

Artificial Intelligence and Its Impact on Clinical Trials

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Outline

- Healthcare
- Experts, expert systems, and learning systems.
- AI architecture
- Machine learning vs. Statistics
- Singularity
- Motivation to use AI
- Illustrations

Healthcare US

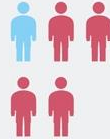
- 12 million misdiagnosis per year
 - Failing to order the right test
 - Misinterpreting a test
 - Not establishing a proper differential diagnosis
 - Missing an abnormal finding
 - Not using available epidemiological information
 - Note. 'Epidemic scale': 2017 AHA & ACC changed the definition of high blood pressure → 30,000,000 more Americans with hypertension without solid evidence to back up the new guideline
- One-third of medical operations are unnecessary
- For every one hundred Medicare recipients (each year)
 - 50 CT scans
 - 50 ultrasounds
 - 15 MRIs
 - 10 PET scans
- 30 to 50% of the 80 million CT scans are unnecessary

Personalized Medicine

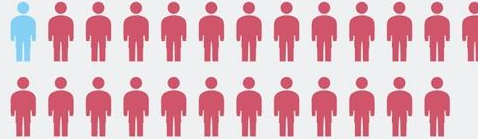
IMPRECISION MEDICINE

For every person they do help (blue), the ten highest-grossing drugs in the United States fail to improve the conditions of between 3 and 24 people (red).

1. ABILIFY (aripiprazole)
Schizophrenia



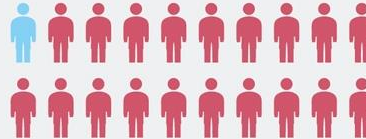
2. NEXIUM (esomeprazole)
Heartburn



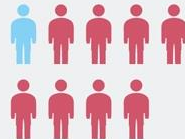
3. HUMIRA (adalimumab)
Arthritis



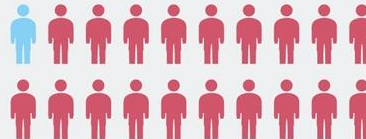
4. CRESTOR (rosuvastatin)
High cholesterol



5. CYMBALTA (duloxetine)
Depression



6. ADVAIR DISKUS (fluticasone propionate)
Asthma



7. ENBREL (etanercept)
Psoriasis



8. REMICADE (infliximab)
Crohn's disease



9. COPAXONE (glatiramer acetate)
Multiple sclerosis

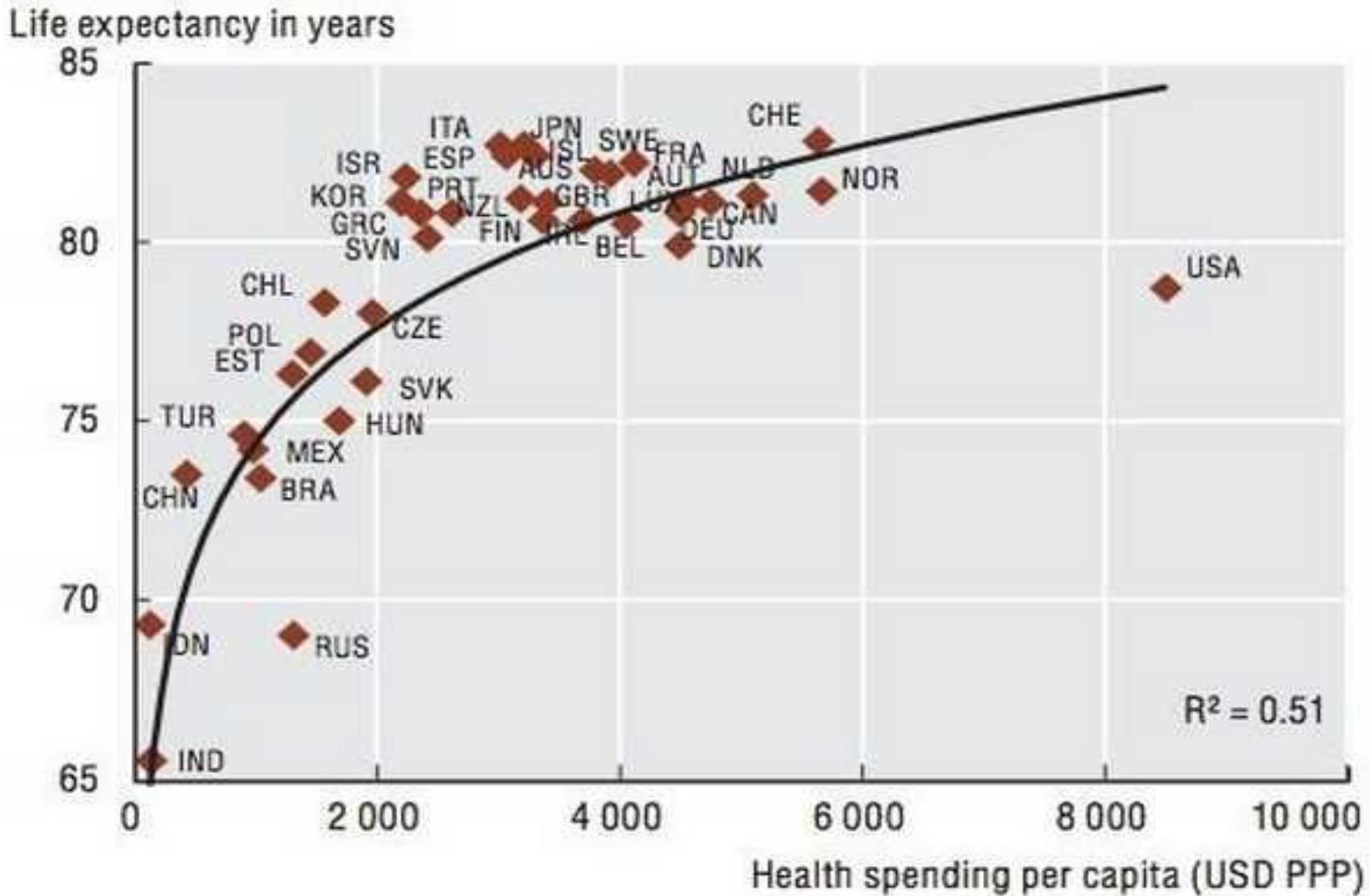


10. NEULASTA (pegfilgrastim)
Neutropenia



Based on published number needed to treat (NNT) figures. For a full list of references, see Supplementary Information at go.nature.com/4dr78f.

An Industry Rife with Inefficiencies...



Example

- Woman brought into emergency WakeMed hospital.
 - Symptoms: Fever, Cough, Chest Pain, Chills, Night Sweats, Headache, Fatigue, Joint Aches, Red Spotty Rash
 - No diagnosis: IV broad spectrum AB and left to go home the next day AB tablets.
 - With no improvement, a week later brought back to the hospital.
 - In critical condition now put in ICU. IV broad spectrum AB and steroids. Fever goes down. Still coughing and very weak. Some blood tests are taken.
 - No diagnosis: Still in critical condition, 3 weeks later transferred to UNC. Valley Fever was ruled out since we don't have that on the East coast.
 - No diagnosis: Still in critical condition, 3 weeks later transferred to Duke University Hospital.
 - Epidemiologist asks the very weak patient if she has recently been to CA. Answer: YES. Test taken for Valley Fever.
 - Positive → Diagnosis.
 - Anti-fungal medication against Valley Fever. Stop of AB and tapering the steroids down.
 - AB and steroid is very harmful to a patient with Valley Fever.
 - 4 weeks in ICU in critical condition.
 - 2 weeks out of ICU she can go home to her husband and 3 children.
 - 1 year of anti-fungal treatment.

Will AI replace human physicians?

