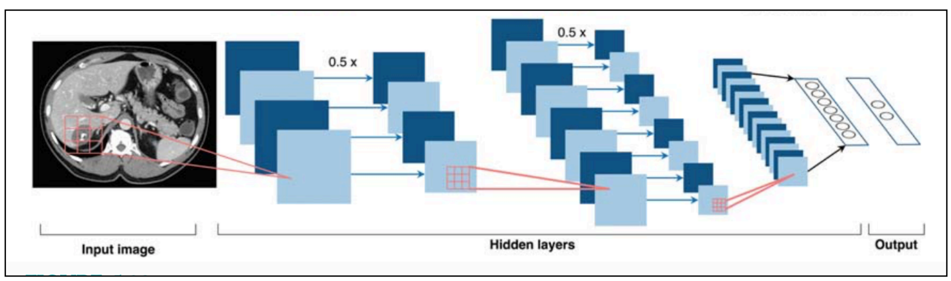

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Module 5.13/Convolutional Neural Network

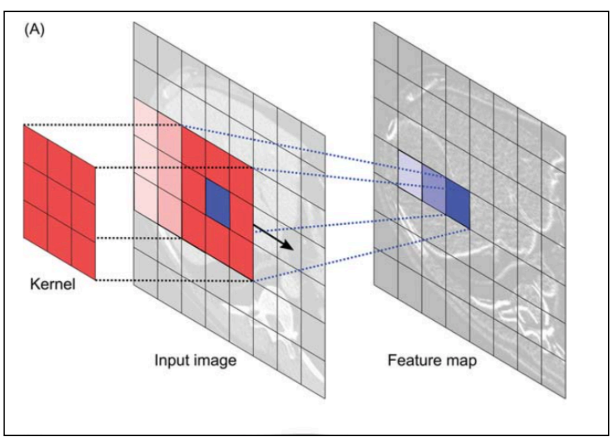
Convolutional neural network (CNN). This is a very popular deep neural network that consists of the characteristic three-dimensional convolutional layers or blocks inspired by cognitive neuroscience and the visual cortex functions. The biological construct of vision as it relates to computer vision is reviewed in a comprehensive fashion by Cox; this review also discussed nuances such as moving images and other elements. CNN is particularly good for computer vision with hierarchical or spatial data (usually images or characters) as well as natural language processing.

CNN can be applied to medical images in three ways: 1) **Classification**- determination of a category (absence/presence of malignancy or type of malignancy); 2) **Segmentation**- identification of pixels/voxels that constitute an area of interest (such as an organ or bleed); and 3) **Detection**- prediction of an area of interest.

Note. **Computer vision** is usually considered a branch of AI and includes image processing, object recognition, optical mark recognition, and other areas but will not be separately covered as the discussion below pertains to computer vision as it relates to medicine.

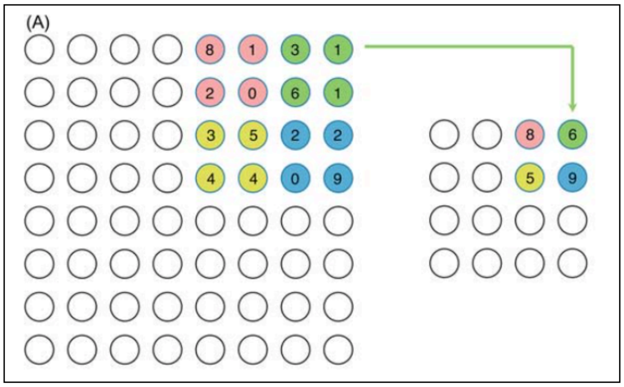
First, it is important to introduce the concept that the computer "sees" a matrix of numbers representing pixel brightness (rather than the shades of gray that the human eye sees)**(see Figure)**.

The building blocks of the **CNN architecture** consists of convolution layers, pooling layers, and fully connected layers as well as rectified linear unit (ReLU) **(see Figure)**. These layers are constructed to enable CNN to learn spatial hierarchies of features and are discussed below:



1) A **convolutional layer (**for **feature map extraction)** involves a convolutional "filter" or "kernel" that is placed over the source pixel or input image. This convolutional filter (or kernel) transforms the source pixel or input image into a new pixel value and it becomes the destination pixel or output feature map. In other words, this layer integrates and transforms the collection of pixels in the images into significant feature characteristics on the output feature map. Essentially, convolution signifies "filtering" and the filter matrix is applied over the image matrix to produce a "convolved" feature map or matrix. In short, a third function (feature map) is derived from two functions (input data and convolutional kernel). A **stride** is the number of pixels to shift or slide over the input matrix (a stride of one signifies a movement of one pixel). There cannot be a stride of 0.

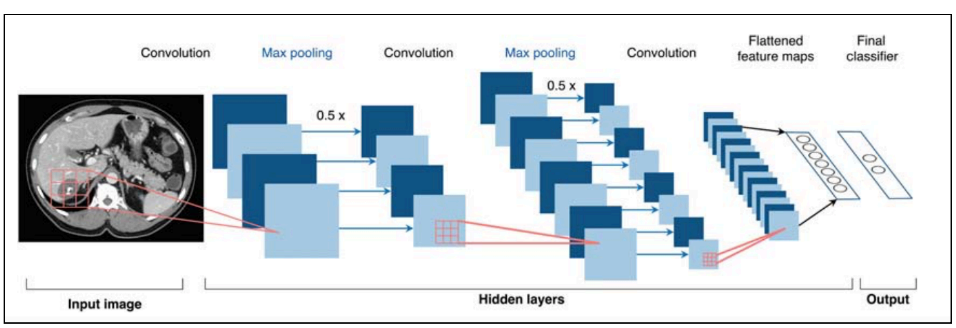
The **rectified linear unit (ReLU)** is an **activation function,** a key component of CNN that ensures a nonlinearity from linear operations; it improves CNN by speeding up its training. The ReLU is unlike the other possible functions (sigmoidal or hyperbolic tangent) in that it is perfectly linear for positive inputs while blocking negative inputs and therefore better suited for CNN.

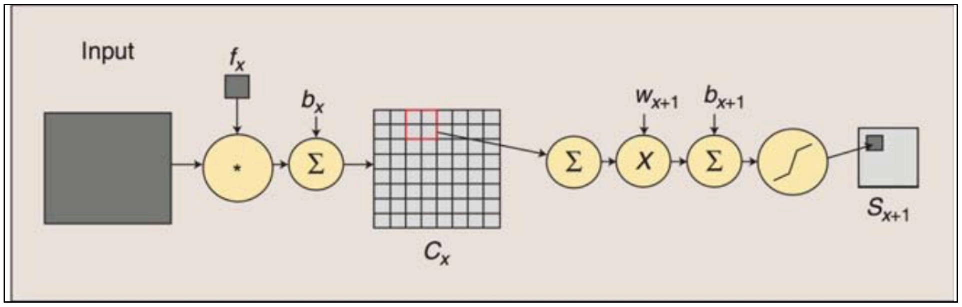


2) A **pooling layer (**for **feature aggregation)** usually follows the convolutional layer described above and receives the output of the convolutional layer as its input, but reduces the number of parameters (in order to reduce overfitting). This process also enables faster computation as the number of input parameters is reduced. Therefore, this "pooling" (also called "downsampling") process reduces the dimensions while retaining important information. A process of **max pooling** (usually preferred over min, average, or sum pooling)**(see Figure)** condenses the more essential information from previous layers into a smaller **tensor** (a tensor is a term for a multidimensional array more complicated than either a simple vector or a higher dimensional matrix). The pooling layer increases the accuracy as well as velocity of training of the model. Overall, the resolution necessarily decreases as the pooling layers progress due to reduction of dimensions but the information of the images (per space) become more and more rich and relevant.

Overall, the first layers of the CNN are more involved with basic image features (such as edges or shapes) while subsequent layers are more focused on abstract features. It is these later layers that contain the robustness as well as the lack of full explainability of deep learning. In other words, CNN features are more generic in the earlier layers and more complex in the later layers.

3) The **fully connected layer (for classification)** maps the features into the final output. A process called **upsampling** in the latter layers increases the resolution of the CNN by reducing the storage and transmission requirements for the images. The last output of the CNN is a topographic display of areas of interest via a process called **flattening.** This is converting the output of the convolutional part of the CNN to a feature vector so that an ANN classifier can be applied. A **softmax activation** is applied to the very last layer (instead of ReLU) so that the output can be converted into a probability distribution **(see Figure)**.





Convolution and Pooling (Downsampling or Subsampling). The convolution process (linear) started with convolving (transforming) an input (image at the early stages of CNN or feature map at the later stages of CNN) with a trainable filter (*fx*) or kernel and subsequently with a trainable bias (*bx*) to produce the convolution layer *Cx*. The subsampling process (nonlinear) then consists of summing a group of pixels (four in this case, outlined in red) and weighting by scalar w_{x+1} (with trainable bias b_{x+1}). Finally, this is passed through a sigmoid function to produce a smaller feature map S_{x+1}. In essence, these two processes convert an input (either an image or a feature map) into something that is reduced in size but retained the information.

Advantages and Disadvantages. CNN is different from conventional machine learning in that CNN requires large amounts of data for model training; CNN, on the other hand, does not require manual (human-derived) **feature extraction** nor image segmentation. While CNN is particularly good at **image recognition** and **classification**, it has difficulty if images have alterations (like rotation or any orientation that is different from previously presented). Other issues with CNN and medical images are its limitation with small datasets as well as its problem with overfitting. Finally, deep learning is difficult to explain and its lack of transparency is a serious issue for CNN adoption.

There are numerous good to excellent review papers on deep learning and medical images (see under Radiology and Cardiology) for in depth discussions with helpful diagrams. An example in the recent biomedical literature of a CNN is the work from Stanford's group on interpretation of ECG across a wide variety of diagnostic classes in 12 rhythm classes using single-lead ECGs from over 50,000 patients with an AUC of the ROC at 0.97 and an average F1 score (harmonic mean of the positive predictive value and sensitivity) of 0.84 ([18]).

[18] Hannun AY, Rajpurkar P, Haghpanahi M et al. Cardiologist-Level Arrhythmia Detection and Classification in Ambulatory Electrocardiograms Using a Deep Neural Network. *Nature Medicine* 2019; 25:65-69.

Questions 5.14/Recurrent Neural Network

1. Recurrent neural network (RNN) is good for all of the following *except*:
a. Musical passages
b. Speech patterns
c. Medical images
d. Continuous physiological data
[ ]

2. Which of the following is best suited for sequential or temporal data?
a. Recurrent neural network
b. Convolutional neural network
c. Support vector machine
d. Auto encoder
[ ]

3. Recurrent neural network is capable of having an active data memory known as:
a. Long short term memory (LSTM)
b. Convolutional layer
c. Pooling layer
d. Fully connected layer
[ ]

4. The following are qualities of a recurrent neural network *except*:
a. Store information
b. Learn sequential data
c. Image recognition
d. Can form hybrid with CNN
[ ]

5. Which of the following can be a good use case for recurrent neural network *except*:
a. ICU blood pressure data
b. Static medical images
c. Heart rate data
d. Notes and language processing
[ ]

Answers 5.14/Recurrent Neural Network

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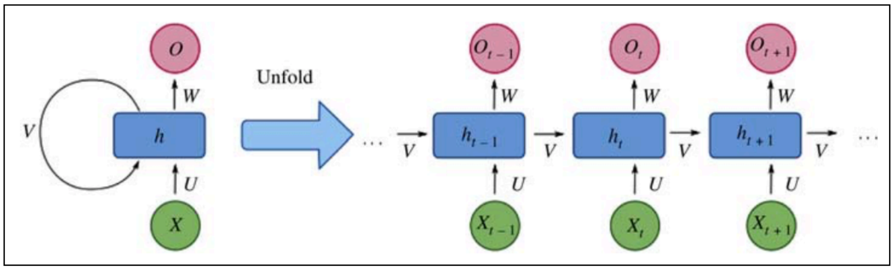
Module 5.14/Recurrent Neural Network



Recurrent neural network (RNN). This is another type of deep neural network that consists of a **feedback loop** (next state depends on the prior state)**(see Figure)**. This architecture shows a feedback mechanism at recurrent layers. Note that the maroon arrows demonstrate a feedback into the nodes of the hidden layer and its therefore the recurrent layer of the RNN. In short, each neuron has an embedded memory of an element. RNN, therefore, is capable of having an active data memory known as **long short-term memory,** or **LSTM**.
A **gated recurrent unit,** or GRU, is a variation of LSTM that is structurally similar to LSTM but simpler (2 "gates" vs 3) and does not possess internal memory. RNN is therefore able to recall a memory as there are longer term dependencies (compared to CNN) so it is good for **temporal** or **sequential data** (financial transaction data, musical passages, or speech patterns as well as serial biometric measurements such as blood pressure and heart rate).

Even a brief discussion of RNN should include two entities: hidden Markov model and neural Turing machine. **Hidden Markov model (HMM)** is more of a stochastic process based on a Markov chain and makes the Markovian assumption (future state is only dependent on the present state, but not before; therefore "memoryless"). HMM, like RNN, deals with sequential data but is a simpler and linear model whereas RNN is a more complex (and adaptive) and non-linear. In addition, RNNs do not have Markovian property so they can accommodate long-distant dependencies. **Neural Turing machine (NTM)** is an RNN that extends the neural network concept and couple this with logical flow and external (infinite) memory sources. The NTM has four components: the controller or neural network; the memory; and the read and write heads.

Advantages and Disadvantages. RNN therefore has two advantages: it can **store information** by using the feedback connections and it can **learn sequential data.** This type of deep learning is used for repeating the same task for **sequential information** that are dependent of each other (like time series in the ICU setting or stock market analyses as well as language generation or translation). The disadvantages of RNN include its slow speed for recurrent computation and often it is difficult to access information in the past.

An example in the recent biomedical literature is the use of the independently RNN to classify seizures (against non-seizures) by EEG with a new approach to expand the time scales with superior results for diagnosis ([19]). Another illustrative example is the RNN work on EHR that showed

[19] Yao X, Cheng Q, and Zhang GQ. A Novel Independent RNN Approach to Classification of Seizures Against Non-Seizures. *arXiv*:1903.09326v1.

accurate predictive models can be built directly from EHR data with the FHIR standard for a variety of clinical scenarios ([20]).

In short, CNN is good for spatial data while RNN is designed for sequential or temporal data. There is, however, a **hybrid "CNN-RNN" model** (also called recurrent CNN, or RCNN but not to be confused with regional CNN, R-CNN) that has some potential in biomedical data, such as **multi-label image classification** and **serial complex biomedical data.**

An example in the recent biomedical literature of RCNN is the ingestible wireless capsule endoscopy technology with use of RCNN for a reliable real-time monocular visual odometer method for endoscopic capsule robot operations ([21]). The novel RCNN architecture models sequential dependence and complex motion dynamics across endoscopic video frames.

[20] Rajkomar A, Oren E, Chen K et al. Scalable and Accurate Deep Learning for Electronic Health Records. *npj Digital Medicine* 2018; 1, Article number :18.

[21] Turan M, Almalioglu Y, Araujo H et al. Deep EndoVO: A Recurrent Convolutional Neural Network (RCNN) based Visual Odometry Approach for Endoscopic Capsule Robots. *Neurocomputing* 2018; 275:1861-1870.

Questions 5.15/Assessment of Model Performance

1. The evaluation of a model with a set of data from the original data set that the model has not seen before is called the:
a. Test set
b. Training set
c. Validation set
d. Final set
[ ]

2. When the original dataset is divided into *k* equal sized subsets called folds so that *k*-1 subsets are used as the training dataset, this methodology is called:
a. Cross validation
b. Holdout method
c. Hyperparameter optimization
d. Hyperparameter tuning
[ ]

3. Examples of a parameter in a model include all of the following *except*:
a. Weights in neural networks
b. Coefficients in linear or logistic regression
c. Support vectors in support vector machines
d. The *k* in *k*-nearest neighbor
[ ]

4. Examples of a hyperparameter in a model include all of the following *except*:
a. Learning rate for training a neural network
b. The *k* in *k*-nearest neighbor
c. Depth of trees in decision tree
d. The coefficients in linear or logistic regression
[ ]

5. The difference between parameters and hyper parameters of a model is:
a. Hyperparameters can be directly learned from the regular training process
b. Hyperparameters are not fixed prior to the training process and these stay dynamic
c. Hyperparameters define higher level concepts such as complexity or capacity to learn
d. An example of a hyperparameter is coefficient in a linear or logistic regression
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Answers 5.15/Assessment of Model Performance

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Module 5.15/Assessment of Model Performance

Assessment Methods. There are several methodologies to assess the prediction model performance but it is good to have the understanding that a perfect score (classification problem with 100% accuracy and regression problem with 0% error) is simply an unrealistic expectation. There will be inevitable error from data issues (inaccurate or incomplete data) or algorithm limitations. A good overall strategy prior to evaluation of the prediction model is to have a good **baseline prediction model** (good predictive models to start with include random forest or gradient boosting, see above under ensemble learning) or simply try all the prediction models that you are familiar with (and then select the best one or few simple ones).

The evaluation of a model with a test set of data (that the model has not seen before) can follow two methods: cross-validation or holdout method. In **cross-validation,** the original dataset is divided into *k* equal sized subsets called **folds,** so that *k*-1 subsets are used as the training dataset. In the **holdout method**, the master dataset is divided into training set, validation set (not always used), and test set (see machine learning workflow section).

Evaluation of Regression Models. For regression models, the performance of the model can be assessed with the **coefficient of determination** (also called R^2 with range 0-1, with 1 being best), which may need to be adjusted for additional independent variables which can increase value of R^2 (without increase in accuracy). In addition, **mean absolute error** (MAE) as well as **root mean square error (**RMSE) are also used: in the former, MAE is the mean of the absolute differences between predictions and actual values and in the latter, RMSE measures the average magnitude of the error by taking the square root of the average of squared differences between again, the prediction and the actual values.

Model **parameters** are configuration variables that are "internal" to the model and are properties that will learn on their own during the training by the model (not set by humans). Examples of these parameters include: weights and biases in neural networks, coefficients in linear or logistic regression, split points in decision tree, and support vectors in support vector machines. A model **hyperparameter,** on the other hand, is a parameter that is prior belief so these are initialized before training a model and are "external" to the model. Examples of these hyperparameters include: *k* in *k*-nearest neighbor, kernel in support vector machine, depth of tree in decision tree, shrinkage factor in ridge regression, and learning rate and number of hidden layers for neural network. In essence, hyperparameters are settings of a model that are adjusted to optimize performance of that model. Finally, the process of an automatic optimization of hyperparameters is termed **hyperparameter optimization** or **tuning**; two examples are grid search and random search.

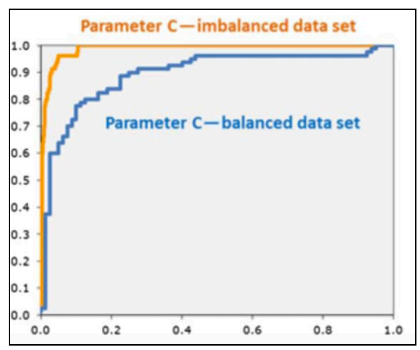
	Parameter	Hyperparameter
Model	Internal to the model	External to the model
Learning	During training	Set before training
Saving of Value	Saved with the trained model	Not saved with the trained model
Dataset Dependency	Dependent	Independent
Examples	Split points in decision trees Coefficients in linear or logistic regression Support vectors in SVM Weights and biases in neural network	Depth of trees in decision trees *k*(number) in *k*-nearest neighbor Learning rate, number of nodes, and layers in neural network Filter size and stride in CNN
Musical Analogy	Akin to playing the violin with data being the notes	Akin to tuning the violin prior to playing the violin

Questions 5.16/Evaluation of Classification Models

1. Which of the following is a *false* statement about sensitivity?
a. It is also called recall
b. It is true positives/(true positives + false positives)
c. It is used in the F_1-score calculation
d. It needs to be high for a cancer screening test
[ ]

2. With a data imbalance situation, the following are all helpful in determining the performance of the model *except*:
a. F_1-score
b. Precision-recall curve
c. Accuracy
d. Precision
[ ]

3. On the right is a curve showing the balanced and imbalanced data set in what kind of plot:
a. Precision-recall
b. True positive rate vs true negative rate
c. Sensitivity vs 1-Specificity
d. Sensitivity vs Specificity
[ ]



4. In the discussion of the imbalanced data set classification problem, which population is usually the one that is overabundant:
a. True positives
b. True negatives
c. False positives
d. False negatives
[ ]

5. The following pairs are correctly matched except:
a. Sensitivity-Recall
b. Precision-Positive predictive value
c. Error rate-misclassification rate
d. Specificity-Negative predictive value
[ ]

Answers 5.16/Evaluation of Classification Models

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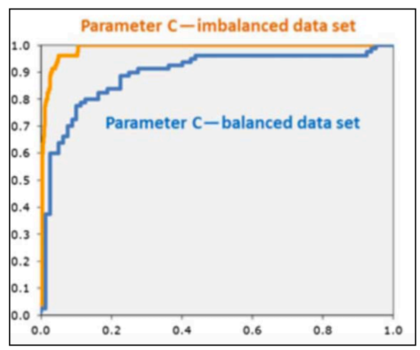
d. Sensitivity vs Specificity
[c]



4. In the discussion of the imbalanced data set classification problem, which population is usually the one that is overabundant:
a. True positives
b. True negatives
c. False positives
d. False negatives
[b]

5. The following pairs are correctly matched except:
a. Sensitivity-Recall
b. Precision-Positive predictive value
c. Error rate-misclassification rate
d. Specificity-Negative predictive value
[d]

Module 5.16/Evaluation of Classification Models

For a binary classification model, the performance is measured by the confusion matrix, the area under the curve (AUC) in a receiver operating characteristic curve (ROC), and AUC in a precision-recall curve (PRC).

Confusion matrix. The **confusion matrix** (aptly named perhaps according to some readers) is a 2x2 table (see below) of predicted vs actual values for the model (most clinicians are familiar with this table from epidemiology and biostatistics)**(see Table)**:

Table. Confusion Matrix

	Actual Positive (for Disease)	**Actual Negative (for Disease)**	
Predicted Positive (based on Test)	True positive	False positive (Type 1 error)	*Total predicted positives*
Predicted Negative (based on Test)	False negative (Type 2 error)	True negative	*Total predicted negatives*
	Total actual positives	*Total actual negatives*	***Total population***

Accuracy = $\dfrac{\text{True positive + true negative}}{\text{Total population}}$

Precision = $\dfrac{\text{True positive}}{\text{True positive + False positive}}$
(Predicted positive)

(Precision also called **Positive Predictive Value**)

Specificity = $\dfrac{\text{True negative}}{\text{False positive + True negative}}$
(Actual negative)

Sensitivity = $\dfrac{\text{True positive}}{\text{True positive + False negative}}$
(Actual positive)

(Sensitivity also called **Recall**)

Error Rate = $\dfrac{\text{False positive + False negative}}{\text{Total population}}$

(Error Rate also called **Misclassification rate**)

F_1 Score = $\dfrac{\text{2 x (Recall * Precision)}}{\text{Recall + Precision}}$

The **F_1-score**, also called **F-measure** or balanced **F-score**, is probably the least familiar to most readers; it is the harmonic mean between precision and recall and can be used to assess binary or multi-class classification models for accuracy. The F_1-score conveniently ranges from 0 to 1 (with higher scores being higher in accuracy). Two other related F measures place more emphasis on either recall or precision and include: 1) **F_2-score** or **measure**, which places more emphasis on recall (high recall model) and therefore more focus on false negatives (false negatives are not acceptable but false positives are acceptable, as in some medical situations) and 2) **$F_{0.5}$-score** or **measure,** which places more emphasis on precision (high precision model) and therefore more focus on false positives (false positives are not acceptable but false negatives are acceptable, as in spam situations). Lastly, the **G-measure** is the geometric mean of recall and precision (as opposed to F-measure being the harmonic mean).

Limitations. In the above confusion matrix, both **accuracy** and **error rate** (or misclassification rate) can appear better than the true underlying performance of the model if the incidence of the disease is very low and therefore the true negatives of the entire population is relatively high (see below for illustrative example). In addition, **recall** (or sensitivity, quantity, completeness) may need to be higher or lower depending on the disease: for instance, one certainly would prefer to have recall be as high as possible for cancer (vs a benign rash) since recall reflects people that were missed in the screening process for cancer. Concomitantly, one would also like **precision** (quality or exactness) to be appropriate for certain disease states: again for cancer, precision reflects that a person who is tested positive actually has the disease so a false positive could be catastrophic for a diagnosis of a brain tumor (but much less significance for mild myopia, for instance). In other words, a disease in which there is no significant penalty for a false positive diagnosis would have less demand on a higher precision. Lastly, the strength of the **F_1 score** is perhaps also its potential weakness: precision and recall are balanced but sometimes this is less than ideal. Depending on the classification prediction model, the F_1 score may need to be weighted so that either precision or recall are given relatively more importance (see above).

We can calculate F_1 for an imaginary test for imaging of cancer (which is a popular classification methodology for CNN) for a cancer that has a low incidence **(see Table)**:

Table 12. Confusion Matrix for a Low-Incidence Disease

	Actual Positive for Disease	Actual Negative for Disease	Low incidence for Disease (4/1000)
Predicted Positive based on Test	3	1	*4*
Predicted Negative based on Test	1	995	*996*
	4	*996*	***1000***

$$\textbf{Accuracy} = \frac{\text{True positive + true negative}}{\text{Total population}} = \frac{3 + 995}{1000} = 0.998$$

$$\textbf{Precision} = \frac{\text{True positive}}{\text{True positive + False positive}} = \frac{3}{3+1} = 0.75$$

$$\textbf{Specificity} = \frac{\text{True negative}}{\text{False positive + True negative}} = \frac{995}{1 + 995} = 0.999$$

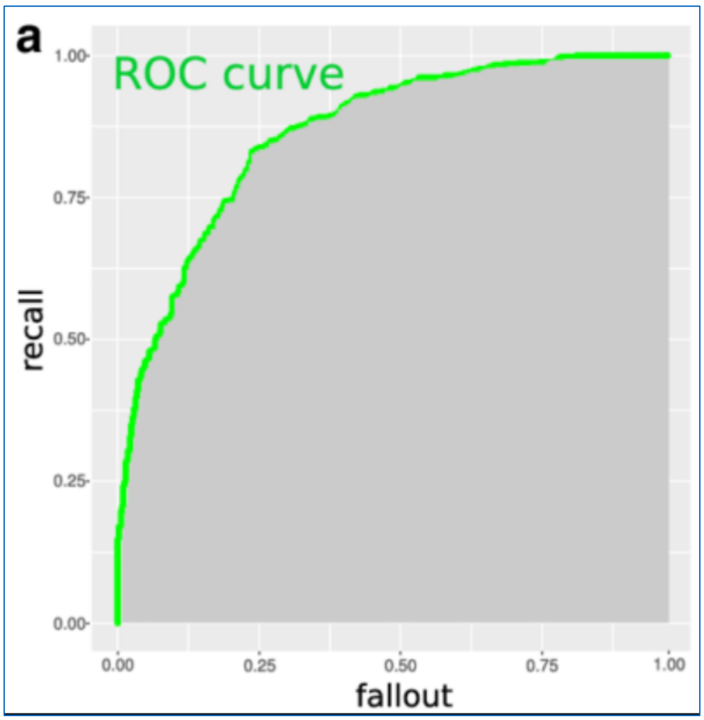
$$\textbf{Sensitivity} = \frac{\text{True positive}}{\text{True positive + False negative}} = \frac{3}{3 + 1} = 0.75$$

$$\textbf{Error Rate} = \frac{\text{False positive + False negative}}{\text{Total population}} = \frac{2}{1000} = 0.002$$

$$\mathbf{F_1}\textbf{ Score} = \frac{2 \text{ x (Recall * Precision)}}{\text{Recall + Precision}} = \frac{2 \text{ x } 0.75 \text{ x } 0.75}{0.75 + 0.75} = 0.75$$

So one can surmise from this specific confusion matrix example that it is relatively easy to have a higher accuracy as well as a lower error or misclassification rate (real and perceived) when the incidence of disease is low because the true negatives is a relatively high number in the calculations for both accuracy and error rate. In short, accuracy and error rate are not good indicators of performance especially when the incidence of disease is very low (like for cancer) because the true negatives, a majority of the cases usually in low incidence disease states, is a relatively high number to make accuracy and error rate look more favorable. This is a good example of how precision and the F_1 score will be more realistic reflection of the classification model prediction performance, especially when there is an imbalance in the classes as in the case of true negatives being a very large number. When the true negatives is a large number, one can also consider the **precision recall curve** (see below).

Receiver operating characteristic (ROC). The most familiar curve and metric for assessing classification models is the **receiver operating characteristic (ROC)** and its accompanying **area under the curve (AUC)(see Figure).** Similar to the aforementioned PR curve, one can compare different predictors by estimating their area under the curve (AUC) with a major difference: in PR curves, the upper right is near perfection with both precision and recall close to 1 but in ROC, it is the upper left part of the graph that is considered better (since the x axis is 1 - specificity to derive the false positive rate). The AUC measures the area under the curve in the ROC plot and is often used to measure the performance of a classification model as it reflects both true positive rate or sensitivity (y axis) and false positive rate or 1-specificity (x axis). True positive rate is also called recall, and false positive rate reflects data that have been misclassified.



ROC and AUC. The ROC plots sensitivity (y axis) against the false positive rate (1-specificity). A perfect model will be close to the upper left corner.

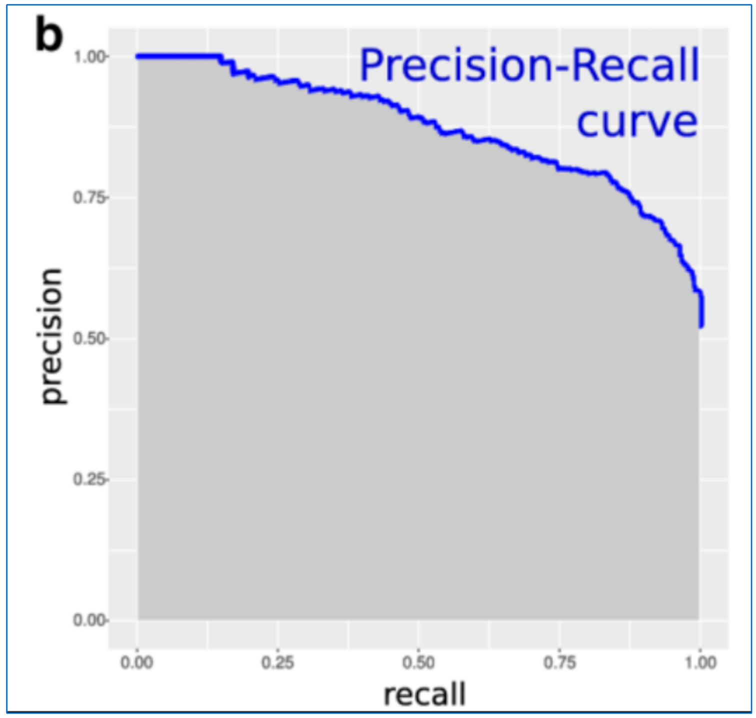
The ROC is, then, a plot of true and false positive rates at various classification threshold so that these thresholds will provide a different pair of true positive and false positive rates. An AUC of 0.5 is essentially a random classifier whereas an AUC of 1 is perfect (conveniently again, like the R^2 coefficient for regression models and F_1 score for classification models, 1 is a perfect score). Usually an AUC of 0.80 or higher is considered good and 0.90 or higher is considered excellent. The higher the AUC, the better the classifier with a few caveats.

A **Gini coefficient** is the ratio between area between the ROC curve and the diagonal line and the area above the triangle:

$$\text{Gini} = 2 \times \text{AUC} - 1 \text{ (where index above 0.60 is considered a good model)}$$

Limitations. Just as accuracy and error rate are vulnerable to a potentially large true negative number, the ROC and AUC are as well since the false positive rate is (1 - specificity), which has true negatives in the denominator (false positives / (false positives + true negatives)). A large true negatives number will lower the false positive rate (x axis), which will push the performance towards perfect classification, or the upper left portion of the ROC curve. In other words, an imbalanced dataset will falsely increase the performance of the classifier when in fact there is no change in the performance. In addition, the ROC does not accommodate changes in prevalence. This is very important as there are rare or unusual diseases in medicine and this does affect the classifier as the false positives will have high level of impact.

Precision recall curve (PRC). As the name implies, this is a curve plotting precision and recall for various threshold values (in a similar fashion to ROC) with both precision and recall values plotted from 0 to 1. Therefore, the upper right part of the graph is precision-recall "nirvana": both values are near 1 **(see Figure)**. The previous discussion on the impact of true negatives on interpretation of metrics and curves is signifi cant in that the much less familiar PRC is more appropriate as an assessment tool when there is an imbalance in datasets; one study even showed that PRC was superior to ROC and even other curves such as concentrated ROC (CROC) and cost curve (CC) in the presence of an imbalanced dataset ([22]). In other words, "stacking" a lot of people who are true negatives for disease (no disease and no positive test) will inflate the ROC curve favorably but without true improvement in sensitivity nor positive predictive value ([23]). This is called the **imbalanced classification problem.**



PRC and AUC. The PRC plots precision (or positive predictive value) on the y axis against recall (or sensitivity) on the x axis. PRC is also shown for two different data sets (for an imagined parameter C). One is balanced (in blue) and the other one is imbalanced (in orange). A perfect model will be close to the upper right corner. In this case, the AUC of the imbalanced data set appears to be about the same as the one for the balanced data set.

Limitations. The precision recall curve is more appropriate for situations in which there is an imbalanced dataset (usually due to large true negatives) but the area under a PRC takes the arithmetic mean of precision values so it is more difficult (vs ROC) to interpret or visualize. In addition, the RPC does not take into account that precision and recall may not have the same significance depending on the situation (but it is considered to be equal in significance).

[22] Saito T and Rehmsmeier M. The Precision-Recall Plot is More Informative than the ROC Plot When Evaluating Binary Classifiers on Imbalanced Datasets. *PLoS ONE* 10(3): e0118432.

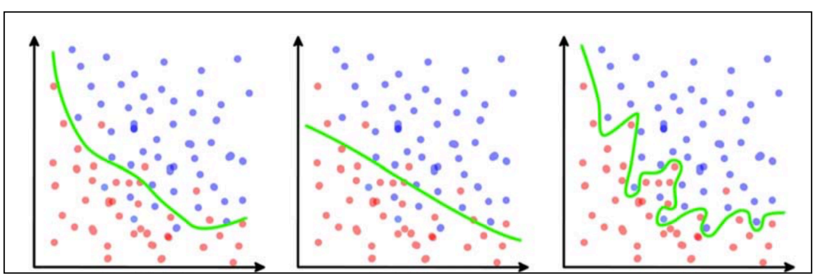
[23] Ekelund S. Precision-Recall Curves: What Are They and How Are They Used? March, 2017. www.acutecaretesting.org.

Questions 5.17/ Fundamental Issues in Machine and Deep Learning

1. Which of the following is most likely to be the *least* explainable?
a. Decision trees
b. Deep learning
c. Support vector machines
d. Bayesian belief nets
[ ]

2. Which of the following is most likely to be the *most* explainable?
a. Decision trees
b. Deep learning
c. Support vector machines
d. Bayesian belief nets
[ ]

3. What is true about a model that demonstrates overfitting:
a. High variance and high bias
b. High variance but low bias
c. Low variance but high bias
d. Low variance and low bias
[ ]



4. The graphs to the left shows:
a. Fit-Underfitting-Overfitting
b. Underfitting-Fit-Overfitting
c. Overfitting-Fit-Underfitting
d. Fit-Overfitting-Underfitting
[ ]

5. To overcome overfitting, data science strategies include all of the following *except*:
a. Use more training data
b. Reduce number of features
c. Use regularization
d. Increase complexity of features
[ ]

Answers 5.17/ Fundamental Issues in Machine and Deep Learning

1. Which of the following is most likely to be the *least* explainable?
a. Decision trees
b. Deep learning
c. Support vector machines
d. Bayesian belief nets
[b]

2. Which of the following is most likely to be the *most* explainable?
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b. Deep learning
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[a]

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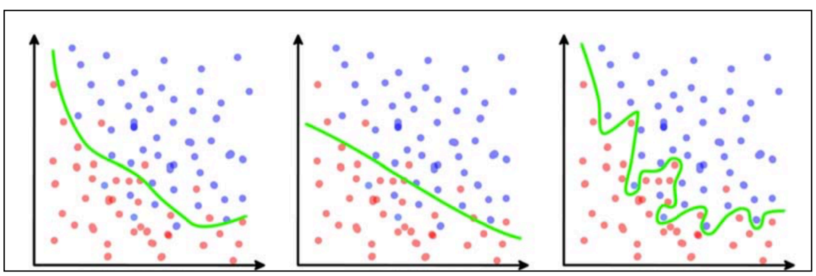

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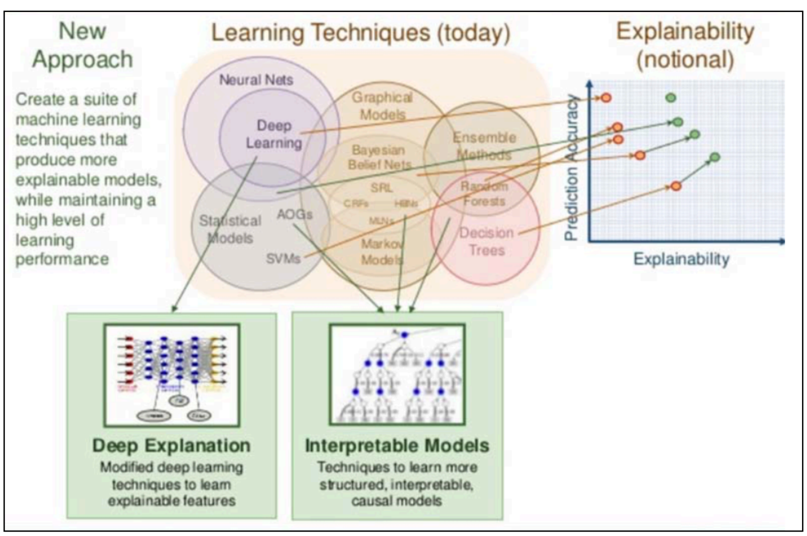
Module 5.17/ Fundamental Issues in Machine and Deep Learning

Interpretability and **Explainability.** A common issue with machine learning resides in its **"black box"** characteristic: for those who are not data scientists or those who have not had education in this domain, it is difficult to understand the many learning techniques that exist today, especially sophisticated machine learning and deep learning **(see Figure)**([24]). While there is a difference between **interpretability** and **explainability,** AI methods need at least interpretability for it to be widely adopted by clinicians. Interpretability is the capability to observe a cause-and-effect while explainability is the understanding of the inner workings of a system or technology. For example, a cardiologist can program a pacemaker and see the consequences of an action (programming the pacemaker and see pacing at the rate that was set), but not necessarily fully understand the engineering aspects of the pacemaker itself (it is helpful to understand the latter but arguably less essential).

Some of the higher prediction accuracy machine learning methodologies (deep learning, random forest, support vector machines, etc) have the least explainability whereas others (Bayesian belief nets, decision trees) have more explainability (but relatively lower prediction accuracy). There is an ongoing effort to elevate explainability in the form of "**explainable AI** or **xAI**") while maintaining (or even increasing) prediction accuracy with a new suite of techniques. The overall strategy to increase explainability is to raise awareness and education of machine learning and other techniques is to generalize algorithms, understand features, and utilize available support tools for explanations like the **Local Interpretable Model-Agnostic Explanations (LIME).** Another methodology is **Shapley Additive exPlanations (SHAP)** that attempts to explain individual predictions and to increase model transparency; a Shapley or SHAP "value" can elucidate the output of a machine learning model.



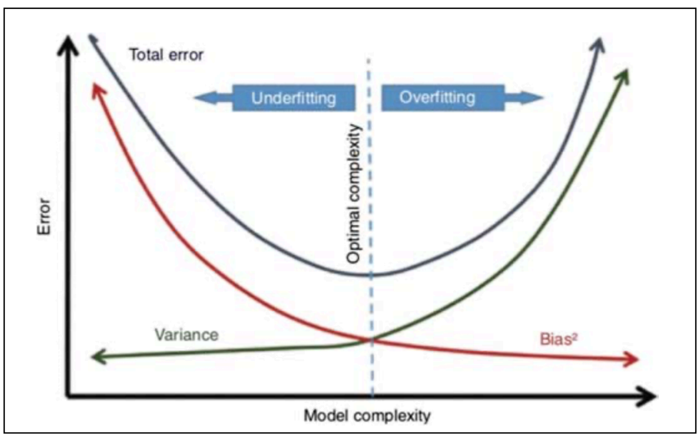
Machine and Deep Learning and Explainability. The figure shows that the learning techniques such as deep learning has relatively higher prediction accuracy (y axis) but also relatively lower explainability. On the other hand, learning techniques such as decision trees are more interpretable models and more easily understood and explained. There is a strategy to increase the explainability for all of these techniques (orange circles with arrow to green circles).

[24] Gunning, David. Talk at DARPA. August 11, 2016.

(AOG- stochastic and-or-graphs; CRF- conditional random fields; HBN- hierarchical Bayesian networks; MLN- Markov logic network; SRL- statistical relational learning)

Bias and Variance Trade-Off. Prediction error can be grouped into two main types. **Bias** is the difference between the expected prediction of the model and the correct value that the model is attempting to predict. Bias is also the inability of a machine learning methodology to capture the true relationship (such as linear regression not reflecting the relationship of data that would be better fitted in a curve). **Variance**, on the other hand, is the difference in the fits between datasets (high complexity models will therefore be more likely to have higher variance). Overall, bias is decreased and variance is increased with increase in model complexity.

The ideal model will have both low bias as well as low variance, but it is usually a trade-off between these two parameters. Bias and variance are manifested in models that demonstrate underfitting and overfitting: the former is a result of high bias and the latter is a result of high variance; therefore, the best balance, fitting, is achieved when there is low bias and low variance **(see Figure)**. Three strategies to have a good bias-variance balance include: regularization, bagging, and boosting.



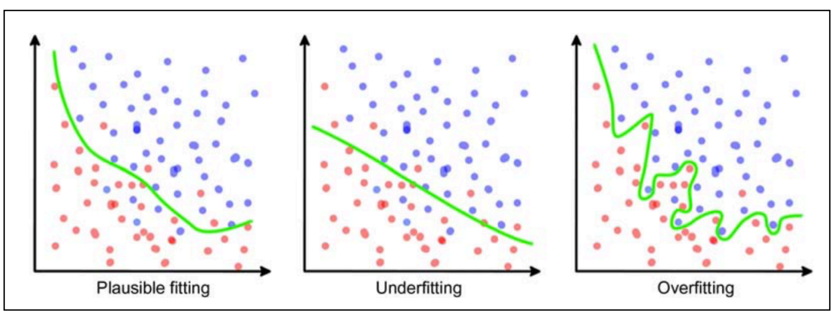
Bias and Variance. In the figure, the y axis is degree of error and the x axis, complexity of the prediction model. As the complexity of the model increases, bias (line in red) decreases while variance (line in green) increases since errors decrease with complexity of the model in bias and the opposite is observed with variance (see text for explanation). The optimal region is a compromise between these two forces and is where bias and variance are both jointly low (not lowest for each)(see optimal complexity). In underfitting, the bias is high but the variance is low and in overfitting, the variance is high but the bias is low.

Model	Bias	Variance	
Ideal	Low	Low	*Ideal model*
Underfitting	High	Low	*Model oversimplifies*
Overfitting	Low	High	*Model cannot generalize*

Fitting. Underfitting occurs when the model is too simplistic: it is poorly trained on sample data (such as a linear model) or when the feature engineering is suboptimal and/or inadequate. The solution will involve a more complex model and a better feature engineering strategy. **Overfitting** occurs when the model is too complex: the results are too tailored to the training data (excessive training or adaptation) so that the model is overly complex for the data (opposite of above situation with underfitting)**(see Figure)**. In other words, the model will not be able to analyze new test data well (does not generalize to other data). This can be the result of a situation in which there is an excessive number of features but not enough samples. Overfitting can also occur with small studies that have concomitantly small number of attributes so the choice of attributes is critical for ideal machine learning.

To overcome overfitting, data science strategies include using more training data or reduce number and complexity of features, pruning, perform cross-validation sampling, and use regularization. **Regularization** is a technique used in machine and deep learning to modulate the model complexity via penalty measures so that overfitting is minimized and that the model retains its capability to predict.

Perhaps a way of thinking about under- and over-fitting is to draw an analogy with clothes: in underfitting, one has a comfortable and loosely fitted T-shirt (high bias as it is not a prefect fit but low variance as most people can fit into this T-shirt) and in overfitting, one has a neatly tailored shirt that is tight-fitting (high variance as it is not a good fit for most people but low bias in that it is a good fit for a few).



Underfitting and Overfitting. The illustrations show plausible fitting first on the left. Underfitting- the separation is too simple and too many samples are on the other (wrong) side so therefore "misclassified". Overfitting- the classifier correctly identifies all the samples but is overly complex and therefore has a high variance.

Curse of Dimensionality. Machine learning often deals with large dimensional space. The **curse of dimensionality** occurs when there is such a large number of features so that the features space is excessively large so that there are not enough samples to fill this space. In general, as the features increase, the amount of data needed to generalize accurately grows exponentially. As the number of features (called dimensionality) increases, the classifier's performance increases until the optimal number of features is reached; this is called the **Hughes phenomenon**. Overall, the ideal number of features depend on the classifier involved and the amount of training data available. Beyond this optimal number of features, additional number of features may not have a positive impact on the performance of the model (even though the sparsity of the observations may make it easier for these to be classified). Overfitting will become an issue with more added features.

There are a few strategies to reduce dimensionality (and thus reducing the curse). One popular methodology involves the **principal component analysis** that was described in detail under unsupervised learning as a method for reducing dimensionality. Other possible methodologies include **locally linear embeddings (LLE)** and **linear discriminant analysis (LDA).** In addition, another strategy involved using domain expertise as a means for more optimal feature engineering. Lastly, there is the obvious strategy of increasing the data available but this last strategy is very limited.

Correlation vs Causation. A correlation measures the relationship between any two variables (see linear regression). A common misconception is that correlation implies that there is causation; events that are correlated, therefore, do not signify that one caused the other. The common dictum is "correlation does not imply causation". This understanding, however, may lead to another misconception: you cannot infer causality from data science.
Causation states that any change in the value of one variable will cause or lead to a change in the value of another variable (cause and effect: a known, observable chain of events). **Reichenbach's common cause principle** states that a correlation between events A and B indicates that 1) A causes B, or 2) B causes A, or 3) A and B have a common (Reichenbachian) cause that induced the correlation. Since causes always occur before their effects, it is therefore assumed that common causes always occur before the correlated events. **Causal networks** represent interdependencies of events.

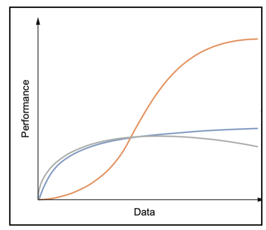
Questions 5.18/Machine and Deep Learning

1. In the table comparing machine with deep learning, which is *incorrect*?

	Machine Learning	Deep Learning
a. Data Needed	+++	++
b. Accuracy	++	+++
c. Plateau in Performance	Yes	No
d. Human Involvement	Feature extraction	None needed

[ ]

2. In the graph to the right, the top orange line is reflective of:



a. Human brain
b. Machine learning
c. Deep learning
d. Statistics
[ ]

3. Classification in supervised learning can be used in healthcare for all of the following except;
a. Medical images
b. Survival prediction
c. Phenotyping
d. Cohort identification
[ ]

4. Disadvantages of deep learning include all of the following *except*:
a. Needs high volume of data
b. Needs long time to train
c. Lack means to represent causal relationships
d. Cannot achieve high accuracy in performance
[ ]

5. Of the following, which requires the *least* amount of data:
a. Deep learning
b. Machine learning
c. Deep reinforcement learning
d. Transfer learning
[ ]

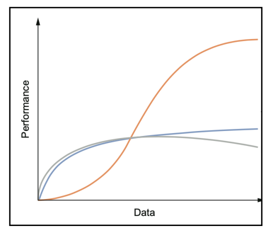
Answers 5.18/Machine and Deep Learning

1. In the table comparing machine with deep learning, which is *incorrect*?

	Machine Learning	Deep Learning
a. Data Needed	+++	++
b. Accuracy	++	+++
c. Plateau in Performance	Yes	No
d. Human Involvement	Feature extraction	None needed

[a]

2. In the graph to the right, the top orange line is reflective of:



a. Human brain
b. Machine learning
c. Deep learning
d. Statistics

[c]

3. Classification in supervised learning can be used in healthcare for all of the following except;

a. Medical images
b. Survival prediction
c. Phenotyping
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[b]

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a. Needs high volume of data
b. Needs long time to train
c. Lack means to represent causal relationships
d. Cannot achieve high accuracy in performance

[d]

5. Of the following, which requires the *least* amount of data:

a. Deep learning
b. Machine learning
c. Deep reinforcement learning
d. Transfer learning

[b]

Module 5.18/Machine and Deep Learning

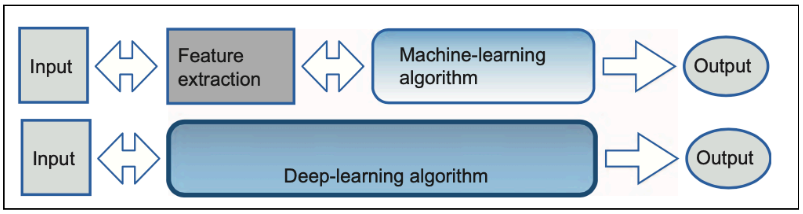
There are significant differences between machine and deep learning **(see Table)**. Whereas **traditional machine learning flow** has manual feature extraction or engineering followed by machine learning algorithm (with a relatively shallow structure) that leads to output, **deep learning flow** involves an artificial neural network that can combine feature extraction with the classification as one step in its algorithm to achieve an end-to-end learning process **(see Figure)**. Deep learning, therefore, requires less domain knowledge to solve the problem assigned, but deep learning is more difficult to comprehend as the algorithms are largely self-directed (so-called "black box").

Machine vs Deep Learning. The workflow for both machine and deep learning are depicted. In machine learning, feature extraction is manually done followed by the use of the algorithm with a shallow structure. In deep learning, there is no separate feature extraction as it is inclusive of the deep learning end-to-end algorithm (which creates a "black box" perception).

Table 13. Machine vs Deep Learning.

	Machine Learning	**Deep Learning**
Era	1980's	2000's
Examples	SVM, Random Forest	CNN, RNN, GANs
Data Needed	++	+++
Accuracy	++	+++
Feature Extraction	Yes	No
Training Time	++	+++
Plateau in Performance	Yes	No
Hardware Requirement	CPU	GPU
Human Involvement	Feature extraction	Training process
Relationship	Linear or Nonlinear	Nonlinear

(CPU- central processing unit; CNN- convolutional neural network; GAN- generative adversarial network; GPU- graphics processing unit; RNN- recurrent neural network; SVM- support vector machine)



Traditional **machine learning**, compared to deep learning, is relatively easy to train and test but its performance is dependent upon its features and is limited with increasing volume of data (**see Figure**). These relatively shallow models are also relatively inefficient as they need a large number of computations and high maintenance in that they require much human work for labeling.
On the other hand, **deep learning** performance can continue to incrementally improve with increasing data (or increasing capacity of the network). While deep learning can learn high-level features representation, it does require large amounts of data for training and can be expensive from a computation usage perspective. Note that with increasing volume of data, human performance remains the same (or even deteriorates from fatigue).

Performance. The data vs performance is plotted for various technologies, including the human brain. Increasing depth of the neural network will increase the level of performance but traditional machine learning will plateau earlier than even shallow neural networks. Deep neural networks will continue to increase in its performance with larger amounts of data. Humans start at a higher level of performance but will fatigue and perform less well with increasing amount of data.

