Machine & deep learning for personalized oncology

Loic Verlingue

MD Medical Oncology

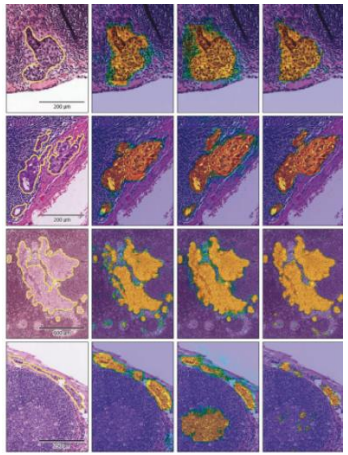
PhDc Data Science

21-22/01/2021

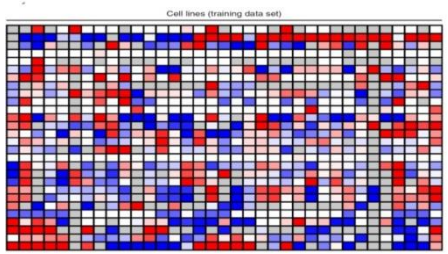
Plan

- A ML / DL workflow
- ML / DL is impacting
  - Diagnosis procedures
  - Drug development
  - Patients' monitoring
- Because of many cool things in deep learning

ML/DL in oncology



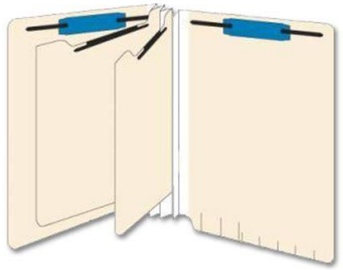
Diagnostics



Molecular biology & prognosis

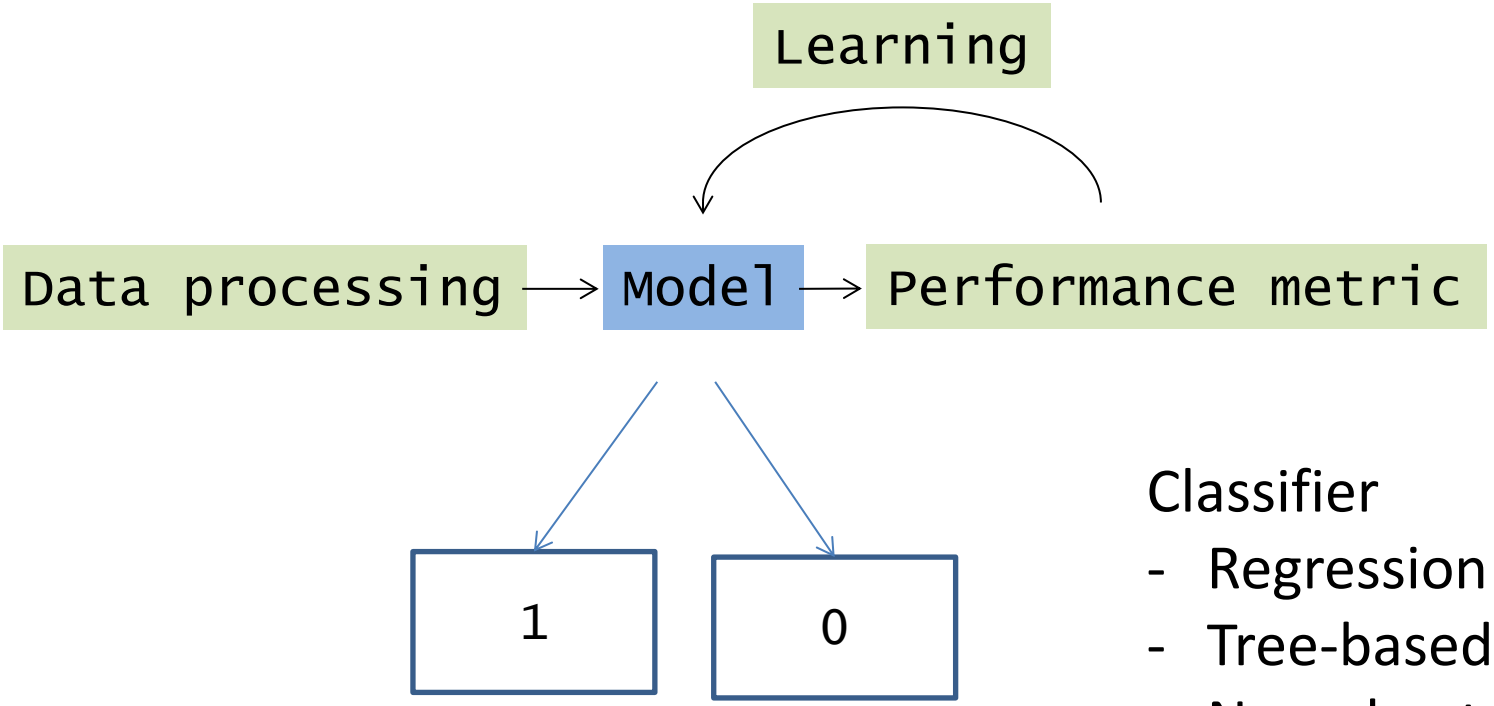
"Here's my sequence"
The New Yorker

Drug development & prediction



Monitoring patients

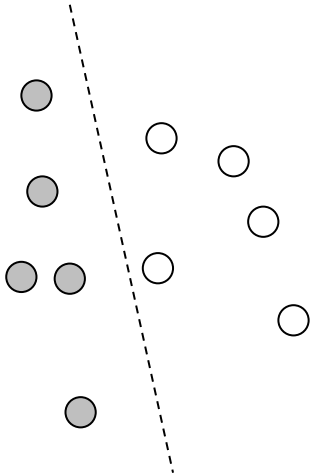
Machine learning workflow



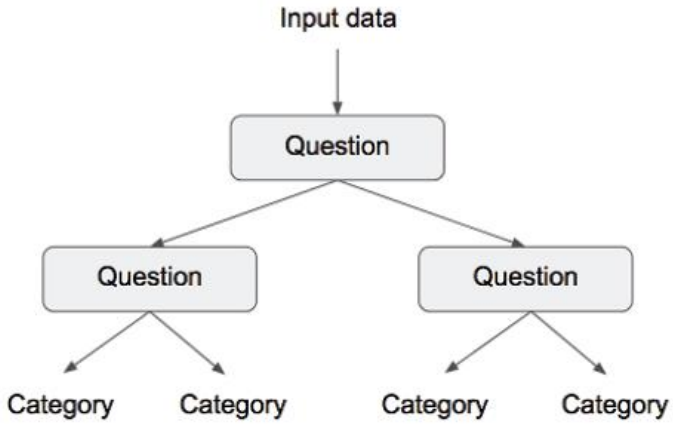
Classifier

- Regression
- Tree-based
- Neural net

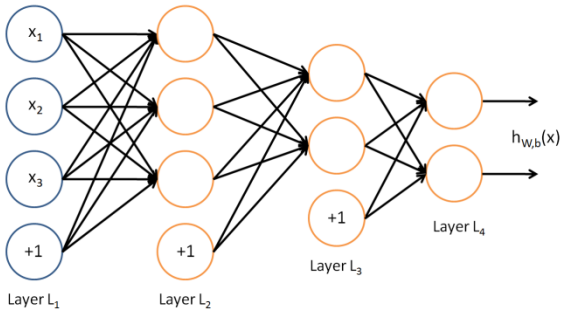
Families of models for classification



Regression /
Kernel approach eg SVM

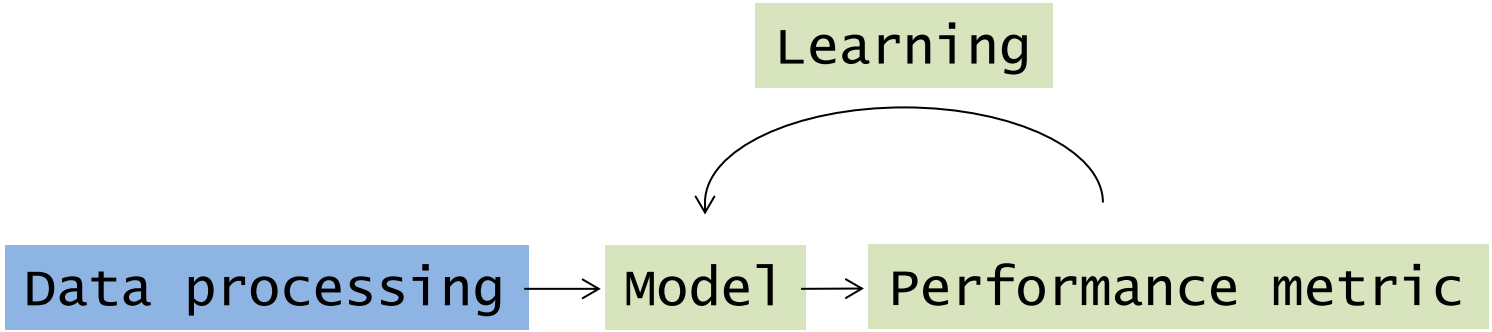


Decision tree /
Ensemble modeling



Multi Layer Percetron =
Artificial Neural Network

Data Processing



Numerical data -> ok for models

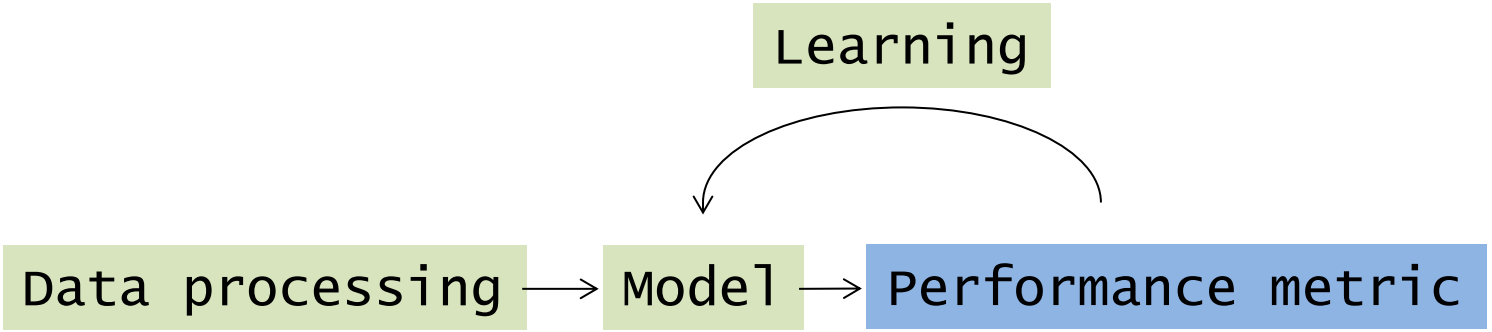
*

Natural langage data -> turn to numerical

*

Images -> use pixels values

Evaluation metrics



Comment évaluer les prédictions du modèle?

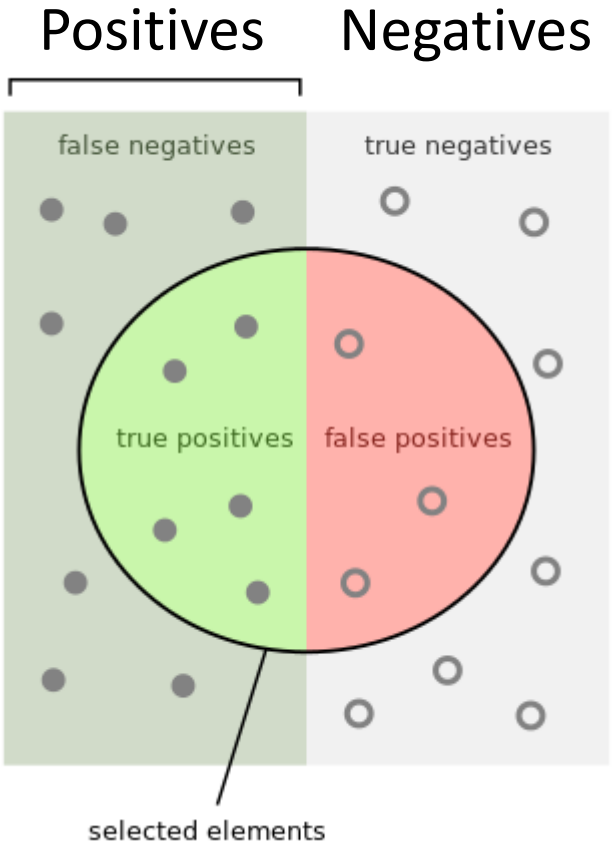
Métriques pour classification binaire

→ Matrice de confusion (1=SF)

		Classe réelle	
		0	1
Classe prédite	0	TN	FN
	1	FP	TP

→ **Que préférez-vous evaluer?**

Métriques pour classification binaire



How many relevant items are selected? e.g. How many sick people are correctly identified as having the condition.

Sensitivity= $\frac{\text{true positives}}{\text{true positives} + \text{false negatives}}$

How many negative selected elements are truly negative? e.g. How many healthy peple are identified as not having the condition.

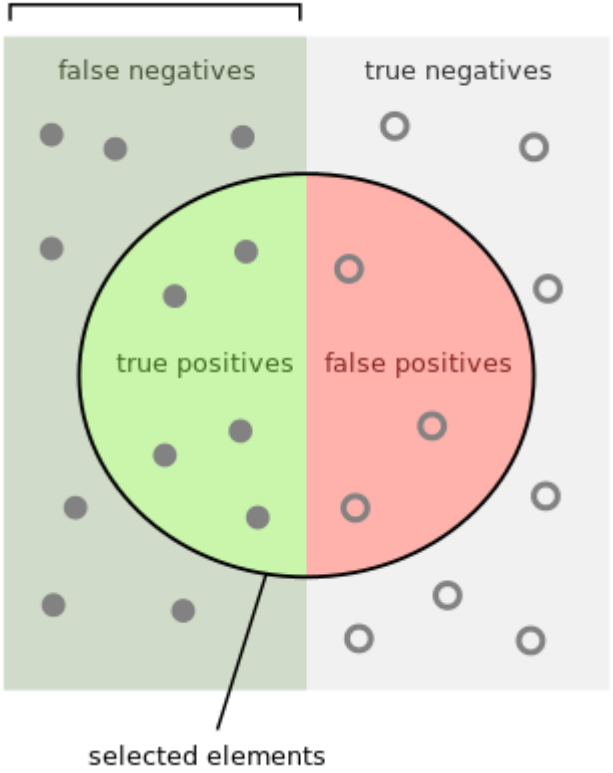
Specificity = $\frac{\text{true negatives}}{\text{true negatives} + \text{false positives}}$

		Classe réelle	
		0	1
Classe prédite	0	TN	FN
	1	FP	TP

wikipedia

Métriques pour classification binaire

Positives Negatives



How many selected items are relevant?

$$\text{Precision} = \frac{\text{true positives}}{\text{true positives} + \text{false positives}}$$

How many relevant items are selected?

$$\text{Recall} = \frac{\text{true positives}}{\text{true positives} + \text{false negatives}}$$

		Classe réelle	
		0	1
Classe prédite	0	TN	FN
	1	FP	TP

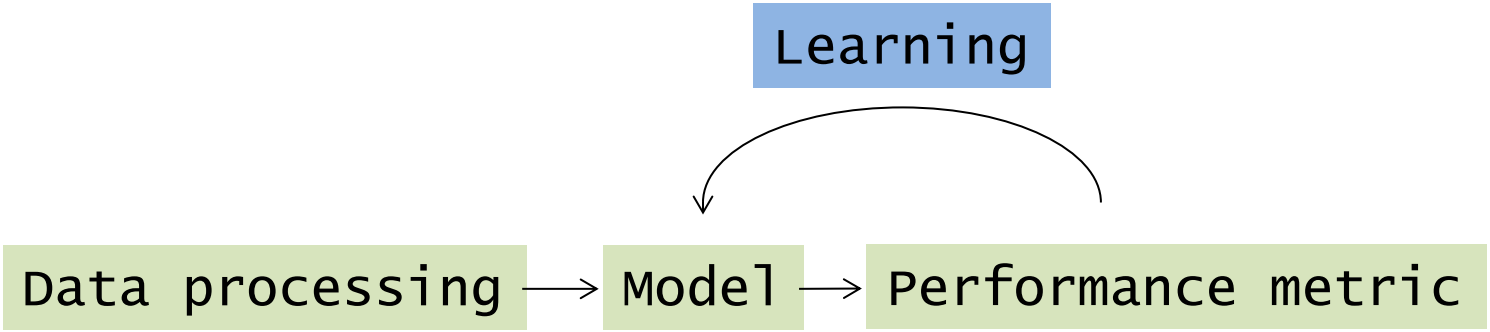
wikipedia

Métriques pour classification binaire

		True condition			
	Total population	Condition positive	Condition negative	Prevalence $= \frac{\Sigma \text{ Condition positive}}{\Sigma \text{ Total population}}$	Accuracy (ACC) $= \frac{\Sigma \text{ True positive} + \Sigma \text{ True negative}}{\Sigma \text{ Total population}}$
Predicted condition	Predicted condition positive	**True positive**, Power	**False positive**, Type I error	Positive predictive value (PPV), Precision $= \frac{\Sigma \text{ True positive}}{\Sigma \text{ Predicted condition positive}}$	False discovery rate (FDR) $= \frac{\Sigma \text{ False positive}}{\Sigma \text{ Predicted condition positive}}$
	Predicted condition negative	**False negative**, Type II error	**True negative**	False omission rate (FOR) $= \frac{\Sigma \text{ False negative}}{\Sigma \text{ Predicted condition negative}}$	Negative predictive value (NPV) $= \frac{\Sigma \text{ True negative}}{\Sigma \text{ Predicted condition negative}}$
		True positive rate (TPR), Recall, Sensitivity, probability of detection $= \frac{\Sigma \text{ True positive}}{\Sigma \text{ Condition positive}}$	False positive rate (FPR), Fall-out, probability of false alarm $= \frac{\Sigma \text{ False positive}}{\Sigma \text{ Condition negative}}$	Positive likelihood ratio (LR+) $= \frac{\text{TPR}}{\text{FPR}}$	Diagnostic odds ratio (DOR) $= \frac{\text{LR+}}{\text{LR−}}$
		False negative rate (FNR), Miss rate $= \frac{\Sigma \text{ False negative}}{\Sigma \text{ Condition positive}}$	Specificity (SPC), Selectivity, True negative rate (TNR) $= \frac{\Sigma \text{ True negative}}{\Sigma \text{ Condition negative}}$	Negative likelihood ratio (LR−) $= \frac{\text{FNR}}{\text{TNR}}$	F_1 score $= \frac{2}{\frac{1}{\text{Recall}} + \frac{1}{\text{Precision}}}$

wikipedia

Quelle méthode d'apprentissage ?