Isabel Symptom Checker



Start 1/ Tell us about your symptoms > 2/

[Find a lab test](#) [Contact a doctor](#)

Symptom details ⓘ [Share](#) [Print](#) [Save](#)

Gender: Female (Not Pregnant), Age: Adult 40-49 yrs [Edit](#)
Country: United States (North America)
Symptoms: Fever, Cough, Chest Pain, Chills, Night Sweats, Headache, Fatigue, Joint Aches, Red Spotty Rash

Show All	Red Flag	Common
Valley Fever		
Lyme Disease		
Brucellosis		
Tularemia	🚩	
Q Fever		
Relapsing Fever		
Non-Hodgkin Lymphoma		
Human Granulocytic Anaplasmosis		
Infectious Mononucleosis		common

Electronic Healthcare Records

Your ATM card works in Outer Mongolia, but your electronic health records can't be used in a different hospital across the street.

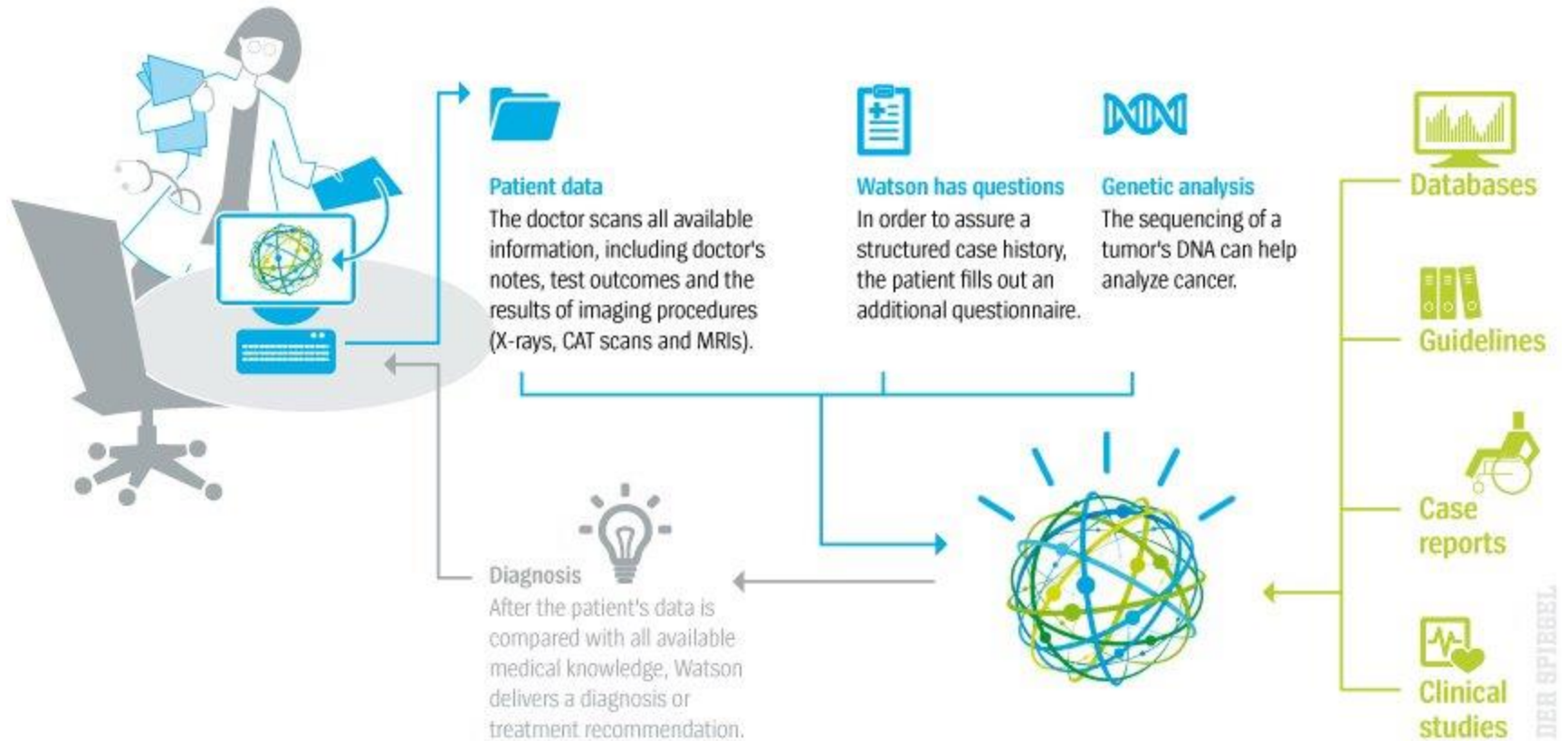
Saurabh Jha on Twitter

Healthcare Data

- AI systems need to 'train'
 - Screening
 - Diagnosis
 - Treatment assignment
 - Demographics
 - Medical notes
 - Electronic recordings from medical devices
 - Physical examinations
 - Laboratory
 - Images

How Watson Works

The ways IBM's system is used in medicine



Expert and Expert System

- An expert is a person who has a comprehensive and authoritative knowledge of or skill in a particular area.
- A computer system that emulates the decision-making ability of a human expert.
- BBN developed RS/Explore and RS/Discover, expert-system software products for data analysis and experimental design.

AI Architecture System

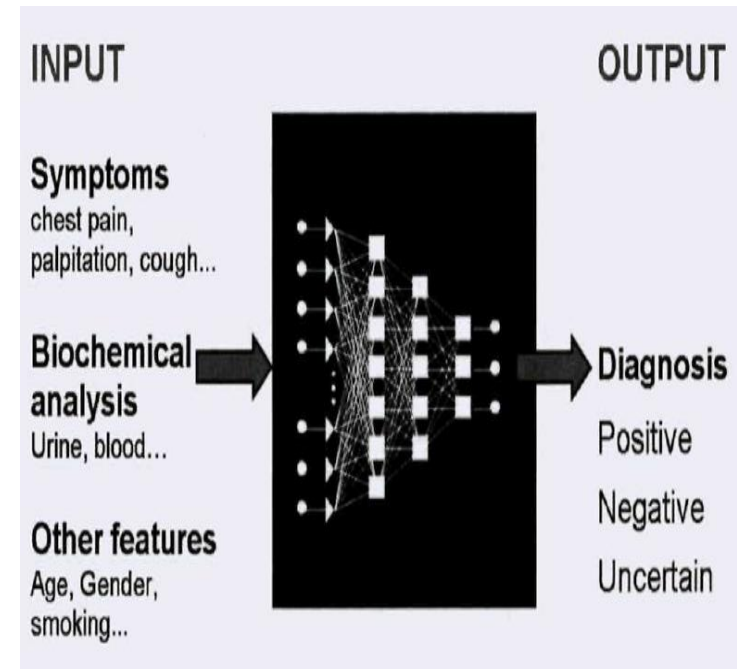
- What is the utility or reward function to be used for optimization?
- How does the system learn? What data does it work with, what learning techniques does it use, and what prior knowledge needs to be built into it?
- How does it maximize its expected reward?

