Biotechnology
Big Data
Artificial Intelligence

Promises, Dangers, Worries, Gotchas

Abhijit Dasgupta, PhD
Chief Data Scientist
Co-Founder

Slides available at https://webbedfeet.github.io/GMU_2019


Biotechnology
DNA
genetic
desired
cells
organisms
altered
bacteria
genetically
diseases
biological
gene
also
processed
products
grown
manufacture
engineering
product
produce
cancer
prolonged
disorders
technology
exploitation
animal
general
Hybrids
United
insulin
bacterial
many
medicine
growth
systems
way
technique
waste
specially
acid
now
antibody-producing
use
foods
medically
cloned
Livestock
used
treat
large
manipulation
applications
manipulate
break
agriculture
studied
insert
nucleic
resistance
created
States
useful
Plants
involved
pests
fields
slicks
solution
material
chronic
hormones
therapy
example
technological
life
normal
attempts
pharming
mass
experimental
problem
splicing
cultured
see
substance
processes
industrial
made
shelf
corn
common
monoclonal
genes
qualities
category
laboratory
substances
inserted
Much
plant
extract
process
living
treatment
field
antibodies
recombinant
soybeans
pharmacology
quantities
hybridomas
oil
techniques
similarly
drugs
development
modified
increased
interferon
inserting
produces
called
includes

Biotechnology
genetic
DNA
desired
cells
organisms
altered
bacteria
genetically
diseases
biological
processed
products
gene
also
product
manufacture
engineering
bacterial
many
United
insulin
technology
prolonged
disorders
exploitation
grown
animal
general
Hybrids
produce
cancer
way
technique
systems
medicine
growth
use
foods
medically
cloned
Livestock
used
treat
acid
now
antibody-producing
specially
waste
large
manipulate
manipulation
applications
studied
insert
break
agriculture
resistance
nucleic
created
States
useful
Plants
involved
pests
fields
slicks
solution
includes
called
produces
inserting
interferon
increased
modified
techniques
similarly
drugs
development
hybridomas
oil
attempts
normal
life
technological
example
therapy
hormones
chronic
material
pharming
mass
experimental
treatment
living
field
process
extract
antibodies
recombinant
soybeans
pharmacology
quantities
Much
plant
inserted
substances
laboratory
category
qualities
genes
monoclonal
common
corn
shelf
made
industrial
substance
processes
see
problem
splicing
cultured

Business needs

- Context (why we need it)
- Discovery (Finding it)
- Evidence of effectiveness
- Reproducibility
- Manufacturability
- Quality

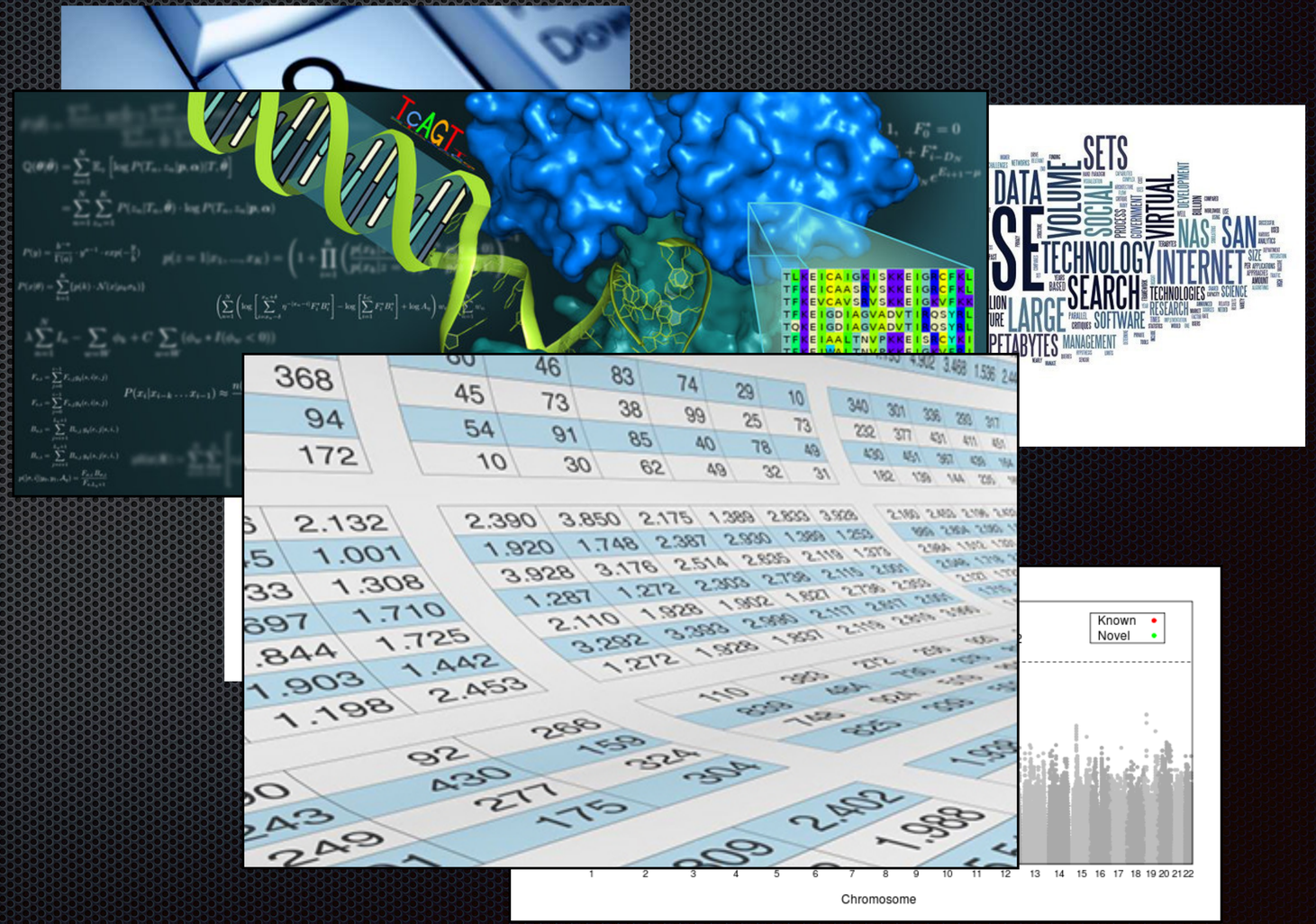
Context (why we need it)

- Market research
- Competition research
- Focus groups
- Gaps in the market
- Market potential

Strengths	Weaknesses
Characteristics of a business which give it advantages over its competitors	Characteristics of a business which make it disadvantageous relative to competitors
Opportunities	**Threats**
Elements in a company's external environment that allow it to formulate and implement strategies to increase profitability	Elements in the external environment that could endanger the integrity and profitability of the business

Discovery (finding it)

- Identifying potential
  - Searching the literature
  - Searching databases
  - Analyzing relationships
  - Culling candidates

