Intelligence artificielle (IA) en médecine et en oncologie : quelques concepts et applications

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IFSBM Module 11

17 décembre 2024

Plan de la présentation

http://www.unehistoiredeplumes.fr/a-vol-doiseau/

- Introduction simple sur l'IA
- IA en médecine
- IA en oncologie
- Exemple : classification des cancers de primitif inconnu par IA
- Conclusions et perspectives

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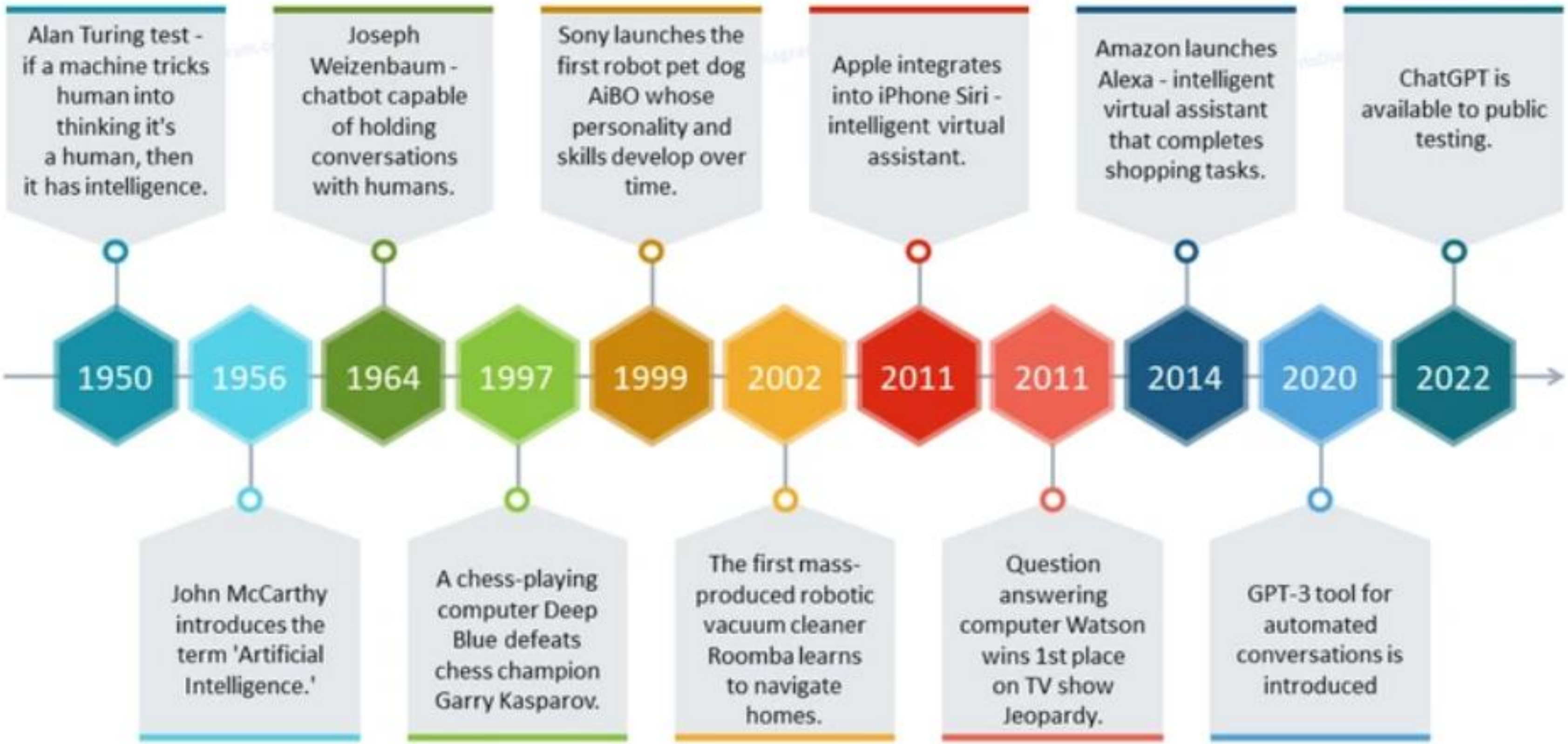
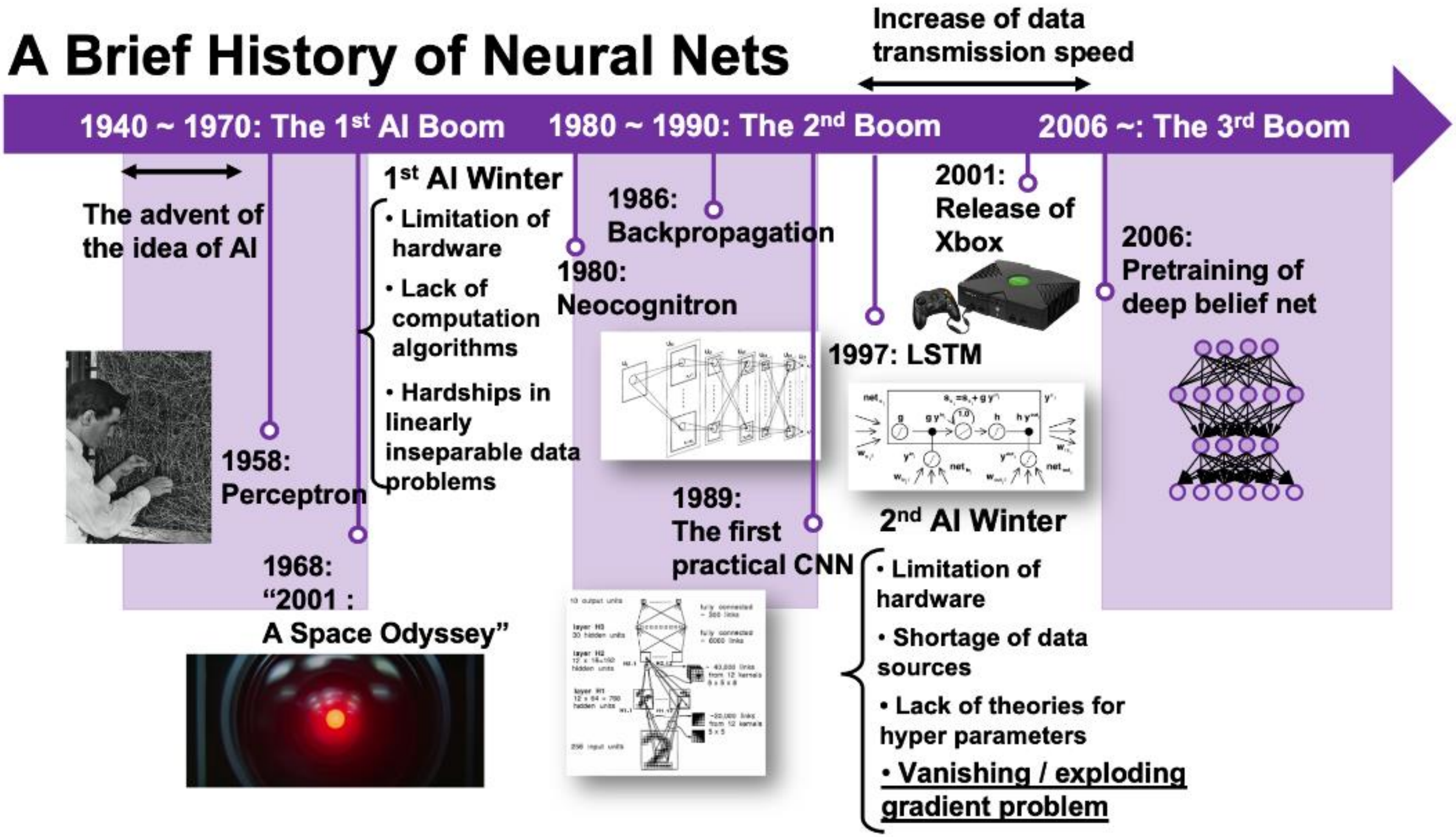
N'hésitez pas à m'interrompre pour poser des questions !

Intelligence artificielle :
brève histoire et concepts de base

Artificial Intelligence Development History Timeline





https://data-science-blog.com/blog/2020/07/16/a-brief-history-of-neural-nets-everything-you-should-know-before-learning-lstm/

Quiz n°1

Quelles sont les utilisations potentielles de l'IA?

- A) Conduire une voiture
- B) Dépister un cancer du sein sur mammographie
- C) Traduire une conversation en temps réel
- D) Résoudre des problèmes de mathématiques de niveau olympiade

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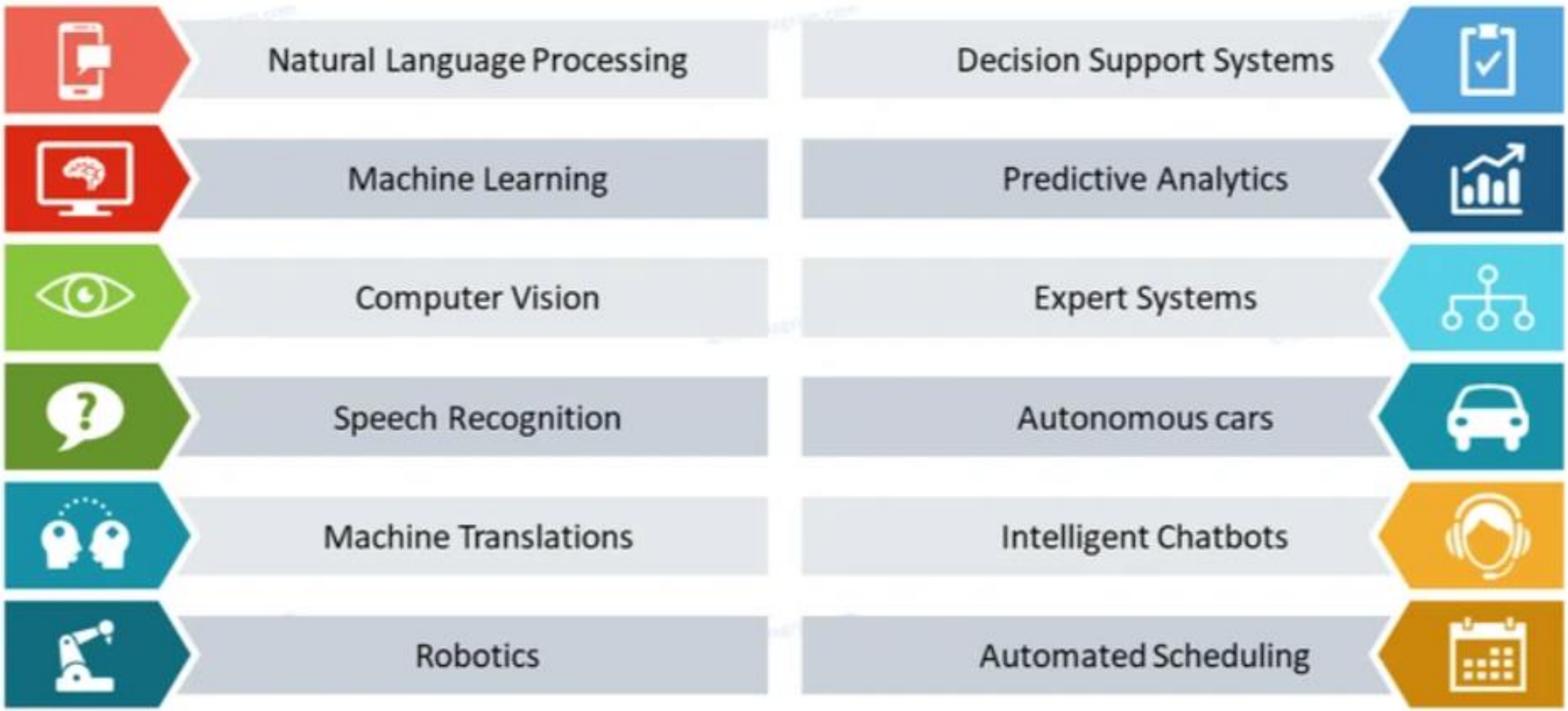
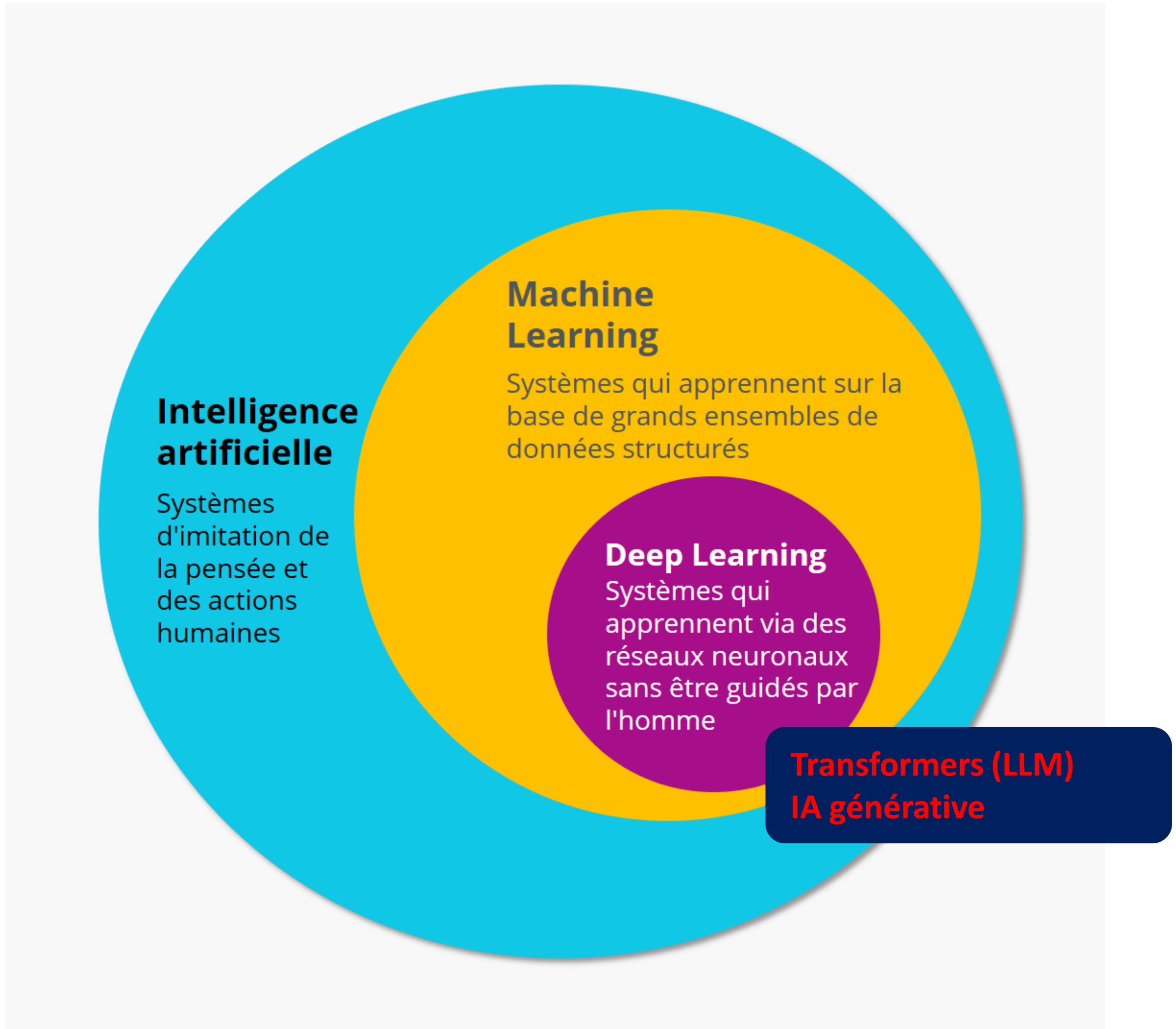
Quelques applications actuelles de l'IA