In summary, the myriad of machine and deep learning tools that are described above have specific applications with advantages and disadvantages. These elements are organized in the table below **(see Table)** (please see individual sections for more details):

Type of Learning	Use in Medicine and Healthcare	Advantages/Disadvantages
Supervised Learning		*Advantages:* Relatively easy to apply *Disadvantages:* Need to generate labels
- Classification	Medical images Phenotyping Cohort identification	
- Regression	Outcome prediction Survival prediction Risk prediction	
Unsupervised Learning		*Advantages:* Relatively easy to apply *Disadvantages:* Difficult to generate performance metric
- Clustering	New patient and therapies Novel phenotype identification Biological hypothesis generation	
- Generalization	Data visualization Variable selection Data compression	
Reinforcement Learning	Process optimization Decision sequence optimization	*Advantages:* Human-like learning *Disadvantages:* Needs large number of simulations
Transfer Learning	Models from other sources	*Advantages:* Requires less data *Disadvantages:* Needs surrogate data

Type of Learning	Use in Medicine and Healthcare	Advantages/Disadvantages
Deep Learning	Image classification Text note classification Sequential prediction	*Advantages:* High level of performance Can model complex relationships *Disadvantages:* Needs high volume of data and long time to train Not able to perform logical inferences Lack means to represent causal relationships

Chapter 6: Other Key Concepts in Artificial Intelligence

Questions 6.1/Cognitive Computing

1. Important AI components of IBM Watson's DeepQA technology as an example of cognitive computing included all of the following *except*:
a. Information retrieval
b. Natural language processing
c. Convolutional neural network
d. Machine learning
[ ]

2. In the following table, which is *incorrect* about cognitive computing and artificial intelligence:

	Cognitive Computing	**Artificial Intelligence**
a. Definition	Systems that are designed to solve problems by simulating human cognitive abilities	Science of making computers do things that require intelligence by humans
b. Purpose	Augments human intelligence	Augments human intelligence
c. Capabilities	Finding patterns in data and performs prediction	Simulating human cognition and advises
d. Applications	IBM Watson	Google DeepMind

[ ]

3. Which of the following characteristics is *true* for cognitive computing and artificial intelligence?
a. Ability to solve problems deemed too complex for human brains
b. Ability of computers to simulate and complement human cognitive abilities
c. Ability to solve a problem through the use of best possible algorithms
d. Finding patterns in data and performs a prediction
[ ]

4. Which statement about cognitive computing is *false*?
a. The cognitive systems era follows the programmable systems era
b. Cognitive computing can excel at natural language
c. Cognitive computing does not involve machine learning
d. Cognitive computing can augment human capabilities
[ ]

5. Cognitive computing has its origin in all of the following *except*
a. Cognitive science
b. Big data
c. Bayes' theorem
d. Knowledge discovery
[ ]

Answers 6.1/Cognitive Computing

1. Important AI components of IBM Watson's DeepQA technology as an example of cognitive computing included all of the following *except*:
a. Information retrieval
b. Natural language processing
c. Convolutional neural network
d. Machine learning
[c]

2. In the following table, which is *incorrect* about cognitive computing and artificial intelligence:

	Cognitive Computing	**Artificial Intelligence**
a. Definition	Systems that are designed to solve problems by simulating human cognitive abilities	Science of making computers do things that require intelligence by humans
b. Purpose	Augments human intelligence	Augments human intelligence
c. Capabilities	Finding patterns in data and performs prediction	Simulating human cognition and advises
d. Applications	IBM Watson	Google DeepMind

[c]

3. Which of the following characteristics is *true* for cognitive computing and artificial intelligence?
a. Ability to solve problems deemed too complex for human brains
b. Ability of computers to simulate and complement human cognitive abilities
c. Ability to solve a problem through the use of best possible algorithms
d. Finding patterns in data and performs a prediction
[a]

4. Which statement about cognitive computing is *false*?
a. The cognitive systems era follows the programmable systems era
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c. Cognitive computing does not involve machine learning
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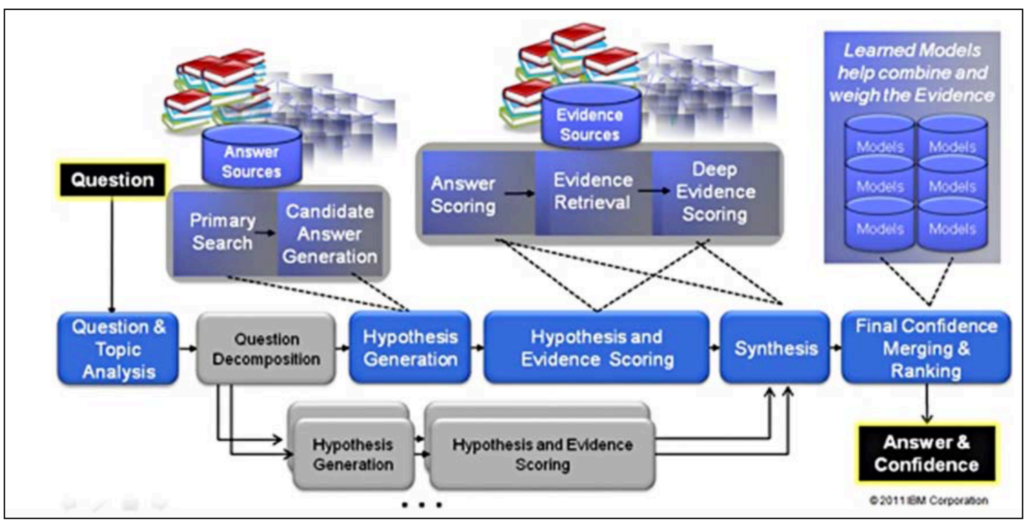
Module 6.1/Cognitive Computing

Cognitive Computing
Cognitive computing is defined loosely as a science that teaches computers to think like a human mind, and therefore an attempt to reengineer the human brain. The cognitive computing **framework** leverages a portfolio of methodologies such as machine learning, pattern recognition, and natural language processing as well as other AI tools to mimic the human brain and its self-learning capability. Cognitive computing is a symbiotic **convergence** of humans (user and expert) and smart technology. The **degrees** of cognitive computing include: first degree that entails understanding natural language and human interactions; second degree that involves generation and evaluation of evidence-based hypotheses; and third degree that possesses adaptations and learning from interactions with users.

In 2011, the iconic supercomputer Watson was able to defeat the human champions on the game show *Jeopardy!*. The **IBM supercomputer Watson** was the first open cognitive platform and heralded the era of cognitive computing with its robust NLP as well as knowledge representation, information retrieval, automated reasoning capabilities along with machine learning; this



supercomputer can also scan an astounding 200 million pages in 3 seconds **(see Figure)**.

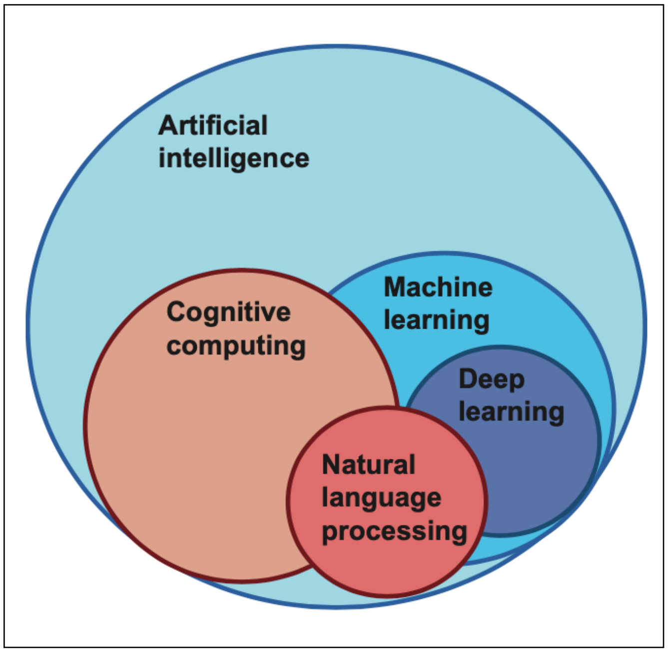
Cognitive Computing (Watson). The DeepQA architecture of Watson involved deconstructing the question and topic analysis, followed by integrating answer sources with evidence sources to lead to a hypothesis and evidence scoring to result in the final answer with confidence scoring.

The essential part of Watson was the **Deep QA technology,** a massively parallel probabilistic evidence-based architecture with more than 100 different techniques for analyzing natural language, identifying sources, finding and generating hypotheses, finding and scoring evidence, and merging and ranking hypotheses. The knowledge for Watson is self-contained as there is no access to the Internet. There are four essential steps in answering the questions posed on *Jeopardy!*:
1) **Question analysis**: parsing the question into words and analyze these parts of the question;
2) **Hypothesis generation**: searching large volume of possible answers and narrowing these down to the more likely possibilities;
3) **Hypothesis and evidence scoring**: collecting positive and negative evidence for passages of word associations and using algorithms to score these possibilities; and
4) **Final merging and ranking**: weighing the evidence and deciding the final ranking of answers.

The DeepQA principles involve massive parallelism to consider multiple interpretations and hypotheses; many experts to facilitate a wide range of loosely coupled probabilistic question and content analytics; pervasive confidence estimation to find a final score and answer; and integration of shallow and deep knowledge. The massively parallel architecture coupled with a dedicated high-performance computing infrastructure of the DeepQA architecture and methodology demonstrated the systems-level approach to research in not only cognitive computing, but also AI.

Just as big data has promulgated machine and deep learning into higher dimensions of performance and scope, big data has also increased the expectations of cognitive computing. The cognitive era (with the two previous computing eras being tabulating and programmable systems) with its cognitive systems have capabilities of learning, reasoning, perception and language processing. The **characteristics** of cognitive computing include: information gathering by integrating data from disparate sources; dynamic training and adaptive by learning and changing as new information is gathered; probabilistic by discovering patterns based on context; meaning-based by performing language processing; and highly interactive by providing advanced communications.

There is sometimes understandable **confusion** between AI and cognitive computing, and in some ways, the latter is even more difficult to define **(see Table)**. While AI does not intentionally mimic human thought processes, cognitive computing with its origin in cognitive science does attempt to simulate the human problem-solving process in a computerized model (via AI tools such as machine learning, neural networks, and NLP as well as sentiment analysis and contextual awareness). In the near future, cognitive computing will sense via networks of smart devices, learn from historical data, infer by generating evidence-based hypotheses, and interact with systems and people with its natural language capabilities. There is great potential for cognitive computing, along with machine and deep learning, to be essential parts of AI in the near future. Cognitive computing is considered under the realm of AI, and conversely, the future direction of AI is in cognitive architecture.



AI and Cognitive Computing. The relationship between cognitive computing and AI is delineated in this schematic diagram. Cognitive computing is usually considered within the AI realm and encompasses machine and deep learning as well as natural language processing.

An example in the recent biomedical literature of cognitive computing is the review article on IBM Watson with a 5-part discussion of: 1) the need for accelerated discovery, 2) the data hurdles that impede discovery, 3) 4 core features of a cognitive computing system, 4) pilot projects applying Watson to life sciences research, and 5) potential applications of cognitive technologies to other life science activities ([25]).

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[25] Chen Y, Argentinis E, and Weber G. IBM Watson: How Cognitive Computing Can Be Applied to Big Data Challenges in Life Sciences Research. *Clinical Therapeutics* 2016; 38(4): 688-701.

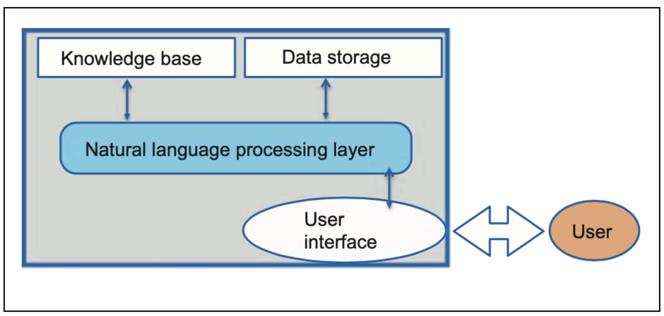
Table. Cognitive Computing and Artificial Intelligence.

	Cognitive Computing	Artificial Intelligence
Definition	Systems that are designed to solve problems by simulating human cognitive abilities	Science of making computers do things that require intelligence by humans
Methodologies	Machine learning Deep learning NLP Rules-based systems Speech recognition Sentiment analysis	Machine learning Deep learning NLP
Purpose	Augments human intelligence	Augments human intelligence
Capabilities	Simulating human cognition and advises	Finding patterns in data and performs prediction
Applications	IBM Watson	Google DeepMind

Questions 6.2/Natural Language Processing (NLP)

1. Natural language processing is involved in all of the following *except*:
a. IBM Watson
b. Chatbots
c. Virtual assistants
d. Image classification
[ ]

2. The following are tasks in natural language processing *except*:
a. Tokenization
b. Lemmatization
c. Regularization
d. Part of speech tagging (POS)
[ ]



3. The diagram on the left is an example of:
a.Chatbot
b.IBM Watson
c.Machine learning
d.Deep learning
[ ]

4. Syntax is the arrangement of words in a sentence so that these make grammatical sense. The techniques involved in syntax include the following *except*:
a. Part-of-speech tagging
b. Parsing
c. Lemmatization
d. Natural language generation
[ ]

5. The following are ways that natural language processing can be used *except*:
a. Image segmentation
b. Speech recognition
c. Sentiment analysis
d. Chatbots
[ ]

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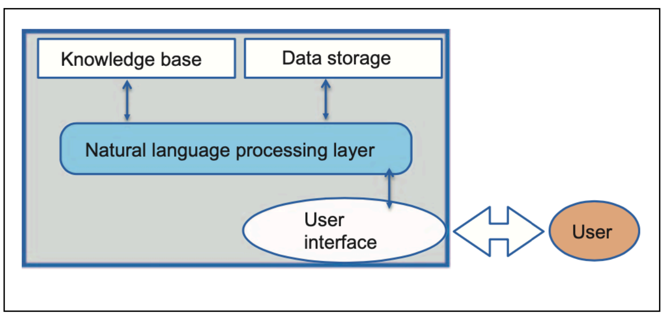

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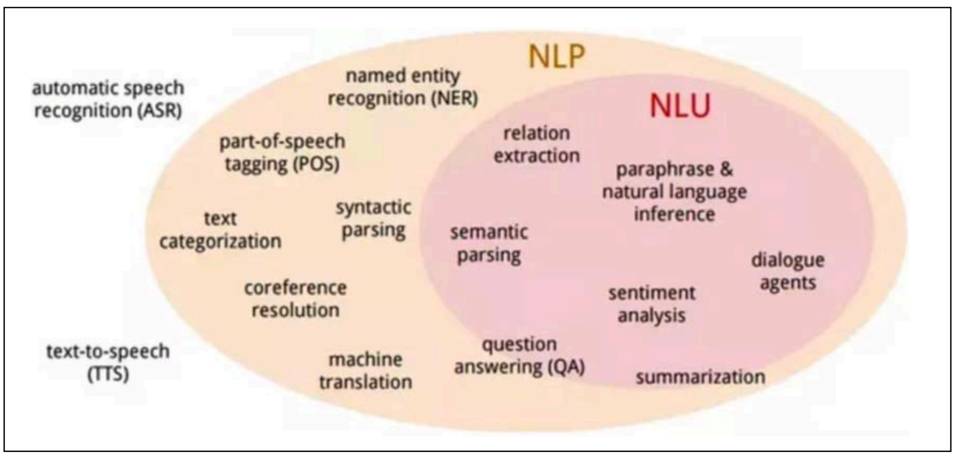
b. Speech recognition
c. Sentiment analysis
d. Chatbots
[a]

Module 6.2/Natural Language Processing (NLP)

NLP is **defined** as the computer to understand spoken as well as written human language through specific set of techniques. In short, NLP is the intersection of AI, computer science, and linguistics and is a good example of human-computer interaction. The **applications** of NLP include: machine translation, information retrieval, document indexing, sentiment analysis, information extraction, chatbots with natural speech, virtual assistants, blocking spam and question answering. Of note, NLP is an essential part of the supercomputer Watson.

The two components of NLP are **natural language understanding (NLU)** and **natural language generation (NLG)**; NLU is usually considered the more difficult component **(see Figure).** Natural language understanding involves mapping of input into a useful representation while natural language generation involves text planning, sentence planning, and text realization.



NLP and NLU. NLU with its parts is a subset of NLP, which has a more complete portfolio. NLU has the diffi cult task to interpret unstructured inputs and covert these words into structured ones for the computer to understand.

The connection of words or phrases to concepts can also be described in terms of tokenization, lemmatization, and mapping. **Tokenization** is a deconstruction of a sentence into words and phrases (or tokens) based mainly but not solely on spaces. For example, *myocardial* and *myocardial infarction* are both tokens. **Lemmatization** is a standardization that maps a token onto a lemma, which is the base form of a word that is found in a dictionary. For example, *MI* can be mapped onto *myocardial infarction*. Finally, the **mapping** of a lemma to a concept is challenging as any word can have different meanings (just as many words can have the same meaning).

The NLP **process** is as follows: speech is deconstructed with phonetic analysis that consists of breaking down the speech into phonemes while text is broken down with combined optical character recognition (OCR) and tokenization. The lexical analysis is analysis of the structure of words. Then, **syntactic analysis,** or **dependency parsing,** is the analysis of words in the sentence for grammar followed by a process of arranging the words that shows the proper relationship between these words. While syntax is the structural role of words, semantics is the meaning of words and semantic interpretation describes a meaning for these words. Next, there is discourse integration, the meaning of sentences in sequence is studied. Lastly, pragmatic analysis occurs when data is interpreted on what it actually means. An even more detailed step-by-step description will be listed (but not delineated in full detail) from the input document to the output: sentence segmentation, tokenization, parts-of-speech tagging (POS), lemmatization, stop words, dependency parsing, noun phrases, named entity recognition, and finally coreference resolution.

Natural Language Processing	**Systactic Analysis**	**Semantic analysis**
	Lemmatization	Named entity recognition
	Morphological segmentation	Word sense disambiguation
	Word segmentation	Natural language generation
	Part of speech tagging	
	Parsing	
	Sentence breakdown	
	Stemming	

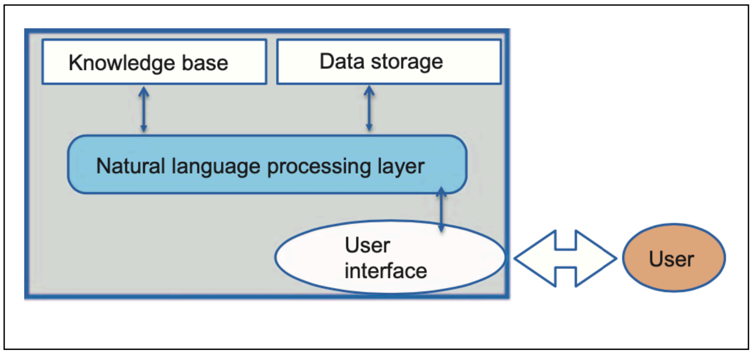
Three strategies can be used in the application of NLP to biomedical data ([26]):
First, a **pattern matching** strategy is perhaps the simplest approach in which a sequence of characters is used for matching. Tokenization and regular expression pattern matching are part of this pattern matching methodology.
Second, a **linguistic approach** can be used for more complex sentences as it treats words as symbols that are constructed together with grammatical rules. Both syntactic (rules for word

[26] Cai T, Giannopoulos AA, Yu S et al. Natural Language Processing Technologies in Radiology Research and Clinical Applications. *RadioGraphics* 2016; 36;176-191.

arrangement in a sentence) and semantic (meaning of word in the context of the sentence) knowledge are used in this strategy to delineate the concepts.

Third, a more recent **machine learning approach** infers rules and patterns directly from the data by the use of elements such as features, training data, and models (discussed previously).

A **chatbot** or automated intelligent agent are intelligent digital assistants that embodies NLP and used for a myriad of purposes including customer communication and information gathering. The parts of a chatbot include: **knowledge base** contains the information needed to answer the queries; **data store** is where interaction history of chatbots with users are stored; an **NLP layer** translates user query into a usable communication; and finally an **application layer** where the application interface is located **(see Figure)**. These components are reminiscent of the early expert systems during the early AI era.



Chatbot Architecture. The chatbot architecture is shown in this schematic diagram. The main components are knowledge base, data storage, and the NLP layer that then connects with the user interface.

An example in the recent biomedical literature of using NLP is the recent report of NLP in extracting clinically useful information from Chinese electronic medical records with the development of rule-based and hybrid methods (with the former showing better results)([27]).

[27] Chen L, Song l, Shao Y et al. Using Natural Language Processing to Extract Clinically Useful Information from Chinese Electronic Medical Records. *International Journal of Medical Informatics* 2019; 124:6-12.

Questions 6.3/Robotics

1. Which of the following is *not* part of Asimov's Laws of Robotics?
a. A robot may not injure a human being, or, through inaction, allow a human being to come to harm
b. A robot must obey the orders given to it by human beings, except where such orders would conflict with the First Law
c. A robot may disobey the orders given to it by human beings if the robot disagrees with the human
d. A robot must protect its own existence, as long as such protection does not conflict with the First or Second Law
[ ]

2. Which of the following is *not* part of the original definition of robotics?
a. A robot is defined as a reprogrammable and multifunctional manipulator
b. A robot is designed to move material, parts, or specialized devices
c. A robot uses variable programmed motions for the performance of a variety of tasks
d. A robot is always guided by an external control
[ ]

3. The following are examples of autonomous systems *except*:
a. Autonomous driving cars
b. Drones
c. Databases
d. Robots
[ ]

4. Robotic process automation (RPA) performs repetitive rule-based tasks that includes all of the following *except*:
a. Filling in forms
b. Reading and writing to databases
c. Taking history from patients
d. Making calculations
[ ]

5. The benefits of robotic process automation include all of the following *except*:
a. Strategy formulation
b. Increased throughput
c. Reduced workload
d. Less errors
[ ]

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a. Strategy formulation
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c. Reduced workload
d. Less errors
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Module 6.3/Robotics

Robotics

The word robot (Czech for worker or servant) initially came from the Czech novelist Karel Capek as a name for a play. A robot is defined (by Robot Institute of America in 1979) as a reprogrammable and multifunctional manipulator designed to move material, parts, or specialized devices through variable programmed motions for the performance of a variety of tasks. Of course the more recent conceptualization of a robot is much more inclusive, and there has been a surge of interest and research concomitant with the more recent era of AI. This discipline involves the utilization of artificial intelligence and engineering to involve the conceptualization and design as well as operation of robots; the interdisciplinary science of robotics includes electrical and mechanical engineering with computer science as well as mathematics, physics, biology, and of course AI. The recent trend in robotics is to yield robots that are more humanlike and less mechanical with living materials. As the field of robotics is vast and its topics heterogenous, a thorough discussion of robotics will not be a focus of discussion in this book, but robotics particularly as it pertains to medicine and health care will be covered later in this book.

A robot shares several basic **elements**: a mechanical frame for a task; a power source and actuation to mobilize; sensing mechanism(s) for both human and robot senses (the latter including force, tilt, proximity sensors), and computer-driven controller with a user interface and computational engine. The **types** of robots include: manipulator (usually fixed), legged and wheeled robots, and autonomous underwater vehicle and unmanned aerial vehicle (UAV). There are many **applications** for robots, but the two main areas are industrial and service with the latter showing more autonomy: industrial, military, aerospace, agricultural, education, and medical along with now even nanorobot, swarm robots, and drones. The field of robotics has converged with others to even include avatars and virtual assistants. There are many **taxonomies** for robots based on control (pre-programmed, remote controlled, supervised autonomous, and autonomous); operational medium (location); or function (military, industrial, etc).

Asimov's three **laws of robotics** have fascinating implications for AI in general and are as follows: 1) A robot may not injure a human being, or, through inaction, allow a human being to come to harm; 2) A robot must obey the orders given to it by human beings, except where such orders would conflict with the First Law; and 3) a robot must protect its own existence, as long as such protection does not conflict with the First or Second Law. One can extend these philosophical premises to AI and its implications for humans.

An example in the recent biomedical literature of robotics use is the review by Nwosu et al for the use of robotics in palliative and supportive care ([28]). These uses include supporting surgical procedures as well as assistive uses in dementia and elderly care.

Autonomous Systems. The convergence of robotics, **mechatronics, and** AI have lead to the advent of **autonomous systems.** Current examples of these systems include: autonomous driving cars, drones, robots in various scenarios, weapons systems, software agents, and even medical diagnostic tools. These advances are engendering many discussions around ethical and legal issues. In addition, future advances in this domain will include digital twins, computer-brain interfaces, cyborgs, and more; most if not all of these advances will have medical or health care applications. Finally, a recent statement from the EU has set up ethical principles and democratic prerequisites for autonomous systems to achieve moral ideals and socioeconomic goals as well as legal governance and regulatory framework ([29]).

An example in the recent biomedical literature of the use of drones include a comprehensive review with uses including delivery of health aid materials such as vaccines and medicines as well as test kits for diagnostic testing, and even defibrillators for cardiac arrest ([30]). In addition, drones can be part of a global telemedicine network for delivery of basic health care.

Robotic Process Automation (RPA). This is a computer-coded program that uses machine learning and artificial intelligence to perform repetitive **rule-based tasks** (such as filling in forms, reading and writing to databases, and making calculations). Its benefits include increased throughput, reduced costs, reduced workload, and less errors. Whereas RPA is more process-driven, machine learning and AI are more data-driven and cognitive. In a way, RPA can function as a gateway to intelligent automation, which is part of any industry's AI-enabled digital transformation with advanced robotics and IoT/IoE. RPA is often coupled with AI as it automates the pre-work for AI.

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[28] Nwosu AC, Sturgeon B, McGlinchey T et al. Robotic Technology for Palliative and Supportive Care: Strengths, Weaknesses, Opportunities, and Threats. *Palliat Med* 2019; Jun 28 [Epub ahead of print].

[29] European Group on Ethics in Science and Technologies. Statement on Artificial Intelligence, Robotics, and Autonomous Systems. March, 2018.

[30] Balasingam M. Drones in Medicine- The Rise of the Machines. *Int J Clin Pract* 2017; 71(9). [Epub].

Questions 6.4/Other Key Technologies Related to Artificial Intelligence

1. An immersive experience of an imaginary physical environment that is completely different than your present physical environment is called:
a. Virtual reality
b. Augmented reality
c. Mixed reality
d. Hybrid reality
[ ]

2. Which of the following statements about blockchain is *false*:
a. Blockchain is a specific type of distributed or decentralized ledger or a database of information with the information stored in many servers in the network.
b. While the identities of the owners are private, the transactions are not.
c. The transactions are secured by a unique cryptographic key so the information is immutable.
d. The convergence of blockchain and artificial intelligence is unproductive.
[ ]

3. The type of cloud that has the security and privacy as well as capital preservation and standardization is called:
a. Hybrid cloud
b. Public cloud
c. Private cloud
d. None of the above
[ ]

4. Artificial intelligence is coupled to all of the following technologies *except*:
a. Cloud computing
b. Internet of things
c. Telemedicine
d. Extended reality
[ ]

5. The recent explosion of physical devices and embedded sensors from equipment, buildings, vehicles, and appliances as well as wearable devices has led to network connectivity which will enable all these devices to collect and exchange data. This advance is called:
a. Digital twin
b. Internet of things (IoT)
c. Cognitive computing
d. Quantum computing
[ ]

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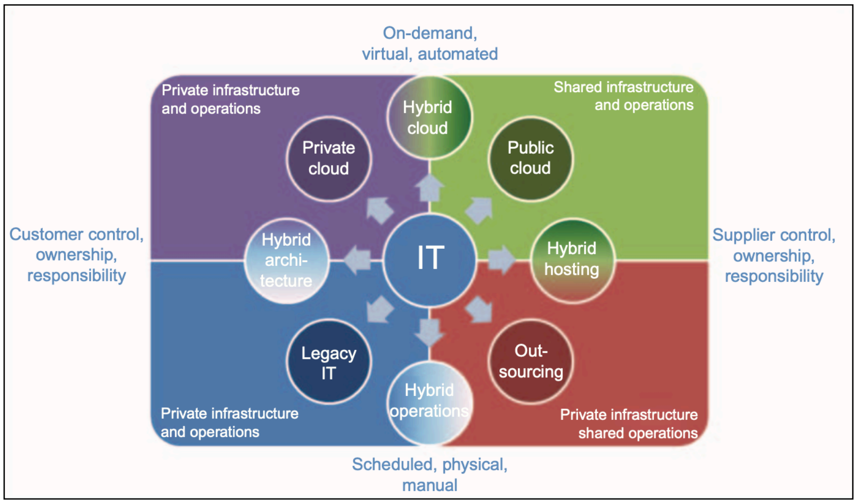
a. Digital twin
b. Internet of things (IoT)
c. Cognitive computing
d. Quantum computing
[b]

Module 6.4/Other Key Technologies Related to Artificial Intelligence

Augmented and Virtual Reality. Augmented reality (AR) is a technology that superimposes a computer-generated digital image on the user's perspective of the real world as to create a composite view (example is the Snapchat lenses). Virtual reality (VR) is an immersive experience of an imaginary physical environment that is completely different than your present physical environment (Oculus Rift is one choice). Finally, mixed reality (MR) combines the elements of both AR and VR so that real world and digital images interact (as observed with Microsoft HoloLens). All of these altered realities can be combined into "XR". AI with its computer vision dimension is essential to allow these advanced XR technologies to interact with the physical milieu with its object recognition and tracking capabilities and is at the heart of these reality altering technologies.

Blockchain. Blockchain is a specific type of distributed or decentralized ledger or a database of information with the information stored in many servers in the network. The **steps** for blockchain to achieve its purpose are: 1) a transaction is requested by a user; 2) the transaction is created on a "block"; 3) the block is then broadcasted to the nodes of the network; 4) the nodes validate the block that was broadcasted; 5) the block is then added to the chain; and 6) the transaction is verified. While the identities of the owners are private, the transactions are not. In addition, the transactions are secured by a unique cryptographic key so the information is immutable. While AI (centralized and lacking in transparency) and blockchain (decentralized and transparent) seem like an odd pairing, the combination of AI with its machine learning tools can enable both to be more efficient. The convergence of these disruptive technologies can create an ideal situation: a distributed computing substrate for AI with a universal anonymous blockchain data for AI work with more equity.



Cloud. Cloud types include public, private, and hybrid types. The **private cloud** (such as hospitals)(see Figure) has potential advantages that include security and autonomy while the **public cloud** (such as Google) has potential advantages that include scalability and cost-effectiveness. There is also the **hybrid cloud** that can potentially offer both security as well as scalability with an attractive cost structure as well. The hybrid cloud combines the customization and efficiency as well as security and privacy of the private cloud with the capital preservation and standardization of the public cloud that could be essential for the biomedical milieu. This strategy can also be dynamic with the private cloud utilizing its public cloud partner(s) on an as-needed basis (the so-called "**dynamic**" hybrid cloud). Logistical challenges of the hybrid cloud include connectivity as well as management of the arrangement on a continuous basis.

With the advent of machine learning capabilities in the cloud, there is a higher attractiveness about storing and managing biomedical data in the hybrid or public cloud. This is especially true now with increased security capabilities of the public and hybrid clouds. A **community cloud**, serving a common interest or purpose, can also be acceptable for a biomedical group or system (such as a specific subspecialty or hospital system). The best alternative cloud infrastructure for medical care, however, may be an even more sophisticated **cloud infrastructure system** that is customized for each need in health care data storage and security. For instance, if supplier control with ownership and responsibility are needed but with shared and private infrastructure, a "hybrid hosting" is desired. Although the storage of genomic data into the public cloud raises issues such as form of security and privacy, initial efforts to secure computation techniques that can enable comparative analysis of human genomes have been productive.

Cybersecurity. Cybersecurity in health care is very vulnerable to attacks and is considered to lag behind other sectors. An issue related to the aforementioned blockchain is AI **security**, which can have different levels of consequences depending on narrow vs general AI failures. In other words, a single isolated failure of a super intelligent system can be utterly catastrophic and fulfill the dire warnings of some of our leaders. There is the additional concern of an **algorithm** being hacked and misinterpret a medical image or misdirect a decision support system.

Internet of Things (IoT). The recent explosion of physical devices and embedded sensors from equipment, buildings, vehicles, and appliances as well as wearable devices has lead to network connectivity which will enable all these devices to collect and exchange data. An **IoT platform** enables connectivity for these devices that are capable of being part of the network. The method of communication is radio-frequency identification (RFID) but can also be wireless, quick response (QR) codes, or other sensor technologies. The connected devices together can form ambient type of intelligence but will need to be AI-enabled. For embedded AI, AI software can be embedded in the applications and devices so that AI is pushed peripherally without the necessity of having all the data pushed into a central repository for machine or deep learning processes.

In **conclusion**, the fast ascent of deep learning performance has promulgated the entire field of data science and AI to new heights. As deep learning usually mandates large training sets and the medical field often lack such large-sized databases, it behooves the medical field to be better organized and more collaborative in such endeavors and concomitantly for the data science stakeholders to accommodate this limitation with innovative approaches in deep learning. The data conundrum in health care is a particularly important issue for AI applications but with efforts such as data sharing and innovations such as graph databases, this can be vastly improved. The assessment as well as transparency of AI tools will need to be mature for wider AI adoption amongst clinicians.

Key Concepts

- The recent advent of an AI “triad” (conveniently “ABC”) consisted of: 1) the emergence of sophisticated algorithms, particularly machine and deep learning with all its variants, 2) the increasingly large volumes of available data that requires new computational methodologies (or simply “Big Data”), and 3) the escalating capability of computational power (with faster, cheaper, and more powerful parallel processing that defied Moore’s Law) with coupling to the widely available cloud computing (with nearly infinite storage). These elements have converged to engender this new resurgence of AI.
- Much of the future of AI in medicine and its success will be rooted in the quality and integrity of biomedical data and databases.
- It is estimated that about 80% of health care data is unstructured.
- Data that have escalated in a myriad of ways to the point that traditional data processing applications are no longer adequate is termed “Big Data”.
- Despite the large volume, variety, velocity, and veracity of big data in biomedicine, there is little dividend in the form of information from this health care big data.
- An ETL (extract, transform, and load) process is employed in order to extract data out of the system and configure the data for the data warehouse that is favored by business professionals as the data is usually structured (but storage usually more costly). A data lake is a lower-cost data storage repository preferred by data scientists and can hold large amounts of raw data, including unstructured data, for later analytic use.
- Interoperability, according to HIMSS, is “the ability of different information systems, devices, or applications to connect, in a coordinated manner, within and across organizational boundaries to access, exchange, and cooperatively use data amongst stakeholders with the goal of optimizing the health of individuals and populations”.
- Most of the present health care data remain embedded in flat files or at best, in relatively simplistic hierarchical or relational DBMS with most of the data centralized and locked into local operating systems that reside in hospitals or offices.
- There are limitations to relational DBMS for health care data: these lack sufficient infrastructural support for the larger health care data (such as time-series data, large text documents, and image/videos). In addition, queries are difficult due to the structure of relational DBMS.
- A graph DBMS can store data in the form of graph elements (nodes, edges, and properties) in order to facilitate relationship definitions for data elements. This type of database is more three-dimensional and has advantages over the traditional relational database.

- The graph DBMS with these search algorithms is especially well designed for complex queries in health care such as chronic disease management, acute epidemiological crises, and health care resource allocation. The location of a similar patient to an index patient can also be performed using this strategy.
- Machine learning, a term initially coined by Arthur Samuel in 1959, is an increasingly popular sub-discipline of AI and is the art of computer programming that enables the computer to learn and improve its performance without an external program instructing it to do so.
- In traditional programming (and statistical analysis), a top-down approach provides rules for the input data and output is derived. In machine learning, both the input data as well as output data (labeled by humans) are entered into the computer and the rules are derived from the data. The new rules are then applied to the new set of data.
- The steps of collecting and processing the data can easily make up the majority of the effort and time needed to do a project for the data scientist, especially in a clinical setting.
- The current paradigm of AI in medicine for biomedical data science is adding another domain of knowledge to computer science and mathematics: the domain knowledge of biomedicine (bioinformatics and clinical informatics as well as biology, genetics and genomics, medicine, and health sciences).
- Machine learning, or more accurately, classical machine learning, is better suited for smaller and less complicated datasets and clinical scenarios with less features. Classical machine learning is categorized into two types of learning: 1) supervised learning and 2) unsupervised learning.
- Supervised learning develops a predictive model from both input and output data (the later labelled by humans) and this model is then used to make predictions on a new set of data.
- These supervised learning methodologies lead to classification (dichotomous or categorical) or regression (to a continuous variable).
- For classification, the popular methodologies are support vector machines, naive Bayes classifier, *k*-nearest neighbor, and decision trees (with boosting or bagging); logistic regression is a misnomer and is in fact a classification methodology. For regression, linear and polynomial regression methods are most commonly used, but other types (such as ridge and lasso regression) may become more popular in the future.
- Unsupervised learning takes unlabeled data and uses algorithms to predict patterns or groupings in the data set without any human intervention. These unsupervised learning methodologies lead to clustering, generalization, association, or anomaly detection.
- A hybrid technique of supervised and unsupervised learning is semi-supervised learning, which uses a small amount of labeled data and then a relatively large amount of unlabeled examples.
- This ensemble learning strategy (bagging, boosting, and stacking) involves training a large number of models that together will surpass the performance of a single model; in

short, it is the creation of a meta-model that has better prediction and more stability. This ensemble of models reduces noise, bias, and variance.

- In addition to the aforementioned supervised (task-driven with classification or regression) and unsupervised (data-driven with clustering) learning, another type of learning is reinforcement learning. Although reinforcement learning is often described as a third or additional type of machine learning along with supervised and unsupervised learning, it is distinctly different than the former two types of machine learning.
- In reinforcement learning, the model is not relating itself to data but rather finding the optimal method via exploration to achieve the most desirable outcome while receiving input data in a dynamic environment.
- Reinforcement learning and its AI congener deep reinforcement learning are particularly valuable assets for biomedicine as these methodologies are well designed to make sequential decisions in an uncertain environment towards a long term goal that can be to minimize error (leading to morbidity and/or mortality).
- Compared to the machine learning techniques just discussed, the more sophisticated neural networks and deep learning techniques (with sometimes hundreds of layers of neurons) are particularly well suited for non-linear and complex relationships, which are not uncommon in biomedicine and health care.
- Current applications of deep learning include speech recognition and natural language processing, computer vision with visual object recognition and detection, speech recognition, and autonomous vehicle driving.
- The building blocks of the CNN architecture consists of convolution layers, pooling layers, and fully connected layers as well as rectified linear unit (ReLU). These layers are constructed to enable CNN to learn spatial hierarchies of features.
- CNN is different from conventional machine learning in that CNN requires large amounts of data for model training; CNN, on the other hand, does not require manual (human-derived) feature extraction nor image segmentation.
- In short, CNN is good for spatial data while RNN is designed for sequential or temporal data. There is, however, a hybrid "CNN-RNN" model (also called recurrent CNN, or RCNN but not to be confused with regional CNN, R-CNN) that has some potential in biomedical data, such as multi-label image classification and serial complex biomedical data.
- The evaluation of a model with a test set of data (that the model has not seen before) can follow two methods: cross-validation or holdout method.
- For a binary classification model, the performance is measured by the confusion matrix, the area under the curve (AUC) in a receiver operating characteristic curve (ROC), and AUC in a precision-recall curve (PRC).
- The F_1-score, also called F-measure or balanced F-score, is probably the least familiar to most readers; it is the harmonic mean between precision and recall and can be used to assess binary or multi-class classification models for accuracy.

- In short, accuracy and error rate are not good indicators of performance especially when the incidence of disease is very low (like for cancer) because the true negatives, a majority of the cases usually in low incidence disease states, is a relatively high number to make accuracy and error rate look more favorable. This is a good example of how precision and the F_1 score will be more realistic reflection of the classification model prediction performance, especially when there is an imbalance in the classes as in the case of true negatives being a very large number. When the true negatives is a large number, one can also consider the precision recall curve.
- While there is a difference between interpretability and explainability, AI methods need at least interpretability for it to be widely adopted by clinicians. Interpretability is the capability to observe a cause-and-effect while explainability is the understanding of the inner workings of a system or technology.
- Some of the higher prediction accuracy machine learning methodologies (deep learning, random forest, support vector machines, etc) have the least explainability whereas others (Bayesian belief nets, decision tress) have more explainability (but relatively lower prediction accuracy).
- The ideal model will have both low bias as well as low variance, but it is usually a trade-off between these two parameters. Bias and variance are manifested in models that demonstrate underfitting and overfitting: the former is a result of high bias and the latter is a result of high variance; therefore, the best balance, fitting, is achieved when there is low bias and low variance.
- Underfitting occurs when the model is too simplistic: it is poorly trained on sample data (such as a linear model) or when the feature engineering is suboptimal and/or inadequate. The solution will involve a more complex model and a better feature engineering strategy. Overfitting occurs when the model is too complex: the results are too tailored to the training data (excessive training or adaptation) so that the model is overly complex for the data (opposite of above situation with underfitting).
- The curse of dimensionality occurs when there is such a large number of features so that the features space is excessively large so that there are not enough samples to fill this space. In general, as the features increase, the amount of data needed to generalize accurately grows exponentially. As the number of features (called dimensionality) increases, the classifier's performance increases until the optimal number of features is reached; this is called the Hughes phenomenon.
- A common misconception is that correlation implies that there is causation; events that are correlated, therefore, do not signify that one caused the other.
- Traditional machine learning, compared to deep learning, is relatively easy to train and test but its performance is dependent upon its features and is limited with increasing volume of data.
- On the other hand, deep learning performance can continue to incrementally improve with increasing data. While deep learning can learn high-level features representation, it

does require large amounts of data for training and can be expensive from a computation usage perspective.

- The cognitive computing framework leverages a portfolio of methodologies such as machine learning, pattern recognition, and natural language processing as well as other AI tools to mimic the human brain and its self-learning capability. Cognitive computing is a symbiotic convergence of humans (user and expert) and smart technology.
- NLP is defined as the computer to understand spoken as well as written human language through specific set of techniques. In short, NLP is the intersection of AI, computer science, and linguistics and is a good example of human-computer interaction.
- A robot is defined as a reprogrammable and multifunctional manipulator designed to move material, parts, or specialized devices through variable programmed motions for the performance of a variety of tasks.
- Traditional regulatory processes are quickly becoming woefully inadequate (and perhaps inappropriate) to be used as a strategy to have oversight over ultrafast-evolving AI software that can change in real-time in a matter of seconds.

Ten Steps to Become More Knowledgeable in Artificial Intelligence in Medicine
These are ten ways one can start to learn and know data science and AI in medicine and health care (not in any particular order so one can pursue these in parallel or in series):

Review data/database and statistics. Much of the data science in medicine is biostatistics "on steroids" so a good foundation in **data** and **databases** (types of data, data deficiencies, types of databases, etc) particularly as it relates to health care and **statistics** (regression, confusion matrix, sensitivity and specificity, etc) is essential for a better appreciation and understanding of data science and AI.

Become familiar with health informatics. Another part of the foundational layers (data-information-knowledge) necessary to have for data science and AI in health care and medicine is information (**informatics**). Informatics, like the aforementioned data, is a key element in the full understanding of data science and AI in medicine. Much of the time spent on AI projects is spent on data and informatics so the ability to navigate in these two domains is helpful and productive.

Identify data science and AI educational resources. There is a comprehensive educational **compendium** that consists of books and textbooks, journals, articles, and websites at the end of this book. There are many helpful **video clips** on the Internet that focus on the many topics that were discussed in this book. There are also ongoing publications and blogs on this topic that can be helpful.

Attend a meeting on data science and AI in medicine or health care. It is important to start a personal educational strategy for yourself (as well as the members of the division or department who may be interested as well). There are several meetings that focus on AI in health care and medicine; for those of you who are not yet fully educated in data science or AI, one caveat is that some of these meetings are very heavy on the data science and you may find some or most of the talks at these meetings too esoteric. Many of the ML/DL and AI papers on subspecialties are not necessarily published in the medical journals but an aggressive search strategy can enable one to find good papers (see list in back of the book).

Meet and get to know a data scientist. It is good to meet a data scientist from the community or at a meeting to simply understand what they do and how they do their projects. If there is good interpersonal dynamic, one can invite each other to their respective domains for a visit. It is usually a valuable experience for a clinician to visit a data science department just as it is usually a meaningful experience for a data scientist to spend time in a clinic or hospital setting with a clinician.

Seek hands-on data science experiences. The next step would be to spend some significant time with a data scientist and see their programming and analyzing skills at work. One can consider taking an **online course** (MOOCs like Coursera, edX, Udemy, and Khan Academy) on data science and/or programming (such as R or Python). Another option is to invite a data scientist to do a **workshop** on computer programming at a frequency that is workable for both you and the data scientist. If you are willing and have the resources and time, a degree in data science at the Masters or PhD level is especially helpful; even more important than the education and experience is the network you form during these years in the program.

Recruit data science support. The initial effort to collaborate with a data scientist does not have to be hiring a full time data scientist but rather some data science resource either part-time or virtual. Often the local colleges and universities have good talent in data science and usually some of these students are very enthusiastic to be involved in health care. Occasionally there is even a premed student who is savvy with programming and computer science.

Start with a small data science project. With the support of a data scientist, one can start a very small project with a small patient population with more straight-forward machine learning for analytics to learn about data mining and analytics. One good strategy is to work with available data sources such as **MIMIC-III**, which is a publicly available ICU database that one can do analytics with. An additional resource is the NIH **Big Data to Knowledge (BD2K) Initiative** which was launched to support research and development of tools for integrating data science into biomedical research.

Select a clinical project. Once you have gained sufficient experience with a small project, one can go bigger with a clinical project with a bigger scope and higher complexity. It is also a good idea to collaborate with a center that already has an active data science program with ongoing projects; these centers usually can use more data which you may have access to so it is a "win-win". The experience and insight one can gain from this arrangement can be more than you expect.

Build a coalition of AI enthusiasts. It is important to start gathering all those interested in the AI domain in your geographical vicinity and have a diversity of leaders to include administration as well a physician and nursing leadership. This **network of networks** effect can be very productive and very often meaningful relationships and even projects can promulgate from these monthly or periodic gatherings.

III. The Current Era of Artificial Intelligence in Medicine

Chapter 7: Clinician Cognition and Artificial Intelligence in Medicine

Questions 7.1/Artificial Intelligence in Medicine-The Why

1. The physicians in this current era are facing the following stresses. Which statement is *not* true?
a. Exponentially increasing medical information makes it difficult for physicians to keep up
b. More patients with higher degree of complexity of chronic diseases creates additional burden
c. Increasingly more data volume of many diverse types in many separate locations creates stress
d. Wide adoption of artificial intelligence in EHR decreases mounting burden of workload
[ ]

2. Factors driving AI adoption in clinical medicine include all of the following *except*:
a. Adaptability of deep learning to analysis of heterogeneous data set
b. Ability of artificial intelligence to help make ethical decisions
c. The promise of deep learning to streamline clinical workflows and empower patients
d. Deep learning technology to deliver improved performance as data sets get larger
[ ]

3. The rate at which medical information is doubling is:
a. 3 days
b. 3 months
c. 3 years
d. 30 years
[ ]

4. Artificial intelligence can assist in decreasing the burden of the clinicians by the following *except*:
a. Discussing end-of-life options with patients
b. Interpreting normal studies
c. Checking laboratory data
d. Communicating with various stakeholders routine information
[ ]

5. Artificial intelligence can surpass human capabilities in tasks in all of the following areas *except*:
a. Endurance
b. Creativity
c. Objectivity
d. Accuracy
[ ]

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b. Creativity
c. Objectivity
d. Accuracy
[b

Module 7.1/Artificial Intelligence in Medicine-The Why

The "Why" for Intelligence-Based Medicine: Sanctuary for The Perfect Storm
The physicians in this era are facing the **perfect storm**: exponentially increasing medical information with a relatively flat trajectory for personal knowledge acquisition due to time constraints; more patients with higher degree of complexity of chronic diseases with increasingly more data volume of many diverse types in many separate locations; mounting pressures to produce work units with diminishing reimbursements and constant denials for procedures and tests; and high level of stress and burnout from the mounting burdens of EHR and workload.

There is a myriad of reasons that physicians in any subspecialty could benefit from incorporation of AI into their practices:

First, AI with the clinician can become a powerful **dyad** (akin to Doctor Watson and Sherlock Holmes or Captain Kirk and Mr. Spock from *Star Trek*) with AI being a very capable second pair of eyes and an additional brain in a myriad of activities ranging from medical image interpretation to decision support. This partner adds perhaps additional dimensions as well as capabilities (such as endurance and objectivity) that can neutralize natural human frailties.

Second, the amount of medical **knowledge** is exponentially increasing and doubling at a rate of a few months, and yet physicians do not have enough time to read and maintain their knowledge capacity. AI can be a useful up-to-date knowledge resource that can be even part of the EHR.

Third, AI can help to reduce the repetitive tasks and therefore inevitable **burden** that physicians do not enjoy performing (clinical fatigue), and this phenomenon is observed especially more senior clinicians as they become very seasoned in their clinical work. This burden includes interpreting normal studies, refilling medications, checking laboratory data, communicating with various stakeholders routine information, etc. An element that can contribute to the weight of this burden is avoiding errors in these tasks.

Fourth, AI can help organize and facilitate the care **coordination** of chronic and complex diseases in many of the patients especially as they have more relevant data from disparate sources such as genomic sequencing, medical imaging, and wearable technology. This also mandates a central repository of data and information that AI can help gather and organize.

Fifth, physicians have currently a high rate of stress and many are facing or having had **burnout** from their careers. The use of AI can mitigate particularly the EHR burden that is often a prime source of frustration and thereby automate and simplify their workload. AI can even help monitor physician burnout with metrics that reflect burnout and dissatisfaction.

Lastly, AI tools can provide an important resource for medical **education** as well as clinical training at all levels with smart tools coupled to the EHR as well as implementation of augmented and virtual reality technologies.

Naylor also identified 7 factors driving **AI adoption** in clinical medicine and health care: 1) the strengths of digital imaging over human interpretation; 2) the digitization of health-related records and data sharing; 3) the adaptability of deep learning to analysis of heterogeneous data sets; 4) the capacity of deep learning for hypothesis generation in research; 5) the promise of deep learning to streamline clinical workflows and empower patients; 6) the rapid-diffusion open-source and proprietary deep learning programs; and 7) of the adequacy of today's basic deep learning technology to deliver improved performance as data sets get larger. Along with these factors, the escalating volume of health care data as well as exponential increase in medical knowledge are additional forces as well.