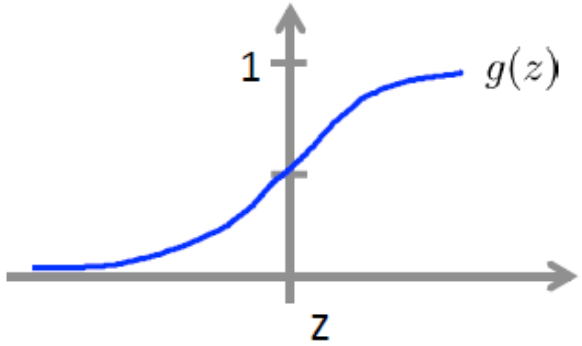


Probability to belong to a class

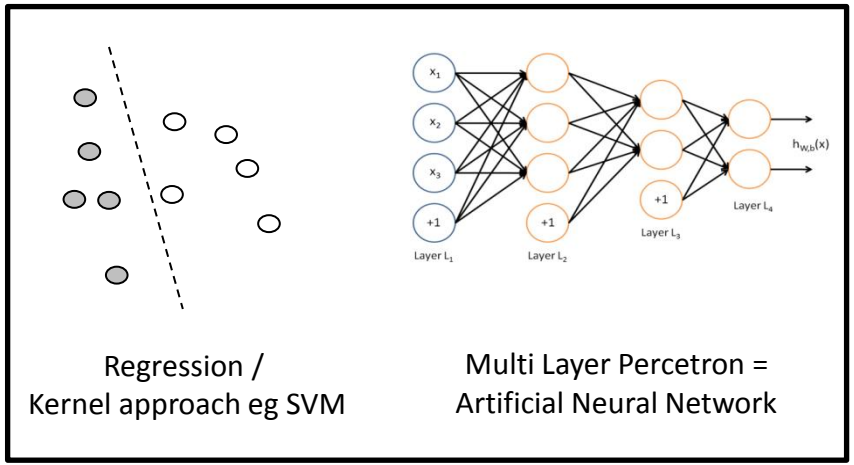
Logistic regression **with a sigmoid function**

$$h_\theta(x) = g(\theta^T x)$$

$$g(z) = \frac{1}{1+e^{-z}}$$



Ok for:

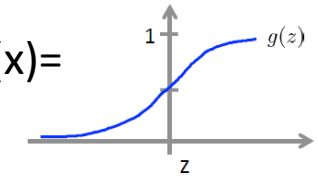


Calculate the cost / error

prediction

Logistic regression cost function

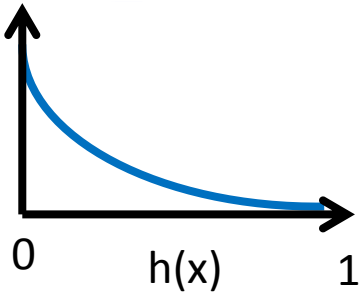
h(x)=



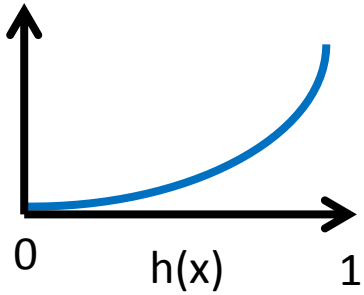
$$J(\theta) = \frac{1}{m}\sum_{i=1}^{m} \text{Cost}(h_\theta(x^{(i)}), y^{(i)})$$ ← truth

$$= -\frac{1}{m}[\sum_{i=1}^{m} y^{(i)} \log h_\theta(x^{(i)}) + (1 - y^{(i)}) \log (1 - h_\theta(x^{(i)}))]$$

If y=1



If y=0



Parameters' updates with gradient descent

Compute the cost $J(\theta) = \frac{1}{m} \sum_{i=1}^{m} \text{Cost}(h_\theta(x^{(i)}), y^{(i)})$

Gradient descent:

Repeat $\{$

$\theta_j := \theta_j - \alpha \frac{\partial}{\partial \theta_j} J(\theta)$

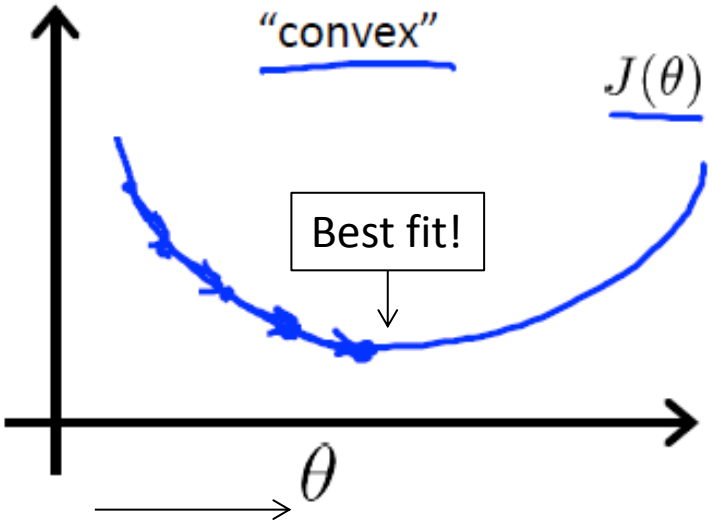
$\}$

Derivative of the cost

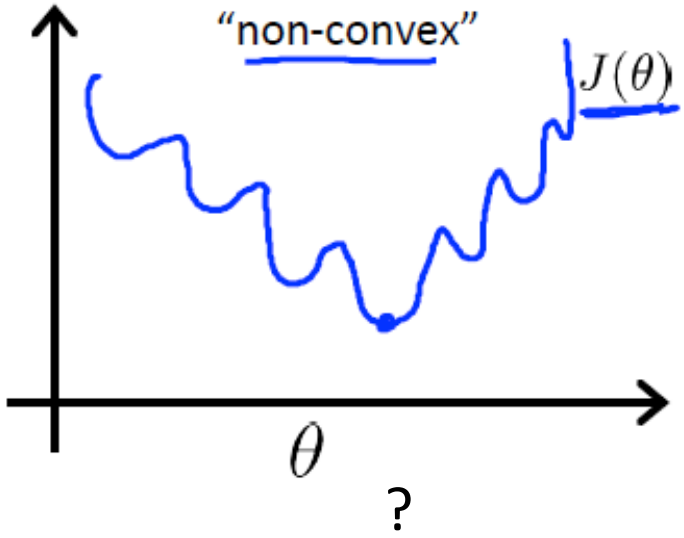
Parameters' updates

Learning rate

Optimisation of the cost



Updates with gradient descent



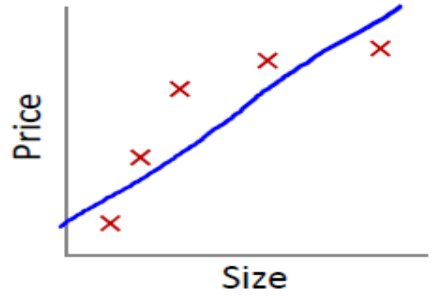
?

Figures from Andrew Ng Coursera

Etes vous sûr que les futurs exemples seront bien prédits?

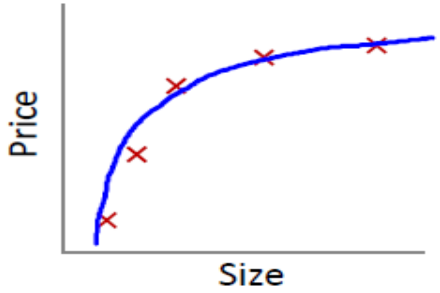
Généralisation du modèle

Biais ⟷ Variance



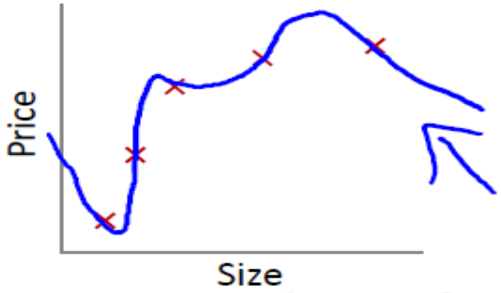
$\rightarrow \theta_0 + \theta_1 x$

"Underfit" "High bias"



$\rightarrow \theta_0 + \theta_1 x + \theta_2 x^2$

"Just right"



$\rightarrow \theta_0 + \theta_1 x + \theta_2 x^2 + \theta_3 x^3 + \theta_4 x^4$

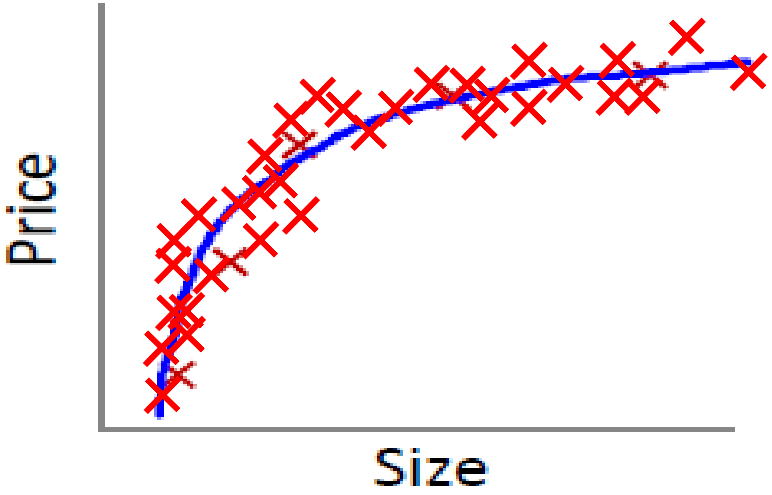
"Overfit" "High variance"

Overfitting: If we have too many features, the learned hypothesis may fit the training set very well ($J(\theta) = \frac{1}{2m} \sum_{i=1}^{m} (h_\theta(x^{(i)}) - y^{(i)})^2 \approx 0$), but fail to generalize to new examples (predict prices on new examples).

Andrew Ng

The problem of overfitting

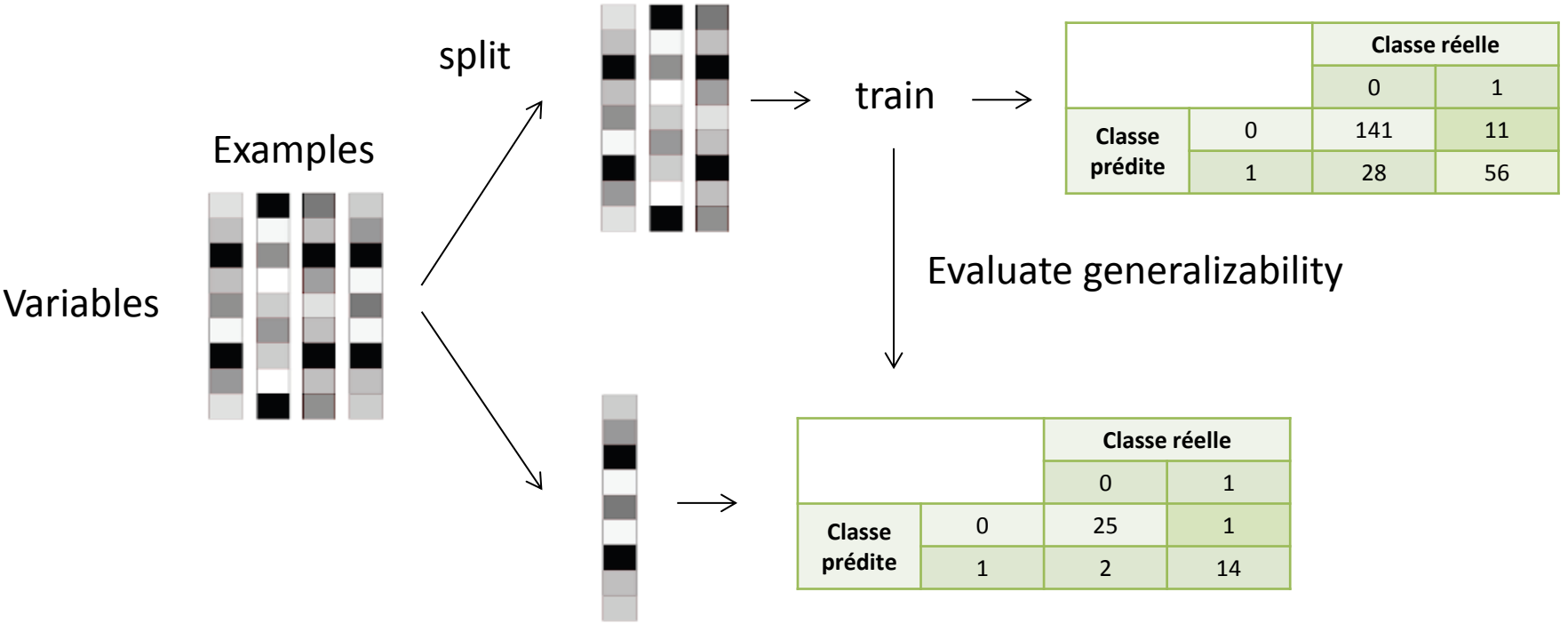
One solution: increase observations



Other solutions: penalize the learning

constrain the model

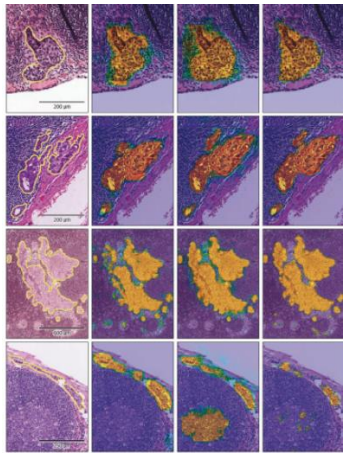
ML generalization testing workflow

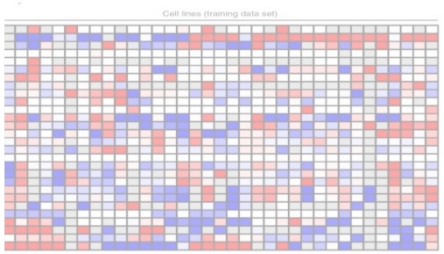


		Classe réelle	
		0	1
Classe prédite	0	141	11
	1	28	56

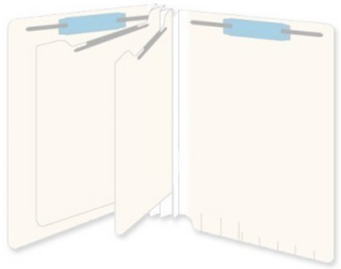
		Classe réelle	
		0	1
Classe prédite	0	25	1
	1	2	14

ML/DL in oncology





"Here's my sequence"
The New Yorker



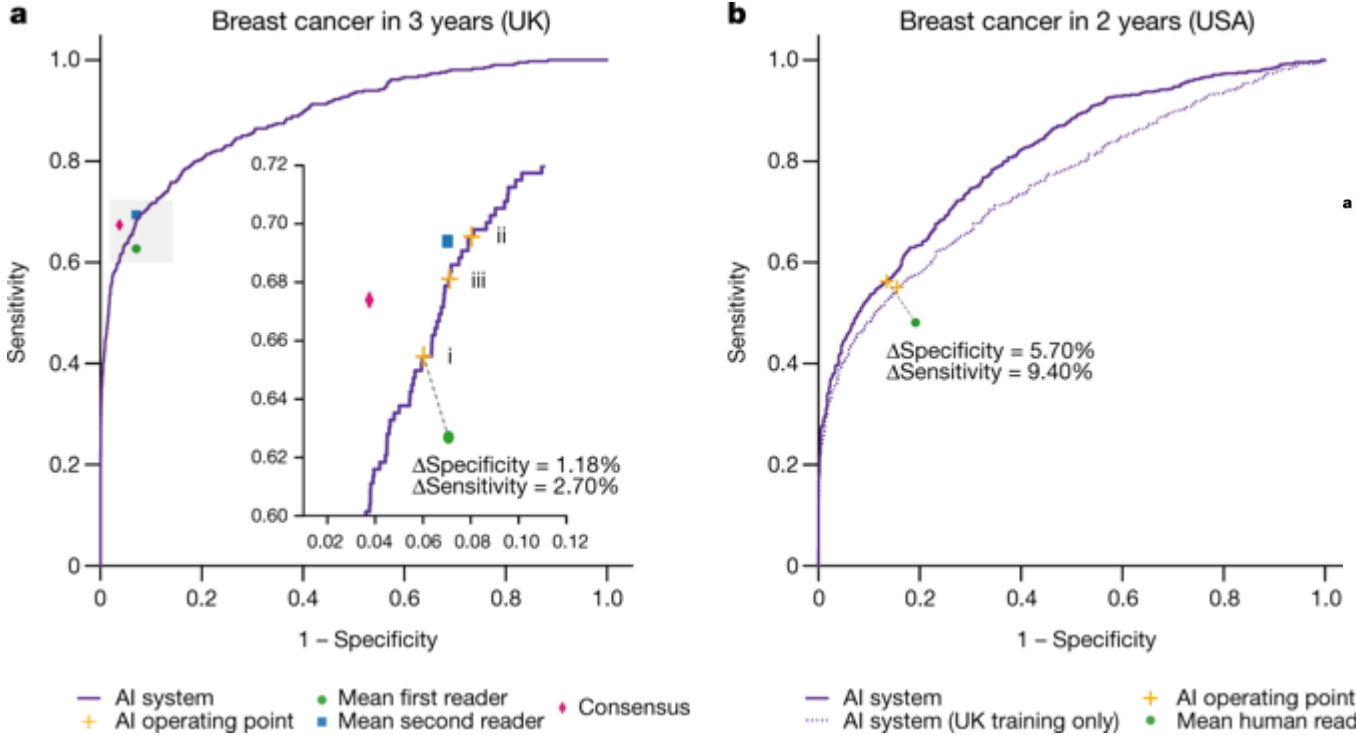
Diagnostics

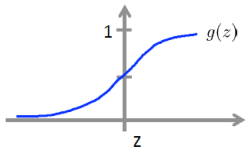
Molecular biology & pronostic

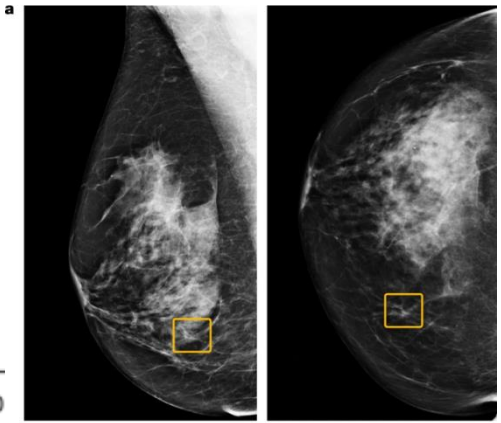
Drug development & prediction

Monitoring patients

Breast cancer screening





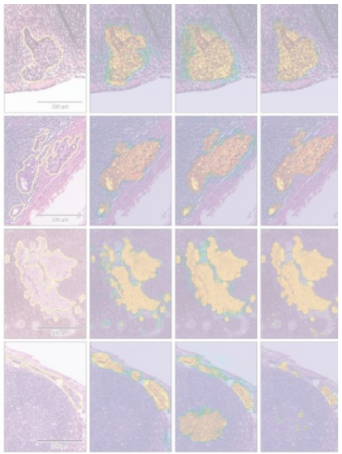


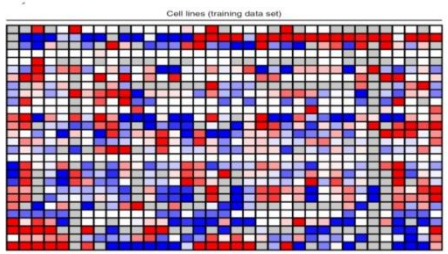
International evaluation of an AI system for breast cancer screening, Scott Mayer McKinney, Marcin Sieniek, […]Shravya Shetty, Nature volume 577, pages89–94(2020)

