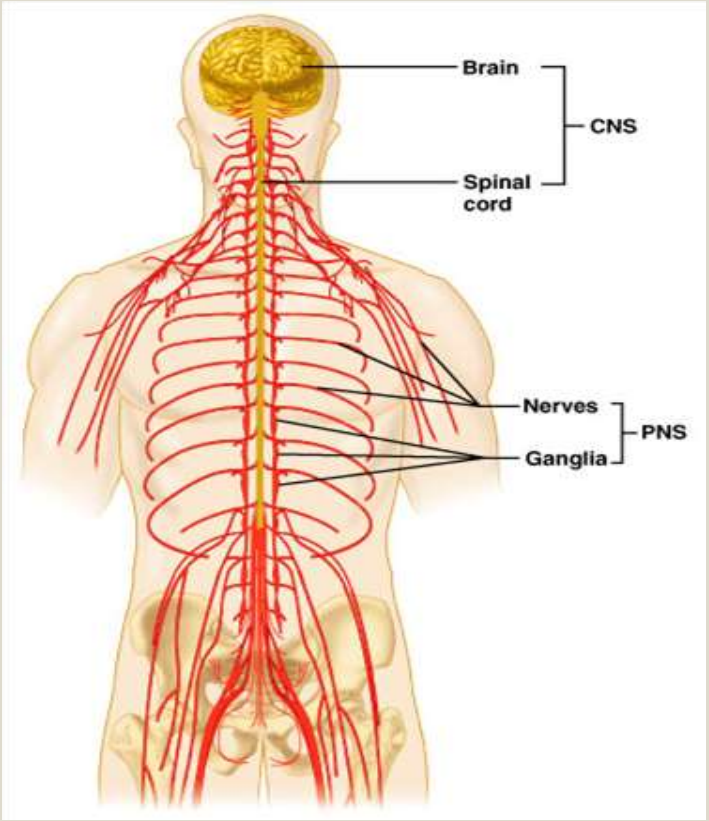
Unit 4- NEUROBIOLOGY

- Basic of Neurons
- glial cells
- Brain and its parts
- Artificial neural networks,-concepts, and differences with biological neural networks
- uses of ANN
- machine learning
- data mining in biology

Nervous system

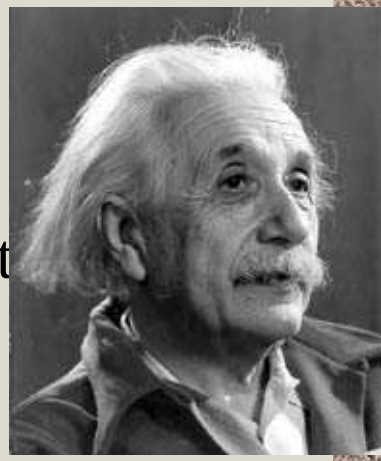
Neurotransmitters
Neuropeptides

- **The task of nervous system is to coordinate the mental processes by which we perceive, act, learn and remember.**
- **The human brain is a network of billions of individual nerve cells interconnected in systems that construct our perceptions of the external world, fix our attention, and control the machinery of our actions.**
- **The nervous system has two classes of cells: *nerve cells (neurons) and glial cells (glia).***



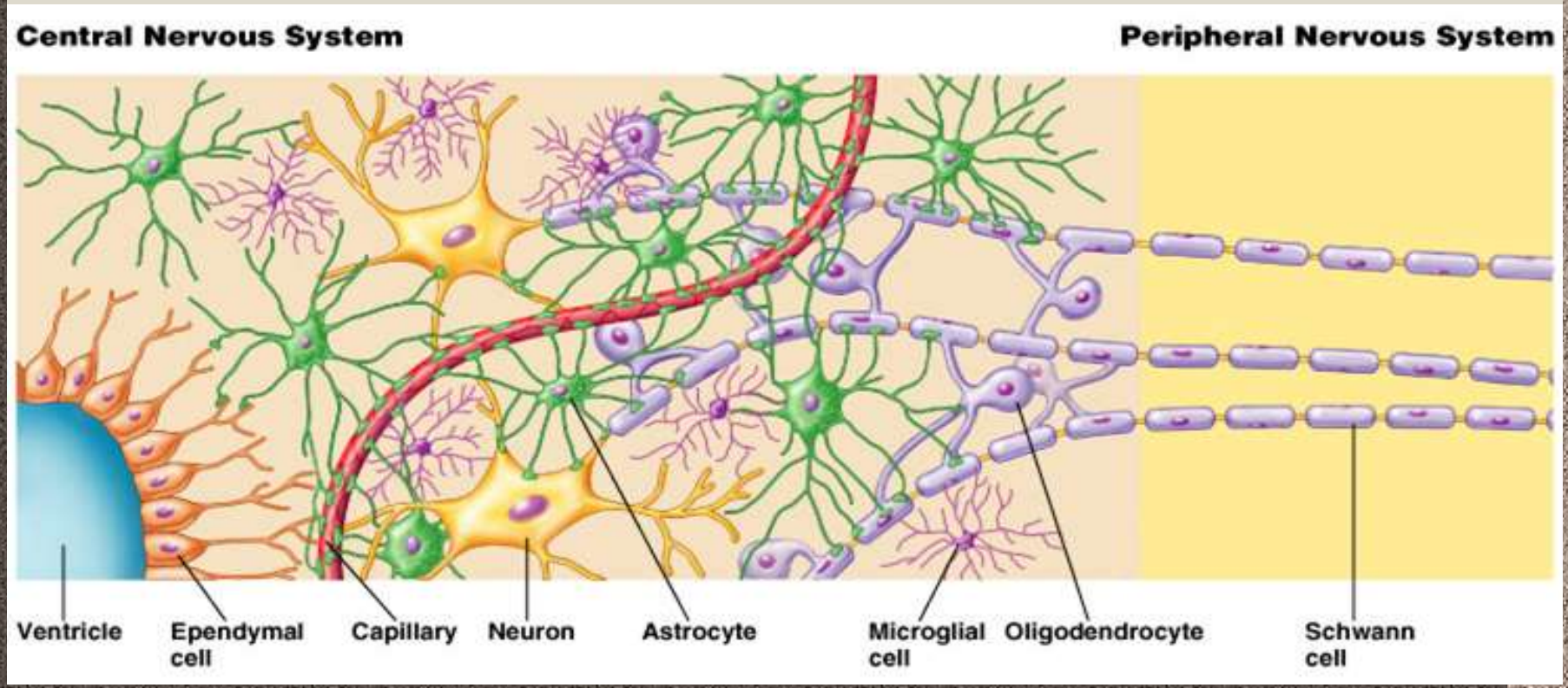
Supporting Cells (Neuroglial Cells) in the CNS

- Neuroglia – usually only refers to supporting cells in the CNS, but can be used for PNS
  - –Glial cells have branching processes and a central cell body
  - –Outnumber neurons 10 to 1 (the guy on the right had an inordinate amount of them).
  - –Make up half the mass of the brain
  - –Can divide throughout life



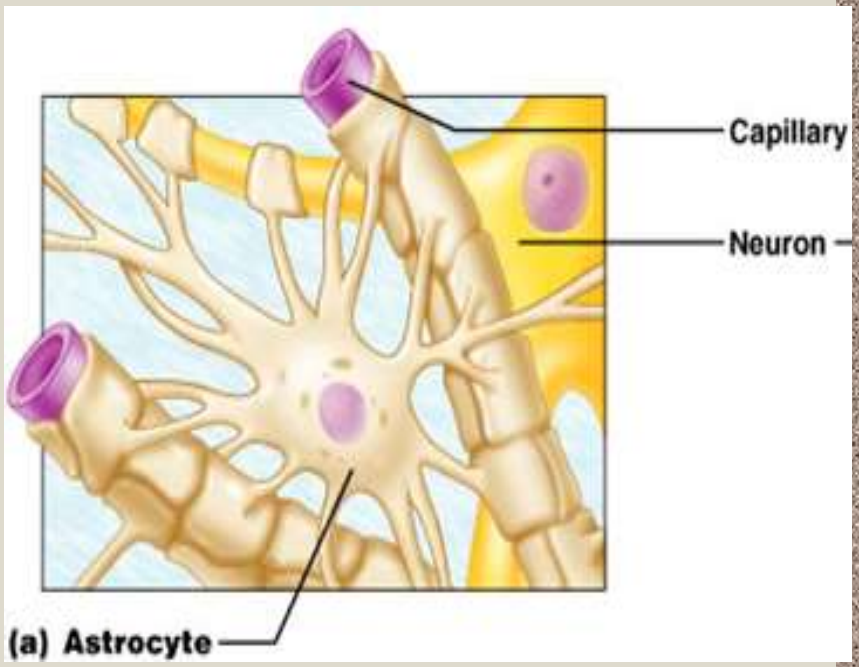
Glial cells

- **Glial cells are support cells.**
- **They are more in number than neurons.**
- **There are between 10 and 50 times more glia than neurons in the brain of humans.**
- **The name for these cells derives from the Greek word for glue. In actual terms, the glia do not commonly hold nerve cells together but surround the neurons.**

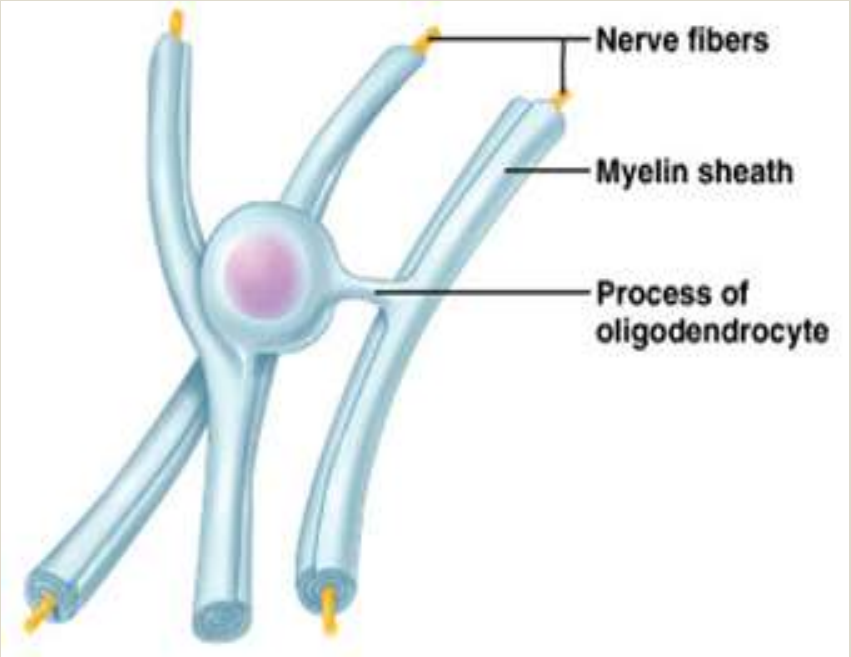


Types of Glial Cells in the CNS: Astrocytes, Oligodendrocytes, and Microglia

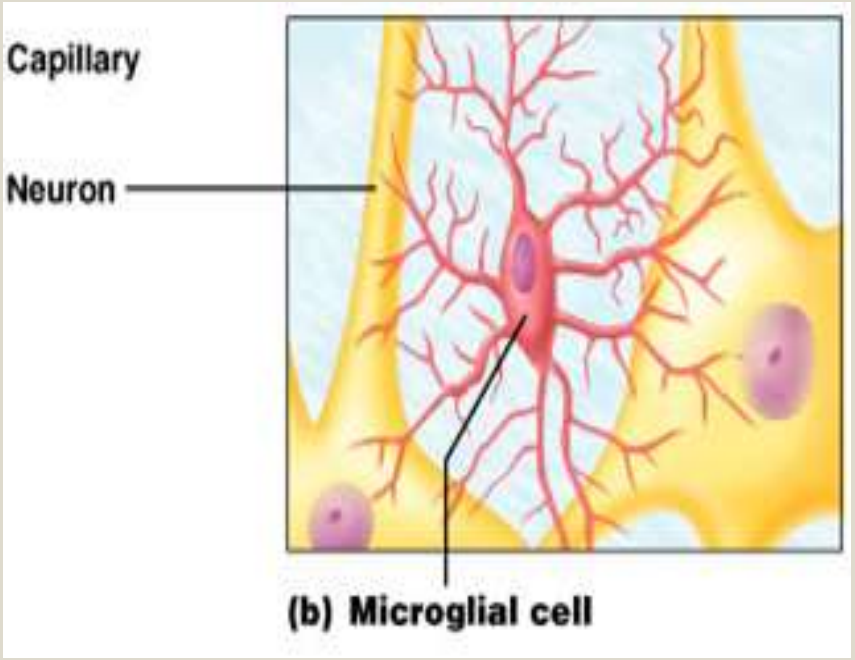
- ***Astrocytes*: Most abundant glial cell type, irregular star-shaped cell bodies .**
  - **Take up and release ions to control the environment around neurons**
  - **Recapture and recycle neurotransmitters**
  - **Involved with synapse formation in developing neural tissue**
  - **Produce molecules necessary for neural growth**
  - **Propagate calcium signals that may be involved in memory**