What is Artificial Intelligence

- Definition--“Use of a computer to model intelligent behaviour with minimal human intervention”
- Machines & computer programs are capable of problem solving and learning, like a human brain.
- Natural Language Processing (“NLP”) and translation,
 - Pattern recognition,
 - Visual perception and
 - Decision making.
- Machine Learning (“ML”), one of the most exciting areas for Development of computational approaches to automatically make sense of data
- Advantage of Machine
 - Can retain information
 - Becomes smarter over time
 - Machine is not susceptible to Sleep deprivation, distractions, information overload and short-term memory loss

Benefits of Artificial intelligence

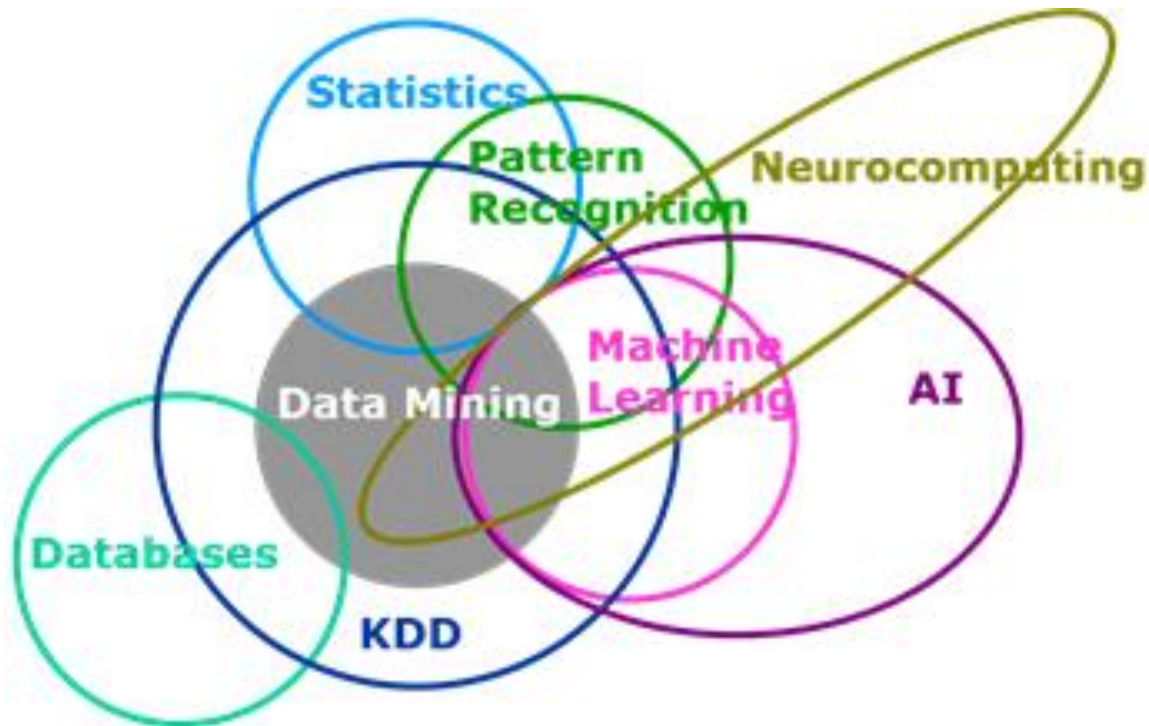
- AI can definitely assist physicians
 - Clinical decision making - better clinical decisions
 - Replace human judgement in certain functional areas of healthcare (eg, radiology).
 - up-to-date medical information from journals, textbooks and clinical practices
 - Experienced vs fresh Clinician
 - 24x7 availability of expert
- Early diagnosis
- Prediction of outcome of the disease as well as treatment
- Feedback on treatment
- Reinforce non pharmacological management
- Reduce diagnostic and therapeutic errors
- Increased patient safety and Huge cost savings associated with use of AI
- AI system extracts useful information from a large patient population
- Assist making real-time inferences for health risk alert and health outcome prediction
- Learning and self-correcting abilities to improve its accuracy based on feedback.



Cancer Classification



Machine Learning vs. Statistics



Building a general purpose learning system

Two approaches

Expert Systems

Relies on hardcoded knowledge

Can't deal with the unexpected, limited to pre-programmed solutions

Inspired by logic systems



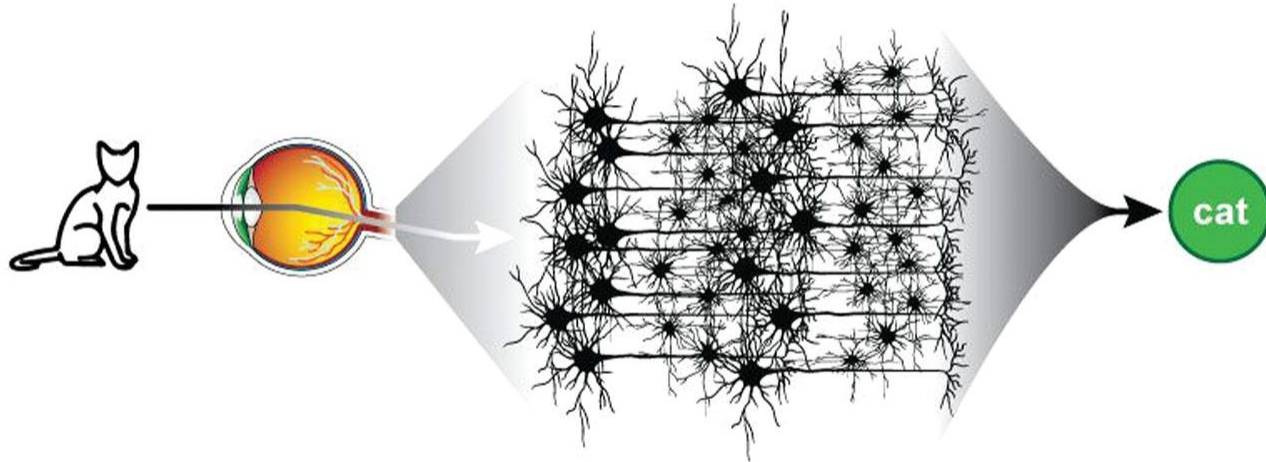
Learning Systems

Learns solutions from first principles

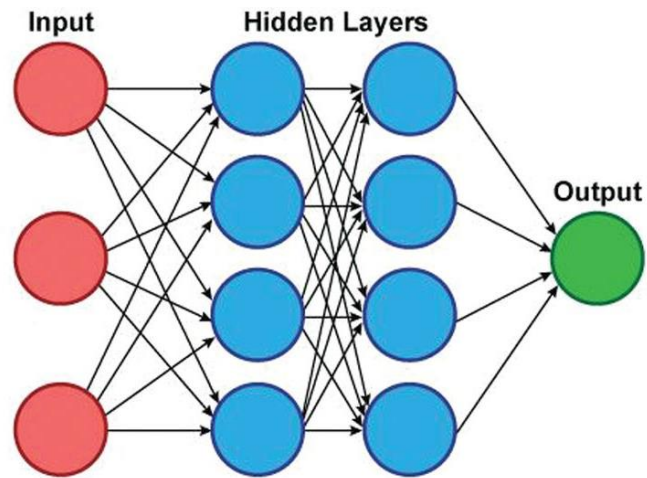
Can generalise to new tasks and solve things we don't know how to