Questions 7.2/Artificial Intelligence in Medicine-The Challenges

1. The following are all challenges about data with relevance to artificial intelligence *except*
a. Data privacy
b. Data integrity
c. Data sharing
d. All of the above are challenges
[ ]

2. Which of the following qualities about artificial intelligence is usually *not* an issue for adoption?
a. Black box perception
b. Algorithm capabilities
c. Regulatory issues
d. Workflow disruption
[ ]

3. All of the following are people-related issues in AI adoption *except*:
a. Lack of clinician champions
b. Shortage of data scientists
c. Domain knowledge differences
d. Lack of mutual respect
[ ]

4. Which of the following is the *correct* order of machine to human involvement:
a. CNN-Random Forest-Logistic Regression-Human Decision
b. Random Forest-CNN-Logistic Regression-Human Decision
c. CNN-Logistic Regression-Random Forest-Human Decision
d. Random Forest-Logistic Regression-CNN-Human Decision
[ ]

5. The general four main principles elucidated in this diagram of the FDA AI regulation (software as a medical device, or SaMD) include all of the following steps *except*:
a. Establish clear expectations on quality systems and good ML practices (GMLP)
b. Expect these manufacturers to monitor the AI/ML devices and incorporate a risk management approach
c. Estimate a 3-5 year assessment period for clinical trials using the SaMD
d. Enable a real-world performance monitoring with transparency
[ ]

Answers 7.2/Artificial Intelligence in Medicine-The Challenges

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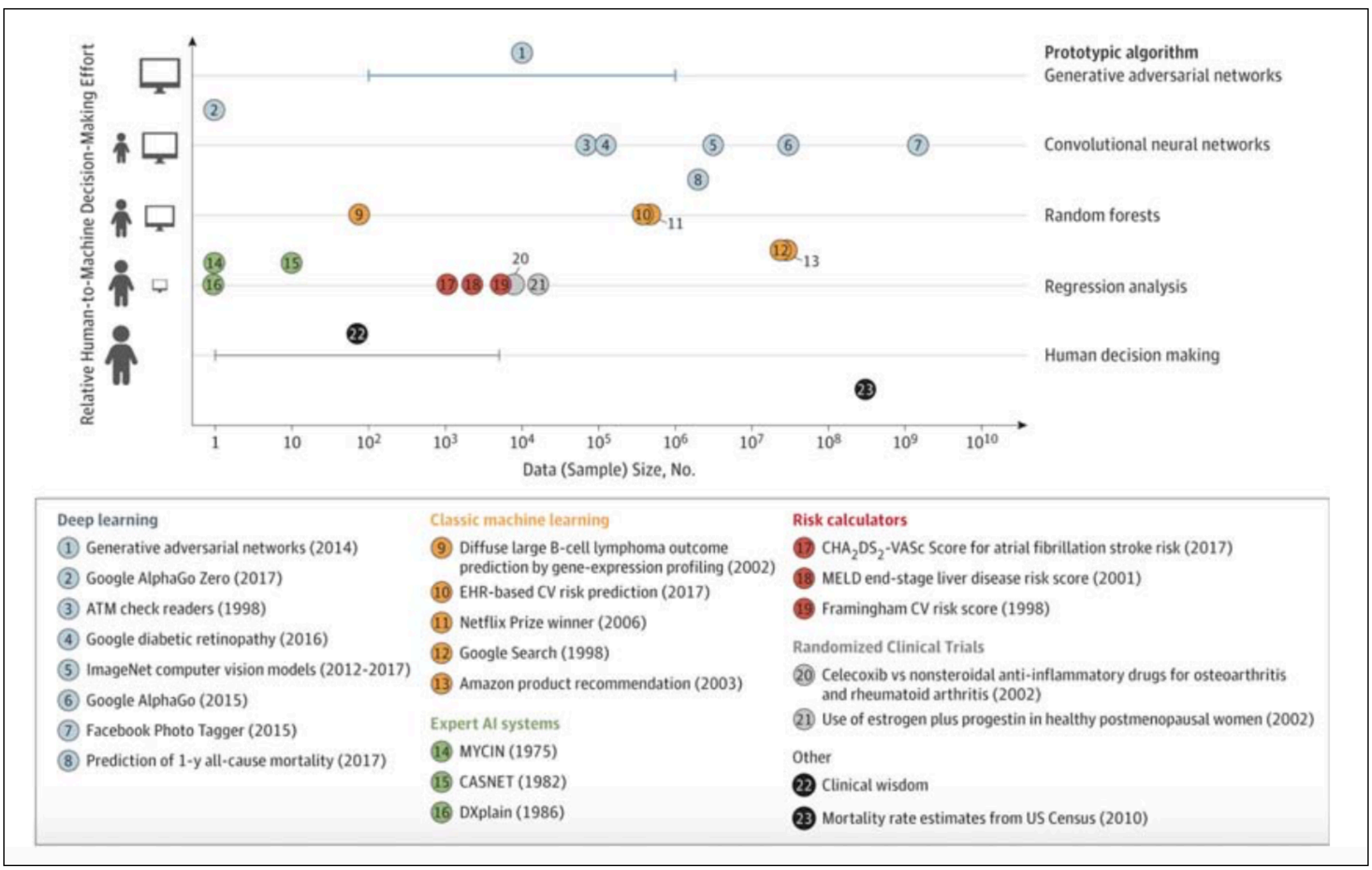
c. Estimate a 3-5 year assessment period for clinical trials using the SaMD
d. Enable a real-world performance monitoring with transparency
[c]

Module 7.2/Artificial Intelligence in Medicine-The Challenges

There are realistic **challenges** for wide AI adoption in biomedicine amongst clinicians **(see Table)**.

Data	Relational database	Data inaccurate	Data incomplete
	Data sharing	Data security	Data standardization
	Data storage and transfer	Data ownership	Data volume
Technology	Black box	Difficult to interpret	Relevance
	Cost	Regulation	Workflow
People	Lack of AI education	Trust	Cultural differences
	Shortage of data scientists	Lack of clinician champions	Hubris
Other	Legal	Bias	Ethics
	Inequity	Data privacy	Business model

Education. First and foremost, there is a lack of focus on data science and AI in the medical school and training program as well as later in continuing medical education (CME). This **knowledge gap,** if it persists, will increase even more as more sophisticated AI technologies are made available for application in medicine and health care. It is important to emphasize that given the present milieu of work burden and escalating knowledge across many other domains, clinicians may simply not have the time nor the desire to learn a difficult domain no matter how interesting or relevant. Perhaps a taxonomy of AI in medicine and health care will be useful for an easier understanding of AI as it pertains to medicine and health care**;** clinicians have a biology mindset and such a classification system can help. To further exaggerate the former issue of under-education and lack of exposure of data science for clinicians, AI (particularly deep learning but to some degree some of the other tools as well) has an inherent “**black box**” nature in that it is not easily explainable nor transparent even to the data scientists themselves (see explainable AI above). These two aforementioned issues combined render AI adoption for clinicians a daunting (but solvable) challenge but also presents a great opportunity to learn an entirely new domain for the willing and even enthusiastic clinician cohort. While regression analyses have yielded some insights into patient risk scores, more sophisticated data science in the form of random forest, CNN, and even GANs will need to analyze these cohorts in the future **(see Figure)**. Overall, some if not most clinicians feel that these AI methodologies should be tested in a clinical setting, either as a randomized controlled trial or as cluster randomization of time periods.



In addition, there are additional challenges that relate more to AI applications in biomedicine that render AI even more complicated than AI in other sectors (see previous section for a more detailed discussion on these topics). The following are major issues from a societal perspective:

Bias. A recurrent theme throughout this book as well as in meetings and discussions on AI in general is the issue of bias (see previous section for a broader discussion). Clinicians are wary of bias as a result of algorithms designed for certain patient populations or single institutions that do not necessarily reflect a more heterogeneous population or additional institutions. There is also the bias that is derived from differences in samples (such as differences in quality of images as well as interpretation of these images by certain groups of specialists).

Equity. There is also an additional issue of inequity (see also previous section). Many aspects of ML in studies may not be fair and equal to all members of the population; these elements can exacerbate health care disparities that already exist. Distributive justice and its principles can potentially be incorporated into the model design and deployment of the models ([31]).

Ethics. An issue related to the aforementioned bias and inequity is ethics (again, see previous section). Among the more often debated areas under this topic for medicine and health care are: 1) Who/what is liable if there is an adverse medical outcome? 2) What if there is an inequity as a result of this new technology not being accessible to everyone, especially those in the third and fourth world? 3) Should/could clinicians and hospitals financially benefit from using patient data to start an AI in medicine startup and company? 4) Who owns and have rights to medical data? There is even discussion of an autonomy algorithm, one which takes data about the patient as input and consequently yields a confidence estimate for a particular patient's predicted health care-related decision as an output with its ethical nuances.

[31] Rajkomar A, Hardt M, Howell MD et al. Ensuring Fairness in Machine Learning to Advance Health Equity. *Ann Intern Med* 2018; 169(12): 866-872.

Regulation. Intertwined with bias and ethics is the area of regulation of this new technology in medicine. Even if we treat AI and its panoply of tools as "**software-as-a-device**", how can we effectively and expediently approve all these upcoming AI tools as these emerge and converge with other advanced technologies (such as AI and augmented reality, see below). Perhaps we need to match this paradigm shift in technology with a parallel philosophical shift in how we regulate. Both the FDA and the AMA deserve much praise for starting just such a shift in the way we conceptualize regulation and oversight in this new technological era ([32]). The **FDA** has proposed new submission type and data requirements based on risk in the form of 510(k) notification, De Novo, or premarket approval application (PMA) pathway, with its Center for Devices and Radiological Health (CDRH) as an important resource. The paper reflects a more innovative strategy (including an algorithm change protocol, or ACP) to the total product lifecycle (TPLC) regulatory approach that will be a more appropriate regulatory process for these new software as a medical devices (SaMD) **(see Figure).** Overall, the FDA and its Good Machine Learning Practices is a much more congruent regulatory strategy with the exponential increase in AI technologies in clinical medicine and health care The **AMA**, on the other hand, has just recently passed its first policy recommendations on augmented intelligence. The recommendations include oversight and regulation of health care AI systems based on risk of harm and benefit accounting for a host of factors as well as payment and coverage for all health care AI systems conditioned on complying with all appropriate federal and state laws and regulations ([33]). In addition, there are also differences in this regulatory domain between regions of the world. For the future, one potential solution is to not regulate device but rather teams or individuals working on the AI tools (akin to clinician licensure). Another possible answer lies in the Turing philosophy of "machines to deal with machines" and devise regulatory algorithms that will overlook algorithms.

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[32] *Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD): Discussion Paper and Request for Feedback.* (regulations.gov).

[33] Personal communications with Sylvia Trujillo and Jesse Ehrenfeld (AMA), 2018-2019.

Figure. FDA and TPLC Regulatory Approach on AI/ML Workflow. The general four main principles elucidated in this diagram include: 1) Establish clear expectations on quality systems and good ML practices (GMLP); 2) Conduct a premarket assurance of safety and effectiveness of those SaMD that require premarket submission; 3) Expect these manufacturers to monitor the AI/ML devices and incorporate a risk management approach; and 4) Enable a real-world performance monitoring with transparency (adapted from FDA white paper).

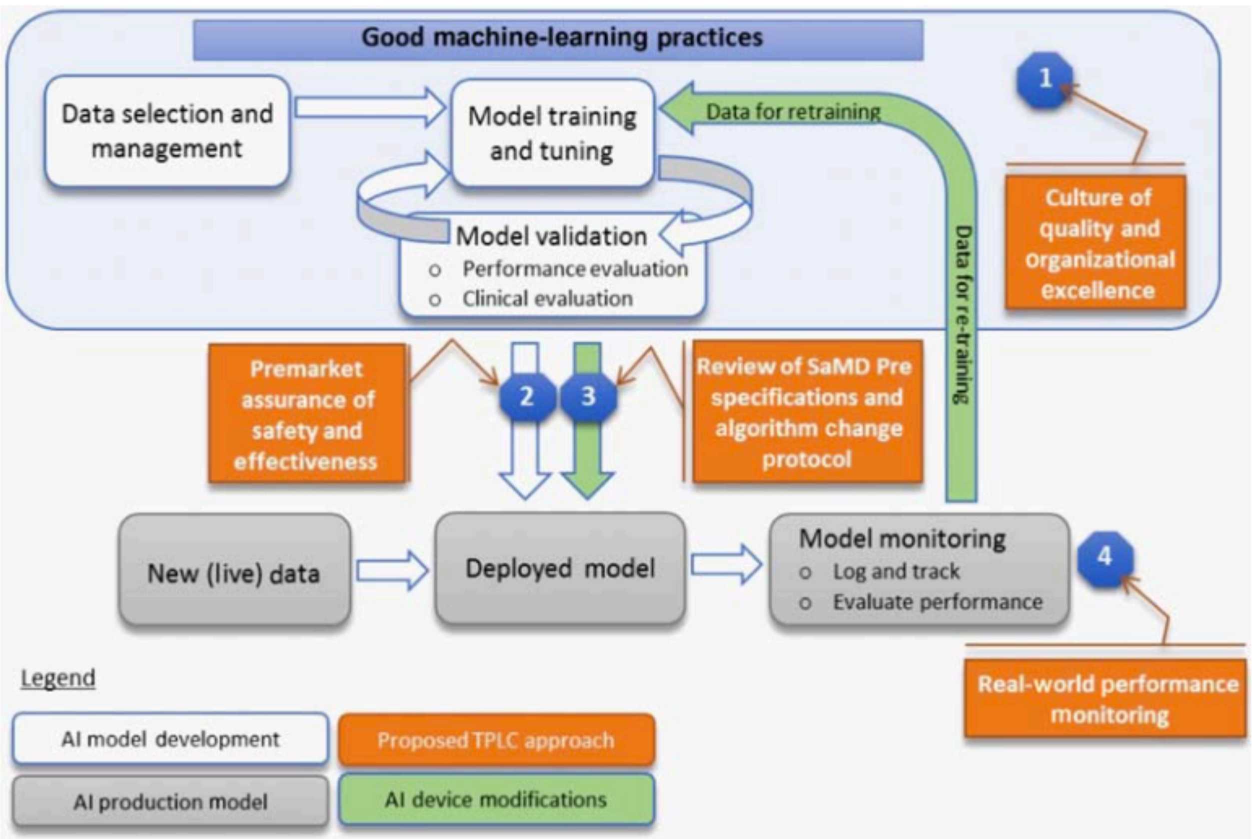

FIGURE 7.2 FDA and TPLC regulatory approach on AI/ML workflow. The general four main principles elucidated in this diagram include (1) establishing the clear expectations on quality systems and GMLP; (2) conducting a premarket assurance of safety and effectiveness of those SaMD that require premarket submission; (3) expecting these manufacturers to monitor the AI/ML devices and incorporate a risk management approach; and (4) enabling a real-world performance monitoring with transparency. *AI*, Artificial intelligence; *FDA*, Food and Drug Administration; *GMLP*, good ML practice; *ML*, machine-learning; *SaMD*, software-as-a-medical-device; *TPLC*, total product lifecycle. Source: *Adapted from FDA white paper*.

Economics. Lastly, and certainly not the least important, is the issue of economics of AI in medicine and health care as it is not clear at present just how the payment models would be designed for AI implementation in health care. One potential solution is to have AI be embedded in a clinical program (and thus overall hospital budget) in the form of an AI-centered team and service. This strategy will enable this team to have a budget and manpower to take on AI-centric projects. Other AI experts have rendered an "AI-as-a-service" model where it is treated as a resource that is utilized when needed (akin to electricity). This concept is especially fitting since Andrew Ng has stated that "AI is the new electricity" (perhaps we can add that health care is a primitive hut with a single lightbulb as the data infrastructure has ample room for improvement). In addition, if AI is deployed in countries in which there is insufficient tertiary and quaternary care, how are procedures, medications, and interventions going to be financed after more new cases are diagnosed?

Overdiagnosis. With all the AI tools that will be available, there can be potential issues of overdiagnosis of diseases that are subclinical. This can lead to the risk-to-benefit ratio not in favor of the patient if therapy has more risk than the subclinical diagnosis of certain conditions. An example would be a subclinical cardiac arrhythmia detected on a wearable device that a primary care or cardiologist decided to treat with an antiarrythmic agent.

Complexity. The nature of biomedicine is intrinsically very complex as it is a biological system with constantly evolving milieu. In addition, many variables in clinical medicine do not have a dichotomous or categorical result and can have a continuous (or fuzzy) nature to the data. Lastly, there is a systems complexity to the person or population with conditions or diseases that may be challenging for any prediction model.

Data Access. Access to data is a significant challenge for stakeholders in AI-related projects due to concerns about data security and privacy as well as hesitation for clinicians and health care organizations to share patient data. **The Health Insurance Portability and Accountability Act of 1996 (HIPPA)** was developed to protect the privacy and security of health information. The purposes of HIPPA include: privacy of health information, administrative simplification, security of electronic records, and insurance portability. There are 18 **HIPPA identifiers** such as name, address, telephone numbers, dates, social security number, photographic image, etc. Projects in AI in health care will need to safeguard these HIPPA identifiers. In addition, clinicians are not accustomed to a culture of sharing patient's data, but recent efforts to have aggregates of data for analytics and AI are being promulgated in collaborative projects such as **PhysioNet**, an online forum for dissemination and exchange of recorded biomedical signals and open-source software and **Virtual PICU** (see under Critical Care Medicine). Additional data resources for projects include: health data.gov., MIMIC Critical Care Database, Broad Institute Cancer Program Dataset, Open Access Series of Imaging Studies (OASIS), and 1000 Genome Project.

Questions 7.3/Clinician Cognition and Artificial Intelligence

1. Which is *incorrect* in System 1 vs 2 thinking:

	System 1	**System 2**
a. **Velocity**	Fast	Slow
b. **Error Rate**	Lower	Higher
c. **Advantage**	Fast	Accurate
d. **Disadvantage**	Biased	Slow

[ ]

2. Tendency to rely or favor an AI decision support system more than human cognition is called:
a. Confirmation bias
b. Automation bias
c. Belief bias
d. Selection bias
[ ]

3. A cardiologist is convinced that a patient with chest pain does not have a myocardial infarction. The EKG did not show obvious ischemic changes so he discharged the patient. He has:
a. Confirmation bias
b. Representative bias
c. Automation bias
d. Availability heuristic
[ ]

4. Rules for good decision making include the following *except*:
a. Be aware of base rates
b. Trust your first intuition for any diagnosis
c. Seek reasons why your decisions may be wrong and entertain alternative hypotheses
d. Ask questions that would disprove, rather than confirm, your current hypothesis
[ ]

5. An ER clinician thinks that the homeless patient has an addiction issue. This is an example of:
a. Representative heuristic
b. Automation bias
c. Confirmation bias
d. Groupthink
[ ]

Answers 7.3/Clinician Cognition and Artificial Intelligence

1. Which is *incorrect* in System 1 vs 2 thinking:

	System 1	**System 2**
a. **Velocity**	Fast	Slow
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d. **Disadvantage**	Biased	Slow

[b]

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c. Confirmation bias
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Module 7.3/Clinician Cognition and Artificial Intelligence

Clinician Cognition and Artificial Intelligence in Medicine
System 1 and System 2 Thinking. Daniel Kahneman, the Nobel Prize-winning psychologist noted for his work on decision making, described System 1 vs System 2 thinking (fast and experiential vs slow and analytical, respectively)(**see Table**). This dichotomy conveniently delineates some of the key differences between clinicians (more prone to System 1 thinking) and data scientists (with their affinity for System 2 thinking). Physicians, especially those in the acute care clinical setting (such as emergency room, ICUs, and operating and procedure rooms) often rely on a fast intuition-based System I thinking that is based on past experiences and judgments. Data scientists, on the other hand, more frequently approach problems with slower and more logical progressive thinking that is rationality-based System 2 thinking. Both of these types of thinking are necessary in medicine, but physicians often lack the time nor the discipline to utilize proportionally more System 2 thinking.

Utilizing different allocations of System 1 and System 2 thinking depending on the situation may be the best strategy; this is a potential future application of AI in aiding this allocation in various case scenarios. For instance, rather than relying on mostly System 1 thinking in urgent or emergent situations, AI can provide the complementary and relatively fast (compared to humans) System 2 thinking to support the former. This combined System 1 and 2 thinking would be ideal in the ICU where urgent and emergent decisions are made often but could always use more System 2 thinking especially in an expeditious manner. On the other hand, excessive or redundant System 2 thinking can be balanced with System 1 thinking to render the entire thinking process more efficient and expedient. For instance, a non-urgent diagnostic dilemma is better off with mostly System 2 thinking than System 1 cognition but perhaps cognitive shortcuts can be made with System 1 input. In short, the human clinician and AI can decide how much System 1 and 2 thinking are necessary to be allocated on a case-by-case basis; this balance or symmetry between the two systems has been termed **dual process thinking**.

Table 2. System 1 vs System 2 Thinking.

	System 1	System 2
Brain Location	Limbic system	Neocortex
Velocity	Fast	Slow
Thinking Type	Intuitive	Rational
	Qualitative	Scientific
	Pattern	Deliberate
Decision Type	Simple	Complex
Conscious State	Unconscious	Conscious
Effort Level	Lower	Higher
Error Rate	Higher	Lower
Characteristic	Associative	Analytical
Advantage	Fast	Accurate
Disadvantage	Biased	Slow

Uncertainty in Biomedicine. One of the major issues with applying data science to biomedicine is the necessary bundling of the **dichotomous** or **categorical element** of the former with the highly empirical and "fuzzy" nature of the latter. There is a relatively high degree of error in human interpretation of medical data in general and this degree of error may even be exaggerated in the future as a result of computer-aided diagnosis (**automation bias**). In addition, there is a high degree of **inter-observer variability** in interpreting medical images or data so any data science applied to this data will need to consider this variability. There is also **intra-observer variability** in which one single clinician may have varying degrees of interpretation for the exact same data. This variability can occur simply from being influenced by medical history attached to the data or innate human mental and perceptual capabilities at different times. Lastly, uncertainty can also occur as a result of a **time continuity** to the patient's health outcome. For example, if an echocardiogram is performed in a teenager with a family history of hypertrophic cardiomyopathy, and is interpreted as "normal", should this study be re-interpreted (to be "not normal") if he turned out to have hypertrophic cardiomyopathy at age 27 years?

Clinician Cognitive Biases and Heuristics. Physicians are often vulnerable to cognitive biases and heuristics with their decision making processes, especially when they are overburdened with their workload and stressed with their expectations to know everything as well as the expediency that they are expected to make decisions today. While cognitive biases distort pure cognition as a result of circumstances based on cognitive factors, heuristics are mental shortcuts to reduce effort in cognition and can therefore lead to biases. In Jerome Groopman's *How Doctors Think* as well as the review on clinicians' biases and heuristics by Klein, both described several cognitive deficiencies in the way physicians think. The table below **(see Table)** delineates some of the common cognitive biases as well as heuristics that may distract the clinician from making the best decision in diagnosis and/or therapy; a few of these biases and heuristics are described in more detail below.

One such cognitive deficiency is **confirmation bias,** which is the tendency for physicians to search for information that confirms one's preexisting hypothesis. In Sherlock Holme's parlance: "It is a capital mistake to theorize before one has data. Insensibly one begins to twist facts to suit theories, instead of theories to suit facts." A clinical example would be a cardiologist thinking that the emergency room patient with chest pain has a myocardial infarction by mistakingly thinking that the borderline EKG is abnormal rather than a normal variant (even if the cardiac enzymes are normal).

Heuristics, on the other hand, are mental shortcuts that anyone who thinks use to decrease the cognitive load. One example such a shortcut that can lead to an error is the **availability heuristic,** or an intellectual shortcut that relies on immediate recall when evaluating a situation. A third cognitive error is **illusory correlation**, or the tendency to perceive two events as causally related when these events are not related and occurred by chance. Klein also further describes the **representativeness heuristic**: this heuristic makes the assumption of a certain conclusion based on available information but without attention to base rates.

In face of all these biases and heuristics, Klein summarized rules for **good decision making** as follows: 1) Be aware of base rates; 2) Consider whether data are truly relevant, rather than just salient; 3) Seek reasons why your decisions may be wrong and entertain alternative hypotheses; 4) Ask questions that would disprove, rather than confirm, your current hypothesis; and 5) Remember that you are wrong more often than you think.

Overall, perhaps the myriad of human biases and heuristics can potentially be neutralized with an objective AI-supported strategy in the decision-making process to reduce the proportion of human-related biases and heuristics that often lead to errors.

Table. Clinician Cognitive Biases and Heuristics

Bias or Heuristic	Description	
Confirmation bias	Proactive and selective seeking of information that confirms our prior and/or existing beliefs	
Availability heuristic	Tendency to rely on events or examples more available in one's memory or experience	
Illusory correlation	Tendency to overestimate a relationship between variables when the evidence is not supportive	
Representativeness heuristic	Rendering a decision based on representativeness of a group and not evidence	
Dichotomous thinking	Situation viewed only in two categories or outcomes instead as a continuum of possibilities	
Automation bias	Tendency to rely or favor automated decision support systems more than human cognition	
Anchoring and adjustment	Tendency to rely too much on one piece of information for decision making	
Selection bias	Bias from selection of data or individuals that renders a randomization not possible	
Affect heuristic	Decisions made with strong influence by emotions that are present	
Groupthink	Group dynamic deficiency when the group desires conformity and makes a suboptimal decision together	
Belief bias	Tendency to judge the strength of the argument based on the plausibility of the conclusion only	
Dunning-Kruger effect	Cognitive bias in which someone mistakenly assesses his/her cognitive ability greater than it really is	
Framing effect	Cognitive bias in which decisions are made depending on situation's positive/negative semantics	
Semmelweis effect	A reflex-like tendency to reject new evidence because it directly contradicts the established paradigm	

Questions 7.4/Levels of Evidence in Medicine

1. When the clinician and investigator have tendencies to submit manuscripts on only studies with a positive diagnostic or therapeutic result, this is called:
a. Confirmation bias
b. Publication bias
c. Representative bias
d. Availability bias
[ ]

2. Which of the following is considered at the *highest* level of the evidence-based medicine pyramid:
a. Double-blinded randomized controlled trial
b. Case-controlled study
c. Case series
d. Non-randomized controlled trial
[ ]

3. What is the order of evidence-based medicine from highest to lowest:
a. Experimental studies> Observational studies> Critical appraisal
b. Critical appraisals> Experimental studies> Observational studies
c. Critical appraisals> Observational studies> Experimental studies
d. Experimental studies> Critical appraisal> Observational studies]
[ ]

4. Which of the following is *not* considered a critical appraisal?
a. Systematic review
b. Meta-analysis
c. Expert opinion
d. Critically appraised individual papers
[ ]

5. A retrospective examination of the condition with diagnosis or therapy implications is called:
a. Case reports
b. Cohort study
c. Randomized controlled trial
d. Case-controlled study
[ ]

Answers 7.4/Levels of Evidence in Medicine

1. When the clinician and investigator have tendencies to submit manuscripts on only studies with a positive diagnostic or therapeutic result, this is called:
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c. Representative bias
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[b]

2. Which of the following is considered at the *highest* level of the evidence-based medicine pyramid:
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c. Critical appraisals> Observational studies> Experimental studies
d. Experimental studies> Critical appraisal> Observational studies]
[b]

4. Which of the following is *not* considered a critical appraisal?
a. Systematic review
b. Meta-analysis
c. Expert opinion
d. Critically appraised individual papers
[c]

5. A retrospective examination of the condition with diagnosis or therapy implications is called:
a. Case reports
b. Cohort study
c. Randomized controlled trial
d. Case-controlled study
[d]

Module 7.4/Levels of Evidence in Medicine

Levels of Evidence in Medicine. Physicians often discuss and perhaps revere **evidence-based medicine (EBM),** which is centered on using evidence to help make sound clinical decisions. The cornerstone of EBM is a hierarchical system of evidence called **level of evidence** and clinicians aim to practice with higher/highest levels of evidence. This system started with the **Canadian Task Force on Periodic Health Examination** in 1979 (levels I, II.1 and II.2, and III with I being at least one randomized controlled trial (RCT) and III being solely expert opinions). Following this, the **United States Preventive Services Task Force (USPSTF)** published its 3-level system with modifications. A **meta-analysis** strategy with the Cochrane Collaboration takes systematic reviews to a higher level of rigor.

The entire continuum or pyramid for EBM is shown below with three broad categories starting from the bottom: **observational studies**, **experimental studies**, and at the highest echelon, **critical appraisals** **(see Table)**. The bottom level is information from anecdotes, publicly available information, and even opinions and recommendations from experts. One level higher is case reports and case series that delineate the conditions and relevant information without a study design of any kind. A **case-controlled study** is a retrospective examination of the condition with diagnosis or therapy implications. A **cohort study** (also called longitudinal study) is a prospective study of patients of a particular condition, disease or risk factor and can also involve an intervention or observation of some kind with before and after study parameters. A **randomized controlled trial (RCT)** is a study with the design involving treated and untreated (or having different interventions) patients in a randomized assignment format and seeing the results of these different groups. RCT, especially in the double-blinded form, is considered the most reliable clinical test of a study. The critically-appraised articles and reviews are highly regarded articles from usually the leaders and experts in that particular realm. Finally, the **meta-analyses** are sometimes performed by the Cochrane Collaboration, which is an international virtual effort to study available information in an unbiased way; this final level of evidence is considered the highest level of evidence in biomedicine.

Major criticisms of EBM include a **publication bias**, which refers to the clinician and investigator tendencies to publish only studies with a positive diagnostic or therapeutic result. In addition, the terms of the criteria for the levels of evidence are not always agreed upon and these **imprecise definitions** are often confusing and misleading. These guidelines or recommendations are very often out of date and do not accommodate more recent ideas and/or study results; in short, the information is not timely and therefore lack **real-time relevance**. Even with well-designed RCTs, often there is no clear **actionable recommendation** and the phrase "further studies or investigations are warranted" is frequently the conclusion. Finally, even with clinical guidelines that are published and discussed in conferences, clinicians often do not have incentives to attain **adherence** to these recommendations. It is entirely possible that EBM, for a myriad of reasons including some not listed above, is simply becoming more obsolete and needs to be modified to reflect current era of AI in medicine (at least as a strategic complement to each other).

Level of Evidence	Level
Critical Appraisal	***Highest***
Meta-Analyses	
Systematic Review	
Critically-Appraised Topics	
Critically-Appraised Individual Articles	
Experimental Studies	
Randomized Controlled Trials	
Non-Randomized Controlled Trials	
Observational Studies	
Cohort Studies	
Case-Controlled Studies	
Case Series and Case Reports	
Expert Opinion and Information	***Lowest***

Questions 7.5/Clinician Perception and Cognition

1. Which of the following tasks would be considered the *most* difficult for artificial intelligence today?
a. Medical image interpretation
b. Integrated data analytics
c. Creative problem solving
d. Automated repetitive tasks
[ ]

2. Which of the following tasks would be considered the *least* difficult for artificial intelligence today?
a. Medical image interpretation
b. Integrated data analytics
c. Creative problem solving
d. Automated repetitive tasks
[ ]

3. Of the following, which would be expected to be the *most* challenging for artificial intelligence?
a. Complex surgical procedure
b. Integrated data analytics
c. Medical image interpretation
d. Automated repetitive tasks
[ ]

4. Of the following brain functions, which is considered the most critical for medical image interpretation?
a. Cognition
b. Perception
c. Operation
d. None of the above
[ ]

5. Of the following brain functions, which is considered the most critical for creative problem solving?
a. Cognition
b. Perception
c. Operation
d. None of the above
[ ]

Answers 7.5/Clinician Perception and Cognition

1. Which of the following tasks would be considered the *most* difficult for artificial intelligence today?

a. Medical image interpretation
b. Integrated data analytics
c. Creative problem solving
d. Automated repetitive tasks
[c]

2. Which of the following tasks would be considered the *least* difficult for artificial intelligence today?

a. Medical image interpretation
b. Integrated data analytics
c. Creative problem solving
d. Automated repetitive tasks
[d]

3. Of the following, which would be expected to be the *most* challenging for artificial intelligence?

a. Complex surgical procedure
b. Integrated data analytics
c. Medical image interpretation
d. Automated repetitive tasks
[a]

4. Of the following brain functions, which is considered the most critical for medical image interpretation?

a. Cognition
b. Perception
c. Operation
d. None of the above
[b]

5. Of the following brain functions, which is considered the most critical for creative problem solving?

a. Cognition
b. Perception
c. Operation
d. None of the above
[a]

Module 7.5/Clinician Perception and Cognition

Clinician Perception/Cognition. Most, if not all physicians in their subspecialties, can be configured by three basic areas of thinking that involves different areas of the brain in which they perform their tasks (how much time they spend in these areas rather than whether they are capable of performing these functions)**(see Figure)**: perception, cognition, and operation.

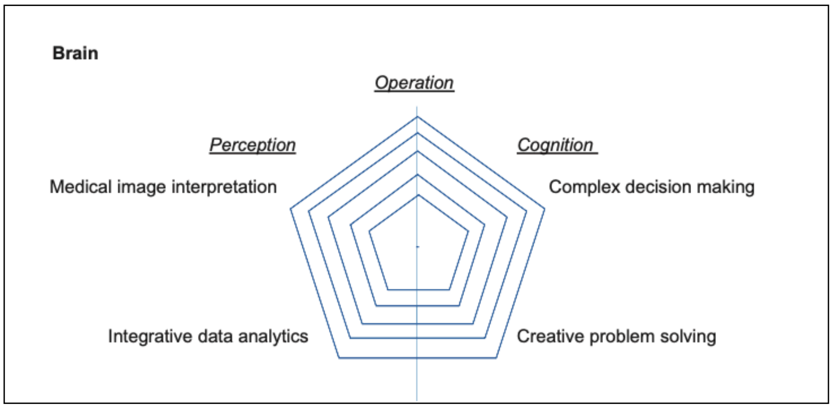

Figure. The Clinician's Brain. A spider diagram can be drawn for each subspecialty to see how much perception, cognition, vs operation that subspecialist does on a day-to-day basis. The concentric pentagons can be levels 1-5 going outward (with "1" the innermost pentagon being no or little activity in that area to "5" being highest level of activity in that area). For instance, a radiologist would rank "medical image interpretation" to be a "5" as a radiologist spends much of the time performing that task.

1) **Perception**- these are tasks clinicians do that machines can currently do with reasonable accuracy and speed. One such task is **medical image interpretation** as computer vision and CNN are able to interpret medical images as good if not better than single or groups of a certain image-focused subspecialty. In addition, **integrative data analytics** with machine and deep learning have capabilities that surpass what humans can do. With deep learning and its variants, some of the traditional image interpretation and integrative data analytics can be performed by machines but humans can still be able to provide oversight and design.
2) **Cognition**- these are tasks that humans are more able to do compared to machines but machines may be able to take on these tasks in the near future. One such task is **complex decision making**, especially in real-time, as biomedicine in most subspecialties is full of this type of task. In addition, **creative problem solving** remains uniquely human and an essential part of many areas in medicine and health care. While deep learning and its variants (such as deep reinforcement learning) are making progress in both of these areas, these methodologies are not yet mature nor sophisticated enough for full deployment in medicine.
3) **Operation-** these are manual tasks, especially advanced tasks, that computers are not able to do at this point. As much as robotics and related technologies have advanced in the past decade, much of **complicated procedures** and **operations** will not be able to be performed entirely by robotic methodologies in the near future. This area can be

explored for a hybrid model in which humans benefit from the relative strengths of the robots (such as better in situ vision, elimination of physiological tremors, better ergonomics for surgeons, etc) while providing creativity and oversight.

In short, perception-focused tasks can be mitigated by AI for the subspecialist so he/she can either have oversight over these tasks or take on tasks in the cognition areas with cognition-centric tasks that can be explored in the near future. Perhaps an AI strategy with more symmetric or individualized task allocation will ensure less burnout for the over-burdened clinician.

Questions 7.6/Current Applications of AI in Medicine

1. Which artificial intelligence methodology is *most* useful for static medical imaging?
a. Logistic regression
b. Convolutional neural network (CNN)
c. Support vector machine
d. Linear regression
[ ]

2. Which of the following statements is *true* about medical image interpretation using artificial intelligence?
a. The main AI methodology is recurrent neural network (RNN)
b. Comparative studies show that AI is as good or even better than human subspecialists
c. Deployment has not yet been possible with moving images
d. Deployment thus far has only been in radiology but not in other areas
[ ]

3. The management of a complex patient with multiple chronic conditions would be best suited for all of the following methodologies *except*:
a. Deep learning
b. Deep reinforcement learning
c. Graph database
d. Logistic regression
[ ]

4. Of the following areas, which has seen the most robust deployment of artificial intelligence?
a. Wearable technology
b. Altered reality
c. Medical imaging
d. Real-time decision support
[ ]

5. For artificial intelligence to recognize a picture of a cat as "cat", the main task involve:
a. Classification and localization
b. Object detection
c. Instance segmentation
d. Semantic segmentation
[ ]

Answers 7.6/Current Applications of AI in Medicine

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c. Graph database
d. Logistic regression
[d]

4. Of the following areas, which has seen the most robust deployment of artificial intelligence?
a. Wearable technology
b. Altered reality
c. Medical imaging
d. Real-time decision support
[c]

5. For artificial intelligence to recognize a picture of a cat as “cat”, the main task involve:
a. Classification and localization
b. Object detection
c. Instance segmentation
d. Semantic segmentation
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Module 7.6/Current Applications of AI in Medicine

The present state of artificial intelligence in medicine includes a myriad of applications, and these application areas will be generalized into ten main categories and separately described in more detail below. This medical applications in AI orientation will be useful to set the framework for the section to follow (*Specific Strategies and Applications of AI for Selected Subspecialties)*.

Medical Imaging. There is much promise in the utilization of AI methodologies such as deep learning (in particular convolutional neural network, or CNN)(see above for details) for automated medical image interpretation and/or augmented medical imaging. The image interpretation tasks include: classification, regression, localization, and segmentation. The images that this AI capability can be made available include not only static images (like a chest X-rays, pathology slides, fundus or skin photographs, and MRI images) but also starting to become available for moving images (such as ultrasound images, pictures during procedures such as endoscopic examinations, and echocardiograms). This AI computer vision capability, already as accurate if not more so than single or groups of clinicians, is especially needed in the image-focused subspecialties such as radiology, pathology, dermatology, ophthalmology and cardiology in the near future as both the volume as well as the complexity of imaging continue to escalate beyond what human specialists (even excellent ones) are able to accommodate and perform at a high level.

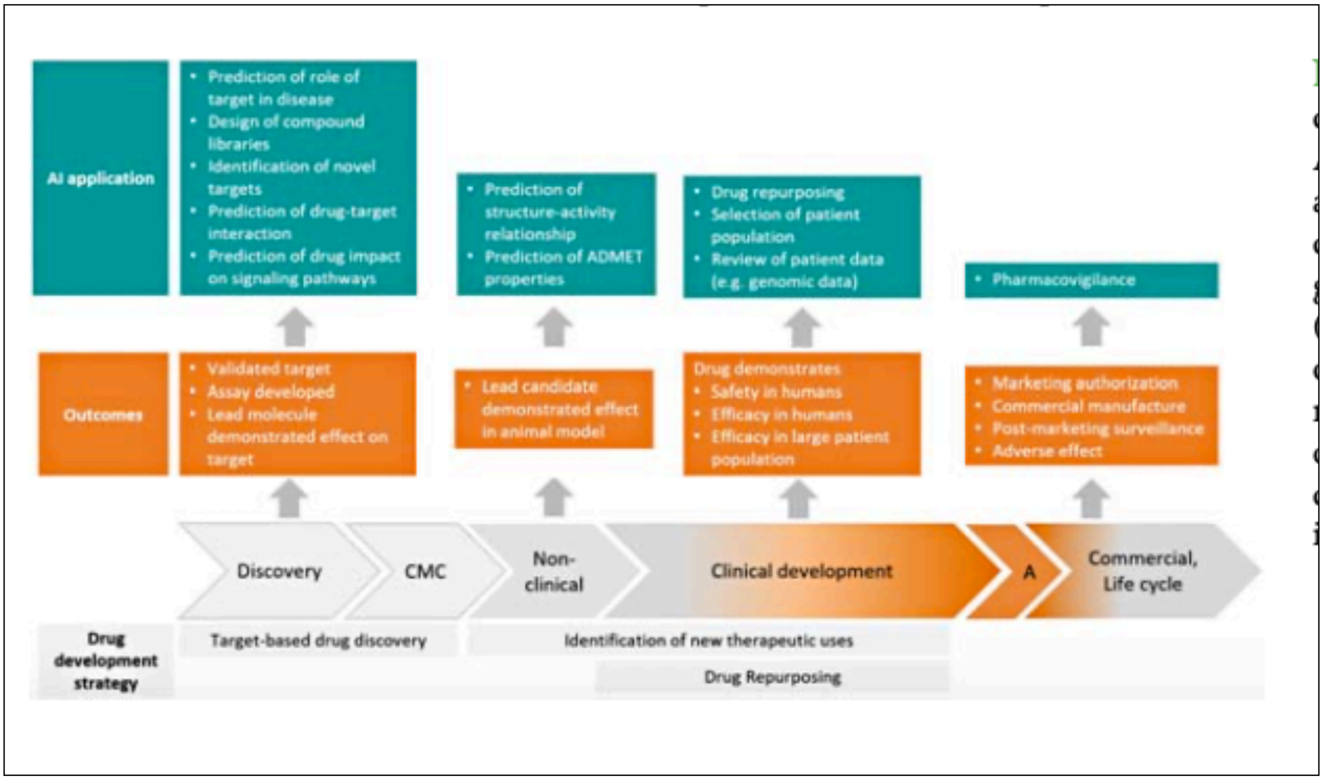
Altered Reality. The area of augmented (AR), virtual (VR), and mixed reality (VAMR) will be able to leverage AI technology and use this resource to the fullest for a variety of purposes; these include education and training as well as simulation and immersive scenarios for all stakeholders (including patients and families) and preoperative and intra-operative imaging and planning for certain medical and surgical subspecialists. In a recent review, the application of virtual reality and AI is especially useful in surgical training (especially laparoscopic and orthopedic surgery), pain management, and therapeutic treatment of mental illnesses. The three altered reality technologies, combined with AI, will enable any clinician to wear a different "lens" in the practice of his/her specialty.

Decision Support. Clinical decision support, especially with an urgent timeline, is one of the most difficult challenges in medicine; just how machine intelligence can help a clinician to solve a difficult and complex clinical situation will be one of the holy grails of AI in medicine. The number of publications and companies now involved in this domain of clinical decision support using AI reflects both the interest as well as the potential in this area, albeit with its nuances and challenges with data and EHR in health care. A recent review of the history of clinical decision support (CDS) states the dramatic improvement in this sector due to the advent of cognitive aids and AI tools to support diagnosis, treatment, care-coordination, surveillance and prevention, and health maintenance or wellness. While it is laudable that AI was able to defeat the human champion in the game *Go*, the practice of medicine, especially in the chaotic domains of the emergency room, intensive care unit, and operating rooms, are more akin to the real-time strategy games like *StarCraft*.

Biomedical Diagnostics. Bedside biomedical monitoring has been unidirectional: displaying data such as vital signs in a continuous fashion but not analyzing and understanding data internally so therefore, not at all "intelligent". AI has the potential to change this paradigm by deploying machine and deep learning to this rich data milieu (with RNN described above) and deriving knowledge and intelligence in a real-time fashion. The hope with monitoring in the hospital setting is for AI to provide real-time analytics coupled with EHR to provide an even more robust decision support tool than either aspect alone. This change in mindset is the concept of AI systems for complex decision-making in acute care medicine, with more focus on time pattern based analysis and decisions by AI and communication to the human team with a feedback loop.

Precision Medicine. The paradigm of precision medicine with its complexity of decisions that can be made and enormity of data to be analyzed is particularly well suited for the portfolio of AI methodologies such as deep learning (especially its AI congener deep reinforcement learning) as similar patients can be identified and assessed. Precision medicine at its highest level will need a disruptive graph or even hypergraph database configuration and a computational platform for new biomedical knowledge discovery. An essential part of the precision medicine paradigm is individualized therapy based on genotype-phenotype coupling and pharmacogenomic profiles that will provide a health "GPS" for every person. A recent review paper on AI and precision medicine emphasizes the key to success of AI for precision medicine is data quality and relevance and also machine learning application in functional genomic studies with physiological genomic readouts in disease relevant tissues with advanced AI. In short, AI can be a very useful tool for individualized risk prediction and medicine can change towards prevention, personalization, and precision.

Drug Discovery. Diverse disciplines such as language, neurophysiology, chemistry, toxicology, biostatistics, and medicine can converge to leverage AI and ML/DL to design novel drug candidates. The cognitive solutions are designed to fully integrate and analyze relatively large data sets such as in life sciences for drug discovery. Such strategies include collecting domain specific content in the form of scientific literature and patents, drug and disease related ontologies, pre-clinical clinical trials, electronic medical records, labs and imaging data, genomic data, and even claims data and social media data. In addition, there are many potential applications of deep learning for large datasets in pharmaceutical research (such as physicochemical property prediction, formulation prediction, and properties such as absorption, distribution, metabolism, excretion, toxicity, and even target prediction) as well as molecular informatics and computer-assisted drug discovery. Mak delineated the entire process of AI utilization in the drug development process with applications of AI at each stage below **(see Figure)**.



AI application
Prediction of role of target in disease
Design of compound libraries
Identification of novel targets
Prediction of drug-target interaction
Prediction of drug impact on signaling pathways
Prediction of structure-activity relationship
Prediction of ADMET properties
Drug repurposing
Selection of patient population
Review of patient data (e.g. genomic data)
Pharmacovigilance
Outcomes
Validated target
Assay developed
Lead molecule demonstrated effect on target
Lead candidate demonstrated effect in animal model
Drug demonstrates
Safety in humans
Efficacy in humans
Efficacy in large patient population
Marketing authorization
Commercial manufacture
Post-marketing surveillance
Adverse effect
Discovery
CMC
Non-clinical
Clinical development
A
Commercial, Life cycle
Drug development strategy
Target-based drug discovery
Identification of new therapeutic uses
Drug Repurposing

Digital Health. The current digital health portfolio entails software as well as hardware, so it includes telemedicine, cellular phone communications, web-based tools, and wearable technology; this will create the futuristic internet of everything in medical and healthier care delivery (see more detailed discussion later). Of particular significance will be the ability to provide data in multiple formats (even videos of patients) via cell phone. An essential part of digital health is the use of information and communication technologies as well as AI in the form of data mining of the incoming data as well as machine and deep learning for anomaly detection, prediction, and diagnosis/decision making in a continuous manner. AI in digital health, if applied strategically and efficiently, also has the potential to revive human-to-human bonding with application of emotional intelligence in health care.

Wearable Technology. The coupling and synergy of AI with wearable technology are essential for both technologies to thrive in the next decades. The data mining process for wearable technology data can be daunting and includes a feature extraction/selection process for modeling/learning to yield detection, prediction, and decision making for the clinician. Expert knowledge and metadata can influence modeling and learning for this incoming data "tsunami". In addition, wearable technology has also taken a different perspective in this time of AI, especially with the possibility of wide adoption of simple AI tools embedded in medical devices (such as the recent FDA-cleared, AI-enabled wearable device that measures multiple vital signs from Current Health that utilizes machine learning algorithms to detect problematic changes in data).

Robotic Technology. Surgical robotics such as the da Vinci system has penetrated even community hospitals and has recently advanced to include 3D visualization and data analytics. Meanwhile, other uses of robotic technology in health care include delivery and sterilization of health care equipment and devices, management of pharmaceutical products, and physical therapy in various venues. Human-robot interaction and relationship are being evaluated in a variety of clinical scenarios such as physical or psychiatric rehabilitation and education and training. There is an ongoing debate about robotics and its ethical implications in the future of society including an exacerbation of health care disparities and creation of new disparities. Lastly, some of the ethics that involve use of robotics are extended for use of AI (see under Ethics above).

Virtual Assistance. AI is very involved in the evolution of virtual assistants as these are dividends of natural language processing (including natural language understanding and generation). There are also AI-inspired software agents that are capable of performing certain tasks or services via text or voice for health care (examples are Apple's Siri, Google Assistant, and Amazon's Alexa). A chatbot (or bot) is a service that is capable of conducting a conversation with a human as a result of using rules governed by AI (see above). Sophisticated chatbots can even use machine learning and therefore can get "smarter" as it converses with people; other names for this entity include: virtual or conversational agent. While it is still relatively early for these virtual assistants to have impact in medicine and health care, it is certainly a robust area ready for future applications.

The following table **(see Table)** summarizes each of the ten application categories as well as examples of applications and the clinicians that would be in the best position to directly benefit from these applications:

AI Application Category	Application Examples (Clinicians with most relevance)
Medical Imaging	Static images (All clinicians, especially image-oriented subspecialties) Moving images (All clinicians, especially image-oriented subspecialties) Hybrid image (All clinicians, especially image-oriented subspecialties) Radiomics with therapy (All clinicians, especially image-oriented subspecialties) Facial recognition of syndromes and conditions (All clinicians)
Altered Reality	Education and training for clinicians (All clinicians, including nurses) Education for patients and families (All clinicians, including nurses) Preoperative planning (Surgery, procedure-oriented subspecialties) Operation visual augmentation (Surgery, procedure-oriented subspecialties) Pain management (Anesthesia, ICU, procedure-oriented subspecialties) Psychiatric treatment (Psychiatry, primary care) Rehabilitation (PM&R, orthopedic surgery, primary care)
Decision Support	ICU patient decisions (ICU, surgery, cardiology) Hospital patient decisions (All clinicians, including nurses) Outpatient chronic disease management (All clinicians, including nurses) Risk prediction and intervention (All clinicians, especially primary care) Calculation of scores (All clinicians) Patient triage (All clinicians, especially emergency medicine)
Biomedical Diagnostics	Real-time data analytics (ICU, ED, anesthesiology, surgery, cardiology) Embedded AI in monitoring (ICU, ED, anesthesiology, surgery, cardiology) AI for biomedical testing (ICU, ED, anesthesiology, surgery, cardiology)
Precision Medicine	Precision medicine including pharmacogenomic profile (All clinicians) New disease subtypes (All clinicians) Chronic disease management (All clinicians, especially primary care) Population health management (All clinicians, especially primary care) Clinical trial candidates (All clinicians, especially primary care)
Drug Discovery	New drugs for therapy (All clinicians, pharmacists, and researchers)
Digital Health	Chronic disease management (All clinicians, especially primary care) Population health management (All clinicians, especially primary care) Telehealth and telemedicine (All clinicians, including nurses)
Wearable Technology	Chronic disease management (All clinicians, especially primary care) Population health management (All clinicians, especially primary care)
Robotic Technology	Robot-assisted surgery (Procedure-oriented subspecialties) Physical rehabilitation (Neurologists, PM&R, orthopedic surgery) Administrative task automation (All clinicians and administrators)
Virtual Assistants	Medical advice and triage (All clinicians, especially primary care) Health coaching and education (All clinicians, especially primary care) Chart review and documentation (All clinicians, including nurses) Psychiatric treatment (Psychiatry, primary care)

Image-oriented sub specialties: cardiology, dentistry, dermatology, gastroenterology, ophthalmology, pathology, and radiology.
Procedure-oriented sub specialties: cardiology, dentistry, dermatology, gastroenterology, ophthalmology, pulmonology, radiology, and surgery.