- ***Oligodendrocytes*: Have few branches.**
- **Wrap their cell processes around axons in CNS**
- **Produce myelin sheaths for rapid conduction of nerve impulses**
    - ***Schwann cells* surround axons in the PNS and form myelin sheath around axons of the PNS**

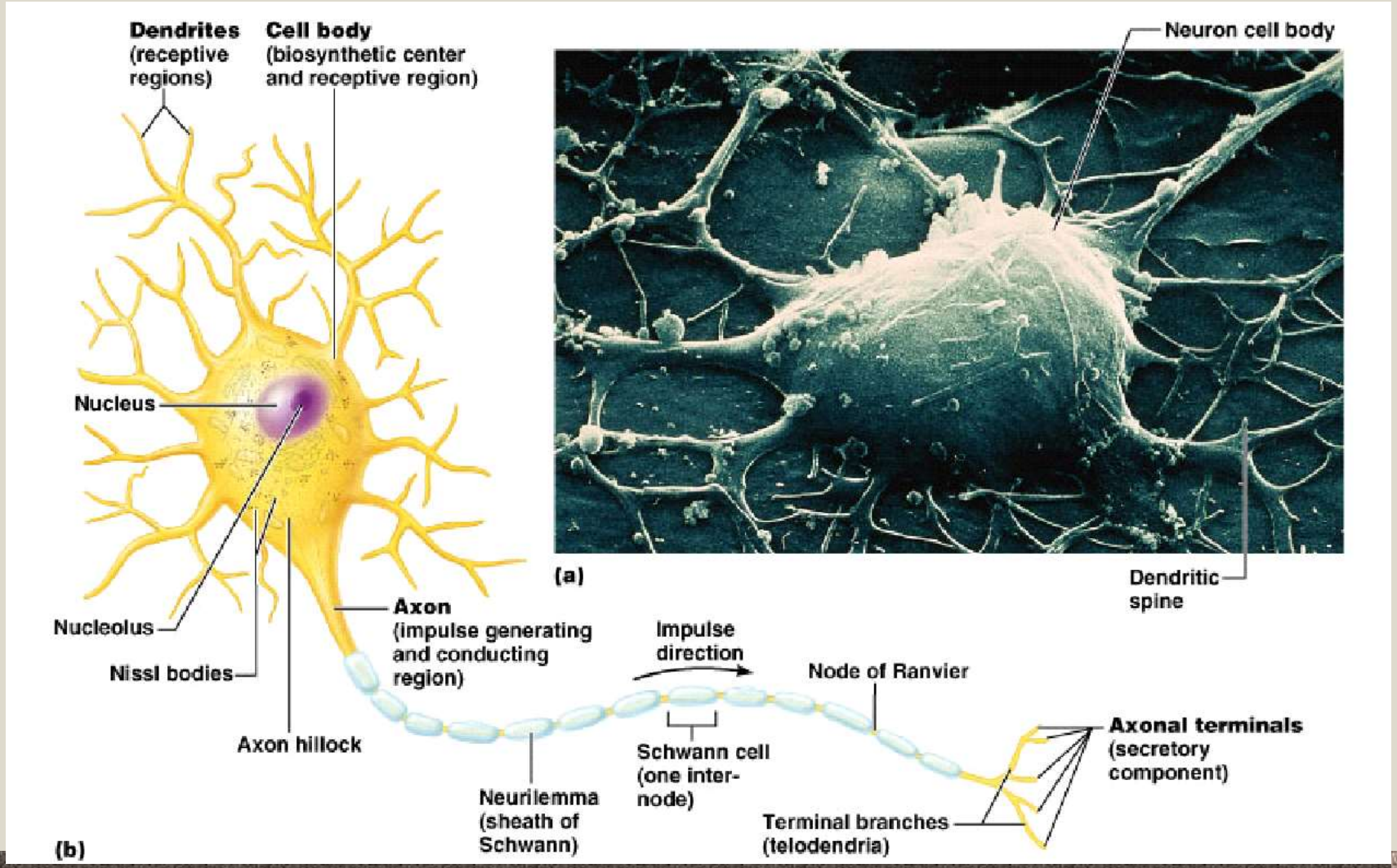


- ***Microglia*: Smallest and least abundant.**
  - **Phagocytes – the macrophages of the CNS**
  - **Engulf invading microorganisms and dead neurons**
  - **Derived from blood cells called monocytes**



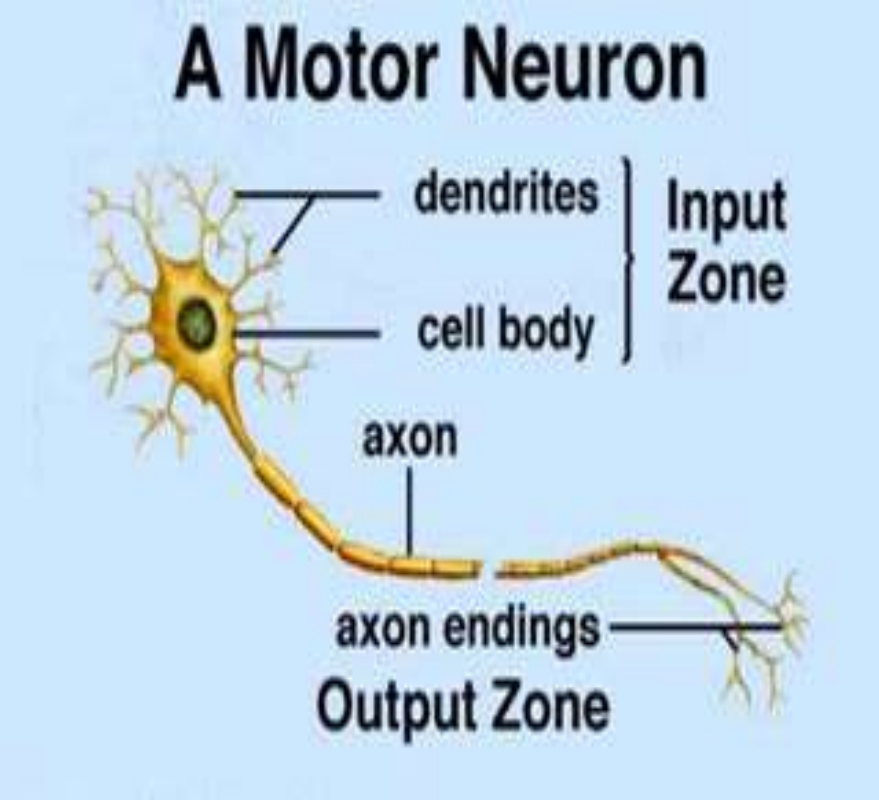
Nerve cells- Neurons

- **Nerve cells are the main signaling units of the nervous system.**
- **A typical neuron has four morphologically defined regions*: the cell body, dendrites, the axon, and presynaptic terminal***
- **The *cell body (soma)* is the metabolic center of the cell. It contains the nucleus which stores the genes of the cell, as well as the endoplasmic reticulum, an extension of the nucleus where the cell's proteins are synthesized.**
- **The cell body gives rise to two kinds of processes: several short *dendrites* and one, long, tubular *axon*.**
- **These processes vary in number & relative length but always serve to conduct impulses (with dendrites conducting impulses toward the cell body and axons conducting impulses away from the cell body as shown in the figure).**


Dendrites
(receptive
regions)
Cell body
(biosynthetic center
and receptive region)
Nucleus
Nucleolus
Nissl bodies
Axon hillock
Axon
(impulse generating
and conducting
region)
Impulse
direction
Node of Ranvier
Schwann cell
(one inter-
node)
Neurilemma
(sheath of
Schwann)
Terminal branches
(telodendria)
Axonal terminals
(secretory
component)
(b)
Neuron cell body
(a)
Dendritic
spine

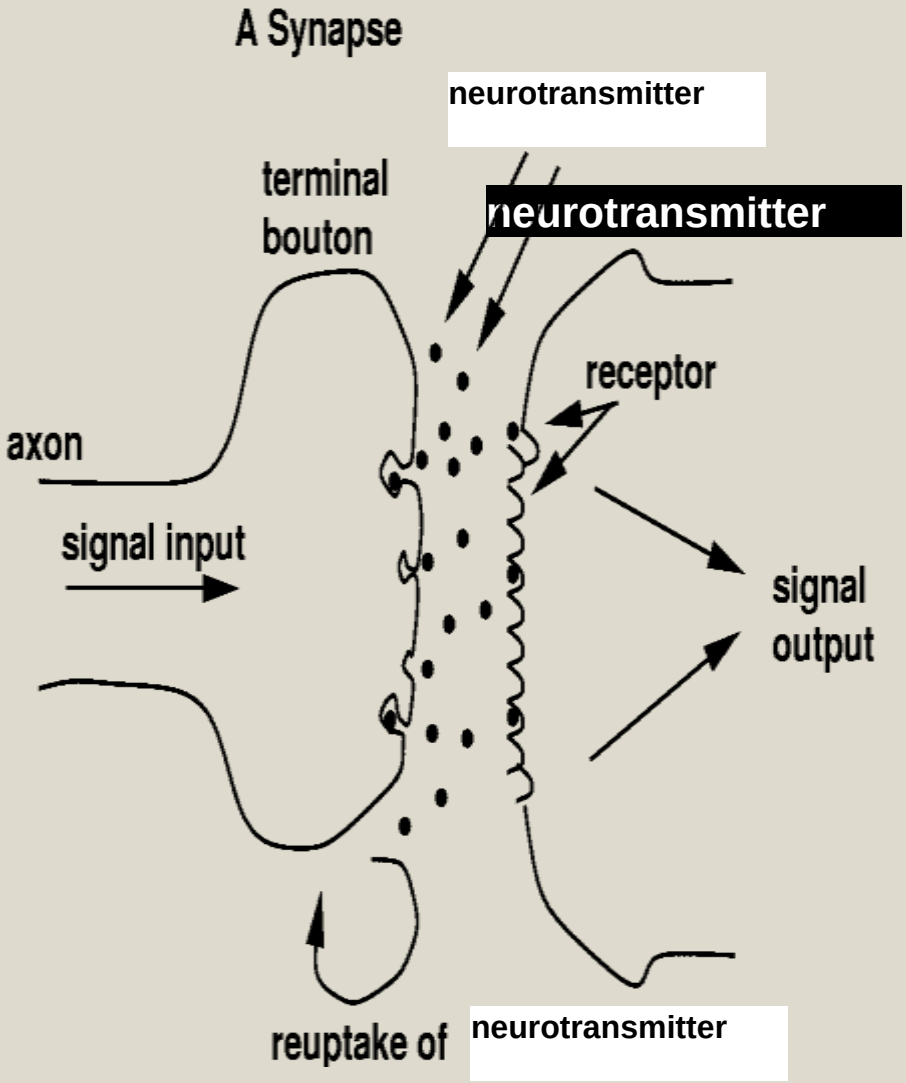
Action Potential

- A neuron receives input from other neurons (typically many thousands). All the input signals are integrated. Once input exceeds a critical level, the neuron discharges a **spike** - an electrical pulse that travels from the body, down the axon, to the next neuron(s) (or other receptors). This spiking event is also called **depolarization**, and is followed by a **refractory period**, during which the neuron is unable to fire.