Many others

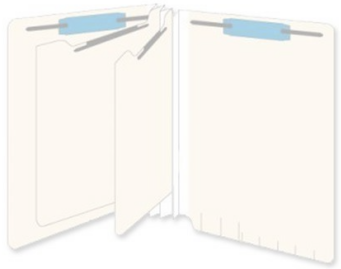
Main Objective	Tumor type	Image Modality	Number of data points (training set + validation/test set)	Endpoints and results	Reference
Diagnosis	Lung cancer	Low dose CT-scan	102 + 70	Prediction of malignancy in lung nodules. Accuracy: 70-77%	Liu et al., 2016[5]
Diagnosis	Lung cancer	CT-scan	312 + 288	Malignant nodules accuracy: 80% Benign nodules accuracy: 79%	Hawkins et al., 2016[6]
Diagnosis	Lung ADK	CT-scan	54 + 86	Correlation with invasive versus non-invasive adenocarcinomas: Spearman R = 0.87-0.89 (p<0.0001)	Maldonado et al., 2013[7]
Diagnosis	NSCLC	CT-scan	81 + 48	Distinguish ADK versus SCC: AUC=0.893-0.905	Zhu et al., 2018[8]
Diagnosis	NSCLC	CT-scan	160 + 235	Discrimination between invasive and non-invasive ADK: Accuracy 84.0-90.8%	Fan et al., 2018[9]
Diagnosis	Prostate Cancer	MRI	54 + 0	Radiomics model for cancer diagnosis: AUC=0.955	Wang et al., 2017[10]
Diagnosis	Prostate Cancer	MRI	147 + 0	Benign versus malignant lesions: Accuracy 93%	Fehr et al., 2015[11]
Molecular characterization	Breast Cancer	MRI	91 + 0	Radiomics features used to predict molecular subtypes, AUC: 0.65-0.89	Li et al., 2016[12]
Molecular characterization	Breast cancer	MRI	48 + 0	Significant correlation between radiomics features and luminal B subtype (p=0.0015)	Mazurowski et al., 2014[13]
Molecular characterization	Breast cancer	MRI	461 + 461	Prediction of molecular subtype: Luminal A, AUC=0.697 TNBC, AUC=0.654 ER status, AUC=0.649 PR status, AUC=0.622	Saha et al., 2018[14]
Molecular characterization	NSCLC	PET-CT	26 + 0	Association with gene expression pathways with an accuracy ranging from 59% - 83%	Gevaert et al., 2012[15]
Molecular characterization	Lung ADK	CT-scan	385 + 0	Prediction of EGFRm status with combination of radiomics signature and clinical variables: AUC=0.778	Liu et al., 2016[16]
Molecular characterization	GBM	MRI	23 + 0	Correlation of radiomics features with multiple molecular pathways	Jamshidi et al., 2014[17]
Molecular characterization	GBM	MRI	22 + 110	Significant associations with tumor hypoxia (p=0.012); proliferation gene-expression signature (p=0.0017); EGFR protein overexpression (p<0.002)	Diehn et al., 2008[18]
Molecular characterization	HNSCC	PET-CT + CT-scan	42 + 79	Correlation with hypoxia: AUC=0.755-0.833 Hypoxia measured by ^{18}F-FMISO PET-CT	Crispin-Ortuzar et al., 2018[19]
Molecular characterization	CRC	CT-scan	61 + 56	Radiomics signature predicts: KRAS mutation, AUC=0.829-0.869 NRAS mutation, AUC=0.757-0.686 BRAF mutation, AUC=0.833-0.857	Yang et al., 2018[20]
Molecular characterization	Rectal cancer	MRI	114 + 0	pCR diagnosis after neo-adjuvant treatment : AUC=0.93	Horvat et al., 2018[21]
Prognosis	NSCLC & HNSCC	CT-scan	474 + 545	Radiomics signature correlates with stage and OS: NSCLC CI=0.65 HNSCC CI=0.69	Aerts et al., 2014[22]
Prognosis	Lung ADK	CT-scan	98 + 84	Risk of metastases relapse CI=0.61	Coroller et al., 2015[23]
Prognosis	NSCLC	CT-scan	22 + 0	Recurrence prediction based on post-treatment imaging: Accuracy 73-77%	Mattonen et al., 2015[24]
Prognosis	NSCLC	PET-CT	70 + 31	Risk of distant metastasis: CI=0.71 When combining with histologic type: CI=0.80	Wu et al., 2016[25]
Prognosis	GBM	MRI	79 + 40	Prognosis OS (p=0.001)	Kickingereder et al., 2016[26]
Prognosis	GBM	MRI	121 + 60	Prognosis prediction errors decreased 36% for PFS and 37% for OS compared to clinical features alone	Kickingereder et al., 2018[27]
Prognosis	GBM	MRI	126 + 165	Significant stratification for OS (p=0.001) and PFS (p=0.000021)	Grossman et al., 2017[28]
Prognosis	Colorectal cancer	CT-scan	326 + 200	Lymph node metastasis prediction: CI=0.78	Huang et al., 2016[29]
Prognosis	Nasopharyngeal carcinoma	MRI	88 + 30	Radiomics signature associated with PFS: CI=0.761	Zhang et al., 2018[30]
Prognosis	Breast Cancer	MRI	84 + 0	Prediction of risk recurrence concordance as assessed by PAM50 or Mammaprint: AUC=0.55-0.88	Li et al., 2016[31]
Prognosis	Breast Cancer	MRI	92 + 54	Sentinel lymph node metastasis based on radiomics features of pre-operative MRI: AUC=0.770-0.863	Dong et al., 2018[32]
Prognosis	Breast cancer	MRI	194 + 100	Radiomic signature correlate with DFS: p=0.002 in the training set P=0.036 in the validation set	Park et al., 2018[33]
Prognosis	High-grade osteosarcoma	CT-scan	102 + 48	OS prognosis: AUC=0.73-0.86	Wu et al., 2018[34]
Treatment effect	NSCLC	PET-CT	47 + 0	Correlation of radiomics features with treatment response (p=0.01)	Cook et al., 2015[35]

ML/DL in oncology





"Here's my sequence"
The New Yorker



Diagnostics

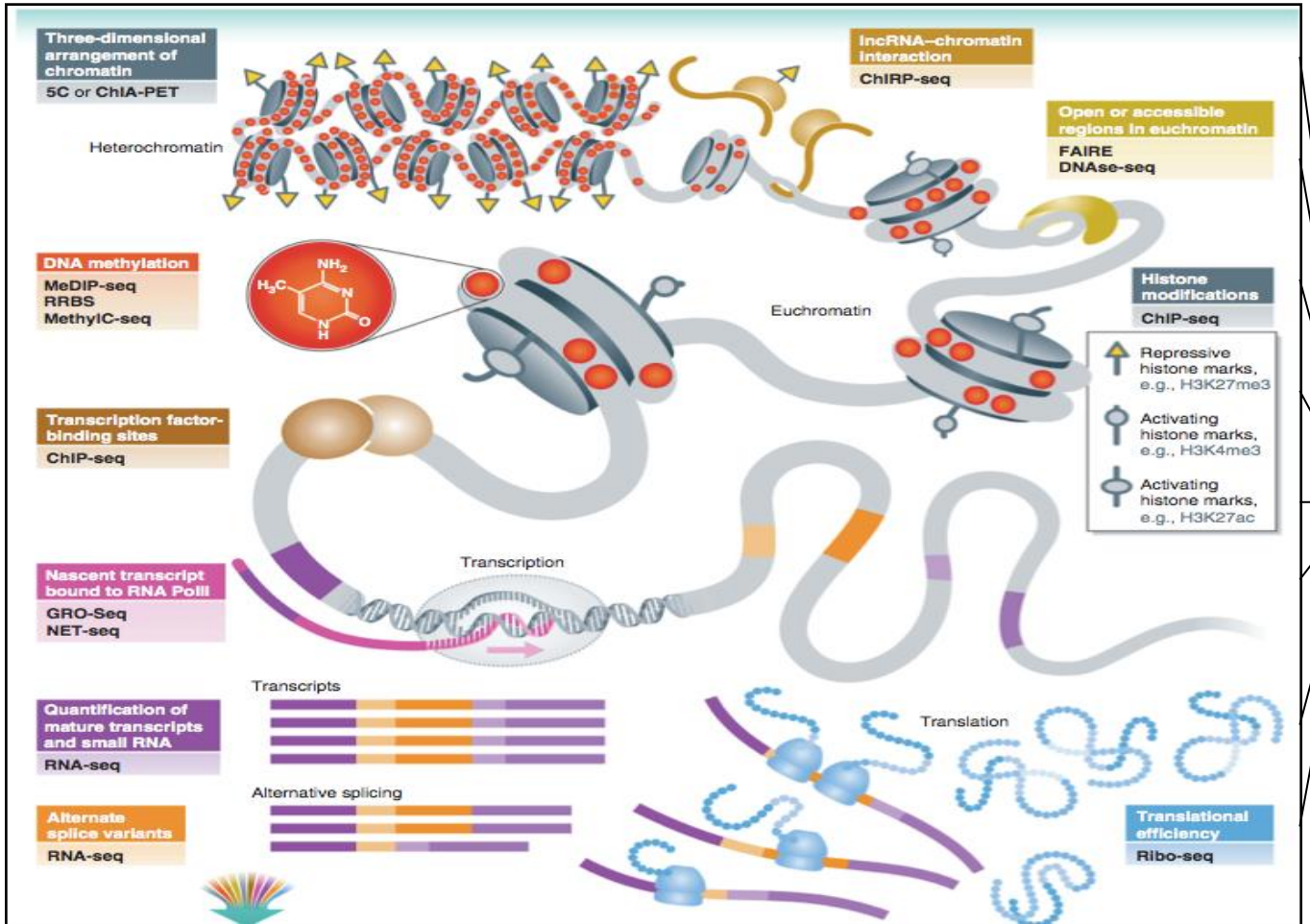
Molecular biology & pronostic

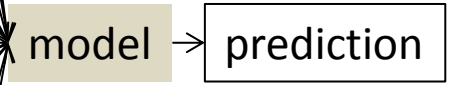
Drug development & prediction

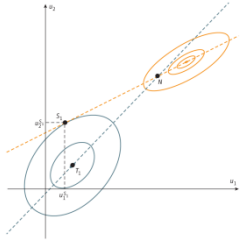
Monitoring patients

Cancer/patient selection

Complexity



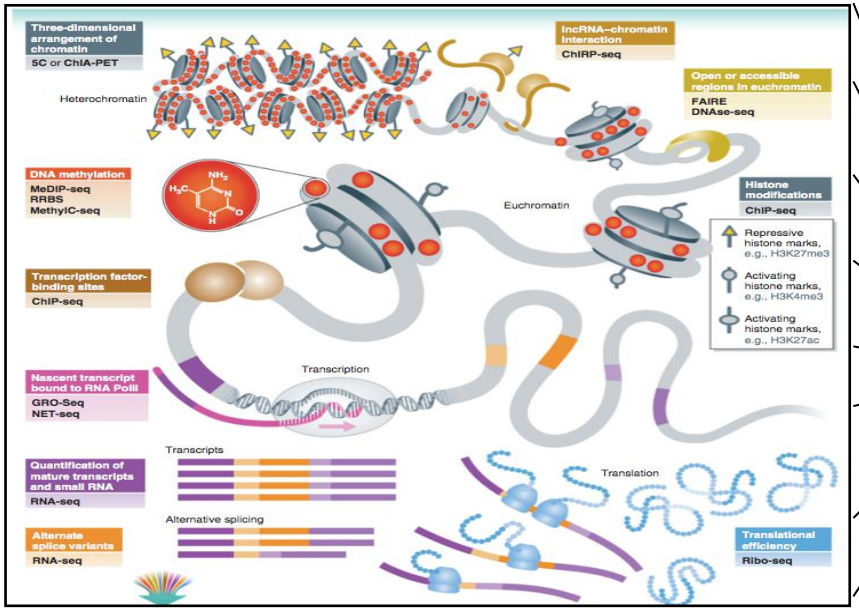


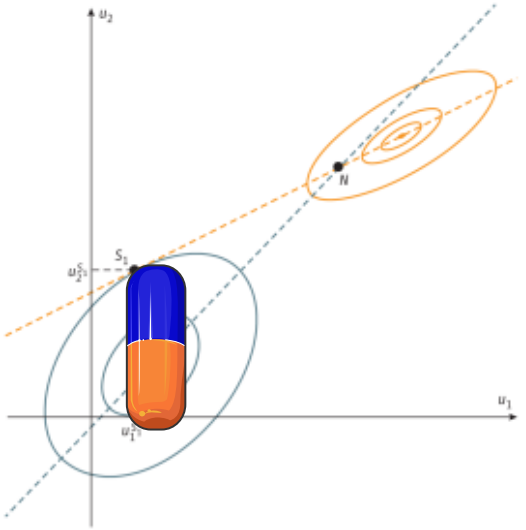


WW Soon et al. 2013

Cancer/patient selection

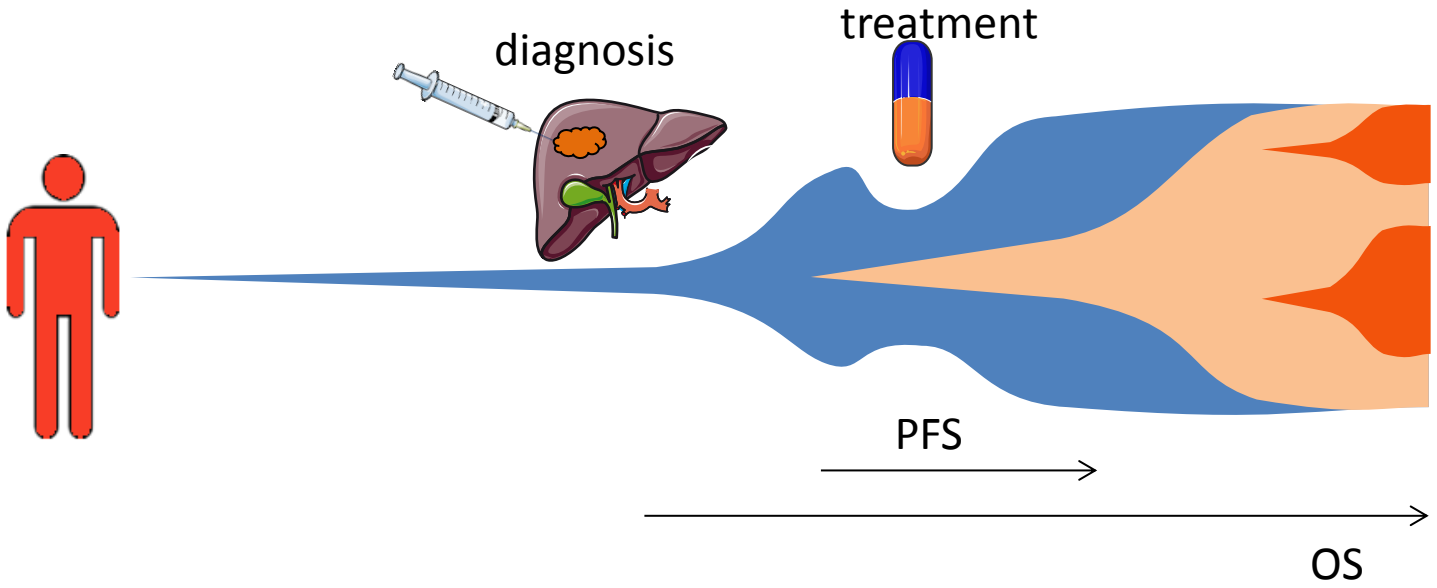
Models



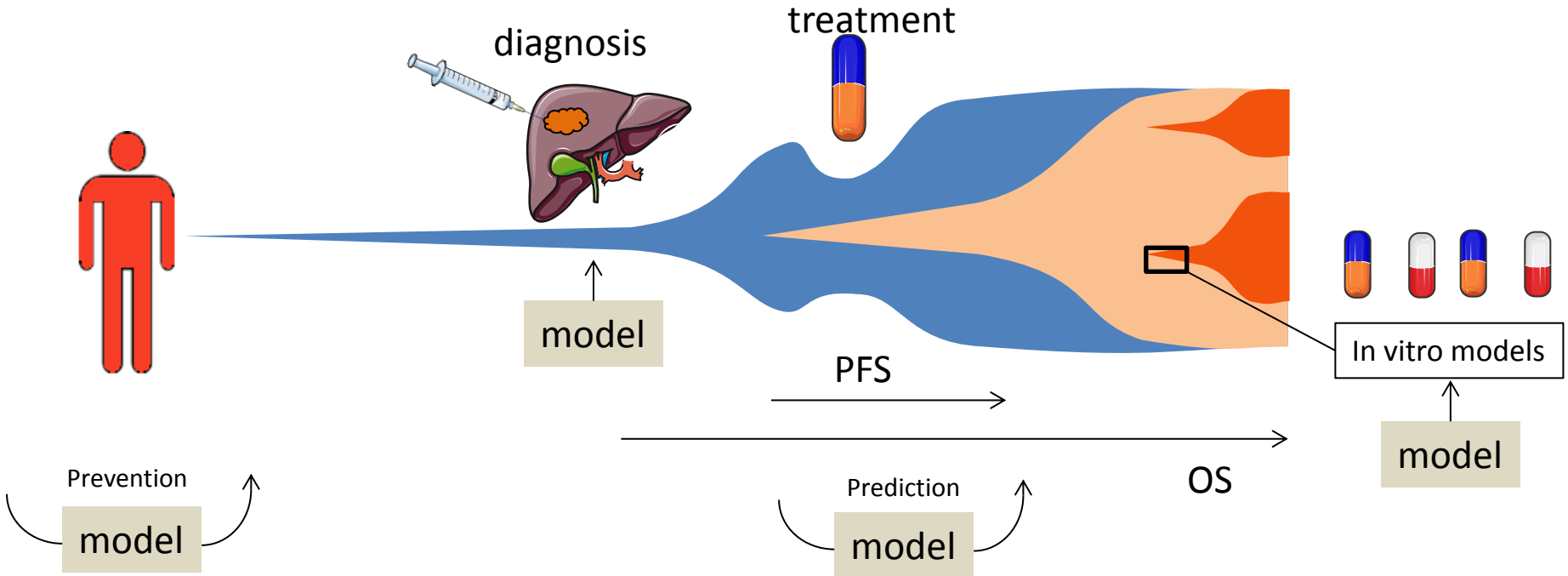


model → prediction

The patient & his tumor's biology



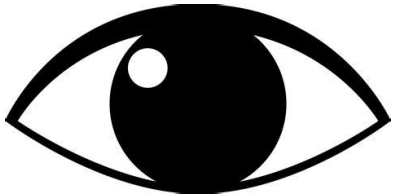
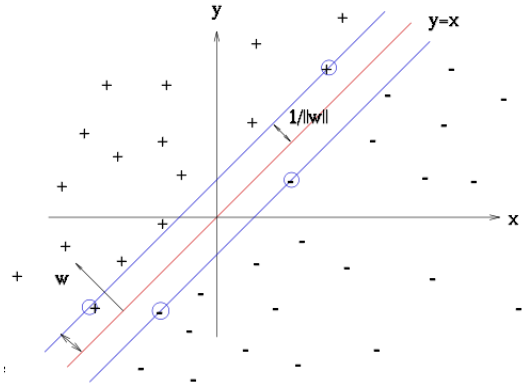
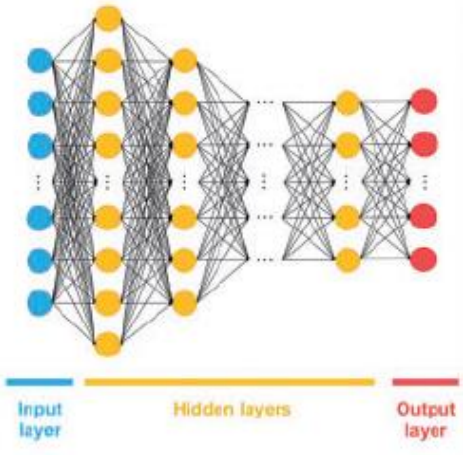
What do we expect from models?



