LOSCHMIDT LABORATORIES

12. Artificial Intelligence in Life Sciences

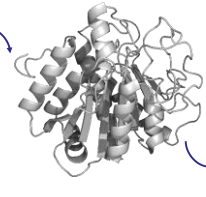
Outline

- Motivation
- Introduction to AI and ML
- Modern challenges in Bioengineering
- Basics of ML
- Recent applications

Motivation

Motivation

MSLGAKPFGEKKFIEIKGRRMAYIDEGTGDPILFQHGNPTSSYLWRNIMPHC
AGLGRLIACDLIGMGDSDKLDPSGPERYAYAEHRDYLDALWEALDLGDRVV
LVVHDWGSALGFDWARRHRERVQGIAYMEAIAMPIEWADFPEQDRDLFQ
AFRSQAGEELVLQD



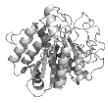
Function

Motivation

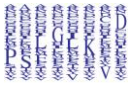
Sequence

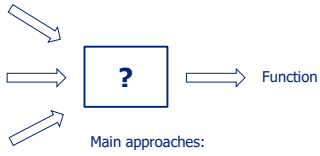
MSLGAKPFGEKKFIEIKGRRMAYIDEGTG
DPILFQHGNPTSSYLWRNIMPHCAGLGR
LIACDLIGMGDSDKLDPSGPERYAYAEHR
DYLDALWEALDLGDRVVLVVHDWGSAL
GFDWARRHRERVQGIAYMEAIAMPIEW
ADFPEQDRDLFQAFRSQAGEELVLQD

Structure



Evolution





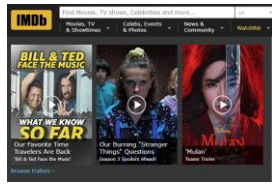
Main approaches:

- Experimental
- Rule-based
- Machine learning

Introduction to AI and ML

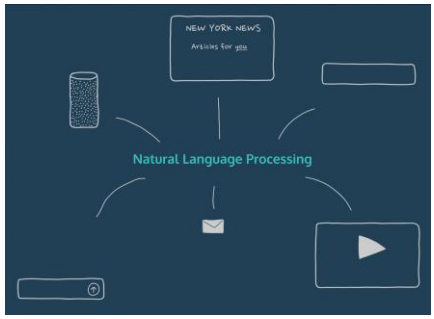
Introduction to AI and ML

- Recommendation engines
- Gaming
- Image & speech recognition
- Anomaly detection
- Natural language processing
- Data mining
- …