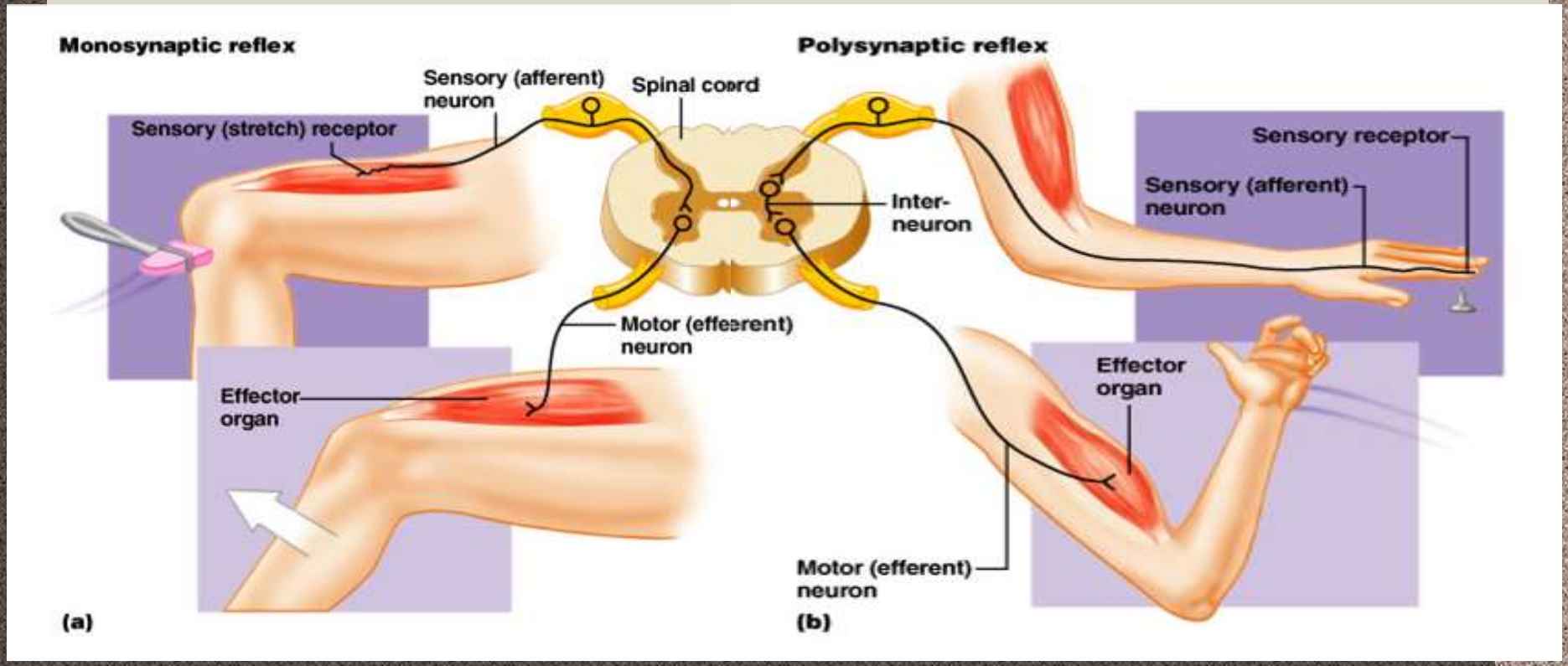
Synapse

- **The axon endings (Output Zone) almost touch the dendrites or cell body of the next neuron.**
- **Transmission of an electrical signal from one neuron to the next is effected by neurotransmitters, chemicals which are released from the first neuron and which bind to receptors in the second. This link is called a synapse.**
- **The extent to which the signal from one neuron is passed on to the next depends on many factors, e.g. the amount of neurotransmitter available, the number and arrangement of receptors, amount of neurotransmitter reabsorbed, etc.**



Sensory Input and Motor Output

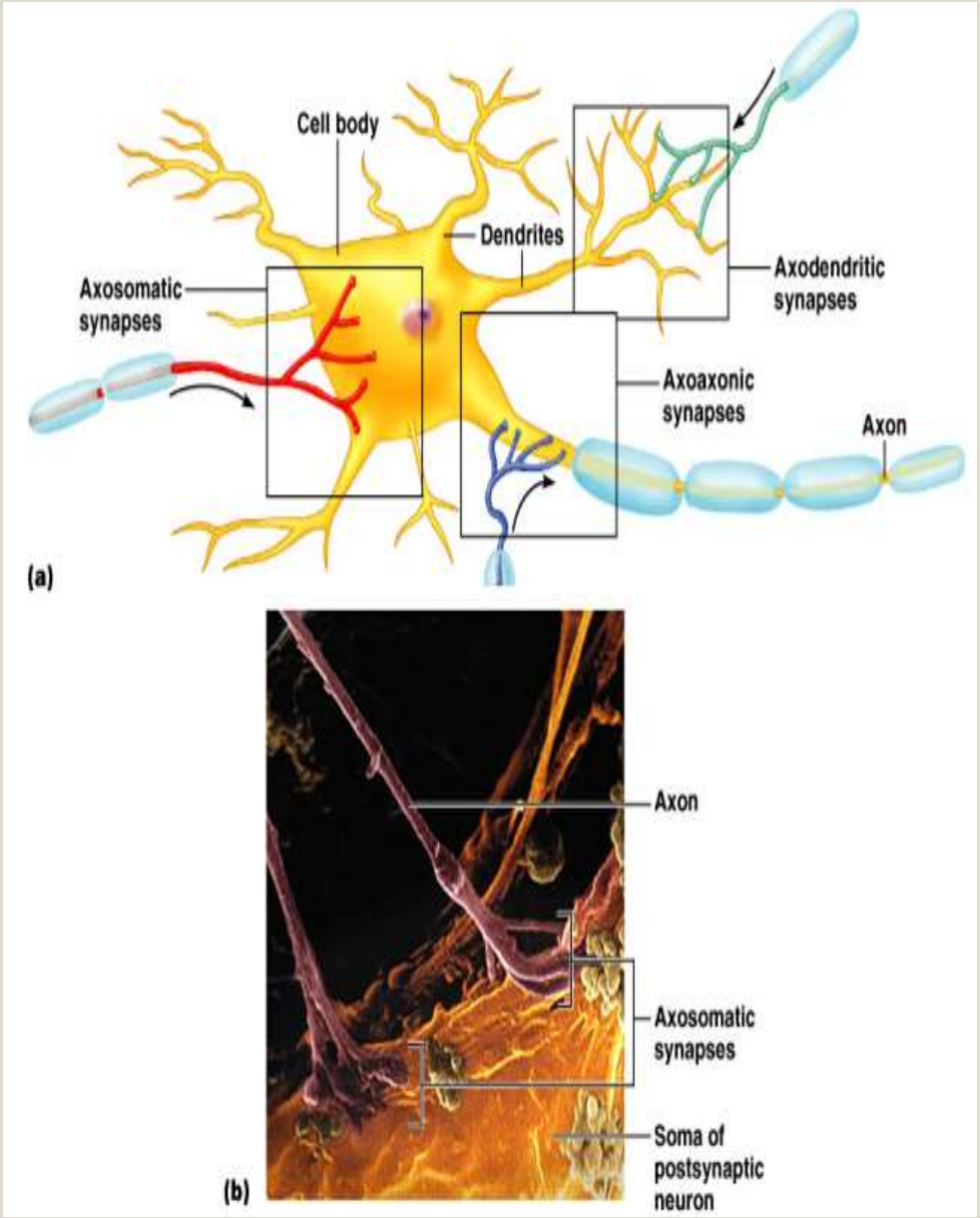
- Sensory signals picked up by sensory receptors
  - Carried by afferent nerve fibers of PNS to the CNS
- Motor signals are carried away from the CNS
  - Carried by efferent nerve fibers of PNS to effectors
  - Innervate muscles and glands



Animation on nerve cells

- https://www.youtube.com/watch?v=NsBaPtemAjs

- The dendrites branch out in a tree-like fashion and are the main apparatus for receiving incoming signals from other nerve cells.
- In contrast, the axon extends away from the cell body and is the main conducting unit for carrying signals for other neurons.



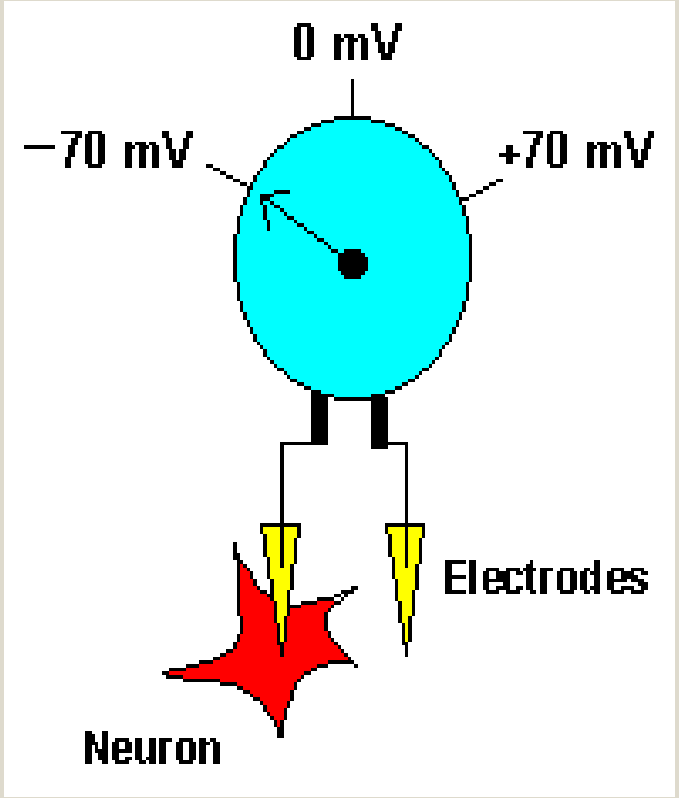
An Animation for nerve impulse

https://www.youtube.com/watch?v=b2ctEsGEpe0

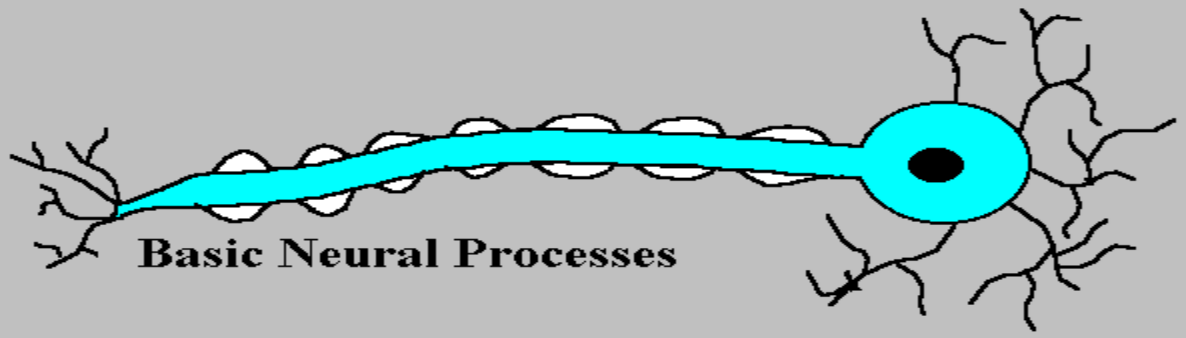
- **An axon can convey electrical signals along distances ranging from 0.1 mm to 3 m. These electrical signals called *action potentials* are rapid, transient with an amplitude of 100 mV and a duration of about 1ms.**