=3P + Personalization!

Models

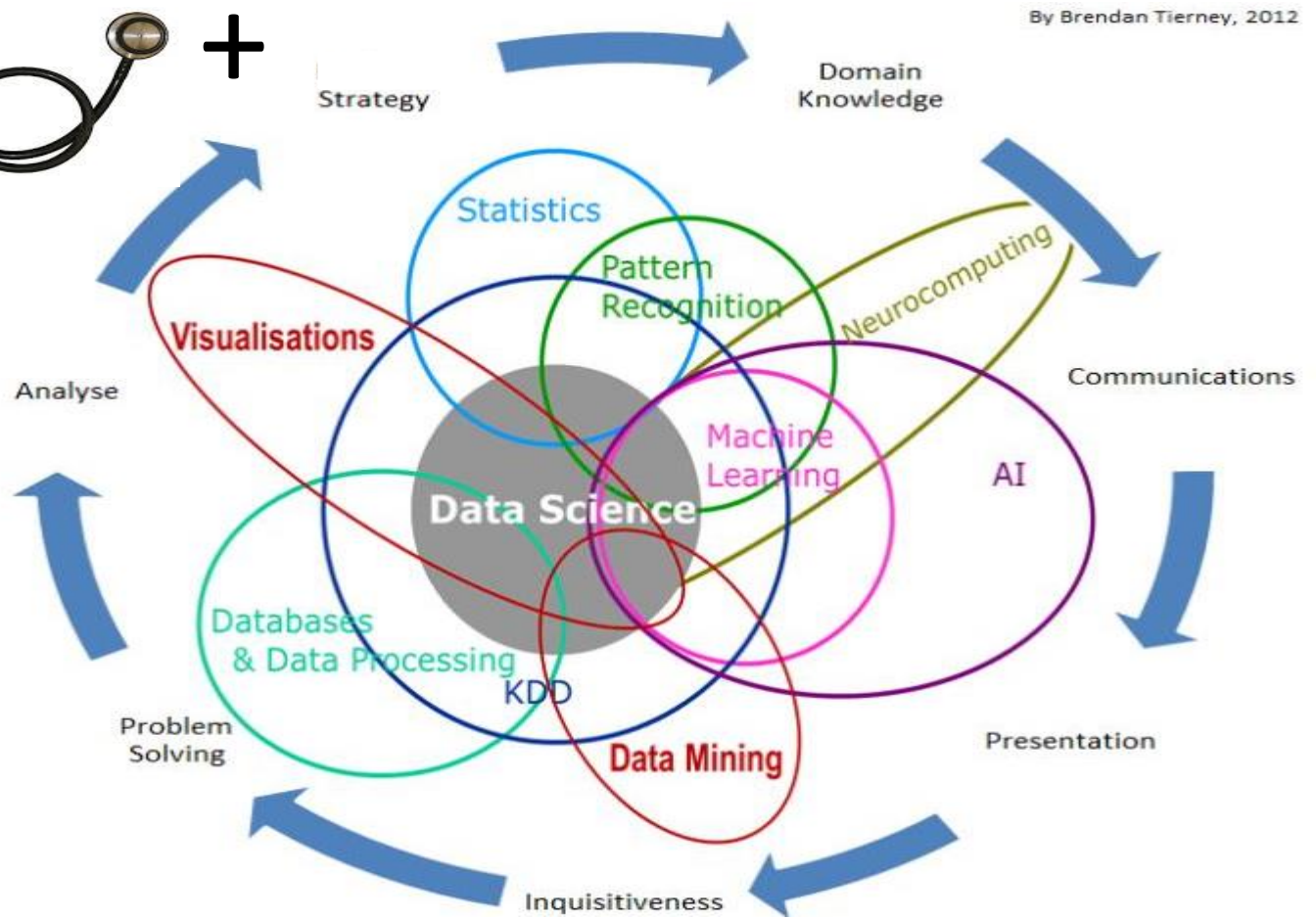
The models you have

	Human	Statistics	Deep learning
			
	Use your knowledge and reasoning	Linear models easy to explain	Non-linear models data-expensive
Examples:	Christophe Massard	Cox model logReg eg: RMH	Deep neural network

Cancer/patient selection

+

The tools you need



What is cool about deep learning?

You can play with formalisms & architectures

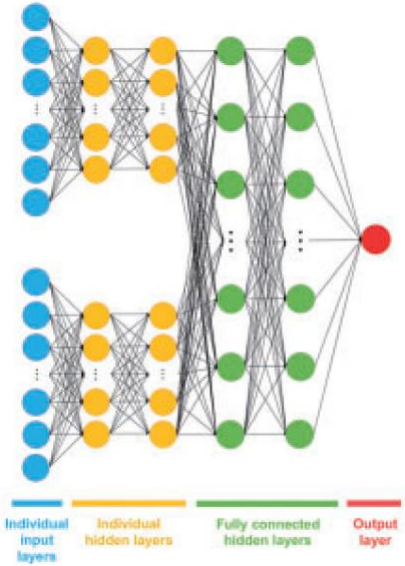
For what ?

To better fit your data and your questions!

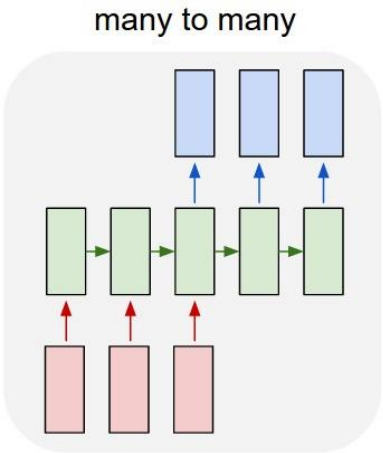
So be innovative!

Find your architecture

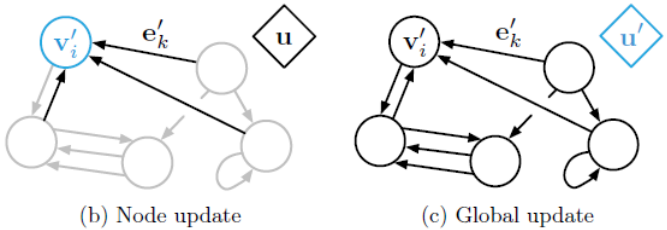
Drugs and proteins
to predict bioactivity
→ **Multitask NN**



Patients' folder
to predict pateints' outcome
→ **Recurrent neural nets**



Molecular data
to predict biological behaviors
→ **Graphical networks**

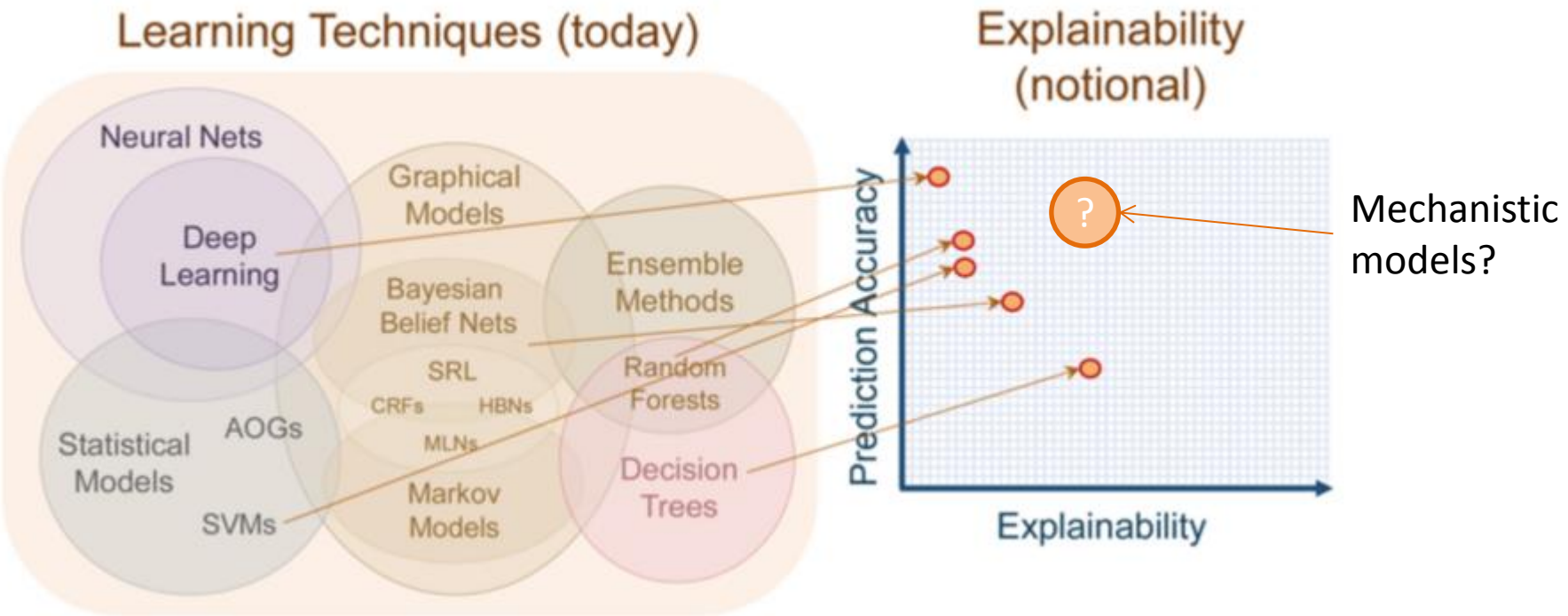


Data science team at

DITEP
Drug Development Department

afaq ISO 9001 Qualité AFNOR CERTIFICATION

Intepretability of ML/DL

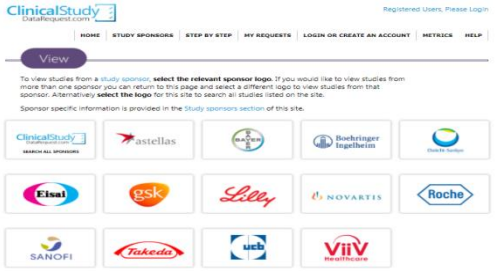


http://nautil.us/issue/40/learning/is-artificial-intelligence-permanently-inscrutable

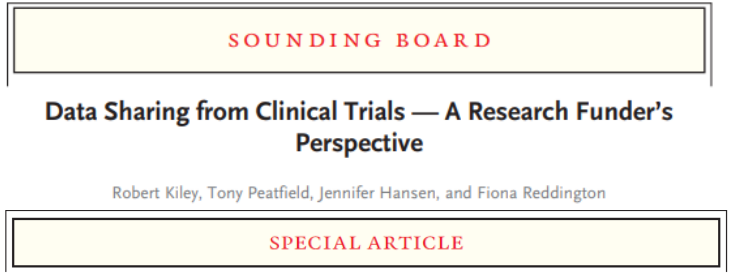
Data

Where are the data?

ClinicalStudy DataRequest.com



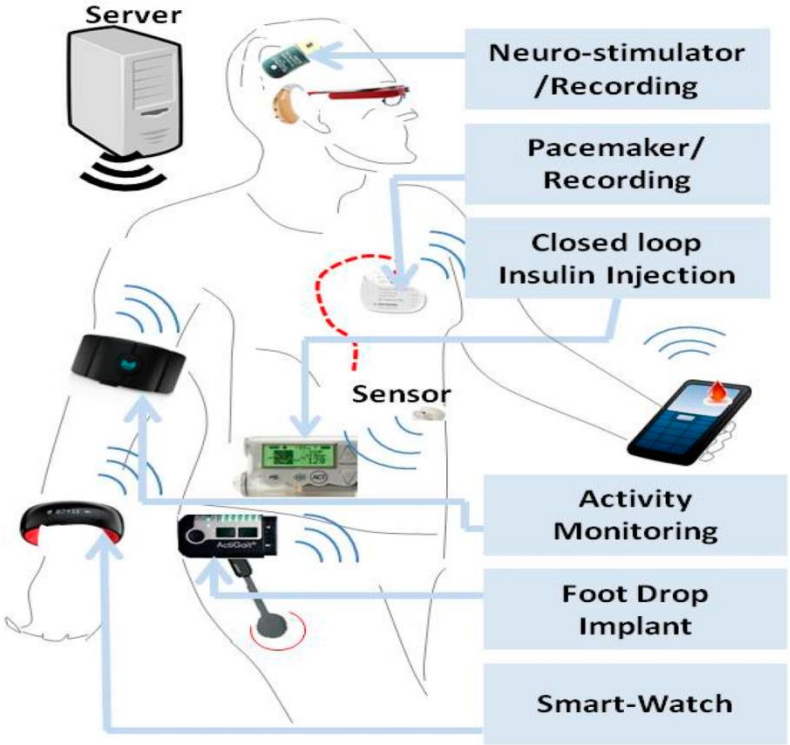
biobank uk
Improving the health of future generations

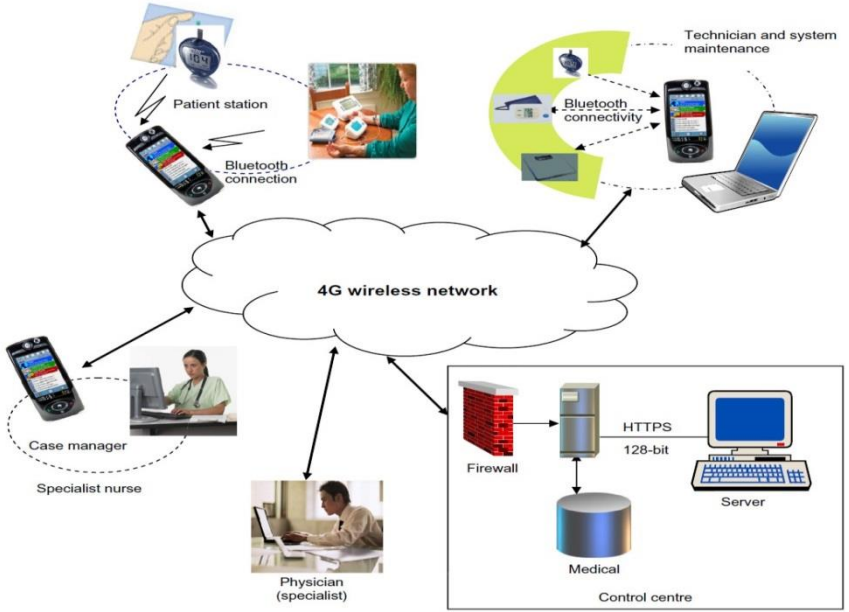


Clinical Trial Participants' Views of the Risks and Benefits of Data Sharing

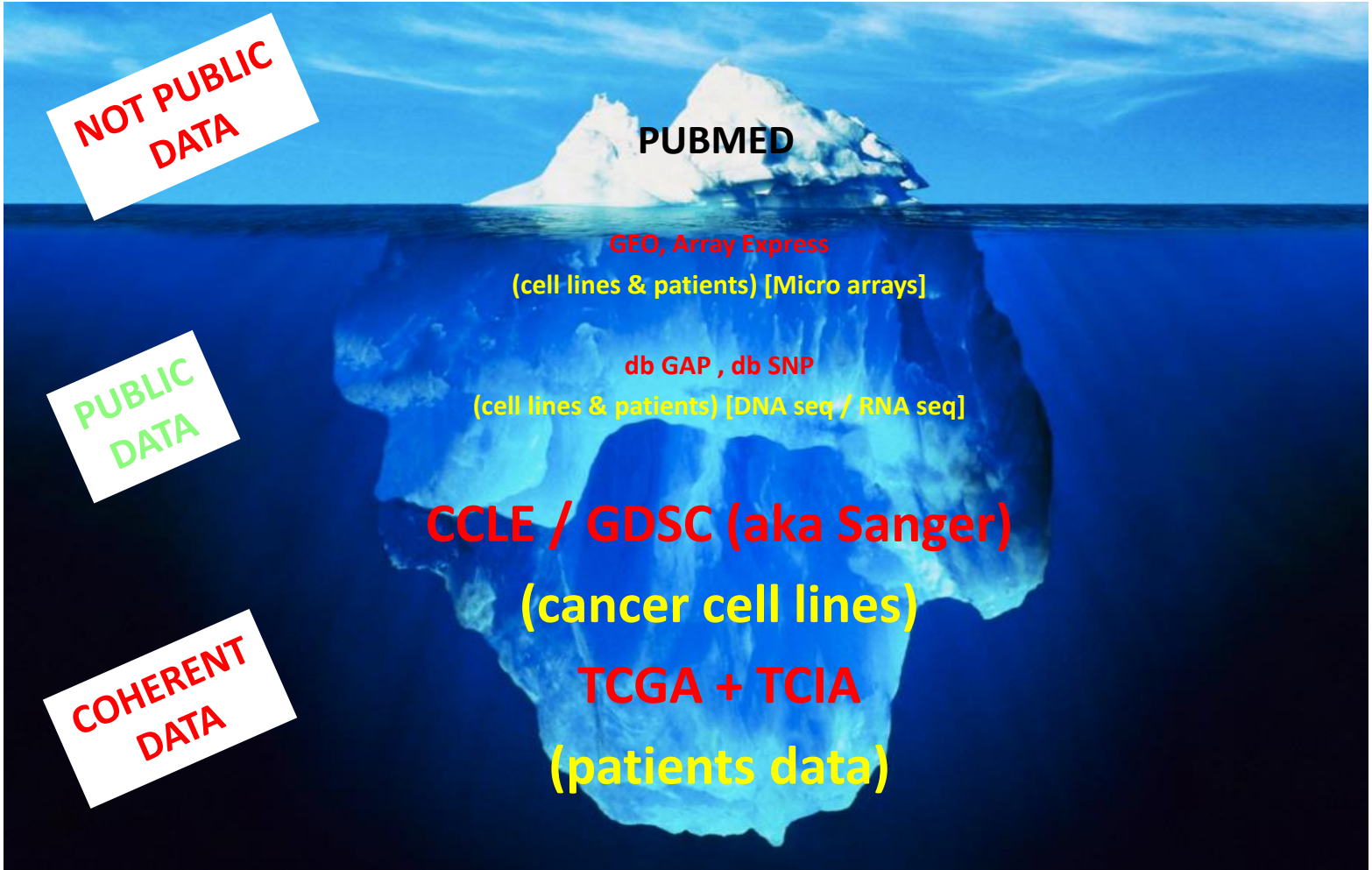
Michelle M. Mello, J.D., Ph.D., Van Lieou, B.S., and Steven N. Goodman, M.D., Ph.D.

New flow of clinical data





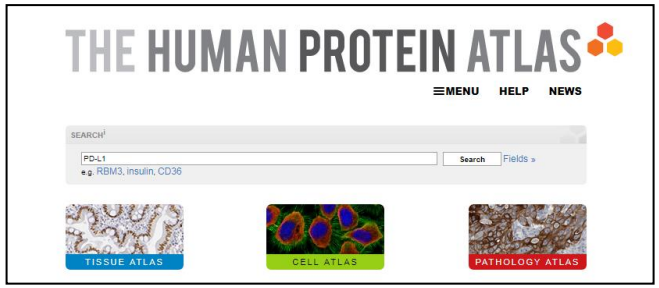
Where are the data?