Inspired & validated by neuroscience

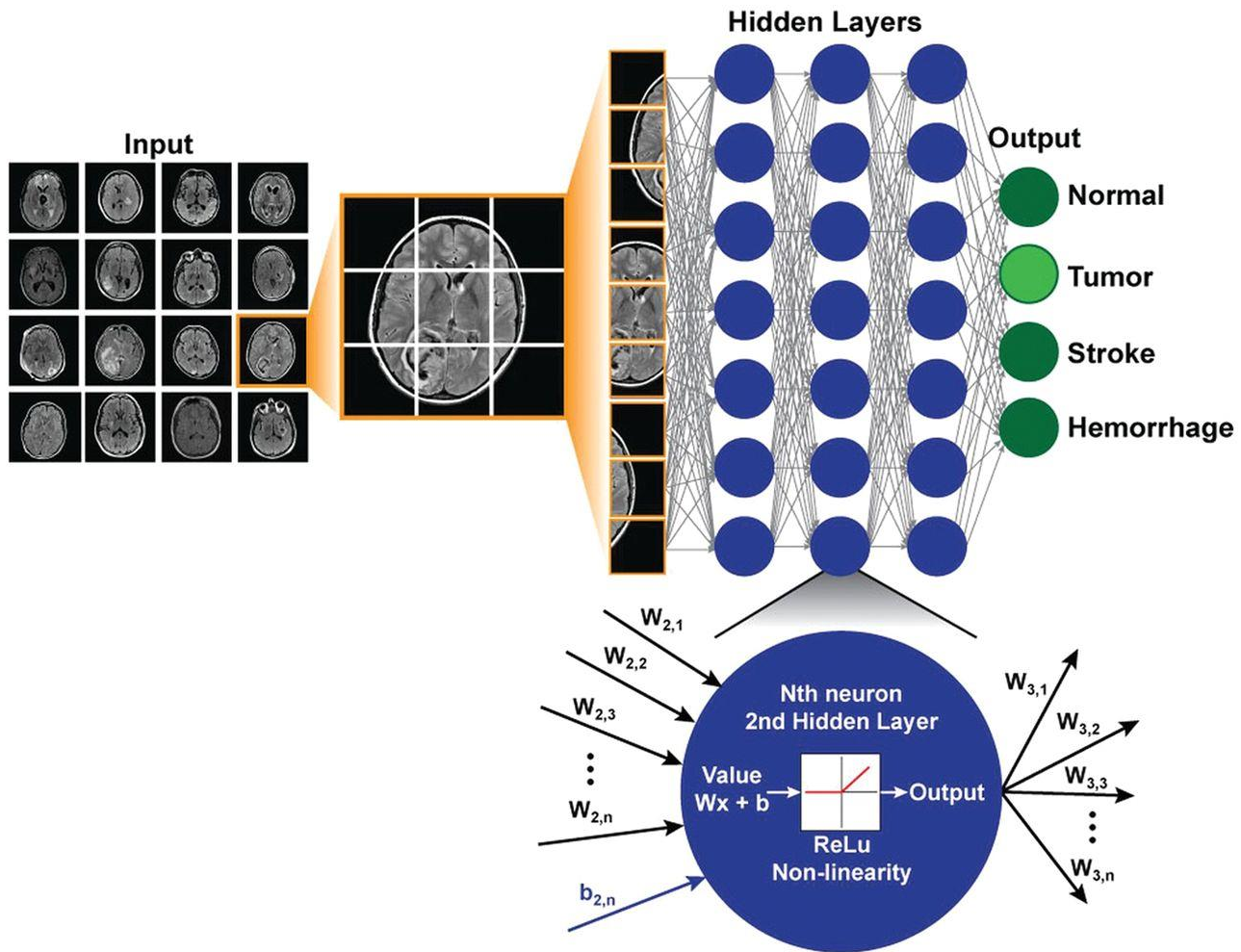
Neural Networks



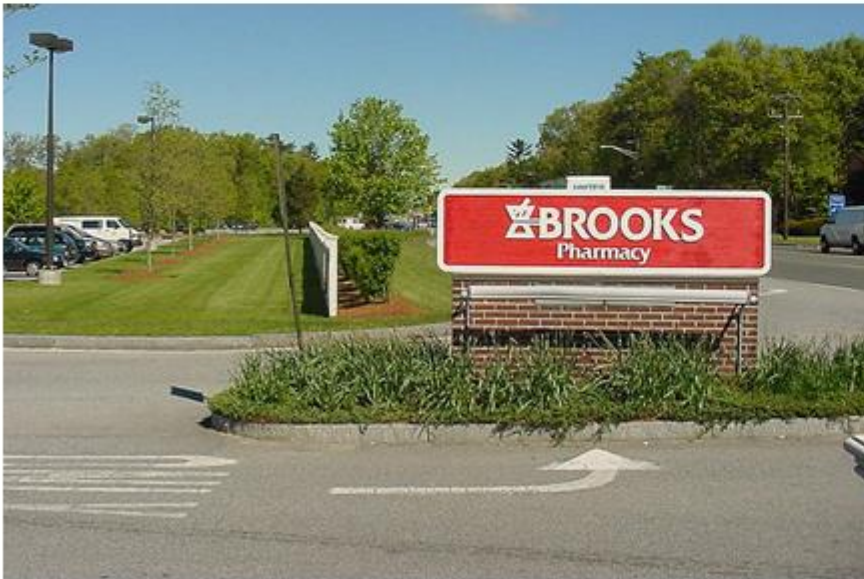
Biological Neural Network



Computer Neural Network



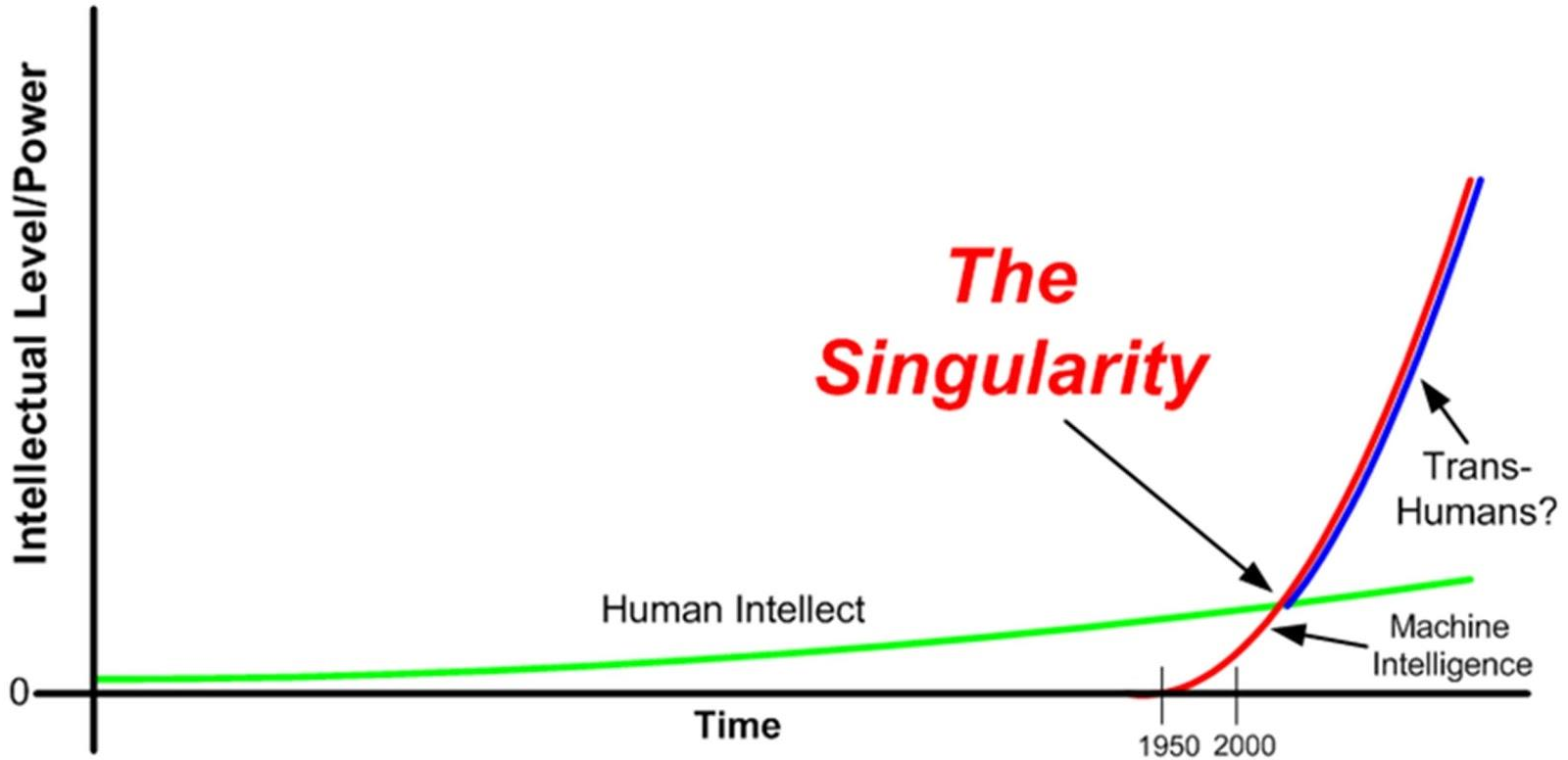
Why is not the future now?