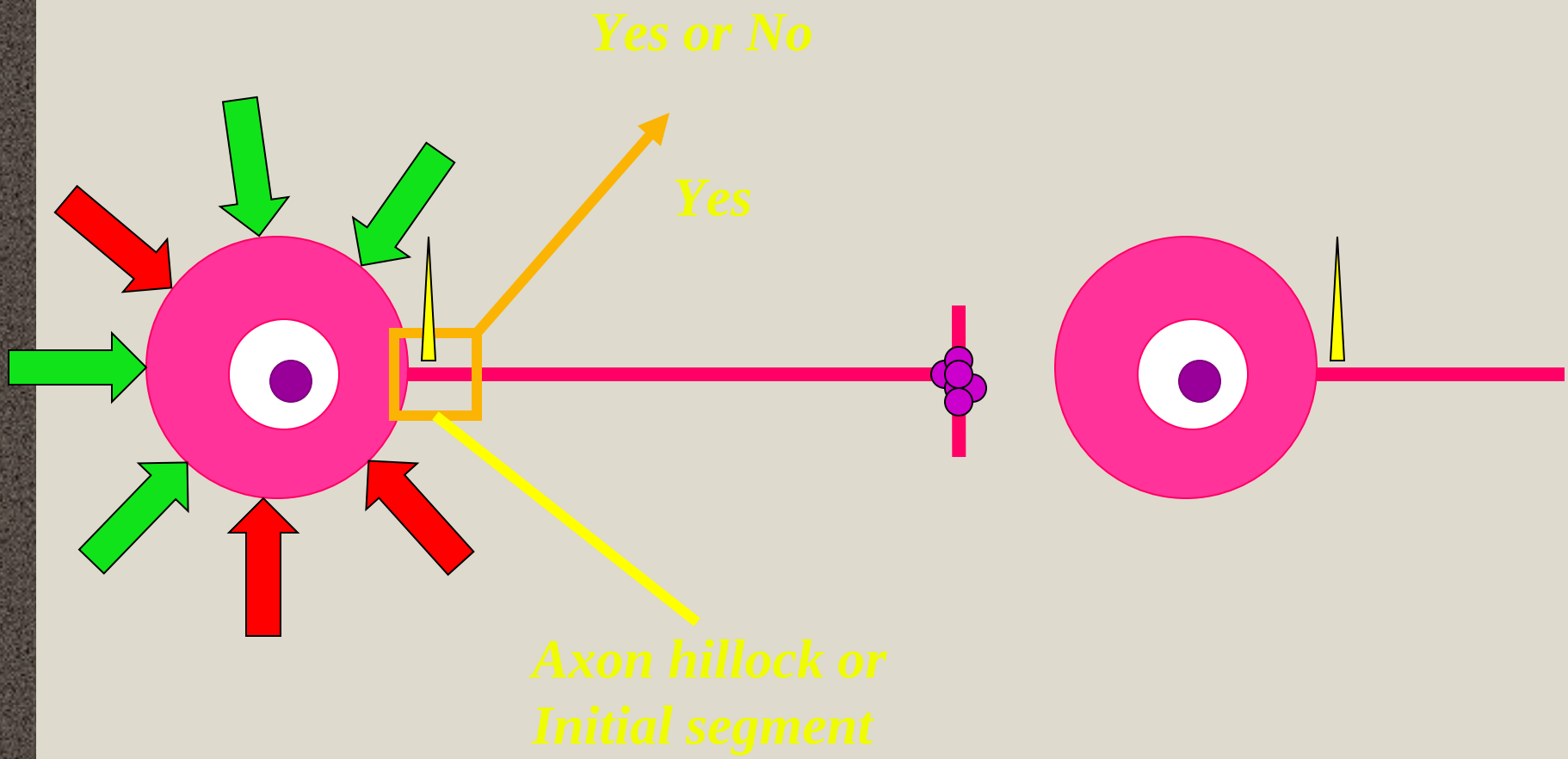
- **Neurons can respond to stimuli and conduct impulses because a membrane potential is established across the cell membrane. In other words, there is an unequal distribution of ions (charged atoms) on the two sides of a nerve cell membrane.**

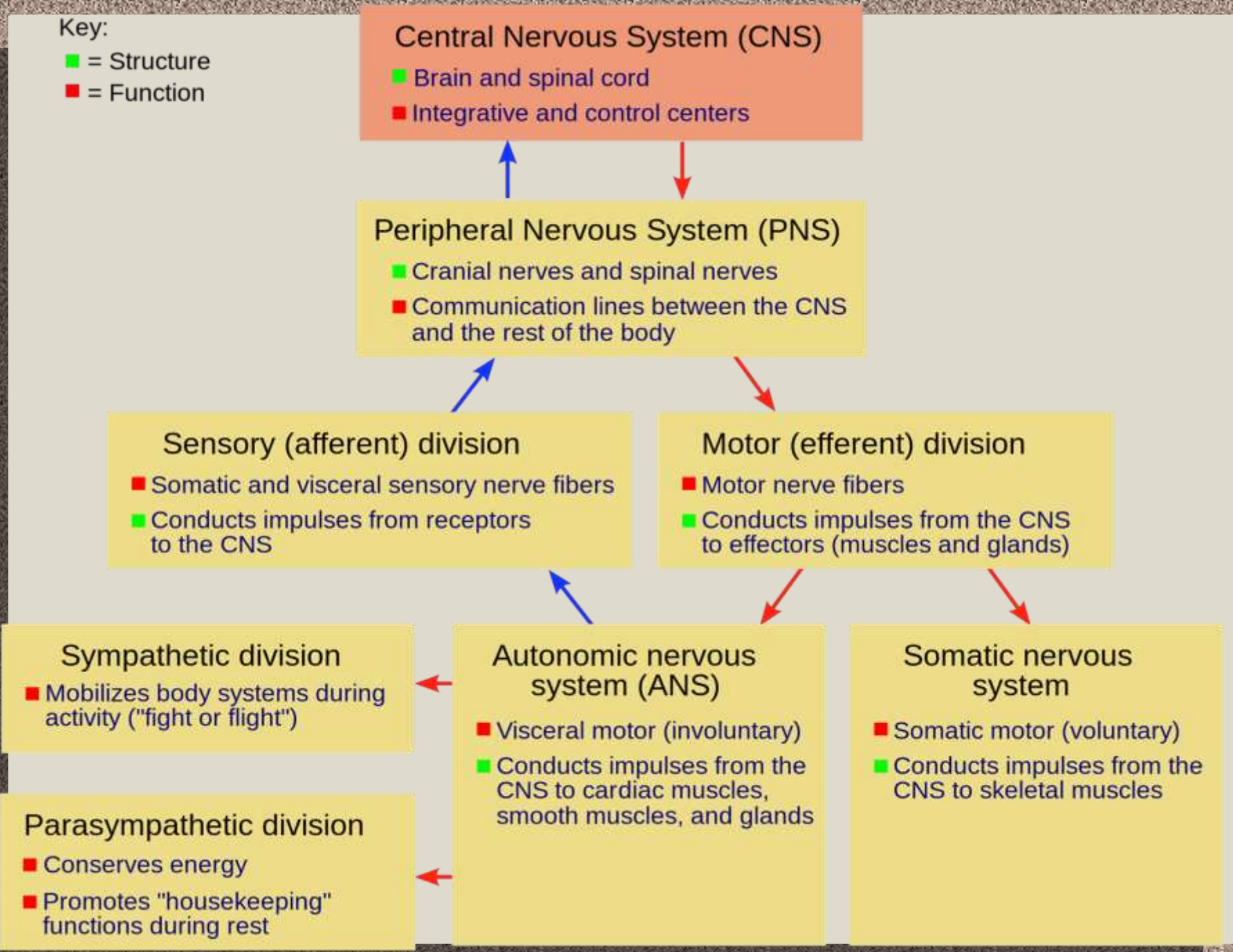
- **This can be illustrated with a voltmeter: With one electrode placed inside a neuron and the other outside, the voltmeter is 'measuring' the difference in the distribution of ions on the inside versus the outside (see the adjoining figure). And, in this example, the voltmeter reads -70 mV (mV = millivolts). In other words, the inside of the neuron is slightly negative relative to the outside. This difference is referred to as the Resting Membrane Potential. It is called a RESTING potential because it occurs when a membrane is not being stimulated or conducting impulses (in other words, it's resting).**



Nerve Conduction



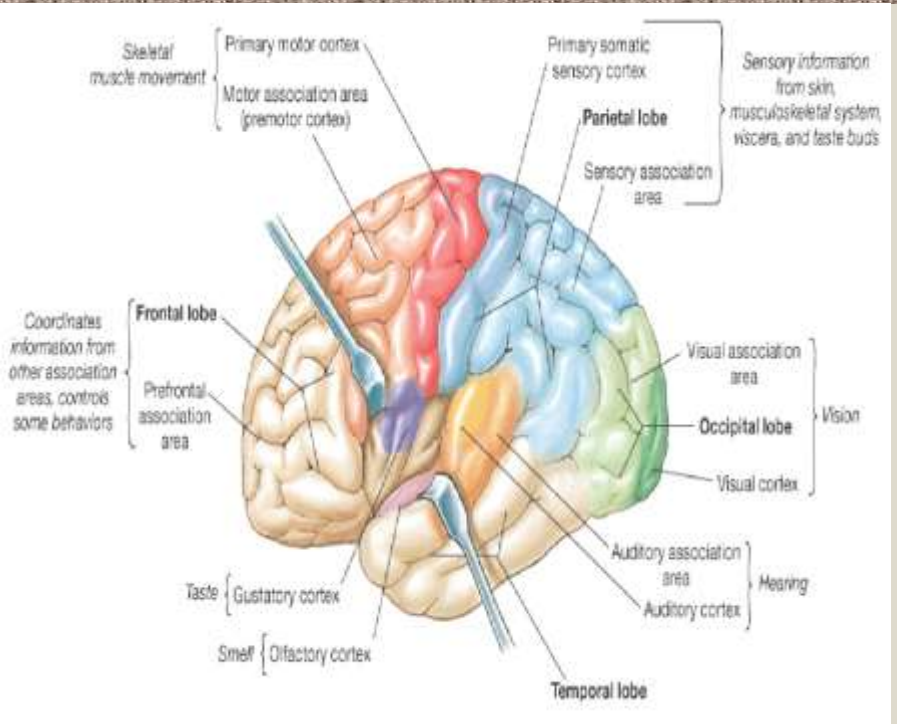



Key:
= Structure
= Function
Central Nervous System (CNS)
Brain and spinal cord
Integrative and control centers
Peripheral Nervous System (PNS)
Cranial nerves and spinal nerves
Communication lines between the CNS and the rest of the body
Sensory (afferent) division
Somatic and visceral sensory nerve fibers
Conducts impulses from receptors to the CNS
Motor (efferent) division
Motor nerve fibers
Conducts impulses from the CNS to effectors (muscles and glands)
Sympathetic division
Mobilizes body systems during activity ("fight or flight")
Autonomic nervous system (ANS)
Visceral motor (involuntary)
Conducts impulses from the CNS to cardiac muscles, smooth muscles, and glands
Somatic nervous system
Somatic motor (voluntary)
Conducts impulses from the CNS to skeletal muscles
Parasympathetic division
Conserves energy
Promotes "housekeeping" functions during rest

Neural Netwo

- The brain is not a homogeneous organ. At the largest anatomical scale, we distinguish **cortex**, **midbrain**, **brainstem**, and **cerebellum**. Each of these can be hierarchically subdivided into many **regions**, and **areas** within each region, either according to the anatomical structure of the neural networks within it, or according to the function performed by them.