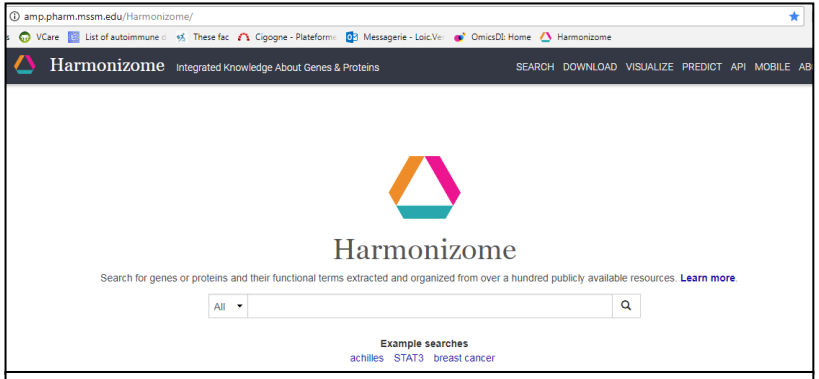
Search is made easy

Traditional databases

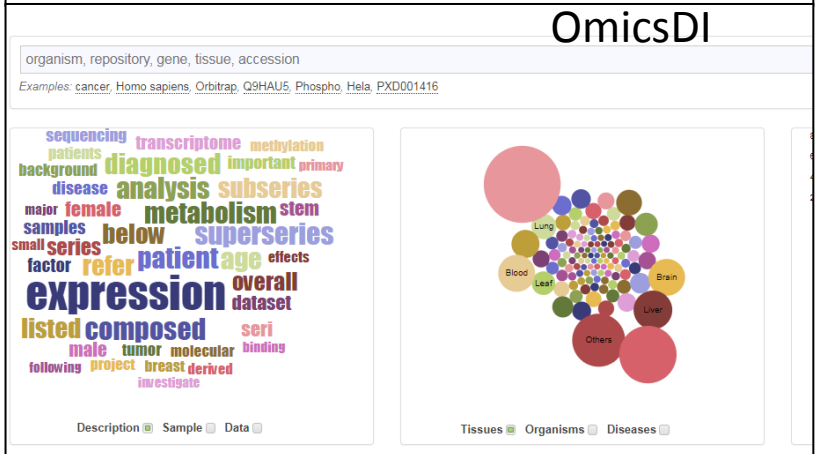
DRUGBANK



Specialized search engine



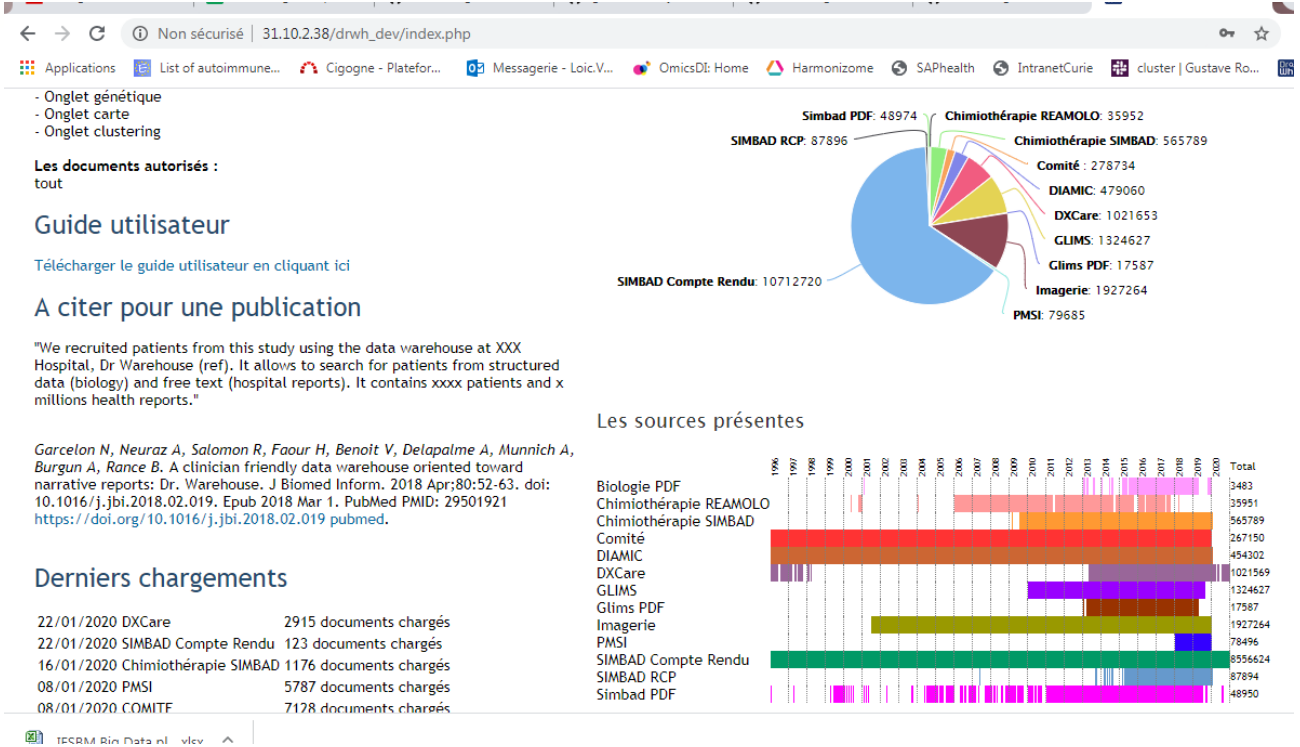
OmicsDI



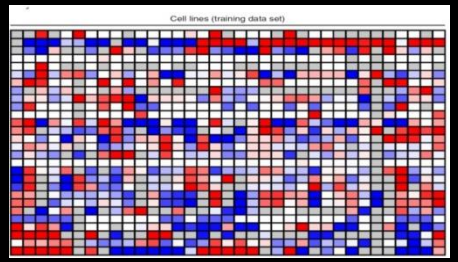
DITEP
Drug Development Department

GUSTAVE ROUSSY
CANCER CAMPUS
GRAND PARIS

At Gustave Roussy



Molecular biology
& pronostic



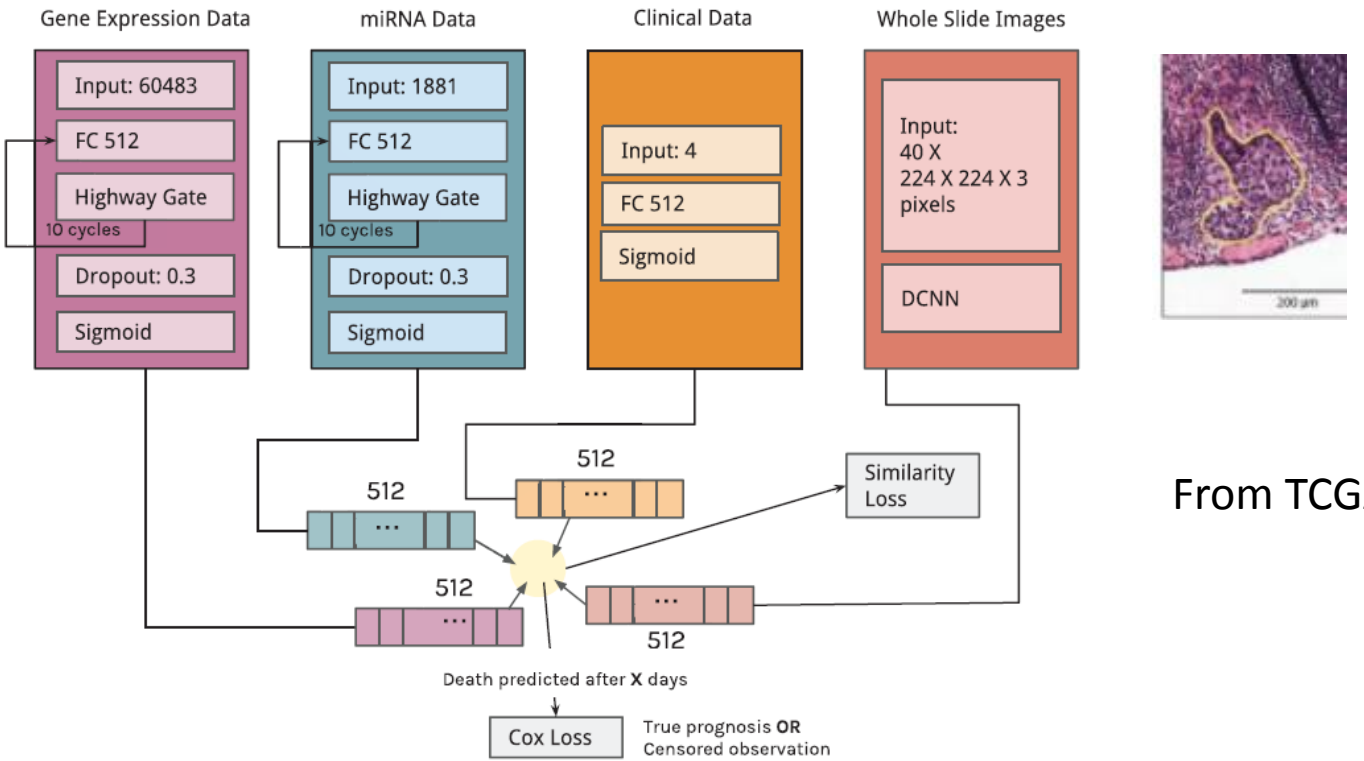
Does it work?

Pan-cancer survival estimation from RNAseq with Deep Learning

Main Objective	Tumor type, data types	Number of examples	Type of model	Endpoints and results	Reference
Patients' survival	4 cancers **TCGA RNAseq**	953 samples	Survival random forest and Cox lasso	Cross-validation C-index ~ 0.60 - 0.75	Yuan Y, et al. Assessing the clinical utility of cancer genomic and proteomic data across tumor types. Nat Biotechnol. 2014
Patients' survival	10 TCGA organs related datasets **RNA-Seq expression**	5031 patient samples (train/test split 80/20%)	MLP with Cox loss	Test C-index ~ 0.62	Ching T, Zhu X, Garmire LX. Cox-nnet: An artificial neural network method for prognosis prediction of high-throughput omics data. PLoS Comput Biol. 2018 Apr
Patients' survival per groups	32 cancer types TCGA **RNA-Seq expression**	6645 patients	Survival	Validation C-index = 0.59-0.75	Ramazzotti D, et al. Multi-omic tumor data reveal diversity of molecular mechanisms that correlate with survival. Nat Commun. 2018 Oct
Patients' survival	20 cancer types TCGA **RNA-Seq expression**	6404 patients	CNN	Clinic + mRNA, test C-index = 0.60	*Deep learning with multimodal representation for pancancer prognosis prediction, Anika Cheerla and Olivier Gevaert, Bioinformatics, 35, 2019*

Pronostic estimation the clinic

Best and most recent try

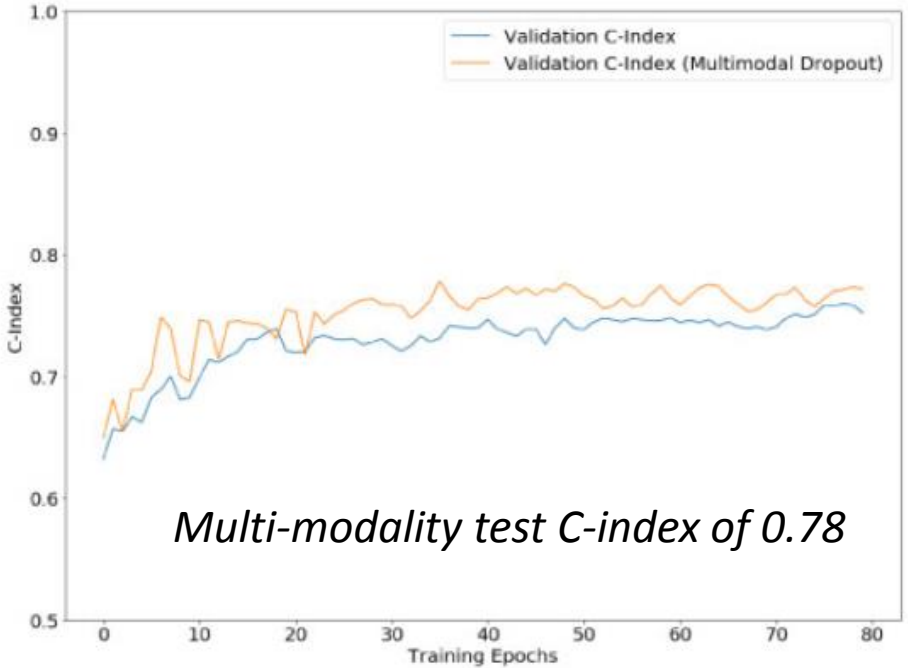


From TCGA

Deep learning with multimodal representation for pancancer prognosis prediction, Anika Cheerla and Olivier Gevaert, Bioinformatics, 35, 2019

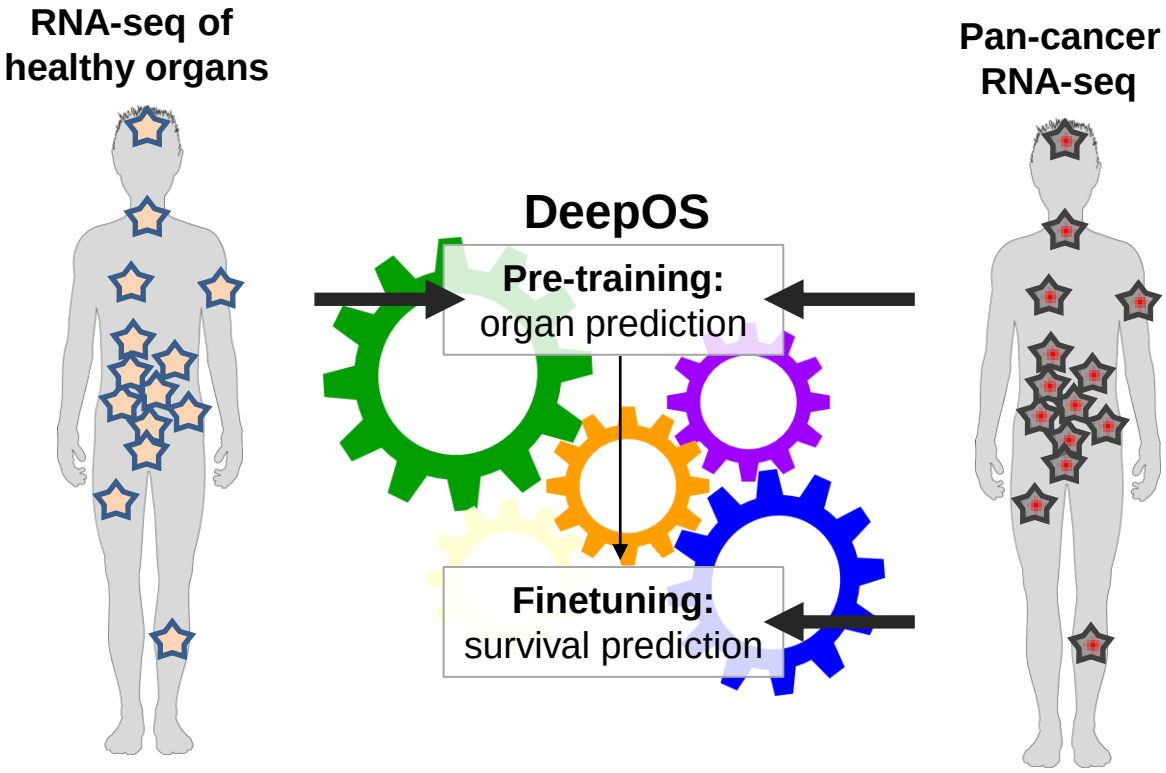
Pronostic estimation the clinic

Best and most recent try

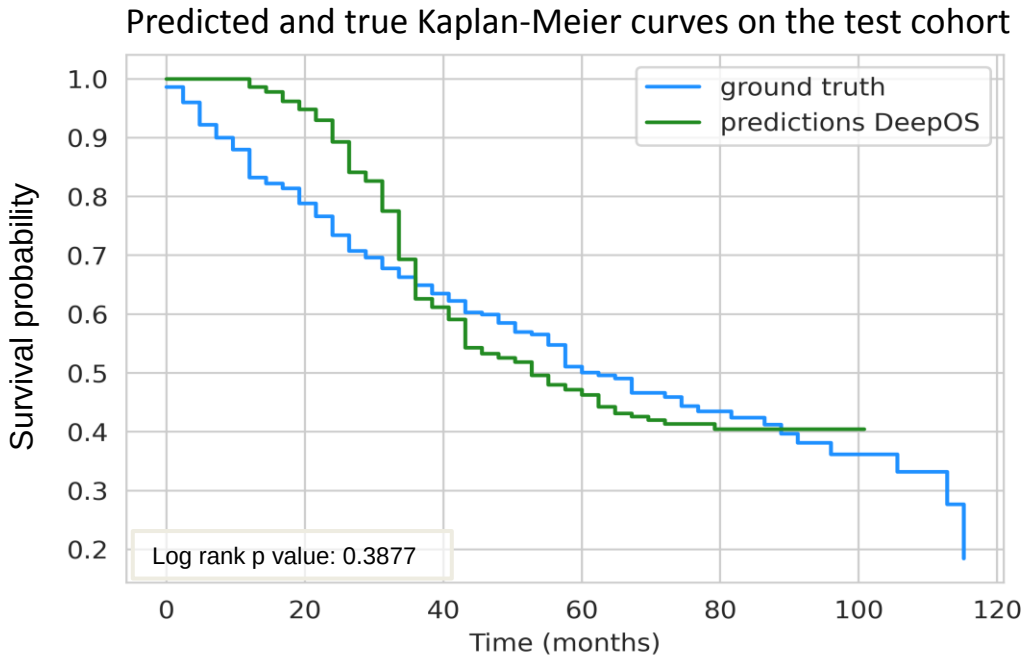


Deep learning with multimodal representation for pancancer prognosis prediction, Anika Cheerla and Olivier Gevaert, Bioinformatics, 35, 2019

DeepOS


RNA-seq of healthy organs
DeepOS
Pre-training:
organ prediction
Finetuning:
survival prediction
Pan-cancer RNA-seq

DeepOS



Test set C-index 0.7147

How to improve models' efficacy?

- Need more samples (cell lines, organoids)
- Need more molecular layers ?
- Need better readouts
- Need more functional (perturbation) data
- Adapt your models to the tasks you want

→ Saez-Rodriguez's take

How to improve models' efficacy?

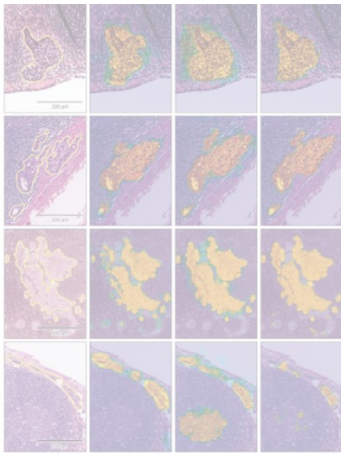
- Focus on your data-analytical approaches
- Use mechanistic prior knowledge
- Adapt your models to the tasks you want

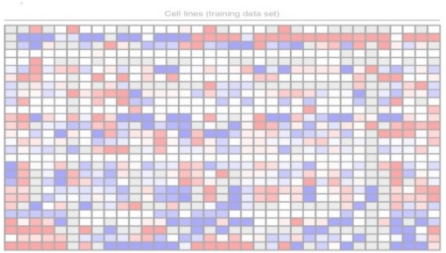
→Camacho, Costello, Collins takes
→ & my take!