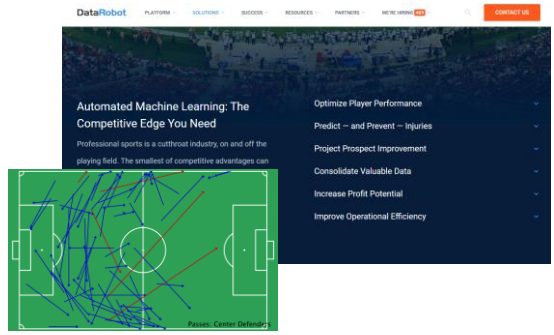
Introduction to AI and ML

Introduction to AI and ML



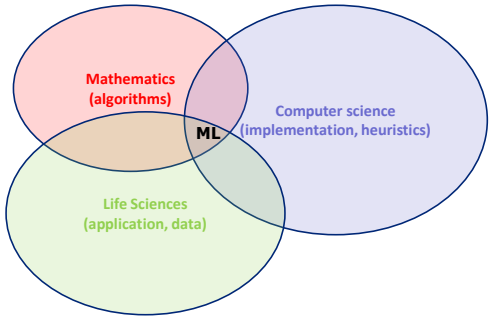
From towardsdatascience.com

Introduction to AI and ML



From www.analyticsindiamag.com/data-mining-strategy-development-football/

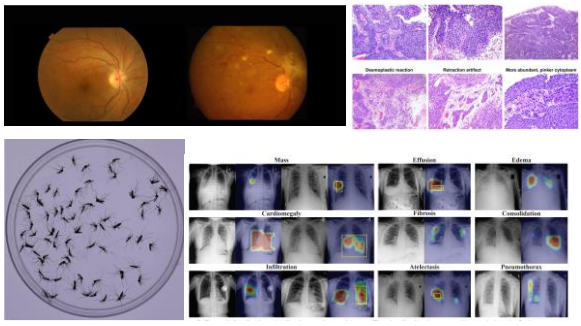
Introduction to AI and ML



Modern challenges

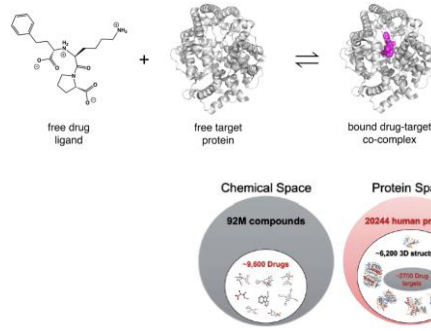
in Bioengineering

Modern Challenges



From ai.google/healthcare/

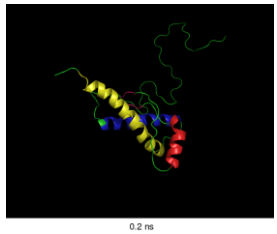
Modern Challenges



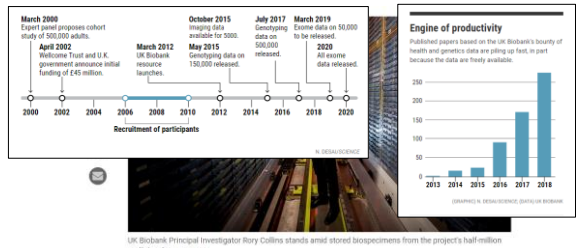
From C4X Discovery

Modern Challenges

- **How to annotate:**
  - **protein structure**
  - **protein function**
  - **protein interactions**
  - **…**
- **How to increase:**
  - **enzymatic activity**
  - **stability & solubility**
  - **substrate specificity**
  - **enantioselectivity**



Modern Challenges



UK Biobank Principal Investigator Rory Collins stands amid stored biospecimens from the project's half-million participants. NIGEL HILIER

Huge trove of British biodata is unlocking secrets of depression, sexual orientation, and more

By Jocelyn Kaiser, Ann Gibbons | Jan. 3, 2019 , 1:20 PM

From sciencemag.org

Modern Challenges

1. A large number of relevant features;
   - From bio-physico-chemical to textual;
   - Heterogeneous data (e.g. clinical, imaging, and genomic data);

2. Complex tasks and large parameter space;
   - A single 300-amino-acid-long protein will have 300·19=5700 single-point variants!
3. Large datasets available and new data are collected.

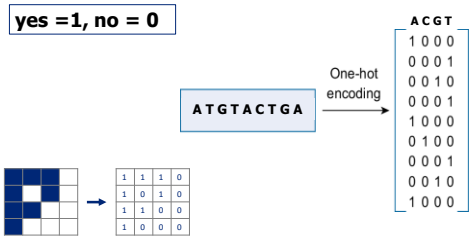
Ideal ML setup = complex tasks + relevant features + abundant data

Basics of ML

Basics of ML: features

- Feature vector: $x = (x_1, x_2, \dots, x_n)$
- All features must be converted to numbers:

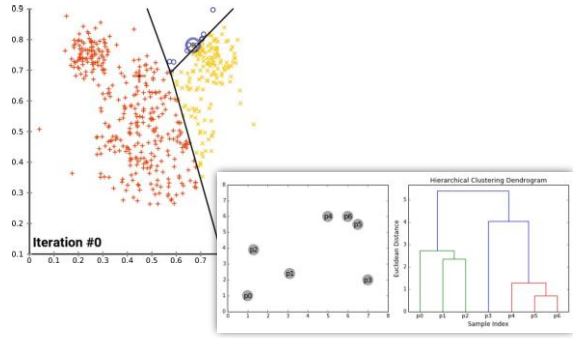
yes =1, no = 0



Basics of ML: types

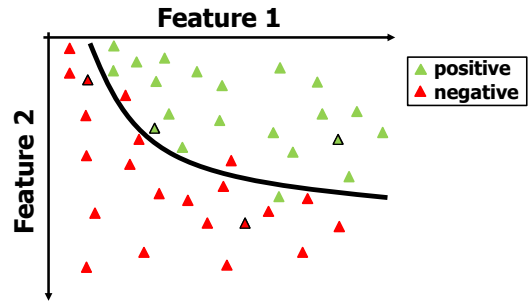
- Unsupervised learning
  - only features are available;
  - goal: cluster the data or reduce their dimensionality;
- Supervised learning
  - features and labels are available;
  - goal: learn to predict the label based on the features;
- Reinforcement learning, feature learning, anomaly detection, etc…

Basics of ML: unsupervised learning



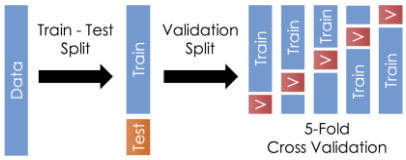
From en.wikipedia.org/wiki/K-means_clustering

Basics of ML: supervised learning



Basics of ML: supervised learning

- We want ML models to be generalizable = good at predicting labels for previously unseen data;
- It is essential to split the data into training set and test sets and use the latter for final evaluation only!
- To fine-tune an algorithm, K-fold cross validation is implemented:



Basics of ML: supervised learning

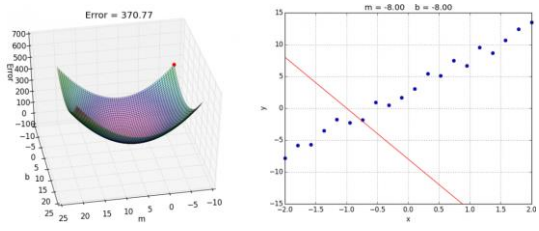
- Let $(x^{(i)}, y^{(i)})$ be our data set, where x are feature values, and y are labels;
- Any ML predictor is fundamentally a function $f(x)$:

$$f(\text{feature values}) = \text{label}$$

- Usually, a generic group of functions $f(x, \beta)$ is chosen, where β is a set of parameters;
- Then we "train" the ML predictor: pick such β^* that $f(x^{(i)}, \beta^*)$ is as close to $y^{(i)}$ as possible.