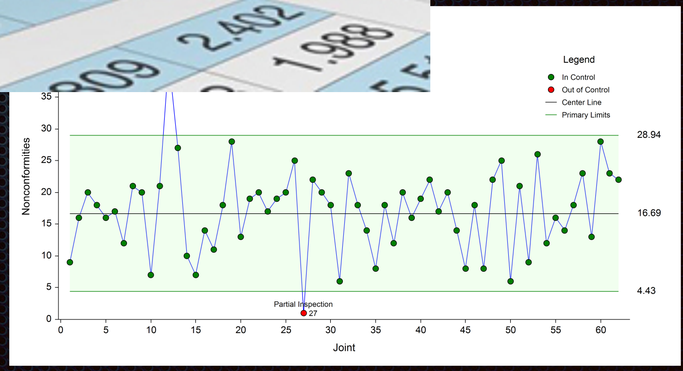


Evidence of effectiveness

- Laboratory experiments
- Field experiments
- Observational studies
- Randomized trials

Manufacturability & Quality

- Translation to a process
- Establishing standards
- Reproducibility
- Quality control / Six Sigma




368
94
172
46 83 74 29 10
45 73 38 99 25 73
54 91 85 40 78 49
10 30 62 49 32 31
2.132
1.001
1.308
1.710
1.725
1.442
2.453
1.198
2.390 3.850 2.175
1.920 1.748 2.387
3.928 3.176 2.514
1.287 1.272
2.110 1.928
3.282
1.272
288
92
159
430
324
277
304
175
249
2.402
1.988
809


data
quality
rules
algorithms
constraints
performance
organizations
system
clusters
business
cloud
crowd
results
MapReduce
repair
identify
techniques
large
many
new
time
using
dependencies
functional
evolved
jobs
inconsistent
evaluate
temporal
keyword
distributed
process
semantics
file
output
detection
work
database
application
entity
set
study
domain
input
constraint
CFDs
used
dirty
important
keywords
real
together
specific
scalability
hold
scale
paper
use
terms
rule
blogs
workflows
workflow
often
evaluation
datasets
scalable
tool
records
approach
intermediate
inconsistencies
known
evolves
evolve
reuse
errors
associated
well
job
join
make
topics
part
several
need
maintenance
search
model
consider
languages
discovery
execution
analysis
Stringer
express
repaired
underlying
case
appear
role
minimal
potentially
designed
within
duplicates
due
change
experimental
clustering
synthetic
Dirty
play
enforced
respect
changes
values
efficiently
understanding
approximate
non-conformant
millions
arises
remain
recognize
become
cost
capture
sometimes
meant
manages
Hence
FDs
contextual
accuracy
continuous
query
years
modern
repairs
ReStore

Data drives

Research

Development

Production

Marketing

Sales

Revisions

Central issue for data-driven business

- The data must be reliable and valid
- Repeating the experiment must yield similar results (reliability)
- We're measuring what we think we're measuring (internal validity)
- The results can be generalized to larger populations (external validity)

Central issue for data-driven business

- This is a matter of trust
- If the foundational data on which the business is built isn't trustworthy, you can't sell anything

theranos

$9 billion

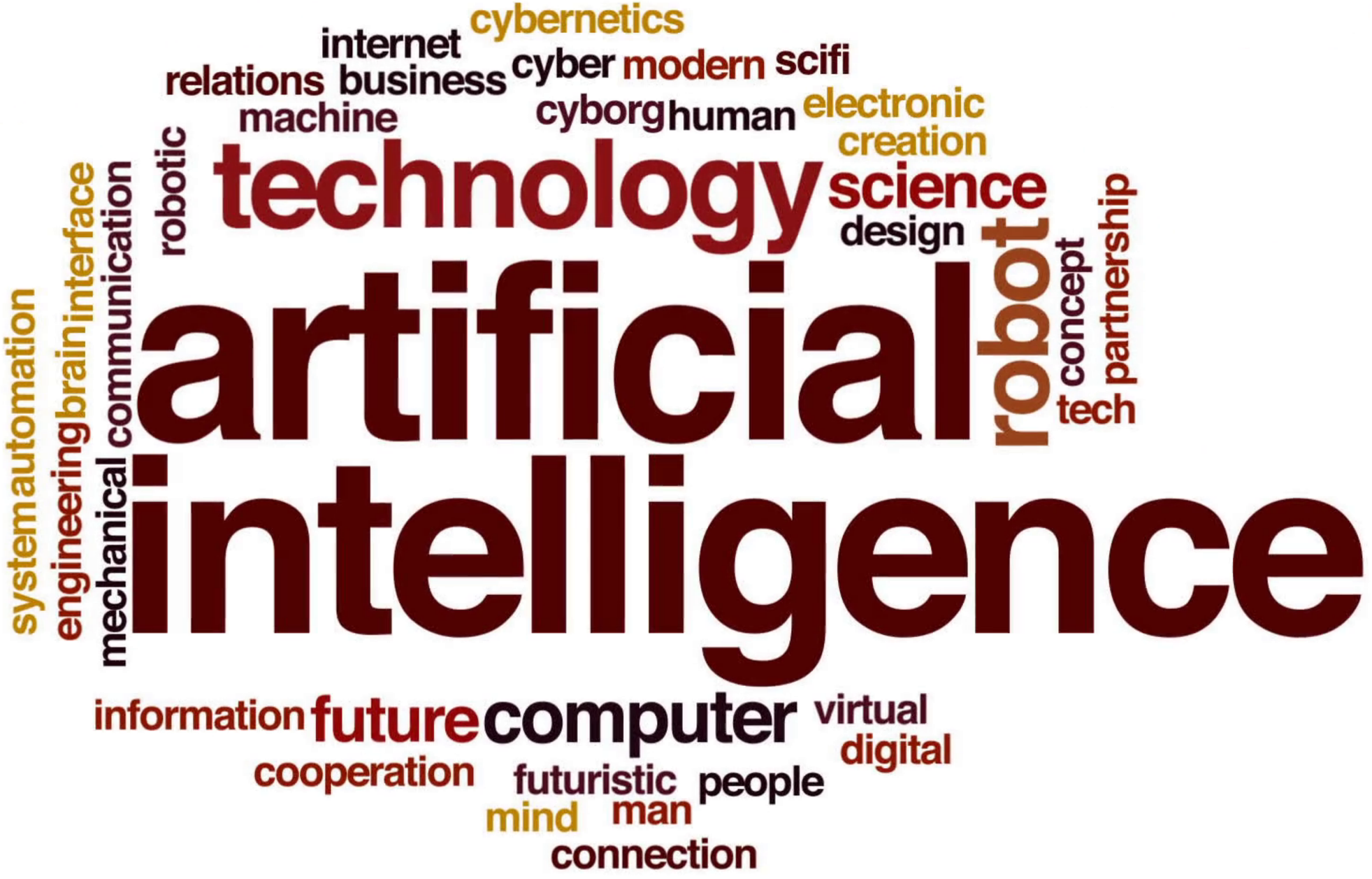
Poof!