For patients’ prognostic estimation

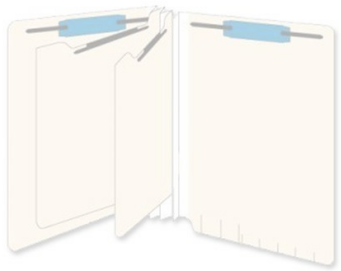
Models are improving…

ML/DL in oncology





"Here's my sequence"
The New Yorker



Diagnostics

Molecular biology & pronostic

Drug development & prediction

Monitoring patients

PLAN

DITEP
Drug Development Department

afaq ISO 9001 Qualité AFNOR CERTIFICATION

Drug discovery → Preclinical Screening → Phase I → Phase II → Phase III

Drug development success rate 2006-2015

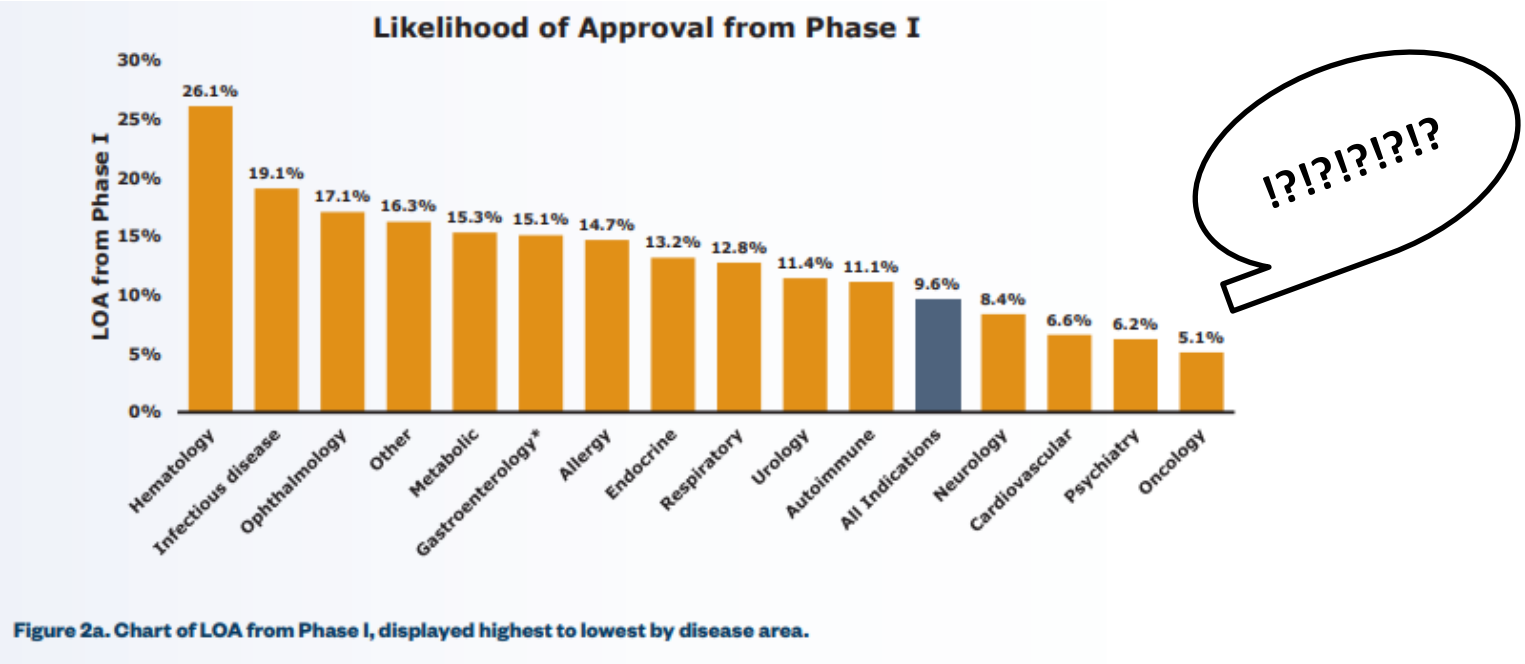
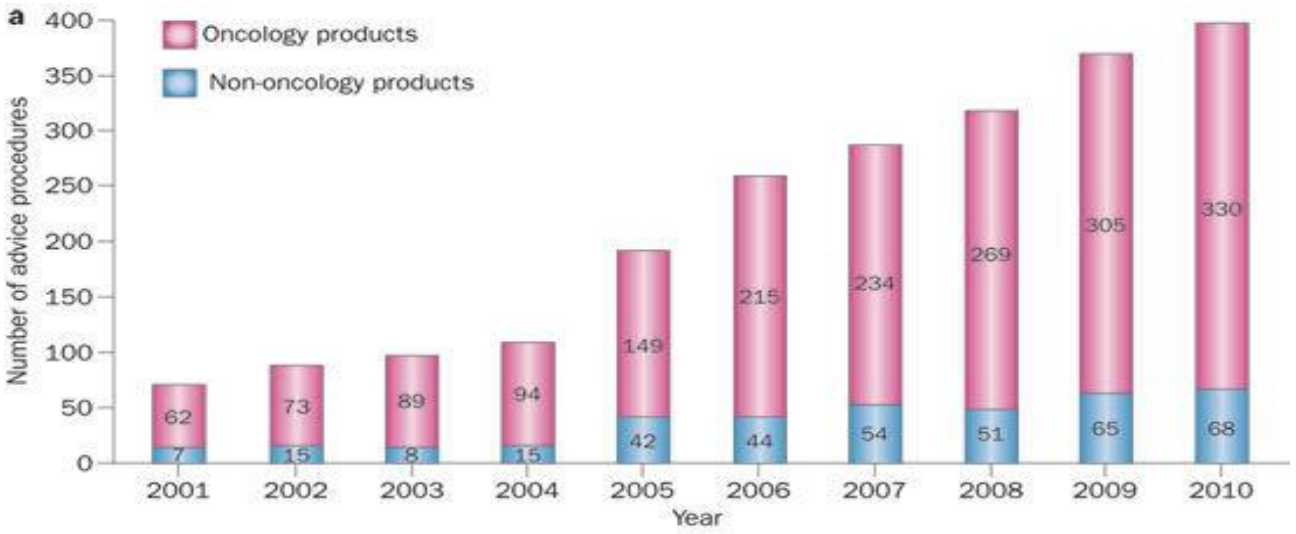
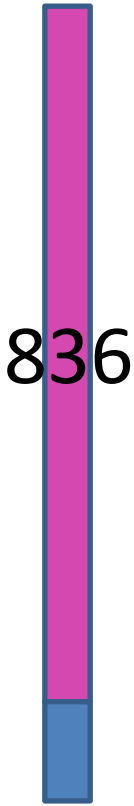


Figure 2a. Chart of LOA from Phase I, displayed highest to lowest by disease area.

Organization BI. Clinical Development Success Rates 2006-2015 Available for dowanload at https://www.bio.org/bio-industry-analysis-published-reports

Drugs' production…





836

2015

73% with identified targets

Jonsson B, Bergh J. Hurdles in anticancer drug development from a regulatory perspective. Nat Rev Clin Oncol. 2012

You are here

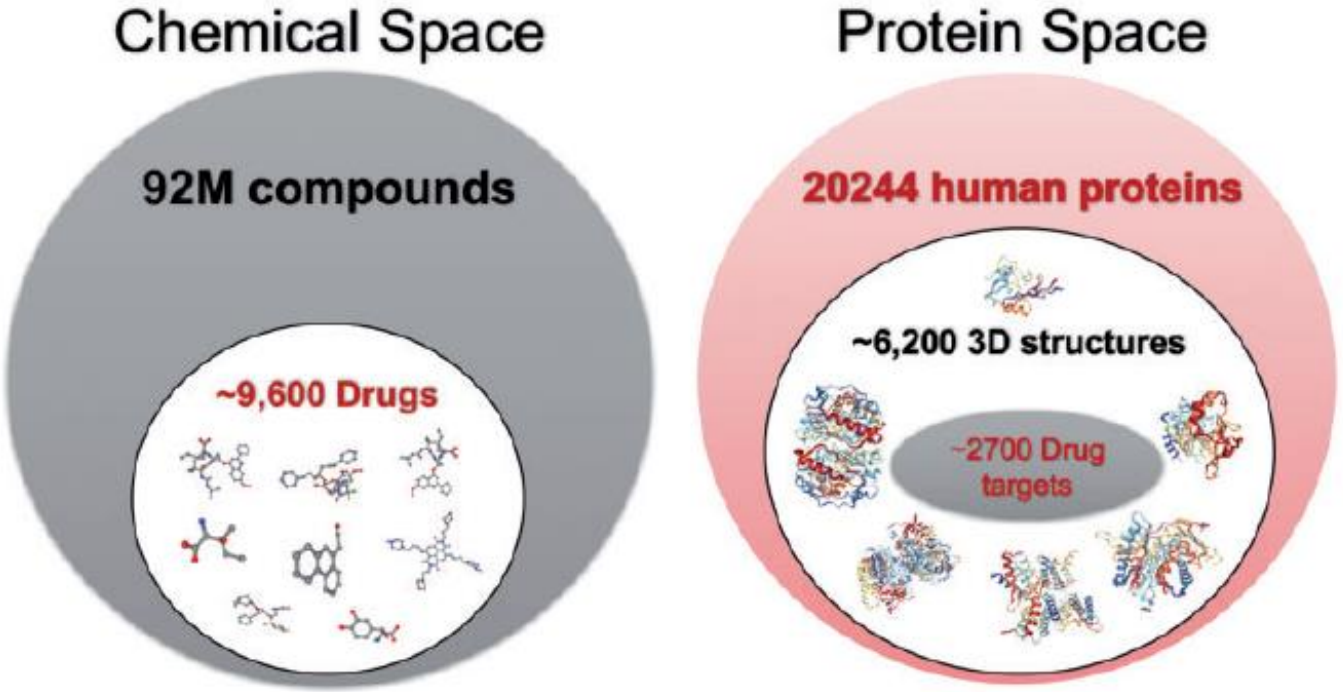
Modèles / ML / IA ?

DITEP
Drug Development Department

afaq ISO 9001 Qualité AFNOR CERTIFICATION

Drug discovery → Preclinical Screening → Phase I → Phase II → Phase III

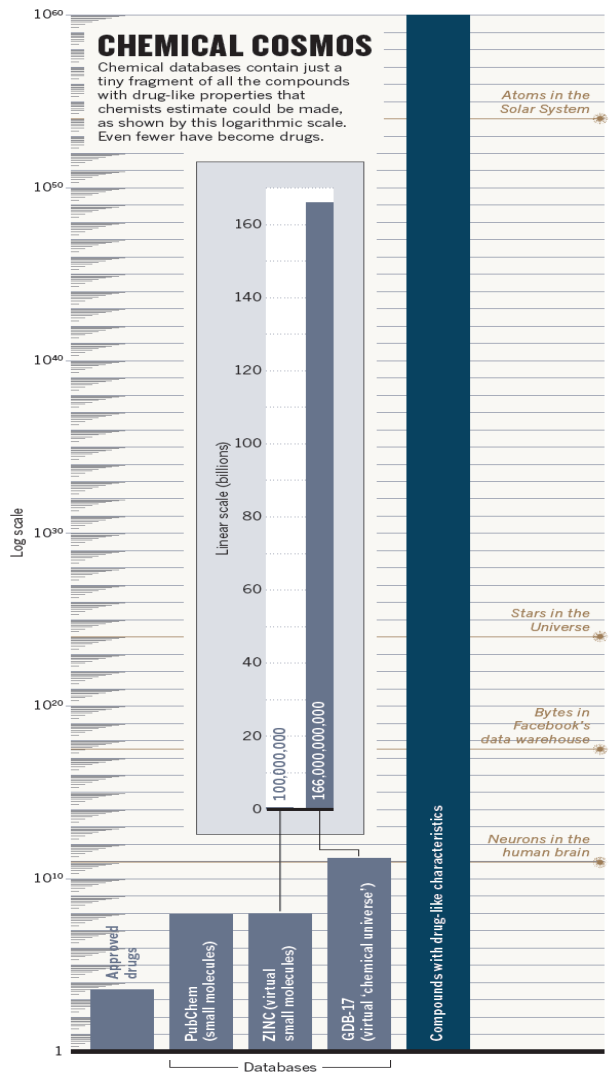
The known space



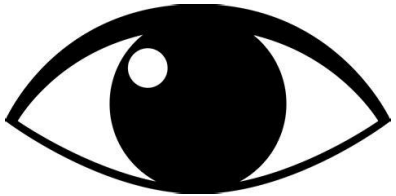
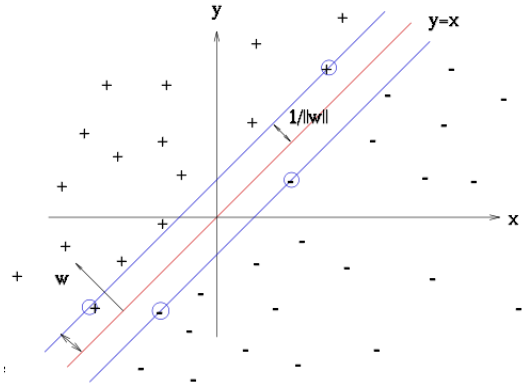
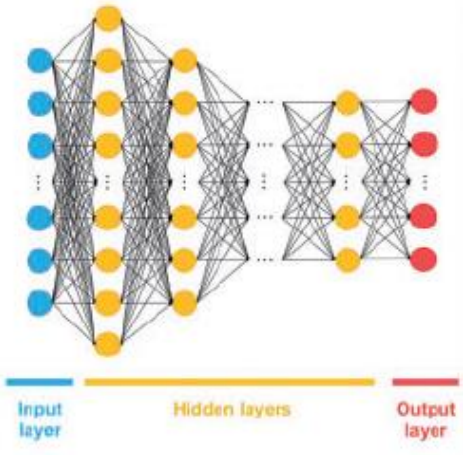
Rifaioglu et al. Recent applications of deep learning and machine intelligence on in silico drug discovery: methods, tools and databases. Brief Bioinform. 2018 Jul 31. PMID: 30084866.

THE DRUG-MAKER'S GUIDE TO THE GALAXY

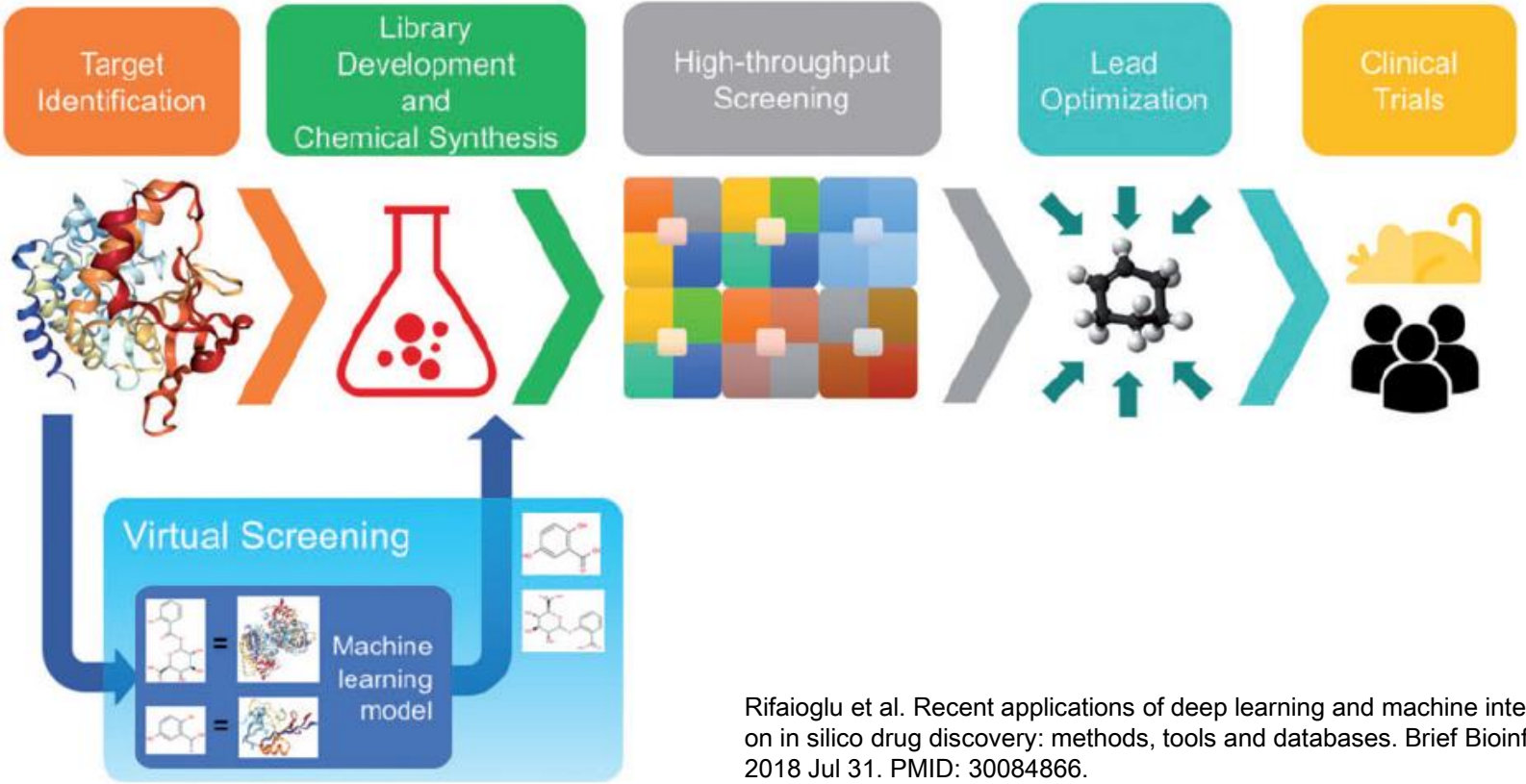
HOW MACHINE LEARNING AND BIG DATA ARE HELPING CHEMISTS SEARCH THE VAST CHEMICAL UNIVERSE FOR BETTER MEDICINES.