ED- emergency department clinicians; ICU- intensive care unit clinicians; PM&R- Physical medicine and rehabilitation

Chapter 8: Artificial Intelligence in Subspecialties

Questions 8.1/Applications of AI for Selected Subspecialties

1. Of the following subspecialties, the one with the *least* activity in AI adoption is:
a. Neonatology
b. Critical care medicine
c. Cardiology
d. Radiology
[ ]

2. An ICU clinician would like to design a project looking at vital sign changes associated with an imminent cardiac arrest. The AI methodology best suited for continuous time series data would be:
a. Convolutional neural network (CNN)
b. Recurrent neural network (RNN)
c. Support vector machine
d. Logistic regression
[ ]

3. For artificial intelligence to recognize a picture of a tumor as "tumor", the main task involves:
a. Classification and localization
b. Identification
c. Visualization
d. Diagnosis
[ ]

4. What task is needed for outlining a tumor on an MRI?
a. Image classification
b. Object detection
c. Instance segmentation
d. None of the above
[ ]

5. Which of the following demonstrates the steps involved in the emerging translational field of radiomics in the correct order:
a. Imaging and segmentation> Feature extraction> Feature selection> Analysis and modeling
b. Imaging and segmentation> Analysis and modeling> Feature extraction> Feature selection
c. Feature extraction> Imaging and segmentation> Feature selection> Analysis and modeling
d. Feature extraction> Imaging and segmentation> Analysis and modeling> Feature selection
[ ]

Answers 8.1/Applications of AI for Selected Subspecialties

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[a]

Questions 8.2/Applications of AI for Selected Subspecialties

1. What task is needed for outlining a mass on a CT?
a. Image classification
b. Object detection
c. Instance segmentation
d. Identification
[ ]

2. Image interpretation tasks include all of the following *except*:
a. Classification
b. Detection
c. Visualization
d. Segmentation
[ ]

3. All of the following are potential dividends of deep learning in radiology *except*:
a. Fast and efficient screening tool for life-threatening diagnoses that need to lead to an acute intervention
b. Novel discoveries in medical images that can help with subtyping, therapy modification, and/or prognostication
c. Add other information (such as EHR or genomic analyses) to enable a radiomic approach to medical image interpretation
d. Perform an interventional procedure such as placing a stent in the renal artery for severe stenosis
[ ]

4. In the ICU setting, which of the following use of artificial intelligence has the *least* experience?
a. Real-time therapy guidance with deep reinforcement learning
b. Risk prediction for ICU patients with machine learning
c. Administrative tasks such as prior authorizations with robotic process automation
d. Chest X-ray interpretation with deep learning
[ ]

5. A promising machine learning methodology for discovery new disease subtypes is:
a. Logistic regression
b. Support vector machine
c. Linear regression
d. Cluster analysis
[ ]

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Questions 8.3/Applications of AI for Selected Subspecialties

1. Which of the following AI-inspired methodologies is the most challenging for artificial intelligence in the field of anesthesiology?
a. Modeling drug behavior
b. Mitigating administrative burden that involves repetitious tasks
c. Providing real-time therapy guidance
d. Configuring a risk-prediction model
[ ]

2. The *most* difficult challenge for artificial intelligence to augment the anesthesiologist practice is:
a. Complex decision support in real-time
b. Medical image interpretation
c. Databases management
d. Communication with other clinicians
[ ]

3. In cardiovascular medicine, artificial intelligence has had the *least* impact in which of the following areas:
a. Advanced cardiac imaging
b. Electrocardiogram and monitoring
c. Altered reality for training and education
d. Decision support with risk score
[ ]

4. The major challenges in ICU data and databases and artificial intelligence projects include all of the following *except*:
a. Compartmentalization of data within and with other institutions
b. Integrity of data (erroneous, missing, and imprecise data)
c. Complexity of data (multimodal data)
d. Quantity of data
[ ]

5. What is *not* true about the Medical Information Mart for Intensive Care (MIMIC) accessible critical care database?
a. It is a multi-center database from over 100 adult ICUs
b. It has information in the critical care unit from over 50,000 adults
c. The data includes general data as well as physiological data and medications and lab tests
d. It has notes and reports (imaging reports, progress notes, discharge summary, etc)
[ ]

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Questions 8.4/Applications of AI for Selected Subspecialties

1. In a landmark paper that compared deep learning vs dermatologists in examining photographs of skin lesions, the deep learning methodology used was:
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b. Recurrent neural network
c. Generative adversarial network
d. Unsupervised learning
[ ]

2. Deployment of artificial intelligence in the emergency room setting includes which of the following:
a. Adverse drug events
b. Emergency room workflow
c. Severity of illness
d. All of the above
[ ]

3. The endocrinological disorder most studied with artificial intelligence methodologies is:
a. Thyroid disorders
b. Diabetes (type II)
c. Adrenal insufficiency
d. Pituitary disorders
[ ]

4. The most productive deployment of deep learning thus far in gastroenterology has been in:
a. Decision support for treatment of gastric ulcers
b. Endoscopy and image interpretation
c. Image interpretation for abdominal ultrasound
d. Staging and treatment for liver cancer
[ ]

5. Contributions by artificial intelligence for treating COVID-19 include the following *except*:
a. Real-time ICU management based on pooled ICU data
b. Protein structure prediction based on genome information
c. Drug discovery for treating disease
d. Prediction modeling using social media and travel records
[ ]

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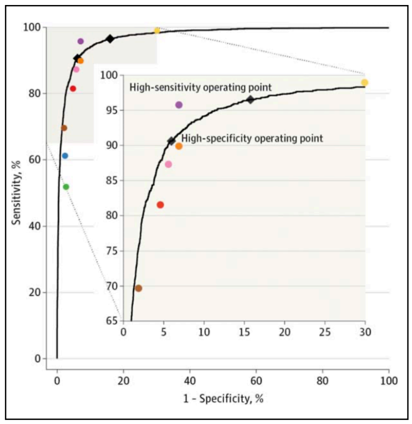
Questions 8.5/Applications of AI for Selected Subspecialties

1. The M.D. Anderson/IBM Watson for Oncology project did not meet expectations for the following reasons *except*:
a. Lack of competitive bidding
b. Insufficient due diligence
c. Lack of total IT department buy-in
d. Lack of clinician champions
[ ]



2. Select the *incorrect* statement regarding the graph on the right of deep learning vs ophthalmologists:
a. This is an AUC of the ROC and demonstrates performance in prediction
b. The methodology was recurrent neural network
c. The black line is the deep learning performance curve
d. The ophthalmologist in purple above the AUC outperformed the deep learning tool
[ ]

3. The first FDA approved fully autonomous AI-based diagnostic tool is used to detect:
a. Heart failure
b. Diabetic retinopathy
c. Melanoma
d. Pulmonary embolism
[ ]

4. Reasons for using AI as a resource in pediatrics include all of the following *except*:
a. The heterogeneity of pediatric disease phenotypes
b. The prevalence of rare diseases
c. The smaller sizes of the pediatric patients
d. The relatively lower resources for care
[ ]

5. The paradigm of AI is a good resource for precision medicine for the following reasons *except*:
a. The complexity of decisions
b. The enormity of data to be analyzed
c. Patients of the same disease can have the exact same therapeutic regimen
d. The heterogeneity of data and sources
[ ]

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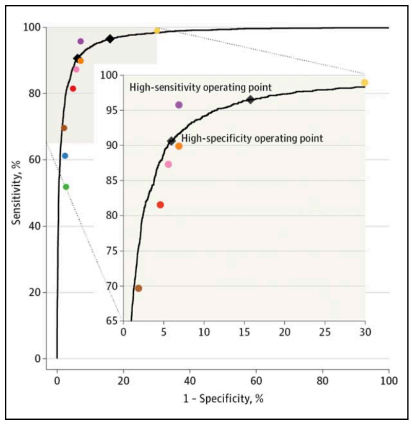

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Module 8.1-8.5/Applications of AI for Selected Subspecialties

The Present State of AI in Subspecialties

AI-related reports in various subspecialties since 1950 **(see Table)** are separated into “high’, “medium”, and “low” use groups based on the current year (2019) published reports. This is a cursory analysis and not an in-depth one with every single reference accounted for (there is much overlap amongst subspecialties in AI-related publications). The subspecialties range from almost 300 reports in radiology (not surprising given its focus on deep learning and computer vision), to only a few in several fields that are not image-intensive (such as infectious disease). Interestingly, the neurosciences (neurology and neurosurgery as well as psychiatry) are on this list of medium/ high user groups that have an AI presence as there is much emphasis of neuroscience currently in artificial intelligence. Finally, most subspecialties, even those in low and medium use subspecialties, have seen a sizable increase in the annual number of published reports in this past decade.

Subspecialty	Total Published Reports (since 1950)	Published Reports (Last 10 years)	Published Reports (Last 5 years)	Published Reports (through 6/2019)
High Level (>100 articles in 2019)				
Radiology	*5778*	*3484*	*2106*	*286*
Oncology	*10825*	*7606*	*3741*	*253*
Surgery	*14390*	*9524*	*3632*	*230*
Pathology	*7861*	*5606*	*3098*	*186*
Medium Level (50-100 articles in 2019)				
Epidemiology	*3168*	*2349*	*1373*	*75*
Neurology	*1110*	*885*	*751*	*64*
Cardiology	*662*	*475*	*370*	*55*
Critical Care Medicine	*1245*	*721*	*464*	*53*
Low Use (<50 articles in 2019)				
Psychiatry	*1268*	*939*	*778*	*49*
Genomic Medicine	*520*	*492*	*425*	*44*
Gatroenterology	*307*	*257*	*202*	*44*
Neurosurgery	*1249*	*788*	*445*	*39*
Internal Medicine/ Primary Care	*852*	*562*	*352*	*32*
Ophthalmology	*367*	*284*	*231*	*31*
Pediatrics	*563*	*447*	*381*	*27*
Pulmonology	*331*	*244*	*204*	*26*
Dermatology	*241*	*190*	*152*	*25*
Emergency Medicine	*298*	*209*	*175*	*21*
Anesthesiology	*444*	*303*	*193*	*20*
Obstetrics and Gynecology	*591*	*473*	*210*	*18*
Infectious Disease	*374*	*306*	*224*	*16*
Endocrinology	*193*	*174*	*130*	*8*

The Subspecialties and AI Strategy and Applications

AI Applications for All Subspecialties. For all subspecialties, however, certain general AI application strategies are listed below for now (or in the near future) and can be considered by almost every clinician from radiology to primary care:

1. **Use of deep learning in medical image interpretation.** This is perhaps the most impressive AI dividend in biomedicine with DL/CNN performing at human (or above) levels of performance (measure by AUC). One of the best potential uses of this methodology is a fast and efficient **screening** tool for life-threatening diagnoses that need to lead to an acute intervention (pneumothorax and drainage or cerebral vascular accident and intervention) for any clinician; this AI capability is ideal for any institution with a large volume of image studies or for a health care facility lacking specialized expertise. Another aspect of this screening is the **accelerated diagnosis** timeline to diagnose non life-threatening diagnoses but nevertheless significant conditions (such as a small pneumonia that can be treated more expeditiously with antibiotics). Of course this screening strategy may be counterproductive if there is automation bias (over reliance on this mechanism) or if the AI tool is not able to pick up small or early findings of these diagnoses. Another dividend from this sophisticated DL-enabled image interpretation is **novel discoveries** in medical images (such as tumor-stroma interfaces) that can help with subtyping, therapy modification, and/or prognostication. Yet another aspect of this DL approach to medical image interpretation is the capability to add other information (such as EHR or genomic analyses) to enable a **radiomic approach** to medical image interpretation. Overall, there is an ongoing question about the absolute validity of the preliminary reports of CNN and medical image interpretation to date as most have not had clinical validation by clinicians nor have these reports been published in a peer-reviewed format; in addition, these early studies have not been clinically tested across many hospitals (outside the study institutions). The FDA, however, has approved the first autonomous diagnosis software (for diabetic retinopathy).

2. **Use of machine or deep learning for decision support.** The complex nature of patient care, especially with escalating amount and types of data as well as increasing number of clinical guidelines and treatment plans, is better suited for ML/DL given enough clinician direction and input. The main use is for **risk prediction** using EHR data for improved allocation of scarce health care resources with so many health facilities and patient cohorts burdened by unplanned hospital admissions with morbidity and mortality risk. One aspect of risk prediction with utilization of DL models is whether these AI tools can be eventually applied to the holy grail of risk prediction: real-time risk prediction. Although there is recent work on deploying deep reinforcement learning in particularly the ICU setting for predictions of events such as septic shock, this work is preliminary and needs more real-world experience. In addition, these AI tools can also be used for workflow in venues such as the emergency department for better resource allocation.

3. **Use of AI tools for administrative support.** AI tools can be utilized for automating processes in health care that are mundane and tedious as performed by humans. Relatively primitive AI tools such as robotic process automation has already made some impact in reducing human burden in administrative tasks in other business sectors and can have the same impact with health care **administrative tasks** such as prior authorization, insurance eligibility, and clinician credentialing.

4. **Use of natural language processing for communication.** Simple tools such as virtual assistants and chatbots can be used for **communication** in various situations like in operating or procedure rooms with all the stakeholders. Physician-to-patient or physician-to-physician or caretaker communications can also be achieved with NLP-related tools. Overall, NLP is relatively under-leveraged and not well understood in the medical and health care arenas but can have impact if this resource is given more appreciation and utilization.

5. **Use of AI tools for mining data.** Use of machine learning, particularly unsupervised learning, can be effective for mining patient data for **new patterns of diseases, novel diagnoses** and therapies, or detecting **variations in clinical practice.** This is a new bottom up approach to medicine (as opposed to traditional diagnosis of diseases based on clinical criteria that clinicians often have to memorize). This paradigm shift to have new subtypes of diagnoses discovered in order to risk stratify as well as to achieve better success with therapeutic interventions can be very productive as these are tenets of precision medicine. In addition, this strategy can also help to detect diseases in patients who may not have met full criteria (especially ones with one significant criterion but perhaps few or none of the other criteria) but nevertheless have the disease. Lastly, mining data can also be used for selection of the appropriate patients for a **clinical trial** for intervention; much of the expenditure and labor for a clinical trial selection of patients can be obviated with intelligent use of ML/DL tools.

6. **Use of natural language processing for medical reports.** Many aspects of **automating reports** as well as organizing these reports can be accomplished with intelligent application of NLP. There is much preliminary work in this area that has already been completed in radiology. In addition, NLP can be used to bring about more consistency in how these reports or notes are generated.

7. **Use of machine or deep learning for risk assessment and intervention.** Another area in terms of expenditures and potential savings is the domain of risk assessment and timely interventions to reduce this risk. One strategy is to delineate patients that would warrant an **alert** for a number of reasons (abnormal vital signs, inappropriate communication, decreased mobility, etc). Another strategy is that ML/DL can be used to detect anomalies is **medication error.** All of this requires sophisticated algorithms and also tools to execute and followup on action plans.

8. **Use of robotic technology for rehabilitation or therapy.** The range of robotic technology for particularly rehabilitation varies from country to country but is advancing quickly. With chronic disease burden increasing and number and availability of specialists not keeping pace, this area can grow further. Uses for robotics already in place include robots used for physical therapy and **rehabilitation** after strokes or injury.

9. **Use of virtual assistants for patient communications.** The proliferation of chatbots and virtual assistants outside of health care will render these tools available for health care as well, especially for chronic disease management. Many aspects of patient communications can be enhanced by these tools and further improved into situations such as **medical triage** and **health advice.**

10. **Use of altered reality in planning and education/training.** There is preliminary work on use of different modes of altered reality for rendering a visual representation of anatomy/physiology or even a procedure for multiple purposes. This strategy can be used for **education, training,** or **pre-procedure planning.**

Anesthesiology. Anesthesiologists work almost exclusively in the operating or recovery room with the surgical (or procedural) team or a critical care setting in conjunction with the critical care team (and therefore very rarely in the outpatient setting). These physicians pay close attention to vital signs and monitor data throughout procedures and care for these patients before and after the procedure as well ("perioperative" care). The anesthesiologist usually has very little time to learn about the patients and their potentially lengthy and/or complicated medical history in great detail prior to the procedure. This subspecialty has been described as "99% boredom, 1% terror" not unlike perhaps airline pilots. These clinicians are amongst the best doctors in dealing with the airway as well as general resuscitations, so there is much overlap with ICU clinicians in practice and scope (although anesthesiologists usually deals with a single patient at a time). As opposed to the ICU clinicians, anesthesiologists usually do not usually know about the short or longer term outcome of these patients after they depart from the operating room or recovery area.

Published Reviews and Selected Works. There is still relatively low publication activity currently in anesthesiology on AI applications (especially since some references are actually in the ICU literature). A recent review paper by Connor astutely emphasized that it is timely for anesthesiologists to learn and to adopt AI now because the practice of anesthesiology embodies a requirement for high reliability as well as a **pressured cycle** of interpretation, physical action, and response (as opposed to a single cognitive act like medical image interpretation) and AI is becoming capable of meeting this practice need of the anesthesiologist. A commentary by Alexander agreed with the prior review and discussed the history of many prior failed attempts to incorporate automation into the practice of anesthesiology due to underlying **complexity** of anesthesia practice as well as inability of **rule-based feedback loops** to influence decisions. Another editorial in Anesthesiology commented on the landmark paper (see Lee et al below) that heralded a new era of ML in clinical anesthesiology. The aforementioned editorial ended with an interesting departing comment: "For those of us who consider ourselves experts in modeling drug behavior, Uber is hiring". Finally, a review that is more extensive on the methodologies in AI but in the critical care medicine literature also placed emphasis on the current AI capabilities for decision support.

One report suggested an interesting collaborative strategy between AI and human intelligence for peri-procedural medical safety in the form of "**simplexity-oriented decisional approach"** where there is fusion of sufficient complexity of thought with necessary simplicity of action. Another group reported their work with an automated, clinically curated surgical data pipeline and repository that can identify high-risk surgical patients from complex data with a machine learning strategy as a **risk prediction model**. The cohort of over 66,000 patients and 194 clinical features were studied with LASSO regression as well as random forest and boosted decision trees methodologies, but LASSO regression was the highest performing risk prediction model with an AUC of 0.92. This ML strategy proved to be superior to traditional heuristics and risk calculators. Finally, a recent landmark paper described a DL approach to link **target controlled infusion** of propofol and remifentanil to the bispectral index (BIS) in 231 patients, and this collection of 2 million data points trained a neural network to predict the BIS based on the infusion rates of these medications. What is impressive about this DL approach is that it is totally independent of pharmacokinetic and pharmacodynamic interaction data and simply matched the input (medication infusions) to the output (BIS).

Present Assessment and Future Strategy. Overall, anesthesiologists are technology-savvy and early adopters of technological advances, but interestingly there has not been wider adoption of AI to date. The main reason is probably that AI technology, while maturing in the area of medical image interpretation, still needs to be more sophisticated in the realm of decision support; **real-time, complex decision support** with feedback mechanism is the crux of the need for AI-enabled anesthesia practice (not medical image interpretation as with other clinicians). This special type of decision support also needs to be inclusive of all data from the patient prior to the procedure for completeness. In addition, anesthesiologists usually have a heavy and hurried workflow and AI still has not had major impact in this domain, although AI has started to have presence in this area. For the future, monitoring in various venues can be embedded with simple algorithms in the form of **embedded AI** so there is less monitor fatigue for the anesthesiologists. ML and DL and deep reinforcement learning will be more sophisticated for both decision support and biomedical diagnostics and will be able to accommodate the challenging **real-time, complex decision making processes** in anesthesia for enthusiastic support for AI by this group. There can be much more clinical application of AI (especially ML and fuzzy logic) with **medication infusions** so often used in anesthesia practice. In addition, there is high potential for the application of AI in altered reality for **pain management,** robotic and virtual assistance in the OR for certain areas such as intubation and other **procedures**, and for the utilization of robotic process automation in automating much of the **workflow** for the OR and anesthesia team.

Cardiology (Adult and Pediatric) and Cardiac Surgery. Cardiology is a multi-dimensional subspecialty that deals with disorders of the heart and blood vessels: while an adult cardiologist sees adults with usually acquired cardiovascular disorders (coronary artery disease, congestive heart failure, elevated cholesterol, atrial fibrillation, or systemic hypertension), a pediatric cardiologist treats fetuses, children and adolescents with both acquired and congenital heart disease. Typical tests that a cardiologist orders include: electrocardiogram (EKG)(a tracing of the heart rhythm), echocardiogram (an ultrasound study of the heart often confused with the former test), CT or MRI of the heart and chest, nuclear imaging, cardiopulmonary exercise testing, and tests that are designed to detect heart rhythm disturbances such as an external (including recent miniature portable devices such as Kardia and the Apple watch) or an internal implanted monitor. Cardiologists also perform cardiac catheterizations for diagnostic purposes as well as for interventional procedures such a balloon angioplasty, stent and/or valve implantation, biopsies, electrophysiologic study (EPS) or a pacemaker insertion. A cardiologist sees patients both in the hospital setting (including often in the ICU setting) or in the outpatient clinic.

Published Reviews and Selected Works. For a subspecialty particularly rich with imaging and clinical data already with more sources to come in the very near future (especially with EKG apps, implantable monitors, and biosensors), cardiology remained relatively dormant in AI-related publications until recently and is in its early discovery stages of adoption of AI. A short review by Bonderman discussed some of the very early AI works in cardiology in the context of reducing both bias and noise in cardiology. A much more comprehensive review by Johnson discussed the many dimensions how AI can affect cardiology: from research to clinical practice and population health. This review also delineated the basics of machine learning (supervised/unsupervised learning and even reinforcement learning). Another review presented a broad and concise overview of AI and its implications in cardiology. An excellent and concise review by Shameer focused on all aspects of cardiovascular medicine in the context of machine learning and another review also showed how effective AI can be in the context of precision cardiovascular medicine. A somewhat esoteric review on an overall deep learning approach (vs rule-based expert systems) in cardiology discussed the advantages and limitations of this new paradigm with an emphasis on the data science aspects such as CNN, RNN, and deep belief networks (DBN) as well as the limitations of data such as standardization and quality. A very recent review of AI in cardiovascular imaging summarizes recent promising applications of AI in cardiac imaging with innovative data visualization.

There is relatively increased use of AI and data science in the domain of **cardiac imaging** ranging from ECG to echocardiography for both diagnosis and prognosis. For **signal modalities**, an arrhythmia detection end-to-end deep learning strategy (accomplished with a 34-layer CNN) with a single-lead ECG (with more than 90,000 single-lead ECGs from over 50,000 patients with 12 rhythm disturbance categories such as atrial fibrillation and ventricular tachycardia) accomplished interpretation at a cardiologist level. Recently, Attia and his group reported a study that paired 12-

lead ECGs with echocardiograms to predict eventual LV dysfunction in patients with asymptomatic LV dysfunction with the use of CNN.

While a prior study described work on automated quantification in **echocardiography (**chamber quantification for left ventricular function and assessment of valve disease), more recent works delineated how CNN was used for automated real-time standard view classification and image segmentation to improve workflow. In addition, machine learning has been applied to the ever so challenging heart failure patients with preserved ejection fraction and helped to set up a new phenotypic risk assessment system for heart failure and also patients with either hypertrophic cardiomyopathy or athletes LV hypertrophy based on expert-annotated, speckle-tracking of echocardiograms. Interestingly, a cognitive machine learning strategy via associative memory classifier was deployed to differentiate patients with constrictive pericarditis from restrictive cardiomyopathy. One study even described using NLP for large-scale, automated, and accurate extracting of structured, semi-structured, and unstructured data from echocardiography reports. Deep learning algorithms have also been applied to **cardiac MRI** as a prognosis prediction tool in patients with pulmonary hypertension and shown to be superior to clinicians' assessment. There is even a report on CNN analyzing retinal fundus photograph**s** (specifically optic disc or blood vessels) as a tool for prediction of cardiovascular risk factors; this is a good example of crossing the boundaries of specialists to attain a higher level of care. In short, while ECGs and static images such as cardiac MRI are relatively straight forward for machine and deep learning, more complicated cardiac imaging such as echocardiograms as well as 3D and 4D images are also being studied with machine and deep learning.

There are also published reports of using AI for **clinical decision support** in various settings in both adult and pediatric cardiology. Decision making in cardiology is often complex and is particularly vulnerable to many heuristics and biases but also traps such as group think, sunk cost trap, and status quo trap. A contribution from AI and data science is detection of a clinical event in electronic health records: one study used a supervised CNN model enhanced with bidirectional LTSM-based autoencoders to detect a bleeding event. Similarly, a deep learning algorithm (called deep learning-based early warning system, or DEWS) that used only 4 vital signs had a high sensitivity and a low false positive rate for detection of patients with cardiac arrest in a multi center study. Choi reported the use of RNN with gated recurrent units (GRUs) to DL models to leverage temporal relations appear to improve the performance of these models to detect **incident heart failure** even with a short observation window of 12-18 months. Finally, machine learning in the form of support vector machine devised an effective risk calculator that was shown to be superior (less recommended drug therapy with less adverse events) to the existing accepted ACC/AHA **cardiovascular disease risk calculator**.

There are relatively few reports of AI-focused publications in children and adults with congenital heart disease although a very early report by Warner delineated a mathematical approach to the diagnosis of congenital heart disease. An early report of utilizing an AI strategy for screening tests such as **electrocardiograms** for sudden cardiac death with a ML/DL approach to maximize accurate diagnosis. An AI-assisted **auscultation algorithm** performed well in a virtual clinical trial but may be difficult to become a routine approach given readily available echocardiographic assessments; in short, an AI strategy for an older technology (the stethoscope) may or may not be adopted by clinicians. Machine learning algorithms were deployed to train a large dataset of adults with congenital heart disease to prognosticate and to facilitate **clinical management**. A similar study to the aforementioned DEWS study revealed that predictive models created by AI can lead to earlier detection of patients at risk for **clinical deterioration** and thereby improves care for pediatric patients in the pediatric cardiac intensive care setting. In addition, four AI-based algorithms were employed to facilitate a **clinical decision support system** for estimating risk in congenital heart surgery. One innovative report described using machine learning and system modeling to facilitate a multi center **collaborative learning project** for rapid structured fact-finding and dissemination of expertise; this forward thinking approach can provide a complement (and perhaps render less necessary) the traditional multi-center, randomized clinical trials that are sometimes challenging to execute.

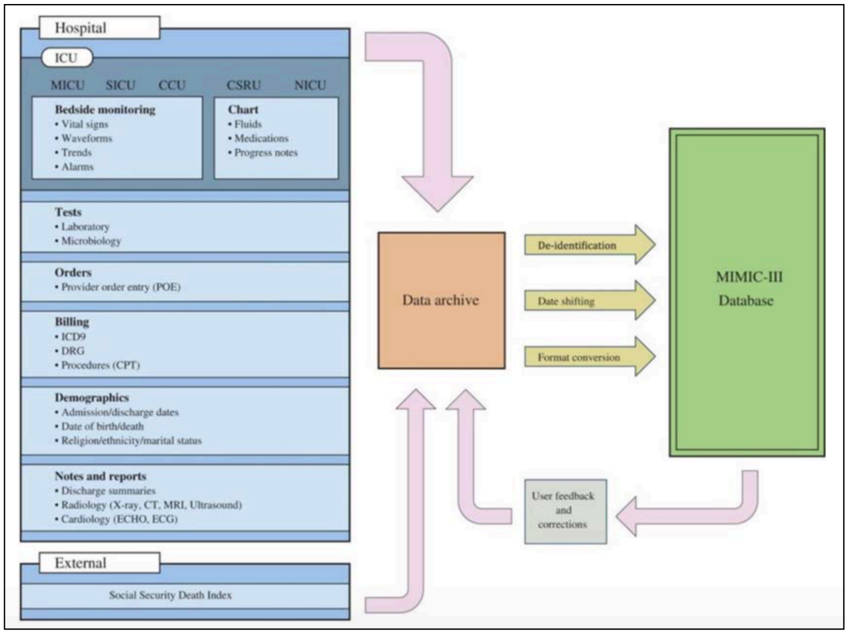
Present Assessment and Future Strategy. Overall, as cardiology is both a perceptual or image intensive field as well as a cognitive or decision making subspecialty with a myriad of procedural tasks, AI is a particularly valuable technology for cardiology with potentially very rich dividends that are vastly under-explored at present but has great promise. Cardiologists presently are curious about AI but have not adopted AI methodologies as have the radiologists even in the image sector. There has been increasing activity in both conferences as well as the publishing domain on AI in cardiology, and there are already algorithms deployed to ECG monitoring on an outpatient basis. In the **medical image** domain, deep learning with CNN is being deployed for not only static images such as EKG, CT and MRI but CNN with modifications (with LTSM) or in combination with RNN can also now interpret **dynamic images** such as angiograms and echocardiograms. These methodologies are direly needed in order to deploy much more sophisticated serial echocardiographic determinations of heart performance than the current conventional metrics of systolic and diastolic function.

For the future, cardiology and cardiologists can benefit greatly from AI as a technological resource. First, the full continuum of cardiac imaging presents serious but solvable challenges for AI deployment if a cardiologist wishes to integrate all of these studies for **hybrid images** or **image fusion** (echocardiogram and cardiac MRI which focuses on physiology and anatomy, respectively). In essence, there will be the emergence of a "**super scan**" in which all imaging modalities lead to a single set of 4D images that can be easily moved and manipulated. AI can also be integrated into the entire continuum, an "**AI image continuum**", from acquisition via operators (AI-enabled or "intelligent" image acquisition) to image interpretation as discussed above and finally on to integration of images into individualized precision health assessment. The cardiologist can also be liberated from the long list of relatively mundane tasks to higher level of medical decision making with full deployment of the various AI tools available. Second, **complex decision making** with AI and the use of deep reinforcement learning can be particularly useful for the ever increasingly complex nature of diagnostic and therapeutic precision cardiovascular medicine in both the intensive care ("precision intensive care") or hospital setting as well as the outpatient arena ("precision cardiovascular care"). This type of individualized medicine will need the many layers of data and information all integrated into an AI-enabled strategy for delivery of key information for knowledge and treatment. Routine individualized **precision cardiovascular medicine** will be practiced in which pharmacogenomic profiles and all aspects of biomedical data (including wearable devices) are combined to yield a precise individual diagnostic and therapeutic strategy as well as risk stratification for cardiovascular disease supported by population data. Third, the application of **altered reality** in cardiology and cardiac surgery for education, training, and trial procedures and interventions prior to the live procedure in heart disease will be made available with AI as a resource. Given the complexity and nuances of operative and interventional procedures in cardiology, perhaps it will be quite some time before a robot will be performing a cardiac procedure in its entirety even with human oversight. Lastly, the **administration** aspects of a busy and complicated heart program can be better managed with some of the robotic process automation tools that are already available. Prediction models can also be in place to prevent unnecessary readmissions and complications. In short, AI is a much needed and very timely resource in cardiology especially since the cardiovascular disease burden remains singularly the largest and continues to climb in an aging population worldwide in both the developed as well as under-developed worlds.

Critical Care Medicine. The intensive care physician has significant overlap with the anesthesiologist in skill set and tasks, and often have had anesthesiology training or board certification. These physicians usually care for patients that are housed in the intensive care setting and usually not in the hospital ward or outpatient setting. The ICU physician and team can work in many types of ICUs, include adult-focused intensive care units such as the medical intensive care unit (MICU), the coronary care unit (CCU), and the surgical intensive care unit (SICU) as well as the intensive care units that are devoted to children such as the pediatric intensive care unit (PICU) and the neonatal intensive care unit (NICU). These physicians are multi-functional within the ICU in that they look at medical images (such as chest X-rays or head CT), perform procedures such as central line or chest tube placements, interpret vital signs and integrate all of this data and make a medical decision, sometimes on an urgent and continual basis.

Published Reviews and Selected Works. Like anesthesiology, critical care medicine is data-rich but there has been only a relatively moderate level of publishing about utilizing AI in the ICU setting (for the same reasons as described earlier for anesthesiology). A review of AI applications in the intensive care unit that was published close to two decades ago, including several older methodologies, is still worth reviewing. Another good review focused on the integration of AI into complex decision-making in the acute care medical arena. The author very astutely pointed out that the future physician and nurse will need to adapt to the AI at the bedside with a new paradigm of **time pattern recognition** (vs the traditional threshold decision making). This new AI-human synergistic thinking requires teaching archives of time pattern phenotypes to be taught and medical education to reflect this paradigm shift. An excellent and thoughtful review discussed not only the potential but also the limitations and pitfalls of Big Data in critical care medicine; the authors strongly advocate an open and collaborative environment for future ICU data efforts. Lastly, Johnson reviewed the limitations of the current ICU databases for precision medicine. These authors contend that the three challenges are: compartmentalization, corruption (erroneous, missing, and imprecise data), and complexity (multimodal data).

An example of application of AI in the hospital setting is the use of machine learning algorithms for training expert-labeled vital sign data streams to automatically classify vital sign alerts as real or artifact in order to clean such data for future modeling.



Another robust illustration of the value of databases coupled with analytics is the **Medical Information Mart for Intensive Care (MIMIC)** accessible critical care database. MIMIC is a large, single-center (Mass General Hospital) database comprising of information in the critical care unit from tens of thousands of admitted patients (over 50,000 adults and close to 8,000 neonates) for data mining and modeling of conditions that resulted in many publications. The data includes general data (such as patient demographic, hospital admissions and discharge dates, death dates, ICD-9 codes); physiological data (such as hourly vital signs, ventilator settings, etc); medications (including IV medications); lab tests (including imaging data); fluid balance; and notes and reports (imaging reports, progress notes, discharge summary, etc). The data can be downloaded as flat files an imported into a database system. The code that underpins the MIMIC-III database is openly available and a Jupyter notebook containing the code is also available. MIMIC-III has been used for "**datathons**" around the world by the MIT group to enable multidisciplinary groups that consist of clinicians and data scientists to answer and solve clinically relevant research queries and clinical problems.

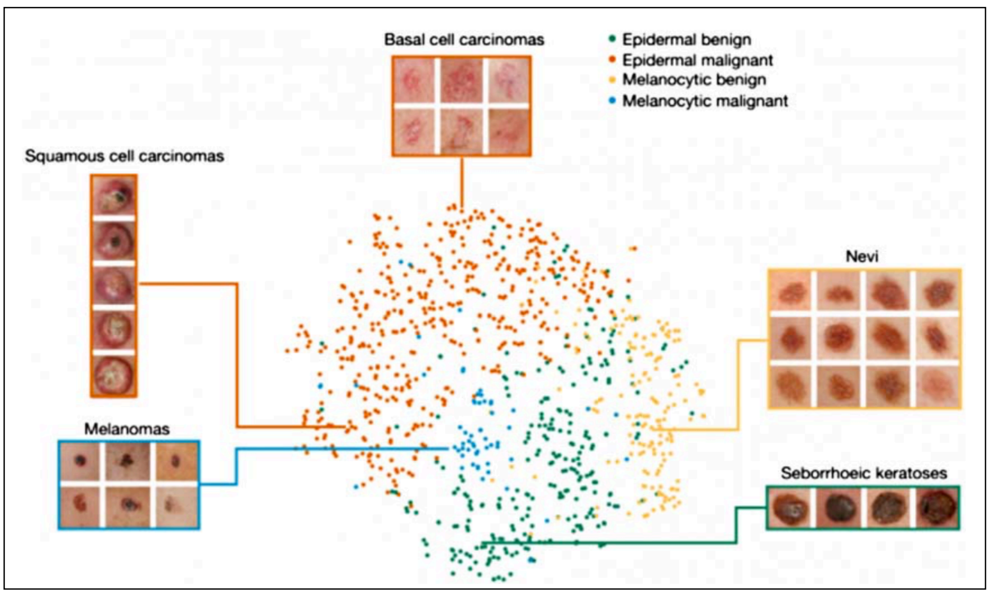
AI is deployed in the form of an intelligent **reinforcement learning agent** (the AI Clinician) that extracted implicit knowledge form patient data that exceeds the experience of a human clinician by many fold. This AI model was able to provide individualized treatment decisions in sepsis that could improve patient outcomes. In addition, **NLP-driven prediction models** with laboratory data and vital signs were successful in yielding better predictive performance for mortality while another ML model emphasized the importance of time in outcome predictions. AI has also been used to enhance the **simulation-based experience** and training in resuscitation medicine. Lastly, there is ongoing interest in forming a dyad between **telemedicine intensive care unit (tele-ICU)** and ML-supported clinical decision support systems (CDSS) (for sepsis prediction and ventilator management) especially with the enormous quantities of data from the tele-ICUs for a generalizable ML-CDSS algorithms.

Pediatric and Neonatal Intensive Care. In the pediatric intensive care setting, there is discussion about using AI more robustly towards "**precision intensive care**" where there is real-time deep learning with cognitive architecture to bring about precision care for each individual ICU patient. One study used AI (in the form of logistic regression, random forests, and CNN) to identify physiomarkers in predicting **sepsis** in the PICU 8 hours earlier than a screening algorithm. In addition, there is ongoing work on the use of AI and predictive modeling for earlier detection of patients at risk for **clinical decompensation** in the pediatric cardiac intensive care setting. This AI strategy used neural network and decision tree classification as well as logistic regression to provide a real-time individualized risk assessment. Another report by Williams described the use of *k*-means clustering unsupervised learning to discover 10 clusters with varying prognostic information. Overall, The PICU community appears to be interested in pursuing AI tools for this complex environment. There is less academic activity in the data-rich milieu of the NICU, but Singh et al described a futuristic iNICU with real time analytics with a Big Data hub and a rules based engine and deep learning.

Present Assessment and Future Strategy. Overall, there is now increasing academic and clinical activity compared to a similar field of anesthesiology but critical care medicine is still under leveraging the entire AI portfolio of tools. Just as in anesthesiology, one major reason is that the AI tools for **real-time, complex decision support** remains suboptimal but can be more sophisticated and mature in the near future. The work by the MIT group and its MIMIC effort has been instrumental in maintaining an AI and ML/DL presence in the ICU domain.
For the future, the clinical relevance and current AI availability profile is similar to that of anesthesiology. Once deep reinforcement learning or other deep learning methodologies are sophisticated enough for the **real-time, complex decision making** challenges of ICU medicine, there will be predictably an even higher level of AI adoption by the physicians in this group. The true value will be a universal **ICU data repository** for an enriched data source for ML/DL and deep reinforcement learning. In addition, AI and **altered reality** variations can also be an important aspect of education and training the clinicians in critical care unit setting with virtual and simulated resuscitations. From the administrative aspects of a busy ICU, robotic and automated assistance can be extremely useful as well to mitigate the escalating burden of documentation and workflow.

Dermatology. A dermatologist deals with the disorders of the skin. The pathology ranges from a simple sunburn or rashes to skin lesions that can be manifestation of systemic diseases (such as lupus) or cancer (such as malignant melanoma). A dermatologist therefore spends much of his/her time interpreting these skin lesions with their observational skills, usually at higher volumes in the clinic compared to other clinicians. A dermoscopy is an examination of skin lesion with a dermascope (also called incident light microscopy or epiluminescence microscopy). The dermatologist also performs minor surgeries such as laser therapy, excision, or biopsy of a lesion.

Published Reviews and Selected Works. There is a relatively low number of publications on AI in dermatology and skin diseases despite the proliferation of DL/CNN in medical image interpretation that is observed in radiology, ophthalmology, pathology, and now in cardiology. There is an excellent review on machine learning and application of AI to imaging and diagnosis with discussion of dermatology and skin lesions. The relatively comprehensive paper reviews the more relevant aspects of ML and image interpretation, including the bias and variance tradeoff, under and overfitting, and loss functions.



A landmark paper was the work published by Esteva et al on the application of deep learning in **skin cancer** in 2017. This paper showed that the authors trained a CNN using a dataset of close to 130,000 clinical images that consisted of over 2,000 different diseases. This CNN was tested against 21 dermatologists in two critical binary classification use cases and performed on par with the experts across both tasks **(see Figure)**. This achievement renders it possible to have cell phones be the low-cost universal access to this important aspect of medical care. Following this publication, a Cochrane Database Systematic Review concluded that prospective comparative studies are needed to evaluate the use of computer-assisted diagnosis (CAD) systems as diagnostic aids vs dermoscopy even though in highly selected patient populations, CADs demonstrated high sensitivity and would serve well as a back-up for specialists to minimize the risk of missing melanomas. Another "human vs machine" comparison was reported by Haenssle, who described a CNN versus an international group of 58 dermatologists with most dermatologists outperformed by the CNN. Lastly, Zhang et al reminded us that the best situation actually entails a combined effort from CNN and human expertise in improving the diagnosis of skin diseases.

Present Assessment and Future Strategy. Overall, there is little AI utilization in dermatology but increasing clinical curiosity and interest for AI to be a second pair of eyes for diagnosis of skin lesions. Based on the dermatologists' meeting agendas and the absence of discussions on AI and image interpretation, this clinical interest is presently perhaps more curiosity than genuine inclination to incorporate AI into the practice (as observed with radiologists and other subspecialties). There are a few efforts to have available an AI-enabled dermatology visual diagnostic aid, and these efforts are likely to increase referrals to the dermatologists as these screening efforts will lead to diagnoses that will need human oversight and possible intervention. For the future, an AI-enabled dermatologist will have routine **CNN-enabled dermoscopy** in the office on a routine basis and this dyad will correctly diagnose skin conditions almost perfectly. This human-machine synergy can also be combined with digital health capabilities to transmit photographs for not only routine screening but also followup; this capability can therefore obviate the need for an excessive number of clinic visits as well as make available a valuable service in global health. A universal visual repository of all skin lesions coupled with accurate labeling can enhance diagnostic capability immensely. The above strategy can also be coupled to a sophisticated decision support tool to achieve **precision dermatology** in terms of diagnosis and therapy. Most if not all procedures performed by the dermatologist can also be enhanced with AI and **altered reality** as to minimize skin trauma and injury. Lastly, AI can also decrease the workflow and administrative burden of a typical busy dermatologist office and clinic.

Emergency Medicine. The emergency room clinician sees a large and heterogeneous group of patients in a short timeframe and often makes many fast medical decisions within this time. Similar to anesthesiologists and ICU physicians, these clinicians often have to make these decisions with inadequate data and information. The emergency room physician often performs minor procedures such as stitching of wounds or insertion of catheters. Like the ICU clinician, emergency medicine clinicians often feel like a real-time strategy game player having to make fast decisions with many complex situations in many patients without all the data. The typical emergency medicine clinician does not see patients in the hospital nor the outpatient clinic, so sometimes the eventual outcome (including death or serious morbidity) of his/her interventions is not known.

Published Reviews and Selected Works. There is little academic or publication activity in emergency medicine in the realm of AI. A recent overview of how AI and machine learning can impact of emergency medicine discussed how essential it is for AI to be integrated into emergency medicine but concomitantly delineated the concerns such as algorithm opacity and data security. Areas of AI incorporation include: public health surveillance, clinical image analysis (including real-time ultrasound), clinical monitoring (with reduction of false alarms), clinical outcome predictions, population and social media analysis, vital signs and warnings, and finally home monitoring; the greatest challenge remains adoption of AI into the complex milieu of the health care system. Another recent review introduced basic AI concepts like ML and NLP in the context of emergency medicine and health informatics as well as clinical and operational scenarios.

A report delineated just exactly how AI can benefit **emergency room operations**: on arrival to accurately triage and risk-stratify in order to reduce waste; during visit to accelerate time to diagnosis in order to assign appropriate level of care; and at discharge to predict adverse events in order to individualize followup planning. In addition, one study compared ML to traditional ED triage and demonstrated that ML (using random forest) was superior in predicting a **higher severity level** that has need for critical care, emergency procedure, or inpatient hospitalization. There was also a report on using ML to predict, detect, and intervene older adults vulnerable for an **adverse drug event** in the emergency department. Finally, Goto reported a ML-based prediction tools (lasso regression, random forest, gradient-boosted decision tree, and deep neural network) for clinical outcomes of children during emergency department triage.

Present Assessment and Future Strategy. Overall, there is very little academic or clinical activity for AI-related topics in this domain (based on recent meeting agendas and personal communications), even though emergency room has a large number of complex decisions and workflow challenges that would benefit from AI tools and methodologies (similar to aforementioned anesthesiologists and critical care medicine clinicians). The medical imaging area in the emergency room setting is now occasionally augmented by CNN and computer vision so this support is exceedingly helpful for the emergency room clinician (who are not as experienced with more sophisticated medical image interpretations such as head CT or echocardiography).

For the future, like the other subspecialties that often require fast thinking and decision making (ICU, surgery, and anesthesiology), emergency medicine can greatly benefit from an AI-enabled strategy of deep reinforcement learning designed for **real-time decision-making**. This AI methodology can augment the clinicians' capabilities to make the best decisions in a busy environment. In addition, the emergency room is similar to the OR for the anesthesiologist and so can benefit from an **AI-enabled workflow augmentation** that can include history taking and triaging as well as discharge planning and followup.

Endocrinology. The endocrinologist deals with the body's endocrine systems and glands that secret hormones (such as thyroid hormone from the thyroid gland and insulin from the pancreas); in essence, the metabolism or biochemical processes of the body. The most common diseases seen by the endocrinologist include diabetes, thyroid disorders, and reproductive organs in adults and diabetes and growth disorders in children. The endocrinologist usually has a large outpatient volume but does not typically perform procedures nor look at large volumes of medical images (but can consult radiologists for various medical image studies such as bone age and certain scans). Outpatient management is a large part of the endocrinologist practice.

Published Reviews and Selected Works. There are relatively few publications on AI utilization in endocrinology, and most of the existing published references are focused on diabetes, especially in the context of diabetic retinopathy. A recent opinion article by Gubbi et al discussed the AI areas relevant to an endocrinologist, including medical image interpretation (especially with diabetic retinopathy), pre-emptive medicine in which the onset of chronic diseases (such as diabetes) is delayed, and proactive diagnosis of endocrine diseases based on phenotypic expressions of these disorders. In addition, AI has been involved in the functional capacity of the artificial pancreas to manage diabetes. In a similar report, AI methodologies and their application to diabetes as a disease entity was reviewed; tools ranged from expert systems to machine learning as well as fuzzy logic in closed-loop systems were discussed. Lastly, a thorough review of the AI in **diabetes** care literature are grouped into four areas: automated retinal screening, clinical decision support, predictive population risk stratification, and patient self-management tools.
A report described the patient experience with the **AI-based diabetic retinopathy screening** tool in an endocrinology outpatient setting. The fundus photographs were automatically read by a DL algorithm and results were provided real-time (vs 2 weeks by traditional retinal grading center); most patients (78%) preferred the automated screening process. In addition, a study examined expert **algorithm-based identification** of type 2 diabetes patients vs a novel data informed framework via feature engineering and machine learning (including *k*-NN, Naive Bayes, decision tree, random forest, and SVM along with logistic regression). The latter performed much higher with an AUC of 0.98 (vs 0.71 for the expert algorithm). Lastly, Li reported a clever approach to **forecasting glucose levels** by using an RCNN model with very short turnaround time for a future artificial pancreas. An example of AI in endocrinology outside of the diabetic patient is a study of ML (rank regression and random forest) and transcriptomics in patients with growth hormone deficiency in disease classification.

Present Assessment and Future Strategy. Overall, aside from some AI-related work on **diabetes** and disease management with fundus imaging and followup, there is little AI work in endocrinology as a subspecialty. This lack of clinical activity outside of diabetes is understandable as most of the attention for AI adoption has been centered on medical imaging interpretation with deep learning and CNN, including some significant work with diabetic retinopathy. There is little imaging focus for endocrinologists so present AI utilization will need to evolve into other areas, such as diabetes and glucose control with ML/DL and fuzzy logic.

For the future, exciting innovative advances with **closed loop systems** and **fuzzy logic** as well as CRNN AI methodologies will all be extremely useful for essentially an **artificial pancreas** to treat diabetes. This will be a highly significant advance in the management of one of the most significant disease burdens in the future. In addition, **AI-enabled population health** with precision medicine will converge for diabetes to minimize population morbidity and mortality by not only improved treatment of the disease but also proactive prevention of the disease. Lastly, as diabetes is a complex disease with many complicated followup strategies necessary to adequately treat this multifaceted disease, automated tools as well as chatbots can be part of the AI portfolio to manage these patients.

Gastroenterology. The gastroenterologist treats patients with not only gastrointestinal disorders (from esophagus to stomach and intestines), but also conditions of the liver gallbladder, and pancreas. The gastroenterologist sees medical imaging studies (such as CT/MRI but also contrast studies of the intestines and bowels) and performs procedures such as endoscopy (upper gastrointestinal tract) and colonoscopy (lower gastrointestinal tract). Common diseases include peptic ulcer, gastritis, gastroesophageal reflux, gastrointestinal bleeding, hepatitis, various types of malabsorption syndromes as well as inflammatory bowel diseases (ulcerative colitis and Crohn's disease) and cancers. In children, diseases include feeding and/or nutritional disorders (including reflux and food intolerances), liver disorders, and diarrhea/constipation.

Published Reviews and Selected Works. An earlier review of ANN in gastroenterology discussed the added value of this AI technology to classification accuracy and survival prediction of diseases. There is recent increased interest in AI in gastroenterology mainly because of the medical imaging work with deep learning. There is review of the use of AI, specifically use of deep learning, for gastroenterology and **gastrointestinal endoscopy**. The use of computer-aided diagnosis as a second observer is better than prior experiences for conditions such as polyps as well as bleeding, inflammation, and infections. The concept of "**optical biopsy**" is presented as a methodology to achieve the diagnosis without biopsy (or at least more precise biopsy with real-time AI-enabled imaging to determine relative health of the observed tissue area)**(see Figure)**. The possible applications of AI in gastroenterology can be summarized as: 1) technical integration of AI with EMR and endoscopy platforms will be essential to optimize clinical workflow; 2) AI systems will need to expand their library of clinical applications to include earlier diagnoses of other disease such as inflammatory bowel disease; and 3) AI systems will need regulatory and ethical considerations.

One report discussed AI as a useful methodology for gastroenterology in clinical decision making with predictive models and in **endoscopy** with deep learning. Another report on imaging and use of AI also discussed a long list of studies of AI (mainly ANN) methodologies for both the upper as well as the lower GI tract, including one also for the **capsule endoscopy**. Lastly, a pediatric paper focused on the use of ML for classifying Crohn's disease and ulcerative colitis in **pediatric inflammatory bowel disease.** This ML approach used endoscopic and histological data from 287 children and applied both supervised and unsupervised learning for delineating disease categories.

Present Assessment and Future Strategy. Overall, based on meeting agendas and discussion with gastroenterologists, there is relatively little clinical AI in gastroenterology activity outside of the use of deep learning and CNN in endoscopic imaging, including real-time support during the procedure. As gastroenterology (along with other subspecialties such as cardiology and pulmonology) can have a very heterogeneous group of patients, AI-enabled precision medicine is underutilized in gastroenterology.

For the future, **AI-enabled endoscopic examinations** should be routinely embedded with CNN as an augmentation for the gastroenterologist. This procedure should involve an entire continuum from acquisition of the image to CNN interpretation of suspicious lesions and decision to biopsy or not. In addition, the examination can also include all data from at home monitoring to EHR from the hospital. In addition, **capsule endoscopy** with miniaturized cameras could play an important role in the future in a strategy to obviate the need for endoscopy or colonoscopy. In the near future, the convergence of AI in the form of CNN (coupled with RNN) and miniaturized capsule technology will finally make these examinations almost entirely noninvasive (perhaps even at home). Lastly, **precision gastroenterology medicine** and care should be provided for all patients with these disorders with an AI-centric strategy that will incorporate all imaging and EMR as well as health data from outside the clinic and hospital settings.

Global and Public Health/Epidemiology. Clinicians who deal with public health around the world is someone who specializes in global health. These clinicians are usually very knowledgeable of infections and chronic diseases (such as diabetes and mental health) as well as basic concepts of epidemiology (including vaccinations and epidemics, public sanitation and environmental health). Common diseases seen by this type of clinician include: respiratory diseases, diarrheal diseases, and malnutrition as well as common infections indigent to the area: malaria, tuberculosis, and HIV. The clinician in the fi eld may view simple medical images (like chest X-rays) as well as perform relatively easy procedures such as minor surgeries and placement of IV lines. The global public health agenda follows the United Nations audacious Sustainable Development Goals.

Published Reviews and Selected Works. There is a paucity of both reviews and published reports utilizing AI in global or public health or epidemiology. Wahl et al published a review with an appropriate question: How can AI contribute to health in resource-poor settings?. This paper informs us that the United Nations convened a global meeting in 2017 to discuss the development and deployment of AI technologies to reduce poverty and improve public health. Although the review has minimal AI substance in the discussion, the paper delineates just how AI can be used in a resource-poor setting: **expert systems** can be used to support health programs; **machine learning** can model certain infectious diseases and their patterns; and **NLP** can be leveraged for surveillance and outbreak predictions using data from EHR and social media sources. Another review focused on AI and Big Data in public health. In this work, the authors delineated the fundamentals of big data and big data and their relevance to public health as well as highlighted the issues that would impact on medical professionals. The authors also conclude that AI and automation are two key elements in a specialized AI in the form of diagnostics but will need to be configured in the future to be generalized AI. Thiebaut et al reported an increase in use of artificial intelligence in public health with a review of over 800 papers in public health and epidemiology in a recent year that included a paper on the use of ANN to de-identify patient notes in EHR that outperformed existing methods. The big data hurdles in **precision public health** mentioned possible solutions as informatics-oriented formalization of study design and interoperability throughout all levels of knowledge inference process. Lastly, a positive discussion on the use of ML in **epidemiology** provided several applications, including predicting risk of nosocomial infections or predicting patients at greatest risk of developing septic shock.