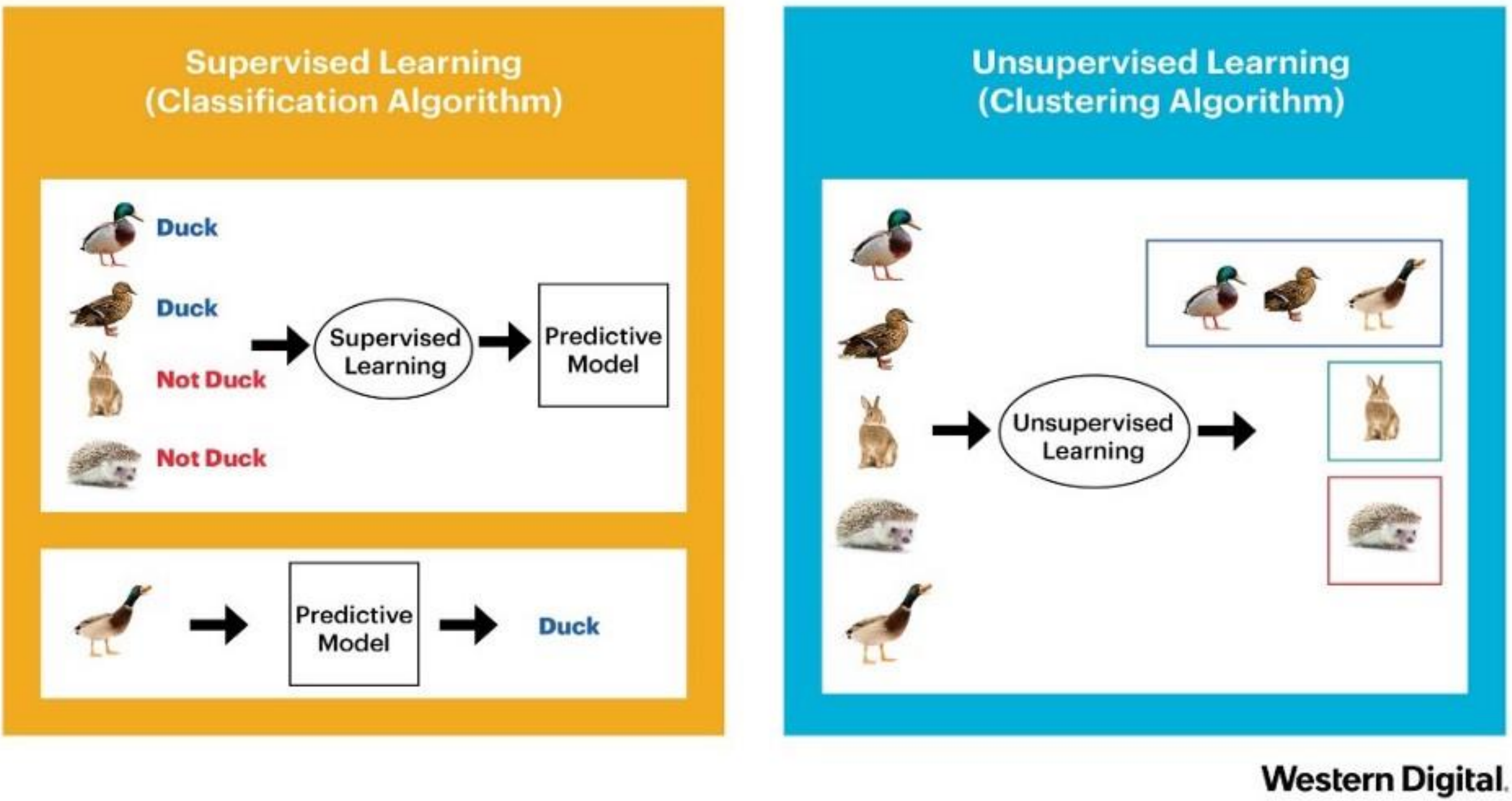


Définitions



https://www.ionos.fr/digitalguide/web-marketing/search-engine-marketing/deep-learning-vs-machine-learning/

Apprentisage supervisé ou non supervisé



https://laptrinhx.com/supervised-vs-unsupervised-learning-1861950659/

Quiz n°2

Je souhaite entraîner un algorithme à discriminer entre lymphome et sarcome à partir du RNA-seq. Quel type d'apprentissage vais-je utiliser ?

- A) Apprentissage supervisé
- B) Apprentissage non supervisé

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Je souhaite entraîner un algorithme à découvrir des sous-groupes de lymphomes à partir du RNA-seq. Quel type d'apprentissage vais-je utiliser ?

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- B) Apprentissage non supervisé

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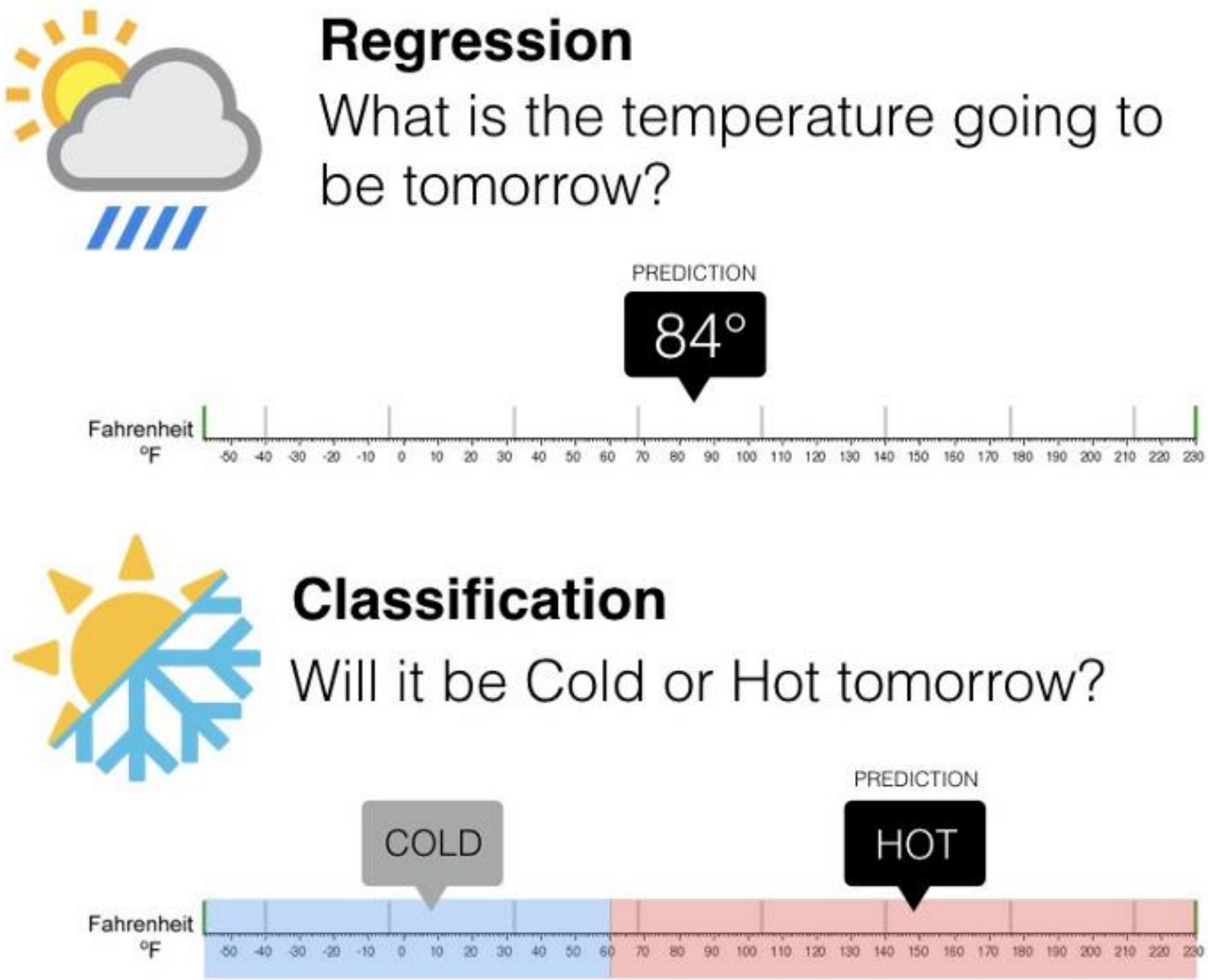
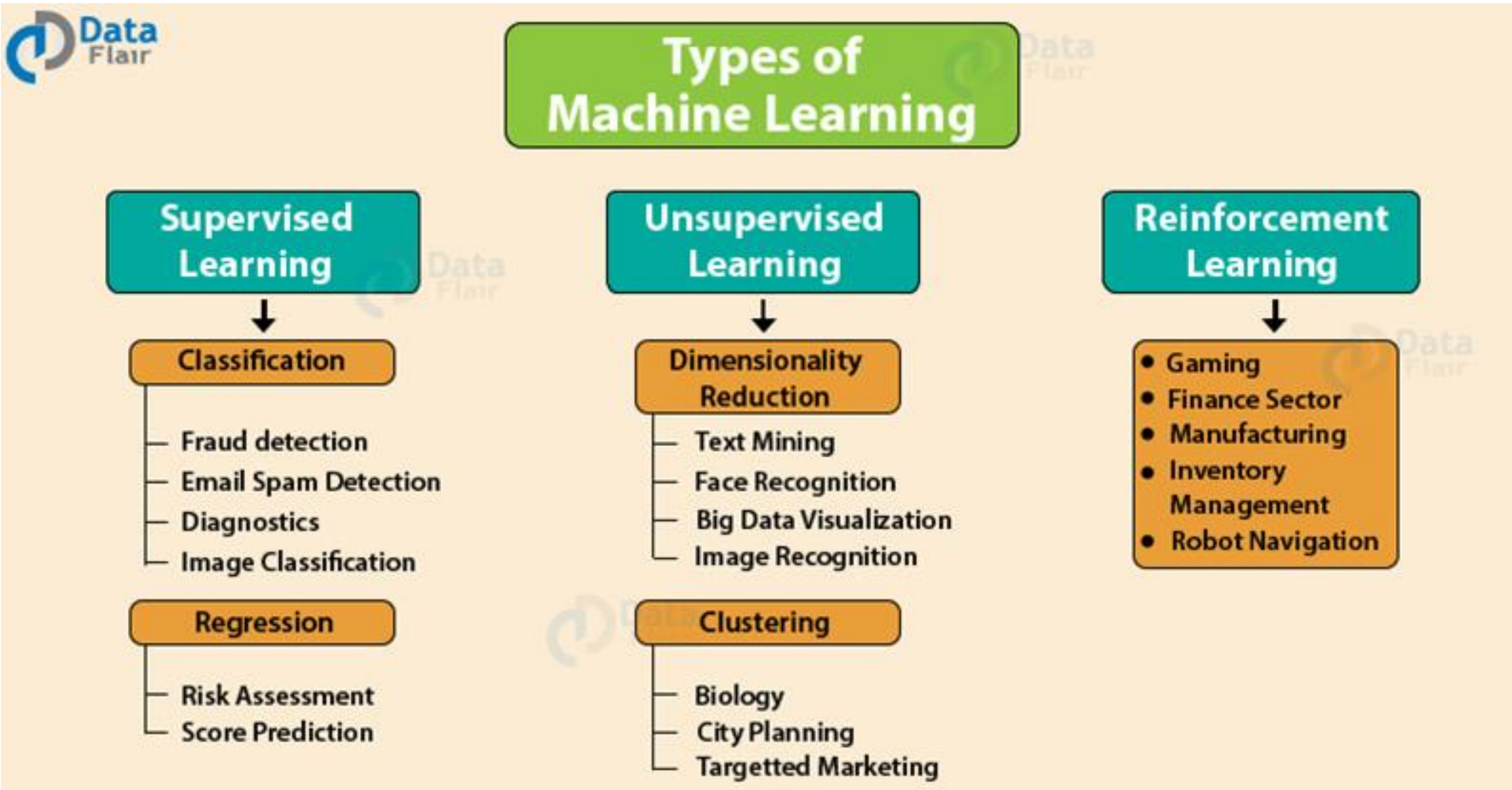
Régression ou classification



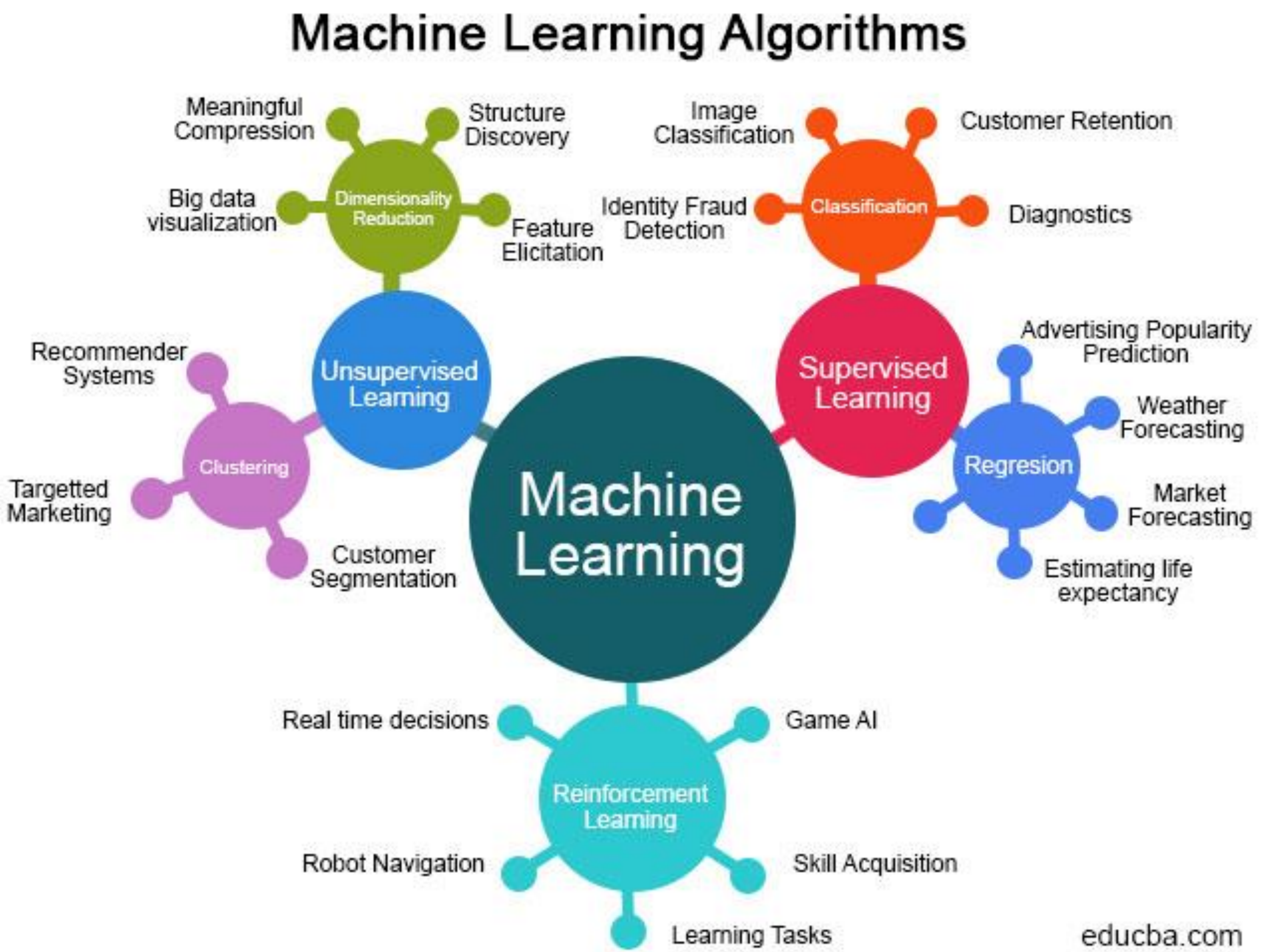
https://towardsdatascience.com/regression-or-classification-linear-or-logistic-f093e8757b9c