Central issue for data-driven business

- It doesn’t matter how much data you can get
- It matters how you got it
  - Experimental design
  - Ethics
  - Provenance

Central issue for data-driven business

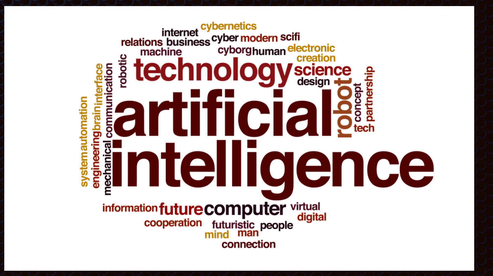
- It doesn’t matter how much data you can get
- It matters how you use it
  - Analytics
  - Translation to business practice
  - Follow-up


cybernetics
internet
cyber
modern
scifi
relations
business
machine
cyborg
human
electronic
creation
technology
science
robotic
design
artificial
robot
concept
partnership
tech
system
automation
engineering
brain
interface
communication
mechanical
intelligence
information
future
computer
virtual
digital
cooperation
futuristic
people
mind
man
connection


internet
cybernetics
relations
business
cyber
modern
scifi
machine
cyborg
human
electronic
creation
technology
science
robotic
interface
communication
system
automation
engineering
brain
mechanical
information
data
analysis
learning
machine
bigdata
deep-learning
modelling
information
systems
simulation
application
government
mathematical
department
intelligence
coastal
wireless
materials
topological
network
software
research
signal
energy
sciences
applications
computer
analytics
networks
development
understanding
design
theory
large
properties
reasoning
process
statistics
processing
methods
space
geometric
technology
performance
science
smart recognition
mining
engineering
machine-learning
statistical
human
pattern
vision
football
management
phenomena
sports
social
wave
allocation
security
computing
collection
interpretation
statistical
Inference
probability
prediction
population
experiments
theory
discipline
pertaining
mathematical
branch
ology
neering
skilled workshop
trainee
industry
robot
control

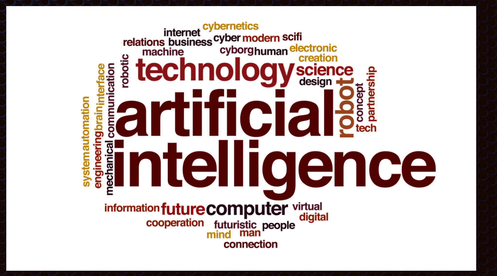
What is AI?

- The ability of machines (computers) to learn, reason and act on their own
- The ability of machines to demonstrate intelligence
- The ability of machines to be autonomous, independent, and make decisions based on their environment



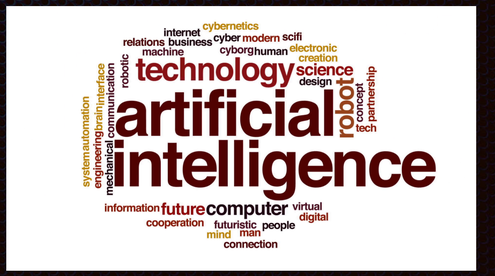
AI in Biotech

- Drug discovery
  - Culling through millions of candidates to identify the next molecule for drug development
- Patient management and decision support
  - Fast analytics to provide likely causes, drug effects and interactions, risks and side-effects based on patient history, EMR mining and literature mining



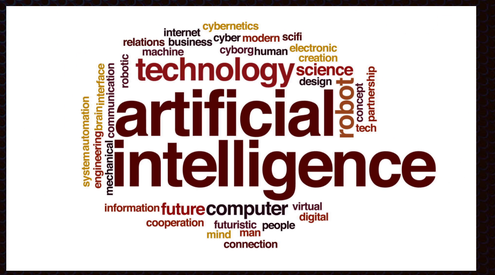
AI in Biotech

- Prosthetics/exoskeletons and predictive movement
- Environmental assessment and closed-loop therapeutic deployment
- Performance optimization through sensing, adaptation and intelligent coaching
- Precision medicine
  - Identifying therapies better targeted at the individual

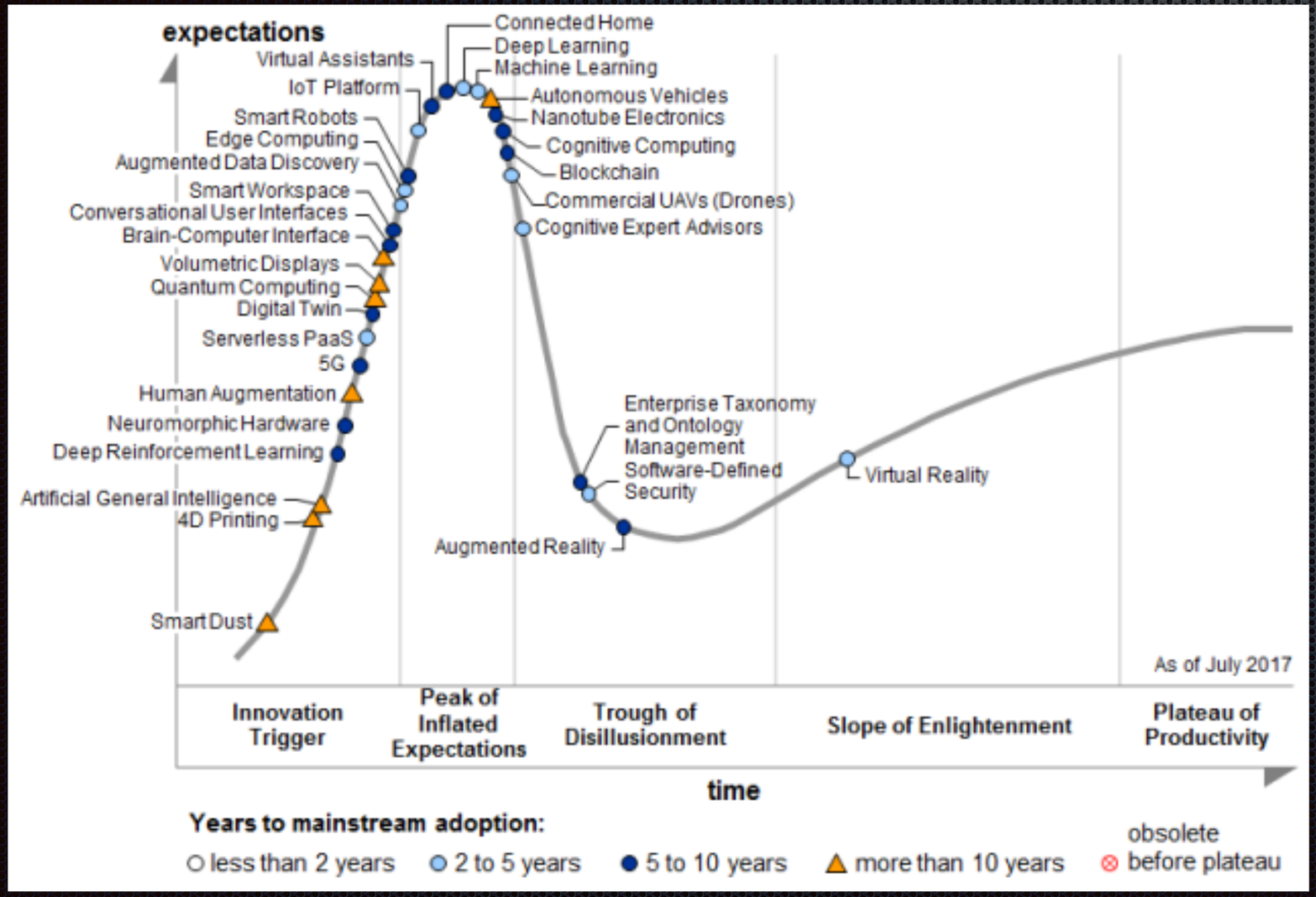


Are we there yet?