Open from 8 am to 6 pm

Open 7/24

Singularity



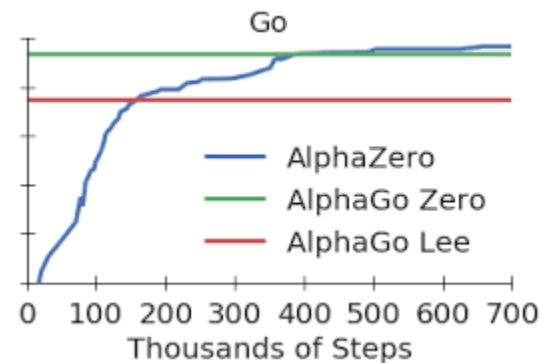
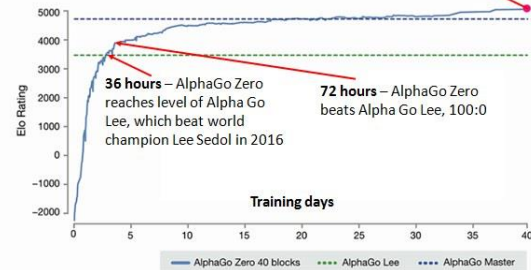
“Let an ultraintelligent machine be defined as a machine that can far surpass all the intellectual activities of any man however clever. Since the design of machines is one of these intellectual activities, an ultraintelligent machine could design even better machines; there would then unquestionably be an ‘intelligence explosion,’ and the intelligence of man would be left far behind.”

Irving John Good, 1965

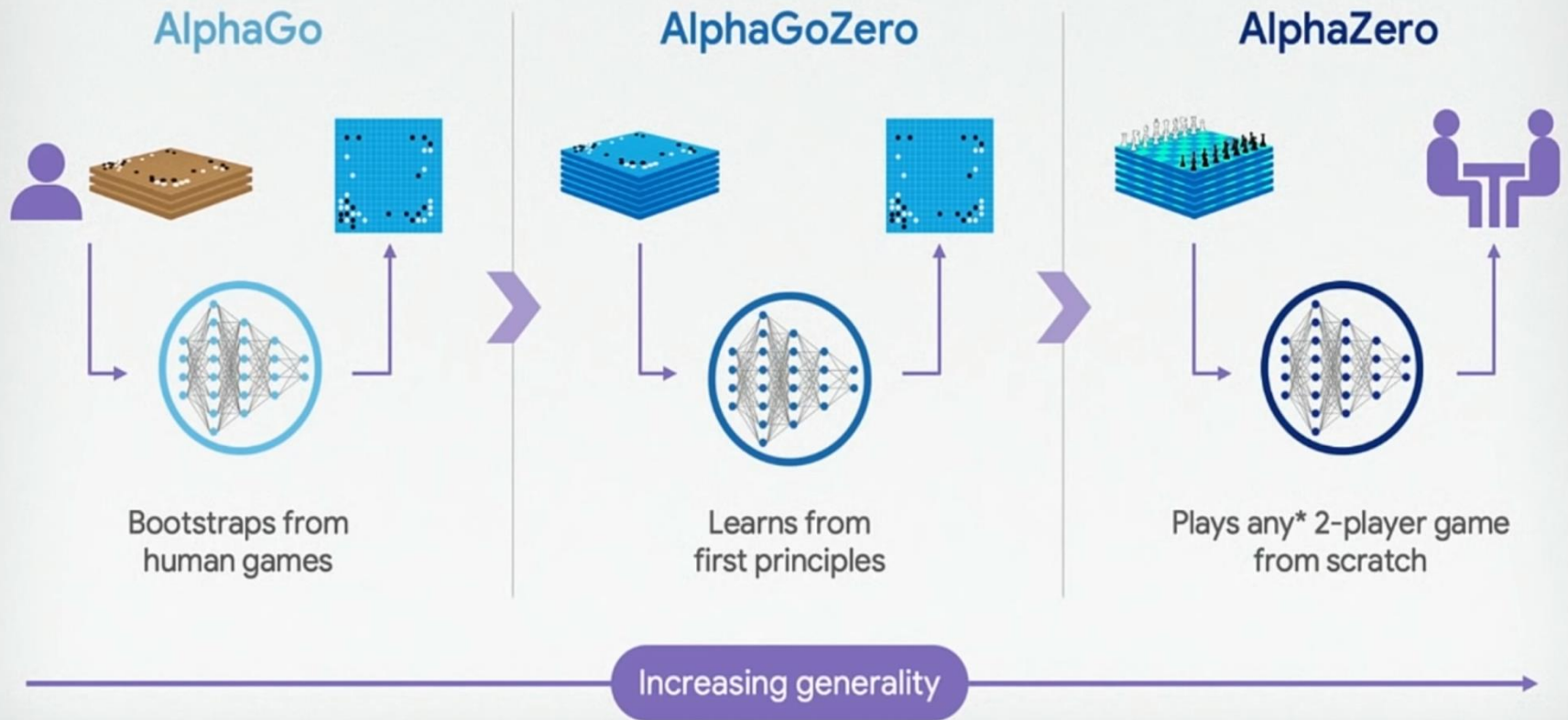
Motivation to use AI - Examples



40 days – AlphaGo Zero surpasses all previous versions, becomes the best Go player in the world