- In addition to these long-range connections, neurons also link up with many thousands of their neighbors. In this way they form very dense, complex local networks:



Computer-based Neural Networks

- The brain's network of neurons forms a massively parallel information processing system. This contrasts with conventional computers, in which a single processor executes a single series of instructions.

- Despite of being built with very slow hardware, the brain has quite remarkable capabilities:
  - its performance tends to degrade gracefully under partial damage. In contrast, most programs and engineered systems are brittle: if you remove some arbitrary parts, very likely the whole will cease to function.
  - it can learn (reorganize itself) from experience.
  - this means that partial recovery from damage is possible if healthy units can learn to take over the functions previously carried out by the damaged areas.
  - it performs massively parallel computations extremely efficiently. For example, complex visual perception occurs within less than 100 ms, that is, 10 processing steps!
  - it supports our intelligence and self-awareness. (Nobody knows yet how this occurs.)

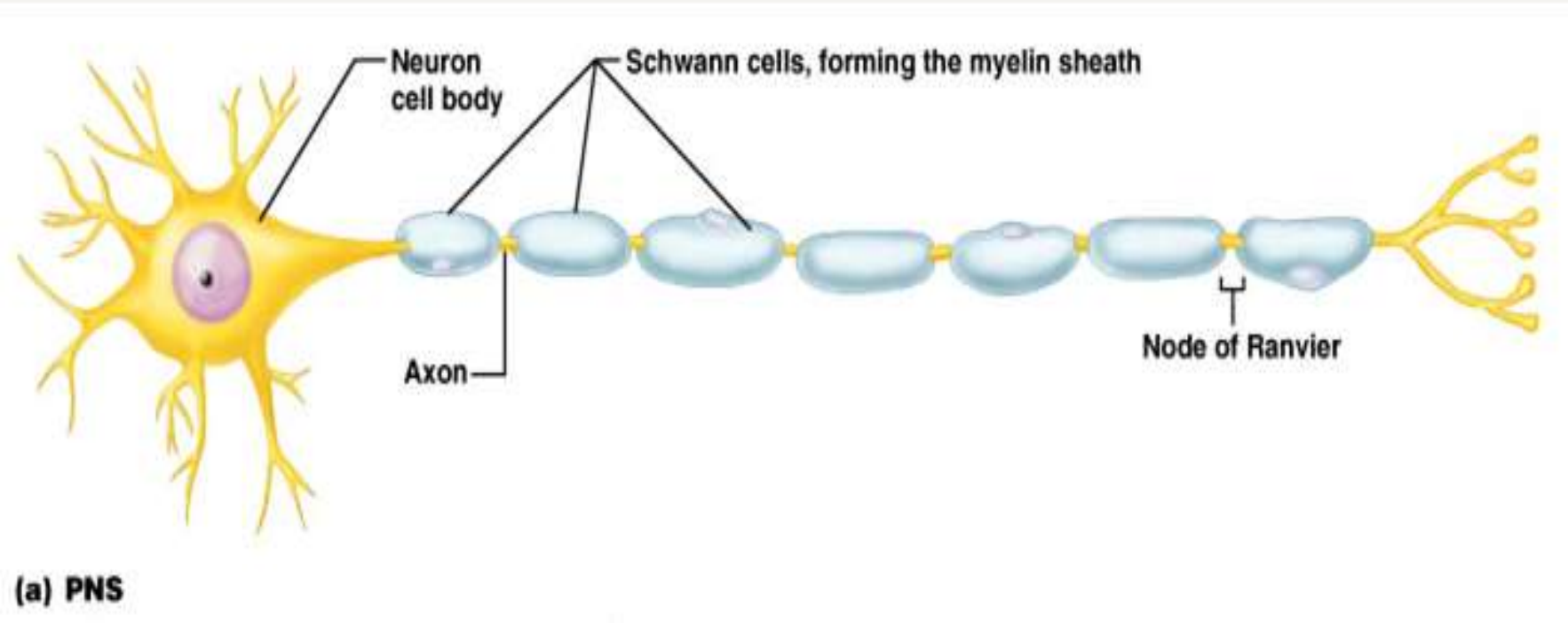
Applications of Neural Networks

- **Aerospace:** High performance aircraft autopilots, flight path simulations, aircraft control systems, autopilot enhancements, aircraft component simulations, aircraft component fault detectors
- **Automotive:** Automobile automatic guidance systems, warranty activity analyzers
- **Banking:** Check and other document readers, credit application evaluators
- **Cognitive science:** Modeling higher level reasoning, language, problem solving, Modeling lower level reasoning, vision, audition speech recognition, speech generation
- **Defense:** Weapon steering, target tracking, object discrimination, facial recognition, new kinds of sensors, sonar, radar and image signal processing including data compression, feature extraction and noise suppression, signal/image identification
- **Electronics:** Code sequence prediction, integrated circuit chip layout, process control, chip failure analysis, machine vision, voice synthesis, nonlinear modeling
- **Entertainment:** Animation, special effects, market forecasting
- **Financial:** Real estate appraisal, loan advisor, mortgage screening, corporate bond rating, credit line use analysis, portfolio trading program, corporate financial analysis, currency price prediction
- **Insurance:** Policy application evaluation, product optimization
- **Manufacturing:** Manufacturing process control, product design and analysis, process and machine diagnosis, real-time particle identification, visual quality inspection systems, beer testing, welding quality analysis, paper quality prediction, computer chip quality analysis, analysis of grinding operations, chemical product design analysis, machine maintenance analysis, project bidding, planning and management, dynamic modeling of chemical process systems

- **Mathematics:** Nonparametric statistical analysis and regression.
- **Medical:** Breast cancer cell analysis, EEG and ECG analysis, prosthesis design, optimization of transplant times, hospital expense reduction, hospital quality improvement, emergency room test advisement
- **Neurobiology:** Modeling models of how the brain works, neuron-level, higher levels: vision, hearing, etc. Overlaps with cognitive folks.
- **Oil and Gas:** Exploration
- **Philosophy:** Can human souls/behavior be explained in terms of symbols, or does it require something lower level, like a neurally based model?
- **Robotics:** Trajectory control, forklift robot, manipulator controllers, vision systems
- **Speech:** Speech recognition, speech compression, vowel classification, text to speech synthesis
- **Securities:** Market analysis, automatic bond rating, stock trading advisory systems
- **Telecommunications:** Image and data compression, automated information services, real-time translation of spoken language, customer payment processing systems
- **Transportation:** Truck brake diagnosis systems, vehicle scheduling, routing systems

Disorders of the Nervous System

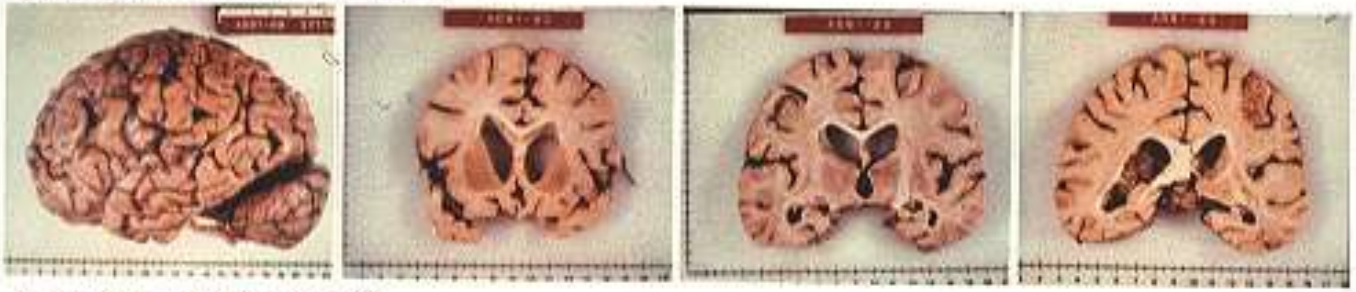
- Multiple sclerosis – common cause of neural disability
  - Varies widely in intensity among those affected
  - Cause is incompletely understood
  - An autoimmune disease
    - Immune system attacks the myelin around axons in the CNS



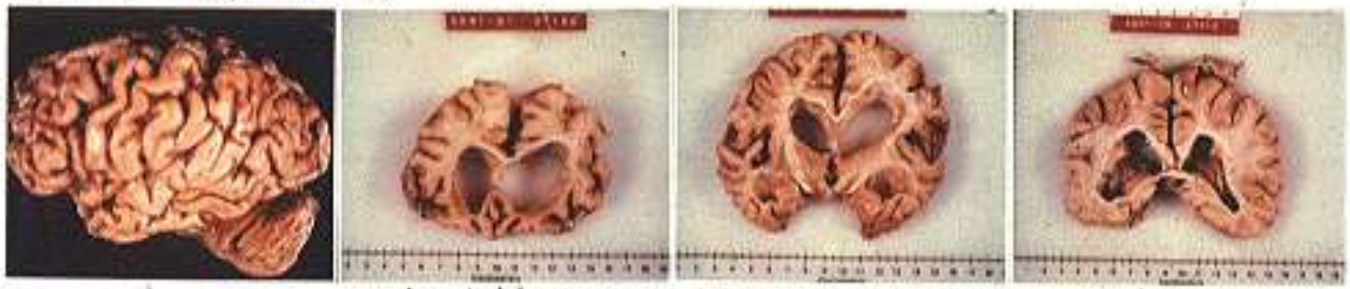
BRAIN ATROPHY VISUAL STANDARDS

GRADE = 1 (NONE, NL FOR AGE)

GRADE = 2 (MODERATE)

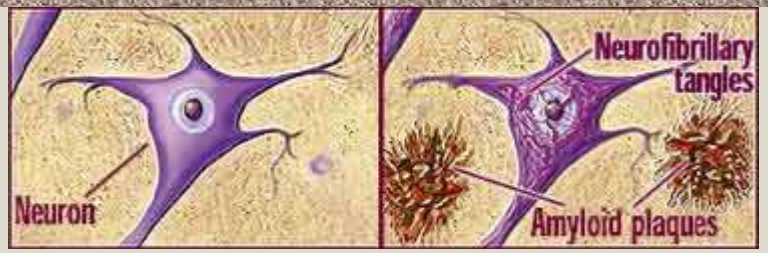


GRADE = 3 (SEVERE)



frontal horns body/temporal horns trigone

- **Alzheimer's Disease:**
  - **Age-associated disorder**
  - **Loss of memory, cognition, and executive performances**
    - **Deposits of amyloid plaques and neurofibrillary tangles that interfere with neuronal functions**
    - **Loss of cholinergic neuronal functions**
- **Parkinson's Disease:**
  - **Age-associated disorder**
  - **Rigidity and incoordination interfering with mobility**
    - **Loss of dopaminergic neuronal functions**