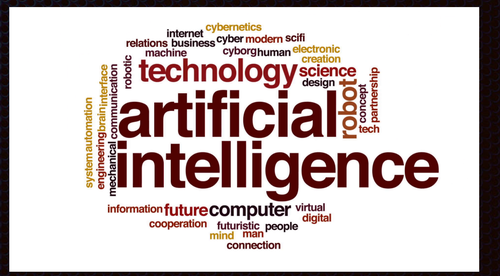
- Not really
  - Self-driving cars and planes on auto-pilot
  - Experimental situations
  - Some medical decision support



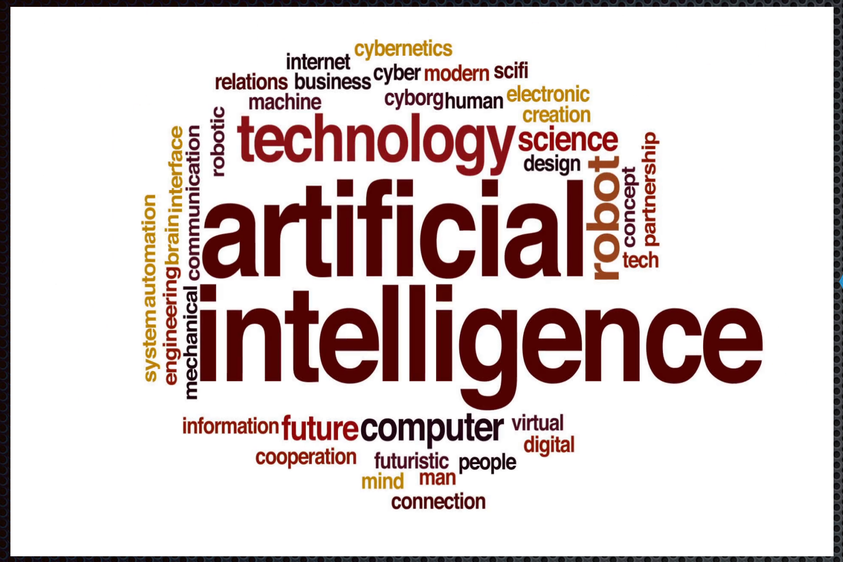
Are we there yet?



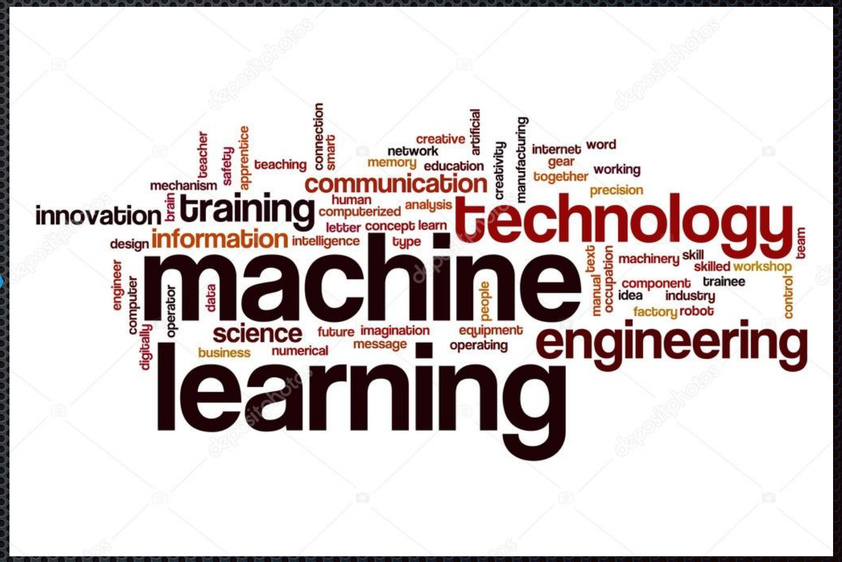
Gartner Hype Cycle 2017



So where are we?

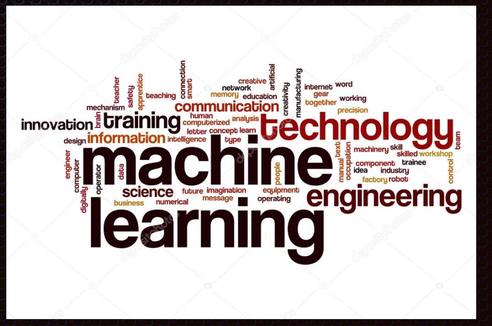


Common use



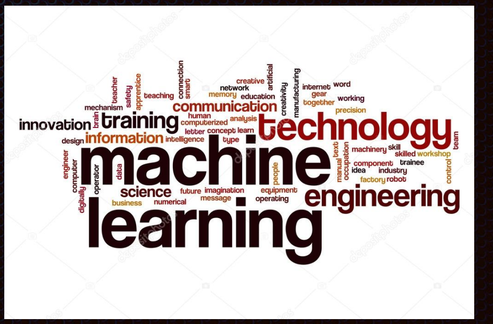
Machine learning

- Artificial intelligence is about learning, reasoning and acting
- We are still trying to get the learning part down well
  - Learning innate patterns in data
  - Learning how an outcome is influenced by different factors
  - Learning to predict the future by observing the past
  - Learning to discern what is real and what is artifact



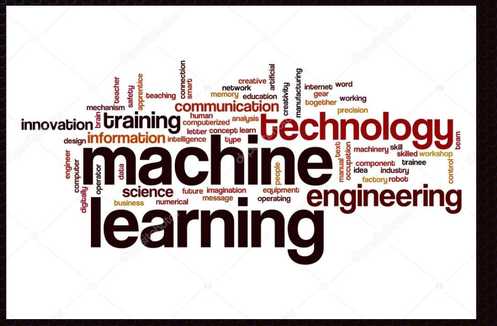
Machine learning success stories

- Breast cancer therapeutics
  - Bioinformatics used to understand innate differences in different types of BrCa, leading to very successful targeted therapeutics
    - Tamoxifen, Herceptin, Fluoracil, Paclitaxel



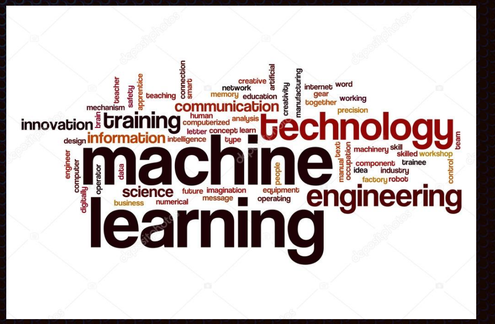
Machine learning success stories

- Identification of subgroups in various diseases, leading to more targeted interventions
  - EGFR & Lung Cancer
  - APoE & Alzheimer's prevention
  - BRCA & Breast cancer prophylaxis
  - Immunotherapies
  - Gene editing (CRISP-R)



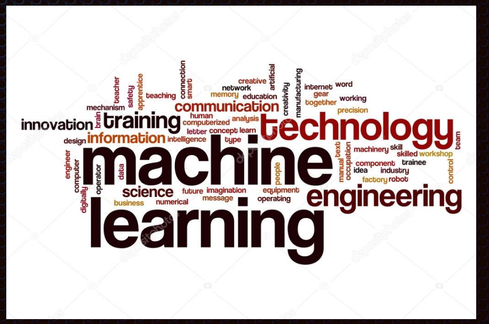
Machine learning success stories

- Risk assessment, epidemiology and causality
  - Cancer risk prediction
    - Gail model for Breast Cancer
  - Impact of inflammation on health
  - Identification of genetic and proteomic risk factors in complex disease



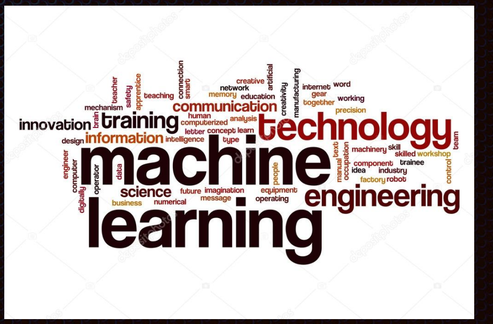
What is ML?