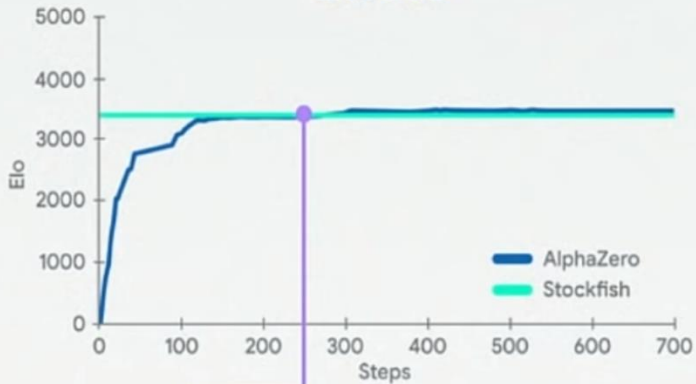


The lineage of AlphaZero



Same system can play any 2-player game

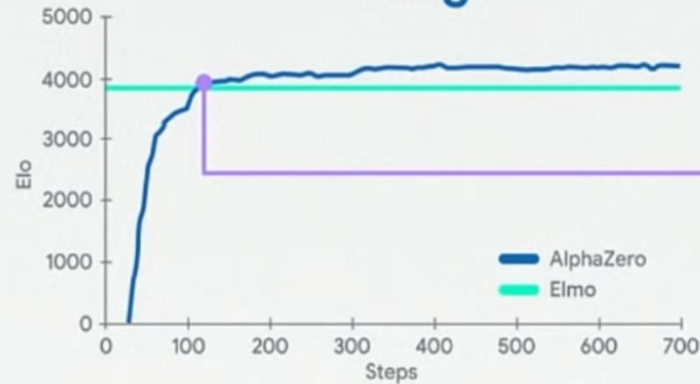
Chess



4 Hours

AlphaZero surpasses StockFish

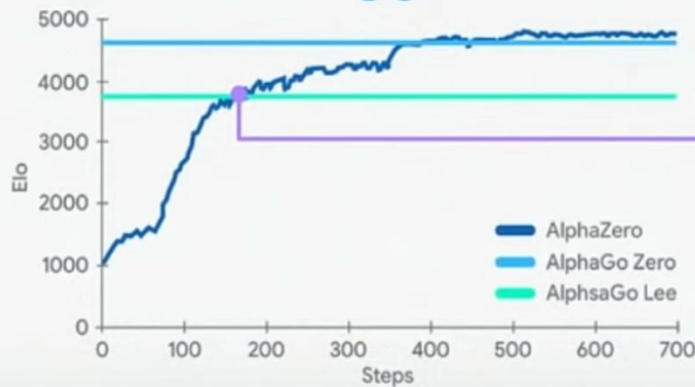
Shogi



2 Hours

AlphaZero surpasses Elmo

Go



8 Hours

AlphaZero surpasses AlphaGo

Motivation to use AI

- AI can use sophisticated algorithms to 'learn' features from a large volume of healthcare data, and then use the obtained insights to assist clinical practice.
- Learning and self-correcting abilities to improve its accuracy.
- Assist physicians by providing up-to-date medical information from journals, textbooks and clinical practices to inform proper patient care.
- Reduce diagnostic and therapeutic errors that are inevitable in the human clinical practice.
- Extracts information from a large patient population to assist making real-time inferences for health risk alert and health outcome prediction.

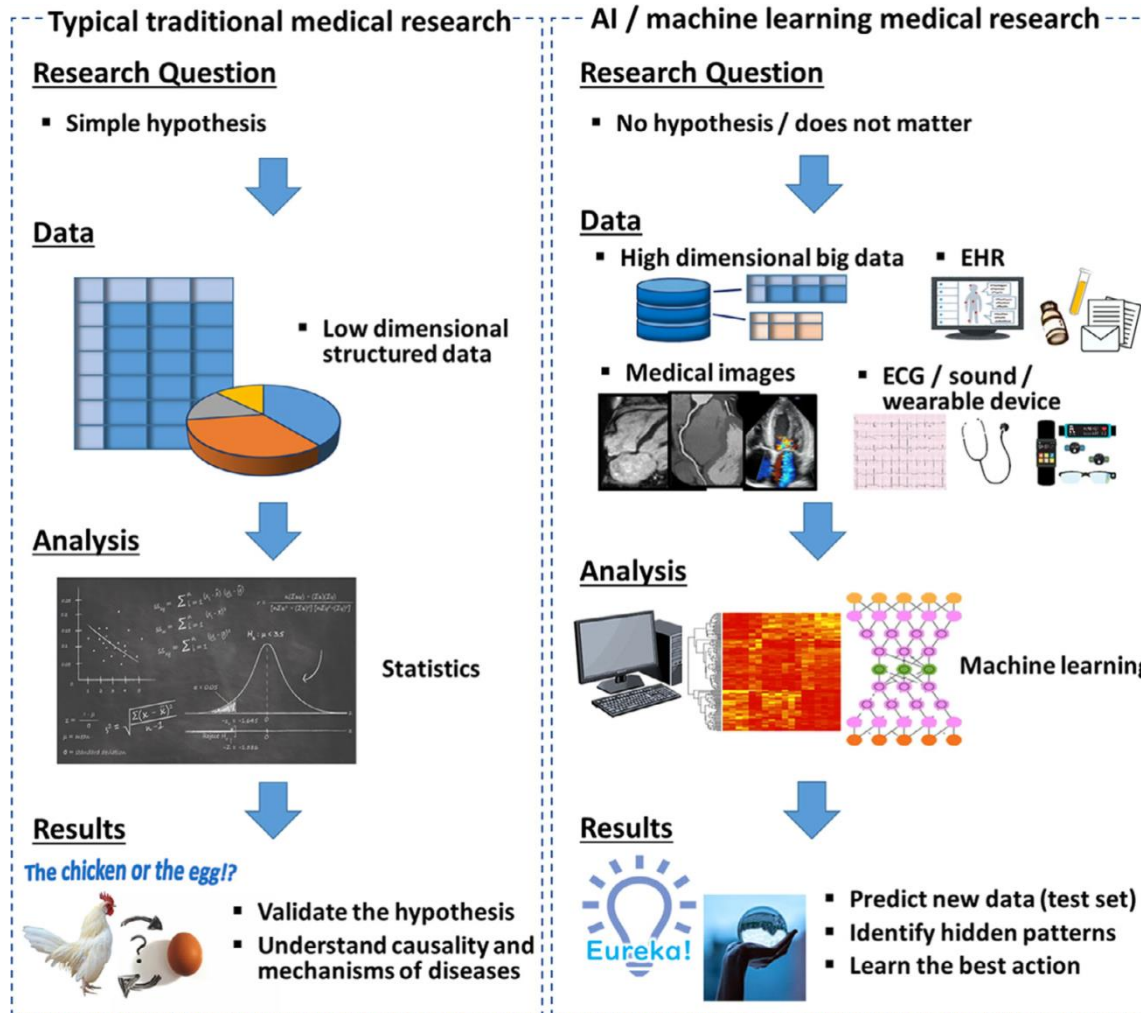
Uncertainty

If the data have their origin in the real world, then the data are likely to be noisy. So machine learning algorithms have to be able to handle uncertainty.

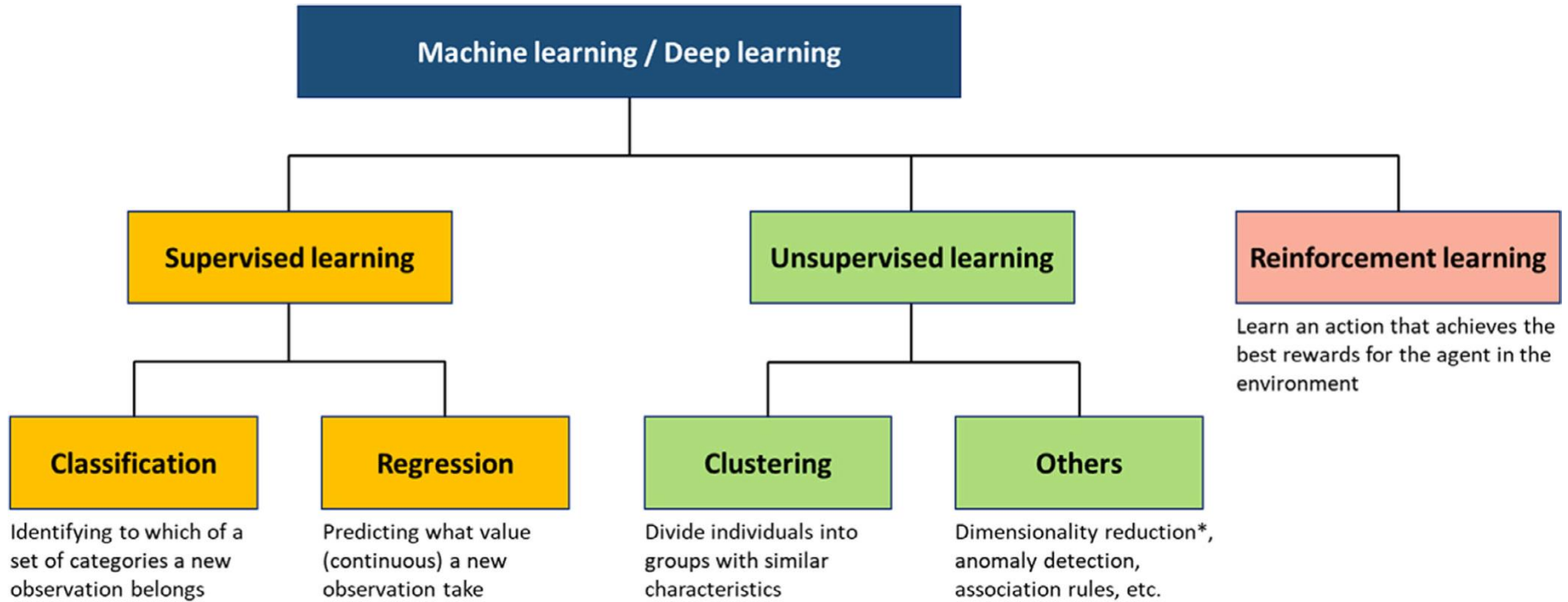
Murray Shanahan, 2015

Electronic health records are noisy, full of errors, and incorrect diagnoses. The algorithms need to overcome these deficiencies.