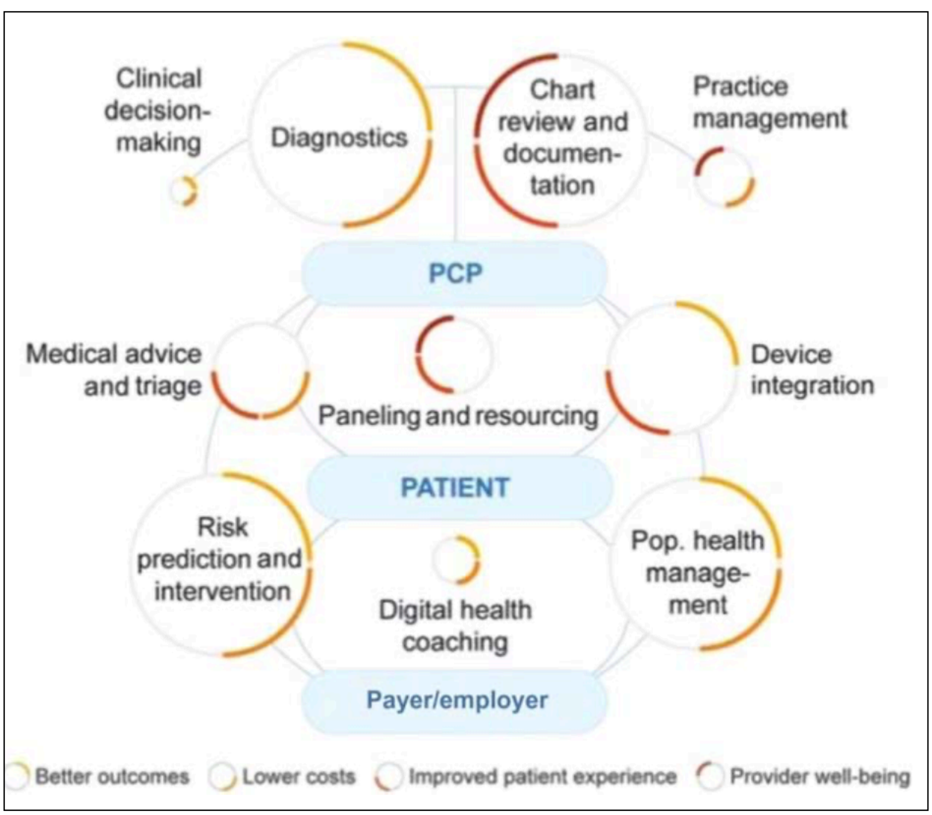
Big data and a global public health intelligence network is described by a Canadian group; this effort and its adoption of big data and capability to detect international **infection disease outbreaks** can provide an early warning system that is life-saving. In addition, Guo reported the ample use of machine learning methodologies in a **Dengue forecast model** in China and discovered that support vector regression had the smallest prediction error rates compared to other methods. Lastly, an interesting new methodology of using unsupervised ML to measure health system proved to be superior to traditional method of health facility surveys and can potentially save resources.

Present Assessment and Future Strategy. Overall, there is only an early appreciation for the possible benefit of AI and related methodologies especially as it relates to big data, analytics, and perhaps image interpretation. There is little evidence of interest, understandably, beyond these topics based on a review of academic programs in public and global health.

For the future, the fields of global and public health as well as epidemiology are ideally structured for use of ML/DL and other methodologies in studying and managing epidemics and natural disasters in the context of large populations. For instance, **epidemics** could be entirely followed and proactively contained with deep reinforcement learning. In addition, as more **population health** and precision medicine experience is gathered with the assistance of AI, these methods can be directly utilized in public and global health as well. Lastly, use of robotic technology including **drones** and orchestrate public health interventions in difficult geographical areas or natural disaster relief.

Internal and Family Medicine/Primary Care. The primary care physicians (internal medicine and family medicine for adults and pediatrics for children) see the patients for their common and usual medical needs. Common adult chronic diseases include heart failure, chronic obstructive pulmonary disease (or COPD), renal failure, diabetes, cancers, Alzheimer's, and infectious diseases. Pediatrics will be discussed separately under Pediatrics.

Published Reviews and Selected Works. Sidey-Gibbons authored an excellent comprehensive review on ML and medicine with a review of ML and its process, including examples of R computer code that accompanied this paper. In a letter to the editor, Krittanawong outlines the ways AI can help physicians: medical imaging, triage, administrative burden, decision support, clinical prediction scores, etc. A review on the use of AI in **medical practice** delineates the applications of AI in internal medicine as not only image interpretation but also cognitive programs and NLP to extract knowledge from the exponentially increasing amount of published works in medicine. In addition, AI can optimize the trajectory of care of **chronic disease patients**, suggest precision therapies for complex conditions, and reduce medical errors. This review ends with an astute reminder that AI will need humans for intelligent use of AI in medical practice. A more recent review on AI and health care reverberates the theme of high potential dividend of AI in medicine and health care, including *in silico* **clinical trials**. Application and exploration of **big data mining** in clinical medicine was reviewed to include methodologies such as fuzzy theory, rough set theory, genetic algorithm, and ANN; these techniques can be used for assessing disease risks and supporting clinical decisions as well as practical drug use guidance. Lastly, one insightful and comprehensive review specifically addressed the ten ways AI can transform **primary care** **(see Figure)**.



According to the authors, the ways that AI will transform primary care will need to augment the patient-physician relationship while freeing up the physicians' cognitive and emotional space for their patients. The ten ways AI will transform primary care include:

1. **Risk prediction and intervention** ($100 billion)- AI technology can be used to make better predictions and save money by avoiding preventable conditions such as unplanned readmissions or prolonged length of stay.
2. **Population health management** ($89 billion)- AI tools can be utilized as a smart platform to manage and execute population health projects.
3. **Medical advice and triage** ($27 billion)- AI methodologies can be used to serve as a medical advice resource for patients and augment the human clinician workforce.
4. **Risk-adjusted paneling and resourcing** ($17 billion)- AI tools can be utilized to determine proper staffing and resource allocation for clinicians and nursing staff.
5. **Device integration** ($52 billion)- AI in its embedded form will need to be part of wearable medical and health devices to enable practitioners to gain insight from this new resource.
6. **Digital health coaching** ($6 billion)- AI-driven fully automated text-based health coaching can increase health and decrease office visits and hospitalizations.
7. **Chart review and documentation** ($90 billion)- AI tools are being deployed to automate chart documentation and reduce the EHR burden of clinicians.
8. **Diagnostics** ($100 billion)- AI-enabled diagnostic tools for a myriad of diseases such as diabetic retinopathy, cardiac disease, and even Parkinson's disease can improve health care and quality of life.
9. **Clinical decision making** ($1-2 billion)- AI-supported decision support tools will be embedded into EHR in the near future and take EHR beyond simply alerts.
10. **Practice management** ($10 billion)- AI-powered automated algorithms will reduce the human burden of repetitive tasks such as prior authorizations and eligibility checks.

In addition, ML has been compared to traditional prediction score for **predicting hospital readmissions** and proved to be superior in even three different hospital settings. This automated strategy in over 16,000 discharges can efficiently target patients at highest risk for readmission. Lastly, even **palliative care** has been demonstrated to improve with DL and EHR via automated screening and notification; this support is justifiably needed since physicians tend to over-estimate prognoses and there is a shortage of palliative care staff. Of course the human and humane aspects of palliative care will need to remain an essential part of the decision making process.

Present Assessment and Future Strategy. Overall, the hype of AI in medicine is mainly focused on medical imaging with deep learning and somewhat focused on decision support as well, so the primary care physician understandably may not perceive AI as very relevant in primary care. As the aforementioned article delineated, however, there are many ways that AI can help the primary care physicians outside of medical image interpretation and decision support. The areas of chart review, practice management, risk prediction, and population health management are large market potentials with growing number of AI-enabled solutions.

For the future, the AI-enabled primary care physician will be in a better position to deliver **precision primary care** with individualized health care planning and disease monitoring. In addition, routine screening using **AI-enabled medical imaging** (such as fundoscopic or dermoscopic examinations) as well as biomedical diagnostics will be automated with high level interpretation but without the requisite sub specialist referral that usually delay the screening process. These screening examinations will be accompanied by the appropriate recommendations for followup. The advent of wearable technology with **embedded AI** will also be a routine part of the health care portfolio for the primary care physician. Finally, a **health avatar** will be available to coach each individual for the health issues that need to be addressed (weight management, mental health issues, smoking cessation, etc).

Neurosciences (Neurology/Neurosurgery and Psychiatry/Psychology). The neurologist sees disorders of the central and peripheral nervous systems. The list of diseases include seizures, peripheral neuropathies, muscular dystrophy, and brain tumors. The neurologist often views electroencephalogram (EEG) as well as various types of brain imaging (MRI including functional MRI, CT, and positron emission tomography, or PET, are the major modalities) with the radiologist. As with cardiologists and cardiac surgeons, neurologists have a special working relationship with neurosurgeons as often medical conditions warrant surgical intervention(s). The psychiatrist sees patients with mental disorders, ranging from mania depression to schizophrenia and can prescribe medications; a psychologist can also follow these patients but usually do not prescribe medications. The Diagnostic and Statistical Manual of Mental Disorders, or DSM-V, classifies mental disorders with well over 200 mental conditions in total.

Published Reviews and Selected Works. There are a few important reviews on the impact of AI on this range of subspecialties, which is ironic given that AI is closest to these fields from a philosophical and scientific perspective. An overview by Ganapathy described that application of AI in the neurosciences mandates a better understanding of the intelligent functioning of the human brain. The authors describe AI applications in neurosciences to include upskilling in neurosurgical procedures, predicting outcome of neurosurgery for seizure disorders, and AI-assisted functional registration for outcome prediction, and other areas (neuro-oncology, neuro-traumatology, imaging services, strokes, and neurorehabilitation). Another review focused on ML and NLP as AI tools that are relevant for the early detection and diagnosis as well as outcome prediction and prognosis evaluation for stroke. An excellent review of AI (as well as natural intelligence) in neurosurgery summarizes neurosurgical implications of machine learning as compared with clinical expertise in several areas (diagnosis, preoperative planning, and outcome prediction). The authors conclude that ML models have potential to augment the decision-making capacity of clinicians but there are several obstacles in this review of ML models (publication bias, ground truth definitions, and interpretability). Another review on ANN in neurosurgery in the realm of clinical decision making showed several applications including diagnosis, prognosis, and outcome prediction. Finally, in the realm of psychiatry, there are two reviews of significance: one review of ML and its role in psychiatry is explored as this field continues to become more and more complex (high-dimensional) and traditional statistical analyses will no longer suffice and the other review focused on DL with CNN for brain imaging as well as RNN for mobile devices and projected future concepts (such as embedding semantically interpretable models of brain dynamics into a statistical ML context).

In children with **autism spectrum disorder**, a robot-based approach showed that children with this disorder are more engaged in the several learning task and seem to enjoy more the task when interacting with the robot compared with the interaction with the adult. In addition, electromechanical and **robot-assisted arm training** for improving activities after a stroke showed improvement of these activities in randomized controlled trials. Much is expected of robots and virtual assistants in the future for both physical rehabilitation and psychiatric therapy as well as health care education and chronic disease management. If accompanied by robust AI tools, these supportive services will be particularly useful in delivering value for the patients.

Present Assessment and Future Strategy. Overall, the area of neurosciences is starting to be aware of and is focused on AI and its full range of capabilities. The academic meetings in neurosciences have an occasional speaker in the AI domain, and the presence of AI in these academic gatherings as well as clinical settings has continued to increase. The neurosciences can advance AI by incorporating cognitive elements and architecture that is so well understood by its members into the current deep learning paradigm.

For the future, with emerging altered reality as well as robotic and virtual assistance technologies, the entire spectrum of neurosciences from neurology and neurosurgery to psychiatry will benefit greatly from these technologies in the therapeutic areas of **precision rehabilitation.** Medical imaging of the brain will advance with multiple modalities converging into a "**superscan**" similar to what was discussed under cardiology. In addition, "**precision psychiatry**" with all the dimensions of precision medicine will mandate strategic use of AI and all its capabilities similar for rehabilitation. Lastly, there will be a necessary convergence and synergy between AI and the neurosciences so that this dyadic relationship will increase the knowledge and capabilities of both of these intimately related sciences.

Obstetrics/Gynecology. These clinicians see female patients at all ages during or after adolescence for regular physical examinations as well as for births or medical conditions that involve the female reproductive system. These physicians are the only clinicians who go from operating in the OR to seeing patients in the clinic as a dually trained surgeon and medical doctor. These clinicians often will follow the fetuses prior to their birth, so fetal monitoring (fetal electrocardiogram used to track heart rate and specifi cally heart rate abnormalities) and fetal echocardiograms are an essential part of fetal followup. Maternal-fetal medicine, or perinatology, involves the medical and surgical management of high-risk pregnancies. Other subareas of focus include reproductive endocrinology and fertility, gynecological oncology, and family planning.

Published Reviews and Selected Works. There are a few published reviews on AI in obstetrics and gynecology. A short commentary mentioned AI and big data to make impact in obstetrics and gynecology and was accompanied by a review of the literature. Wang discussed AI in the context of assisted **reproductive technology** as well as its limitations and challenges. AI applications in reproductive medicine include: evaluation and selection of oocytes; sperm selection and semen analysis; embryo selection; and finally prediction of in vitro fertilization.

One manuscript focused on AI and its use in the interpretation of **intrapartum fetal heart rate tracings**. The analysis concluded with the observation that the use of AI for fetal heart rate monitoring during labor showed that the agreement between the AI tool and human observers was moderate but AI assistance did not improve neonatal outcomes (neonatal acidosis, APGAR scores, or death), which is worth remembering as an important aspect of AI (outcome vs performance of algorithm). Another review published prior to proliferation of deep learning networks focused on use of ANNs in **gynecological diseases**. Even in 2010, the authors appreciated the robust ANN in evaluating multifactorial data from multiple sources to derive at subtle and complex patterns and nonlinear statistical modeling that was superior to conventional logistic regression. Categories of ANN application in gynecological diseases include gynecological oncology (especially early detection and prognosis), assisted reproduction and reproductive endocrinology, and gynecological urogynecology (prediction of surgical outcome). Another area of interest in exploring computational science in reproductive medicine is **in vitro fertilization (IVF).** Simopoulou et al reviewed the necessary leap of evolution from basic mathematics to bioinformatics for analyzing complex models for embryo selection in IVF. Lastly, an interesting reference to the use of fuzzy cognitive maps, which combines fuzzy logic with neural networks, in obstetrics is suggested as a medical decision support system that includes cause and effect relationships among concepts.

Present Assessment and Future Strategy. Overall, much of the interest in the use of AI in obstetrics and gynecology has been in the areas of **fetal monitoring**, which as a very small signal-to-noise ratio (similar to electrocardiograms and electroencephalograms), and **in vitro fertilization.** Similar to many of the aforementioned clinical areas, obstetrics and gynecology has a very heterogeneous group of patients, and even include fetuses as an essential part of the clinical scope. This level of complexity is well suited for more sophisticated ML/DL to decrease the burden and stress of decision making for the clinician.

For the future, an **AI-enabled fetal monitoring** strategy will reduce the human burden and concomitantly increase diagnostic accuracy for fetal events in a proactive manner. Advances in monitoring technology will lead to continuous at home monitoring that is both accurate and non-invasive. For all aspects of gynecological as well as obstetrical conditions and situations, support from AI tools will enable the clinicians to render better decisions in **precision medicine** format.

Oncology. These physicians follow patients who are diagnosed with cancer and set up their diagnostic as well as therapeutic strategies; primary care physicians (internists, pediatricians, family practitioners) usually are the clinicians that screen patients for cancer. The oncologists are essentially specialized internists who focus on the specifi c cancer and all that is required of that cancer in terms of continued surveillance and therapy (including complications and sequelae). Radiation oncologists treat cancer with use of high energy radiation therapy. There are also pediatric oncologists who focus on children and young adolescents with cancer. There is sometimes clinical overlap between oncology and hematology (see above).

Published Reviews and Selected Works. There are a large number of publications on the use of AI in oncology; this may be due to the interest in precision medicine and therapy for cancer patients as well as in cognitive computing (IBM Watson) and its application in cancer. A discussion of AI in oncology discussed this topic in terms of virtual (ML and algorithms) and physical (robots and medical equipment) AI. Areas for AI and its impact in oncology include tumor segmentation, histopathological diagnosis, tracking tumor development, and prognosis prediction. The authors concluded by discussing the power of cancer-related platforms to track **tumor progression** and treatment effects. Another good review of machine learning and imaging discussed also AI in oncology. This review covered not only machine learning but also deep learning with discussion on handcrafted vs machine-engineered feature extraction in **radiomics**; three cases were presented at the end of the review. The domain of **cancer genomics** and precision medicine with AI applications was reviewed by Xu; there is a myriad of ways AI can be applied to this area. There are also many review papers on radiation oncology, and one review paper that focused on **radiation oncology** discussed the various aspects of how AI can be applied to this domain: image segmentation, treatment plan generation and optimization, normal tissue complication probability modeling, quality assurance, and adaptive re-planning. As natural language processing is essential in AI projects in oncology, a review on NLP appeared to encourage oncologists to automate unstructured data from their practice. Lastly, a commentary by Kantarjian succinctly summarized potential applications of AI in cancer care and research, ranging from developing national/ international cancer registries and pathways to uncovering genomic or molecular events that render certain cancer patients more or less sensitive to treatments.

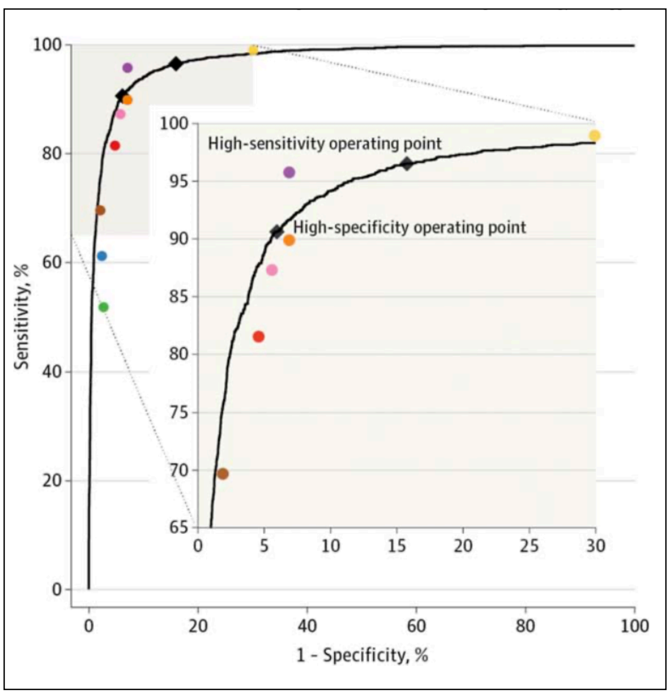
Important papers were published on the experience (good and less than good) with **Watson for Oncology (WFO).** The system was demonstrated to be effective in having high concordance with a tumor board after incorporating data from over 500 breast cancer cases. In addition, the **Watson for Genomics (WfG)** tool was used to demonstrate that human curation is not sufficient to interpret somatic next-generation sequencing and that a molecular tumor board empowered by cognitive computing can improve patient care by being more expedient. Lastly, WFO had significant issues with the system's inability to solve data quality problems in unstructured data (such as doctors' notes and written case reports) and departed from the well-known M.D. Anderson Hospital. In **breast cancer**, the combination of computer-aided diagnosis of image-omics (pathological images) and functional genomic features improved the classification accuracy by 3%. In this study, support vector machine for differentiating stage I breast cancer from other stages are learned with use of computer-aided diagnosis that enables joint analysis of functional genomic information and image from pathological images. In another study, the entire biomedical imaging informatics framework consisted of image extraction, feature combination, and classification. In addition, a deep learning set of algorithms were used to examine hematoxylin and eosin-stained tissue sections for detection of lymph node metastases and achieved better diagnostic performance than a panel of 11 pathologists who interpreted without time constraints. The fascinating aspect of this study is that it was part of an international contest (Cancer Metastases in Lymph Nodes Challenge, or CAMELYON16) with 23 teams competing, with most teams using a deep CNN for the image interpretation. Lastly, an exciting development in the area of precision oncology is **dynamic risk profiling** using serial tumor biomarkers for personal outcome prediction in the strategy called continuous individualized risk index (CIRI).

Present Assessment and Future Strategy. Overall, there remains to be relatively little academic or clinical activity in AI in oncology other than the activity generated by **Watson for Oncology.** The relatively negative publicity that promulgated from the M.D. Anderson/IBM Watson for Oncology project did have significant repercussions and offered an important lesson in AI adoption and accountability. Launched in 2013, this partnership garnered much publicity in the media and the hyped promise to cure cancer was never realized. Issues involved in this failure include: lack of competitive bidding, insufficient due diligence, and decision made without IT department buy-in. The seemingly obvious questions regarding whether it would improve patient outcomes and lower costs were not adequately answered by the institution.

For the future, AI promises to be an essential resource for oncology in many ways since oncology is multi-system and multi-dimensional as a subspecialty. Using NLP, key discoveries can be made via EHR data for early cancer detection as part of **population health management** as well as for ascertaining **patient-chemotherapy coupling** to be maximally efficient and efficacious. Medical imaging and radiology, an important component of cancer care, will become extremely sophisticated and perhaps be even closer with pathology. This will form an **AI-enabled image continuum** (radiology to pathology) that will even include multiple layers of additional information such as response to therapy and outcomes. As with most other subspecialties, a precision medicine approach to cancer (**precision and translational oncology**) to include pharmacogenomic profiles including immunotherapy is even more critical in oncology as it can provide a differential advantage towards survival. Finally, there is also altered **reality-enabled strategies** for treating therapy-related side effects in patients receiving chemotherapy, which may change in the future as well.

Ophthalmology. An ophthalmologist examines the eyes (including a fundoscopic examination which is a detailed examination of the retina) and cares for the diseases that pertain to the eye. Optical coherence tomography (OCT) is another imaging in ophthalmology. There is a myriad of diseases that affect the eye, with most common ones being glaucoma, cataracts, diabetic retinopathy seen in patients with diabetes, and macular degeneration seen in older patients. In addition to corrections for near sightedness (myopia), far sightedness (presbyopia), and astigmatism, an ophthalmologist can perform operations that include laser surgery and other procedures that deal with eye pathology.

Published Reviews and Selected Works. With the advent of deep learning and CNN in medical imaging, there is a relative increase in the number of publications in this area; most of the works focus on the deep learning aspect of **fundoscopic examination**. A review by Kapoor et al reviewed the current state of the art in AI in ophthalmology. The review not only focused on ophthalmology but briefly reviewed AI and its impact in a few other fields in medicine as well. The major areas of impact for AI in ophthalmology include: **teleophthalmology** for various eye diseases such as retinopathy of prematurity and glaucoma screening as well as use of AI and deep learning in eye diseases. Another review discussed the use of AI and patient metadata for rapid diagnosis and followup with an ophthalmologist. There are additional reviews on AI in ophthalmology.



One of the most significant studies published in the application of AI in medicine was the study by Gulshan that validated the accuracy of a deep learning algorithm for detection of **diabetic retinopathy** in retinal fundus photographs. The study showed that the algorithm is as good as board-certified ophthalmologists in making the diagnosis with high specificity and sensitivity and an area under the ROC of 0.99 **(see Figure)**. The deep CNN algorithm used over 100,000 retinal images for its data set and it had high sensitivity and specificity for detecting diabetic retinopathy in test sets. In 2018, Abramoff published a study of his **autonomous diagnostic system** (IDx-DR), which was later approved by the FDA in 2019 as the first fully autonomous AI-based diagnostic tool in biomedicine.

Present Assessment and Future Strategy. Overall, the public and the subspecialty have been enthusiastic about the first **autonomous AI-enabled diagnostic tool** (see above) and therefore screening of certain common eye conditions such as diabetic retinopathy can be achieved with good accuracy. The global health implications are sizable: the deep learning algorithm improves in the scope of eye conditions it can help diagnose, and the referrals may increase for the ophthalmologist to treat eye disorders.

For the future, the AI-enabled ophthalmologist may need to adopt the same strategy as the radiologist in that the non-perceptive as well as the procedural parts of the job will become even more important. The **automated screening eye examination** may be done at local centers with automated interpretation rather than in the clinical office of the ophthalmologist with delayed results. **Precision ophthalmology** care will involve appropriate followup of significant findings on the fundus examination that will routinely include patient metadata. It is possible that with widespread screening for common eye disorders that we will have a significant increase in the incidence of eye disorders; the increase in prevalence will need to be configured into national and international health budgets as well as treatment strategies to avoid over diagnosis and over treatment.

Pathology. A pathologist typically reviews many types of medical images of biopsies or sections of tissues in the form of microscopic slides (microscopic morphology remains the gold standard in diagnostic pathology). In addition to image interpretation, a pathologist also performs autopsies (called "gross" pathology). Lastly, many aspects of laboratory testing fall under the auspices of the pathologist and his/her division. The recent advent of digital pathology has expedited the workflow of the pathologist: whole-slide imaging, faster networks, and cheaper storage solutions have enabled pathologists to manage digital slide images.

Published Reviews and Selected Works. There is a robust body of literature on the use of AI in the form of deep learning and computer vision in pathology as it is an image-focused domain. A recent review of artificial intelligence and relevance to pathology recognized the significance of deep learning in incorporating clinical, radiological, and genomic data to pathology data. Much of the review focuses on CNN and computer vision for pathological specimens. In addition, a review of automation and AI in laboratory medicine emphasize the robust coupling of these two technologies can increase efficiency and lead to personalized medicine as well as precision public health. Different levels of automation in the laboratory ranges from inoculation to partial and complete laboratory automation. Additionally, reviews of digital pathology and AI delineated the integration of digital slides into the pathology workflow coupled with advanced algorithms and computer-aided diagnostic techniques.
There is also a report on the use of combined automation and AI in the **clinical laboratory**. The authors pointed out that both of these technologies will disrupt the clinical laboratories with development of new diagnostic and prognostic models that will be essential aspects of personalized medicine. Another review on use of AI in laboratory medicine focused on not only workflow but also regulation. A third review focused on basic concepts of ML as well as how these ML models can relate to laboratory medicine. Similar to a "human vs machine" landmark papers in other areas, a report compared DL algorithms to a group of 11 pathologists in a simulated workflow interpreting whole-slide images of lymph nodes in women with **breast cancer**; some of the ML algorithms proved better. In addition, automated interpretation of blood culture **gram stains** by use of CNN can be extended to all Gram stain interpretive activities in the clinical laboratory. Furthermore, a report on prostate cancer risk stratification and treatment section pointed out that multi parametric MRI and digital pathology should together can enable advanced characterization of disease through a combined **AI-enabled pathology-radiology assessment**. Nir reported recently that patch-based training and evaluation of CNN models may be flawed and that **multi expert data** should be used to obtain a more realistic performance evaluation of the model. Finally, O'Sullivan suggested the interesting integration of AI and autopsy via autonomous robots that can use a trained algorithm for a **robotic autopsy**. This development can have valuable insight into surgical procedures that are partly robotic as well.

Present Assessment and Future Strategy. Overall, the present situation warrants the pathologist to accommodate deep learning as a partner in image interpretation perhaps as much as the radiologist, if not more so. This accommodation will need all the pathology images to be digitized and stored in the cloud. It is entirely possible that the pathologist job description is even more vulnerable than that of the radiologist if the pathologist is not open to adoption of AI (as much of the pathologist focus is medical images). The laboratory data part of the pathologist portfolio can be improved with education for both the patient as well as the caretaker; in addition, the laboratory data should be one of the essential layers of data used for precision medicine.

For the future, while there is perception that some or even most of the pathologist work can be displaced by computer vision, there are several strategies. Perhaps the most intriguing is to have a new **medical image subspecialist** in the future who has a strong background in computer vision and deep learning that will entail the work of the present day pathologist and radiologist combined. This will be a sub specialist who will study the **medical image continuum** from the molecular and microscopic to the human-sized anatomic images. In addition, it is conceivable that the future laboratory will be entirely devoid of humans as full automation and AI will be an **end-to-end AI-enabled laboratory.**

Pediatrics. Pediatric physicians are either primary care pediatricians or a sub specialist in a specific field such as pediatric cardiology or pediatric infectious disease. Pediatric patients are challenging due to the heterogenous patient population (size and age) as well as the prevalence of pediatric rare diseases. Some pediatric subspecialties also accommodate adult patients with pediatric diseases.

Published Reviews and Selected Works. There has been only a few published works in pediatrics and artificial intelligence. There is, however, a growing number of AI-related publications predominantly within certain pediatric subspecialties such as radiology, cardiology, oncology, neurology, ophthalmology and pathology. In addition, there are publications in the realm of global health and infectious disease that are good realms for data mining as well as precision medicine which is ideal for certain pediatric diseases. A recent concise "synthetic" mini review by Kokol et al showed the evolution of AI-related pediatric medicine papers through several time periods and concluded that AI still has not been widely adopted in pediatrics due to a myriad of factors. The major AI themes as it related to children were: brain mapping, pattern recognition, developmental disorders, emergency care, machine learning, and oncology and gene profiling. In addition, a more comprehensive review by Shu et al covered a myriad of topics in the use of AI in pediatrics: decision support and hospital monitoring; medical imaging and biomedical diagnostics; precision medicine and drug discovery; cloud computing and big data; digital medicine and wearable technology; and robot technology and virtual assistants. Lastly, a review of the importance of data science in child health discusses the three unique features of child health for impact by data science: imperative for data sharing given less volume of relevant data, rareness of congenital diseases, and importance of potentially sensitive temporal information. This review also raises the interesting prospect of utilizing transfer learning with models developed on non-pediatric data.
A few important works are worth noting in AI in pediatric medicine. A recent publication from China focused on the use of AI and analysis of diverse and massive electronic health records (symptoms and signs, history, laboratory data, and PACS report) in over 1 million children visits. This paper revealed that machine learning classifiers can query medical records in a similar fashion to hypothetico-deductive reasoning of clinicians to make a diagnosis by using a deep learning-based natural language processing **information extraction model** that also includes a disease hierarchical logistic regression classifier in order to predict a clinical diagnosis for the encounter. This model was capable of out-performing junior pediatricians in diagnosing common pediatric diseases and may have a role for triaging based on severity of illness. An earlier study of ML (with 9 ML algorithms) used for medical decision support for early detection of **neonatal sepsis** found that 8/9 algorithms exceeded the physicians in terms of treatment sensitivity and specificity. Another good illustrative example of innovative application of AI tools is the mobile detection of **autism** through machine learning on home video. In this study, use of machine learning on 162 two-minute home videos speed the diagnosis without compromising accuracy of the autism diagnosis. The home video is uploaded and three raters (via a web portal) tagged all features (such as eye contact, stereotyped speech, or echolalia) to generate feature vectors to run each of the 8

classifiers automatically for diagnosis of autism. The 5-feature logistic regression classifier showed to be superior to other models that used decision trees or support vector machines.

Recently, a report on girls with suspected **central precious puberty** and their response to the gonadotropin-releasing hormone (GnRH) stimulation test with use of extreme boosting and random forest classifiers proved to be useful; to render the algorithm more interpretable, a LIME modification was deployed. Lastly, the use of NLP to recognize **Kawasaki disease** showed this methodology to be superior to manual review of charts by physicians and the authors astutely pointed out that this tool should be embedded in EHR as a support mechanism.

Present Assessment and Future Strategy. Overall, the field of pediatrics, both primary care and subspecialty care, underutilizes AI but certain areas are starting to adopt AI (cardiology, PICU, etc). Major obstacles to adoption include lack of understanding of AI and appreciation of AI tools amongst particularly pediatricians. The combination of heterogeneity of the population with the enigma of rare diseases renders pediatrics and the care of children ideal for deployment of AI for faster diagnoses and more accurate decision making process.

For the future, there can be several AI-related projects that will be impactful: 1) With AI and facial recognition capabilities as well as genomic sequencing, **undiagnosed genetic syndromes** in pediatrics can be a phenomenon of the past; 2) With lifelong **precision medicine** as a goal, multi-layered information such as genomic profile, family history, imaging data, laboratory data, etc will not only be the strategic for diagnosis and therapy in childhood, but throughout the entire lifespan of the individual; and 3) sophisticated AI tools can be deployed to accelerate speed of **AI-enabled diagnosis** of common childhood diseases (such as pneumonia, heart disease, diarrheal illnesses, etc) in areas of clinician shortage. In addition, medical images of children are often low in number, especially for certain rare diseases; a convergence of medical image types as well as pooling of such medical images can create a universal deep learning library for rapid **diagnosis and interpretation.** Lastly, **altered reality** as well as robotic technology can be useful AI tools in the therapy for children.

Pulmonology. These sub specialists are educated and trained to diagnose and treat diseases of the lungs and chest. Common disorders that they treat include reactive airway disease, lung cancer, and chronic obstructive lung disease (COPD). These clinicians often perform and/or overlook pulmonary function tests that measure lung function and capacity. In addition, they also perform bronchoscopy, a procedure that involves endoscopic examination of the airways and lungs. These clinicians work closely with the ICU physicians, and sometimes are even boarded in ICU medicine.

Published Reviews and Selected Works. There is a paucity of systematic reviews as well as reports of AI in pulmonary medicine. There is no comprehensive review that focuses on the use of AI in pulmonology.
A commentary on the use of AI and chest imaging (in the form of chest CT) discusses the enormous potential of AI by incorporating algorithms into standardized workflows and estimating **COPD burden**, exacerbation risk, and mortality in any given geographical area. Gonzalez et al in this same issue reported on their experience with deep learning-based analysis of CT scans of the chest can directly predict outcomes including respiratory events and mortality. Interestingly, this group also utilized transfer learning to have another cohort use the same methodology. Lastly, a recent report used AI for predicting **prolonged mechanical ventilation** and tracheostomy placement in adults. The AI methodology used was gradient-boosted decision trees algorithm for the classifier. Lastly, a pediatric study using physiological data and ML showed that this pediatric **automated asthma respiratory score** with ANN had a good predictive accuracy and another pediatric study discovered pediatric asthma **phenotypes** based on response to controller medications.

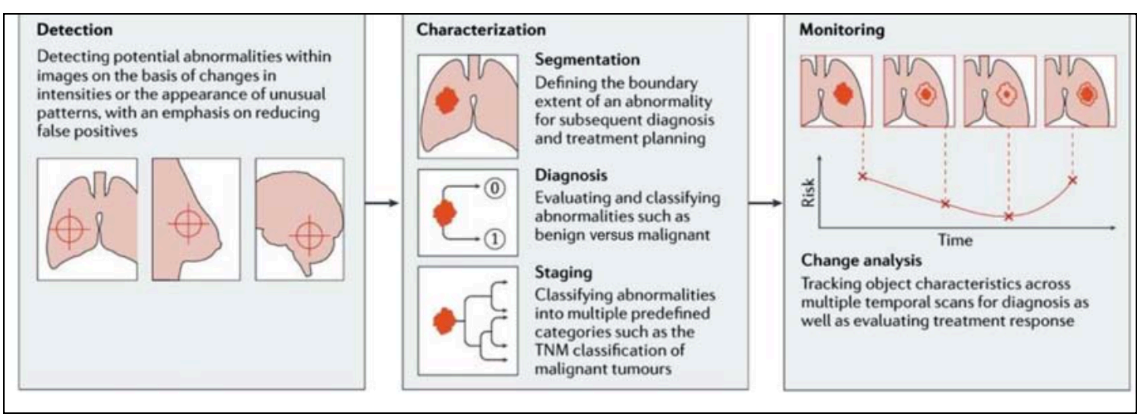
Present Assessment and Future Strategy. Overall, there is little academic or clinical activity on the use of AI in pulmonology. In addition to utilizing AI and DL/CNN for CT and MRI of the chest, pulmonologists can also leverage AI more for its image-related procedures, such as bronchoscopy

For the future, there are many areas that can be explored for AI applications in pulmonary medicine. Even though there are not as many types of imaging for the pulmonologist (as compared to radiologist or cardiologist), there are many possible advances from **precision pulmonology** and testing. For instance, an easy at home pulmonary function testing capability can be interpreted with an **AI-embedded pulmonary function device**.

Radiology. Radiology is a field dedicated to interpretation of medical images ranging from an Xray to more advanced images (such as CT and MRI) as well as some types of ultrasound (the exception being an echocardiogram, or an ultrasound of the heart, which is usually interpreted by a cardiologist). Some radiologists also perform procedures (called "invasive" as these procedures involve entering the vasculature or body organ) such as biopsies or interventions (such as vascular occlusions of certain blood vessels or aneurysms or insertion of catheters into veins). The field of nuclear medicine involves use of radioactive materials to diagnose or treat diseases.

Published Reviews and Selected Works. Radiologists are very familiar with **computer-aided detection and diagnosis** (CADe and CADx, respectively) software that are explicitly programmed to detect specific presentations of a disease on the medical image. As this field has been the most enthusiastic about AI especially as it relates to CNN with medical image interpretation, this is reflected in the number of publications as it has been exponential in its increase. In short, radiology is now the leading subspecialty in the number of new publications in the AI in biomedicine realm per annum (followed by oncology, surgery, and pathology in order). There are a number of review articles as well as substantive commentaries on AI in radiology and related subareas, but only a few will be mentioned here.

A recent review of AI and ML in radiology reviewed not only the imaging aspects of AI but also **workflow and surveillance**. The paper defined success of AI in radiology as: increased diagnostic certainty, faster turnaround, better outcomes for patients, and better quality of work life for radiologists. Another review discussed the evolution of AI vs human intelligence and put this in the context of **image-based tasks** with excellent diagrams for these processes (see Figure). The basic differences between traditional machine learning (with feature engineering and classification) and deep learning for radiology image interpretation is also shown. Yet another review in the same year focused on ML and its impact in workflow, specifically scheduling and triage, clinical decision support systems, detection and interpretation of findings, post processing and dose estimation, examination quality control, and radiology reporting. The review piece by Liew added the legal and ethical issues within health policy applied to AI systems.



There are several excellent overviews of ML/DL in imaging. A comprehensive primer on deep learning for radiologists by Chartrand is both comprehensive as well as easy to understand, with exquisite and concise explanations of key concepts as well as excellent diagrams to illustrate the many nuances in this domain. Other good reviews of varying lengths and details in DL in radiology have been published since 2015. Finally, an excellent AI guide of medical image analysis for the user (as well as authors and reviewers) offers excellent best practices, covering technical, statistical, and other aspects of evaluation and application of AI tools in radiology.

Another key area for radiologists is **natural language processing** as much of the workflow is focused on reporting and communicating the image findings. Cai et al provided an overall primer on NLP as it pertains to radiology research and clinical applications (see previous citation) and Pons provided a similar review of NLP with focus on workflow elements such as diagnostic surveillance, case recall, and quality of practice.

A landmark paper in radiology was the CheXNet study that developed an algorithm for detecting **pneumonia** on chest X-rays with performance that proved superior to radiologists. The algorithm was a 121-layer CNN trained on the largest publicly available chest X-ray dataset called ChestX-ray14 (with over 100,000 frontal-view chest X-ray images with 14 diseases). Although there have been many appropriate criticisms of this study (such as accuracy of ChestXray 14 dataset, medical meaning of labels, etc), it raised awareness amongst radiologists that a new era of AI-enabled medical image interpretation has arrived.

Titano reported use of CNN and weakly supervised classification for screening head CT images for acute neurologic events and was able to reduce the time to diagnosis from minutes to seconds. GE Health care partnered with Boston Children's Hospital to develop an AI-backed decision support platform with cloud computing for the diagnosis and treatment of **pediatric brain diseases**. This AI strategy of having a reference library of normal pediatric MRI brain scans coupled with deep learning is particularly helpful for pediatric brain imaging as disorders can be misinterpreted as normal brain maturation while the opposite is also true (normal brain maturation can be misdiagnosed as abnormal changes and lead to misdiagnoses and inappropriate treatment). This decision support platform will be available worldwide for all pediatric brain imaging as pediatric neuroradiologists are scarce. In addition, a recent report described a DL language modeling approach to attain a **radiology-pathology correlation** by taking reports of each domain and use Universal Language Model Fine-Tuning for Text Classification methodology. A recent study in JAMA showed that in diagnostic study of **intracranial aneurysms** with augmentation with a DL segmentation model, clinicians showed significant increases in sensitivity, accuracy, and inter-rater agreement when augmented with neural network model-generated segmentations while a study of cerebral arteriovenous malformations showed ML was able to provide best possible predictions of AVM radio surgery outcomes and to identify a novel radiobiological feature. A brief paper described the innovative Data Science Institute and AI Advisory Group under the American

College of Radiology. Finally, Jha suggested that radiologists (as well as pathologists) learn to adapt to AI to become "information specialists".

Present Assessment and Future Strategy. Overall, AI in radiology is extremely robust with some if not most of the radiologists very cognizant of the significance of AI in their future work. A milestone was reached when FDA granted approval of the AI radiology software called **ContaCT** (Viz.ai) in 2018; this software is able to decrease the time to make diagnosis of a major stroke. Even though there had been some discussion regarding whether radiology will be an attractive field for future students and trainees, the prevailing thinking is that radiology remains a secure field but with AI being an ever important partner in the practice. Despite what was said about not training any more radiologists, it is entirely conceivable that AI will render radiology even more enticing as a medical field. The American College of Radiology's **Data Science Institute** deserves much praise for its conceptualization and agenda as an AI-centric center of resources and education for radiologists. There is an ongoing discussion or even debate about the performance of single-site AI tools in medical image interpretation and whether these studies are applicable to other sites. In addition to the present work on **CNN and medical image interpretation**, there is also progress on **NLP applications** in radiology for less prose in reports and data mining. Some focus is now directed to **workflow inadequacies** in radiology that can potentially be neutralized by AI techniques.

For the future, a key concept for radiologists and medical image interpretation is the creation of a **"AI-enabled, end-to-end imaging**" that creates a continuum from image acquisition to reconstruction and segmentation and then on to image interpretation so that AI is embedded in all aspects of image acquisition and interpretation. Of note is the AI-enabled acquisition of images so that a poor image or study will potentially be an observation of the past; in addition, the future acquisition of images will be accompanied by labels that will be already in place. A concept that was discussed earlier under Cardiology is the emergence of a "**super scan**" in which static images such as CT or MRI as well as dynamic images as seen in ultrasound can converge into one modality with an AI-enabled strategy. A future concept also entails incorporation of this image interpretation into precision medicine and population health **(precision radiology or imaging)** so that followup studies will be based on data rather than intuition alone. It is possible that there will be a closer dyadic relationship between radiology and pathology so a future field of **medical image specialist** could emerge. In areas outside of imaging, AI can decrease the dosage of nuclear materials needed in **nuclear medicine**. Lastly, AI can also mitigate the administrative burden of a busy program by automating certain aspects of the radiology **administration** (such as deployment of RPA).

Surgery. While there are general surgeons, surgery is a large domain that encompasses many subareas, such as plastic surgery, orthopedic surgery, thoracic surgery, and neurosurgery. These subareas of surgery focus on a particular body area or organ (such as the heart for cardiac surgery) or a specific system (such as urologic surgery for the genitourinary system). A surgeon often interprets medical images although often with consultation with a radiologist but at times without such a support (such as during emergencies).

Published Reviews and Selected Works. The majority of current published works on AI and related topics concentrate on aspects of robotic surgery, but there are few reviews and published reports on AI in surgery (Neurosurgery and cardiac surgery will be discussed separately under neurosciences and cardiology, respectively). One recent review on AI in **surgery** emphasized that four AI areas outside of robotics are particularly relevant to surgeons: machine learning, NLP, artificial neural network, and computer vision. The implications for surgeons include: more precise selection of patients for procedures, especially biopsies; higher level of precision care as part of preoperative care; and increased surgical community collaboration via video and EMR data sharing and analytics. The integration of multimodal data with AI can significantly augment the surgeons' capability to improve care: preoperative comprehensive risk score calculation; intra-operative event detection and predictive analytics; and post-operative morbidity and mortality detection and prediction. Another general review in surgery but primarily focused on the transition from laparoscopic surgery to **robotic surgery** that is integrated with AI. These robots will need to be able to perceive surroundings, recognize problems, implement appropriate action plans and finally, produce solutions to new problems.
A similar review in **otolaryngology** encourages surgeons to put forth more efforts to collaborate with data scientists. The author correctly pointed out the pitfalls of AI in health care, such as the inflated expectation of Watson in oncology as well as the somewhat comical nuances in medical image interpretation (such as chest tubes in pneumothorax and rulers in malignant lesions). In addition, a focused review of AI in **plastic surgery** emphasized the importance of precision medicine and AI in plastic surgery in order to use patient data to formulate an individualized plan of intervention while another review of AI in the same surgical subspecialty focused on not only surgical applications but also resident training. Patients discussed in this review include: those undergoing breast surgery (and risk for associated anaplastic large cell lymphoma as well as over diagnosis of breast cancer); wound care (via use of imaging and CNN as well as AI-assisted evaluation for surgical flaps); and craniofacial surgery (perioperative and intraoperative surgical planning for craniosynostosis). A comprehensive review of AI and ML in **orthopedic surgery** is a thorough systematic literature review from the past two decades of 70 journal articles with the caveat that AI, like any other technology, needs to adhere to the tenets of health technology assessment while a word of caution was raised as well to balance the positive outlook. An excellent review of AI in **spine research** also covered a wide range of topics, from ML to image segmentation and prediction of outcomes.

Present Assessment and Future Strategy. Overall, with the exception of neurosurgery, most of the surgical disciplines remain relatively dormant in the area of AI. The field of **robotic surgery** does involve AI and is the sector that has garnered the most attention by the surgeons in general.

For the future, in addition to evolution of higher sophistication of robotic surgery, there are many areas that can be developed in the surgical areas. The surgeons would benefit from computer vision and **medical image interpretation** especially in the absence of a qualified radiologist. In addition, **preoperative planning** with the use of AI and virtual or augmented reality could reduce suboptimal surgical results and/or unnecessary complications. Data mining can be used for **risk assessment and stratification** to provide both the patients and payors a more precise prediction of outcome and resource allocation. Lastly, altered reality and AI can provide a resource for **preoperative planning** as well as **education and training** in surgery.

Digital Health. Digital health heralds the era of technological advances such as apps, wearable technology and remote monitoring, telemedicine and communication tools, and other diagnostic devices to affect a more optimal quality of care as well as a more timely response to any situation. While it is not a subspecialty per se, there are concentrated efforts and meetings in this domain to promote the use of existing technologies for population health and personalized medicine.

Published Reviews and Selected Works. There is a number of reports in digital health coupled with AI that clearly demonstrates not only proof of concept in applying AI to an app or device but also clinical benefit. A recent editorial in *Lancet* cautions the use of AI in digital medicine and strongly recommends a continual evaluation of digital health interventions for both clinical effectiveness and economic impact. A more positive review by Fogel discussed how AI in digital medicine can improve not only basic **health screening and prevention** as well as **medication adherence** but also the human-to-human experience of health care. Another review in this domain focused on the concept of a **medical internet of things (mIoT)** in digital health care that is imbued with AI-related tools. In order to reduce overall costs for both prevention and management of chronic diseases, devices are needed to execute this strategy: to monitor health biometrics, to auto-administer therapies, and to track real-time health data during therapy. Along with these devices, mobile applications for access to medical records as well as tools for telemedicine and telehealth for this new paradigm of medical IoT. All of these devices and equipment will need an AI-centric strategy for data integration and interpretation for delivering optimal health care advice and direction. While chronic diseases such as diabetes care can benefit greatly from a coordinated and efficient strategy, use of technology including AI remains fragmented at present due to a myriad of issues: lack of supportive policy and regulation, unsustainable reimbursement, inefficient business models, and concerns regarding data security and privacy. The advent of wearable devices and sensors to continuously track physiologic parameters can provide an overall patient care strategy that will improve outcome and lower health care costs in cardiac patients with heart failure. This new paradigm of cardiovascular disease management can also improve the physician-patient relationship. Machine learning algorithms have also been applied to large-scale wearable sensor data in neurological disorders such as Parkinson's disease to significantly improve both clinical diagnosis and management. This sensor-based, quantitative, objective, and easy-to-use system for assessing Parkinson's disease has potential to replace traditional qualitative and subjective ratings by human interpretation.

Present Assessment and Future Strategy. Overall, the present digital medicine sector is gradually being developed with interaction with basic analytics and AI tools. Most of the wearable devices are not embedded with analytics. As this domain also requires data infrastructure to be well organized, some of the efforts in this area have been also challenging. An overall strategy for preliminary and continual **evaluation** of AI applications in digital medicine has been ongoing as the barrier to entry may continue to be low for some apps and devices. This evaluation process will need insight from not only organizations such as the AMA or the FDA, but perhaps also by an international consortium of multidisciplinary experts. Finally, attention is being directed towards the **cybersecurity** of these intelligent devices to mitigate the risk of data breaches and therefore intentional harm to patients and caretakers.

For the future, **embedded AI (eAI)** and machine learning algorithms evolve toward the **internet of everything** (IoE) and will bring together people, process, data, and things; this strategy will allow the accrued data be streamlined and organized in the cloud proactively in an overall paradigm of **personalized precision medicine.** As these devices become more intelligent, increasingly higher levels of sophistication in decision support can also be part of both 1) **preventive medicine** (such as retinal images for retinopathy screening or skin lesions for melanoma detection) as well as 2) **chronic disease care management** (such as diabetes, hypertension, or heart failure).

Genomic Medicine and Precision/Personalized Medicine. Genomic medicine involves using genomic information of an individual as part of the clinical diagnosis and therapy, and has had impact on oncology, pharmacology, rare and undiagnosed diseases, and infectious disease. Genomic medicine is also an important part of precision or personalized medicine. There is some understandable confusion between personalized medicine and precision medicine: while the former is an older term, the latter is a more current term to reflect an approach to medicine that incorporates genetic, environmental, and lifestyle factors. Phamacogenomics, the study of how genes can affect a person's response to drugs, is an important part of precision medicine.

Published Reviews and Selected Works. There is significant academic activity focusing on AI in this burgeoning domain. A recent review on AI utilization in precision medicine discussed the importance of data quality and relevance. The authors contend that much of the effort to advance AI in precision medicine has been focused on algorithms and generation of genomic sequence data and EHR but should also be on **physiological genomic readouts** in disease-relevant tissues as well. Another review discussed advances in ML and AI are vital for the understanding of **epigenetic processes**, specifically deep learning for the generation and simultaneous computation of novel genomic features. Grapov et al reviewed deep learning in the context of omics and EHR and astutely pointed out that the challenges of DL is akin to those observed in **biological message relay systems** such as gene, protein, and metabolite networks. In biomedical diagnostics, medical geneticists are often frustrated by the tedious nature of genotype-phenotype interrelationships among syndromes, especially for extremely **rare syndromes**. Now, medical geneticists are able to use a visual diagnostic system that employs machine learning algorithms and digital imaging processing techniques in a hybrid approach for automated diagnosis in medical genetics, especially in rare diseases. One such proposal is the **BioIntelligence Framework** proposed by Farley et al. In this model, a scalable computational framework leverages a hypergraph-based data model and query language that may be suited for representing complex multi-lateral, multi-scalar, and multi-dimensional relationships. This hypergraph-like store of public knowledge is coupled with an individual's genomic and other patient information (such as imaging data) to drive a personalized genome-based knowledge store for clinical translation and discovery. Patients of very similar genomic and clinical elements can be discovered and matched for diagnostic and therapeutic strategies.

Present Assessment and Future Strategy. Overall, the field of genomic medicine with its extension into precision medicine has increased its focus on AI as it embodies the principles of Big Data and integration of this data for knowledge discovery in a **multi-omics data integration strategy.** The necessary complex work for all the disparate data to converge and for the prediction models to work creates a daunting challenge for the data scientist in this domain but concomitantly an exciting opportunity. For the future, there is optimism that precision medicine that is enabled by AI can lead to precision medicine from birth. This **lifelong precision medicine continuum** means that we can perhaps one day prevent diabetes starting from birth. In short, precision medicine as a paradigm for the future of medicine is attainable with full deployment of AI methodologies.