Principales catégories de machine learning



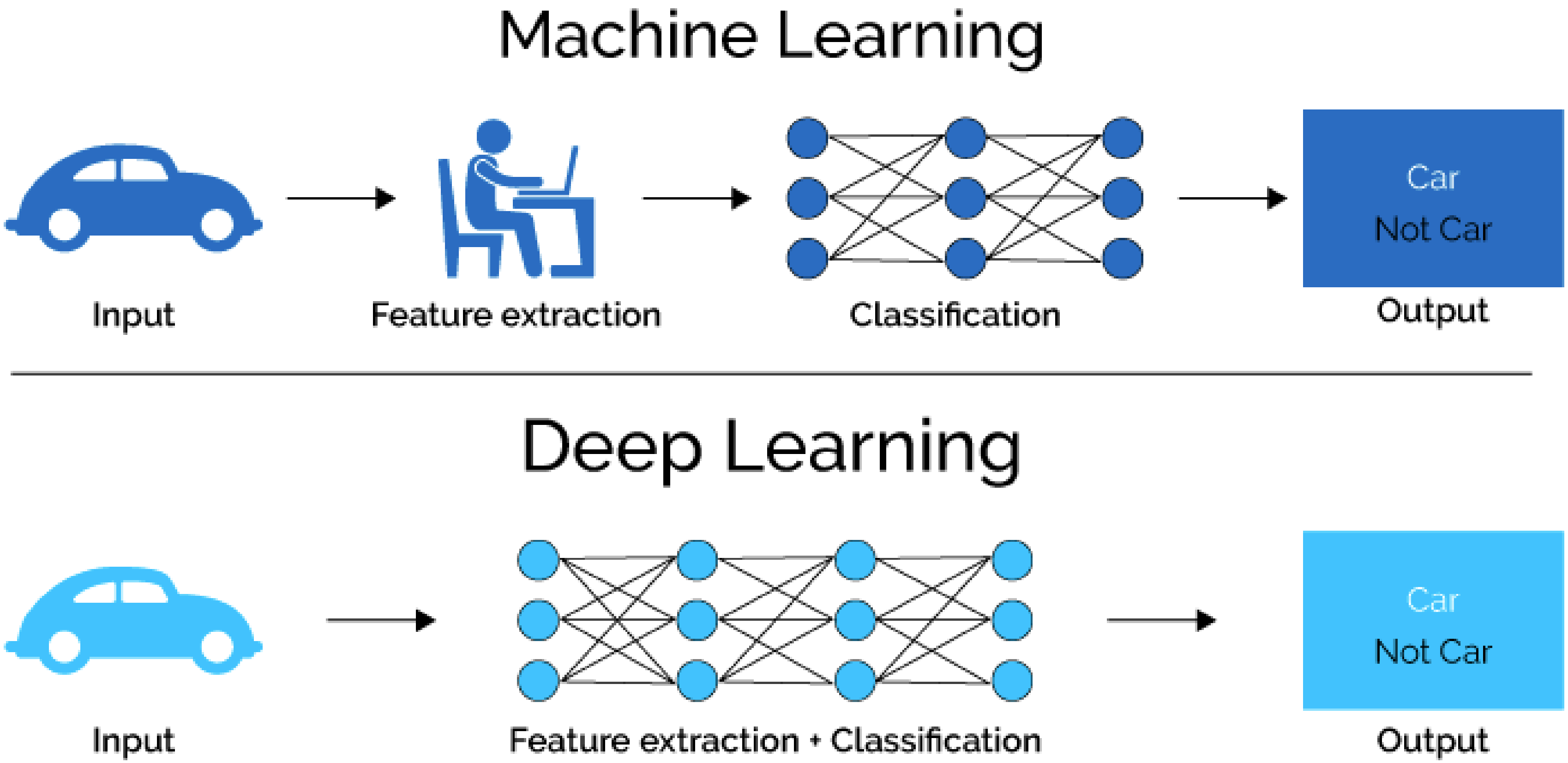
https://data-flair.training/blogs/types-of-machine-learning-algorithms/

Une prolifération d'algorithmes…



https://www.educba.com/machine-learning-algorithms/

Machine learning vs deep learning



https://lawtomated.com/tag/unsupervised-learning/

La nourriture des algorithmes : le « Big data »

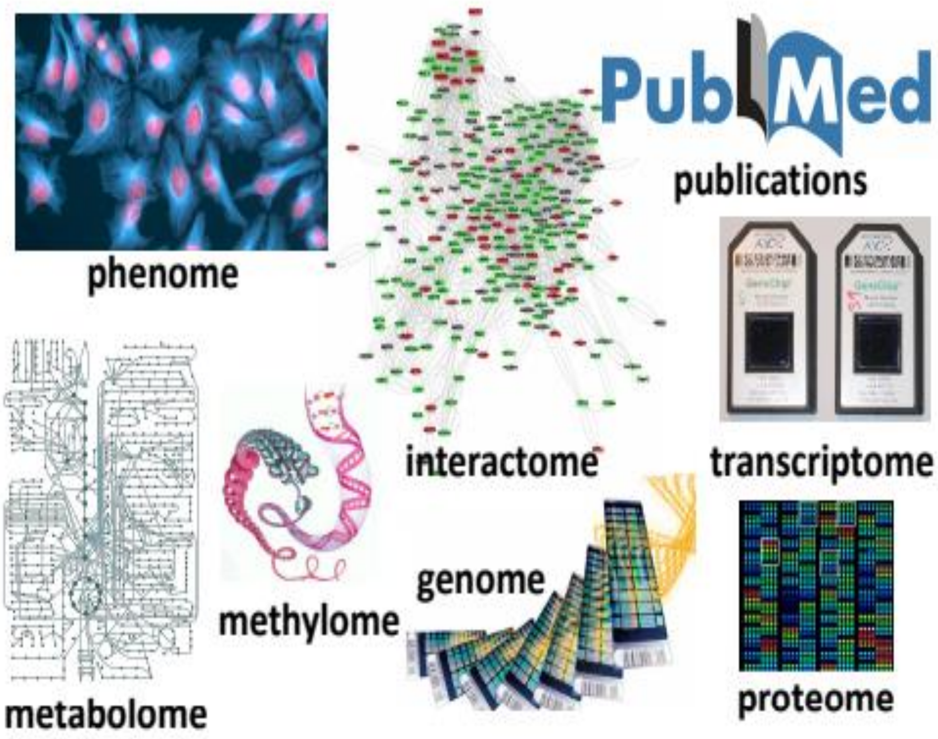
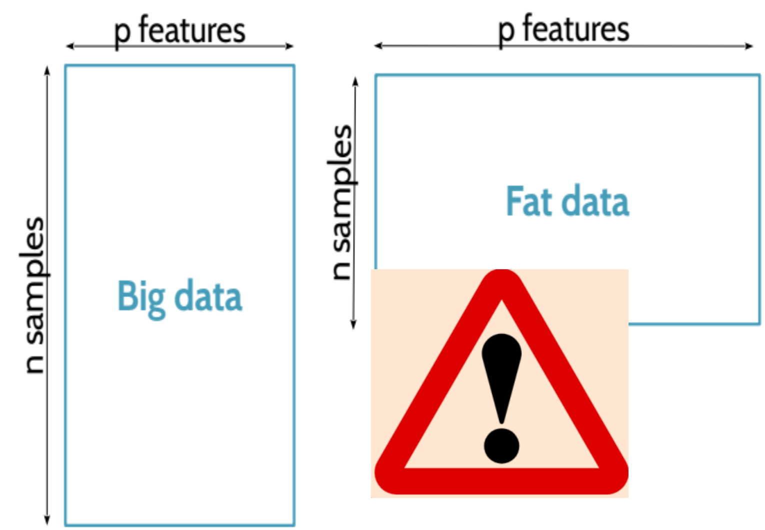


Image sources: ajc1@ flickr; Zlir'a@wikimedia

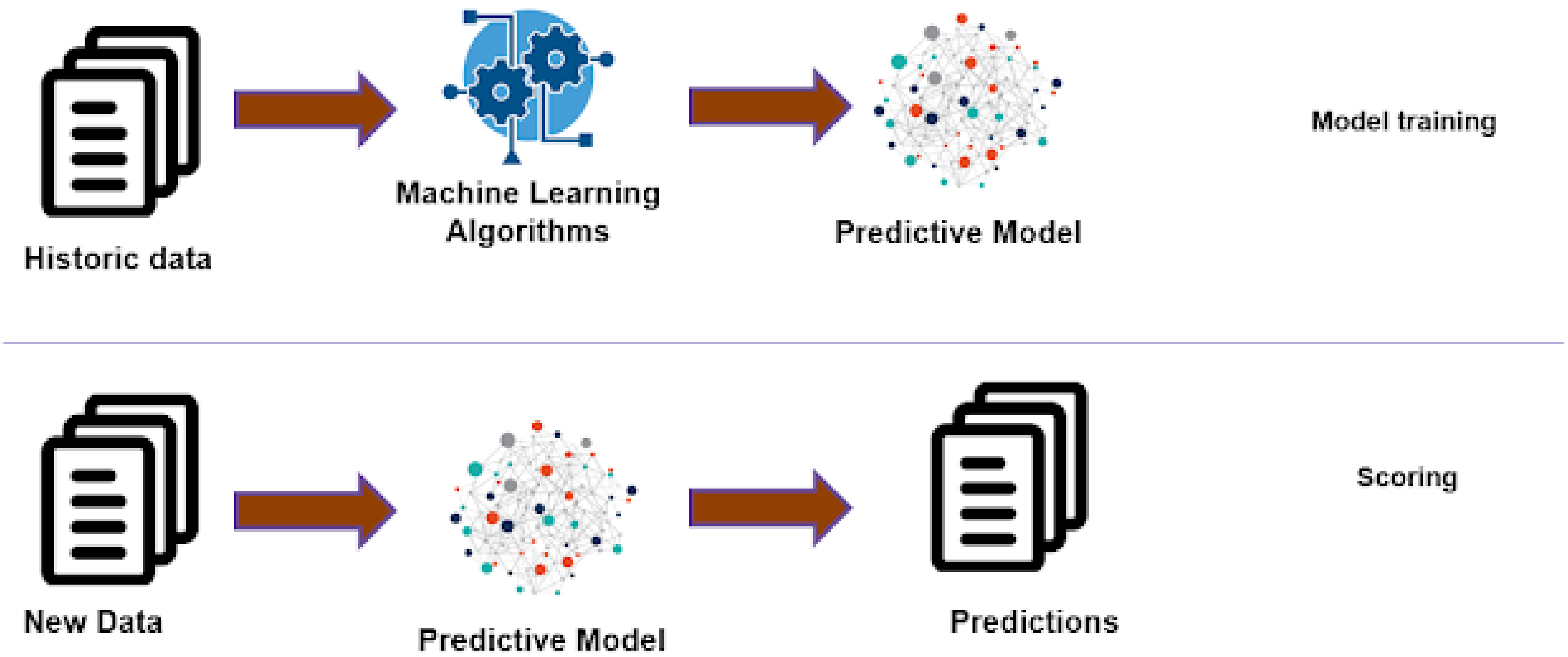


E.g. **G**enome-**W**ide **A**ssociation **S**tudies (GWAS):

- $p = 10^5 - 10^7$ **S**ingle **N**ucleotide **P**olymorphisms (SNPs)
- $n = 10^2 - 10^4$ samples.

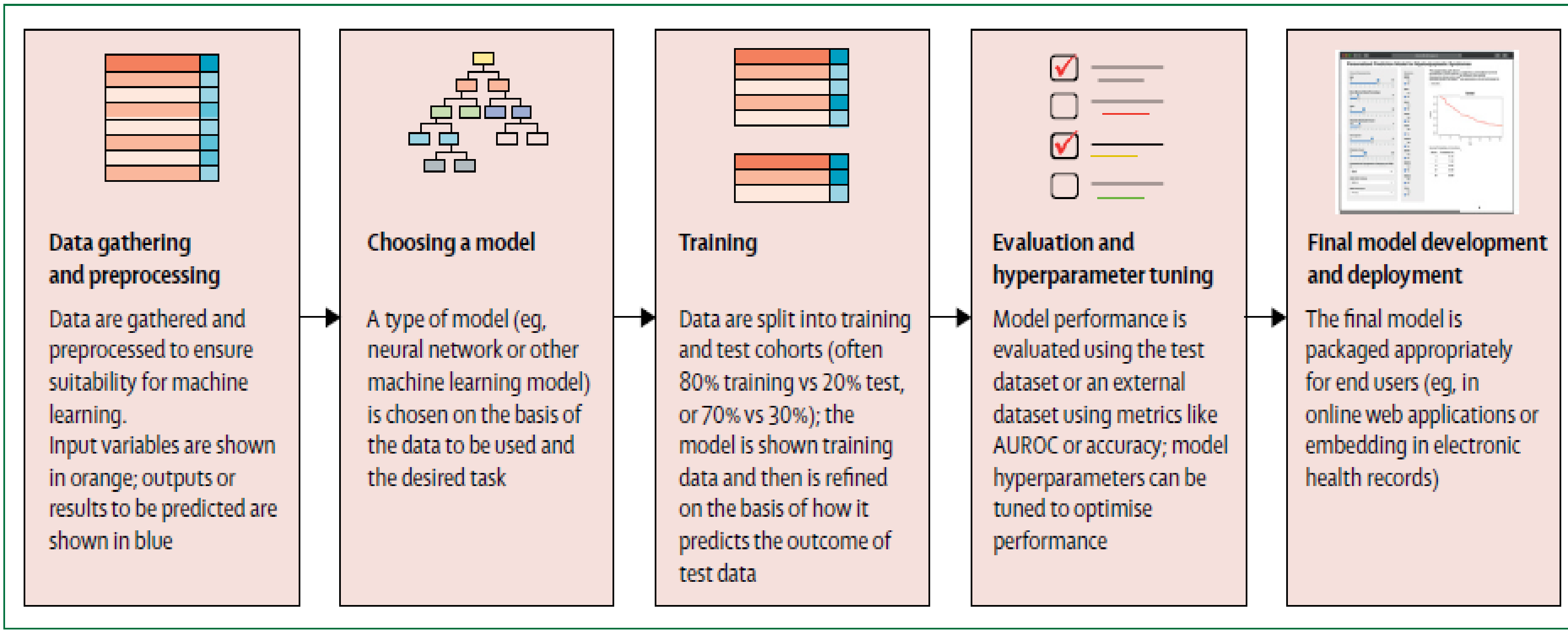
http://cazencott.info/dotclear/public/publications/2016-01-13-azencott.pdf

Workflow typique de machine learning



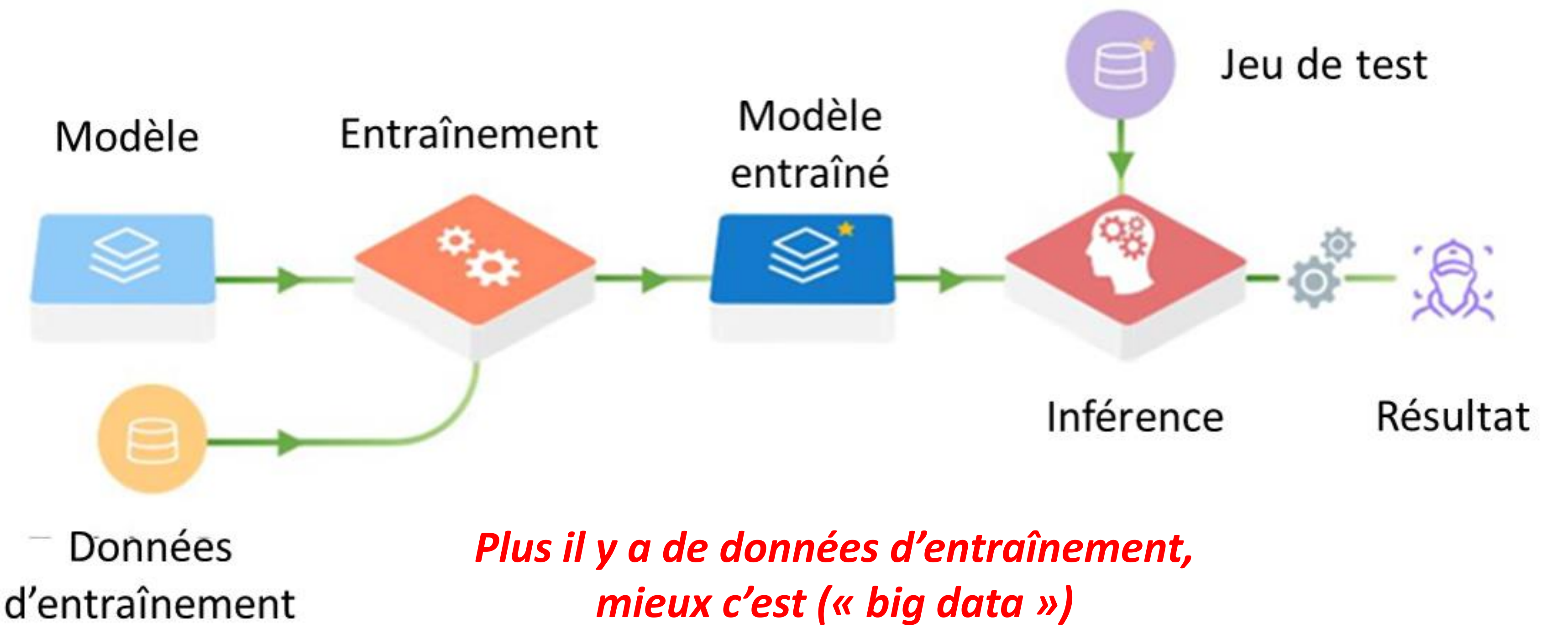
http://singaporebusinessintelligence.blogspot.com/2018/10/what-is-automated-machine-learning.html