- Algorithms that ingest data and adapt to mimic and express inherent data patterns
  - Learns from data
  - Can provide predictions
- Algorithms can be
  - Simple (linear regression)
  - Complex (decision trees)
  - Indecipherable or magical (neural networks / deep learning)



What is ML?

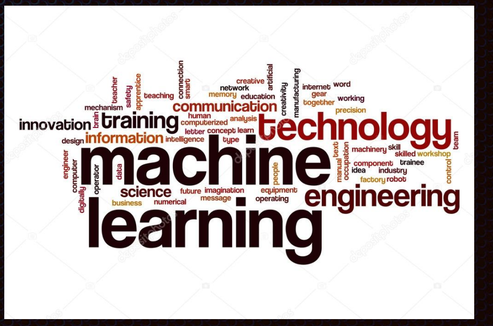
- Algorithms that are mainly meant for prediction
  - Supervised learning
- They cannot often express why the predictions happen
  - What factors influenced the prediction in what way?
  - It’s a function of the complexity of the model and our inability to express or comprehend that complexity easily



ML and Big Data

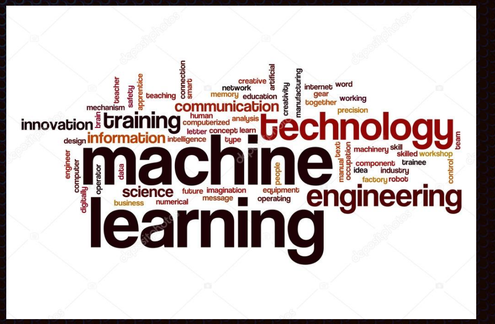
Machine learning is a greedy, hungry, voracious animal

with respect to data



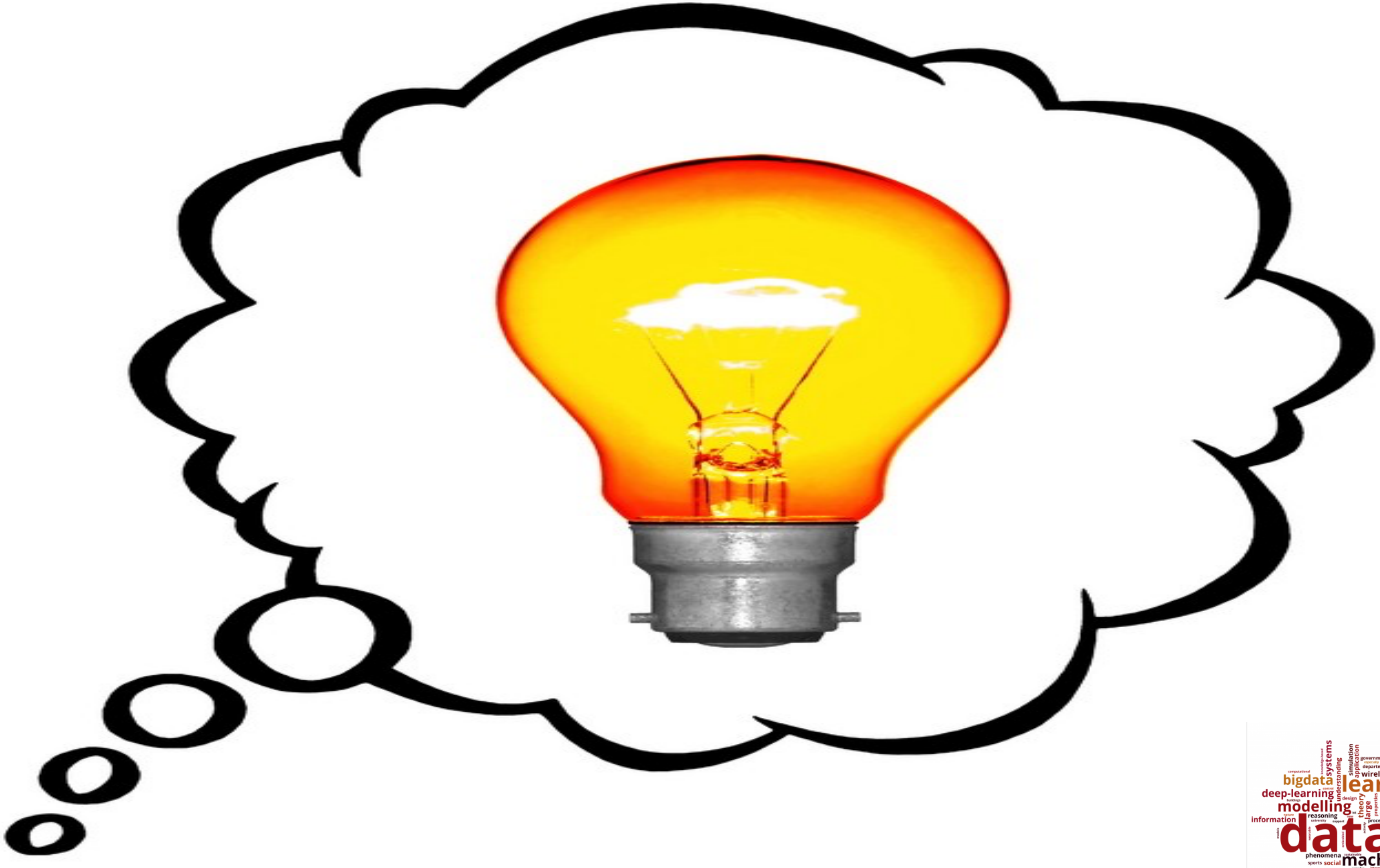
ML and Big Data

- Complex models require a lot of data to work well
  - Deep learning works for Google and Facebook because of their data stores
- So we have been collecting lots of data in the hope (and prayer) that we can learn from it
- And, by lots, I mean….