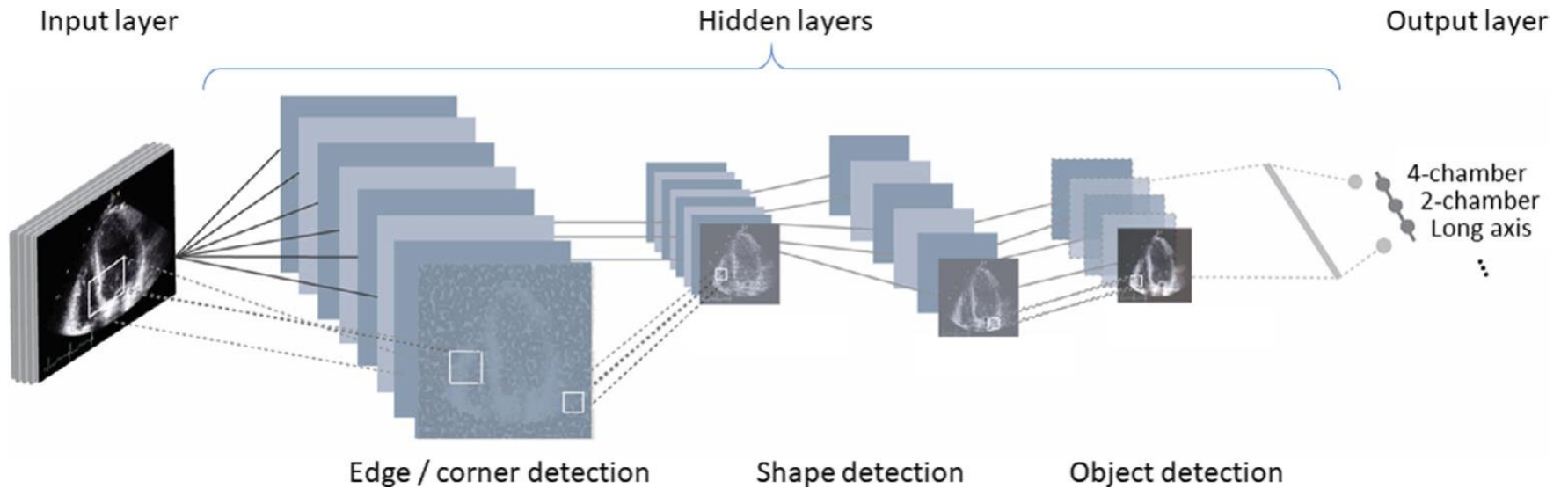
Medical Research



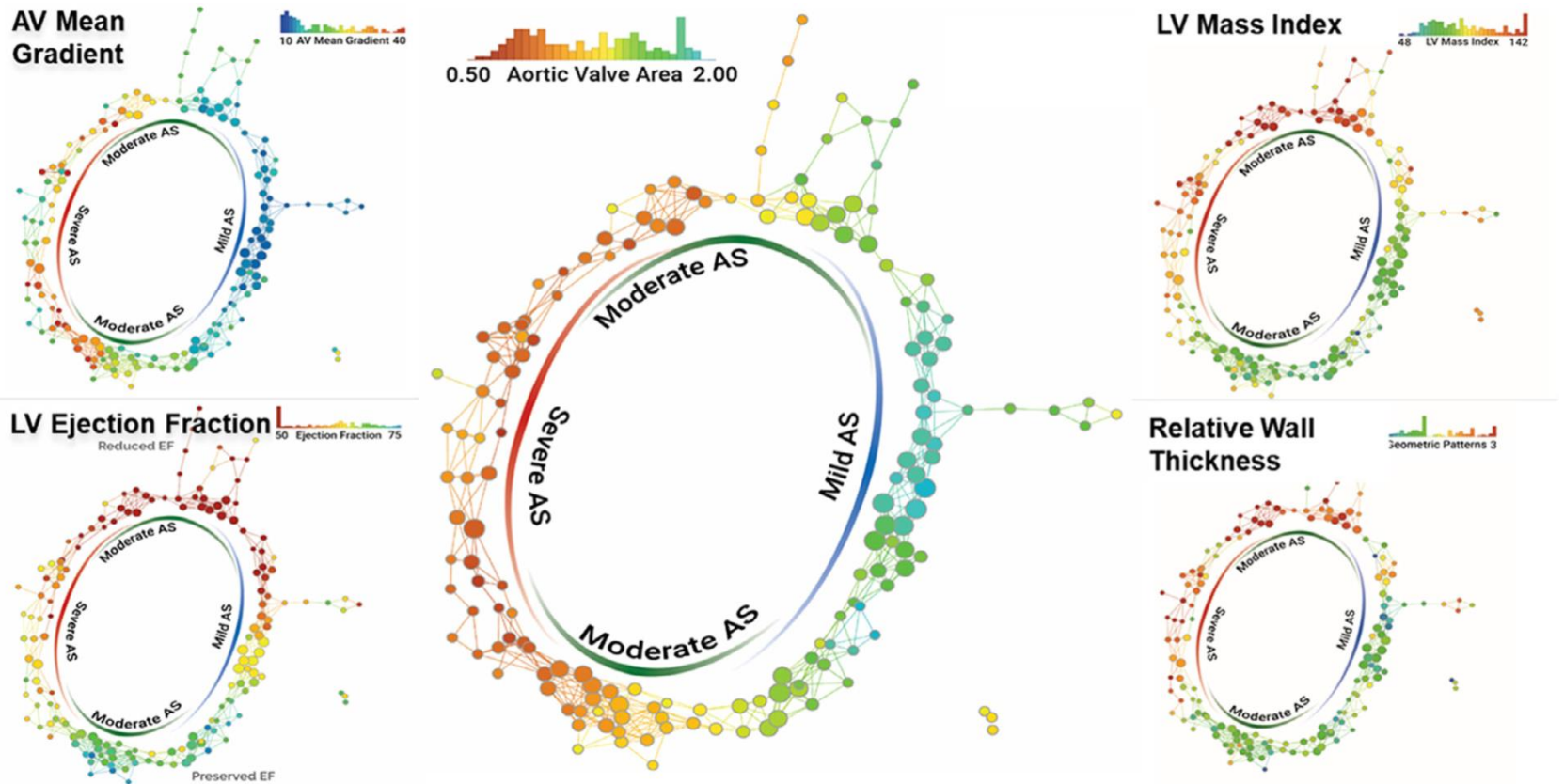
Learning Methods



Structure of Deep Learning



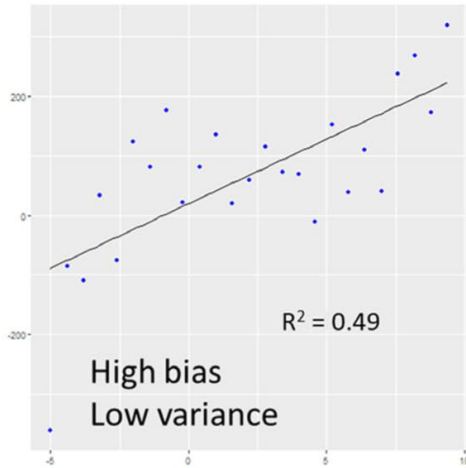
Topological Data Analysis in Patients with AS