Workflow typique de machine learning (2)



Radakovich et al., Lancet Haem 2020

Développement d'un modèle d'IA

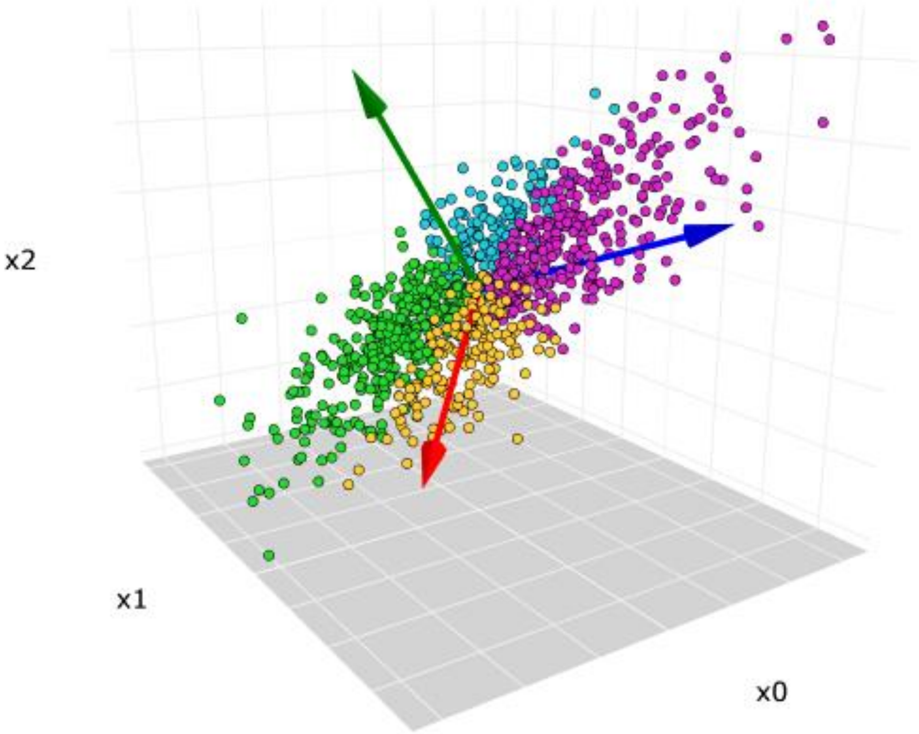


Plus il y a de données d'entraînement, mieux c'est (« big data »)

https://www.le-cortex.com/media/articles/lintelligence-artificielle-comment-ca-marche

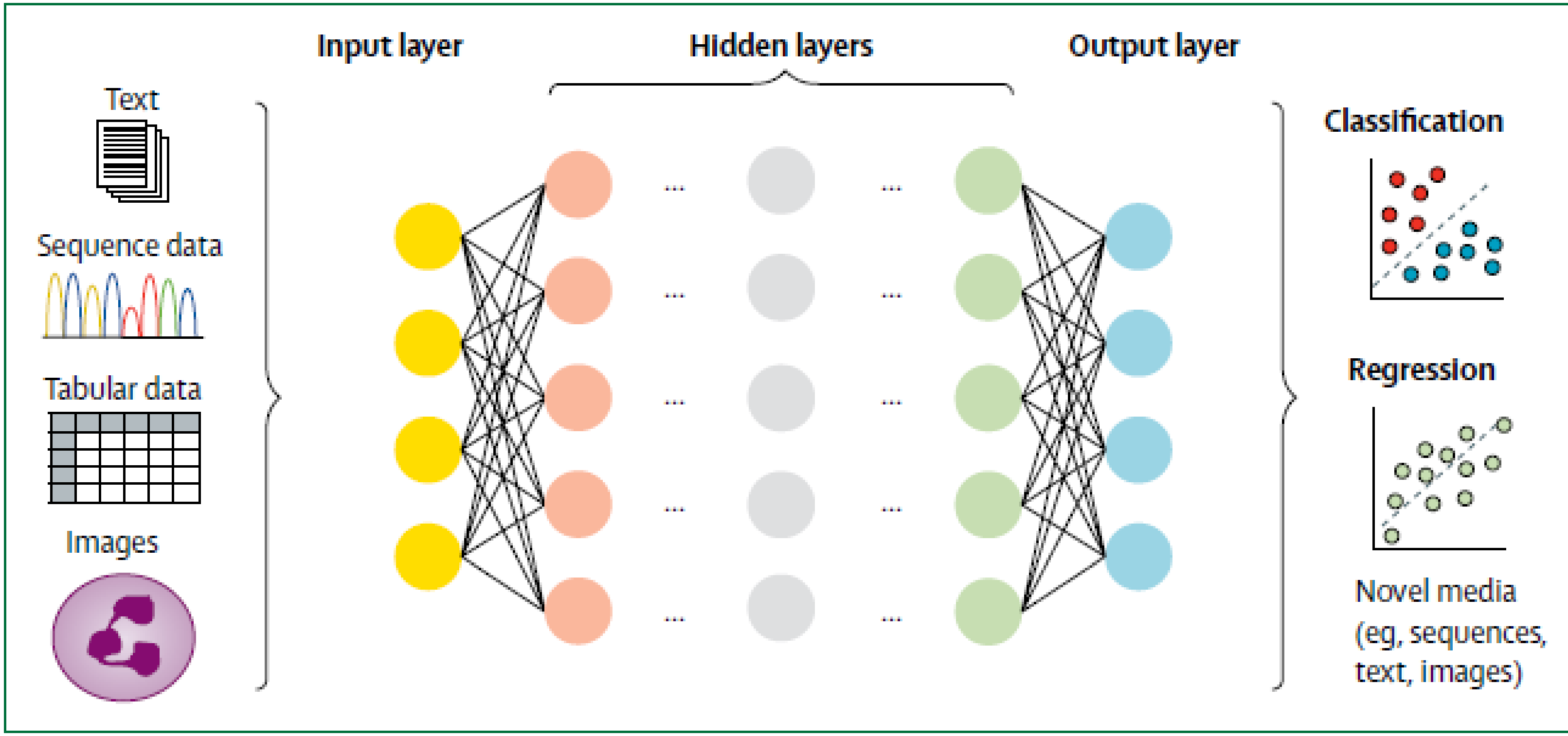
La réduction de dimension

- L'IA est aussi capable de « réduire » la dimension d'un jeu de données <u>pour le rendre plus interprétable</u>



https://towardsdatascience.com/principal-component-analysis-pca-explained-visually-with-zero-math-1cbf392b9e7d

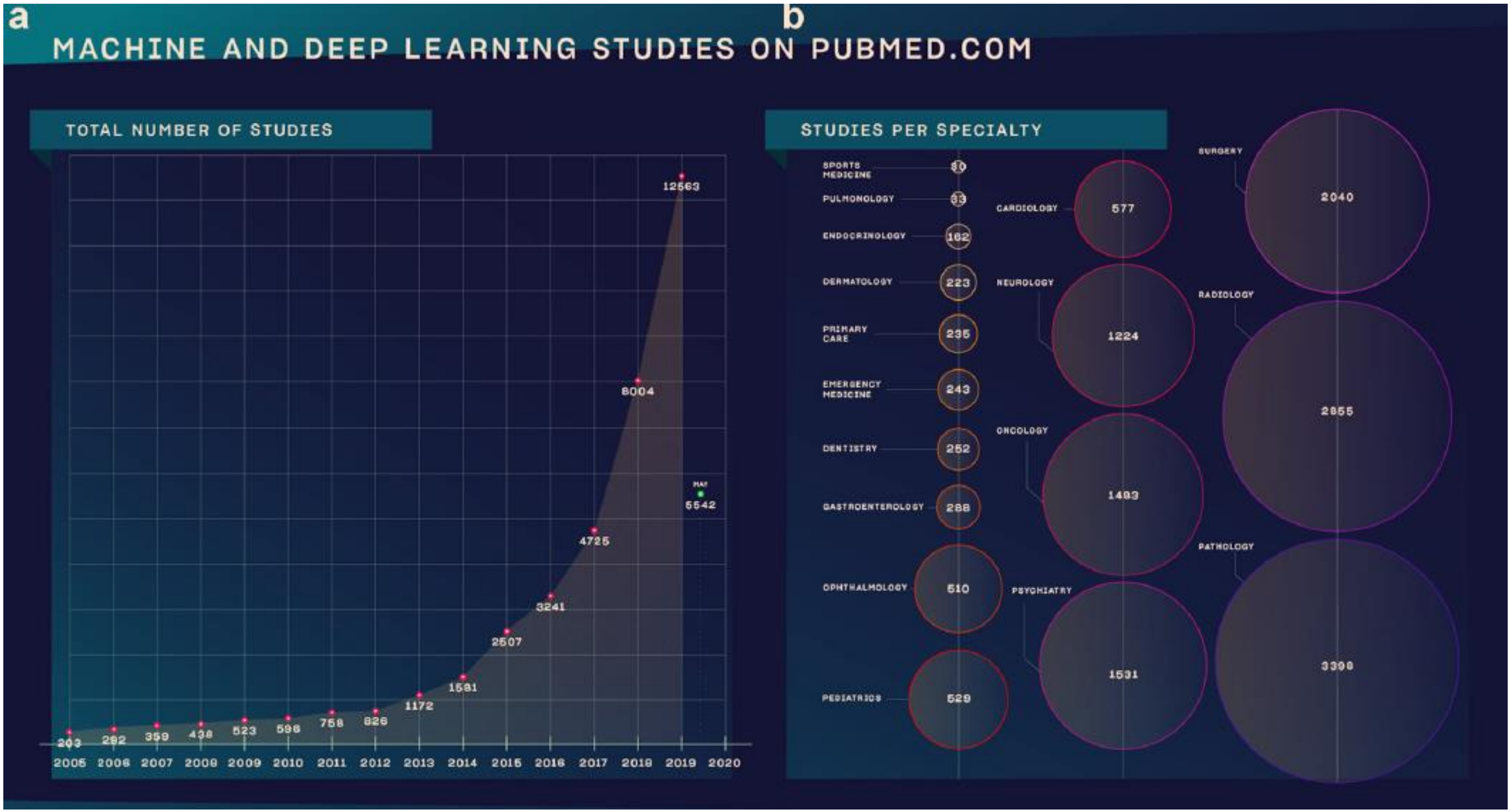
Schéma type de deep learning



Radakovich et al., Lancet Haem 2020

Intelligence artificielle en médecine : quelques applications

IA et médecine : une prolifération d'articles…



Mesko et al., Npj Digital Med, 2020

Applications potentielles en médecine (non exhaustives)

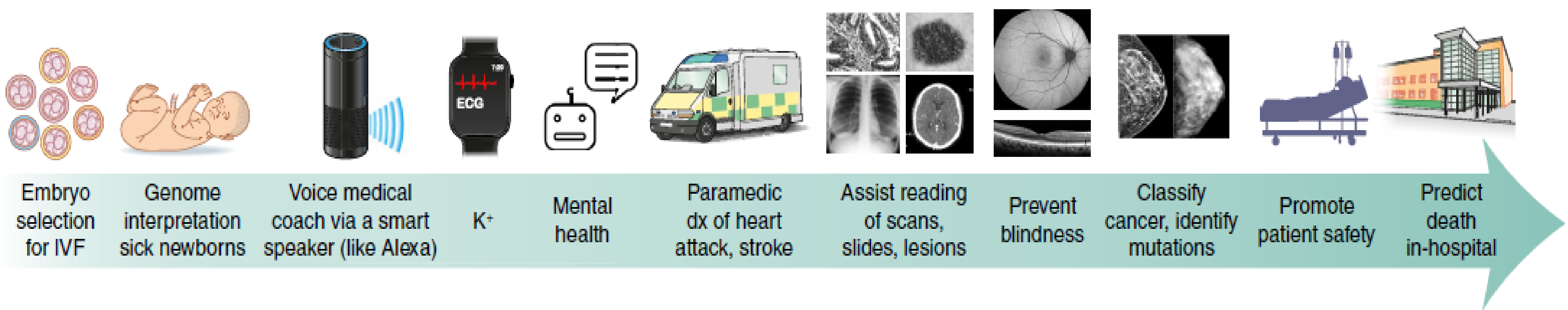


Fig. 2 | Examples of AI applications across the human lifespan. dx, diagnosis; IVF, in vitro fertilization K^+, potassium blood level. Credit: Debbie Maizels/ Springer Nature