Alzheimer's Disease

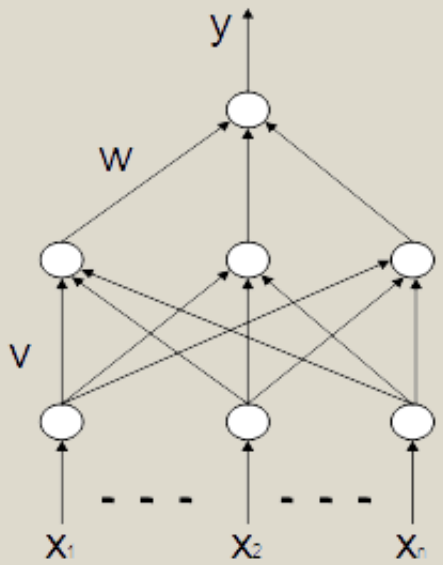
Parkinson's Disease

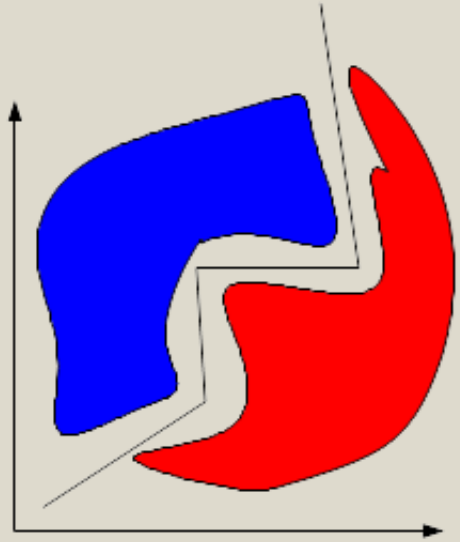
List of neurodegenerative diseases

- Alexander's disease
- Alper's disease
- Alzheimer's disease
- Amyotrophic lateral sclerosis
- Ataxia telangiectasia
- Batten disease (also known as Spielmeyer-Vogt-Sjogren-Batten disease)
- Bovine spongiform encephalopathy (BSE)
- Canavan disease
- Cockayne syndrome
- Corticobasal degeneration
- Creutzfeldt-Jakob disease
- Huntington's disease
- HIV-associated dementia
- Kennedy's disease
- Krabbe's disease
- Lewy body dementia
- Machado-Joseph disease (Spinocerebellar ataxia type 3)
- Multiple sclerosis
- Multiple System Atrophy
- Narcolepsy
- Neuroborreliosis
- Parkinson's disease
- Pelizaeus-Merzbacher Disease
- Pick's disease
- Primary lateral sclerosis
- Prion diseases
- Refsum's disease
- Schilder's disease
- Subacute combined degeneration of spinal cord secondary to Pernicious Anaemia
- Schizophrenia
- Spielmeyer-Vogt-Sjogren-Batten disease (also known as Batten disease)
- Spinocerebellar ataxia (multiple types with varying characteristics)
- Spinal muscular atrophy
- Steele-Richardson-Olszewski disease
- Tabes dorsalis

Neural Networks

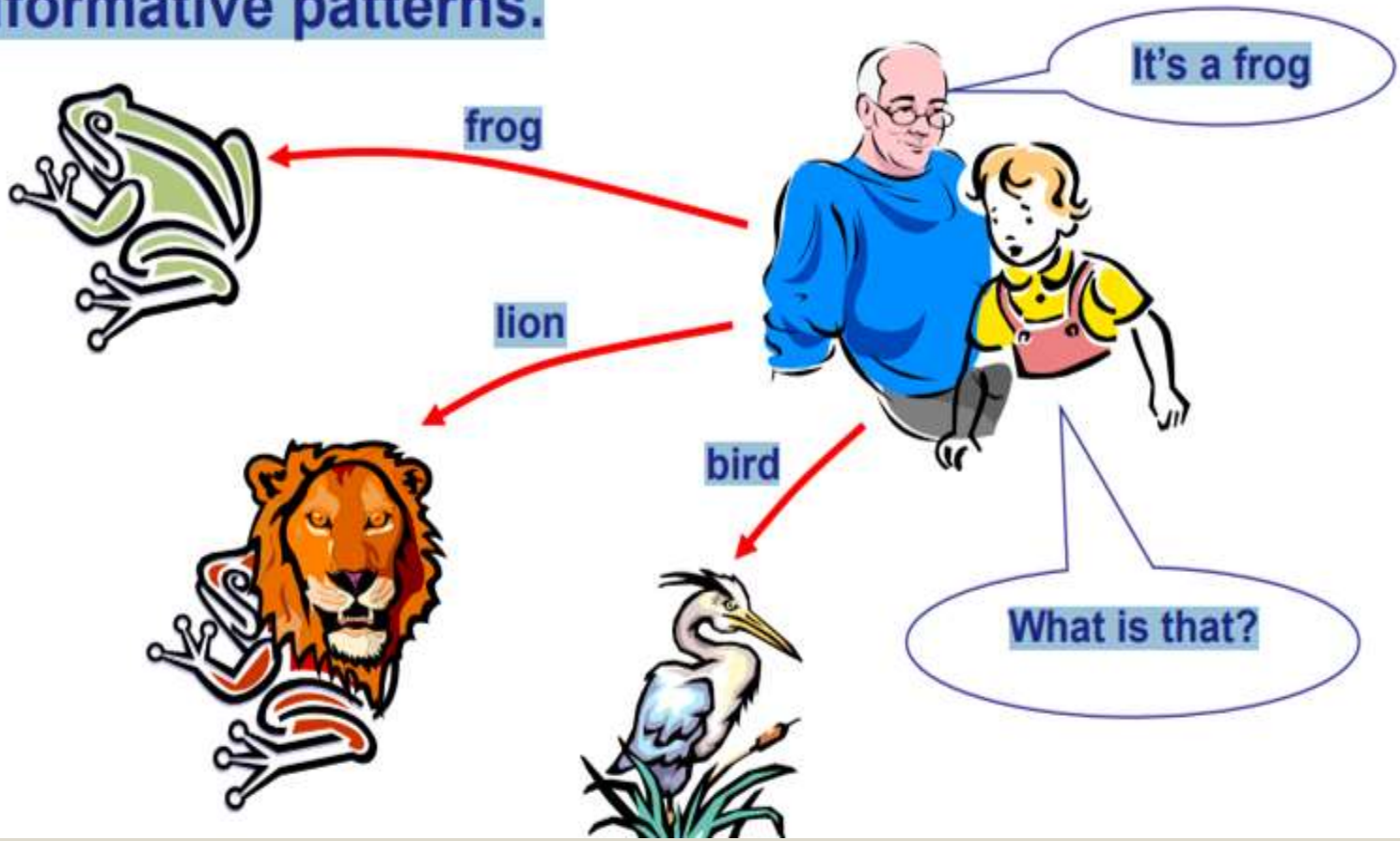
- Good at tasks such as pattern matching, classification, function approximation, and data clustering
- Good at tasks in bioinformatics such as coding region recognition, protein structure prediction, gene clustering





The idea of ANNs..?

- NNs learn relationship between cause and effect or organize large volumes of data into orderly and informative patterns.



Neural networks to the rescue…

- **Neural network:** *information processing paradigm inspired by biological nervous systems, such as our brain*
- Structure: large number of highly interconnected processing elements (*neurons*) working together
- Like people, they learn *from experience* (by example)

- Neural networks are configured for a specific application, such as pattern recognition or data classification, through a learning process
- In a biological system, learning involves adjustments to the synaptic connections between neurons

→ same for artificial neural networks (ANNs)

Artificial Neurons

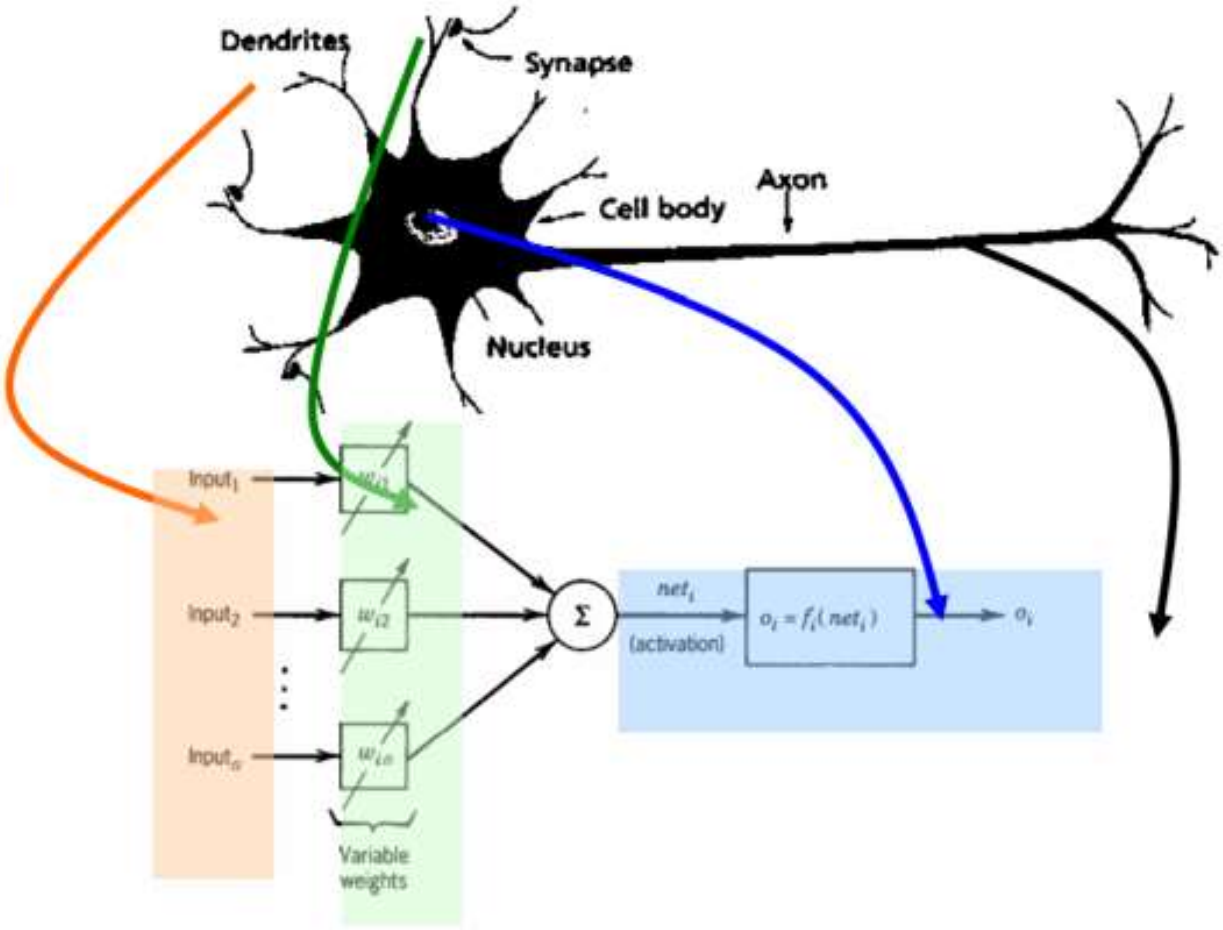
- ANN is an information processing system that has certain performance characteristics in common with biological nets.
- Several key features of the processing elements of ANN are suggested by the properties of biological neurons:

1. The processing element receives many signals.
2. Signals may be modified by a weight at the receiving synapse.
3. The processing element sums the weighted inputs.
4. Under appropriate circumstances (sufficient input), the neuron transmits a single output.
5. The output from a particular neuron may go to many other neurons.