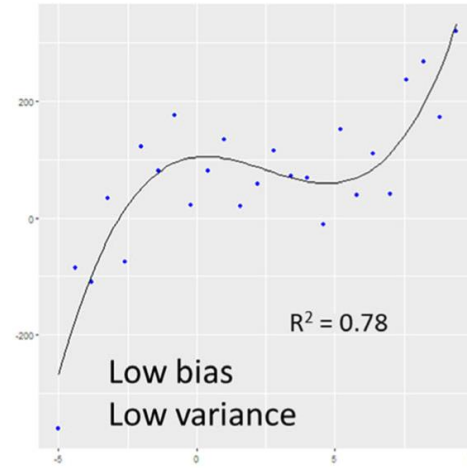
Fitting

Sample data

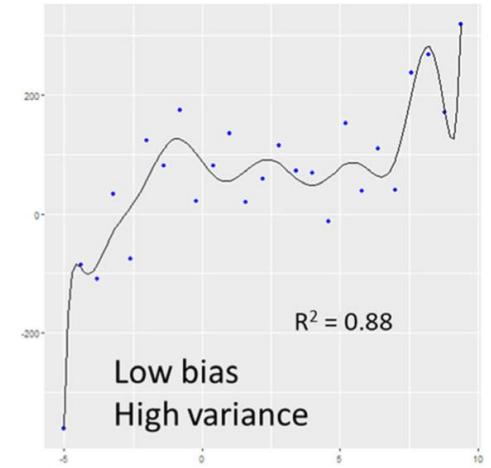
Underfitting



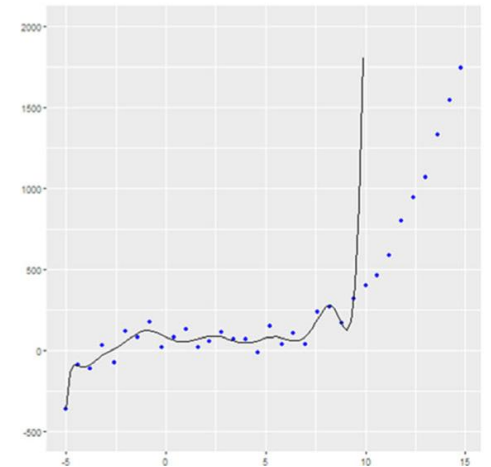
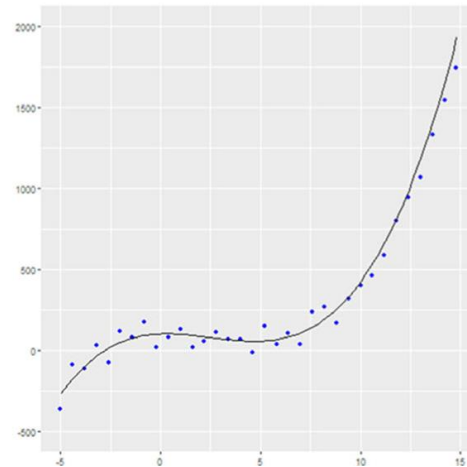
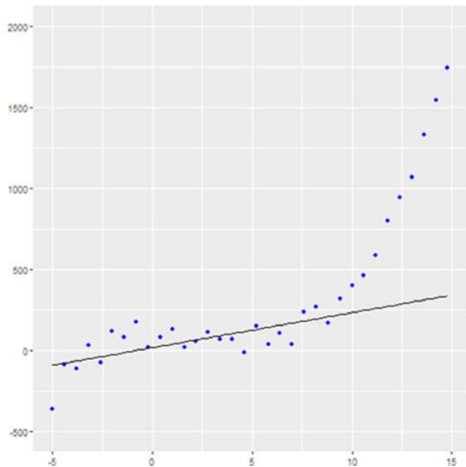
Optimal fitting



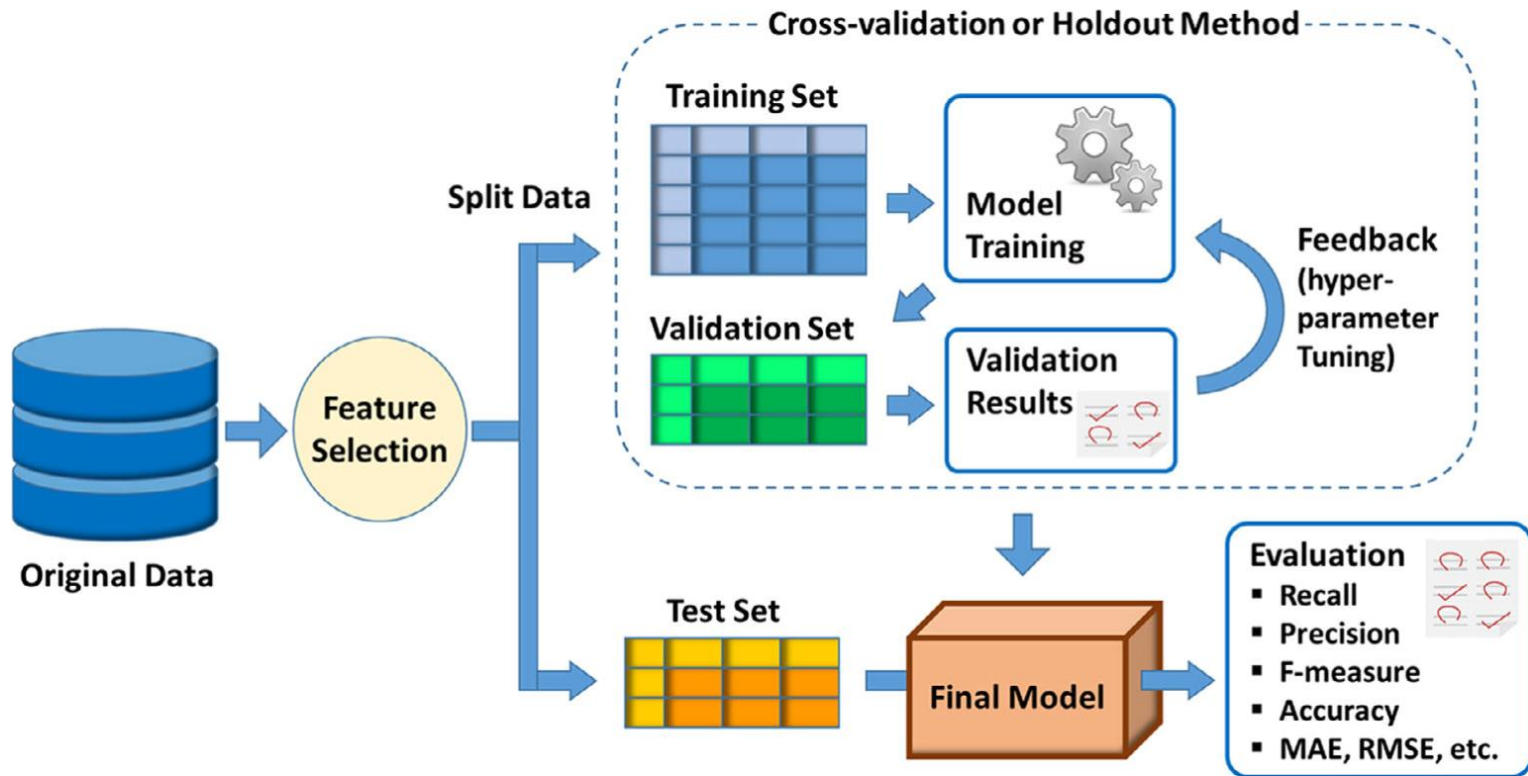
Overfitting



When new data are added



Development and Evaluation



Thank You!
Questions?