Topol, Nat Med 2019

Applications potentielles en médecine

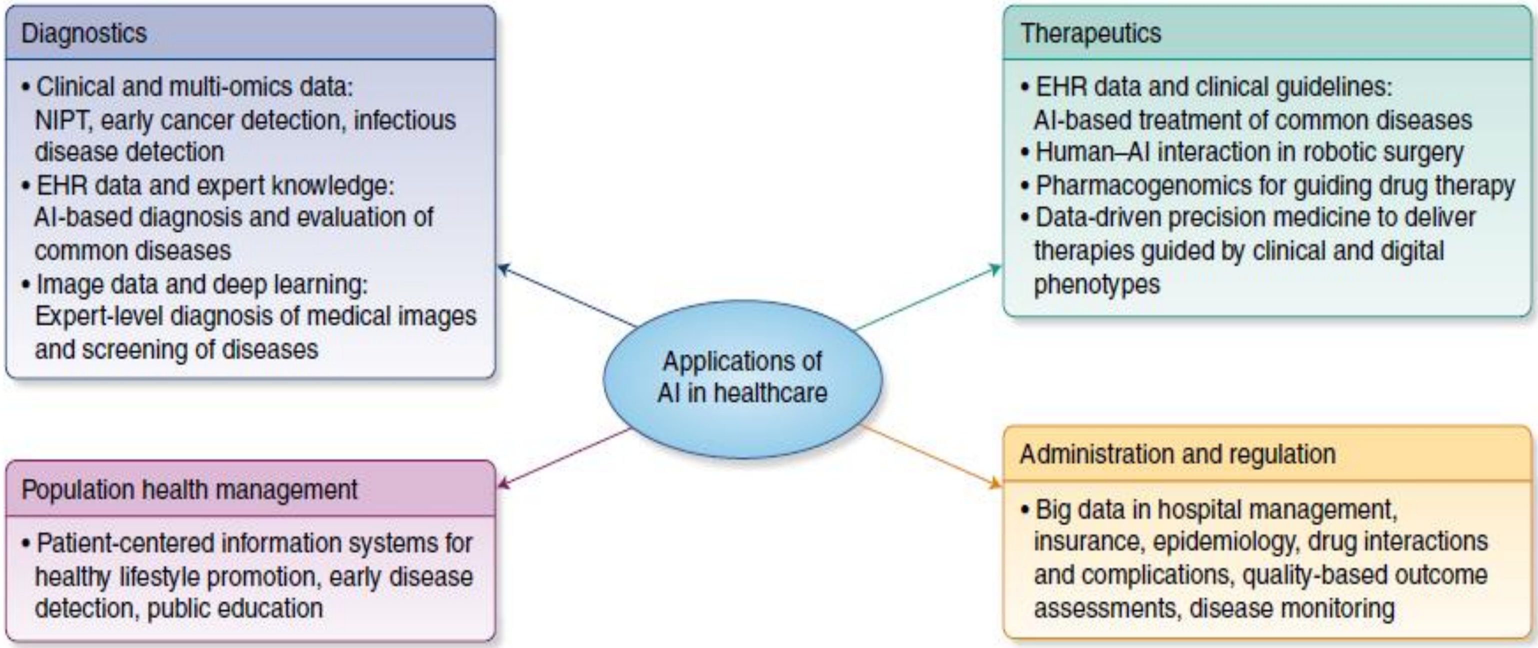
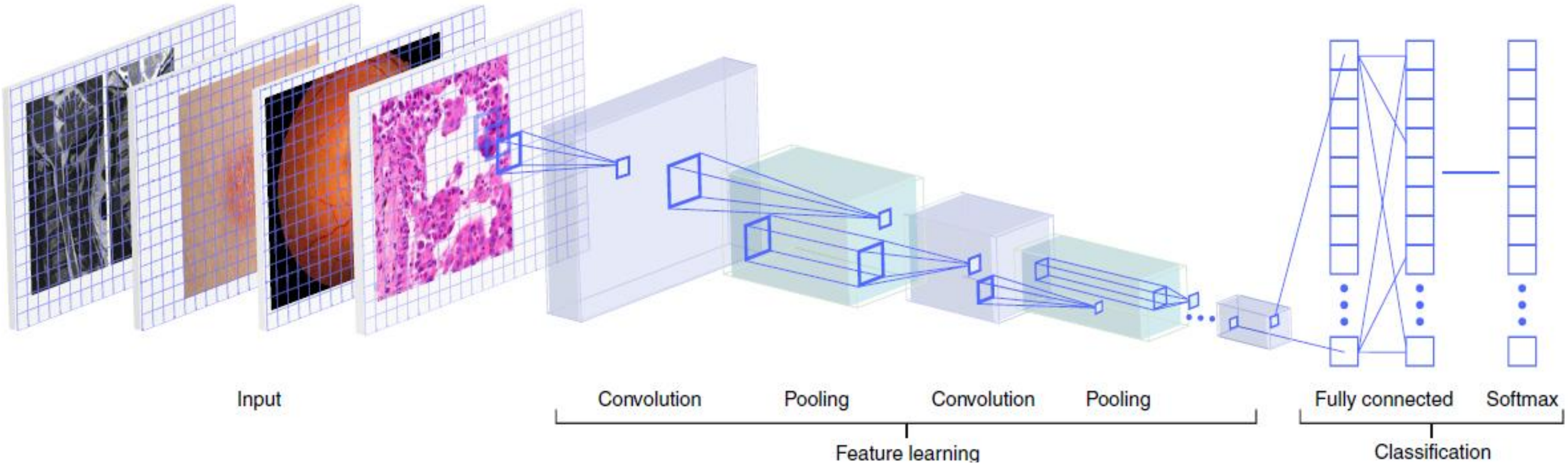
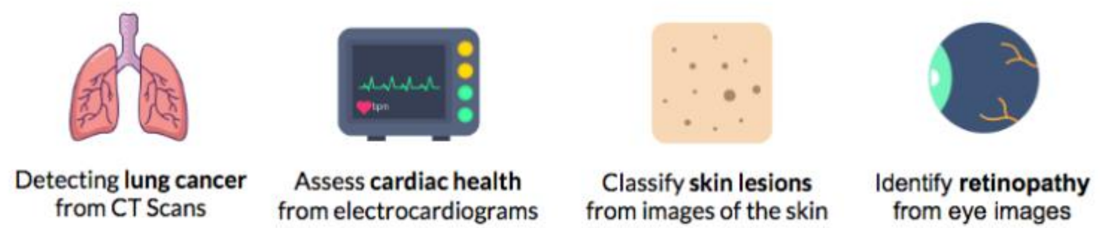


Fig. 1 | Potential roles of AI-based technologies in healthcare. In the healthcare space, AI is poised to play major roles across a spectrum of application domains, including diagnostics, therapeutics, population health management, administration, and regulation. NIPT, noninvasive prenatal test. Credit: Debbie Maizels/Springer Nature

He et al., Nat Med 2019

Un domaine pionnier : l’analyse d’images





https://www.datarevenue.com/en-blog/artificial-intelligence-in-medicine

Esteva et al., Nat Med 2019

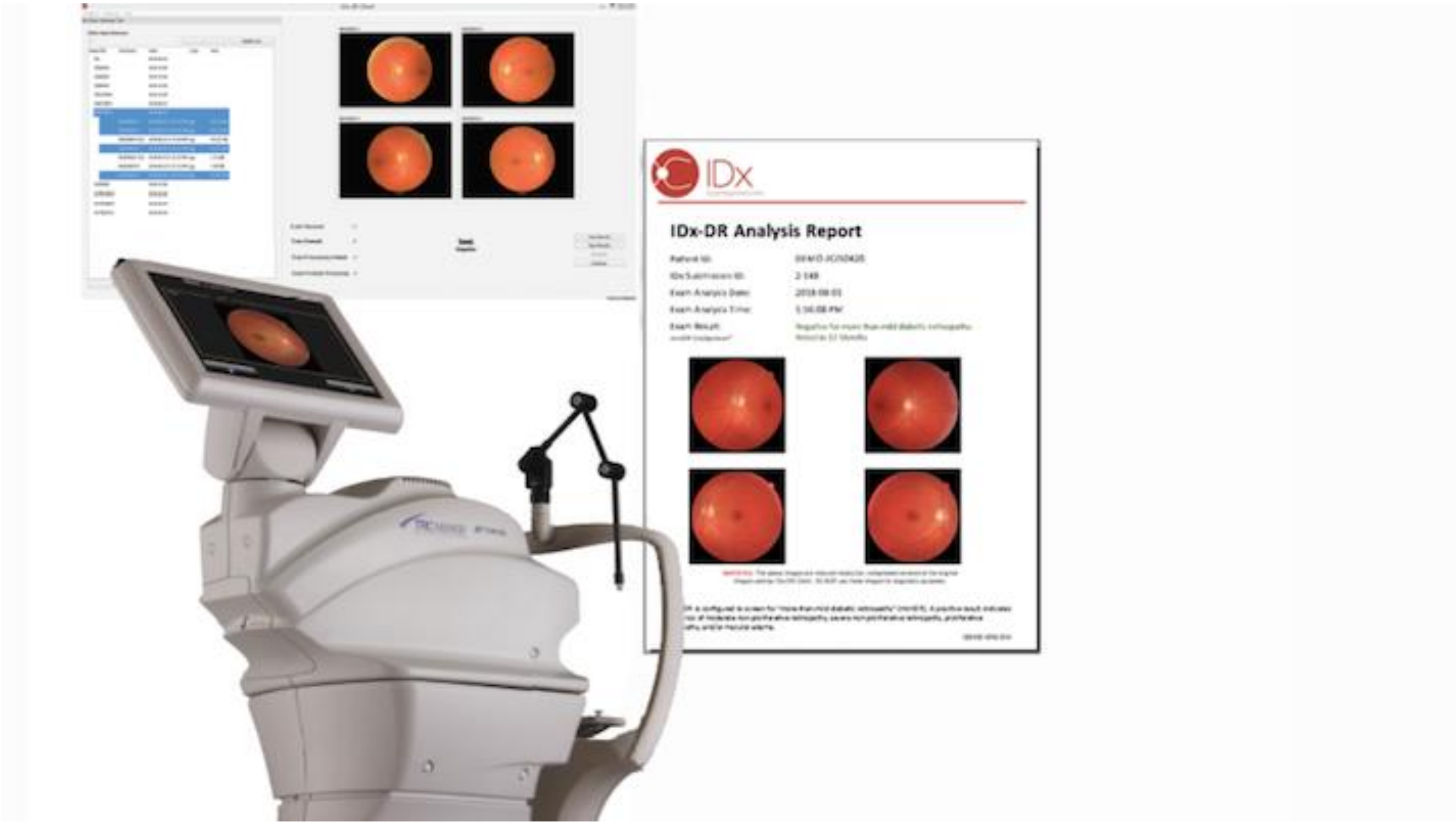
Certains outils d'IA sont déjà en pratique clinique

Table 2 | FDA AI approvals are accelerating

Company	FDA Approval	Indication
Apple	September 2018	Atrial fibrillation detection
Aidoc	August 2018	CT brain bleed diagnosis
iCAD	August 2018	Breast density via mammography
Zebra Medical	July 2018	Coronary calcium scoring
Bay Labs	June 2018	Echocardiogram EF determination
Neural Analytics	May 2018	Device for paramedic stroke diagnosis
IDx	April 2018	Diabetic retinopathy diagnosis
Icometrix	April 2018	MRI brain interpretation
Imagen	March 2018	X-ray wrist fracture diagnosis
Viz.ai	February 2018	CT stroke diagnosis
Arterys	February 2018	Liver and lung cancer (MRI, CT) diagnosis
MaxQ-AI	January 2018	CT brain bleed diagnosis
Alivecor	November 2017	Atrial fibrillation detection via Apple Watch
Arterys	January 2017	MRI heart interpretation

Topol, Nat Med 2019

Dépistage de la rétinopathie diabétique (IDx)



https://dxs.ai/

Perspective :
le « coach médical virtuel »

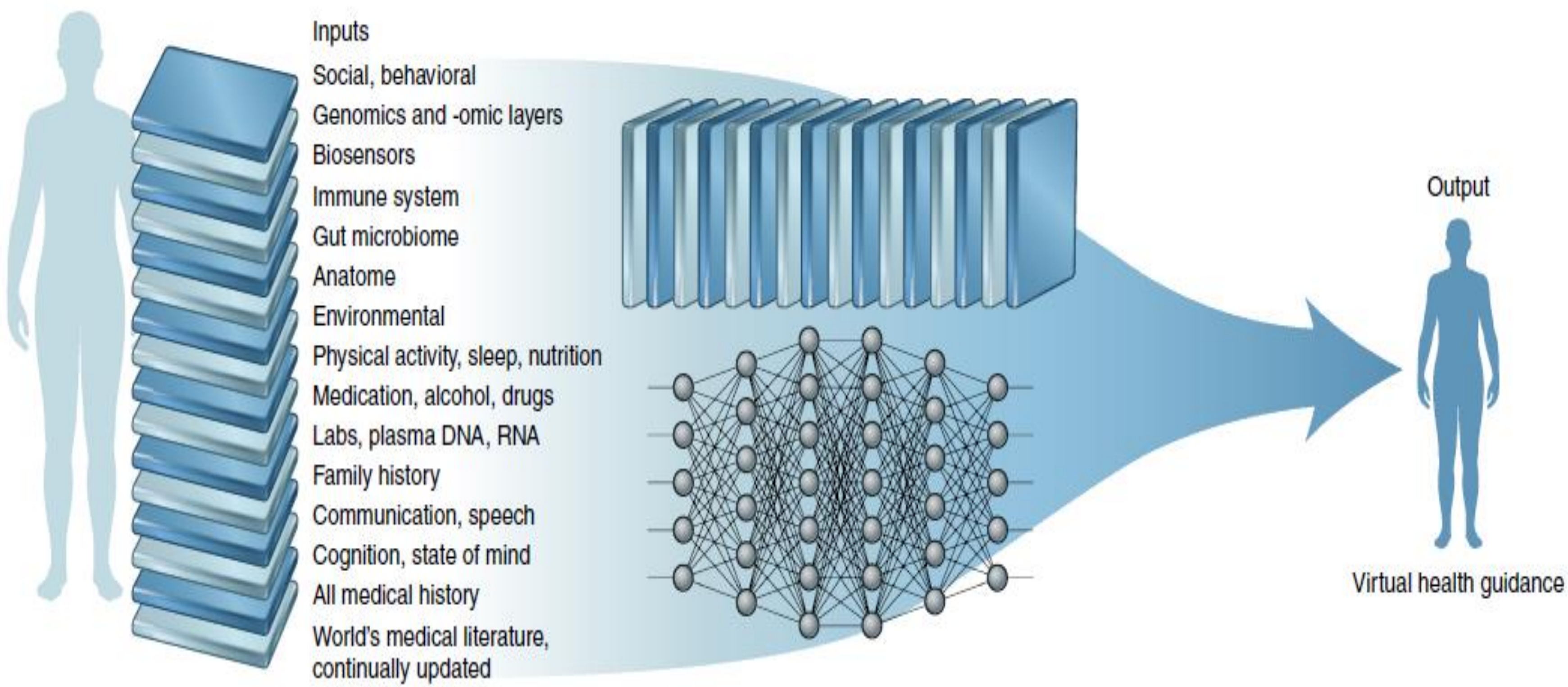
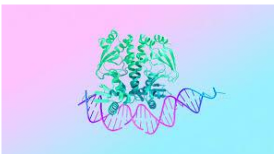


Fig. 3 | The virtual medical coach model with multi-modal data inputs and algorithms to provide individualized guidance. A virtual medical coach that uses comprehensive input from an individual that is deep learned to provide recommendations for preserving the person's health. Credit: Debbie Maizels/ Springer Nature

Topol, Nat Med 2019

IA en oncologie : quelques applications

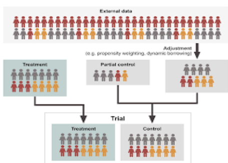
Applications potentielles de l’IA en oncologie

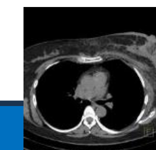


Médecine de précision (diagnostic, pronostic, thérapeutique)

Découverte de nouveaux médicaments

Anatomopathologie



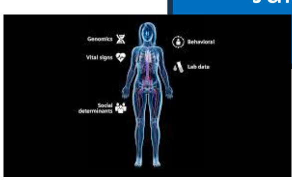


Design d’essais cliniques (bras synthétiques)

Intelligence artificielle

Imagerie

Jumeaux virtuels

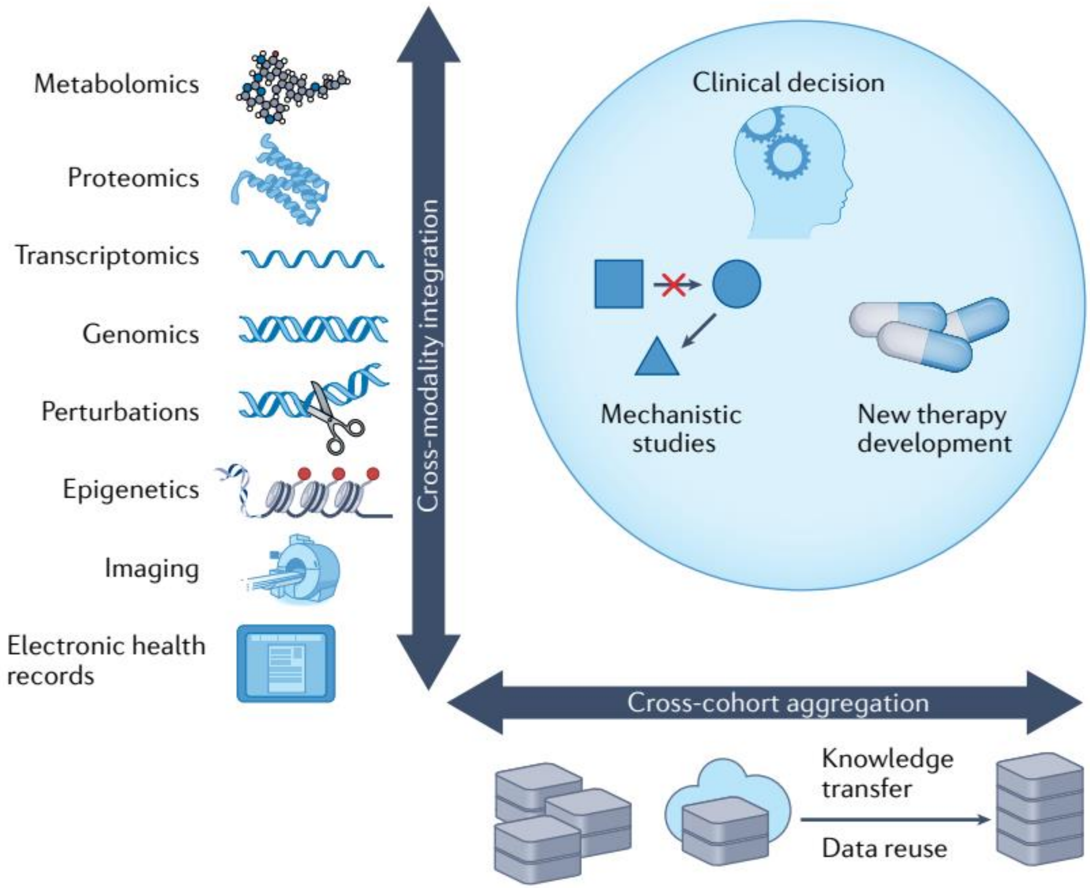


Planification du traitement (chirurgie, radiothérapie)