Artificial Neurons

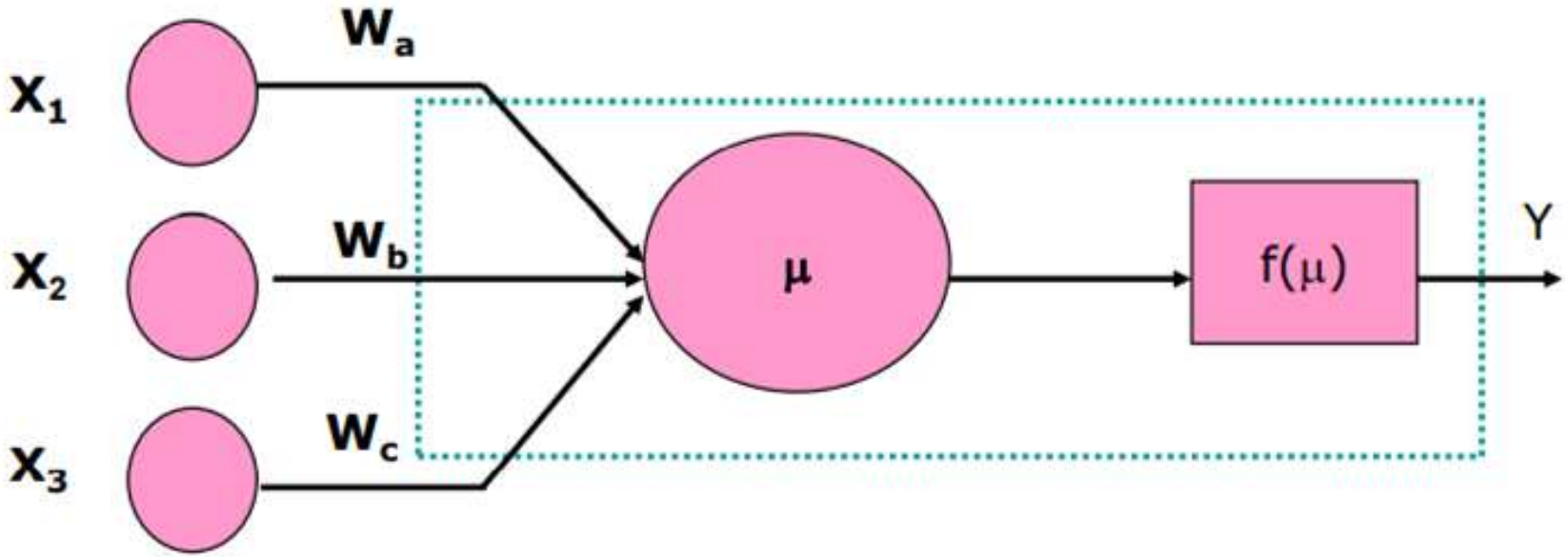
- From experience: examples / training data
- Strength of connection between the neurons is stored as a weight-value for the specific connection.
- Learning the solution to a problem = changing the connection weights

A physical neuron



An artificial neuron

Model Of A Neuron



Input units — Connection weights — Summing function — computation

(dendrite) (synapse) (soma) (axon)

Learning Processes in Neural Networks

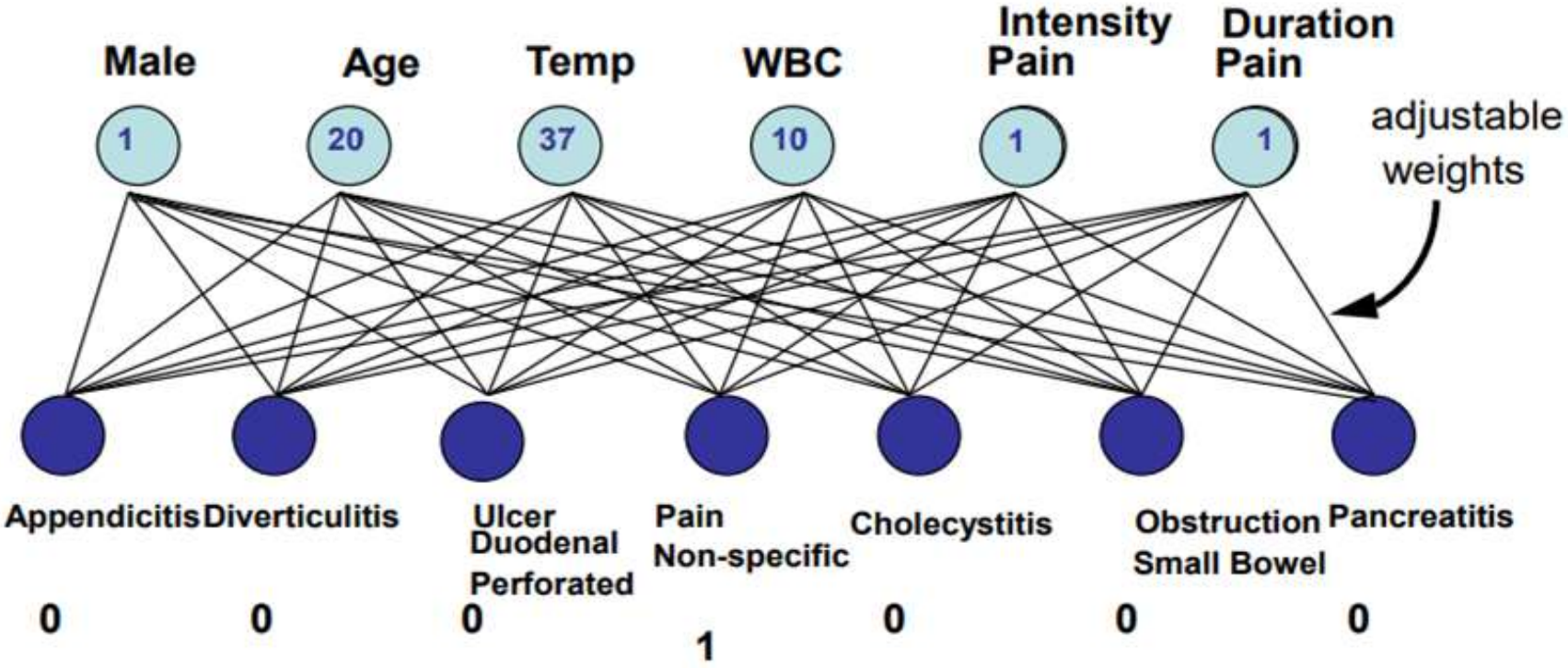
Among the many interesting properties of a neural network, is the ability of the network to learn from its environment, and to improve its performance through learning. The improvement in performance takes place over time in accordance with some prescribed measure.

A neural network learns about its environment through an iterative process of adjustments applied to its synaptic weights and thresholds. Ideally, the network becomes more knowledgeable about its environment after each iteration of the learning process.

There are three broad types of learning:

1. Supervised learning (i.e. learning with an external teacher)
2. Unsupervised learning (i.e. learning with no help)
3. Reinforcement learning (i.e. learning with limited feedback)

Abdominal Pain Prediction

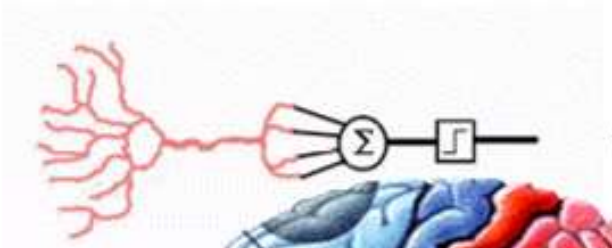


-A neuron receives input, determines the strength or the weight of the input, calculates the total weighted input, and compares the total weighted with a value (threshold)

-The value is in the range of 0 and 1

- If the total weighted input greater than or equal the threshold value, the neuron will produce the output, and if the total weighted input less than the threshold value, no output will be produced

ANN Applications



Medical Applications

Chemistry

Information
Searching & retrieval

Education

Business & Management

Neural Network Applications

Brain modelling

Aid our understanding of how the brain works, how behaviour emerges from the interaction of networks of neurons, what needs to "get fixed" in brain damaged patients

Real world applications

Financial modelling – predicting the stock market

Time series prediction – climate, weather, seizures

Computer games – intelligent agents, chess, backgammon

Robotics – autonomous adaptable robots

Pattern recognition – speech recognition, seismic activity, sonar signals

Data analysis – data compression, data mining

Bioinformatics – DNA sequencing, alignment

MACHINE LEARNING

- Machine Learning is the field of study that gives computers the capability to learn without being explicitly programmed.

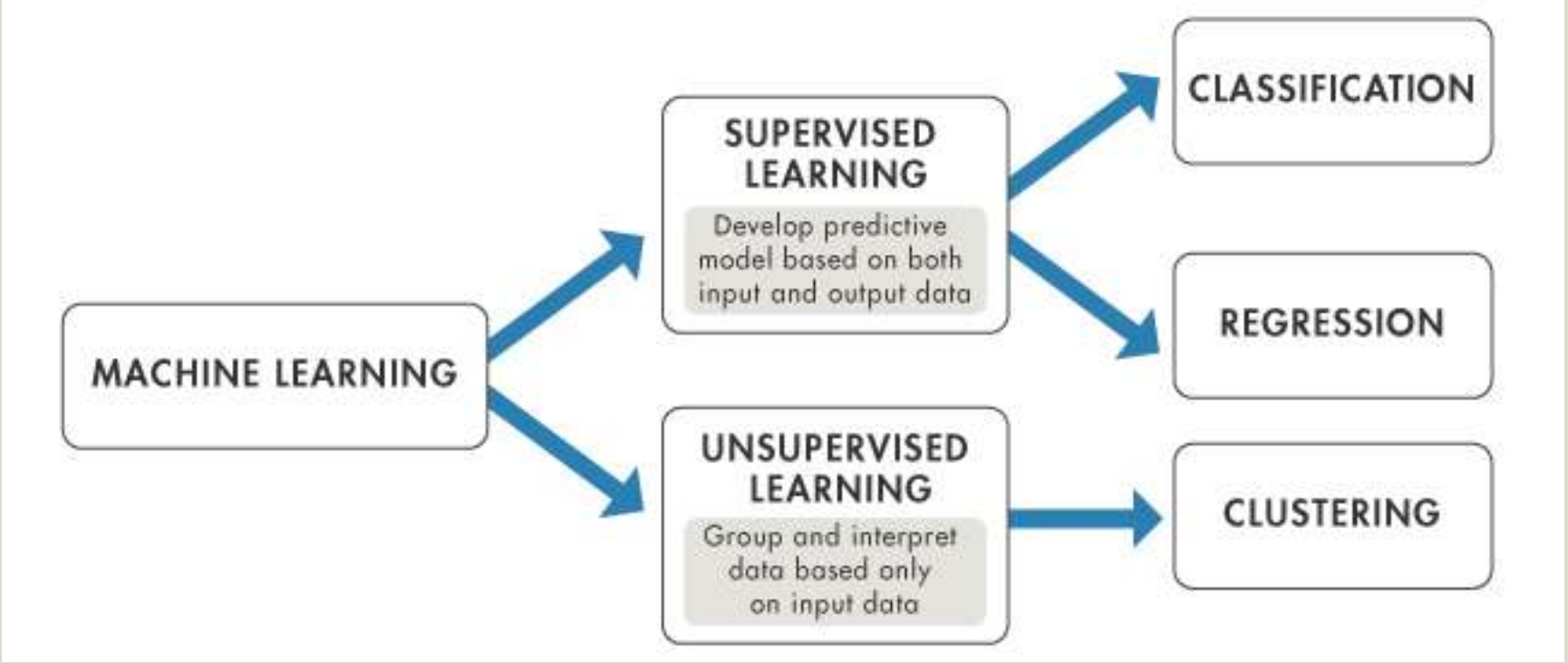
- Machine learning and statistics are closely knit.

TYPES

- **Supervised machine learning algorithms** require external assistance.
- The external assistance is usually through a human expert who provides curated input for the desired output to predict accuracy in algorithm training.
- The expert or data scientist determines the features or patterns that the model would use. Once the training is completed, then it can be applied to test another data for the prediction and classification. It is supervised because the algorithm learns from the training data set akin to a teacher supervising the learning process of a student
- e.g., decision tree, support vector machine, and neural network.

TYPES

- **Unsupervised learning algorithms** infer patterns from data without a dependent variable or known labels.
- In unsupervised learning algorithms no external assistance is required.
- The computer program automatically searches the feature or pattern form the data and groups them into clusters.
- When we introduce new data for the prediction, then it uses previously learned features to classify the data. This method is very useful in the era of big data because it requires huge amount of training data.
- E.g.,Clustering and principle component analysis



- Regression and Classification are types of supervised learning algorithms while Clustering is a type of unsupervised algorithm.