Big Data in Drug Discovery

- Pharma is losing patent control
- Getting a drug to market requires many years and billions of dollars
- However, we have plenty of clinical, bioinformatic, molecular and trial data




data
analysis
learning
machine
bigdata
deep-learning
modelling
information
systems
research
networks
processing
statistics
materials
energy
mining
performance
science
computer
applications
development
wireless
signal
topological
coastal
mathematical
government
simulation
application
understanding
theory
large
reasoning
technology
human
vision
football
wave
social
sports
phenomena
engineering
smart recognition
statistical
machine-learning
management
security
allocation
pattern
intelligence
department
space
analytics
linked
design
process
methods
geometric
network
sciences

A bright idea

- Let’s mine this data for good candidate molecules
- No assays, just data
- To confirm, outsource to do targeted assays

Grab public data.
Start a company.
Sell the company.
Repeat

Dr. Atul Butte, UCSF, 2015

Data sitting still is useless
Data needs to stay in motion
Data needs to get us someplace

Where’s the data

Where’s the data

- Our bodies
  - Genetic/proteomic/molecular code (1.5 Gb per cell)
  - Movement / behavior
    - Sleep
    - Gait
    - Sounds

Where’s the data

- Interactions with the world
  - Health records and Insurance
  - Government data
  - Telecommunication
  - Social media
  - Economic behavior

Where’s the data

- Data we voluntarily give, maybe inadvertently
  - Sensors we wear and carry
  - Movement through GPS (Google Maps, anyone
  - Electronic communication
  - Economic activity

Where’s the data

- Data we voluntarily give, by choice
  - Medical and health data
  - Surveys

All told, 2 Zb* per year

**A Zb is 10^{21} bytes*

Can we trust scientific discoveries made using machine learning?

Rice U. expert: Key is creating ML systems that question their own predictions

RICE UNIVERSITY

Statistician: Machine Learning Is Causing A "Crisis in Science"

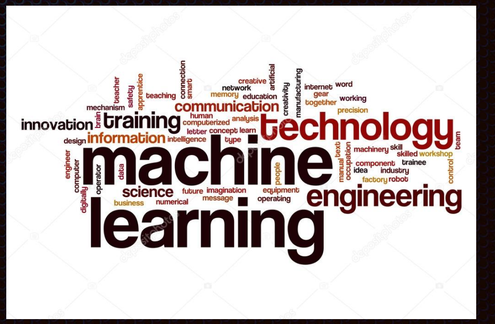
Many researchers now use machine learning to analyze data. There's just one glaring problem.

Jon Christian | February 18th 2019

Science & Environment

AAAS: Machine learning 'causing science crisis'

By Pallab Ghosh
Science correspondent, BBC News, Washington



February 16, 2019

Open access, freely available online

Essay

Why Most Published Research Findings Are False

John P. A. Ioannidis

Summary

There is increasing concern that most current published research findings are false. The probability that a research claim is true may depend on study power and bias, the number of other studies on the same question, and, importantly, the ratio of true to no relationships among the relationships probed in each scientific field. In this framework, a research finding is less likely to be true when the studies conducted in a field are smaller; when effect sizes are smaller; when there is a greater number and lesser preselection of tested relationships; where there is greater flexibility in designs, definitions, outcomes, and analytical modes; when there is greater financial and other interest and prejudice; and when more teams are involved in a scientific field in chase of statistical significance. Simulations show that for most study designs and settings, it is more likely for a research claim to be false than true. Moreover, for many current scientific fields, claimed research findings may often be simply accurate measures of the prevailing bias. In this essay, I discuss the implications of these problems for the conduct and interpretation of research.

Published research findings are sometimes refuted by subsequent evidence, with ensuing confusion

factors that influence this problem and some corollaries thereof.

Modeling the Framework for False Positive Findings

Several methodologists have pointed out [9–11] that the high rate of nonreplication (lack of confirmation) of research discoveries is a consequence of the convenient, yet ill-founded strategy of claiming conclusive research findings solely on the basis of a single study assessed by formal statistical significance, typically for a *p*-value less than 0.05. Research is not most appropriately represented and summarized by *p*-values, but, unfortunately, there is a widespread notion that medical research articles

It can be proven that most claimed research findings are false.

should be interpreted based only on *p*-values. Research findings are defined here as any relationship reaching formal statistical significance, e.g., effective interventions, informative predictors, risk factors, or associations. "Negative" research is also very useful. "Negative" is actually a misnomer, and the misinterpretation is widespread. However, here we will target relationships that investigators claim

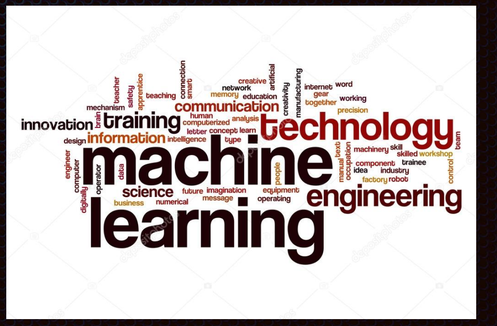
is characteristic of the field and can vary a lot depending on whether the field targets highly likely relationships or searches for only one or a few true relationships among thousands and millions of hypotheses that may be postulated. Let us also consider, for computational simplicity, circumscribed fields where either there is only one true relationship (among many that can be hypothesized) or the power is similar to find any of the several existing true relationships. The pre-study probability of a relationship being true is $R/(R+1)$. The probability of a study finding a true relationship reflects the power $1-\beta$ (one minus the Type II error rate). The probability of claiming a relationship when none truly exists reflects the Type I error rate, α. Assuming that c relationships are being probed in the field, the expected values of the 2×2 table are given in Table 1. After a research finding has been claimed based on achieving formal statistical significance, the post-study probability that it is true is the positive predictive value, PPV. The PPV is also the complementary probability of what Wacholder et al. have called the false positive report probability [10]. According to the 2×2 table, one gets $\mathrm{PPV} = (1-\beta)R/(R-\beta R+\alpha)$. A research finding is thus