Optimisation du workflow clinique

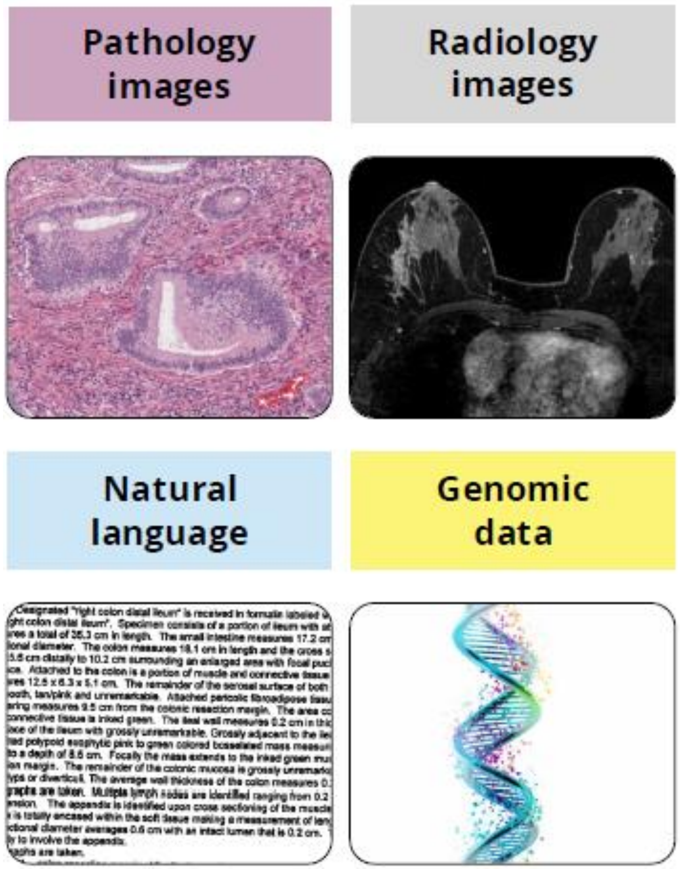
Chatbots pour les patients et leur suivi

Intégration et agrégation de données



Jiang, Nat Rev Cancer, 2022

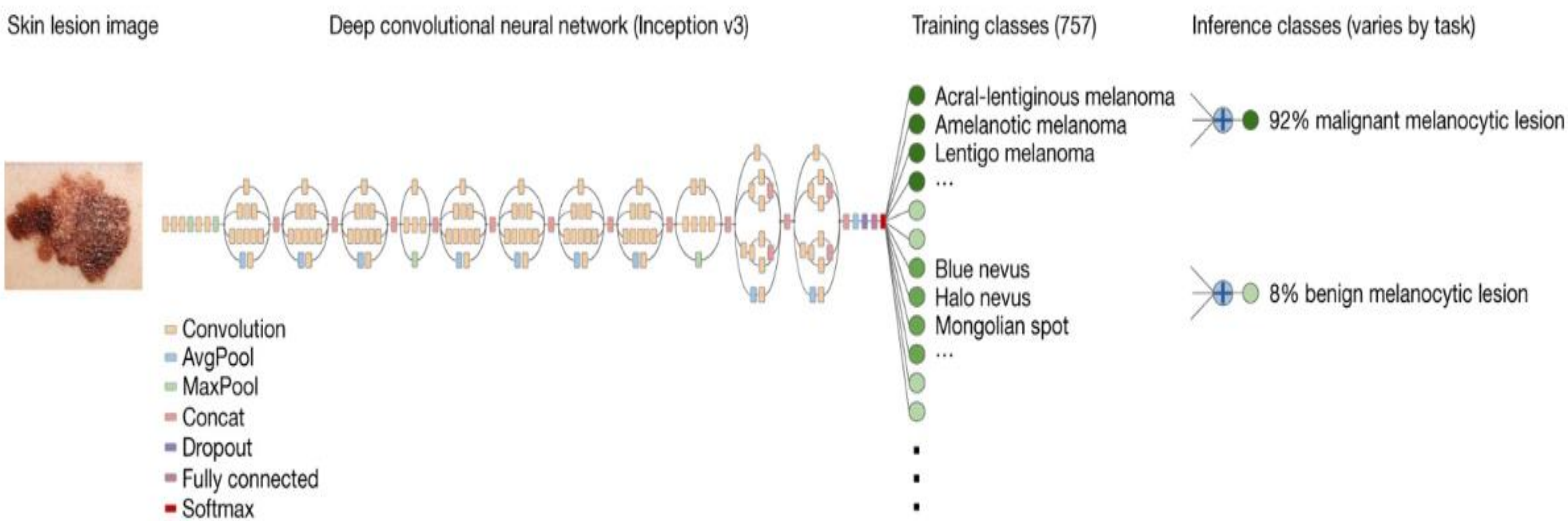
Données « AI-able » en oncologie



Jakob Kather

Classification des cancers dermatologiques

From: Dermatologist-level classification of skin cancer with deep neural networks



Esteva et al., Nature 2017

IA à visée diagnostique : analyses d’images

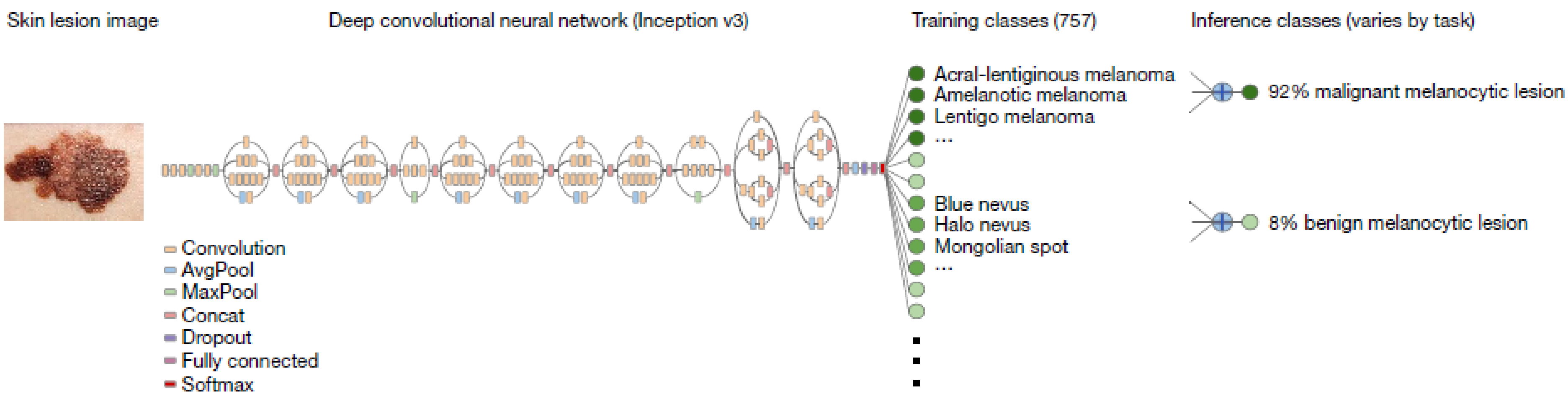
LETTER

doi:10.1038/nature21056

Dermatologist-level classification of skin cancer with deep neural networks

Andre Esteva[1*], Brett Kuprel[1*], Roberto A. Novoa[2,3], Justin Ko[2], Susan M. Swetter[2,4], Helen M. Blau[5] & Sebastian Thrun[6]

Données d’entraînement :
129 450 images, 757 maladies



IA à visée diagnostique: analyses d'images

LETTER

doi:10.1038/nature21056

Comparaison algorithme vs 21 dermatologues

Dermatologist-level classification of skin cancer with deep neural networks

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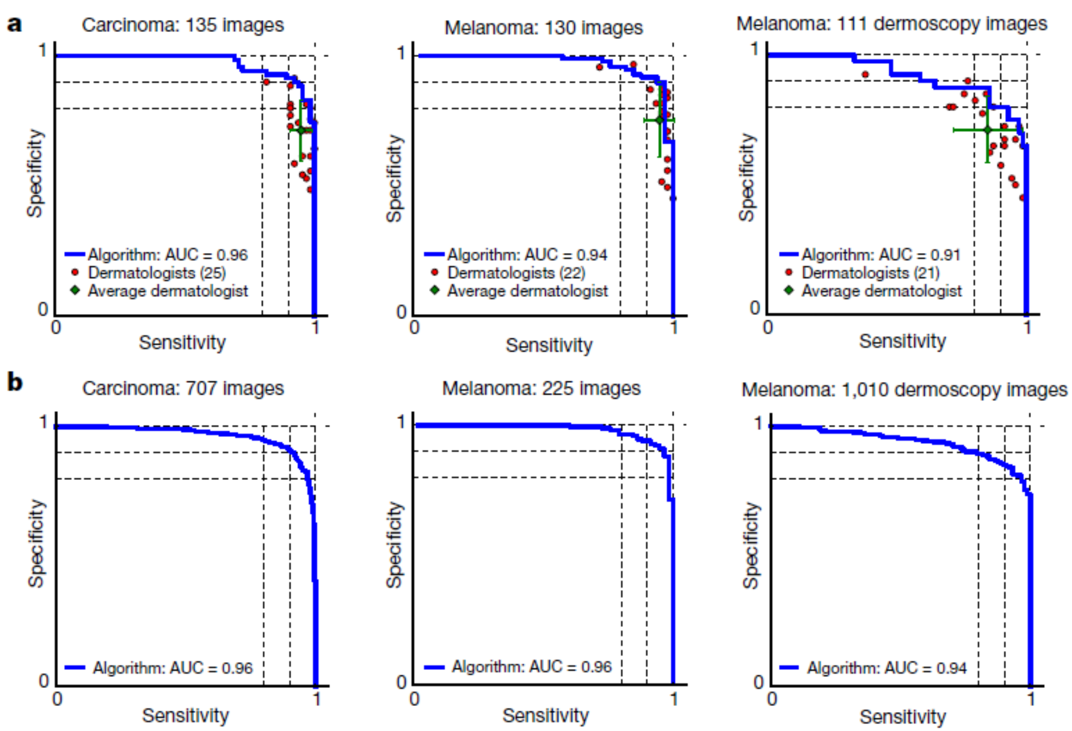


IA à visée diagnostique: radiologie

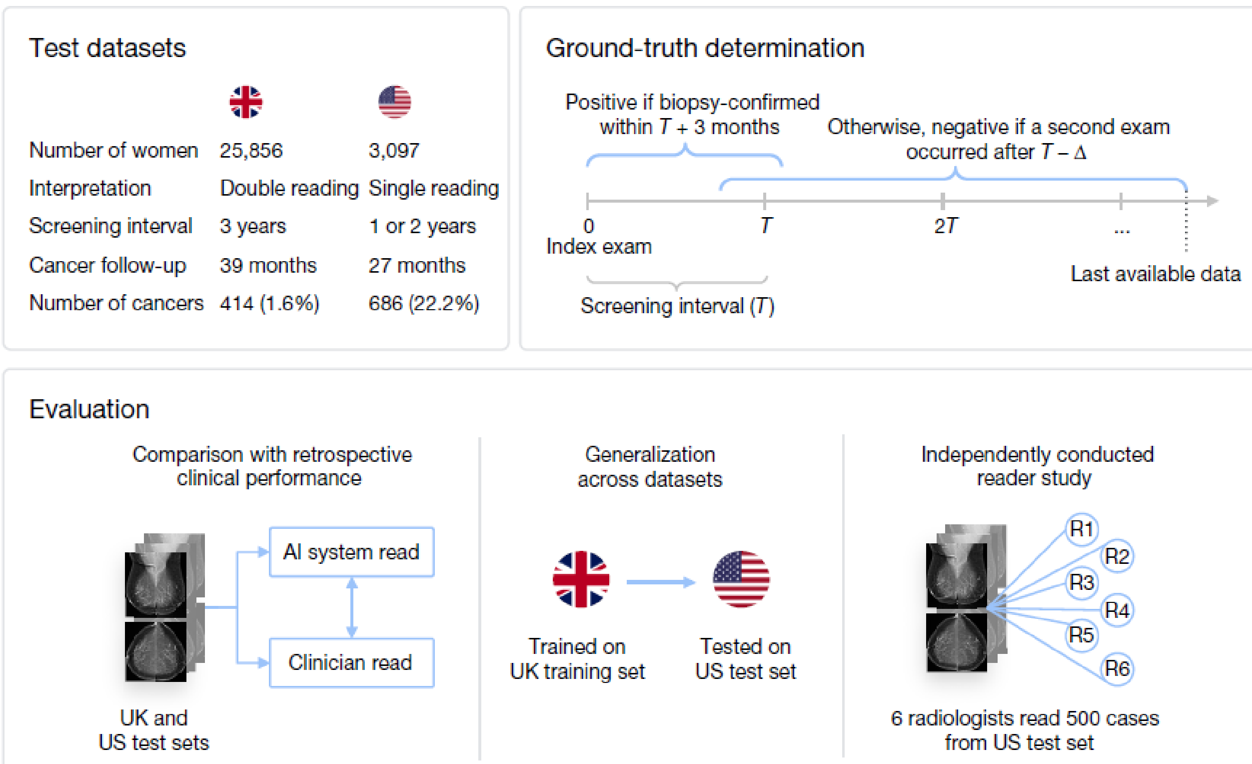
Données d'entraînement :
mammographies de 25 856 femmes (UK)
Données de test :
mammographies de 3097 femmes (US)

Article

International evaluation of an AI system for breast cancer screening

https://doi.org/10.1038/s41586-019-1799-6
Received: 27 July 2019
Accepted: 5 November 2019
Published online: 1 January 2020

Scott Mayer McKinney[1,14*], Marcin Sieniek[1,14], Varun Godbole[1,14], Jonathan Godwin[2,14], Natasha Antropova[2], Hutan Ashrafian[3,4], Trevor Back[2], Mary Chesus[2], Greg S. Corrado[1], Ara Darzi[3,4,5], Mozziyar Etemadi[6], Florencia Garcia-Vicente[6], Fiona J. Gilbert[7], Mark Halling-Brown[8], Demis Hassabis[2], Sunny Jansen[9], Alan Karthikesalingam[10], Christopher J. Kelly[10], Dominic King[10], Joseph R. Ledsam[2], David Melnick[6], Hormuz Mostofi[1], Lily Peng[1], Joshua Jay Reicher[11], Bernardino Romera-Paredes[2], Richard Sidebottom[12,13], Mustafa Suleyman[2], Daniel Tse[1*], Kenneth C. Young[8], Jeffrey De Fauw[2,15] & Shravya Shetty[1,15*]