Physical Medicine and Rehabilitation (PM&R). This is a subspecialty that focuses on physical rehabilitation of usually medical and surgical patients after procedures and/or with disabilities (temporary or permanent). This field is also known as physiatry and the physician who practices physiatrcy a physiatrist. Common diagnoses of patients seen by physiatrists include those with brain or spinal cord injuries, neuromuscular disorders, strokes, multiple sclerosis, burn injury, and others. The overarching goal of this sub specialist is to restore functional capacity of and quality of life of any individual in need of interventions to achieve that goal. A sub specialist in this domain needs to have working knowledge of not only musculoskeletal system but also other systems, such as neurological, circulatory, and rheumatological.

Published Reviews and Selected Works. There are very few papers on the use of AI in this subspecialty. Barry reviewed the use of AI in this subspecialty and emphasized that adaptation, cooperation, and trust are at the center of rehabilitation and that AI and use of robots and other equipment can therefore enhance adaptation with guidance for movement as well as other elements such as cues for sensation and control of environment. Applications for AI in PM&R include: exoskeletons and neuroprosthetics; exercise and movement control with robots; telepresence, social robots, and smart environments (including smart homes). In addition, use of AI along with wearable technology and patient biometric measurements can improve efficiency and efficacy of musculoskeletal physiotherapy. Other papers focused on the use of robotics in rehabilitation but will not be covered in detail here.

Present Assessment and Future Strategy. Overall, there are some activities in this domain but limited to robotics but little in combining robotics and advanced AI methodologies or other emerging technologies. For the future, since **AI-enabled robotics** loom large in the coming decades, this subspecialty will see a large panoply of robots and equipment that will be made available for rehabilitation of patients with handicap and/or functional impairment. Additional technologies such as **altered reality** will also provide an additional innovative dimension to rehabilitation strategies.

Regenerative Medicine. This field of medicine, like genomic medicine, can be an element in some if not most subspecialties. Regenerative medicine is the discipline of creating living and functional tissue to repair or replace the patient's own tissue (due to congenital defect, injury, or disease). Progress has been made in bone, soft tissue, and corneas as well as organ transplantation but the future will bring many more possible therapies (such as tissue-engineered vascular grafts, stem and precursor cells for myocardial infarction, and even artificial pancreas, kidney, and even spinal cord).

Published Reviews and Selected Works. There is a moderate amount of published works on AI in regenerative medicine. One review in **pediatric cellular therapy** and regenerative medicine discussed use of predictive modeling for personalized treatment in children.

Present Assessment and Future Strategy. Overall, there is some activity in the area of regenerative medicine and AI in that this is a necessary cornerstone of precision medicine for the future. Regenerative medicine can be enabled by AI as computational modeling in both cellular immunotherapy and genetic engineering in addition to regenerative medicine can yield major dividends in the decade to come for precision medicine. For the future, promises loom large for this branch of medicine and many improvements in diagnosis will necessarily lead to therapy. An AI-enabled strategy for regenerative medicine will complement precision medicine with individualized medical and surgical therapy from the converging sciences of *tissue engineering, 3D-printing,* and AI as "**organ printing**". The AI strategy can be extended into the artificial organ such as pancreas and kidneys as AI will be a necessary coupling for not only its **morphological genesis** but also **functional maintenance** in the form of fuzzy logic and deep learning.

Medical Education and Training. Medical school education consists of a four year curriculum that consists of two years of basic sciences prior to two years of subspecialty exposure. Medical education consists of preclinical and clinical parts, with the former involving courses like anatomy, physiology, biochemistry, pharmacology, and pathology and the later rotations such as surgery, internal medicine, pediatrics, and radiology. After one graduates from medical school, one enters a residency program for subspecialty training and further on to a fellowship program for some areas such as cardiology, critical care medicine, or specialized surgical subspecialties. The length of residency and fellowship training after graduation from medical school depends on the subspecialty; it can be as short as three years for primary care (pediatrics or family practice) to as long as seven or more years for: 1) some surgical subspecialties like neurosurgery or cardiothoracic surgery; 2) some medical subspecialties that require additional fellowship training (such as pediatric cardiology); or 3) someone who desires multiple subspecialty board certification (such as cardiology and intensive care). After their specialized training, the typical physician is required to take a board examination to be certified in that particular subspecialty and then is required to take a recertification examination every 5-10 years. Physicians attain board certification and recertification as well as continue their education with continuing medical education (CME). In the United States, the Association of American Medical Colleges (AAMC) leads the academic medicine effort for the education of medical school students. With the exponentially increasing medical knowledge, the doubling time for medical knowledge has substantially shortened to the point where the average clinician does not have enough time to keep up with knowledge even in his/her own field.

Published Reviews and Selected Works. It is more than 100 years since the Flexner report that shaped our present medical school education strategy, and it is now more important than ever to reassess our medical educational strategy. A report by Wartman emphasized the timeliness of AI in medical education and its role in the future of clinical work. In addition, some subspecialties have also discussed the need for AI education also during clinical training as residents as well as the use of VR and AI in medical education. On the other hand, a review showed that AI can also be effectively utilized for assessing physician competence at different levels; surgeons and radiologists seem to be the subspecialties that used this strategy the most. Lastly, Johnston astutely pointed out that the training of the physicians of the future needs both information technology and analytics knowledge but also the humanistic aspects of medicine (the art of caring) is more essential than ever before.

Present Assessment and Future Strategy. Overall, there is very little education of data science or AI in medical education or training; in addition, much more use of AI and altered reality would also be ideal for both education and training (such as use of altered reality for virtual dissection of anatomy). For the future, medical education and training is ripe for a major disruption to maintain pace with the exponentially increasing medical knowledge as well as the rapid rise in modern technologies. The altered reality technologies with gaming and deep reinforcement learning can radically change the medical education experience as well as the clinical learning and training effectiveness. The advent of AI is a precious gift from our technological colleagues, and while AI is not necessarily going to replace clinicians, it should be part of every medical student's educational curriculum as well as every physician's clinical portfolio from this point forward.

Nursing. Nurses carry the main burden of health care delivery, and ranges from bedside nursing to outpatient nursing, and even home nursing. A nurse practitioner (NP) has obtained additional training and education and is able to write orders and serve as a physician's partner. A physician's assistant (PA) is a similar partner to the physician but may have additional capability to perform clinical and procedural tasks.

Published Reviews and Selected Works. The academic interest in AI for nursing is fairly robust. One paper details the potential of augmented intelligence in nursing. This review of AI focused on cognitive computing and IBM Watson but also discussed other AI tools in use. The essence of the review is on AI as a resource to place the locus of meaning back at home and with the patient. Another report reviews applying AI technology to support decision making in nursing.

Present Assessment and Future Strategy. Overall, the interest in AI from the nursing colleagues is relatively high. One potential reason is the number of challenges that nurses face on a day-to-day basis can have AI-enabled solutions. For the future, the domain of robotics and robotic assistance can be very robust in the future for nursing. In addition, the domain of chronic disease management and the possible role of virtual assistants will also be valuable for nursing care.

Health Care Administration. Like medical education and training, there is very little use of AI in hospital administration with the exception of some analytics (see earlier section). The typical hospital administrator is usually not enlightened on aspects of AI with the exception of an administrator who has a technology and/or AI background or had experience working with a data science team. An important aspect of health care administration is the complicated process (made even more so with the new ICD-10 codes) of **revenue cycle management (RCM)** that starts with the interaction and ends with hospital payment**:** processing, patient pre-authorization, eligibility and benefit verification, claims submission, payment posting, denial management, and finally reporting. Other aspects of health care administration with IT infrastructure includes HIS, RIS, VNA, CPOE, EHR and PACS, supply chain management, CRM, fraud and claims management.

Published Reviews and Selected Works. There is a paucity of published works on the use of current AI tools in health care administration. One review of AI in health care delivery has a section on health care administration. This review and section acknowledges that the complex nature of health care with its administrative burdens and resource constraints are in need of AI tools. New approaches such as transfer learning, contextual analysis, knowledge injection and distillation can be proposed to mitigate the health care imbroglio that has persisted and escalated the past few decades. In addition, a report discussed the use of ML-enabled complex high-dimensional models to assess and predict **hospital attendance** and found that gradient boosting machine-based models were the most accurate. In addition, there are many applications for **robotic process automation (RPA)**, which are intelligent software robots that can automate most repetitive tasks. These include processes such as physician credentialing, enrollment and patient eligibility, coding, claims administration, accounts receivable, and secondary claims management. The aforementioned RCM process can be managed with RPA with steps of the RCM automated (such as denied claims management).

Present Assessment and Future Strategy. Overall, there is much improvement that can be done in the administrative aspects of the hospital with deployment of AI. One main resource is the use of AI in the form of robotic process automation to increase operational efficiency. For the future, AI in a hospital should be the formation of an embedded **intelligence unit** that encompasses all aspects of data analytics at a cognitive level and in real-time mode. There will no longer be a necessary difference between business intelligence and clinical analytics as both will be part of the intelligence in the hospital.

Chapter 9: Implementation of AI in Medicine

Extreme uncertainty and dissatisfaction in data and information exists in the **imbroglio** of the practice of medicine and the world of health care especially with the increased incorporation of electronic health records (EHR) into the hospital and clinics and limited input into the few EHR vendors. Some of the data issues facing the present day practitioner include: escalating and missing data, exponentially increasing information, rigid regulatory policies, and decreasing access to information. He described the main implementation obstacles of artificial intelligence in medicine as: data sharing and standardization, transparency, patient safety, financial issues, and education. Medical providers lack sufficient insight and **education** in the realm of data science and this ignorance results in an inadequate knowledge from the rich data that now exist in health care and medicine. To date, there has not been wide acceptance of data science or artificial intelligence in the medical school or clinical training program curriculum. Finally, there is also a significant cultural and intellectual **schism** between the clinical world and data science domain: most medical meetings lack data science or artificial intelligence discussions on application and gatherings of devotees of machine learning or data science in health care or medicine also lack strong clinician presence.Practitioners require accurate data as well as up to date information and sharing of ideas to ensure best **outcomes** for the patient population and not solely be distracted by high performance of these tools. In the future, the data domain in health care will also be more inclusive of non-traditional sources such as social media and home monitoring especially with the proliferation of applications. In addition to the aforementioned issues above, Maddox posed several very relevant **questions** in this nascent domain: 1) What are the right tasks for AI in health care? 2) What are the right data for AI? 3) What is the right evidence standard for AI? and finally 4) What are the right approaches for integrating AI into clinical care?

In **conclusion**, the convergence of Big Data, improved algorithms, computational power, and cloud storage in health care has started to yield robust machine learning projects and reasonable results in biomedicine and health care. There is a wide range of subspecialty focus and interest level in AI applications to date, with radiology surging ahead with particularly deep learning in medical image interpretation. There are also many nuances between clinicians and data scientists in culture and understanding in being partners in this domain. Best practice in the near future will involve the use of AI to answer the clinical questions (intelligence-based medicine) rather than current practice of solely relying on published reports and other resources (evidence-based medicine or expert groups).

Key Concepts

- There is currently an escalating interest and enthusiasm for AI in medicine and health care, particularly in a few areas such as medical imaging and decision support; the origin of this surge in accommodation of AI in medicine has been mostly the rapid proliferation as well as adoption of machine and deep learning in many areas.
- Overall, the FDA and its Good Machine Learning Practices is a much more congruent regulatory strategy with the exponential increase in AI technologies in clinical medicine and health care.
- This dichotomy conveniently delineates some of the key differences between clinicians (more prone to System 1 thinking) and data scientists (with their affinity for System 2 thinking). Physicians, especially those in the acute care clinical setting (such as emergency room, ICUs, and operating and procedure rooms) often rely on a fast intuition-based System I thinking that is based on past experiences and judgments. Data scientists, on the other hand, more frequently approach problems with slower and more logical progressive thinking that is rationality-based System 2 thinking.
- Overall, perhaps the myriad of human biases and heuristics can potentially be neutralized with an objective AI-supported strategy in the decision-making process to reduce the proportion of human-related biases and heuristics that often lead to errors.
- Major criticisms of EBM include a publication bias, which refers to the clinician and investigator tendencies to publish only studies with a positive diagnostic or therapeutic result. In addition, the terms of the criteria for the levels of evidence are not always agreed upon and these imprecise definitions are often confusing and misleading. These guidelines or recommendations are very often out of date and do not accommodate more recent ideas and/or study results; in short, the information is not timely and therefore lack real-time relevance.
- Most, if not all physicians in their subspecialties, can be configured by three basic areas of thinking that involves different areas of the brain in which they perform their tasks: perception, cognition, and operation.
- There is much promise in the utilization of AI methodologies such as deep learning (in particular convolutional neural network, or CNN) for automated medical image interpretation and/or augmented medical imaging. The image interpretation tasks include: classification, regression, localization, and segmentation.
- The area of augmented (AR), virtual (VR), and mixed reality (VAMR) will be able to leverage AI technology and use this resource to the fullest for a variety of purposes; these include education and training as well as simulation and immersive scenarios for all stakeholders (including patients and families) and preoperative and intra-operative imaging and planning for certain medical and surgical subspecialists.
- While it is laudable that AI was able to defeat the human champion in the game *Go*, the practice of medicine, especially in the chaotic domains of the emergency room, intensive care unit, and operating rooms, are more akin to the real-time strategy games like *StarCraft*.

- Bedside biomedical monitoring has been unidirectional: displaying data such as vital signs in a continuous fashion but not analyzing and understanding data internally so therefore, not at all "intelligent". AI has the potential to change this paradigm by deploying machine and deep learning to this rich data milieu (with RNN described above) and deriving knowledge and intelligence in a real-time fashion.
- Human-robot interaction and relationship are being evaluated in a variety of clinical scenarios such as physical or psychiatric rehabilitation and education and training.
- AI is very involved in the evolution of virtual assistants as these are dividends of natural language processing (including natural language understanding and generation).
- The paradigm of precision medicine with its complexity of decisions that can be made and enormity of data to be analyzed is particularly well suited for the portfolio of AI methodologies such as deep learning (especially its AI congener deep reinforcement learning) as similar patients can be identified and assessed.
- Diverse disciplines such as language, neurophysiology, chemistry, toxicology, biostatistics, and medicine can converge to leverage AI and ML/DL to design novel drug candidates. The cognitive solutions are designed to fully integrate and analyze relatively large data sets such as in life sciences for drug discovery.
- An essential part of digital health is the use of information and communication technologies as well as AI in the form of data mining of the incoming data as well as machine and deep learning for anomaly detection, prediction, and diagnosis/decision making in a continuous manner.
- Wearable technology has also taken a different perspective in this time of AI, especially with the possibility of wide adoption of simple AI tools embedded in medical devices.
- AI technology, while maturing in the area of medical image interpretation, still needs to be more sophisticated in the realm of decision support; real-time, complex decision support with feedback mechanism is the crux of the need for AI-enabled anesthesia practice.
- Overall, as cardiology is both a perceptual or image intensive field as well as a cognitive or decision making subspecialty with a myriad of procedural tasks, AI is a particularly valuable technology for cardiology with potentially very rich dividends that are vastly under-explored at present but has great promise.
- Once deep reinforcement learning or other deep learning methodologies are sophisticated enough for the real-time, complex decision making challenges of ICU medicine, there will be predictably an even higher level of AI adoption by the physicians in this group. The true value will be a universal ICU data repository for an enriched data source for ML/DL and deep reinforcement learning.
- For the future, an AI-enabled dermatologist will have routine CNN-enabled dermoscopy in the office on a routine basis and this dyad will correctly diagnose skin conditions almost perfectly. This human-machine synergy can also be combined with digital health capabilities to transmit photographs for not only routine screening but also followup; this capability can therefore obviate the need for an excessive number of clinic visits as well as make available a valuable service in global health.

- For the future, like the other subspecialties that often require fast thinking and decision making (ICU, surgery, and anesthesiology), emergency medicine can greatly benefit from an AI-enabled strategy of deep reinforcement learning designed for real-time decision-making.
- For the future, exciting innovative advances with closed loop systems and fuzzy logic as well as CRNN AI methodologies will all be extremely useful for essentially an artificial pancreas to treat diabetes. This will be a highly significant advance in the management of one of the most significant disease burdens in the future.
- AI-enabled endoscopic examinations should be routinely embedded with CNN as an augmentation for the gastroenterologist. This procedure should involve an entire continuum from acquisition of the image to CNN interpretation of suspicious lesions and decision to biopsy or not.
- The fields of global and public health as well as epidemiology are ideally structured for use of ML/DL and other methodologies in studying and managing epidemics and natural disasters in the context of large populations.
- There are some clinical and organizational activities in deploying AI and ML/DL in infectious diseases but not in an organized global manner. The field of infectious disease with its many sources of data is ideally suited for big data and ML/DL with some expert knowledge oversight for many dividends.
- There are many ways that AI can help the primary care physicians outside of medical image interpretation and decision support. The areas of chart review, practice management, risk prediction, and population health management are large market potentials with growing number of AI-enabled solutions.
- Similar to the artificial pancreas discussed under endocrinology, the artificial kidney will need real-time decision support and predictive modeling with biofeedback and embedded AI in the device. Elements need to be incorporated in this model will include anemia, total body water, and intradialysis hypotension.
- There will be a necessary convergence and synergy between AI and the neurosciences so that this dyadic relationship will increase the knowledge and capabilities of both of these intimately related sciences.
- Much of the interest in the use of AI in obstetrics and gynecology has been in the areas of fetal monitoring, which as a very small signal-to-noise ratio (similar to electrocardiograms and electroencephalograms), and in vitro fertilization. Similar to many of the aforementioned clinical areas, obstetrics and gynecology has a very heterogeneous group of patients, and even include fetuses as an essential part of the clinical scope. This level of complexity is well suited for more sophisticated ML/DL to decrease the burden and stress of decision making for the clinician.

- Overall, the public and the subspecialty have been enthusiastic about the first autonomous AI-enabled diagnostic tool and therefore screening of certain common eye conditions such as diabetic retinopathy can be achieved with good accuracy. The global health implications are sizable: the deep learning algorithm improves in the scope of eye conditions it can help diagnose, and the referrals may increase for the ophthalmologist to treat eye disorders.
- The relatively negative publicity that promulgated from the M.D. Anderson/IBM Watson for Oncology project did have significant repercussions and offered an important lesson in AI adoption and accountability. Issues involved in this failure include: lack of competitive bidding, insufficient due diligence, and decision made without IT department buy-in. The seemingly obvious questions regarding whether it would improve patient outcomes and lower costs were not adequately answered by the institution.
- While there is perception that some or even most of the pathologist work can be displaced by computer vision, there are several strategies. Perhaps the most intriguing is to have a new medical image subspecialist in the future who has a strong background in computer vision and deep learning that will entail the work of the present day pathologist and radiologist combined. This will be a sub specialist who will study the medical image continuum from the molecular and microscopic to the human-sized anatomic images.
- The field of pediatrics, both primary care and subspecialty care, underutilizes AI but certain areas are starting to adopt AI (cardiology, PICU, etc). Major obstacles to adoption include lack of understanding of AI and appreciation of AI tools amongst particularly pediatricians. The combination of heterogeneity of the population with the enigma of rare diseases renders pediatrics and the care of children ideal for deployment of AI for faster diagnoses and more accurate decision making process.
- Even though there are not as many types of imaging for the pulmonologist (as compared to radiologist or cardiologist), there are many possible advances from precision pulmonology and testing. For instance, an easy at home pulmonary function testing capability can be interpreted with an AI-embedded pulmonary function device.
- In addition to the present work on CNN and medical image interpretation, there is also progress on NLP applications in radiology for less prose in reports and data mining. Some focus is now directed to workflow inadequacies in radiology that can potentially be neutralized by AI techniques.
- Wearable technology and embedded AI can provide valuable real time and daily information for AI-enabled chronic disease management that can be designed to be patient-centric. In addition, diagnostic dilemmas that frequently encountered by the rheumatologist can be aided by an AI resource in the form of updated information as well as an able cognitive partner. Lastly, as many of these patients have chronic disability, the AI tools in robotic technology and virtual assistants can be valuable as assisting dimensions for patient care.

- For the future, in addition to evolution of higher sophistication of robotic surgery, there are many areas that can be developed in the surgical areas. The surgeons would benefit from computer vision and medical image interpretation especially in the absence of a qualified radiologist. In addition, preoperative planning with the use of AI and virtual or augmented reality could reduce suboptimal surgical results and/or unnecessary complications.
- Embedded AI (eAI) and machine learning algorithms evolve toward the internet of everything (IoE) and will bring together people, process, data, and things; this strategy will allow the accrued data be streamlined and organized in the cloud proactively in an overall paradigm of personalized precision medicine.
- The multidimensional genomic and clinical data can be configured (mapped and projected though an ontology graph data structure) to search for individualized therapy. Clinical and molecular profiles from individuals are used along with their EHR data for a three-dimensional approach (horizontal knowledge planes or search space and vertical mapping with ontology layers) to recover concepts to infer therapeutic options. The basis for this framework is a hierarchically organized and ontologically based knowledge representation schema.
- For the future, since AI-enabled robotics loom large in the coming decades, this subspecialty will see a large panoply of robots and equipment that will be made available for rehabilitation of patients with handicap and/or functional impairment. Additional technologies such as altered reality will also provide an additional innovative dimension to rehabilitation strategies.
- The altered reality technologies with gaming and deep reinforcement learning can radically change the medical education experience as well as the clinical learning and training effectiveness.
- The domain of robotics and robotic assistance can be very robust in the future for nursing. In addition, the domain of chronic disease management and the possible role of virtual assistants will also be valuable for nursing care.
- AI in a hospital should be the formation of an embedded intelligence unit that encompasses all aspects of data analytics at a cognitive level and in real-time mode. There will no longer be a necessary difference between business intelligence and clinical analytics as both will be part of the intelligence in the hospital.

Ten Elements for Successful Implementation of Artificial Intelligence in Medicine

These are ten necessary elements and solutions to solve issues and problems for artificial intelligence in medicine to be an ultimately successful paradigm shift:

Improving data access, storage, and sharing strategies in health care. Much of the data in health care is missing, inaccurate, and disorganized as well as fragmented. In addition, patients need to be empowered to own their data as often health care data are sequestered in a hospital or clinic with virtually no access. Finally, all the stakeholders must come together and be willing to provide access and share health care data. If AI is the rocket to launch us into orbit and onto moonshot projects, data is the fuel we need yet this fuel is not centrally collected. Timing is key as major data sources are still yet being formed, such as genomic data, wearable technology data, and socioeconomic data. While AI methodologies are ahead of schedule, data in health care has been in disarray for decades and will require effort to be improved. One key strategy will be the deployment of a revolutionary data infrastructure (graph or **hypergraph databases**). All of this discussion of health care data being collected and stored will require close attention to cybersecurity and the emergence of blockchain technology may be timely. In short, good AI in medicine mandates good not merely basic data and database foundation but also some level of **connectivity** via IoT and IoE.

Fostering AI in medicine awareness and education. Even with escalating increases in venture capital in the area of artifi cial intelligence in health care and medicine, particularly in the areas of decision support and medical imaging, hospital administrators and clinicians as well as investors still lack suffi cient education about artifi cial intelligence methodologies applied to health care and medicine. There is a paucity of data science classes in medical schools and residency programs. In addition, computer and data scientists are also less than fully enlightened in the realm of clinical medicine and what clinicians actually need most for artificial intelligence to be utilized in order to lessen their burden. An overall higher level of knowledge will also prevent procuring AI solutions that are "Mechanical Turks".

Understanding human-to-human (H2H) collaboration for AI-driven agenda. In the work of artifi cial intelligence in medicine, it is vital that human to human interactions and relationships drive these agendas and projects. From sharing data to doing projects using artifi cial intelligence in health care and medicine, human champions and leaders from a myriad of domains need to be the drivers of these joint agendas.

Increasing clinician-to-data scientist synergy. There is a general lack of awareness and education for clinicians about deep learning (try to find a clinically active physician who even understands what deep learning is) and concomitantly for data scientists about clinical medicine (try to find a data scientist who interfaces with a physician more than once in a while and who actually spends time in the clinical domain). This clinician-to-data scientist distance is further increased with at times human hubris on both sides. One example is the preliminary machine learning work in atrial fibrillation: this has the potential to lead to over diagnosis if there is not enough discussion between the clinical and data science domains. A great fictional comparison is that of Sherlock Holmes (the data scientist) and Dr. Watson (the clinician), the dyad of inspectors that work well together as both neutralize each other's weaknesses. Lastly, the present state of imbroglio in medicine and its future solutions based on artificial intelligence mandates a special duality and synergy of clinicians and data scientists (like the double helices of DNA) with their respective different modes of processing contributing without hubris. Take the integer of "5" and have the clinician and data scientist each be this integer: If the two parties are antagonistic, then it is 5/5 or 1; if the two parties are complementary but not synergistic, then it is 5+5=10; if the two parties are synergistic, then it is 5x5=25. The future clinician may benefit from a dual education in data science and artificial intelligence. These dual-trained scientists can then serve as valuable liaisons between the clinical and data science domains. It is possible that deep learning and AI can render the clinicians less clinically astute so these clinician-data scientists can mitigate this loss of clinical acumen. Lack of a dual perspective can easily lead to false presumptions; over-diagnosis is a potential problem such as studies that have excluded a clinician input. This cohort will also be useful to demystify the "black box" issue of artificial intelligence. The cohort is helpful to police false discovery with finding spurious associations in the training set that have little relevance to new data.

Appreciating small (and not always big) data in biomedicine. Finally, for the future, if we have sustained human-to-human collaboration and if we have design deep learning in health care and medicine, we will need to utilize not only deep learning but also variants of deep learning for solutions as there cannot be always Big Data to satisfy the ideal situation for deep learning. We need to work with "small" data (individual patients' serial data for example) that is extremely important for many clinicians in serial followup. We also need to think of innovative deep learning methods such as one-shot learning and deep reinforcement learning for less than Big Data.

Making the visible invisible and the invisible visible as well as being able to explain AI. The AI projects should render present day paraphernalia such as computers and biometric devices obsolete (making the visible invisible). One such AI-inspired tool is the **intelligent agent** (or chat bots) that will replace many humans. Conversely, the signal in the noise will be picked up by deep learning and other techniques to make the invisible knowledge and intelligence in health care and medicine more discernible. It is good to have someone knowledgeable to triage the situations to see which will be best suited for AI methodologies. Lastly, we need **explainable AI,** or xAI, to minimize the "black box" perception of AI and in particular, deep learning amongst stakeholders who do not have a data science education or background.

Utilizing all aspects of AI tools in the AI portfolio (not only deep learning). Despite the attention, It is not always about machine or deep learning in biomedicine. The lack of a meaningful continual human (clinician)-to-human (data scientist) interface then results in a paucity of best solutions to real problems in health care and medicine with a full understanding of all the nuances. In addition, we have the possibility of creating a myriad of over-diagnoses which can result in inappropriate therapy and its inherent complications. In short, we do not, in health care, have **"design" thinking**. It is prudent to implement basic techniques in statistical analysis rather than always thinking that deep learning is the only methodology. Some of the knowledge can be culled from good basic data analytics without heavy duty deep learning and it is important to appreciate when situations do not demand AI. Conversely, many future problems in biomedicine and health care will need to be solved with a cognitive solution and not simply deep learning.

Understanding the complex nature of biomedicine. In spite of the success of AlphaGo in defeating the human Go champion, biomedicine can arguably be even more complex than the Go game. The "deep" phenotype of biomedicine will include hundreds of layers of data including genomic and pharmacogenomic profile, socioeconomic milieu, psychological profile, etc. This deep phenotyping necessary to demystify the imbroglio of clinical biomedicine and precision medicine will become far more complex as the years of AI in health care and medicine become more omnipresent (see Figure). There is a potential mismatch between precision medicine and population health; AI in biomedicine may be useful to reconcile these two forces.

Introducing elements of cognition in AI in medicine. All stakeholders involved in AI in medicine and health care should have a rudimentary understanding of the types of artifi cial intelligence and all their nuances and limitations. Appreciation of the third wave (neuroscience) of AI will be vital for all practitioners of AI in health care and medicine. The advent of internet of things (IoT) will evolve into the AI-inspired **internet of everything (IoE)** in which devices will have some **embedded AI (eAI)** capabilities; this is analogous to afferent peripheral nerves connecting to a central nervous system. With this capability, each person's health care could be provided a "**clinical GPS**" with illnesses being "traffi c congestions" to be navigated around.

Executing more realistic projects as well as grand vision projects. It is essential to have a portfolio of AI in medicine projects especially ones that are field-proven automation projects (administrative tasks such as obtaining authorizations and credentialing health care workers) using **robotic process automation.** The AI team should have a balanced portfolio of projects that include both easier to accomplish ones as well as more ambitious deep learning projects that focus on medical image interpretation or decision support in various clinical venues. This approach will increase adoption from both the administrative as well as the clinical leadership as there will be an ROI as well as value from the portfolio of projects.

Ten Obstacles to Overcome for Implementation of Artificial Intelligence in Medicine
Here are ten potential obstacles (there are obviously more but these are some of the common ones observed) for successful implementation of AI projects or agendas in any organization or group:

Cultural differences between clinicians/hospital administrators and data scientists. Physicians, especially ones in acute care settings, prefer to make decisions expediently as they may have many such decisions to make within a short time (rounds or conferences). Data scientists usually have a less aggressive **timeline** and tend to work with more flexibility (although startups have a similar attention to timelines). There is also a difference in the **hierarchical structure** of these two groups.

Value proposition of AI projects and services. It is sometimes very difficult and/or tedious to convince all stakeholders the value proposition of individual AI projects from various services. This obstacle is usually easier to overcome when a previous AI service or project has been productive or has returned some value on investment. It is also helpful to have at least a few clinician champions in the organization to emphasize value in terms of quality of **patient care delivery**.

Knowledge deficit on both sides. Clinicians are mostly familiar with statistics from their medical education but are not usually well educated in data science. Data scientists, on the other hand, can search for knowledge in medicine but at times do not comprehend the many nuances and intrinsic **complexities** and **uncertainties** of clinical medicine nor how physicians think. This creates a sizable domain knowledge schism that can exaggerate the cultural differences.

Trust in new technology. The clinicians sometimes feel somewhat antagonistic towards certain technologies that had great promise but resulted in much lower delivery. One constant comparison is that of **EHR** and AI as the latter technology is sometimes bundled with the former. Clinicians naturally still harbor some discontent with EHR due to its increased burden and lack of perceived value. AI can focus on mitigating this burden or at least bring value as much as feasible.

Explainability of AI tools (and the "black box" perception). There is a perception that there is a lack transparency of AI tools. It may be unfair to expect AI tools to be fully elucidated as clinicians do not always have that expectation for all technologies (pacemakers for example). If clinicians attain a basic understanding of AI and if the data scientists work on rendering these AI tools more understandable, perhaps an acceptable middle ground of **interpretability** can be reached.

Workflow affected by AI. There is low tolerance amongst clinicians for more burden of any kind due to a relatively high rate of professional **burnout** from many reasons (one major reason is the EHR burden). The ideal AI project would not only decrease the burden, but also improve patient care and bring the cost of care down. The only sure way to get adoption for an AI project that would increase burden is if the project will clearly demonstrate improved quality of care.

Access to large volume of high integrity data. Biomedical data, in its cleanest and most complete form, is very difficult to secure in high volumes. Even very large biomedical datasets can have very inaccurate labeling as well as many other issues. Clinicians can help to overcome this limitation by collaborating with other institutions, which is rarely done but hopefully will be more routine in the near future. Data scientists can also be more flexible with working with **small data**.

Interoperability and EHR infrastructure issues. Aside from the aforementioned data size and integrity issue, there are logistical hurdles of data access and gathering that can have high levels of time and resource demands. Lack of full **interoperability** between hospitals and health care venues makes it difficult to have full access to the data as well as to gather all the data. There is also an understandable lack of full collaboration amongst EHR vendors that will facilitate data sharing.

Lack of clinician champion(s). Just as with any project, it is much more difficult to get AI adoption if there is no clear clinician champion who would be very committed to the AI project. Even with a clinician champion, that person will still need to gather several co-champions that will not only support but also sustain the project. The champion(s) will need to maintain constant **communication** with the AI stakeholders to have circular feedback throughout the project.

Fear of AI taking over and displacing clinicians (and others). There is a concern amongst health care workers that part or most of their job descriptions can be displaced by **automation** and AI. The premature public declaration by a vocal few that doctors will be replaced was not widely accepted nor appreciated by clinicians. The more realistic concept is that AI will complement the skill sets of health care workers and reduce the excessive burdens that they face on a daily basis.

In addition, here are a few more obstacles from Kevin Lyman of Enlitic:
1. Radiology data is highly nuanced and unintended bias is hard to avoid without proper education.
2. More time is spent building tools that enable us to build clinical AI than actually building clinical AI.
3. Most hospitals do not design their software infrastructure with ease of AI integration in mind.
4. Models do not get regulatory approvals, claims around very specific uses of a model do.
5. Privacy and security are subjective measures with moving targets, especially on a global scale.

IV. The Future of Artificial Intelligence & Application in Medicine

Questions 10.1/Key Concepts of the Future of Artificial Intelligence

1. According to Peter Voss, what is the next (third) wave or phase of AI:
a. Cognitive architecture
b. Deep learning with advances
c. Good old fashioned AI (GOFAI)
d. Deep reinforcement learning
[ ]

2. An altered reality that is coded by a special language and is a computer-generated artificial simulation or recreation of a situation (mainly via vision and hearing) is called:
a. Augmented reality
b. Virtual reality
c. Mixed reality
d. Immersive reality
[ ]

3. An enhanced reality that is a result of computer-generated enhancements atop of reality is called:
a. Augmented reality
b. Virtual reality
c. Mixed reality
d. Immersive reality
[ ]

4. Which of the following statements about blockchain is *not* true?
a. It is the use of cryptography to allow a collection of blocks or records to be maintained in such a way that is difficult to modify
b. This strategy was initially used for bitcoin as a public ledger
c. Blockchain is a disruptive innovation in information registration that utilizes three existing technologies: private key cryptography, peer-to-peer network, and the blockchain protocol
d. Blockchain and AI will not have any synergy in the future
[ ]

5. Which of the following phenomena is *not* thought to be complex?
a. A pandemic
b. The heart
c. The weather
d. A computer
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Questions 10.2/Key Concepts of the Future of Artificial Intelligence

1. Healthcare exemplifies a complex adaptive system. Which of the following is *not* a characteristic of this kind of system:
a. Systems thinking
b. Centralized control
c. Self-organizing
d. Dynamic
[ ]

2. The computing technology that enables devices to collect and analyze data in real time locally so that it is processed outside the cloud data center is called:
a. Edge computing
b. Quantum computing
c. Data lake
d. Data warehouse
[ ]

3. The technological paradigm of integrating machine learning or other AI tools into the device itself to attain a certain desired function is called:
a. Robotic process automation
b. Embedded artificial intelligence
c. Internet of things
d. Cognitive computing
[ ]

4. Which is *not* a true statement about swarm intelligence?
a. It is intelligence derived from many individuals based on self-organizing group behavior
b. The collective behavior illustrates that unified systems outperform the majority of individuals
c. This group dynamic results in ad-hoc information gathering and sharing
d. This type of intelligence cannot be combined with machine intelligence
[ ]

5. Instead of training a deep neural network from the beginning, one can take a previously trained network on a different domain for a source task and adapt it for a target task with smaller amount of data. This is called:
a. Generative adversarial network
b. Autoencoder
c. Transfer learning
d. Recurrent neural network
[ ]

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b. Autoencoder
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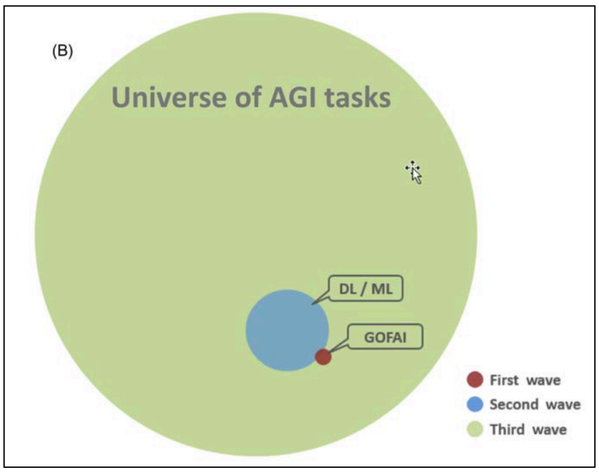
d. Recurrent neural network
[c]

Module 10.1-2/Key Concepts of the Future of Artificial Intelligence

The future of artificial intelligence and its applications in biomedicine is very promising but also full of challenges. This premise of advances in AI is based on rapid improvement and accelerated deployment of advanced computer technology (such as quantum computing and neuromorphic chips) and rapid development and evolution of artificial intelligence techniques (such as deep learning and it many variants) as well as cognition-influenced architecture that have lead to a current Cambrian explosion of AI.



Peter Voss so aptly described the future of AI as the "**third wave**": the first wave of AI was **good old fashioned AI (GOFAI)** that focused on traditional programming followed by the second wave of AI of the current **deep learning** so that this third wave will be reliant on many **cognitive architectures (see Figure)**. While this third wave of cognitive architecture is much more complex as it incorporates the relevant elements of human cognition, the former two waves do lack the biological completeness and integration of the third wave. Machine learning alone in medical decision making can be dangerous if it is performed without human cognition and "common sense". In this third wave, cognitive architectures will need to possess: general learning ability; real-time and interactive learning; dynamic goals and context; transfer learning; and abstract reasoning in order to reach AGI. In addition, human-like intuition AI developments designed to be between machine and deep learning and rule-based programming are helpful; these AI advances include interactive networks (a model that can reason about how objects in complex systems interact), neural physics engine (an object-based neural network architecture fore learning predictive models), and **recursive cortical networks** (discussed below).

In addition to cognitive architecture, there are additional areas of development of AI that are particularly relevant to clinical medicine and health care (in alphabetical order):

5G
This is the next generation mobile internet connectivity that will provide much faster speed (100x faster than 4G) and more reliable connections on devices. This future capability will accommodate the exponential rise in internet of things and medical devices with the infrastructure necessary for the large amount of data to come. Increased speed and data transfer as well as more bandwidth is the end result of having 5G capability; this will be essential as more devices become more sophisticated. The countries most active in bringing in 5G are US, China, and South Korea.

Augmented and Virtual Reality
The future of AI will enable both augmented and virtual reality. **Augmented reality (AR)** is an enhanced reality that is a result of computer-generated enhancements atop of reality. **Virtual reality (VR),** coded by a special language called virtual reality modeling language (VRML), is a computer-generated artificial simulation or recreation of a situation mainly via vision and hearing (Facebook Oculus is an example). Both of these AI-enabled reality methodologies will become commonplace in the near future and will have many possible applications in medicine and health care, such as medical education (both clinicians and families), training (including simulation), and preoperative or pre-procedural planning.

Blockchain and Cybersecurity
Blockchain is the use of cryptography to allow a collection of blocks or records to be maintained in such a way that is difficult to modify. This strategy was initially used for bitcoin as a public ledger. Blockchain is therefore a disruptive innovation in information registration that utilizes three existing technologies: private key cryptography, peer-to-peer (P2P) network, and the blockchain protocol. A successful deployment of technologies such as blockchain to improve cybersecurity in health care will facilitate data sharing amongst stakeholders in the near future. Additional future cloud and data security concepts to be adopted for the future will need to include novel concepts as blockchain as well as: 1) **Homomorphic encryption**. This is an encryption strategy that allows for certain computations to be performed on medical data while they are still encrypted. One significant limitation for this security solution is that the processing speed is slowed during this process. 2) **Differential privacy**. This security process uses sophisticated algorithms to add sufficient “noise” to the data to render it less vulnerable to linkages to other databases for matching purposes. Mamoshina (see reference above) proposed to create a large secure health care data ecosystem that is enabled by a convergence of blockchain and AI.

Brain-Computer Interface (BCI)

The other terms for this concept include mind-machine interface (MMI), brain-machine interface (BMI), or direct neural interface (DNI). These are all communication pathways between the brain and an external device to augment natural intelligence. An example of this type of device is the one proposed by Elon Musk called "**neural lace**". This area of development is of particular interest to many areas of physical rehabilitation as these interfaces with AI capabilities can improve patients who are disabled in any way with augmentation of their capabilities.

Capsule Network

This is Hinton's recent description of neural network and a **capsule** with an element of biomimicry that can be "smarter" with less input data. This aspect is potentially ideally suited for biomedical data. The conventional CNNs were instrumental in the popularity of deep learning but have significant limitations. One such drawback is the lack of spatial hierarchies between the objects. Capsules, which are groups of neurons that will encode spatial information, essentially can introduce the cognitive element of "intuition" to deep learning as these entities improves model's spatial information and hierarchical relationship.

An example in the very recent biomedical literature of this new development of capsule network with CNN is in Alzheimer's disease diagnosis with MRI and CNN with capsule network for superior performance (compared to 3D CNN with an auto encoder).

Cloud AI

Cloud computing has been thus far a public cloud model (exemplified by Amazon Web Services (AWS) or Salesforce's CRM system), but the cloud of the future will enable virtualization and management of software-defined data services. Future AI applications, therefore, will be in the cloud so AI will be in the form of AI-as-a-service (AIaas). The other aspect of cloud computing that will be essential for AI is its role in the formation of internet of everything (IoE)(see below) to create a ubiquitous decentralization of devices and sensors.

Complexity and Chaos

It is very essential to understand the difference between "complicated" and "complex", both of these contexts reside between "simple" and "chaos" in the systems science's order continuum; these terms, however, are often used interchangeably and thus create an understandable confusion (see Table and Figure). A **complicated** problem can usually be clearly defined and be deconstructed to its component parts (system equal to the sum of its parts), and each part can be analyzed (and improved) as part of the whole system (therefore "reductionistic"). The process is ordered and linear with an attainable equilibrium and the outcome is usually predictable or deterministic. Examples of complicated systems include: cars, planes, and cardiac pacemakers. A **complex** problem, on the other hand, is less clearly defined (therefore 'fuzzy") and cannot be easily deconstructed meaningfully into separate component parts as each part is interdependent with the other parts (therefore “holistic” with dynamic relationships), Here, the process is unordered and nonlinear without an attainable equilibrium and the outcome is highly unpredictable or stochastic. Examples of complex systems include the immune system, the stock market, and the heart. While the SpaceX launch and booster return is duly “complicated” as an engineering system with many decisions and parts, the inclement weather that preempted its original launch is a “complex” organic phenomenon with highly unpredictable elements. The simple-complicated-complex-chaotic continuum is aptly delineated in John Snowden’s article on the **Cynefin framework** which helps leaders the appropriate context to facilitate their decision making process.

	Complicated	Complex
Context	Static	Unstable
Discipline	Mechanical	Organic
Order	Repetitive	Spontaneous
Problem	Definable	Fuzzy
Protocol	Adequate	Limited
Outcome	Predictable	Unpredictable
Process	Deterministic	Stochastic
Structure	Formal	Flow
Expertise	Necessary	Helpful
Situation	Reproducible	Unique
Reducibility	Sum of its parts	More than sum of its parts
Management	Analytical	Pattern
Linearity	Newtonian	Nonlinear
Equilibrium	Yes	No
Cause/Effect	Present	Retrospective
Parts	Process	Relationships
Characteristic	Static	Dynamic
Strategy	Reductionist	Holistic
Mode	Analysis	Adaptation
Work	Agile	Scrum
Interdepency	Some	Dense
Practice	Emergent	Good
System	Systems thinking	Complex adaptive system
Action	Sense-analyze-respond	Probe-sense-respond
Examples	Airplane Rocket Computers	Medicine Weather Markets

As we head into the era of attempting to solve some of the enigmas and nuances of biomedical systems with artificial intelligence, we will need to realize that even more advanced methods (such as deep reinforcement learning) will be insufficient. Three mathematics-based concepts: chaos, complexity, and complex adaptive systems (CAS) will need to be recruited to be part of this intelligence (artificial and natural) portfolio.

Traditional science possesses a predictable set of phenomena that can be assembled in explaining more complex phenomena; this philosophy, exemplified by Newtonian mechanics, is termed **reductionism**. **Chaos** and chaos theory, on the other hand, challenges traditional science as it describes an underlying pattern and interconnectedness with self-organization and feedback mechanisms (albeit governed by deterministic rules) within a dynamical system that appears to have randomness; these rules are sensitive to minute changes in initial states. Chaos describes therefore, a nonlinear science that renders it much more difficult to predict outcomes. An early practitioner of modern chaos theory was the American meteorologist and mathematician Edward Lorenz, who used this theory to help predict weather in the 1960s. One of the main underpinnings of chaos theory is the **butterfly effect**: in a deterministic dynamical system, a small change in initial conditions (such as a butterfly flapping its wings in California) can lead to sizable alterations in another area (in this case, a typhoon in Asia).

Complexity is a study of both structure as well as dynamics of systems in which the diverse elements interact with each other (as well as the outside world) and possess local rules without instructions from a leader. Examples of complex systems include the market economy, traffic, weather, internet, and society as a whole while biomedical examples include biological systems, brains, ants and birds, and immune system. Complex systems with its characteristics of emergent behavior, spontaneous order, and small world principle ("six degrees of separation") are often confused with complicated systems (such as a computer or an airplane), which have elements that do not interact nor respond to each other. Additional characteristics of complex systems include non-linearity (with sudden transitions and tipping points), path dependence, limited predictability with fundamental uncertainty, and evolutionary dynamics. The **Stacey matrix** (formulated by Ralph Stacey, a British organizational theorist), with its horizontal axis of degree of certainty and the vertical axis of level of agreement, illustrates that there is a continuum from simple, rational decision making (high degrees of certainty and high level of agreement) to complicated and then complex decision making (medium or low degree of certainty and medium or low level of agreement), and finally chaos at the other end (little degree of certainty and low level of agreement). In medicine, there is very little certainty and agreement so the zones of complicated and complex decision making are far bigger than that of simple decision making.

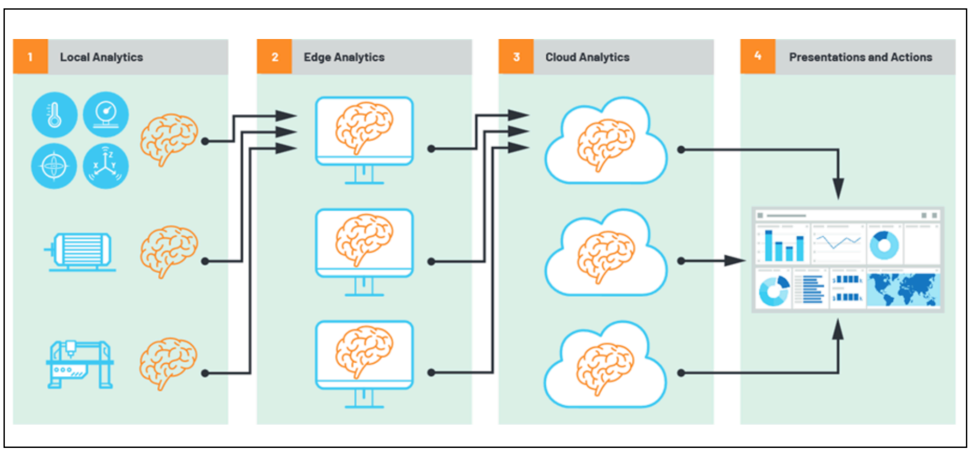
In **complex adaptive systems** (CAS), a dynamical system adapts to an uncertain and changing environment by exhibiting complex adaptive behavior (self-organization) that "emerges" from local interactions of its members within a boundary and with rules. Feedback (both positive and negative) occurs between the members and the group complex adaptive behavior. This ultimately results in a quasi-equilibrium between the CAS and the environment. A CAS possesses the following characteristics: systems thinking; lack of centralized control; dense low-level connectivity; trust; continual learning; and co-evolution. A good healthcare example of a CAS would be individual, social, and environmental determinants of health in primary care. As we become more cognizant of the utterly amazing biomedical world with its many elegant nuances and processes, perhaps someday we will begin to understand and appreciate even more the complex aspects of Mother Nature in both health and disease.

Edge Computing

As a counterbalance and a coupling to cloud computing, edge computing technology enables devices to collect and analyze data in real time locally so that it is processed outside the cloud datacenter. This is akin to having a peripheral nervous system with local signal processing (as opposed to having every signal going to the central nervous system for analysis). In addition to being more efficient, this process can also increase the level of security as the data can be processed without going to the cloud. Disadvantages of this edge computing include more sites that will need to be configured and monitored as well as issues with decentralization.

Embedded AI (or IoE)

Data in health care will concomitantly escalate as well from the advent of wearable and home monitoring technology leading to **internet of everything** (IoE). There are now an estimated 100,000 mHealth apps available. While the **internet of things** (IoT) is the interconnection of billions of physiologic devices to the Internet, IoE will be essentially a "network of networks" to incorporate people, processes, and data to these devices to enable automation in data acquisition and analytics without human intervention. All of these "smart" devices with wireless sensor networks (WSNs) will add to the collective intelligence of medical data and information. The internet of everything is basically intelligent connection of people, process, data, and things; it builds on IoT by adding **network intelligence** and turning information into actions. The future of AI will need to involve the IoE just as the brain needs a nervous system.



Embedded artificial intelligence is the technological paradigm of integrating machine learning or other AI tools into the devices to attain a certain desired function. Embedded AI is advancing beyond the internet of things (IoT), which is devices communicating with each other and generating data. With biomedical devices, especially ones with continuous monitoring, the amount of physiological data received would be unmanageable by caretakers unless there is an "upstream" intelligent algorithm built in to the device to filter all the noise from the signal (for instance, filtering out normal sinus rhythm and sending an alert to the cardiologist only when there is an abnormal rhythm like atrial fibrillation or ventricular tachycardia).

Fuzzy Cognitive Maps (FCM)
Fuzzy logic, combined with neural networks, can form fuzzy cognitive maps that is an efficient and robust AI technique for modeling complex systems in medicine. FCM can be helpful in designing medical decision-support systems by focusing in four areas: decision-making, diagnosis, prediction, and classification. The advantage of FCM is in its unique specification of integrating human knowledge and experience with computer-aided techniques so that one can achieve a human-machine synergy that is ideally suited for the complexities of medicine.

Generative Query Network (GQN)
GQN is a very significant foray into how machines can learn like a child from Google's DeepMind. This is a framework for a machine to learn on its own (based on data) to perceive their surroundings without any human labeling. This is accomplished by having two different networks: a **representation network** (in which an agent makes observations) and a **generation network** (in which these observations are turned into predictions). This autonomous process will facilitate training for neural networks and have a sizable impact in medical imaging.

Hypergraph Database
As elucidated in an earlier section, traditional relational databases are weak in complex hierarchical data and processing graphical data structures. A graph database is designed to neutralize these disadvantages by processing data in a graphical (with nodes and edges) strategy and enable queries across the data network. In order to model even more complex and highly interconnected data, a new paradigm of data representation called **hypergraphs** will need to be implemented. A hypergraph is a graph model in which the relationships (called a hyperedges) can connect any number of nodes. Future applications of AI will become increasingly more sophisticated and the data in biomedicine will need a paradigm shift to a graph and even hyper graph format with graph algorithms that will take graphs as inputs.

Low-Shot Learning
Popularized by facial recognition work, **one-shot learning** is an advanced methodology of supervised learning algorithm that uses a siamese neural network to be able to learn from one or very few images. In addition, Fei-Fei Li of Stanford promulgated one-shot learning that can bring a special dimension to unique cases in medicine as it will not require the usual large dimensionality of data that the previous types of learning will need. There is work on one-shot learning with both memory-augmented neural networks (MANN)(see Neural Turing Machines, or NTM above under neural networks) and also Siamese neural networks (SNN). Siamese neural network contains two or more identical subnetworks (same parameters and weights). One-shot learning would be particularly useful in biomedicine as CNN are based on large and labeled datasets that may not be scalable for some diseases.
Even more interesting, **zero-shot learning** is a supervised learning that is able to predict labels that are not in the training data by using embedding vectors called word embeddings. In other words, this type of learning is able to solve a task by not having received any training data. All of these

low-shot learning methodologies that do not require Big Data can be particularly useful in clinical medicine and health care.
An example in the recent biomedical literature of one-shot learning is the deployment of this learning for cervical cell classification in histopathology tissue images in patients with cervical cancer with a 94.6% accuracy in detection.