Basics of ML: supervised learning

$$f(x) = m \cdot x + b$$



Recent applications

Recent applications: decision tree

Gene Pair	Interact?	Expression correlation	Shared localization?	Shared function?	Genomic distance
A–B	Yes	0.77	Yes	No	1 kb
A–C	Yes	0.91	Yes	Yes	10 kb
C–D	No	0.1	No	No	1 Mb

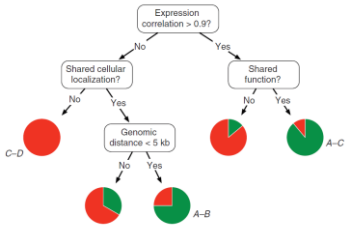


Figure 1 A hypothetical example of how a decision tree might predict protein-protein interactions.

Kingsford, Carl, and Steven L. Salzberg. "What are decision trees?." *Nature biotechnology* 26.9 (2008): 1011.

Recent applications: neural networks

Recent applications: ANNs for drug design

- **QSAR modeling for ligand binding activity;**
- **Structure generation;**
- **Synthetic pathway generation;**

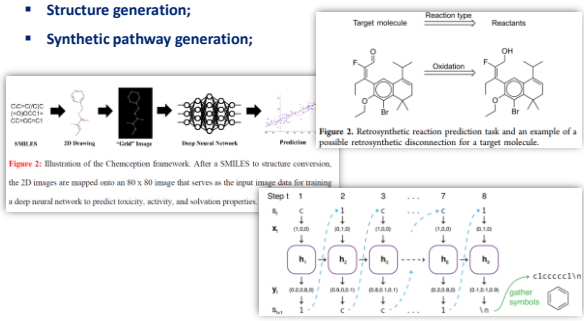
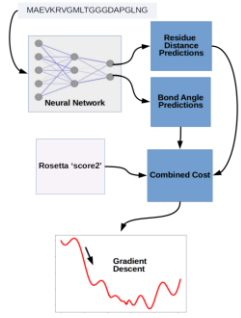


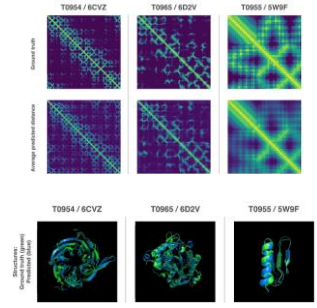
Figure 2: Illustration of the Chemception framework. After a SMILES to structure conversion, the 2D images are mapped onto an 80 x 80 image that serves as the input image data for training a deep neural network to predict toxicity, activity, and solvation properties.

Figure 2. Retrosynthetic reaction prediction task and an example of a possible retrosynthetic disconnection for a target molecule.

Goh et al. 2017 Chemception: a deep neural network with minimal chemistry knowledge matches the performance of expert-developed QSAR/QSPR models
Segler et al. 2018 Planning chemical syntheses with deep neural networks and symbolic AI. Nature

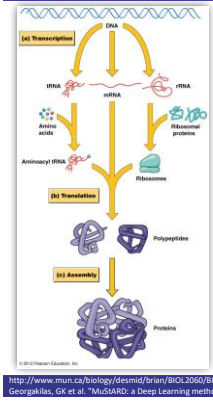
Recent applications: AlphaFoldfor protein folding

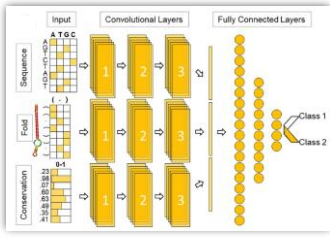




https://deepmind.com/blog/article/alphafold
https://dzone.com/articles/a-summary-of-deepminds-protein-folding-upset-at-ca

Recent applications: MuStARD for genome annotation





http://www.mun.ca/biology/desmid/brian/BIOL2060/BIOL2060-21/CB21.html
Georgakilas, GK et al. "MuStARD: a Deep Learning method for intra-and inter-species scanning identification of small RNA molecules." bioRxiv (2019)

Reading

- **Eraslan G et al. 2019 "Deep learning: new computational modelling techniques for genomics." Nature Reviews Genetics. (especially pages 2-6)**