GUSTAVE ROUSSY
CANCER CAMPUS GRAND PARIS

IA à visée diagnostique: radiologie

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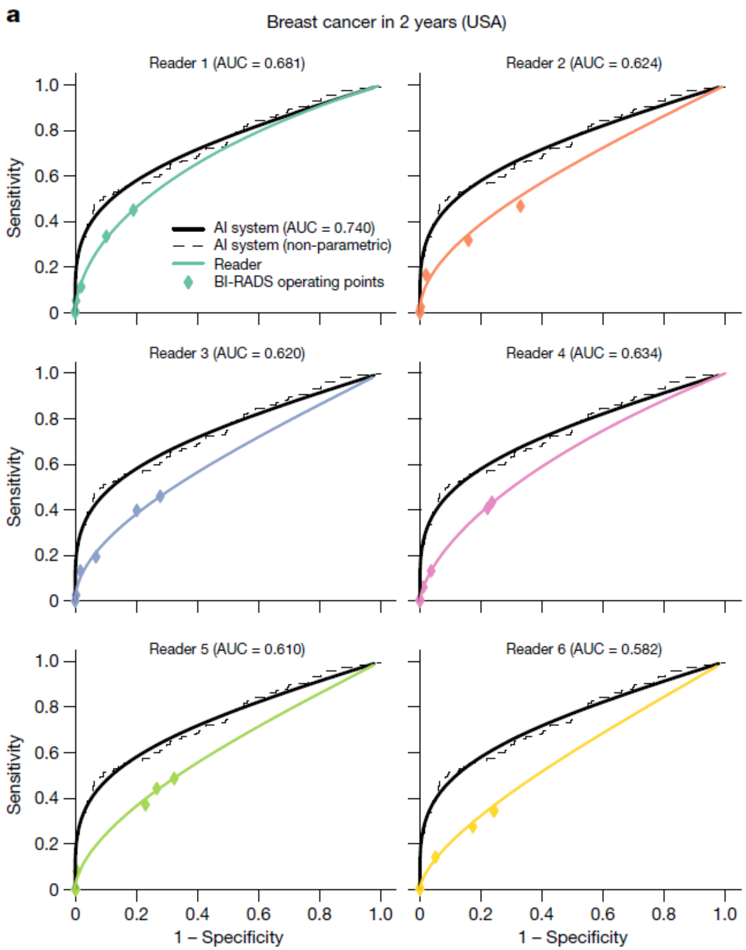
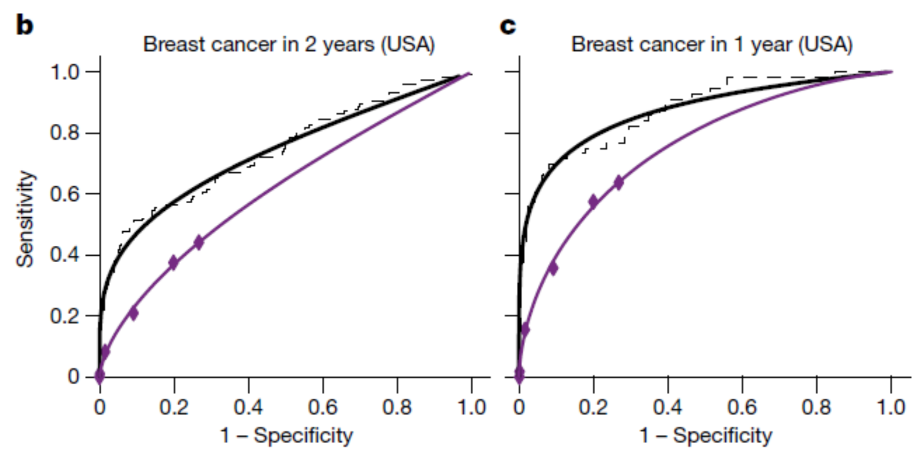


Comparaison aux performances de 6 radiologues indépendants sur 500 examens



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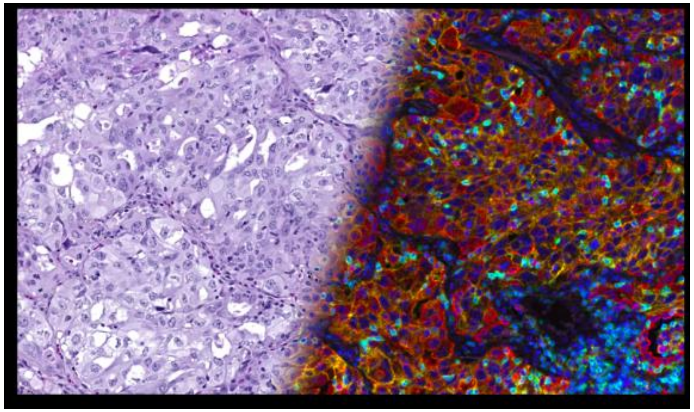
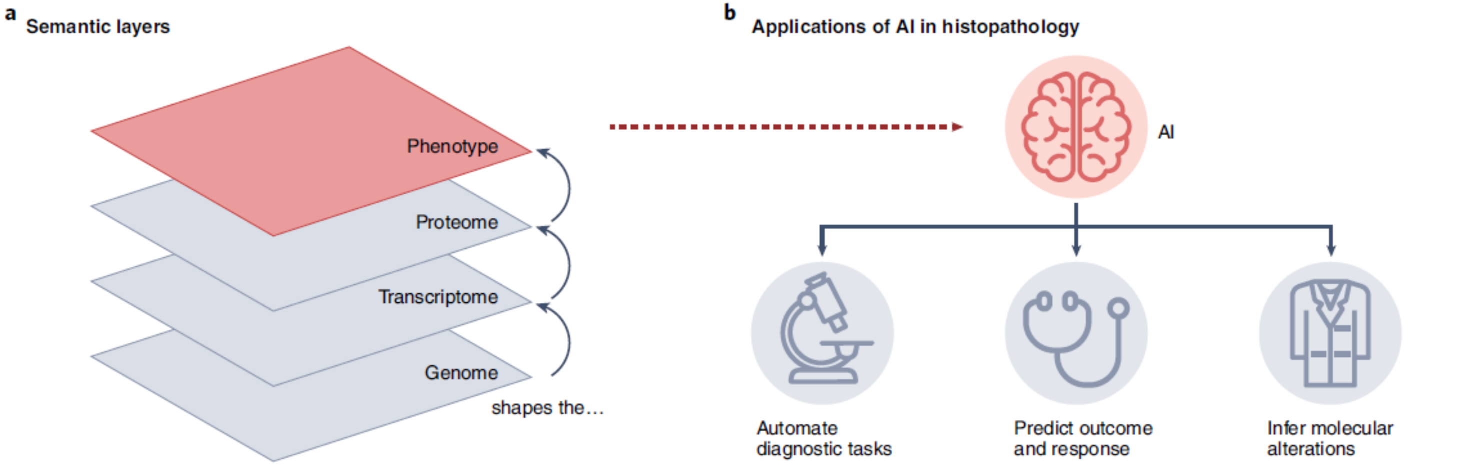
IA et pathologie digitale