Neuromorphic Computing
Also known as neuromorphic engineering, this is a concept in which computer chips can mimic the brain by communicating in parallel using "**spikes**", which are bursts of electric current that the neuron can control. These neuromorphic chips have the advantage over traditional computer CPUs in that these chips require far less power to process AI-inspired algorithms. Advances in AI in medicine in the future will require technological improvements such as neuromorphic computing.

Quantum Computing
Another type of futuristic computing is a new approach to process information and is much more powerful than the conventional computer. A quantum computer utilizes **quantum bits** (or qubits) instead of the conventional bits (that is in 0 or 1 states) used in digital computing. Quantum computing takes advantage of the quantum phenomenon that subatomic particles can exist in more than one state at a time. A quantum computer like the D-Wave computer is 100 million times faster than a conventional laptop. As the demand for computation exponentially increases in biomedicine as we head into the cognitive era of AI, quantum computing (and other types of computing such as DNA computing) will be a necessary technological tool.

Recursive Cortical Network (RCN)
This is a generative model (structured probabilistic graphical model to be exact) that differs from deep learning in that it has a **scaffolding** (rather than learning from scratch, or *tabula rasa*, as in deep learning). RCN is thus an object-based model that can be much more efficient in learning and was able to break the text-based CAPTCHA (completely automated public Turing text to tell computers and humans apart). The result of this model is that it has a **contour hierarchy** of features that is guided by neuroscience and the visual cortex.

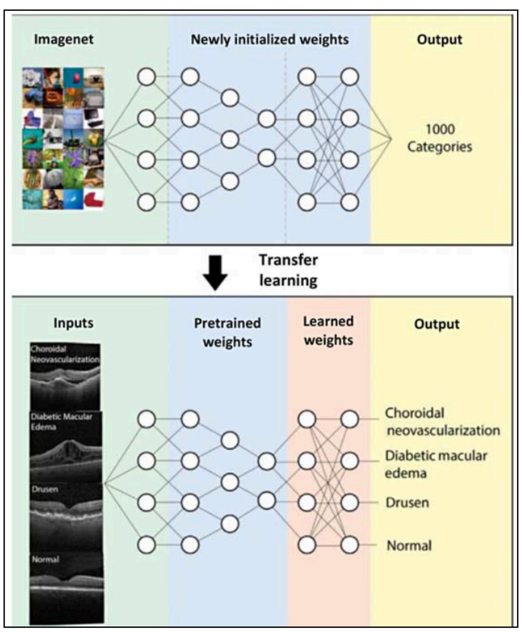
Spiking Neural Network (SNN)
SNNs, called the third generation of neural networks, operate with events called **spikes**, which are discrete events that occur at certain points in time; it therefore is more biological than machine learning in that the neural network often relies on the timing of individual action potential of neurons. This is work that is now more in the realm of **brain-inspired AI**.
An example in the recent biomedical literature of SNN is the Kasabov study: It is suggested that SNN, with its innovative spatio-temporal architecture, can serve as a framework to improve processing velocity as well as accuracy for spatio-temporal brain data (such as EEG) for earlier diagnosis of degenerative brain diseases such as Alzheimer's disease.

Swarm Intelligence

Swarm intelligence is intelligence derived from many individuals based on **self-organizing group behavior**. The collective behavior illustrates that unified systems outperform the majority of individual members, but since humans do not naturally have these connections as observed in ants or fish, swarm AI is executed by technology to provide feedback to human members. This group dynamic results in ad-hoc information gathering and sharing, and consensus is based on dissemination of the pool of knowledge. In short, this type of intelligence leverages the "**wisdom of the crowd**" and this philosophy is direly needed to answer the numerous queries we have in medicine and health care.

Temporal Convolutional Nets (TCN)

Up to now, RNNs have been involved with sequence problems such as language and speech. Temporal convolutional nets are CNNs with some added new features and are challenging RNNs for the sequence problem category. In addition, video-based action segmentation has been previously dealt with in two steps: low-level features for each frame by using CNN followed by an RNN as a classifier for higher level temporal relationships. A unified approach with TCN and capture all levels of time scales. This flexibility with TCN can be ideal for a myriad of situations in medicine.



Transfer Learning

Transfer learning involves adaptation of a trained model to predict examples from a different dataset; this phenomenon is particularly favorable with deep learning networks since deep learning requires so much time and resources for its training. In other words, a model that is previously trained on a type of task is now repurposed on a different type of task. The type of learning is called inductive transfer**.** Transfer learning can be accomplished with both image and language data. Compared to traditional machine learning, transfer learning is very different as it accomplishes learning of a new task by relying on a previously learned task so that it has acquired knowledge (whereas machine learning does not retain that knowledge of a learned task). This knowledge of solving one problem is applied to a different (but related) problem **(see Figure)**. Finally, transfer learning can be accomplished in minutes compared to hours for deep learning, and can be done with small datasets (vs large datasets for deep learning). Instead of training a deep neural network from the beginning, one can take a previously trained network on a different domain (like ImageNet) for a source task and adapt it for a target task with smaller amount of data (retinal images). The transfer of learned knowledge renders the target model able to use small amount of data.

Data and Databases

For all of these aforementioned advanced AI tools to effectively create a paradigm shift in medicine, we still need to vastly improve health care data and databases:

First, health care databases can utilize the above graph DMBS (see above) mapped into networks of autonomous databases as a **federated** or **virtual meta-database** management system for interoperability and collective intelligence. Many subspecialties lack such a coordinated network of stakeholders but will benefit immensely from such a collaboration. The advantage of such as network is incorporation of a Web-enabled semantic search and global query capability with data discovery is that it is ideally suited for biomedicine especially with rare diseases and with complex imaging data. In addition, this federated approach using Internet-based networking technologies can provide excellent collaborative research in epidemiology and public health even at the international level. Lastly, this federated system provides an excellent framework for the IoT networking paradigm of interconnected smart objects. This data discovery capability can eventually mature into artificial intelligence possibilities embedded into the database. One key future development of big data analytics is **real time analytic processing (RTAP)**. This is a process in which the data is captured and processed in a streaming fashion using online analytical processing (OLAP) and complex machine learning algorithms.

Second, each configurable **cloud infrastructure** in the biomedical system should retain the following essential characteristics of cloud computing: on-demand self-service, broad network access, resource pooling, rapid elasticity, and measured service. The cloud infrastructure that is best suited for each situation will be configured to meet that need. Health care with its big data and data analytical needs that concomitantly demands privacy and security can use this flexible cloud infrastructure to meet the challenges.

Third, little in the biomedical data domain is truly virtualized at present. There is, however, a report of **software-defined network** (SDN) in a hospital setting in Japan using *OpenFlow*™ as the hospital in-house LAN (one of major technical specifications of SDN published by Open Network Foundation). In short, SDN decouples the control plane from the data plane and creates a more dynamic resource utilization with better oversight of network bandwidth and with direct programmability. One limitation of SDN is its requirement for network architecture and design skills. In addition, the storage of heterogeneous health care data sources can be abstracted into designated data pools, with this process being an app-centric policy-based automation (**software-defined storage**)(such as *IBM*'s *Big Blue Elastic Storage*). This strategy is ideal for the biomedical system with its data-intensive applications that require immediate access and rapid analytics as well as matching the storage capability with the type of data. As an example, this strategy has been implemented at Maimonides Medical Center with *DataCore's SANsymphone-V* software with savings in hardware and personnel costs and increased performance of applications. The aforementioned SDN concept has evolved into a **software-defined data center (SDDC)** architecture (with server virtualization, software-defined networking, and storage hypervisor) that can be entirely virtualized so that all of the infrastructure and the management can be automated by software. In short, the SDDC frees the application layer from the hardware layer.

Fourth, an entirely virtualized infrastructure can include compute, network, security, and storage abstractions such that it is **IT as a service** (ITaaS) and its cloud infrastructure also managed by automation. One advantage of such a system is its **remote programmability** to render it agile and automated as well as global and continuous. All of the components are essentially decoupled from the hardware as a ubiquitous software for all users in various hospitals and programs at any given time. Another advantage is the **accelerated service delivery** (from weeks/days to even hours). The dynamic configuration of SDDC can optimize resource allocation and improve efficiency in health care.

The future of software-define data systems will be a federated system with more standardized network protocols and more automated interfaces for management. With emerging sophisticated database management systems and cloud and virtual computing technology, medical data can be efficiently organized into a virtual intelligent **biomedical data "ecosystem"** to better serve the needs of hospitals and health systems. In addition, the wireless sensor networks as well as other patient-generated data will need to be virtualized to provide effective solutions in health care. This virtual strategy will enable medical data to converge with **artificial intelligence** methodologies to promulgate true medical intelligence in the cloud. One major area of concern will always be **data security** in the cloud as present data shows 94% of health care institutions having had breach of data. The **exponential convergence** of existing biomedical data with both genomic and biophysiologic data will render medical data to be even more voluminous, complex, and heterogeneous. This explosion of medical data will need a more sophisticated database management strategy as well as cloud and virtual environments to enhance data discovery as well as ensure data security and privacy.

In summary, the future of biomedicine can include a proposal for an artificial intelligence-inspired cloud continuum of data-information-knowledge-intelligence (a "medical intelligence" as a service, or "MIaaS"). First, future medical data can be managed in a **graph-based meta-database management system** with real time analytic processing for both its storage capability and its query flexibility to accommodate the large and complex medical data in the ensuing decades. Second, future medical data in the **customized cloud infrastructure** will be far more sophisticated than a simple public-private dichotomy and can be customized from a cloud infrastructure system based on customer vs supplier control, ownership, and responsibility as well as private vs shared infrastructure and operations; cloud security can be further enhanced by mechanisms such as homomorphic encryption and differential privacy. Third, a **software-defined data center (SDDC) architecture** can be entirely virtualized so that the infrastructure that includes compute, network, and storage abstractions will result in IT as a service (ITaaS). The future medical data system will be entirely in a virtual synergy with humans and contribute to medical intelligence.

By embedding intelligence into all aspects of medical data from graph database and meta-database management system to customized cloud infrastructure and to software-defined data center and virtualization, the aforementioned strategies can accelerate this transformation in biomedicine from fragmented and unstructured data sets to cohesive and agile information imbued with **medical intelligence**.

Questions 11.1/The Future of Artificial Intelligence in Medicine

1. According to Oren Etzioni, the three rules for AI that are inspired by Isaac Asimov's three rules for robotics include all of the following except:
a. An AI system must be subject to full gamut of laws that apply to its human operator
b. An AI system must clearly disclose that it is not human
c. An AI system cannot retain or disclose confidential information without explicit approval from the source of that information
d. An AI system can be legally liable for its mistakes if a human is not accountable
[ ]

2. Bias can be neutralized in which part of the machine learning workflow?
a. Data input
b. Algorithm
c. Data output
d. All of the above
[ ]

3. The advent of the newly enacted policy and its mandate to require specific informed consent for personal data use in Europe is called:
a. European General Data Protection Regulation (GDPR)
b. European Privacy Act
c. The HIPPA-Europe Provision
d. None of the above
[ ]

4. Which of the following is *least* likely to be the AI methodology expected to have impact in clinical medicine
a. Deep reinforcement learning
b. Generative adversarial network
c. Few-shots learning
d. Expert system
[ ]

5. Which of the following is *not* a quality that machines are superior to humans at:
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b. Objectivity
c. Creativity
d. Digital
[ ]

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Module 11.1/The Future of Artificial Intelligence in Medicine

The myriad of issues in the application of artificial intelligence mentioned in previous sections will need to be addressed, perhaps on a grander scale, in the future.

One issue is the **ethics** of its use in the variety of sectors and the accompanying debates amongst scholars and scientists as well as the public. Elon Musk and Stephen Hawking both predict dire consequences while other Silicon Valley titans argue the other way. The truth may very well be in the middle: we need to be respectful of the power of AI and not be careless in its deployment. One approach is that suggested by Oren Etzioni to have three rules for AI that are inspired by Isaac Asimov's three rules for robotics: 1) An AI system must be subject to full gamut of laws that apply to its human operator; 2) An AI system must clearly disclose that it is not human; and 3) An AI system cannot retain or disclose confidential information without explicit approval from the source of that information.

Another issues is the **economics** of such a paradigm shift in work and compensation. Artificial intelligence is a prediction technology so cost of goods and services that rely on prediction (such as inventory management and demand forecasting) will fall. But since all human activities rely on not just data and prediction but also judgment, action, and outcome, prices for the latter three can increase as the demand for these three capabilities go up. The issue of singularity (in which the computers will be more intelligent than all of mankind and replace its intellectual capacity) and how we accommodate this epoch will need to be discussed. The economic impact of such an event especially with countries which do not have large investments in AI needs to be examined.

The issue of **bias** in the formation and application of AI for all uses will need to be scrutinized. Biased data feeding into machine learning algorithms can lead to biased systems in AI. Bias can also be in the form of a patient population being too homogenous and therefore models become less valid for a more heterogenous population.

Another concern is that of **data** protection and privacy. The advent of the newly enacted European General Data Protection Regulation (GDPR) and its mandate to require specific informed consent for personal data use may herald an equivalent movement elsewhere in the world. In addition, HIPPA does not regulate health care data generated outside the health system so new guideline are needed for this upcoming data tsunami.

There is also the issue of **transparency** for AI in medicine methodologies. The perception, fair or unfair, of AI techniques having a black box and lack of transparency breeds mistrust amongst the various stakeholders. Some explainability will be necessary for wide adoption amongst clinicians as well as patients and families.

Lastly, AI and specific ethical issues in health care include not only bias, inequity, and other issues but also **fiduciary relationship** of patients and machine learning systems and potential changes in the physician-patient dyadic relationship. There are close to if not over 200 companies around the world in this domain of AI in clinical medicine and health care, so this aspect is looming larger by the month.

The One Hundred Year Study on Artificial Intelligence (AI100) is a long-term study of AI and its impact on people and society. The eight relevant areas that are considered most salient include health care (the other seven being transportation, service robots, education, low-resource communities, public safety and security, employment and workplace, and entertainment). Already used in areas such as radiology, pathology, genomic medicine, cardiology, outpatient services, and intensive care, AI will continue to have escalating impact in medicine albeit with concomitant fear amongst stakeholders for an AI "takeover", especially their jobs.

In Nick McKeown's parlance, medical data and analytics need to be transformed from a "vertically integrated, closed, proprietary, slow innovating" data system to that of a "horizontally integrated, open interfaces, and rapid innovation" data ecosystem. To put it into biological lexicon, the biomedical data system needs to transform from a rudimentary musculoskeletal system to an intelligent nervous system. In addition, cloud computing and storage will be vital to facilitate the panoply of AI techniques for multi-institutional collaborations that will be essential for the future of AI in biomedicine and health care.

Perhaps clinicians and medical educators can embrace rather than distrust AI and allow its capacities to transform how we teach and deliver health care, especially in the changing health care milieu to fee-for-value systems. An effective AI in medicine strategy will liberate clinicians from the burgeoning burden of electronic health records and allow a return to an ideal physician-patient relationship. In addition, since computers are excellent at handling data and making predictions, the human judgment will become even more valuable. This philosophy of accommodating emerging technologies will need to be indoctrinated early in the clinician's career.

In **conclusion**, the future of artificial intelligence in medicine is extremely propitious with a myriad of advanced AI techniques such as deep reinforcement learning, generative adversarial network, one-shot learning, and cognitive methodologies that will need to be in synergy with clinicians with cognitive thinking to allow data to be an enabler of new knowledge and intelligence in biomedicine and health care. All health care data will need to be liberated and shared without any obstacles so that AI can be ubiquitous and invisible in the future health care arena and discover new knowledge from all sources of data and information. In short, for us to fulfill our vision of precision medicine and population health for the next century, we need to change the paradigm of evidence-based medicine to that of a data science-driven **intelligence-based medicine** **(see Figure)**.

Key Concepts

- This premise of advances in AI is based on rapid improvement and accelerated deployment of advanced computer technology (such as quantum computing and neuromorphic chips) and rapid development and evolution of artificial intelligence techniques (such as deep learning and it many variants) as well as cognition-influenced architecture that have lead to a current Cambrian explosion of AI.
- Peter Voss so aptly described the future of AI as the “third wave”: the first wave of AI was good old fashioned AI (GOFAI) that focused on traditional programming followed by the second wave of AI of the current deep learning so that this third wave will be reliant on many cognitive architectures.
- A successful deployment of technologies such as blockchain to improve cybersecurity in health care will facilitate data sharing amongst stakeholders in the near future.
- As a counterbalance and a coupling to cloud computing, edge computing technology enables devices to collect and analyze data in real time locally so that it is processed outside the cloud datacenter. With biomedical devices, especially ones with continuous monitoring, the amount of physiological data received would be unmanageable by caretakers unless there is an “upstream” intelligent algorithm built in to the device to filter all the noise from the signal.
- The advantage of FCM is in its unique specification of integrating human knowledge and experience with computer-aided techniques so that one can achieve a human-machine synergy that is ideally suited for the complexities of medicine.
- In order to model even more complex and highly interconnected data, a new paradigm of data representation called hypergraphs will need to be implemented. A hypergraph is a graph model in which the relationships (called a hyperedges) can connect any number of nodes.
- All of these low-shot learning methodologies that do not require Big Data can be particularly useful in clinical medicine and health care.
- As the demand for computation exponentially increases in biomedicine as we head into the cognitive era of AI, quantum computing (and other types of computing such as DNA computing) will be a necessary technological tool.
- This is a generative model (structured probabilistic graphical model to be exact) that differs from deep learning in that it has a scaffolding (rather than learning from scratch, or *tabula rasa*, as in deep learning).
- SNNs, called the third generation of neural networks, operate with events called spikes, which are discrete events that occur at certain points in time; it therefore is more biological than machine learning in that the neural network often relies on the timing of individual action potential of neurons.
- Swarm intelligence is intelligence derived from many individuals based on self-organizing group behavior. The collective behavior illustrates that unified systems outperform the majority of individual members.

- Transfer learning involves adaptation of a trained model to predict examples from a different dataset; this phenomenon is particularly favorable with deep learning networks since deep learning requires so much time and resources for its training.
- One key future development of big data analytics is real time analytic processing (RTAP). This is a process in which the data is captured and processed in a streaming fashion using online analytical processing (OLAP) and complex machine learning algorithms.
- The aforementioned SDN concept has evolved into a software-defined data center (SDDC) architecture (with server virtualization, software-defined networking, and storage hypervisor) that can be entirely virtualized so that all of the infrastructure and the management can be automated by software.
- By embedding intelligence into all aspects of medical data from graph database and meta-database management system to customized cloud infrastructure and to software-defined data center and virtualization, the aforementioned strategies can accelerate this transformation in biomedicine from fragmented and unstructured data sets to cohesive and agile information imbued with medical intelligence.
- Medical data and analytics need to be transformed from a "vertically integrated, closed, proprietary, slow innovating" data system to that of a "horizontally integrated, open interfaces, and rapid innovation" data ecosystem.
- The future of artificial intelligence in medicine is extremely propitious with a myriad of advanced AI techniques such as deep reinforcement learning, one-shot learning, and cognitive architecture that will need to be in synergy with clinicians with cognitive skills to allow data to be an enabler of new knowledge and intelligence in biomedicine and health care.
- For us to fulfill our vision of precision medicine and population health, we need to change the paradigm of evidence-based medicine to that of a data science-driven intelligence-based medicine.
- The final stage of human-to-machine relationship is convolution, a term that describes the sinuous ridges of the brain in biological terms but conveniently a third function that is promulgated from two existing functions in mathematical terms. In our lifetime, we will observe human and machine intelligences be harmoniously intertwined and difficult to discern which contributed to what aspect of this endeavor. We may even stop calling anything "artificial" intelligence.

Conclusion

This *esprit de corps* of the AI in medicine community reminds us how essential relationship and collaboration is in this domain. While we discuss “machines” and “artificial” intelligence, there are humans behind these entities (at least for now). Relationship needs to be fostered in AI in medicine and health care at all levels and across all dimensions. Often, the best strategy entails forming **dyadic relationships or hybrids:**

First and foremost, it needs to be between **human and machine**. There are numerous published manuscripts in which there are no clinicians amongst the authors as if data science in medicine can be an entirely isolated discipline and science. This hubris, albeit unintentional, is unacceptable. On the other hand, clinicians need to be much more knowledgeable and accommodating of this new AI paradigm in medicine.

Second, the relationship needs to be between **human and human.** The clinician and data scientist dyad needs to be engendered and much more effective in creating an important interface between data science and clinical medicine and health care. The universal theme that prevailed around the world is: empowering patients and enabling clinicians to use AI to be innovative and transformative. From a plastic surgeon in Toronto who leveraged deep learning in medical images to improve her care of burn patients to the data scientist from Senegal who is working on reinforcement learning models in health care, these global AI in medicine citizens continue the mission of creating an AI in medicine and health care ecosystem and community to affect transformative change.

Third, the relationship needs to be between **machine and machine.** The advent of internet of things is leading to the need for AI to be embedded in wearable technology. Thus, the future will be machine collaborating with machines to become internet of everything. In addition, deep learning algorithms will need to be in synergy with those principles of cognitive architecture to maximize the yield of AI in medicine and health care.

Even though AI programs such as *AlphaZero* have now heralded the advent of high-level, self-learning AI that relies more on cognition and algorithms than brute pattern recognition of data, artificial intelligence remains at least partly a human intelligence imprinted into machines that reflect human thinking. The clear message from recent events is that we need to continually define and clarify the human to machine relationship. Interestingly, there are biological terms for this anthropocentric relationship. The first stage of this special human-machine relationship is **symbiosis**, or the living together of two dissimilar organisms. We are mostly at this stage currently. The second stage is **synergy** in which the total combined effect is usually greater than the sum of the parts. Muscles and nerves are often “synergistic”. We already have the early underpinnings for this level of relationship.

We need to reach the final stage of human-to-machine relationship: **convolution.** This is a term that describes the sinuous ridges of the brain in biological terms but conveniently a third function that is promulgated from two existing functions in mathematical terms. In our lifetime, we will observe human and machine intelligences be harmoniously intertwined and difficult to discern which contributed to what aspect of this endeavor. We may even stop calling anything "artificial" intelligence.

Much has happened even in the few years since the inception of this book and *AlphaGo* vs Lee Sedol matches in 2016. *AlphaGo Zero*, the followup and much more capable version of *AlphaGo*, learned to play Go without the benefit of learning from human-played Go games in the past and was able to defeat its predecessor *AlphaGo* 100 games to 0. It was evident that *AlphaGo Zero* (named for its *tabula rasa* inception) played the game Go with innovative moves not previously seen amongst human Go players (so "new intelligence"). What was absolutely astounding was that *AlphaGo Zero* learned to play Go in 40 days and surpassed all human players with about 2,500 years of learned history. *AlphaZero,* the congener of *AlphaGo Zero,* is also a self-learning program but can play more two-player games (specifically chess, shogi, and Go) and play with a style not observed with human players before, and easily win with an uncanny flexibility and adaptation. Lastly, *AlphaStar* has very recently soundly defeated human champions in yet another game that was deemed nearly impossible for AI to conquer: the Real-Time Strategy (RTS) game of *StarCraft II*. This was perhaps an even more impressive an AI feat as the previous programs since RTS games have additional challenges compared to the game Go: imperfect information, long term planning, real-time, and large action space. These AI feats have very significant implications for clinical medicine and health care as clinicians face very similar situations as complex RTS games on a daily basis.

What was enlightening about the human vs *AlphaGo* competition discussed at the beginning of this book was not only the brilliant and innovative 37th move made by *AlphaGo* during the second game, but also the 78th move of the meaningless fourth game (as *AlphaGo* had already won three games in the five-game match) in which Lee Sedol made an equally brilliant and creative move. This move was not widely publicized as the 37th move but clearly demonstrated that the computer had a positive influence on man and a man-to-computer synergy would yield the best result for artificial intelligence, perhaps especially in clinical medicine and health care. The biologist E.O. Wilson would remind us that the ultimate union of sciences, including biological sciences and artificial intelligence, is with the humanities in the form of **consilience.** Perhaps the best reward of artificial intelligence and its essence in our lives, akin to children, is a more in depth understanding and appreciation of ourselves as human beings.

Machines have computation, instructions, and objectivity while humans have purpose, creativity, and passion. With AI in clinical medicine and health care and intelligence-based medicine, it should never be human *versus* machine, but always human *and* machine.

Questions 12.1/Miscellaneous Topics in AI in Healthcare

In Agarwal's *Prediction Machines*, as the cost of predictions falls, complementary services that are expected to increase in value include all of the following *except*:

a. Human judgment
b. Human prediction
c. Action
d. Data collection

[ ]

In McAfee and Brynjolfsson's *Machine, Platform, Crowd*, what does machine replace?

a. Minds
b. Products
c. Core
d. Organizations

[ ]

How would one describe the growth in training of artificial intelligence programs?

a. Linear with upward trajectory
b. Linear with flat trajectory
c. Exponential
d. Linear with downward trajectory

[ ]

In Kotter's model for creating change, which of the following is the very first set of steps:

a. Finding resources and people (configuring a budget and ask for volunteers)
b. Engaging and enabling the whole organization (communicate the vision, empower action, and create quick wins)
c. Implementing and sustaining change (build on the change and make it stick)
d. Creating a climate for change (create urgency, form a powerful coalition, and create a vision for change)

[ ]

The state with high degree of uncertainty in technology but medium range of agreement, according to the Stacey Matrix, would be:

a. Complex
b. Complicated
c. Simple
d. Chaos

[ ]

Answers 12.1/Miscellaneous Topics in AI in Healthcare

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Questions 12.2/Miscellaneous Topics in AI in Healthcare

In the hype cycle, what follows the period of peak of inflated expectations?
a. Technology trigger
b. Slope of enlightenment
c. Trough of disillusionment
d. Plateau of productivity
[ ]

According to Gartner's hype cycle for emerging technologies in 2020, which of the following AI technologies is at the peak of inflated expectations and will plateau the earliest (2-5 years)?
a. Embedded AI
b. Explainable AI
c. Generative adversarial networks
d. Self supervised learning
[ ]

In Rogers' innovation diffusion model, when does the "chasm" between early and mainstream markets occur?
a. Between late majority and laggards
b. Between early adopters and early majority
c. Between innovators and early adopters
d. Between early and late majority
[ ]

Metcalfe's law of network states:
a. The value of a telecommunications network is proportional to the square of the number of connected users in the system
b. The performance of hardware (or technology) doubles about every two years
c. We tend to overestimate the effect of a technology in the short run and underestimate the effect in the long run
d. A man with a watch knows hat time it is, but a man with two watches is never sure.
[ ]

In the startup financing lifecycle, which of the following is *not* part of pre-seed funding?
a. Angel investment
b. Mezzanine funding
c. Founders, friends and family (FFF)
d. Seed capital
[ ]

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Questions 12.3/Miscellaneous Topics in AI in Healthcare

According to the Kim and Mauborgne, blue ocean strategy includes all of the following *except*:
a. Create uncontested market space
b. Make the competition irrelevant
c. Exploit the existing demand
d. Align the whole system of a firm's activities in pursuit of differentiation and cost
[ ]

According to Michael Porter, the strategies for an entrance into a market is all of the following *except*:
a. Cost leadership strategy
b. Differentiation strategy
c. Focus strategy
d. Blue ocean strategy
[ ]

The five dysfunctions of a team, according to Lencioni, include all of the following *except*:
a. Absence of trust
b. Lack of commitment
c. Fear of conflict
d. Lack of hierarchy
[ ]

Which is true of Amara's law that examines effects of technology short and long term:
a. We tend to underestimate the effect of technology in the short term
b. We tend to overestimate the effect of technology both short and long term
c. We tend to underestimate the effect of technology both short and long term
d. We tend to underestimate the effect of technology in the long term
[ ]

Which of the following is *not* an element for transformation in Jim Collins' work, *Good to Great*:
a. Level 5 leadership
b. Denial of risk
c. Hedgehog concept
d. Culture of discipline
[ ]

Answers 12.3/Miscellaneous Topics in AI in Healthcare

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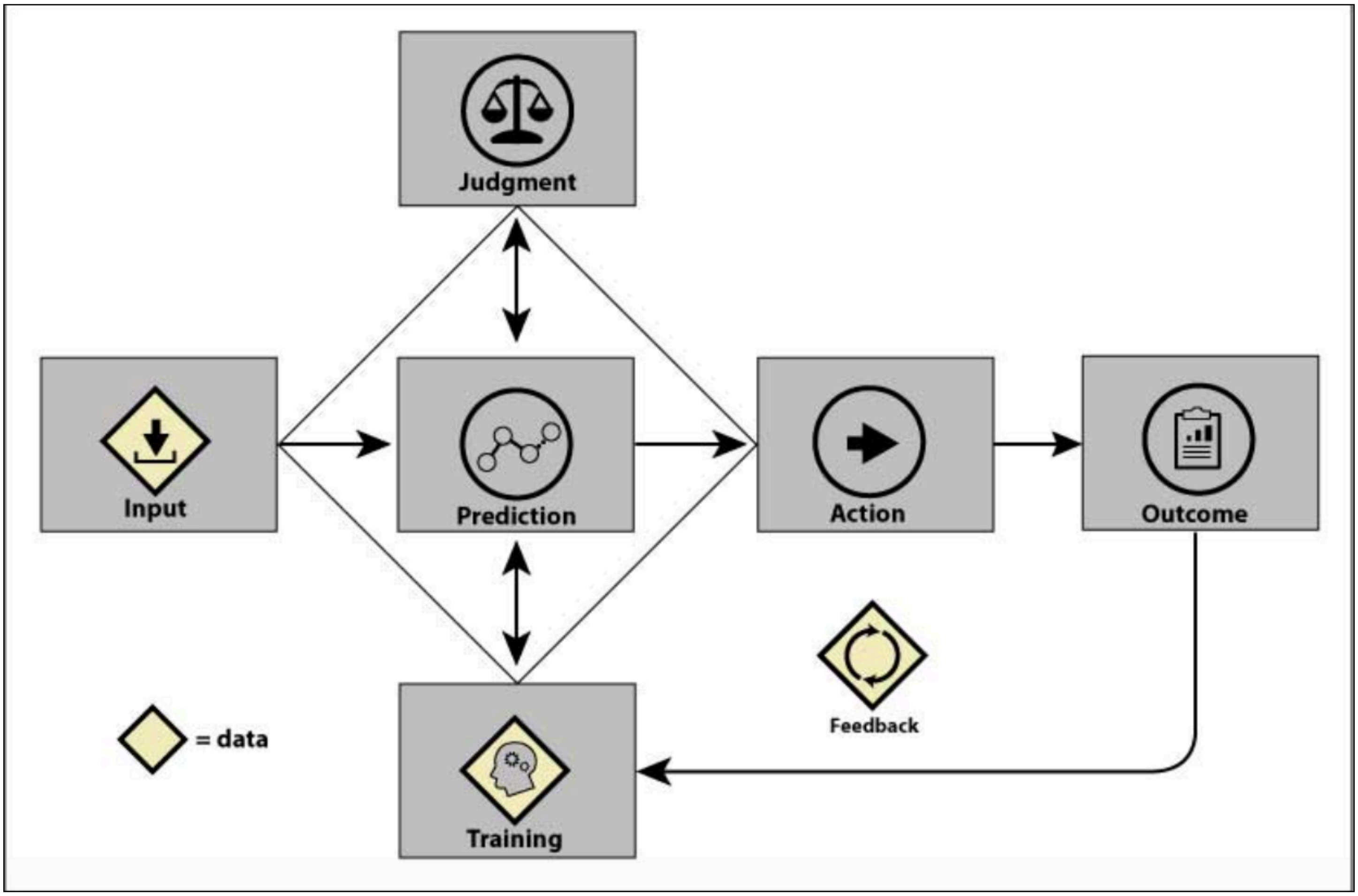
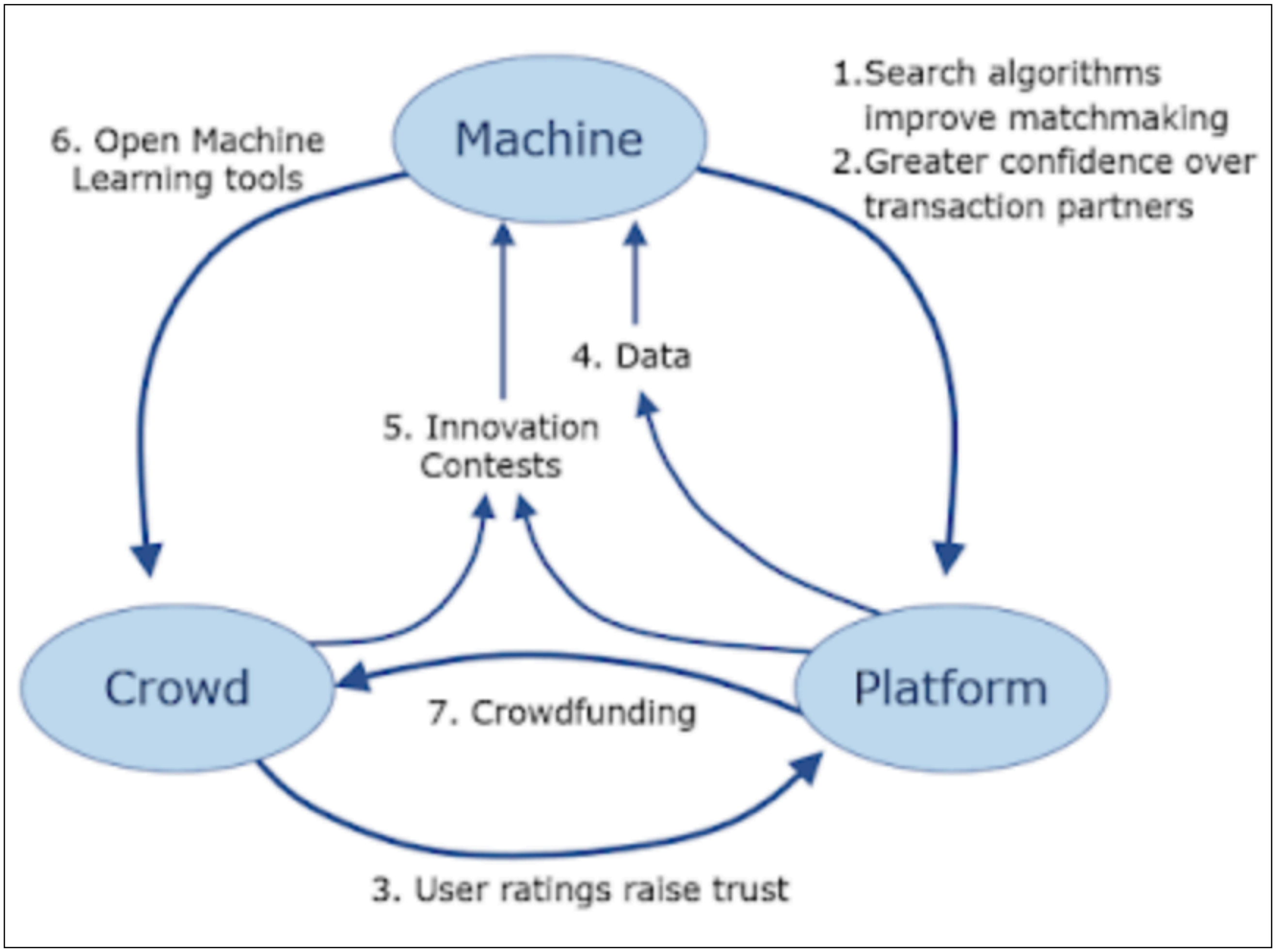
Module 12.1-3/Miscellaneous Topics in AI in Healthcare

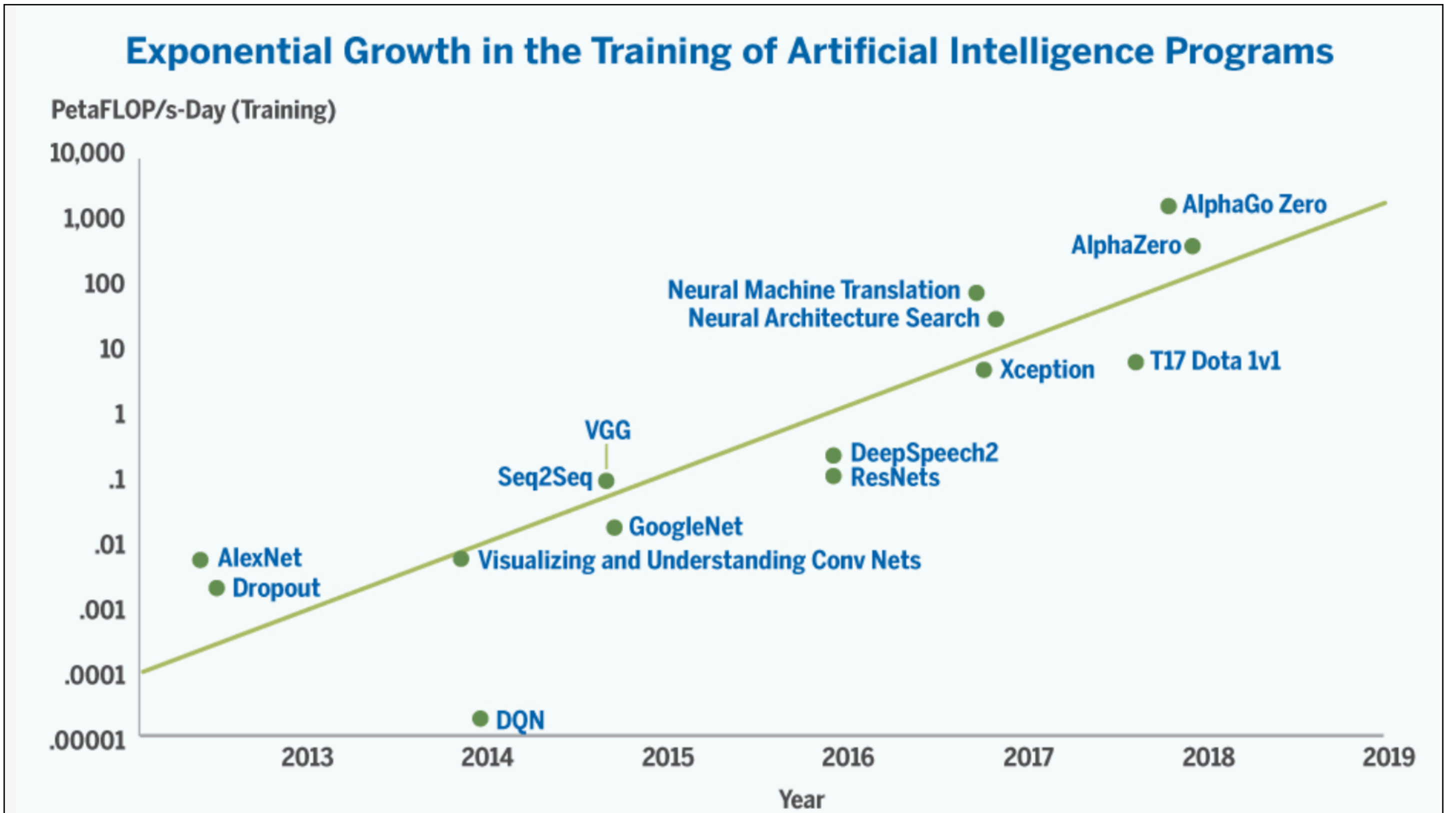
Artificial Intelligence (Ajay Agrawal et al in *Prediction Machines*)



Artificial Intelligence (Andrew McAfee and Erik Brynjolfsson in *Machine, Platform, Crowd*)

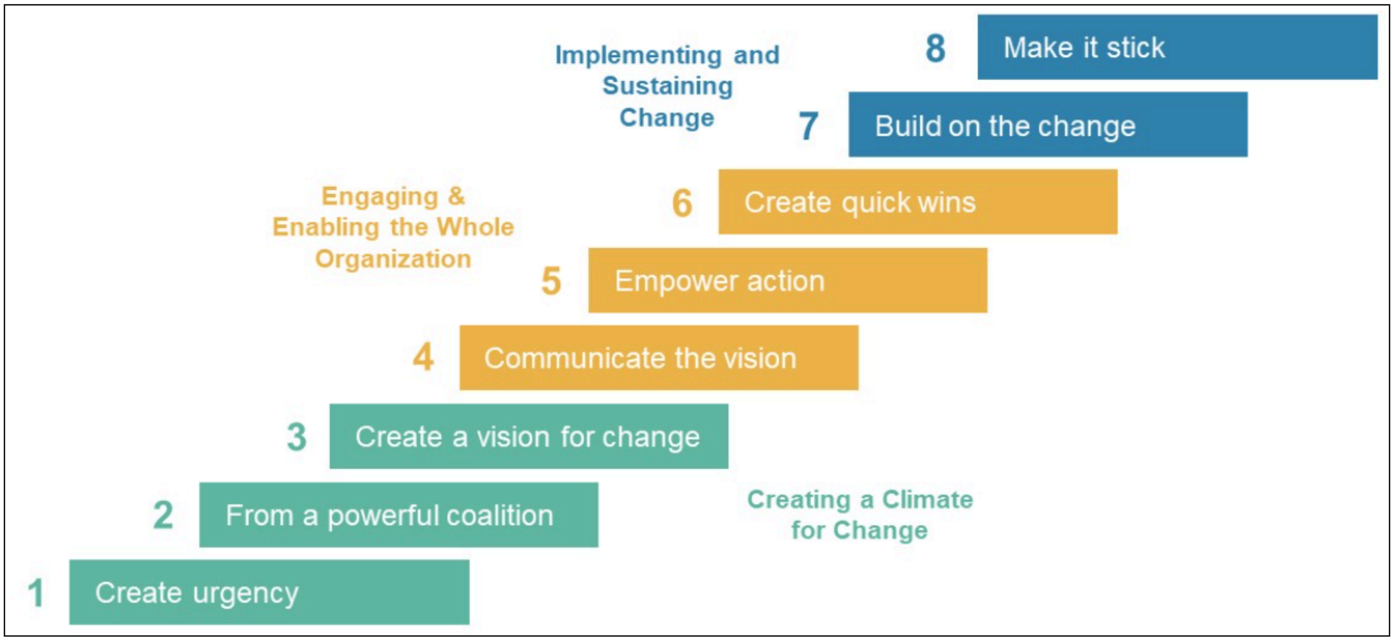


Artificial Intelligence (Training and exponential growth)

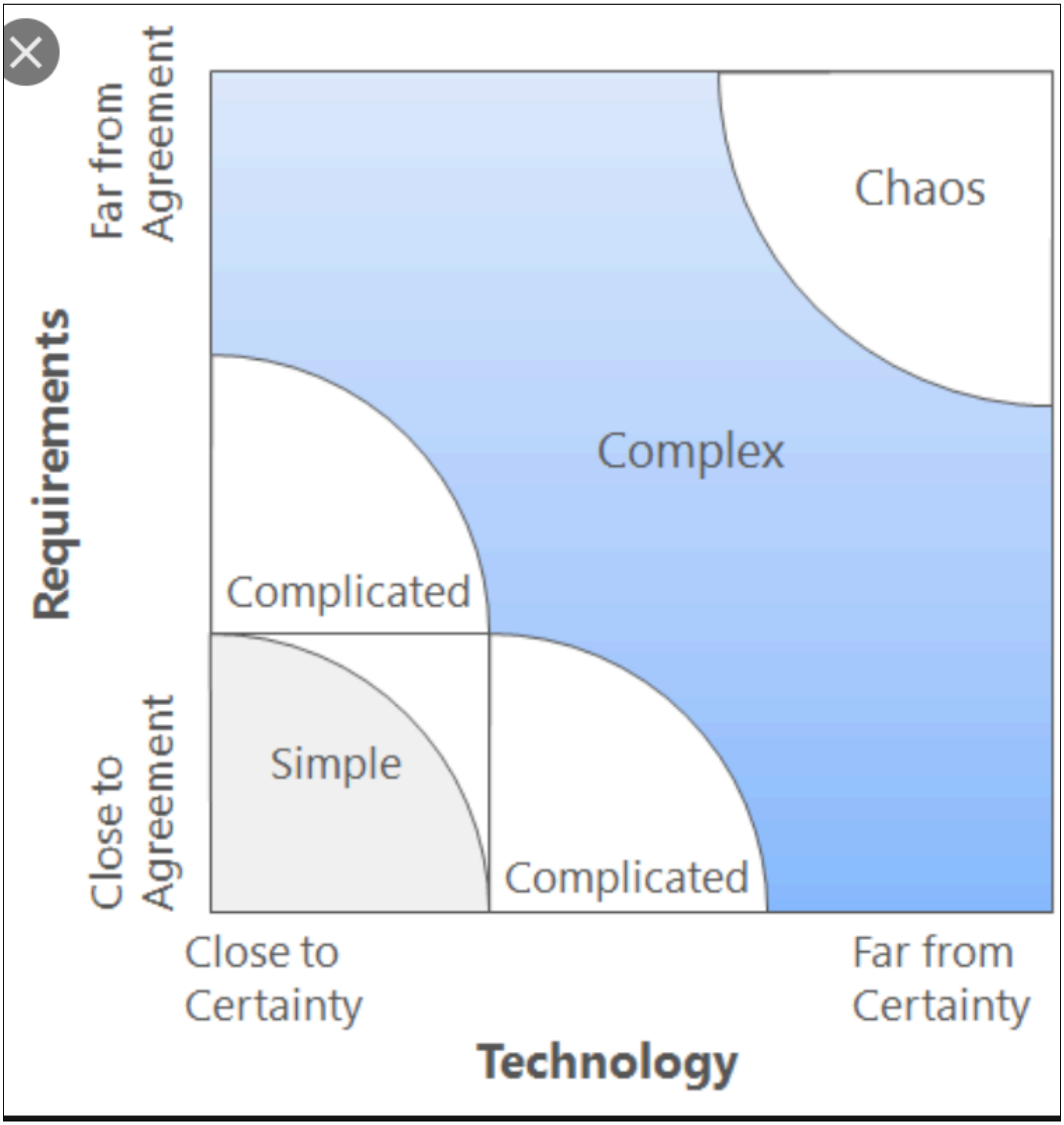


Source: https://openai.com/blog/ai-and-compute/
Note: A petaFLOPS is a unit of computing speed equal to one quadrillion FLOPS, floating operations per second, a measure of computer performance.