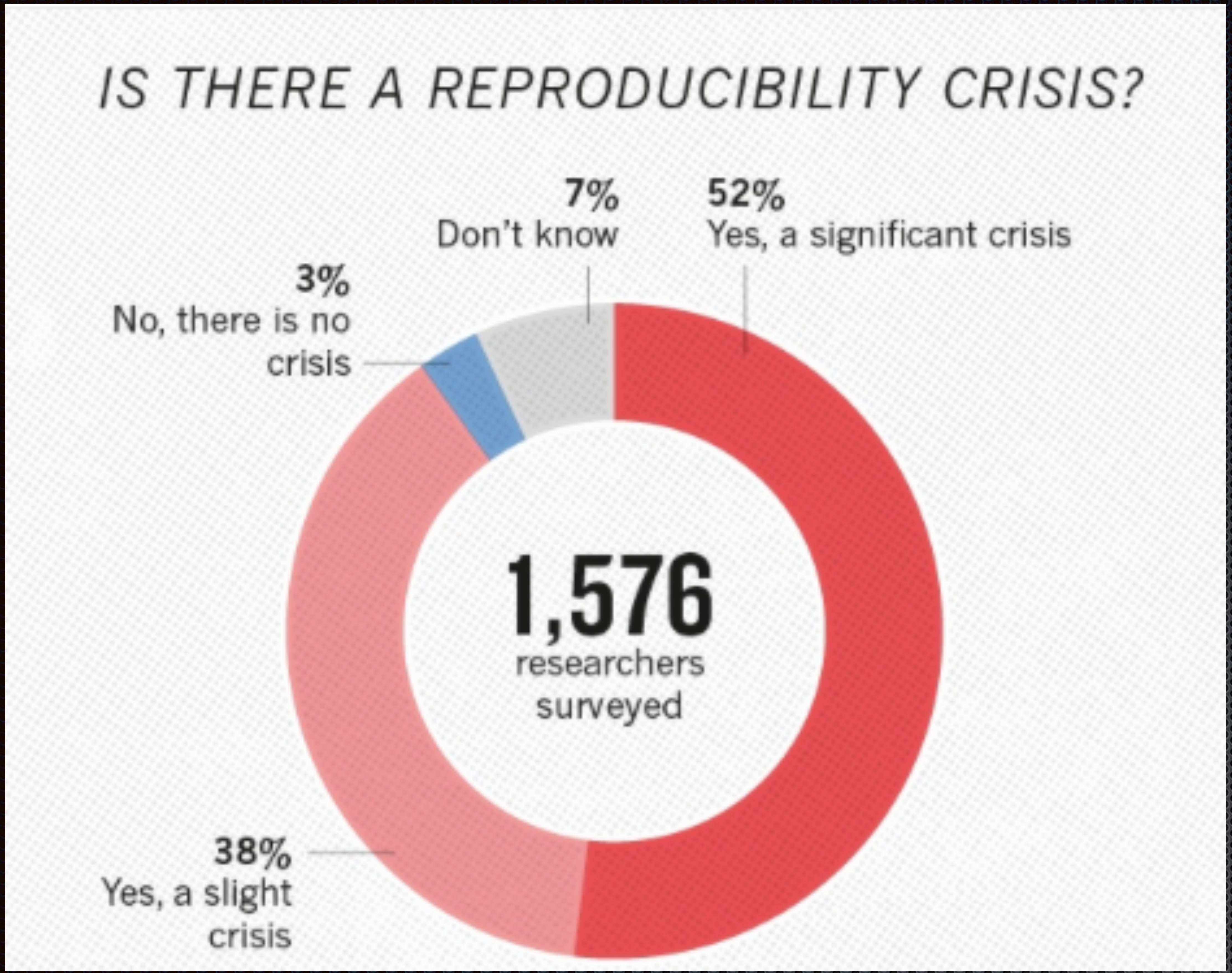
Citation: Ioannidis JPA (2005) Why most published

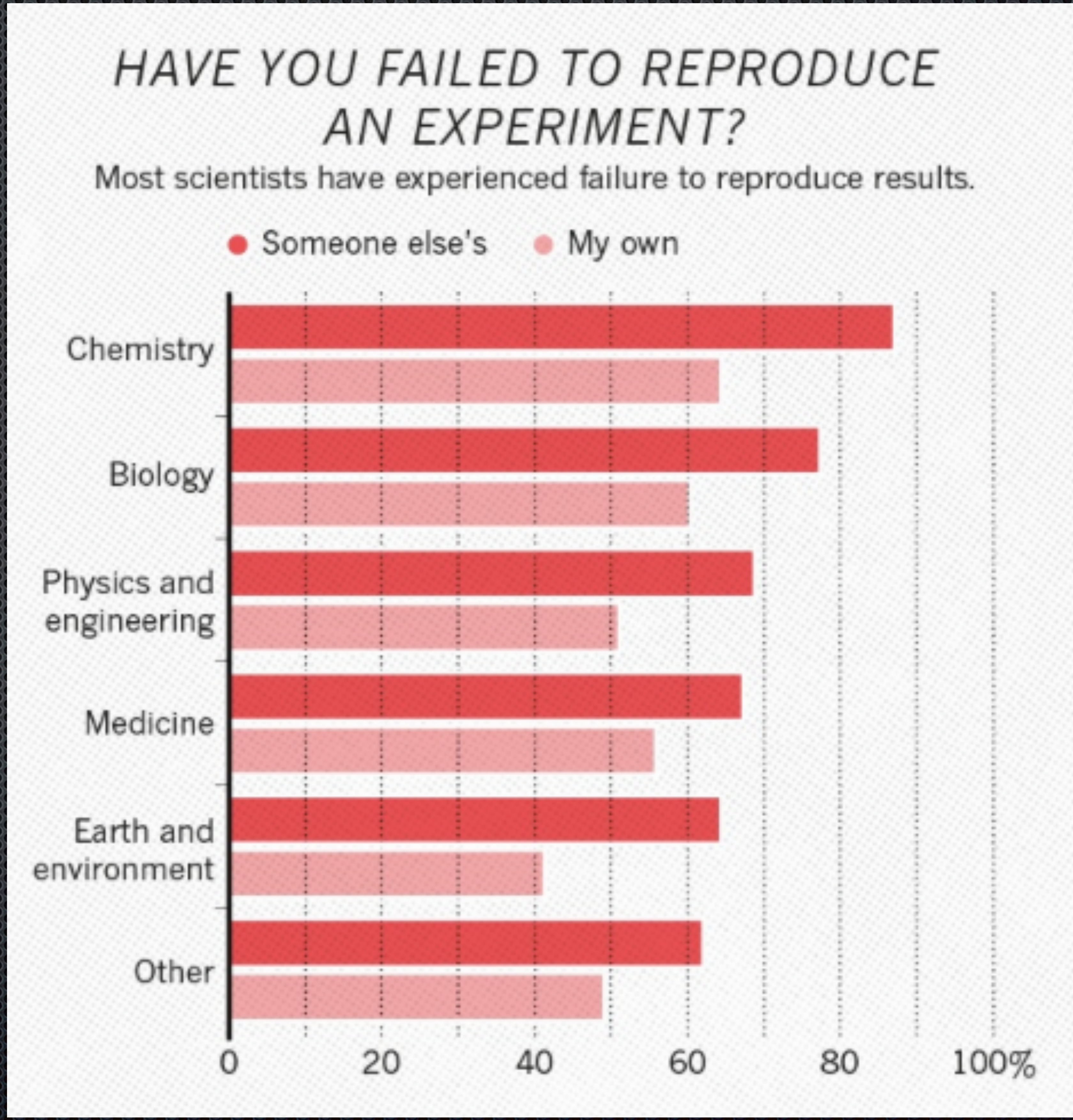
Pharma report:

89% of research findings are not reproducible

This has huge implications for biotech and pharma development, right?!!




IS THERE A REPRODUCIBILITY CRISIS?
7%
Don't know
52%
Yes, a significant crisis
3%
No, there is no crisis
1,576
researchers surveyed
38%
Yes, a slight crisis


HAVE YOU FAILED TO REPRODUCE AN EXPERIMENT?
Most scientists have experienced failure to reproduce results.
Someone else's
My own
Chemistry
Biology
Physics and engineering
Medicine
Earth and environment
Other
0
20
40
60
80
100%


data
analysis
machine
learning
modelling
bigdata
deep-learning
processing
statistics
mining
research

Issues with Big Data

- Variability — Inconsistencies in the data
- Veracity — Poor data quality
- Complexity — Data management challenges

These are really the more pressing challenges

This is behind most of the problems!