The models you have

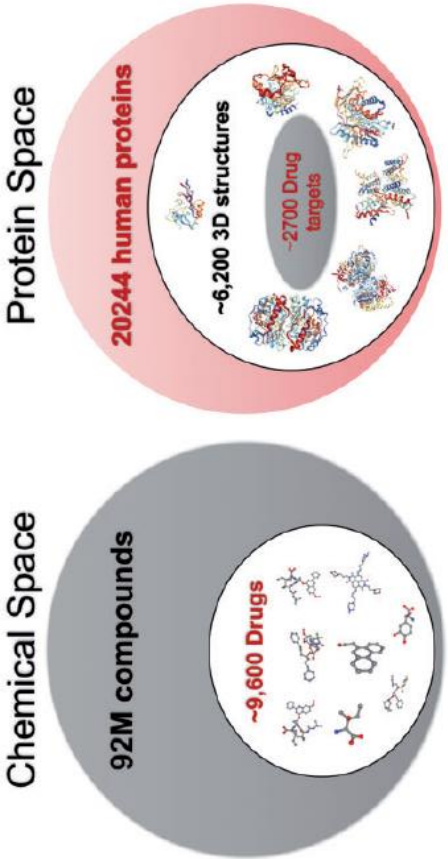
	Human	Statistics	Deep learning
			
	Use your knowledge and reasoning	Linear models easy to explain	Non-linear models data-expensive
Examples:	Christophe Massard	Cox model logReg eg: RMH	Deep neural network

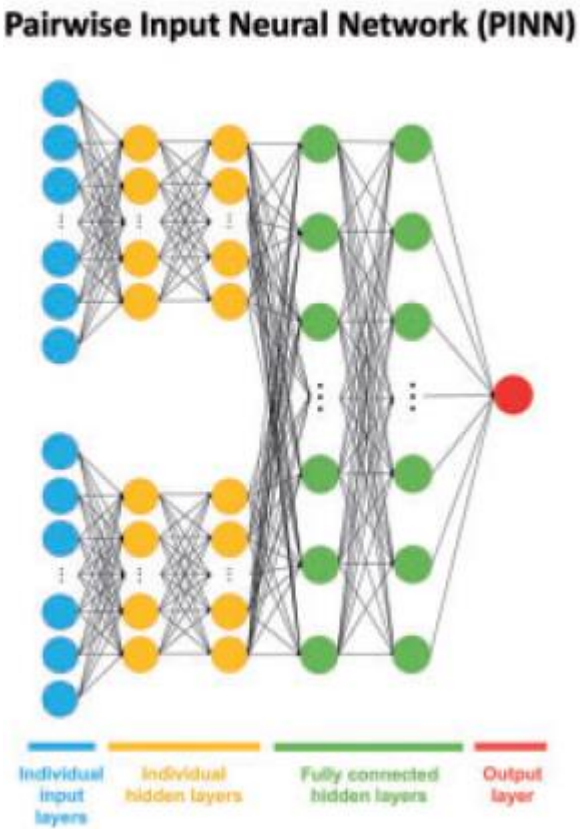
Drug discovery in details



Rifaioglu et al. Recent applications of deep learning and machine intelligence on in silico drug discovery: methods, tools and databases. Brief Bioinform. 2018 Jul 31. PMID: 30084866.

Overview

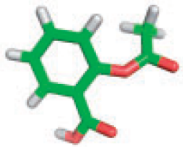
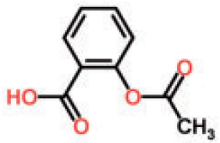




Bioactivity

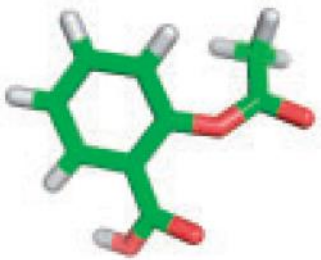
How to encode drugs

Table 1. Chemical formula, 2D/3D graphical representation, SMILES and InChI notations of aspirin

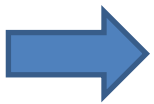
Category	Representation
Compound name	Aspirin
Chemical formula	$C_9H_8O_4$
3D/2D structure	 
SMILES	CC(=O)OC1=CC=CC=C1C(=O)O
InChI	InChI=1S/C9H8O4/c1-6(10)13-8-5-3-2-4-7(8)9(11)12/h2-5H, 1H3, (H, 11, 12)

Rifaioglu et al. Recent applications of deep learning and machine intelligence on in silico drug discovery: methods, tools and databases. Brief Bioinform. 2018 Jul 31. PMID: 30084866.

How to encode drugs or proteins?



fingerprints



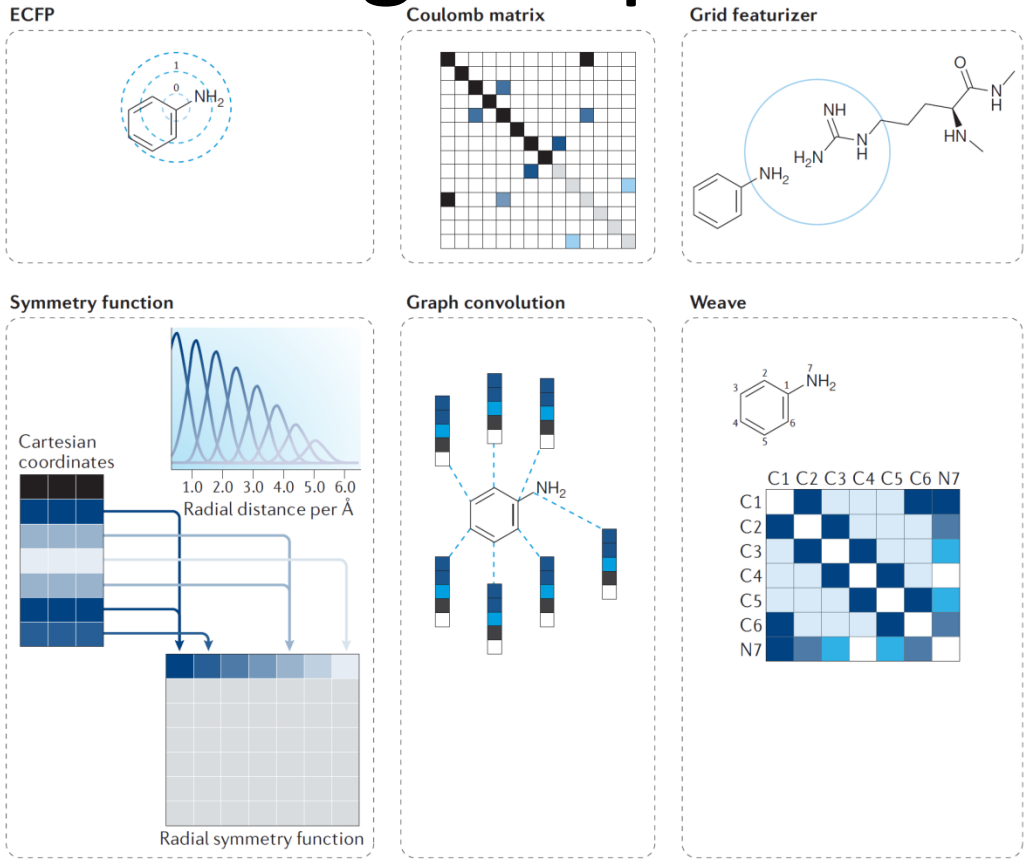
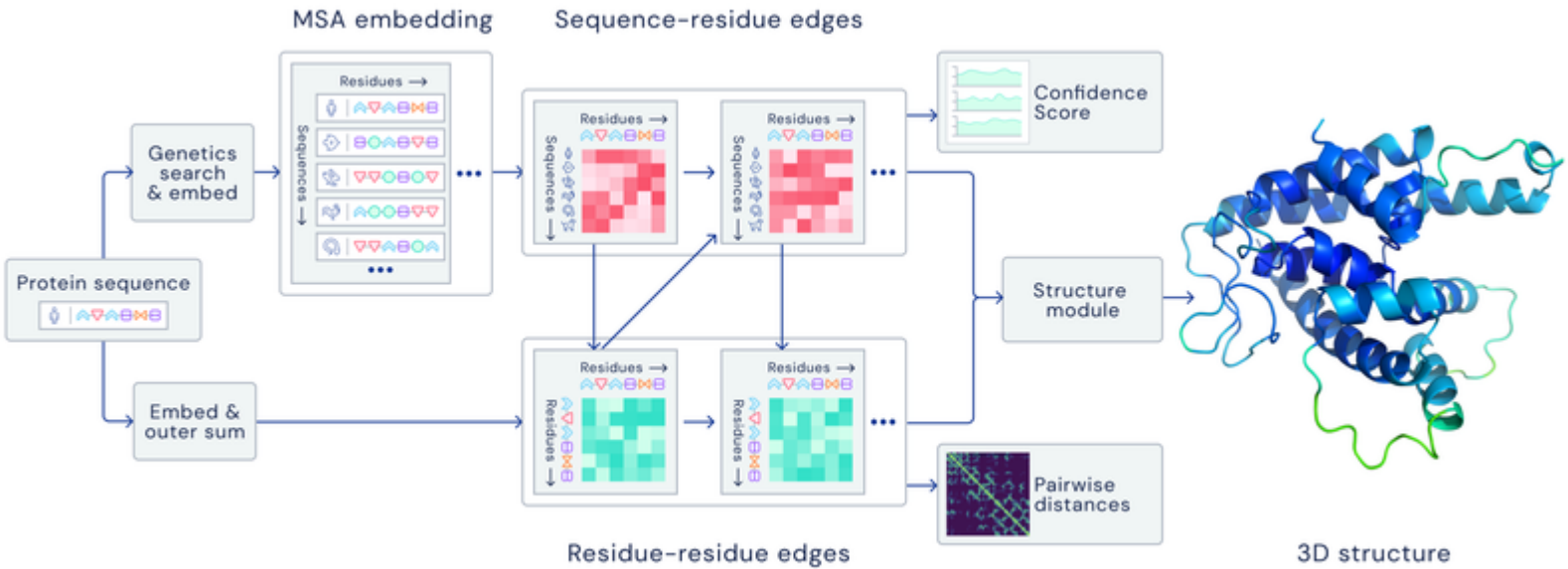


Fig. 3 | **The challenges of compound structure representation in machine learning models.** The appropriate

Protein folding prediction

Prediction of ‘spatial graph’: eg backbone atom distance matrices and torsion angles



AlphaFold’s architecture in schematic form. Image Credit: DeepMind

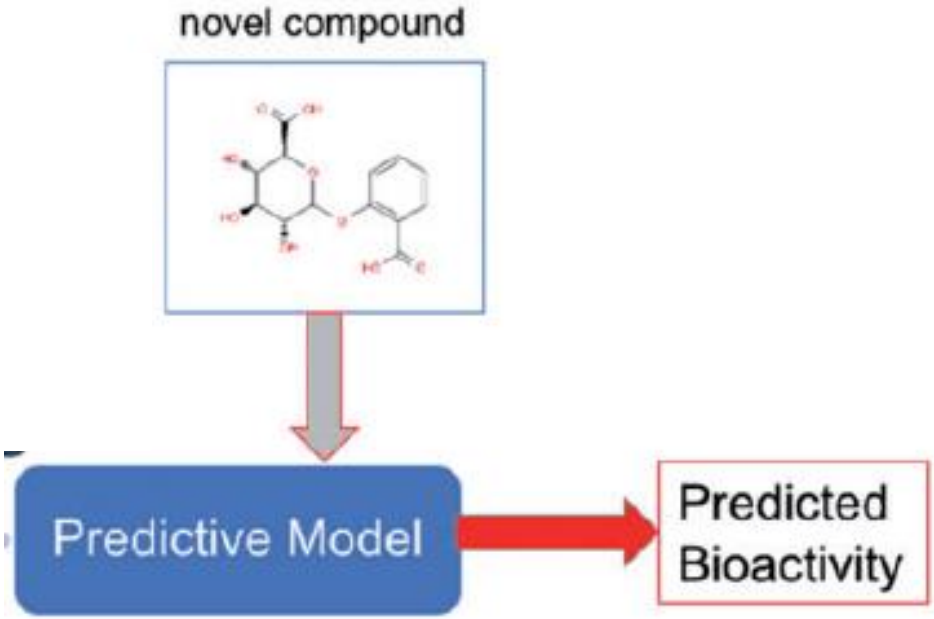
other: arXiv:1911.05531 [q-bio.BM]

Gold standard databases

- **DUD-E**
  - 22 886 ligands and their affinities against 102 targets retrieved from the ChEMBL database
- **TOX-21**
  - 12 000 compounds screened for their toxic effects (in bioassays)
- **MoleculeNet**
  - ~ 700 000 compounds retrieved from publicly available databases

Compound and bioactivity databases	Statistics[a]			Website	Version
	Compounds	Targets	Interactions		
PubChem [1]	93 977 773 (C) 235 653 627 (S)	10 341 (P)	233 799 255 (I) 1 252 820 (E)	https://pubchem.ncbi.nlm.nih.gov	03.12.2017
ChEMBL [2]	1 735 442 (C)	11 538 (P)	14 675 320 (I) 1 302 147 (E)	https://www.ebi.ac.uk/chembl	v23
DrugBank [5]	9591 (D)	4270 (P)	16 748 (I)	http://www.drugbank.ca	v5.0

Predictions



Rifaioglu et al. Recent applications of deep learning and machine intelligence on in silico drug discovery: methods, tools and databases. Brief Bioinform. 2018 Jul 31. PMID: 30084866.

Deep learning wins

2 studies on multitask NN for bioactivity measures
~ hidden layer sizes: [1000, 2000, 3000]

- 743 336 compounds & 5069 targets
- 2.1 million bioactivity measurements
- Compounds were represented by 43 x 340 dimensions ECFP12 fingerprints

Method	AUC	p-value
Deep network	**0.830**	
SVM	0.816	1.0e-07
BKD	0.803	1.9e-67
Logistic Regression	0.796	6.0e-53
k-NN	0.775	2.5e-142
Pipeline Pilot Bayesian Classifier	0.755	5.4e-116
Parzen-Rosenblatt	0.730	1.8e-153
SEA	0.699	1.8e-173

J&J + univ Austria 2014

Unterthiner T, Mayr A, Klambauer G, et al. Deep learning as an opportunity in virtual screening. Deep learn Represent Learn Work NIPS 2014;2014:1–9.

- 1.6 million compounds & 259 targets
- 37.8 million experimental compound–protein interactions
- Compounds were represented by ECFP4 fingerprints

Model	PCBA ($n = 128$)	MUV ($n = 17$)	Tox21 ($n = 12$)	Sign Test CI
Logistic Regression (LR)	.801	.752	.738	[.04, .13]
Random Forest (RF)	.800	.774	.790	[.06, .16]
Single-Task Neural Net (STNN)	.795	.732	.714	[.04, .12]
Pyramidal (2000, 100) STNN (PSTNN)	.809	.745	.740	[.06, .16]
Max{LR, RF, STNN, PSTNN}	.824	.781	.790	[.12, .24]
1-Hidden (1200) Layer Multitask Neural Net (MTNN)	.842	.797	.785	[.08, .18]
Pyramidal (2000, 100) Multitask Neural Net (PMTNN)	**.873**	**.841**	**.818**	

Google + Standford 2015

Ramsundar B, Kearnes S, Edu K, et al. Massively Multitask Networks for Drug Discovery. arXiv 2015; arXiv: 1502.02072.

DITEP
Drug Development Department

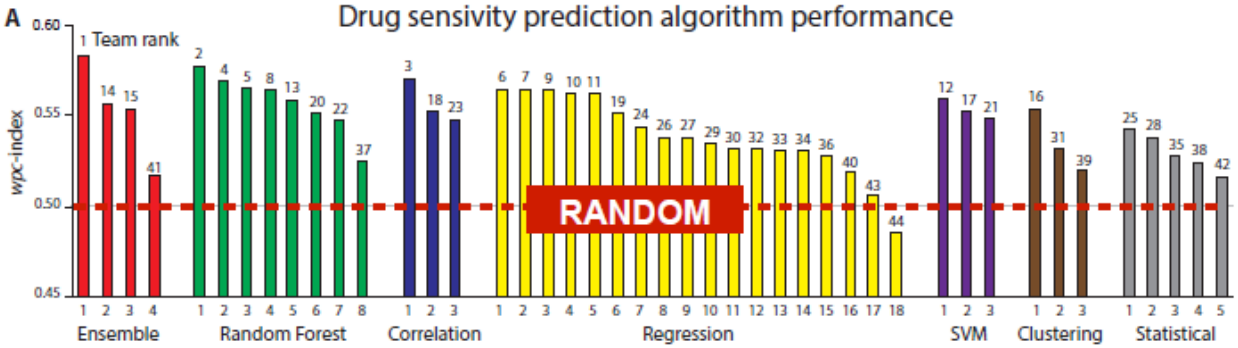
afaq ISO 9001 Qualité AFNOR CERTIFICATION

You are here

Drug discovery → Preclinical Screening → Phase I → Phase II → Phase III

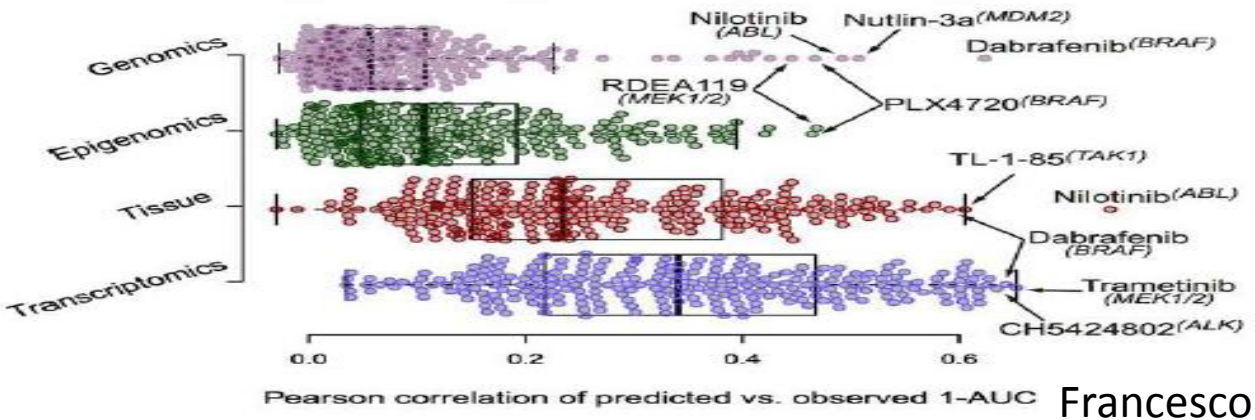
Treatment prediction in cell lines

Saez-Rodrigez « predictability is very low »



DREAM CHALLENGES
powered by Sage Bionetworks

Costello JC, et al. A community effort to assess and improve drug sensitivity prediction algorithms. Nat Biotechnol. 2014