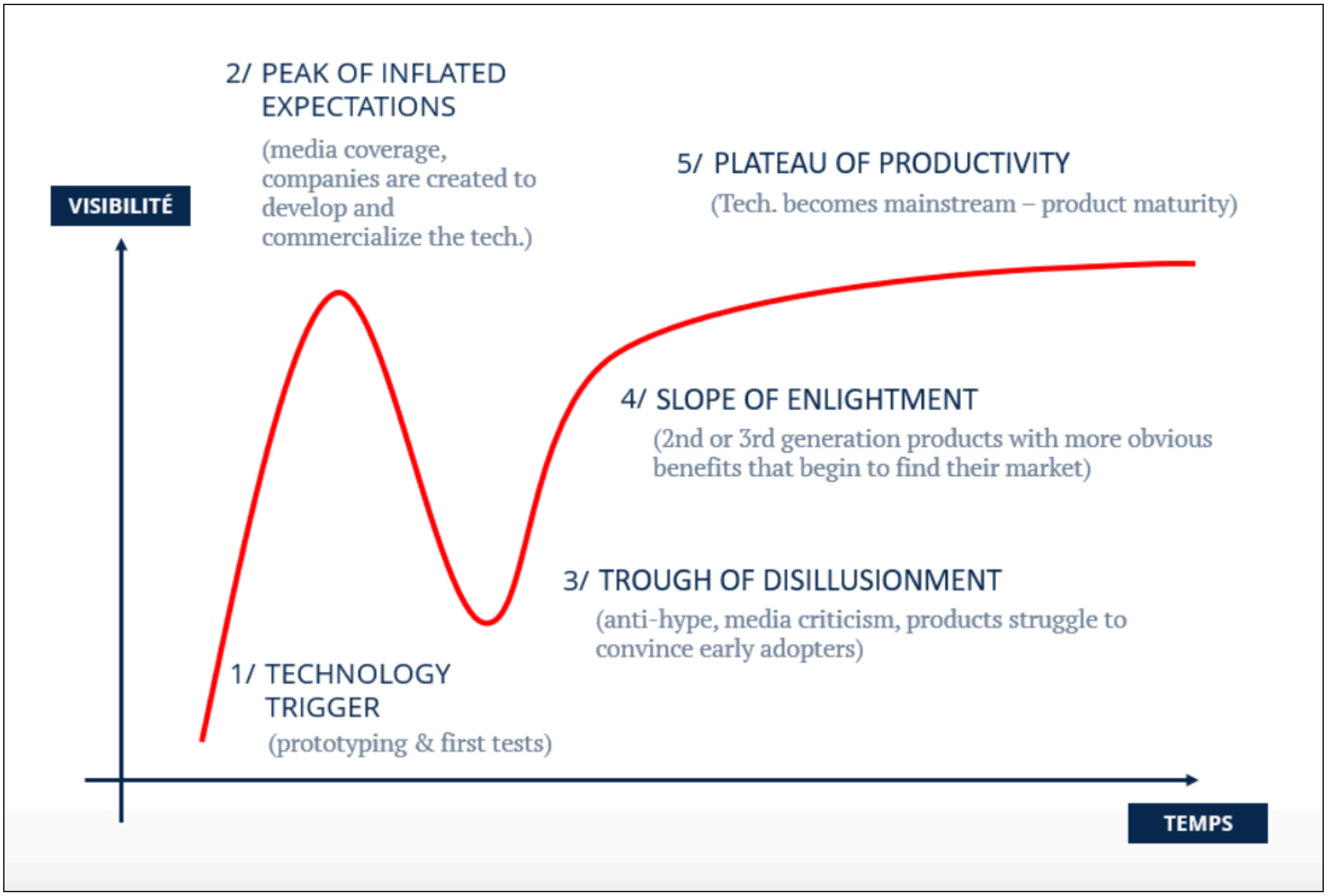
Change Management (John Kotter in *Leading Change*)



Complexity (Stacey Matrix)



Hype Cycle (Gartner)



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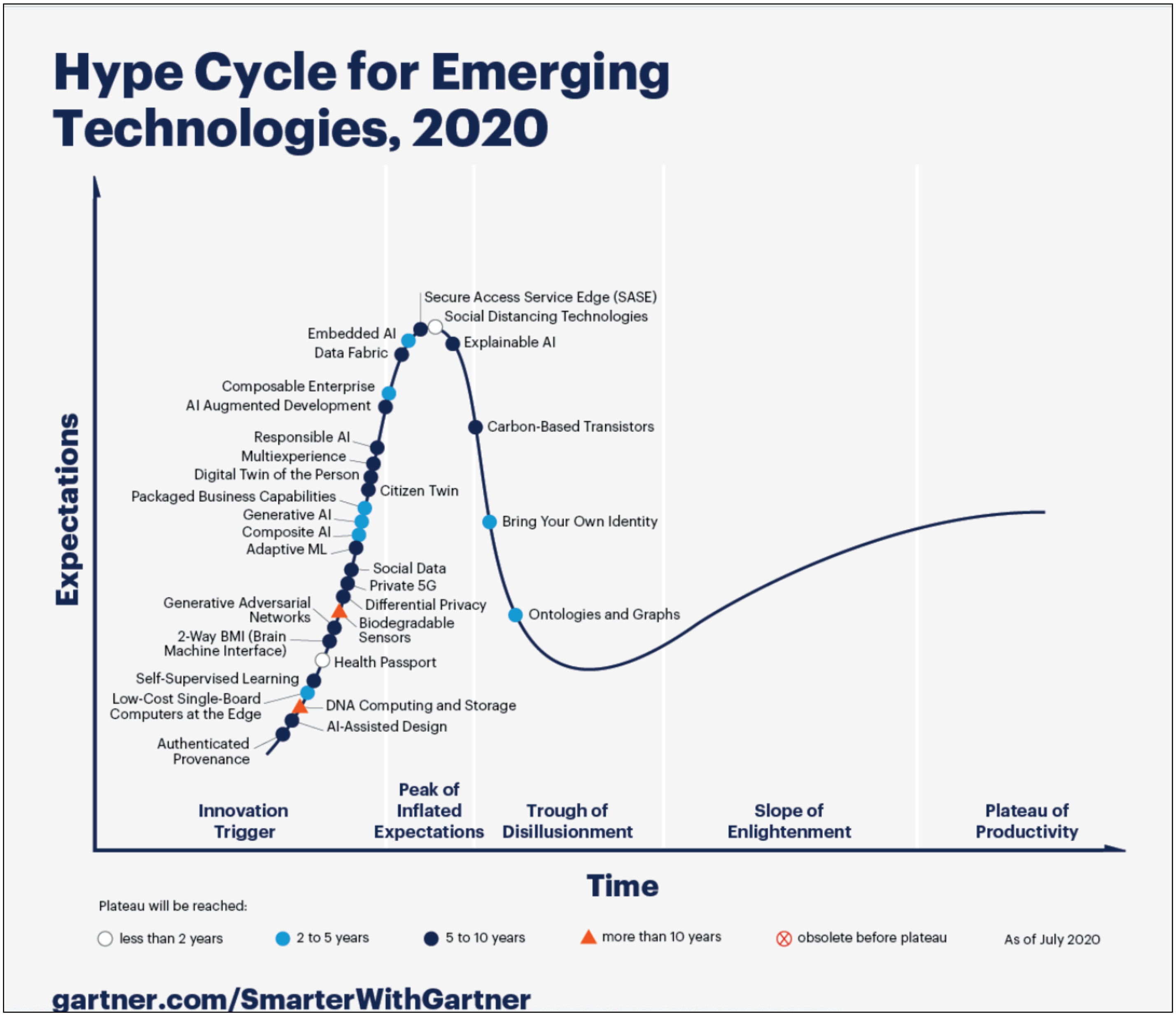
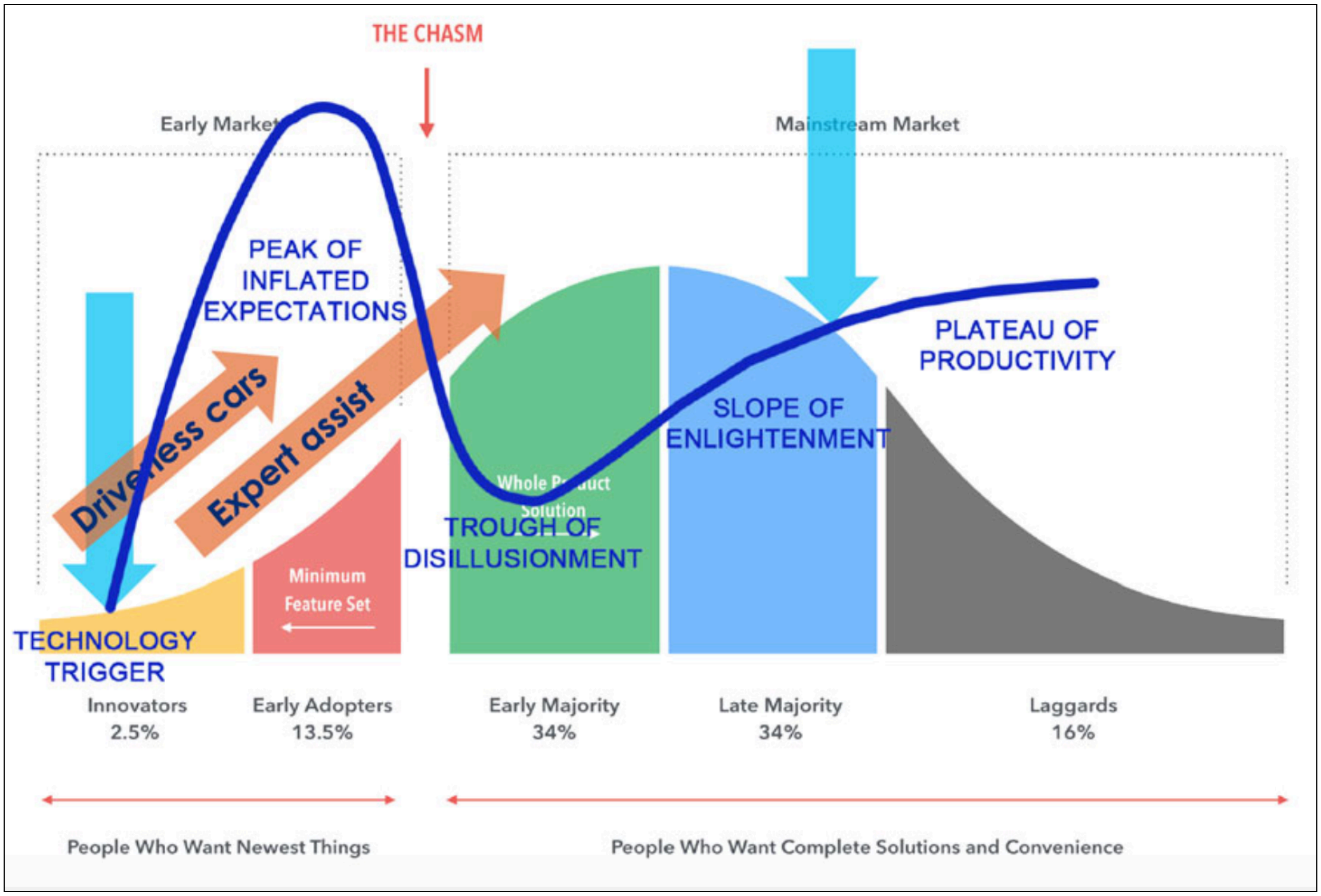
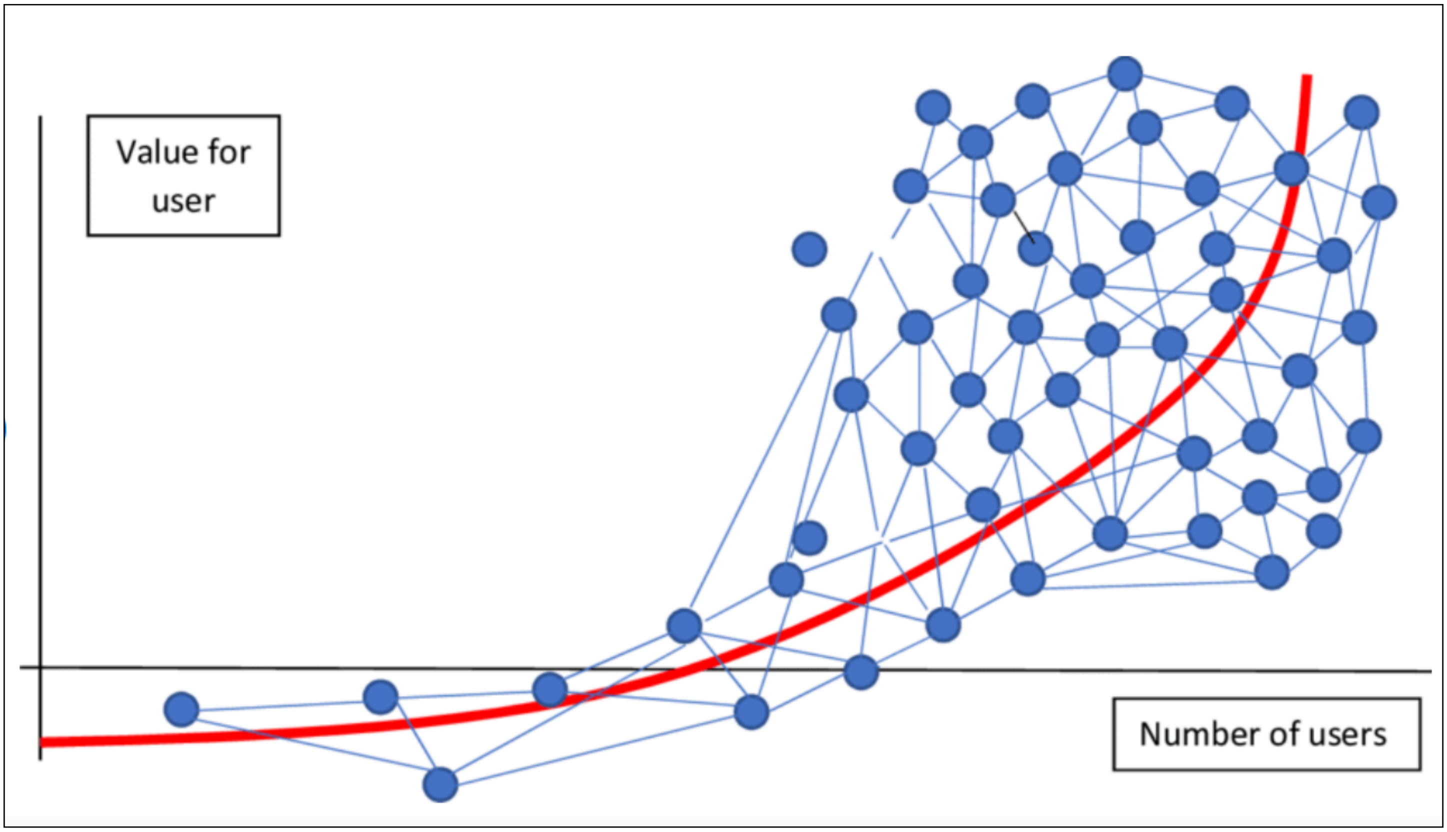


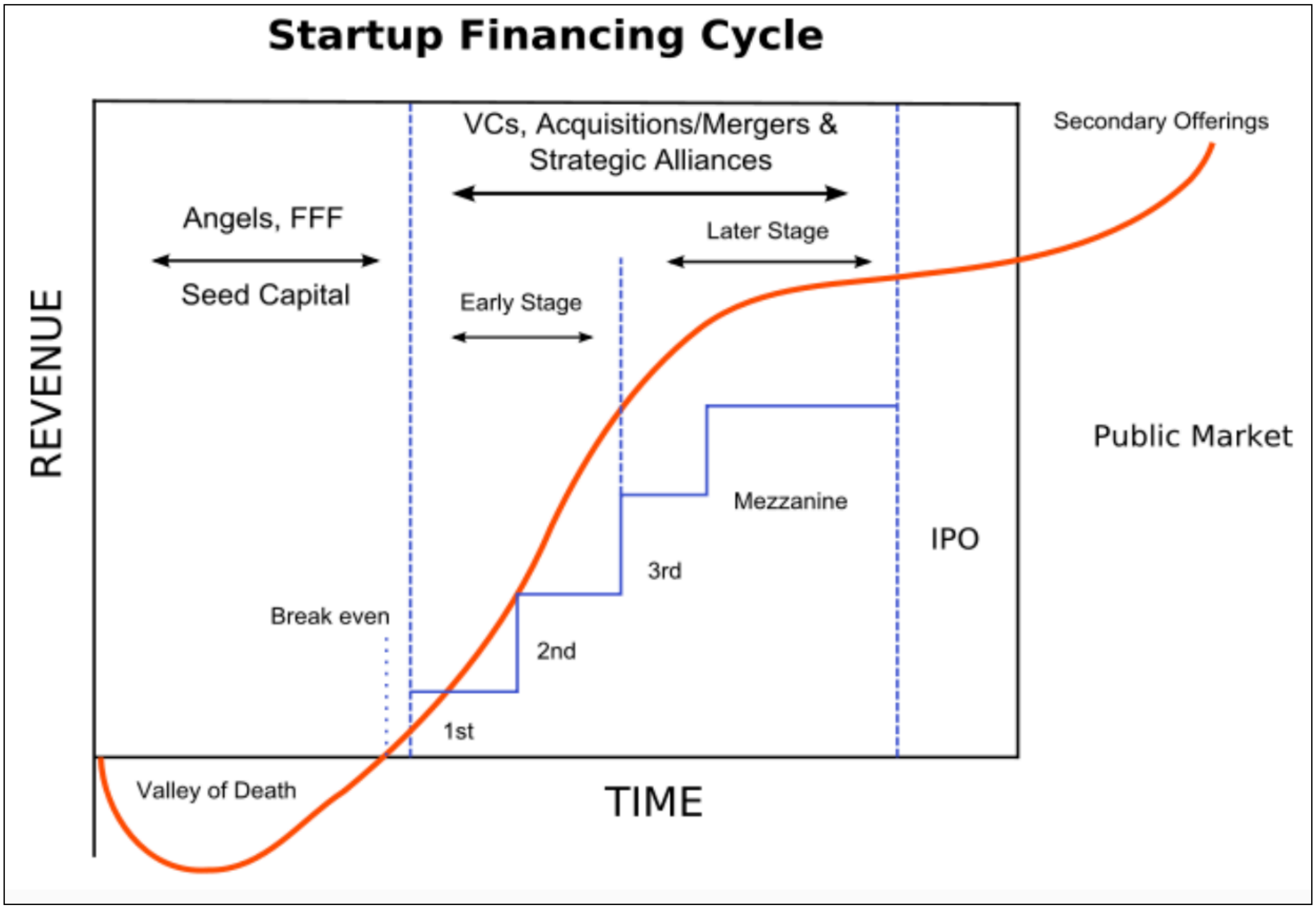
Innovation Diffusion (Everett Rogers in *Diffusion of Innovation*)



Network (Metcalfe's Law)



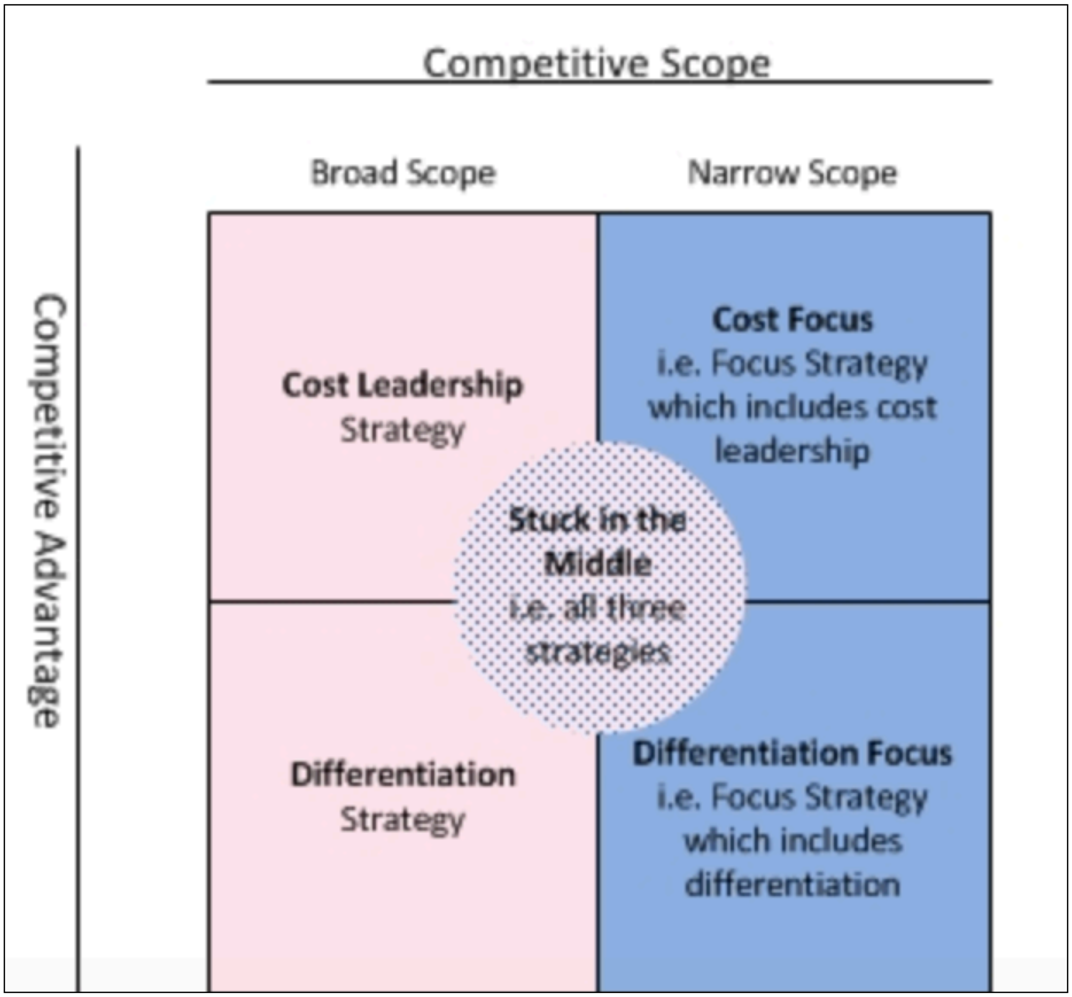
Startup Lifecycle



Strategy (Chan Kim/Renee Mauborgne in *Blue Ocean Strategy*)

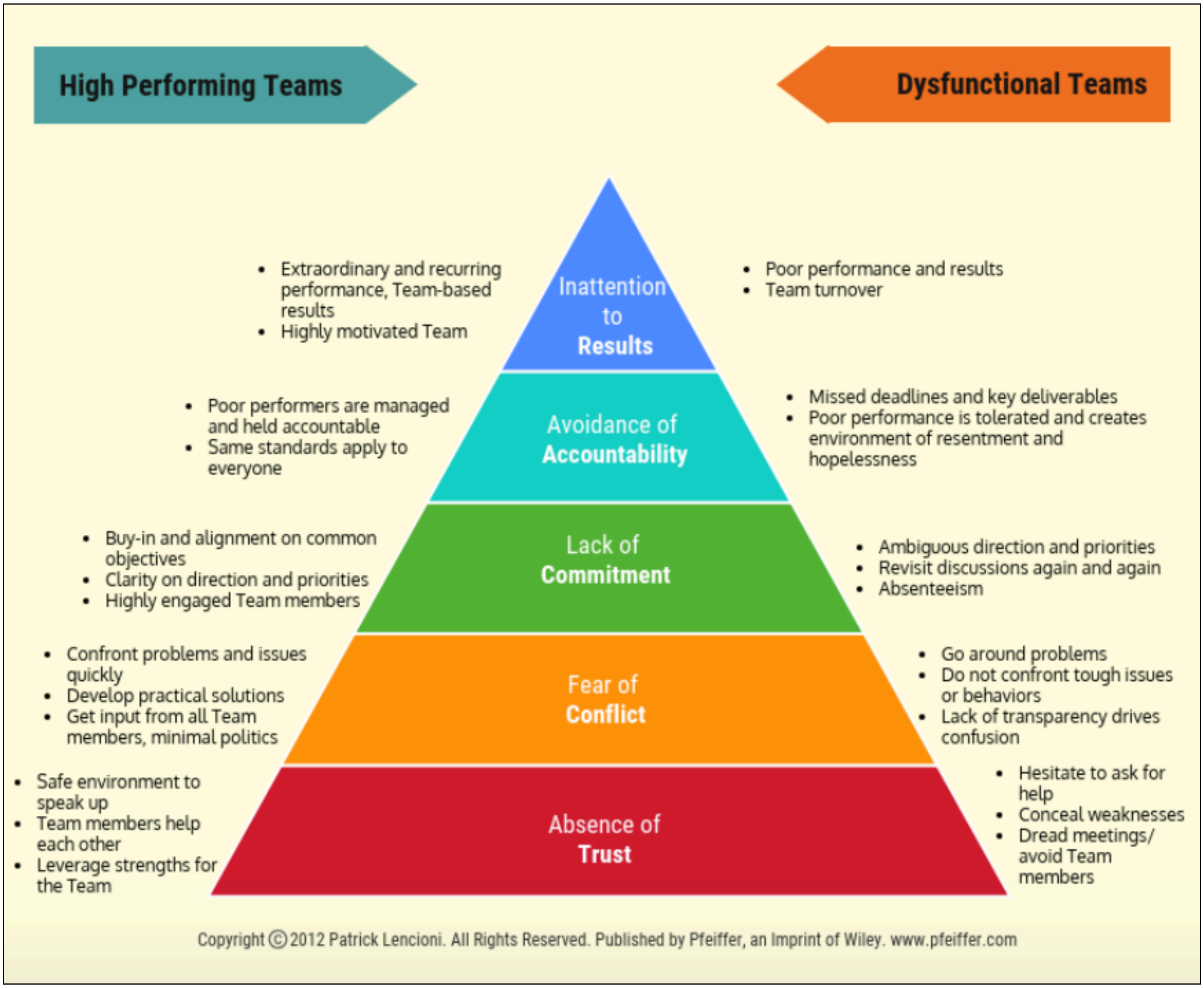
Red Ocean Strategy	Blue Ocean Strategy
Compete in **existing** market space.	Create **uncontested** market space.
Beat the competition.	Make the competition **irrelevant**.
Exploit **existing** demand.	Create and capture **new** demand.
Make the value-cost trade-off.	**Break** the value-cost trade-off.
Align the whole system of a firm's activities with its **strategic choice of differentiation or low cost**.	Align the whole system of a firm's activities in **pursuit of differentiation and low cost**.

Strategy (Michael Porter in *Competitive Strategy: Creating and Sustaining Superior Performance*)

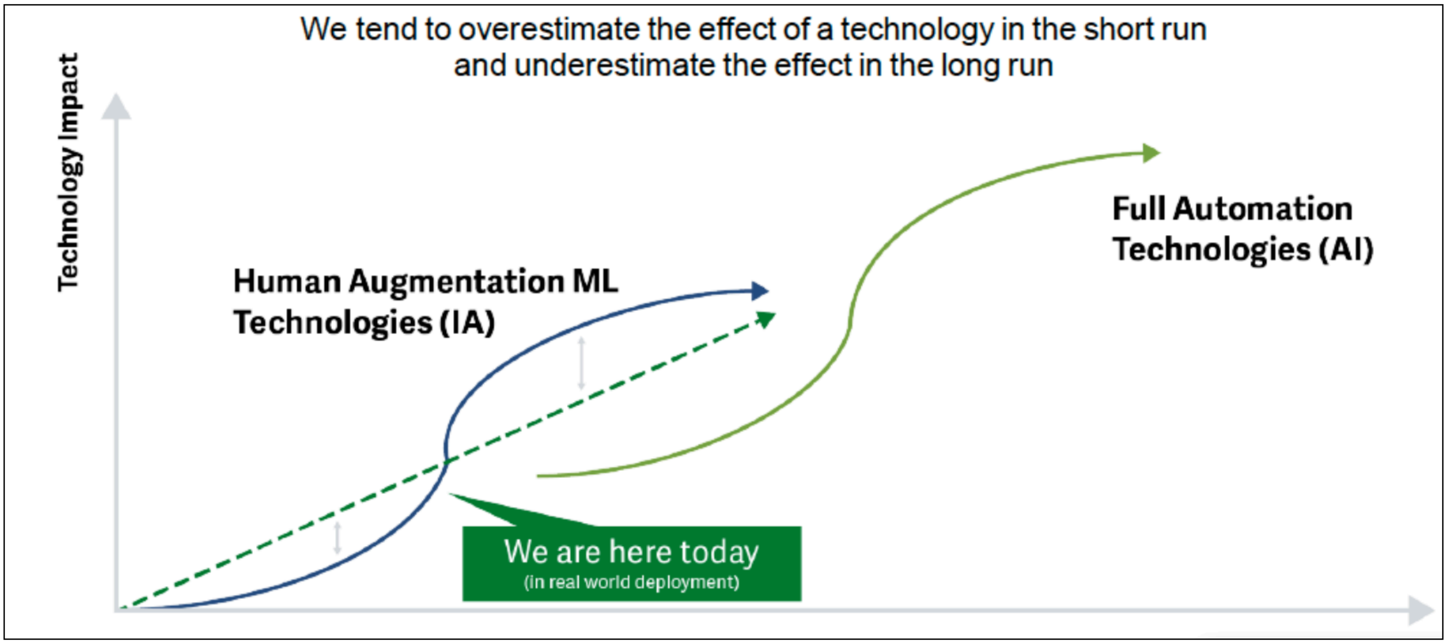


[redacted]

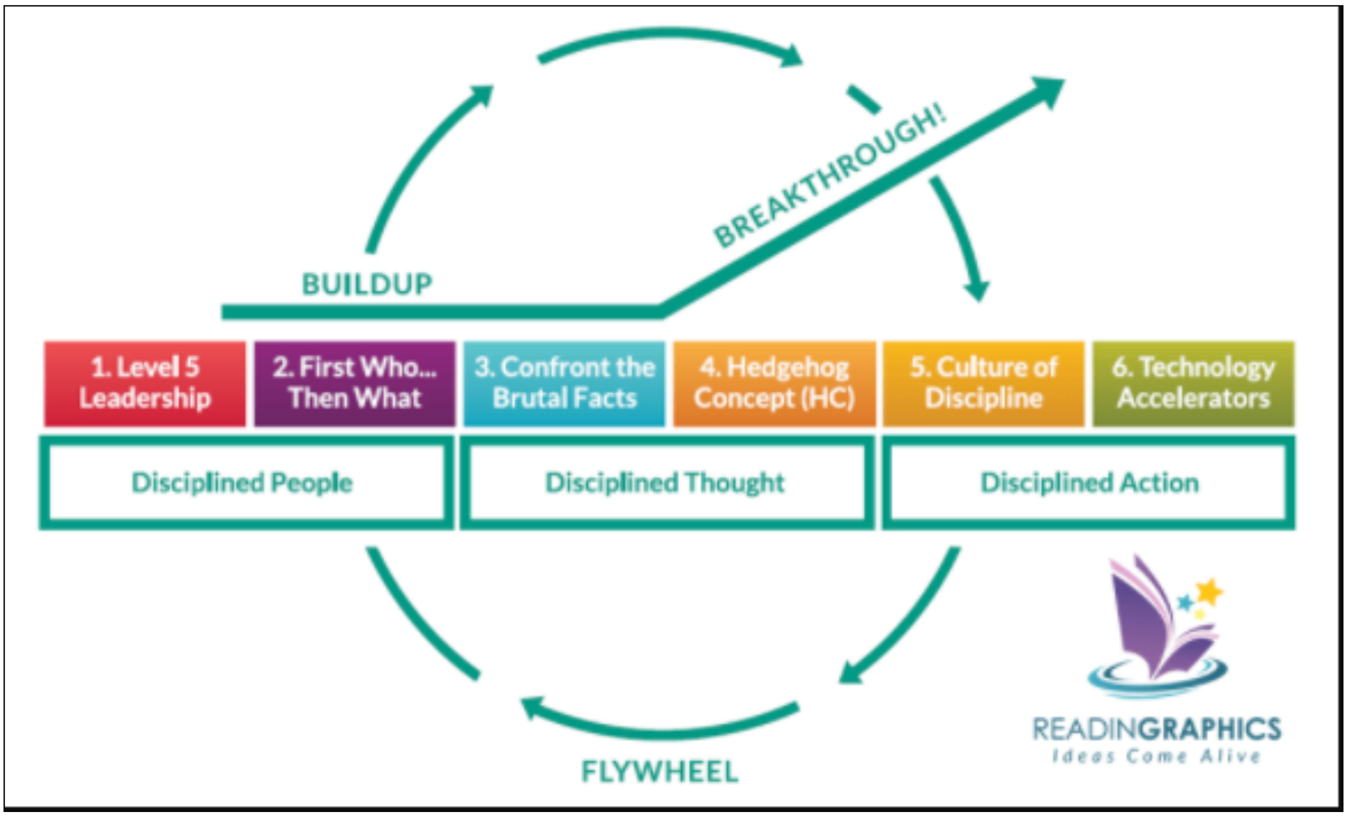
Team (Patrick Lencioni in *Five Dysfunctions of a Team*)



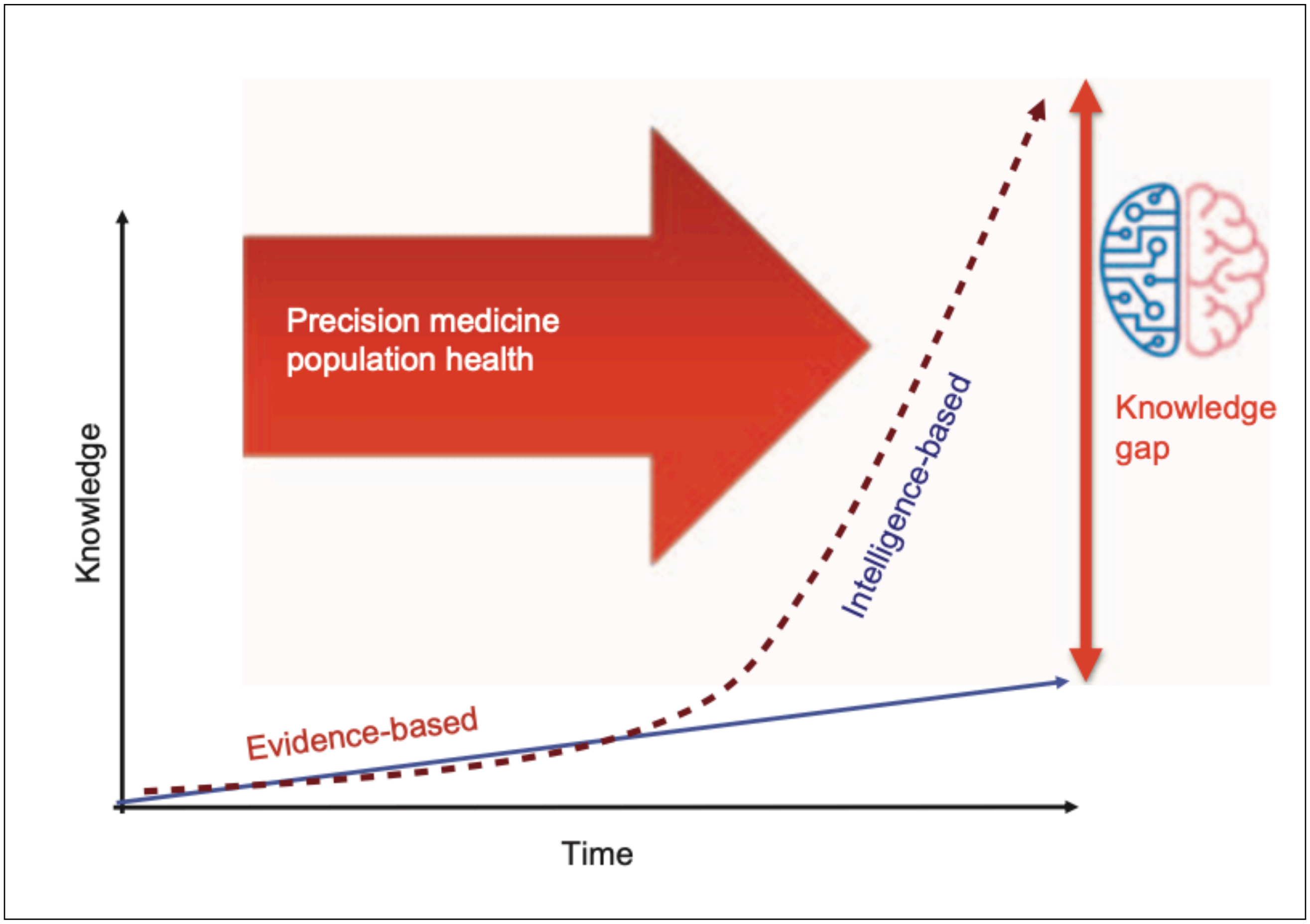
Technology (Amara's Law)



Transformation (Jim Collins in *Good to Great*)



Intelligence-Based Medicine (ACC and Spyro Mousses)



Major Takeaways in AI in Clinical Medicine and Health Care

After this long decades long journey and meeting/discussing AI in clinical medicine and health care at many international venues and with thousands of clinicians, data and computer scientists, informatics experts, AI experts, educators, researchers, investors, hospital administrators, IT specialists, students, these are the major takeaways (not in any particular order and a few principles may be duplicated from above but worth repeating):

Deep learning is very good for selected situations. As impressive as DL is for medical image interpretation and complicated **nonlinear situations** with large volume of data, ML may be better suited for simpler models with less data. In addition, DL faces significant challenges for projects like EHR. Lastly, **RPA** is adequate for tasks that have repeated steps that would benefit from automation.

Cognitive elements in AI will be needed. Clinicians will need to be much more engaged with the next wave of AI in medicine projects that will be more focus on cognitive architecture. *AlphaGo Zero* from Google DeepMind was much more about **algorithms** than big data. Important **cognitive elements** include memory, relationships, imagination, creativity, and abstract concepts.

Sharing of data will be essential. Collaboration amongst centers and pooling of data on a global scale will contribute significantly to the overall AI in medicine effort. Data in health care fragmented and disorganized to begin with, but some of this deficiency can be neutralized with pooling of health care data into **data reservoirs**, perhaps with **blockchain** and AI for privacy can security.

A human-to-machine convolution, not synergy, will advance biomedicine. We need to balance machine intelligence with human cognition so that a third realm, "**medical intelligence**", can result from this hybrid process. A good algorithm improves human decisions but a human can improve the algorithm by creatively solving its failures. Human and machine can be intertwined to **convolve**.

We overestimate AI in the short term (Amara's Law). There is some hype about AI in biomedicine especially given the performance of DL and CNN in medical image interpretation. We need to be careful with the AI hype as we can easily create an artificial **AI in medicine winter**, which may exhaust the valuable resources we need for a long term investment in AI.

But we will underestimate AI for the long term The longer term gain is very high so we need to "pace" ourselves for the longer journey in AI in medicine. In the coming decades, a myriad of new discoveries in the areas of **disease knowledge**, **drug discovery**, and **protein folding** will lead to new heights of understanding that will be impressive to even scientists.

Data overload is complicated by system complexity. The data conundrum in health care is a delicate balance: while more good (accurately labelled) data will be what is needed for the DL methodologies to yield good to excellent performances of predictions, the **system complexity** of biological systems and biomedical scenarios is an additional daunting challenge to overcome.

We need to push the AI in medicine agenda together. The two main domains (clinical medicine and data science) need to understand each other's cultures and domains; the more we can collaborate and trust each other, the better. In these days of incessant texting and emails, we are **hyper-connected** but **under-communicating.**

We need a major educational effort in AI in health care. A group of champions need to facilitate an **interface** between the clinician and data scientist groups for educational and training **curricula** for both domains. The chasm between clinical medicine and data science is huge but surmountable if we remain patient and put aside any hubris.

Big Data in health care is limited. Although the clinicians need to work collaboratively to gather as much as the biomedical data as possible (national and international levels), our data scientist colleagues need to appreciate that a large volume of good data is not possible sometimes, especially with rare diseases. **Innovative solutions** are needed to get around the data conundrum.

The AI technology is surging forward but other dimensions are not keeping up. The AI technology is rapidly improving, but regulation, ethics, and laws are not keeping up with this **exponential trajectory**. Regulatory agencies, ethics groups, and legal entities will all need to appreciate that AI is an ultra-fast moving methodology and traditional strategies and timelines are simply out-of-date.

Performance of a prediction tool should not be only AUC of ROC. Almost never are other important indices about performance discussed: AUC of the **precision-recall curve** and the **F_1 score** (see text). The reason is that if the population is unbalanced (usually a large number of true negatives), metrics can appear to be superior. Performance also does not correlate with **outcome**.

Data and databases in health care need a major makeover. Most of health care data and databases are still in relational database structure and will be much better in the more flexible and dynamic graph or **hypergraph format** for the future. This change is especially necessary for DL and its variants as well as cognitive architecture tools to better accommodate health care data.

AI and neurosciences will need to be in more synergy. The recent successes with Google DeepMind projects are simply astounding, and these **self-learning general AI tools** are likely to be influential in medicine. These tools are the "smart" AI tools (with intuition, creativity, and "common sense") that everyone has been waiting for, but perhaps with some appropriate trepidation.

It is more about AI interpretability, not explainability. Much has been written about AI explainability, and work is being done to have the best of both worlds (explainability and performance). It is more about **interpretability**, however, which is being able to observe a **cause and effect** without intricate knowledge of all the details inside the technology or device.

Clinicians will need to participate in this major paradigm shift in biomedicine. Clinicians will need time and resources to explore this new resource of AI and to observe **clinical validation studies** to be entirely convinced of the value of this new paradigm. Physicians and their **clinical wisdom** alone is valuable and they do not need to be facile with data science to be part of this movement.

Wearable and implantable technology will need embedded AI. The upcoming **data "tsunami"** from the panoply of wearable and implantable medical and health devices will be generating a large volume of continuous and real-time physiologic data; all of this data will need to be organized, stored, and analyzed peripherally in the form of peripheral or **embedded AI**.

Future of AI will be more about synthesis of data, not big data. There is already a trend to synthesis data and not have over reliance on available labelled data for learning. There simply will not be enough human labeled data, especially in rare diseases and small patient populations. The **generative AI tools** like GANs will help to navigate around this limitation in medicine.

Relationships will become increasingly important in AI models. Often in clinical situations, features that have a relationship are sometimes not associated in ML/DL models. This aspect of clinical medicine is a dimension will need to be duplicated or mimicked by **neural AI models** (such as **recursive cortical networks**) in the near future to increase relevance in medicine.

Medicine needs real-time AI tools. While medical imaging has been successful coupled with AI, subspecialties with more focus on **real-time decision making** need AI tools that can accommodate these time-series data and decisions that are also often based on too little information that constantly change. There is hope that **self-learning DRL** can provide the AI resource that is vital.

AI can be the equalizer in clinical medicine and health care. The present health care ecosystem fosters a mindset for hospitals to compete and be part of ranking systems (akin to college sports teams). With strategic use of AI, the concept of venerable experts only at the premiere institutions will be neutralized so that this special **AI-generated expertise** can be democratized.

AI needs to be in the minds of many, not in the hands of a few. Just as personal computers became ubiquitous, AI will need to have the same level of **adoption** in clinical medicine. In the future, programming will not be needed, making AI available will elevate primary care physicians into mini subspecialists and subspecialists into multi-dimensional experts all over the world.

Deep learning has performed well with medical images, but other applications will be more challenging. The much more complex nature of **unstructured EHR** (compared to medical images and its pixels/voxels) and other data in biomedicine and health care render this realm significantly more challenging for DL even though its **nonlinear capability** is a good strategy.

We need to learn from the earlier AI in medicine era and remember these lessons. GOFAI (in the form of **expert systems**) failed to be widely adopted in the earlier era not only because it was too slow and cumbersome and not useful for new and/or complex cases, it also failed to meet lofty expectations. We need to incorporate the strengths of GOFAI into current data science and AI.

AI can be used for most if not all subspecialties and areas in medicine. The image-focused subspecialties (radiology, ophthalmology, pathology, cardiology, etc) are among the first adopters because of the impressive performance of the CNN work. For the next wave of subspecialties to fully adopt AI, **real-time decision support tools** and other applications will need to mature.

Despite all the advances of AI, medicine and health care are behind other sectors. Due to intrinsic challenges (such as **data access** and **knowledge deficits**), AI has not been widely adopted by clinical medicine and health care; activity and interest, however, are increasing substantially in certain subspecialties (especially ones that are image-focused) and areas around the world.

The recent surge of AI in medicine is a derivative of the AI triad. The three elements of AI: **sophisticated algorithms** (especially deep learning), **big data**, and **computational power/cloud storage** have promulgated the recent AI revolution. The relative success of DL and specifically CNN in medical image interpretation has launched AI in medicine in this era.

AI is much more than just the well-publicized tools. Despite **IBM Watson** and its publicity (both positive and negative) as well as **CNN** and its early successes in medical image analytics, AI is a full "symphony" of "instruments": **NLP** for language, **RPA** for automation of repetitive tasks, and many types of machine and deep learning (such as self-learning **deep reinforcement learning**).

Medicine is not a dichotomous or categorical science. While the experience thus far with CNN and medical images have been relatively straightforward, much of clinical medicine is not based on dichotomy (such as alive-dead). Many cases of diseases are subclinical (with a **time element**) and/or have **gradations** of disease; this level of complexity and nuance creates a challenge for ML/DL.

There is information in what we do not see in EHR. In clinical medicine, often the **absence** of a significant positive piece of evidence is sometimes paradoxically the best evidence for a diagnosis; this aspect may or may not be adequately captured in an ML/DL model unless domain expertise in disease processes are directly involved in the model.

Resist the temptation to design AI tools before defining the problem. Problems in need of a solution is pervasive in health care. If one were to wear an "**AI lens**", some of these problems can be readily solved with an AI solution. This approach is aligned with the **design thinking process** in which the initial steps of problem solving are to empathize with people and to define the problem.

AI tools can rehumanize medicine. There is an undercurrent of AI dehumanizing medicine but AI can actually "rehumanize" medicine. If clinicians are partly relieved of their burden with data and information from EHR with AI strategies (such as **DL information tools** embedded into the EHR or **NLP-directed dictation tools**), they will have more time with their patients.

Learning about AI enables us to learn about ourselves. As we delve into ethical and issues about AI and human elements of thinking, creativity, imagination, consciousness, and ethics, we are in essence bringing **clarification** (or at least more discussions and intellectualization) into what humans need to define going into the next century with our AI partners.

When AI works well and humans trust it, we will no longer call it AI. With increasing trust and familiarity with AI tools, these tools will become commonplace and we will gradually cease calling it AI but rather simply accept these tools as part of our devices or practices. This will be particularly evident with wearable devices as well as hospital monitors that will be smart with **embedded AI**.

We humans sometimes have an unfair expectation of our machine partner. When we critique an AI tool with an AUROC of 0.83, we need to be reminded that humans usually perform much lower (the few accidents with autonomous vehicles are in the headlines even though sometimes humans are partly to blame for not being vigilant). This performance expectation should be **fair**.

There is a tendency to trust electronic data more than one should. There are many humans involved with the EHR in the data inputting so it can be full of errors. It is perhaps more accurate if we remove at least some if not all the humans from the loop of entering or validating various types of data in the EHR. **Real-time analytics** in the form of data correction should be in place.

An AI hybrid or even ensemble with two or more methodologies can be a winning strategy. There are several examples of a hybridization of two or more methodologies, like **deep reinforcement learning**. Other examples include **semi-supervised learning** and CRNN. In the future, it will be routine to have several specialized AI tools together (similar to instrument sections of an orchestra).

It is useful to look at AI tools in other sectors and adopt these tools for health care. AI is deployed in many sectors and some of the innovations in AI are not known to health care AI stakeholders. **DeepMind**'s work on *AlphaStar* and *AlphaZero* and Event Horizon Telescope work on the image of the black hole have implications for many situations in biomedicine and health care.

The future role of randomized controlled trials (RCT) needs to be reconfigured. The future of clinical research will be more **data-driven** and bottom-up rather than top-down designed. Recruitment of patients will also needs to be enabled by AI and not be human-driven as this process is too tedious and too slow without AI.

A dually educated cohort of clinician-data scientists can be the catalyst for this domain. A small cohort of dually educated clinician-data scientists can help solidify this interface between the two domains and this expertise and perspective result in a **geometric** (not additive) **gain** in both insight and knowledge. This can be analogous to a musician-composer in music industry.

AI in medicine is in its very early era. If AI in medicine is compared to music, we are presently in the equivalent of the **Renaissance period** (after the Medieval period) and about to enter the Baroque era. If we all remain dedicated and patient, we can see the wondrous AI in medicine accomplishments in the Classical (Mozart) and Romantic (Chopin) periods to follow.

AI is the exit velocity we need to leave the present health care conundrum. It is not possible to escape the **gravitational forces** of the present set of weighty issues in medicine and health care. AI coupled with emerging technologies can be the potent force we need in order to have the escape velocity to leave the present milieu.

The future CIO will be Chief Intelligence Officer. As AI becomes more pervasive and less enigmatic in health care, organizations will need a cohort of experts in the realm of AI in medicine and health care. In addition to the new type of CIO, there will also be new related careers such as a health care **AI architect** or **data strategist** to accommodate the demand of more sophisticated AI.

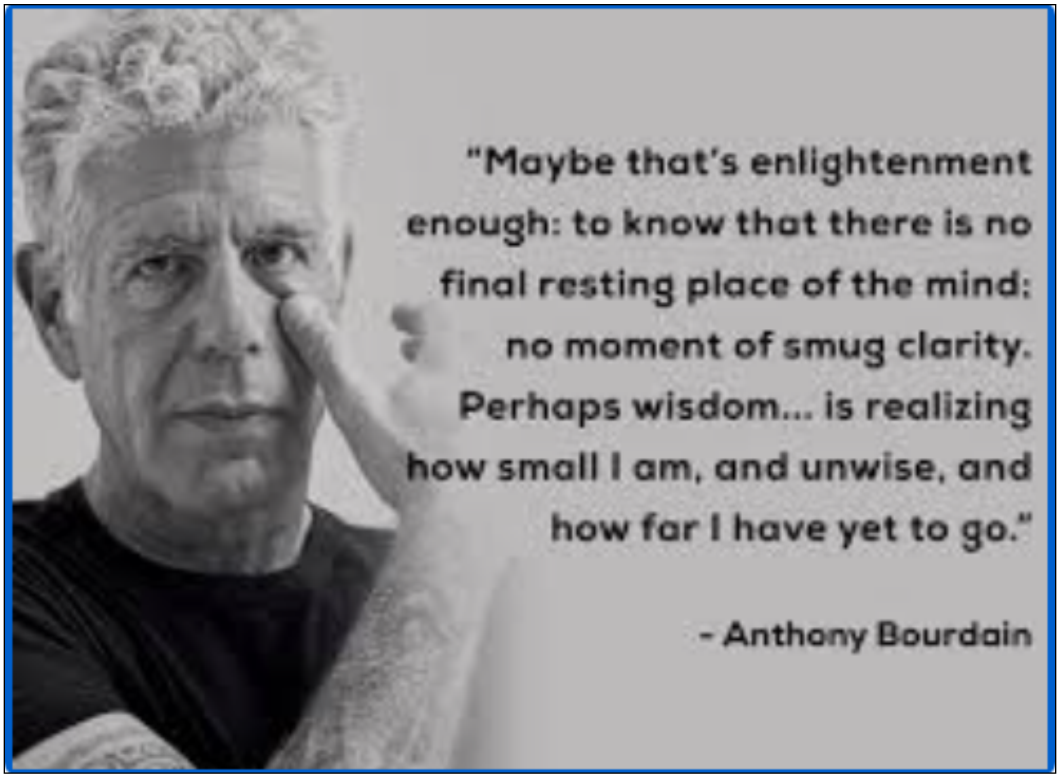
AI-related stakeholders need to spend time with clinicians. There are many examples of startup companies failing to follow this strategy and end up with an AI service that is adequate or even good but not congruent with what the clinicians actually need in their practice. This data science-to-clinical medicine **misalignment** is not infrequent.

Superior prediction does not mean better outcomes. It is important to understand that a higher AUC of the ROC does not automatically translate to better outcome, and a diagnosis is only the beginning of an opportunity to improve survival or outcome. There are many necessary steps in this **health care chain** that will need to be executed from diagnosis of a medical image.

AI and its tools do not change human behavior. Some AI tools can lead to better prediction of disease (such as 36.8% chance of diabetes in the next 5 years), but there are only a few AI tools that are coupled to an effort to change human behavior (such as weight management to reduce the likelihood of diabetes).

And finally,

The human-to-human (H2H) is more essential than ever before. The best moments during this long journey have been meaningful **social interactions** with many special people in this domain (always without machines) who took the time: an intimate dinner in Vienna with data science colleagues, coffee in Boston with a young aspiring surgeon, late evening soiree in London with technophiles, and tea in Hangzhou with a startup group.


"Maybe that's enlightenment enough: to know that there is no final resting place of the mind; no moment of smug clarity. Perhaps wisdom... is realizing how small I am, and unwise, and how far I have yet to go."
- Anthony Bourdain

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(In the spirit of crowd wisdom and "swarm intelligence", no author has more than one article listed)

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Websites of Interest

Organizations

American Medical Informatics Association
(AMIA.org)

Artificial Intelligence in Medicine (AIMed)
(AI-Med.io)

Artificial Intelligence in Medicine
(www.journals.elsevier.com/artificial-intelligence-in-medicine)

Association for the Advancement of Artificial Intelligence (AAAI)
(www.aaai.org)

Data Science Institute (DSI) at American College of Radiology (ACR)
(www.acrdsi.org)

Machine Learning for Health Care (MLHC)
(www.mlforhc.org)

Health Care Data Sets

Big Cities Health Inventory Data
(www.bchi.bigcitieshealth.org)

Child Health and Development Studies
(www.chdstudies.gov)

Data Elements for Emergency Department Systems (DEEDS)
(www.stacks.cdc.gov)

Health Plan Employer Data and Information Set (HEDIS)
(www.ncqa.org)

Healthcare Cost and Utilization Project (HCUP)
(www.hcup-us.ahrq.gov)

HealthData.gov
(www.healthdata.gov)

Human Mortality Database
(www.mortality.org)

Medicare Provider Utilization and Payment Data: Physician and Other
(www.cms.gov)

MHEALTH Dataset Data Set
(www.archive.ics.uci.edu)

MIMIC III
(MIMIC.physionet.org)

Outcomes and Assessment Information Set (OASIS)
(www.cms.gov)

Surveillance, Epidemiology, and End Results (SEER)-Medicare Health Outcomes survey (MHOS)
(www.healthcaredelivery.cancer.gov)

Uniform Ambulatory Care Data Set (UACDS)
(www.aspe.hhs.gov)

Uniform Hospital Discharge Data Set (UHDDS)
(www.medicalbillingcodingworld.com)

University of California at Irvine (UCI) Data Set

Videos of Interest

Introductory

How Researchers are Teaching AI to Learn Like a Child (AAAS)
(https://www.youtube.com/watch?v=79zHbBuFHmw)

AlphaGo (Documentary, 2017)

Do You Trust This Computer? (Documentary 2018)

Artificial Intelligence: Mankind's Last Invention
(https://www.youtube.com/watch?v=cM8Nk7b_X1o)

Three Principles for Creating Safer AI (TED2017/ Stuart Russell)
(https://www.ted.com/talks/stuart_russell_3_principles_for_creating_safer_ai?language=en)

What Happens When Our Computers Get Smarter Than We Are? (TED2015/Nick Bostrom)
(https://www.ted.com/talks/nick_bostrom_what_happens_when_our_computers_get_smarter_than_we_are?language=en)

IBM Watson: The Science Behind an Answer
(https://www.youtube.com/watch?v=DywO4zksfXw)

A Gentle Introduction to Machine Learning
(https://www.youtube.com/watch?v=Gv9_4yMHFhI)

StatQuest series

ML TensorFlow Zero to Hero

More Advanced

Machine Learning Fundamentals: Bias and Variance
(https://www.youtube.com/watch?v=EuBBz3bI-aA)

The Rise of Artificial Intelligence Through Deep Learning (TEDxMontreal/Yoshua Bengio)
(https://www.bing.com/videos/search?q=artificial+intelligence+and+TED&qpvt=artificial+intelligence+and+TED&view=detail&mid=C0477628C68142A174BFC0477628C68142A174BF&&FORM=VDRVRV)

But What is a Neural Network? Deep Learning, Chapter 1 (3Blue1Brown series)
(https://www.youtube.com/watch?v=aircAruvnKk)

Gradient Descent, How Neural Networks Learn. Deep Learning, Chapter 2 (3Blue1Brown series)
(https://www.3blue1brown.com/videos-blog/2017/10/16/gradient-descent-how-neural-networks-learn-deep-learning-chapter-2)

What is BackPropagation Doing Really? Deep Learning, Chapter 3 (3Blue1Brown series)
(https://www.3blue1brown.com/videos-blog/2017/11/3/what-is-backpropagation-really-doing-deep-learning-chapter-3)