Regression

- When the output variable is continuous, then it is a regression problem whereas when it contains discrete values, it is a classification problem
- The ultimate goal of the regression algorithm is to plot a best-fit line or a curve between the data. The three main metrics that are used for evaluating the trained regression model are variance, bias and error

Classification

- For any given input, the classification algorithms help in the prediction of the class of the output variable. There can be multiple types of classifications like binary classification, multi-class classification, etc. It depends upon the number of classes in the output variable.
- The classification techniques help make predictions about the target values' category based on any input provided. Usually, the term "classification" is used to narrate the predictive modeling in which the sample annotation is definite.

Clustering

- Clustering is a type of unsupervised machine learning algorithm. It is used to group data points having similar characteristics as clusters.
- the data points in the same cluster should exhibit similar properties and the points in different clusters should be as dissimilar as possible.

	SUPERVISED LEARNING	UNSUPERVISED LEARNING
Input Data	Uses Known and Labeled Data as input	Uses Unknown Data as input
Computational Complexity	Very Complex	Less Computational Complexity
Real Time	Uses off-line analysis	Uses Real Time Analysis of Data
Number of Classes	Number of Classes are known	Number of Classes are not known
Accuracy of Results	Accurate and Reliable Results	Moderate Accurate and Reliable Results

Deep Learning

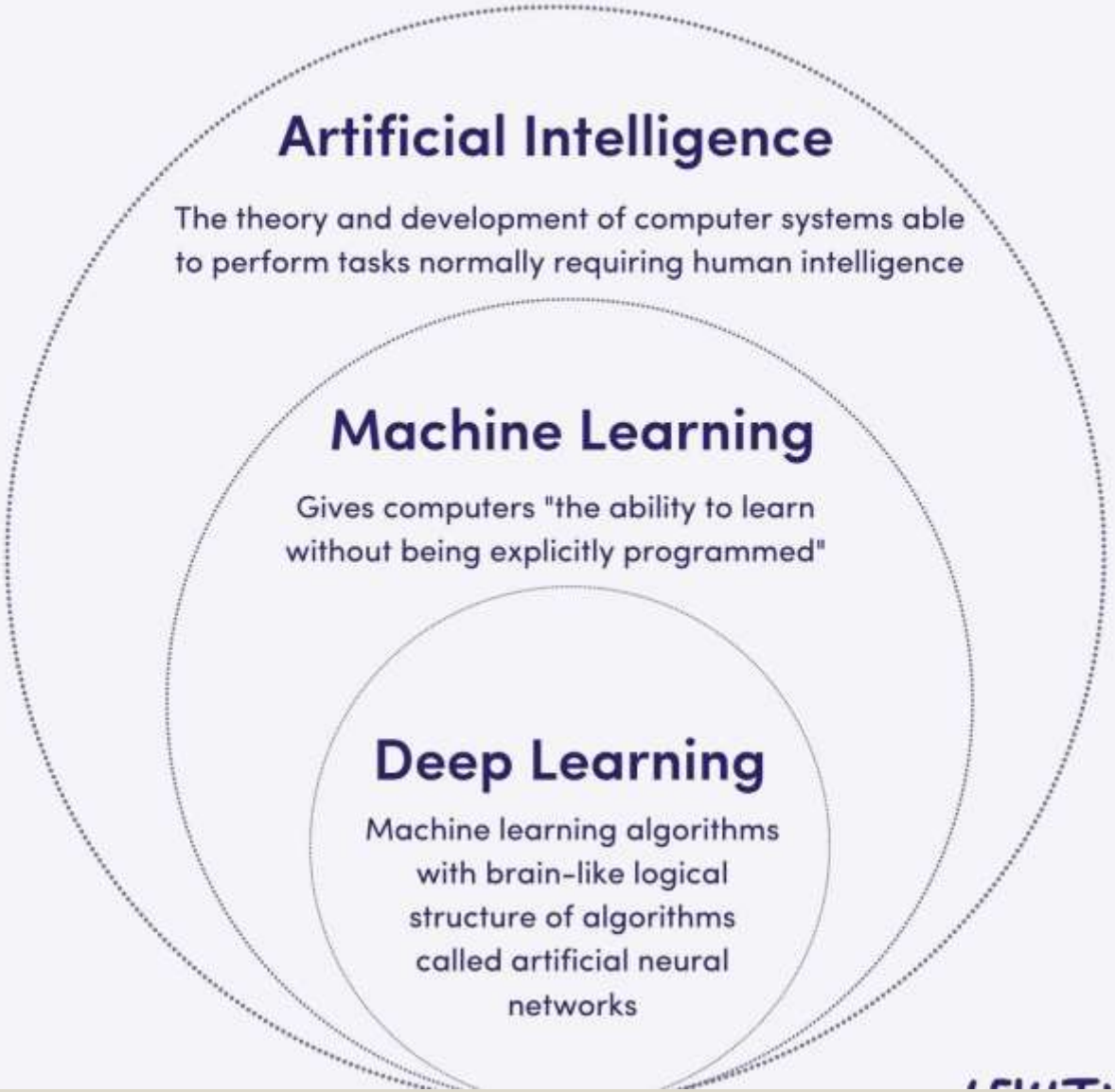
- **Deep learning** is a more recent subfield of machine learning that is the extension of neural network. In deep learning “deep” refers to the number of layers through which data is transformed. So, deep learning is similar to neural network with multi-layers. These multi-layers nodes try to mimic how the human brain thinks to solve the problems.

Applications of ML

- The ML algorithms are used for selecting relevant features in biological data which are high dimensional in nature
- The second major application of ML in biology has been found in classification of biological data
- Third major ML application in bioinformatics is clustering of biological data like gene data

Examples of Application of ML

- **Structure prediction of proteins-**the use of machine learning in structure prediction has pushed the accuracy from 70% to more than 80%.
- **Stroke diagnosis-** Machine learning methods for the analysis of neuroimaging data are used to help diagnose stroke. Historically multiple approaches to this problem involved neural networks**.**
- Machine learning and AI are being used extensively by hospitals and health service providers to improve patient satisfaction, deliver personalized treatments, make accurate predictions and enhance the quality of life. It is also being used to make clinical trials more efficient and help speed up the process of drug discovery and delivery


Artificial Intelligence
The theory and development of computer systems able to perform tasks normally requiring human intelligence
Machine Learning
Gives computers "the ability to learn without being explicitly programmed"
Deep Learning
Machine learning algorithms with brain-like logical structure of algorithms called artificial neural networks

DATAMINING IN BIOLOGY

- Data mining refers to extracting or “mining” knowledge from large amounts of data. Data Mining (DM) is the science of finding new interesting patterns and relationship in huge amount of data.
- It is defined as “the process of discovering meaningful new correlations, patterns, and trends by digging into large amounts of data stored in warehouses”.
- Data mining is also sometimes called Knowledge Discovery in Databases (KDD). Data mining is not specific to any industry. It requires intelligent technologies and the willingness to explore the possibility of hidden knowledge that resides in the data.

- **primary** goals of data mining, in practice,
  - prediction and description.

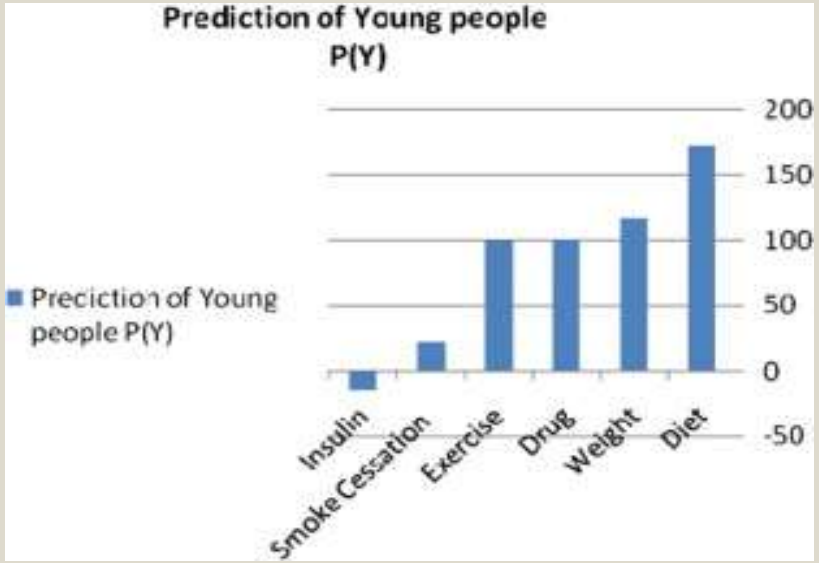
The main tasks well suited for data mining, all of which involves mining meaningful new patterns from the data, are:

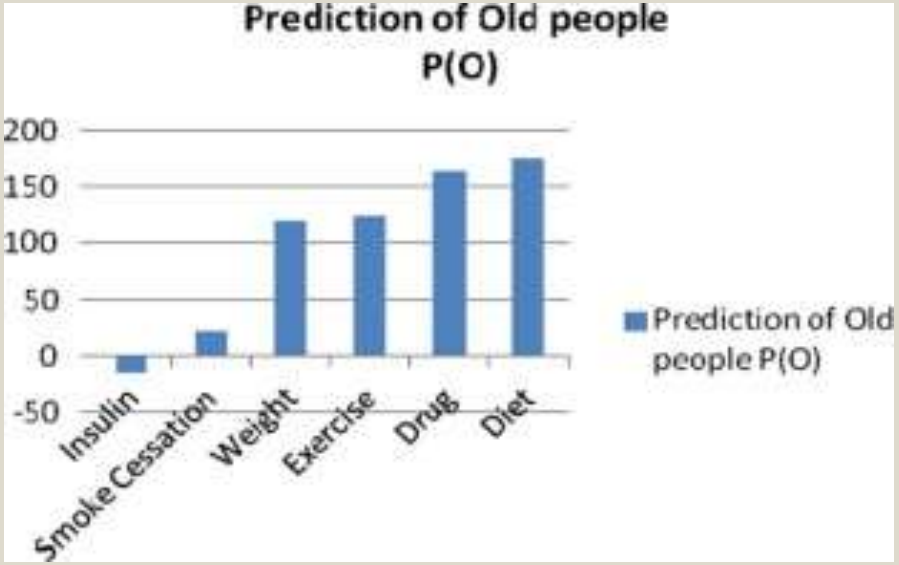
- Classification: Classification is learning a function that maps (classifies) a data item into one of several predefined classes.
- Estimation: Given some input data, coming up with a value for some unknown continuous variable.
- Prediction: Same as classification & estimation except that the records are classified according to some future behaviour or estimated future value).
- Association rules: Determining which things go together, also called dependency modeling.
- Clustering: Segmenting a population into a number of subgroups or clusters.
- Description & visualization: Representing the data using visualization techniques.

Case study: DATAMINING in DIABETES

- Diabetes is the most common endocrine disease across all population and age groups.
- This disease has become the fourth leading cause of death in developed countries and there is substantial evidence that it is reaching epidemic proportions in many developing and newly industrialized nations
- Regression analysis was done on data available in WHO for diabetes patients of different age groups and their treatments
- The effect of available treatments on younger and older population was predicted

Cited from: Abdullah A. Aljumah, Mohammed Gulam Ahamad, Mohammad Khubeb Siddiqui,Application of data mining: Diabetes health care in young and old patients,Journal of King Saud University - Computer and Information Sciences,Volume 25, Issue 2,2013,Pages 127-136, https://doi.org/10.1016/j.jksuci.2012.10.003





- The young age group, *p*(*y*), is predicted to have a preferential order of treatment namely diet control, weight control, drug treatment, exercise treatment, smoke cessation, and finally, insulin.
- The preferential order of modes of treatment for old age group patients, *p*(o), differs from *p*(*y*). The predictions indicated here are diet control, drug treatment, exercise, weight control, smoking cessation, and finally, insulin.

THANKYOU