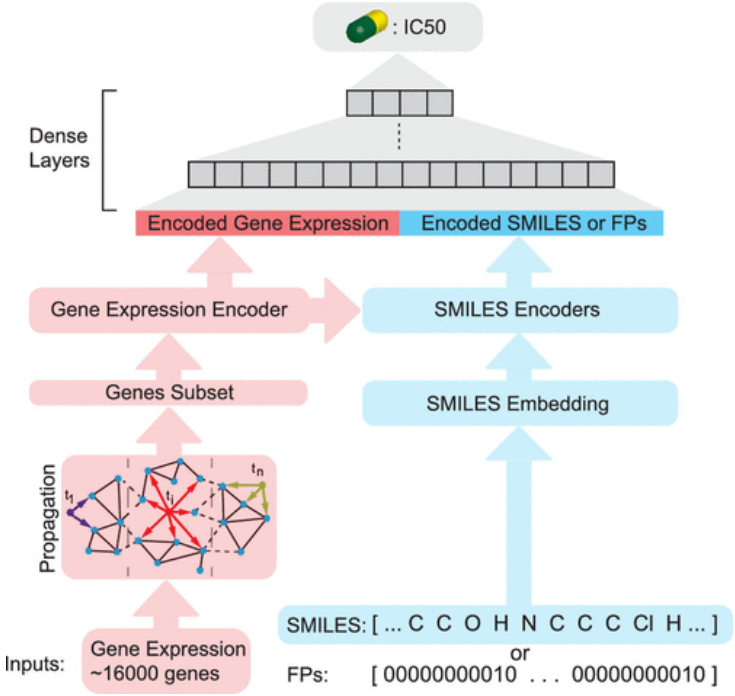


Francesco Iorio et al, Cell, 2016

Treatment prediction in cell lines

Best and most recent try

Data:
985 cell lines
208 drugs
= 175 603 pairs

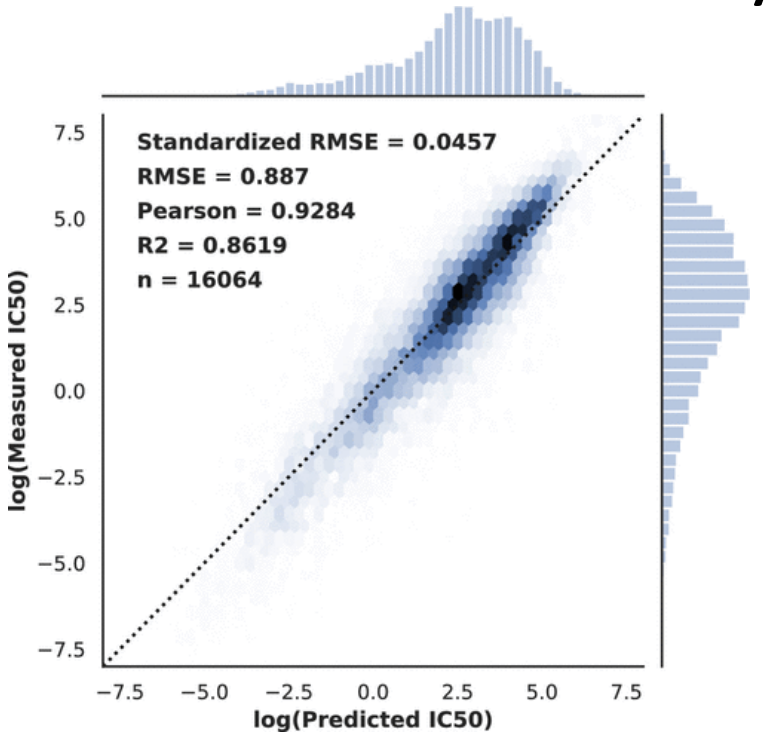


Manica M, Oskooei A, Born J, Subramanian V, Sáez-Rodríguez J, Rodríguez Martínez M. Toward Explainable Anticancer Compound Sensitivity Prediction via Multimodal Attention-Based Convolutional Encoders. Mol Pharm. 2019 Oct 31

Treatment prediction in cell lines

Best and most recent try

Test set



Manica M, Oskooei A, Born J, Subramanian V, Sáez-Rodríguez J, Rodríguez Martínez M. Toward Explainable Anticancer Compound Sensitivity Prediction via Multimodal Attention-Based Convolutional Encoders. Mol Pharm. 2019 Oct 31

You are here

DITEP
Drug Development Department

afaq ISO 9001 Qualité AFNOR CERTIFICATION

Drug discovery → Preclinical Screening → Phase I → Phase II → Phase III

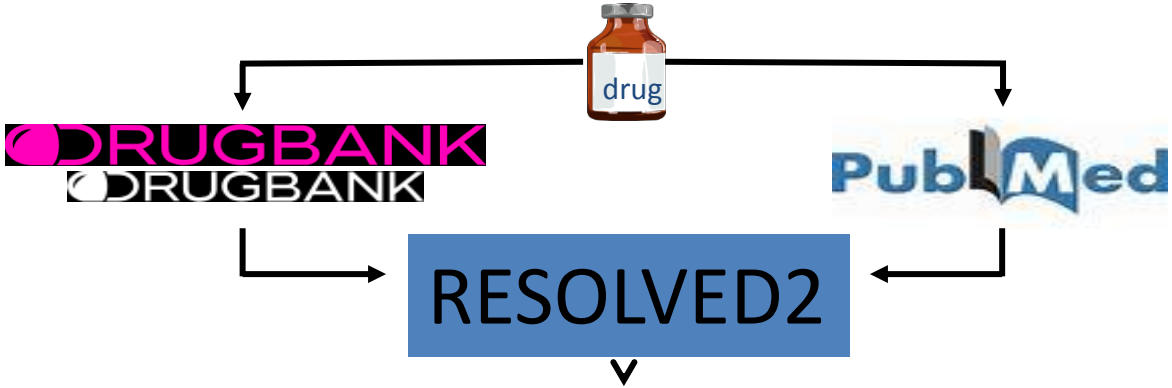
Les enjeux à la fin de la phase I: la décision

Phase I

Phase II-III

Prediction of Drug Approval After Phase I Clinical Trials in Oncology: The RESOLVED2 model

Is this new drug likely to be approved in the future?



Under submission

DITEP
Drug Development Department

afaq ISO 9001 Qualité AFNOR CERTIFICATION

Target identification, validation

Study agent identification, validation

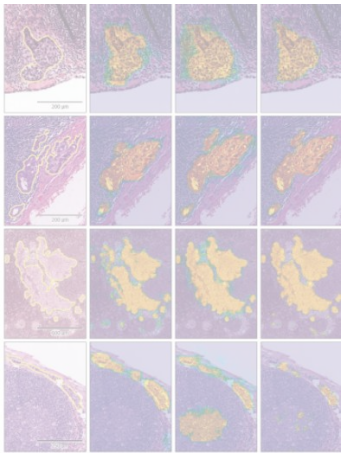
Phase I

Phase II

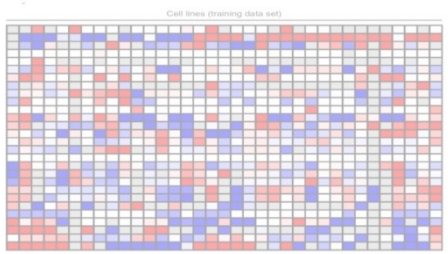
Phase III

?

ML/DL in oncology



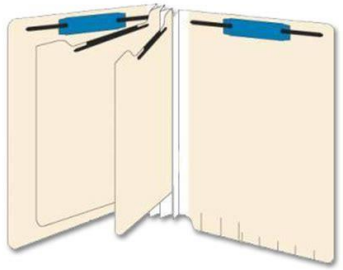
Diagnostics



Molecular biology & pronostic

"Here's my sequence"
The New Yorker

Drug development & prediction



Free text & Monitoring patients

Tasks with EHR

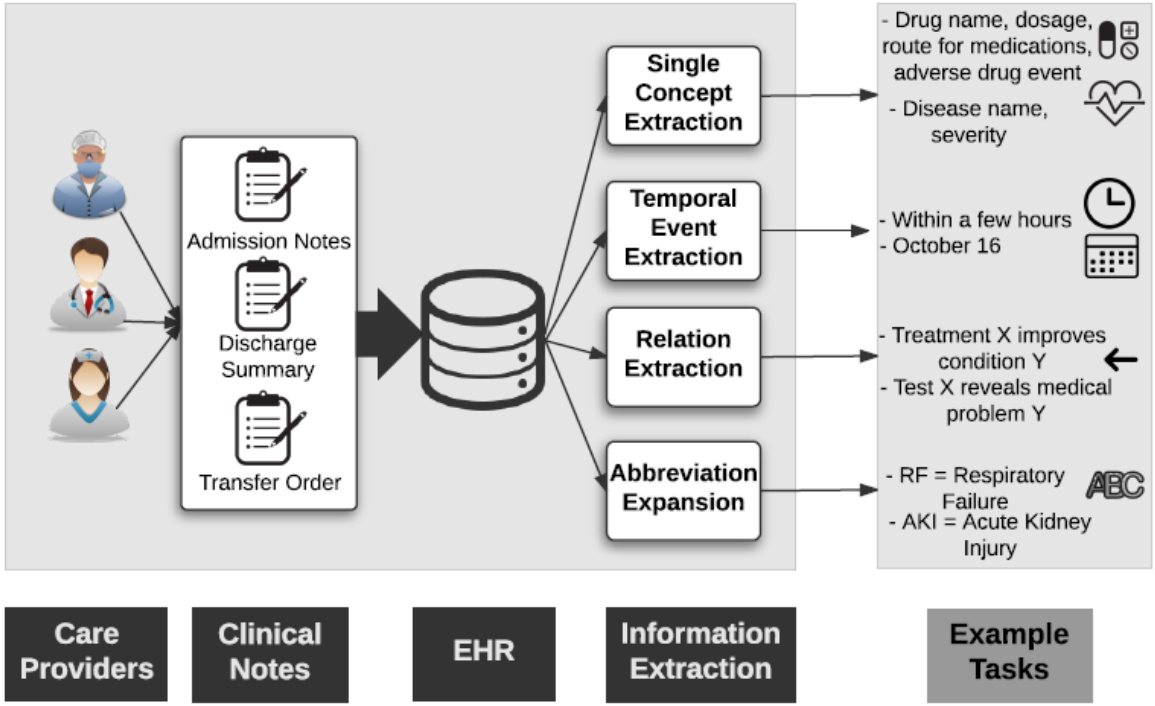
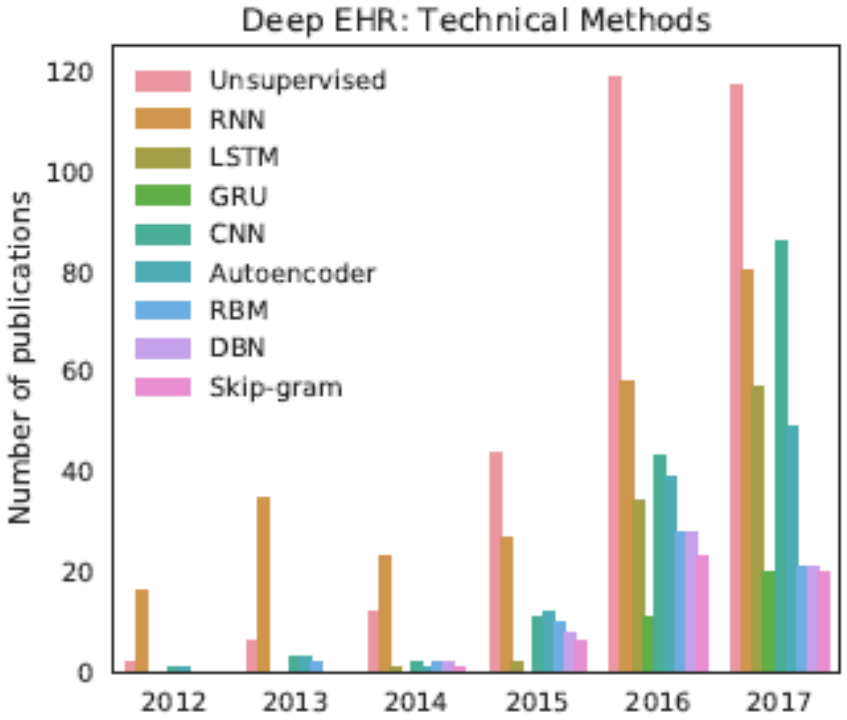


Fig. 7. EHR Information Extraction (IE) and example tasks.

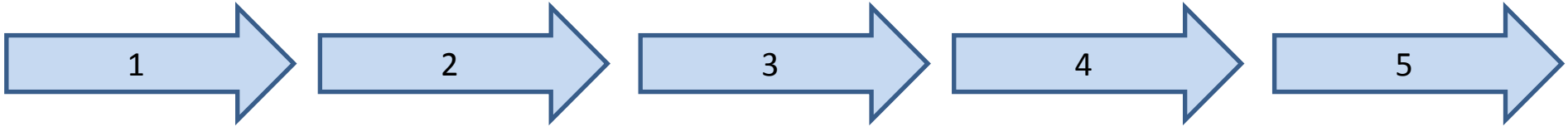
Deep EHR: A Survey of Recent Advances in Deep Learning Techniques for Electronic Health Record (EHR) Analysis. Benjamin Shickel, Patrick J. Tighe, Azra Bihorac, and Parisa Rashidi. arXiv:1706.03446v2

Methods for EHR



Deep EHR: A Survey of Recent Advances in Deep Learning Techniques for Electronic Health Record (EHR) Analysis. Benjamin Shickel, Patrick J. Tighe, Azra Bihorac, and Parisa Rashidi. arXiv:1706.03446v2

Taux d'attrition des patients



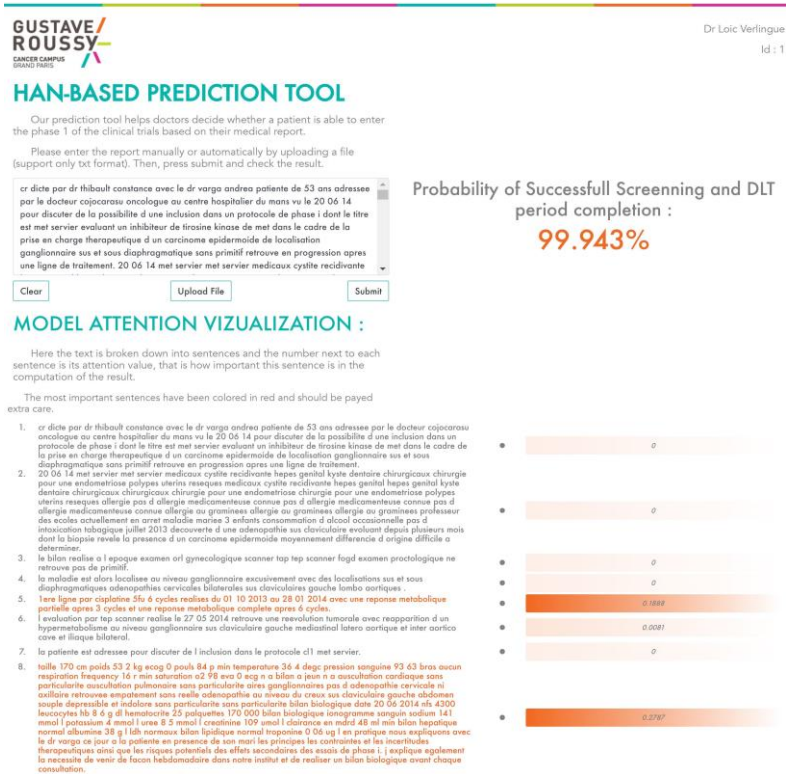
Consultation d'inclusion	Phase de screening	C1J1	Période de DLT	Sortie d'essai
100%	85% - 75%		~65%	0%
	- (15%, 25%)		-16%	
	Screen fails		Mortalité	

- Mckane A, et al: Determinants of patient screen failures in Phase 1 clinical trials. Invest New Drugs
- Kempf E et al: A Case-Control Study Brings to Light the Causes of Screen Failures in Phase 1 Cancer Clinical Trials. PLoS ONE

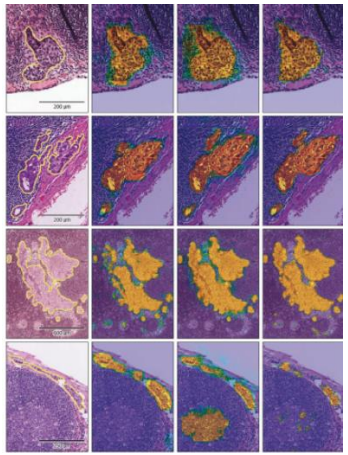
Olmos D, A'hern RP, Marsoni S, et al: Patient selection for oncology phase I trials: a multi-institutional study of prognostic factors. J Clin Oncol

Softwares : prediction of succesful screening and DLT period completion (SSD)

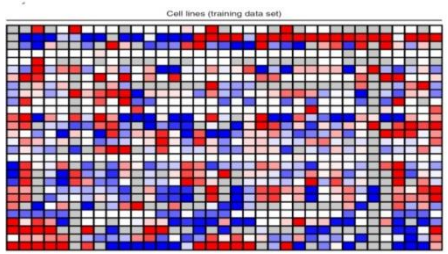
En cours de développement
DITEP Data Science Team
DTNSI



ML/DL in oncology



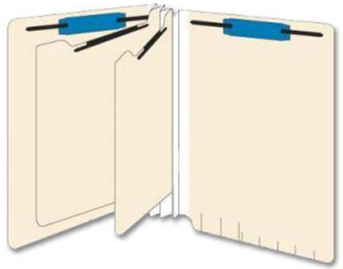
Diagnostics



Molecular biology & pronostic

"Here's my sequence"
The New Yorker

Drug development & prediction



Monitoring patients

Review for AI in medicine

REVIEW ARTICLE | FOCUS
https://doi.org/10.1038/s41591-018-0300-7
nature medicine

High-performance medicine: the convergence of human and artificial intelligence

Eric J. Topol

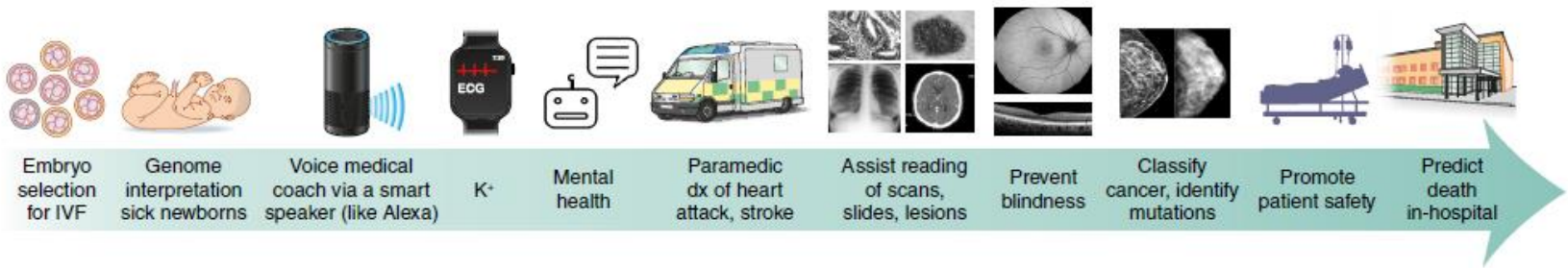
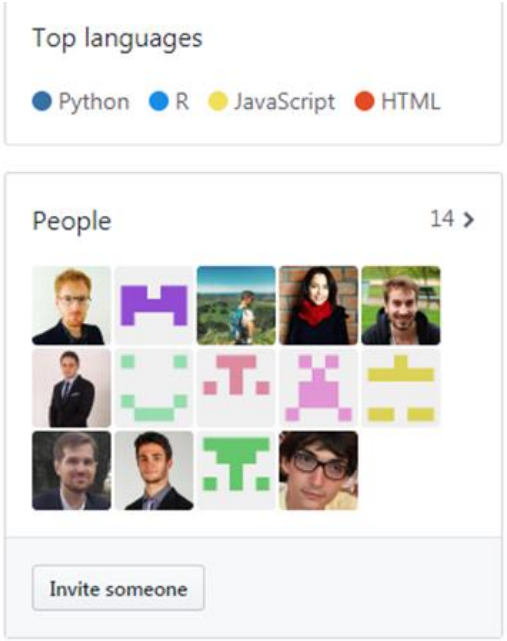


Fig. 2 | Examples of AI applications across the human lifespan. dx, diagnosis; IVF, in vitro fertilization K^+, potassium blood level. Credit: Debbie Maizels/ Springer Nature

Data Science & DITEP

Medical team

Data Science team



loic.verlingue@gustaveroussy.fr

Info https://github.com/DITEP