Data is NOT information

- Data is just that, data
- It only contributes to information when given a context (your question)
- In that context, the data-derived information can be translated into action
  - Products
  - Services

The question drives the learning

Not the other way around

My personal experience

- You've got data
- I need data and a question
- 80% of my time will be to help you figure out the question
- 80% of the remaining time will be spent getting your data into a usable state for your question

Need to find the right Big Data for your question

Need to see if your question is answerable given available data

Biases and ethics

- Our learning is only as good as the training data that is used
- Training data is often biased
  - Funding biases
  - Historical biases
  - Incompatibilities

Biases and ethics

- Genomic and pathway databases ingest the scientific literature
- The relative volume of literature in various fields is driven by funding
  - Databases are biased to cancer, heart disease and diabetes
  - Good luck if you have a rarer disease to treat

Biases and ethics

- Historically, minorities had lower chances of getting loans, mortgages, etc.
- This is reflected in the historical data
- This data is used to train ML models
- Now the historical racial bias is codified, since the models will make predictions based on patterns it saw in the training data
- Similar issue with clinical trials
  - Most studies were done on middle aged white men
  - Do these data apply to women, children, other ethnicities?
- Huge issue recognized in data ethics

Biases and ethics

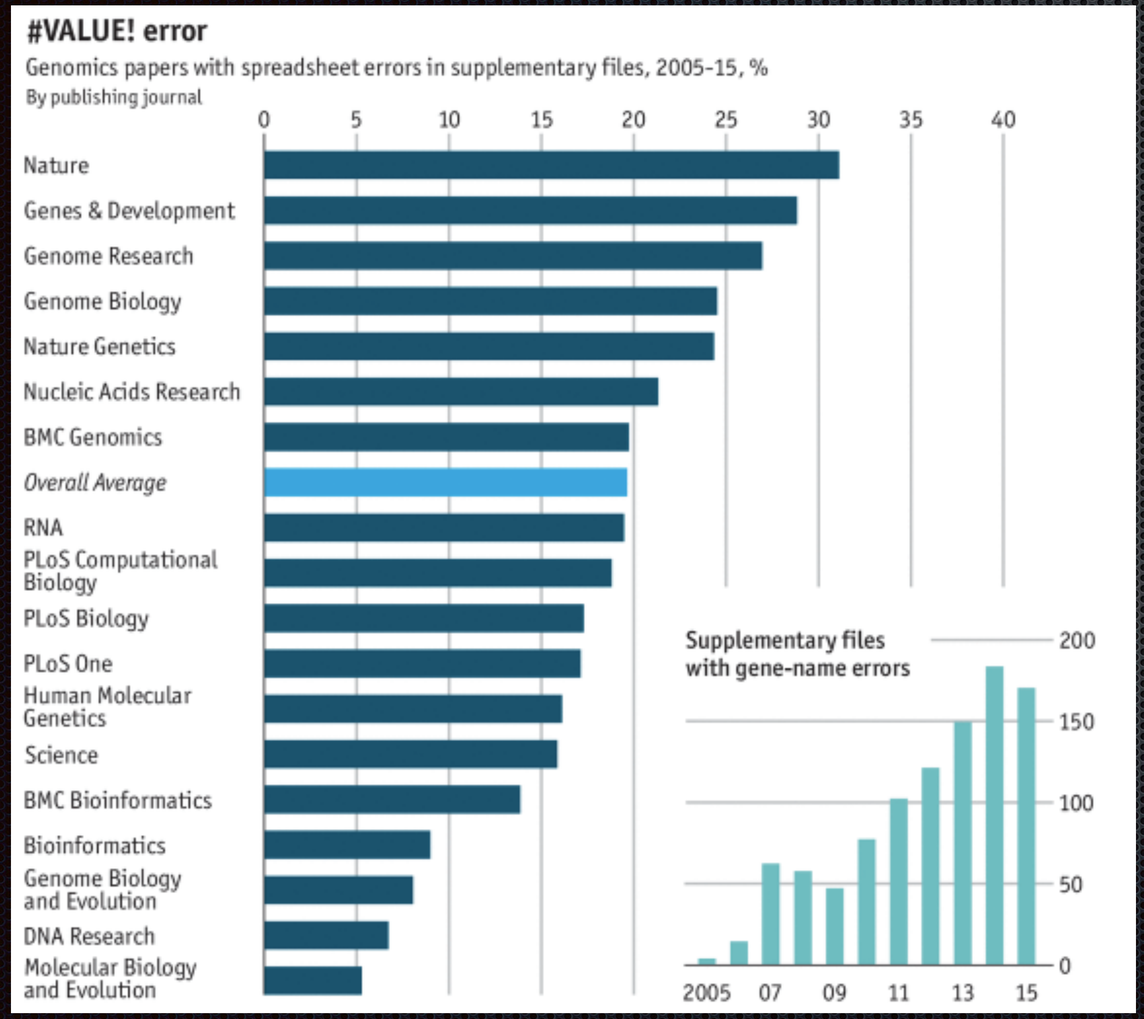
- aka, we like shiny new things

- Historical bioinformatic data incompatible with currently produced data
- We have lost the opportunity to use this large corpus of data
  - Billions of dollars in international funding
- We can’t tell how these data relate to current findings easily

Garbage in, garbage out

- Make sure the data you're leveraging for your business and your career is of the highest quality
  - Provenance
  - How it was collected
  - How it is stored

Garbage in, garbage out



Garbage in, garbage out

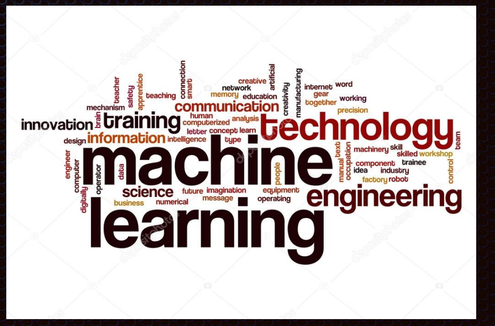
- Make sure you use the data
  - Appropriately
  - Ethically
  - Really think through and understand your data, your question, and how they relate
  - Don’t just dump things into AI just because it’s the cool thing

Big Data + ML/AI ≠ Sorceror's Stone

- Big Data can mean Big Noise
  - No signal to be had
  - ML will give spurious, irreproducible answers
  - Dietary studies are notorious for this, as are psych studies

Big Data + ML/AI ≠ Sorceror's Stone

- Finding and assessing rare events is VERY HARD
- Suppose an event occurs in 1 out of 10,000 people
- You fit a ML model to this huge database (think Medicare)
- I use the amazing "Ostrich Method": Just say no
  - I'll have an accuracy of 99.99% in this scenario
  - Beat that, you fake intelligence.



The crystal ball

- Storage costs are a huge issue
- Analytic methods need progress
  - Still leveraging methods from 20 or more years ago
  - A fast moving area

The crystal ball

- Lots of unusable data
  - Lack of compatibility
  - Lack of documentation
- More efficiency and focus needed
  - Data generation
  - Data analysis
  - Data products

Symbiosis

“Begin with the end in mind”

- Find a problem that needs solving
- Find the tools, data and methods that will help you figure it out
- Create a diverse team (in skills, talent and background)
- Work as a team to develop a product that solves it
- Use evidence-based best practices to convince the market that your’ve solved it

Contact info

- abhijit@zansors.com
- @webbedfeet / @Zansors
- https://webbedfeet.netlify.com

Abhijit Dasgupta

Director/Chief Data Scientist

ARAASTAT

Zansors