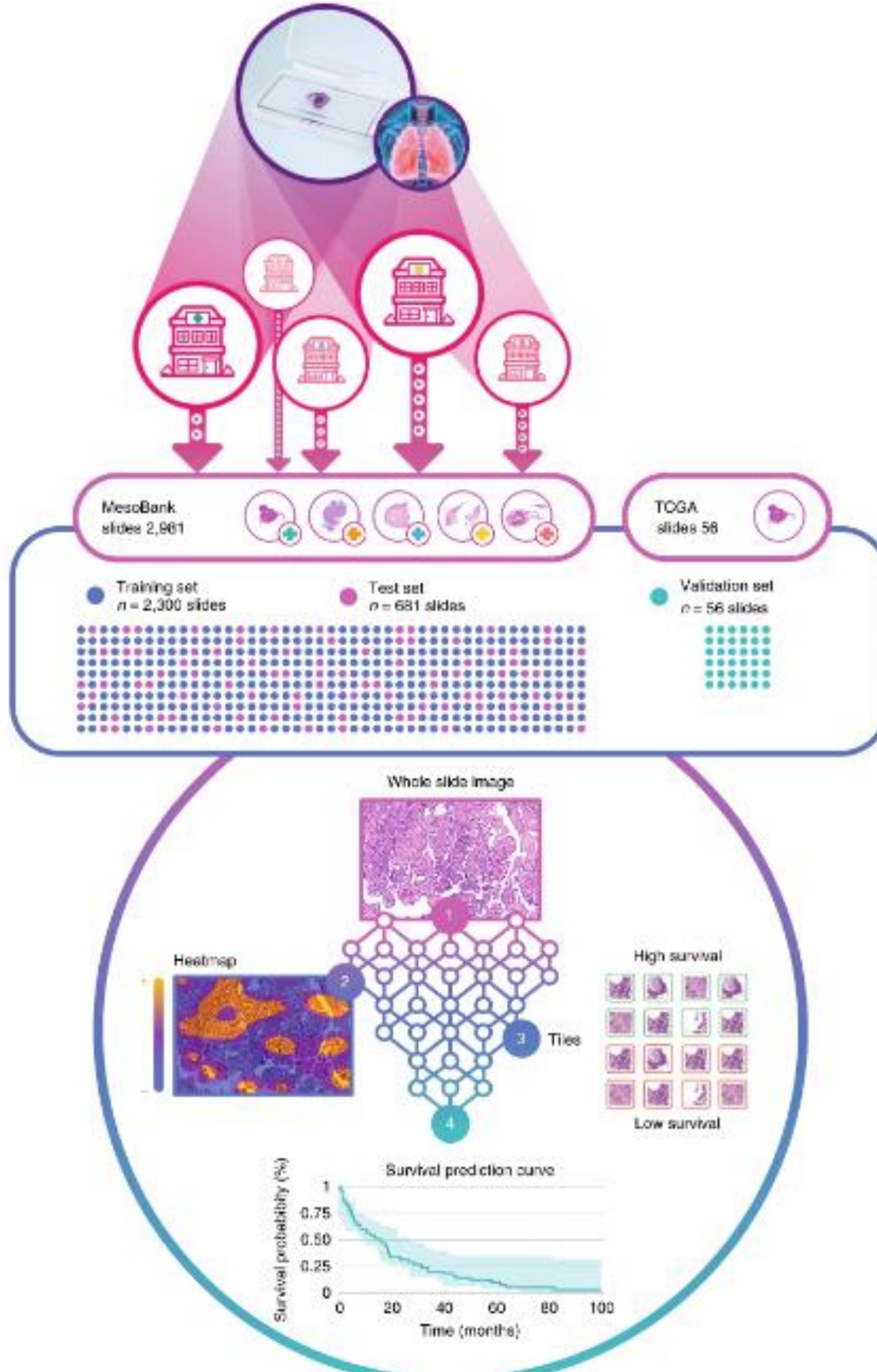




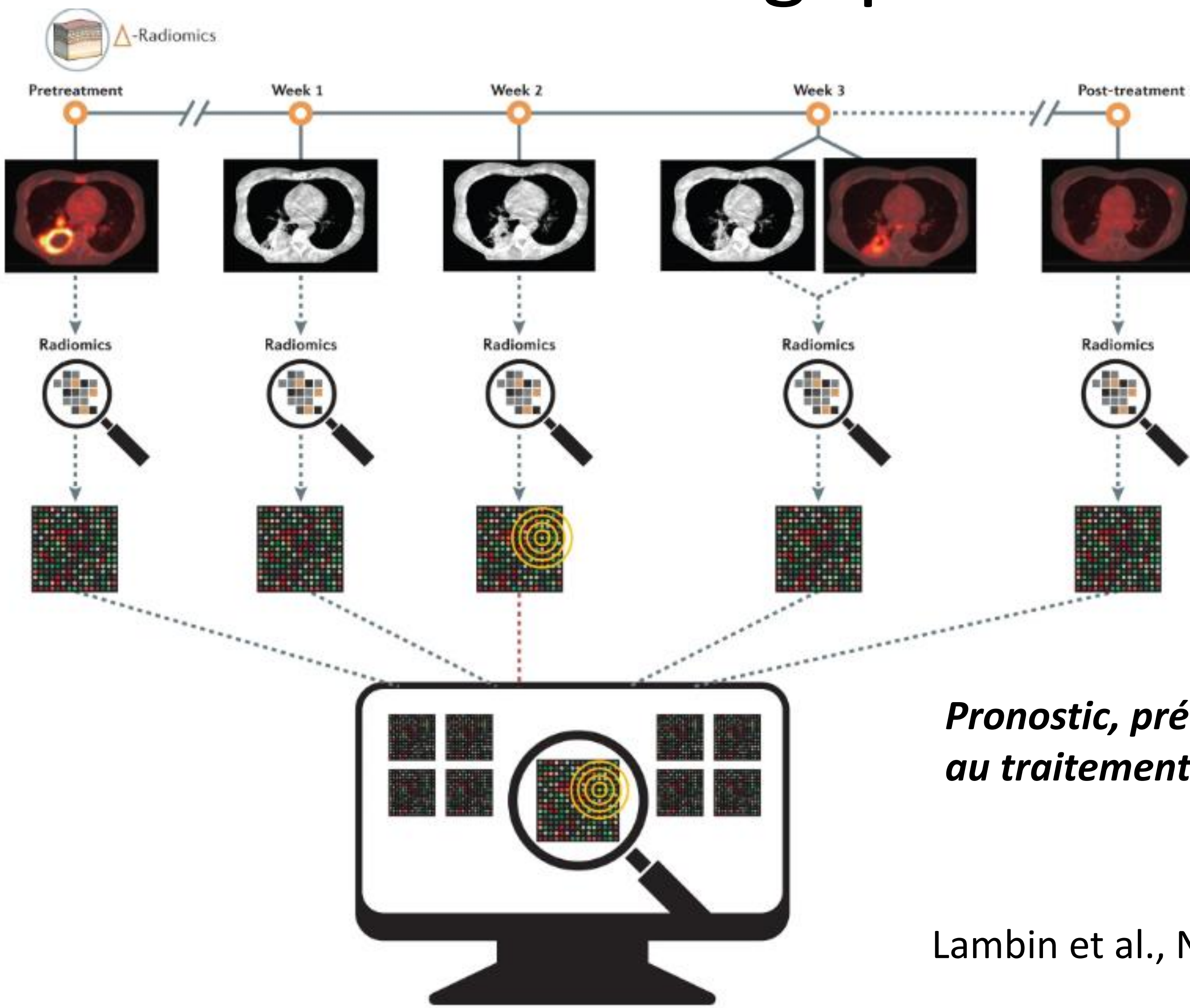
Shmatko, *Nature Cancer* 2022

Prédiction du pronostic des mésothéliomes à partir de lames histologiques

Courtiol et al.,
Nature Med 2019



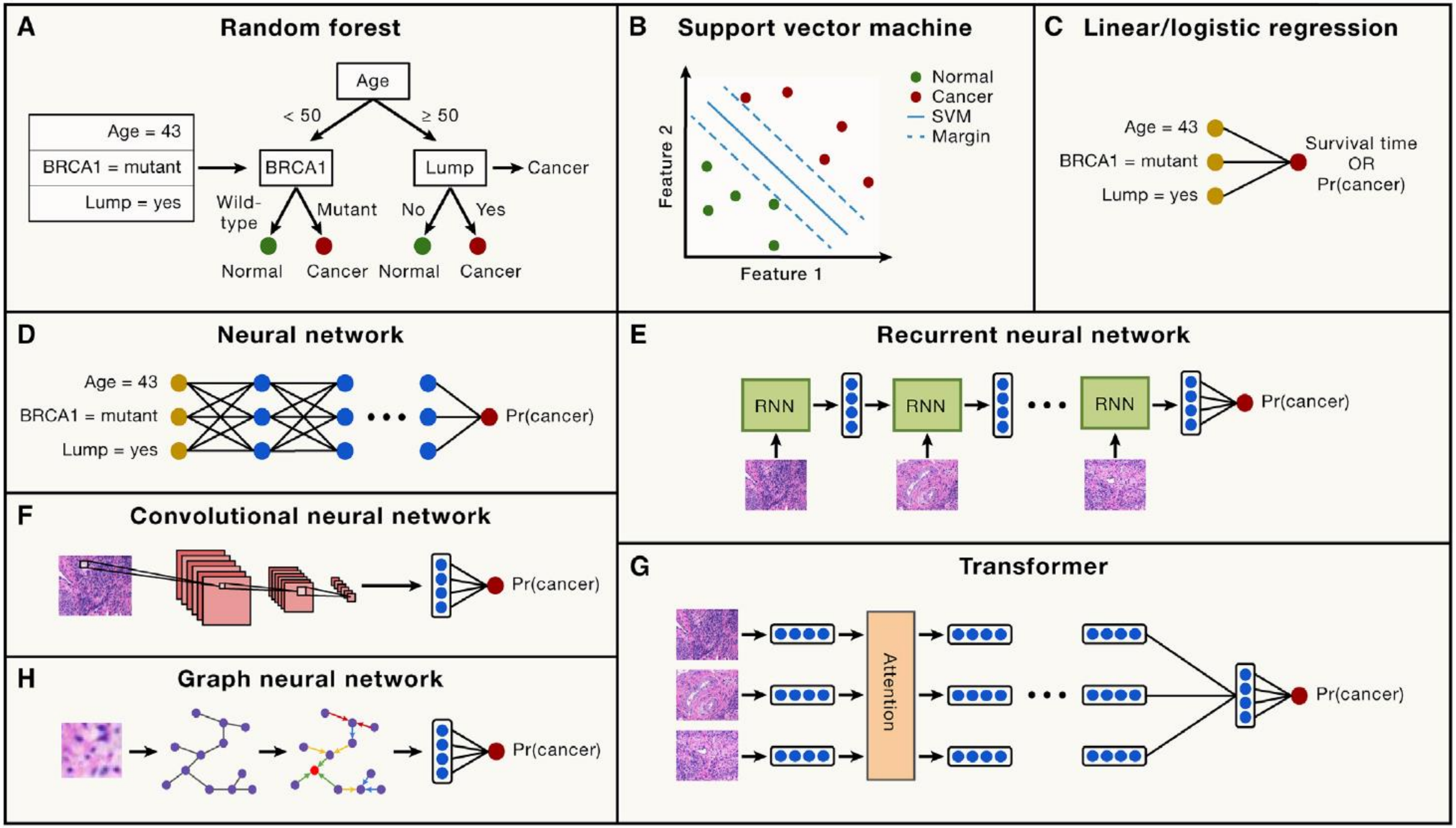
Radiomique : analyse fine d'images radiologiques



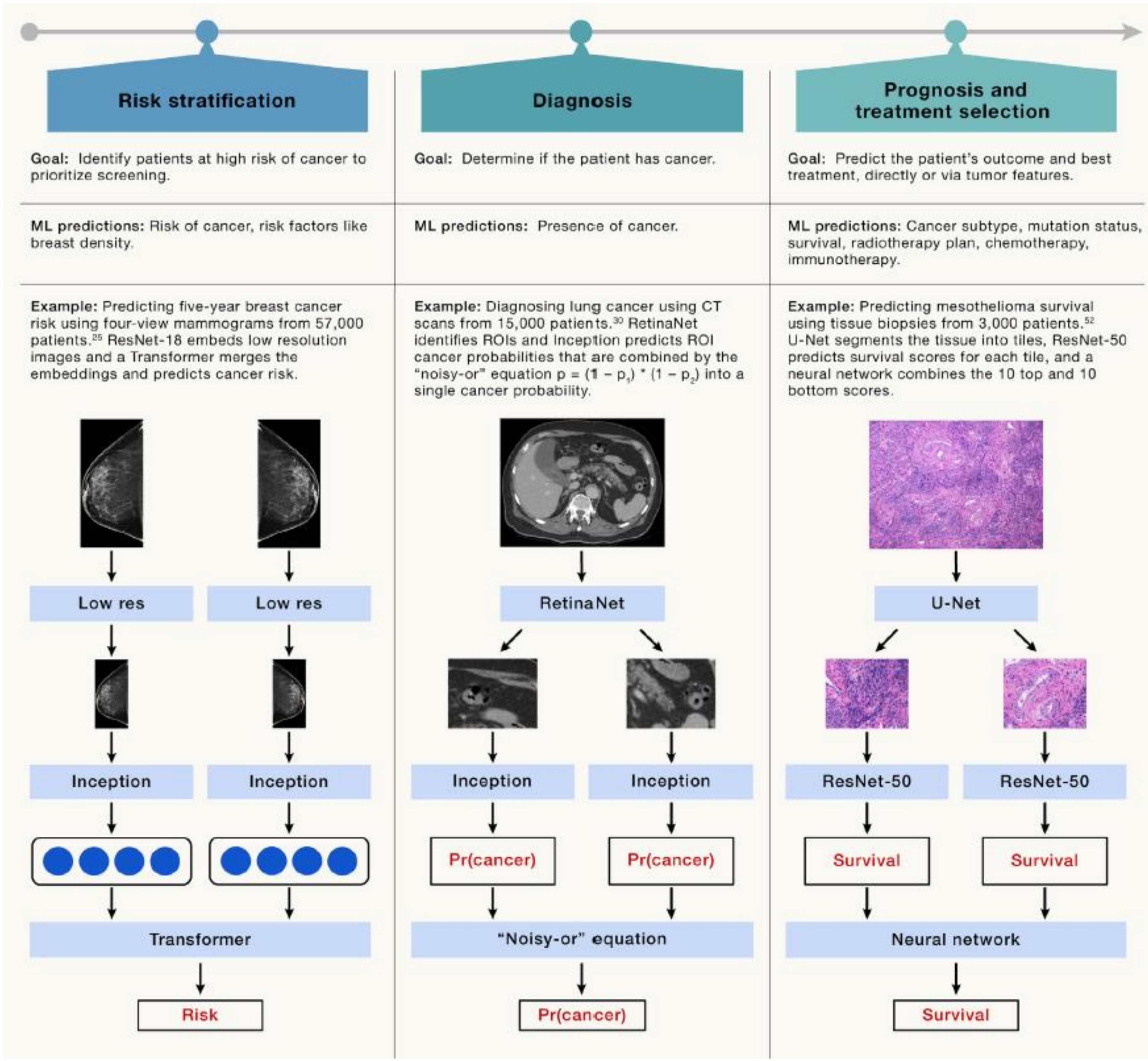
Pronostic, prédiction de réponse au traitement…

Lambin et al., Nat Rev Clin Onc 2017

Principaux algorithmes de ML utilisés en oncologie



Swanson et al., Cell 2023



Swanson et al., Cell 2023

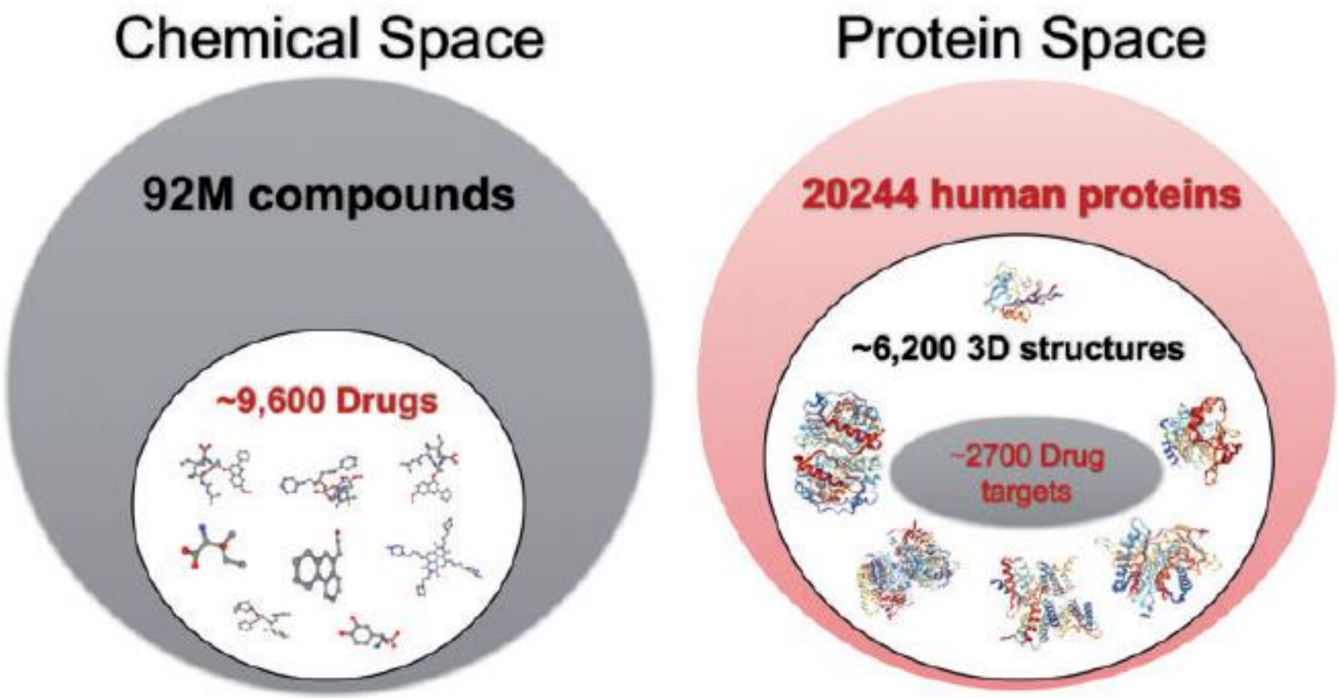
IA en hématologie

	Sample size	Application	Method	Results
Kimura et al (2019)[21]	3261 peripheral smears	Leucocyte classification; distinguishing aplastic anaemia and myelodysplastic syndrome	CNN, gradient boosting	Sensitivity vs specificity was 93·5% vs 96·0% for leucocyte detection, and 96·2% vs 100% for aplastic anaemia vs myelodysplastic syndrome differentiation
Achi et al (2019)[22]	128 patients	Differentiating diffuse large B-cell lymphoma, small lymphocytic lymphoma, Burkitt lymphoma, and normal lymph nodes	CNN	95% accuracy per slide; 100% accuracy per patient
Li (2019)[23]	41 patients	Detection of acute myeloid leukaemia bone marrow involvement via PET-CT	Manual feature engineering (PyRadiomics)	Sensitivity vs specificity was 87·5% vs 89·5% for bone marrow involvement; outperformed visual inspection of scans
Milgrom et al (2019)[24]	251 patients	Predicting refractory Hodgkin lymphoma from PET-CT	CNN	AUROC of 0·95 for model vs 0·78 for tumour volume; 0·65 for standardised uptake value
Moraes et al (2019)[25]	283 patients	Differential diagnosis of chronic lymphocytic leukaemia and B cell lymphomas via flow cytometry	Decision tree	95% inclusion of correct diagnosis in differential diagnosis; 66% definitive diagnosis
Ni et al (2016)[26]	51 patients	Detection of MRD in acute myeloid leukaemia via flow cytometry	Support vector machine	Similar performance with manual flow analysis (concordance=0·986)
Fuse (2019)[27]	217 patients	Prediction of acute leukaemia relapse after allogeneic stem cell transplantation	Decision tree	0·75 AUROC for relapse after transplantation
Goswami et al (2019)[28]	347 patients	Risk stratification for autologous stem cell transplantation in multiple myeloma	Decision tree	Significant risk-stratification and identification of high-risk features
Nazha (2019)[29]	433 and 113 patients	Predicting resistance to hypomethylating agents in patients with myelodysplastic syndrome on the basis of NGS myeloid malignancy panel	Recommender algorithm	Improved stratification of patients by risk of resistance to a hypomethylating agent
Gal et al (2019)[30]	493 patients	Response to induction therapy in paediatric acute myeloid leukaemia	K-nearest neighbours	0·84 AUROC for response to induction
Candia (2015)[31]	60 patients	Unsupervised analysis of microRNA expression signatures in acute myeloid leukaemia and acute lymphocytic leukaemia	Dimension reduction, network analysis	Identification of novel microRNA signatures in acute myeloid leukaemia and acute lymphocytic leukaemia

AUROC=area under the receiver operating characteristic curve. CNN=convolutional neural network. MRD=minimal residual disease. NGS=next-generation sequencing.

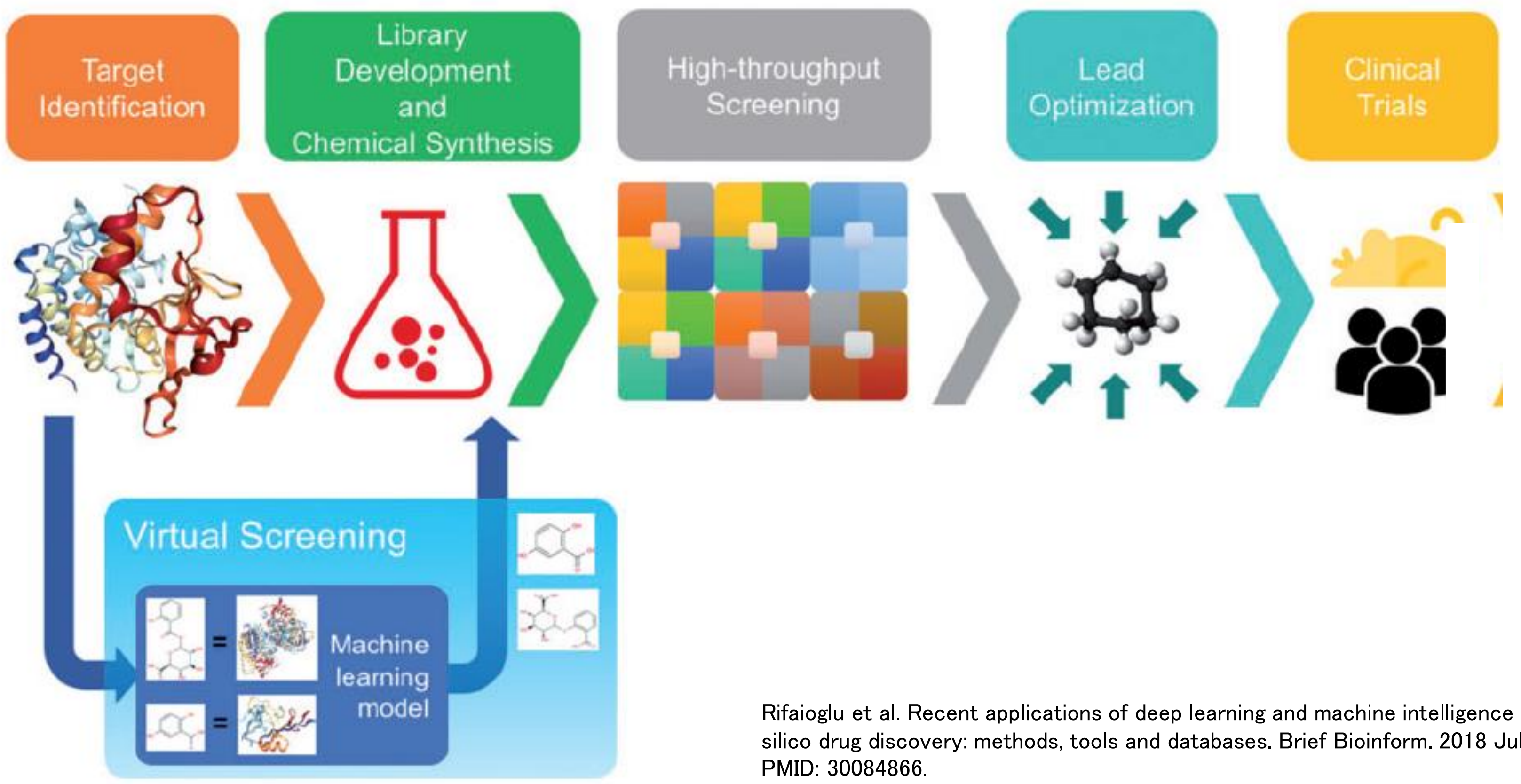
***Table:* Representative artificial intelligence in malignant haematology publications**

Drug development



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.

IA et développement du médicament



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.

IA et dossiers médicaux électroniques

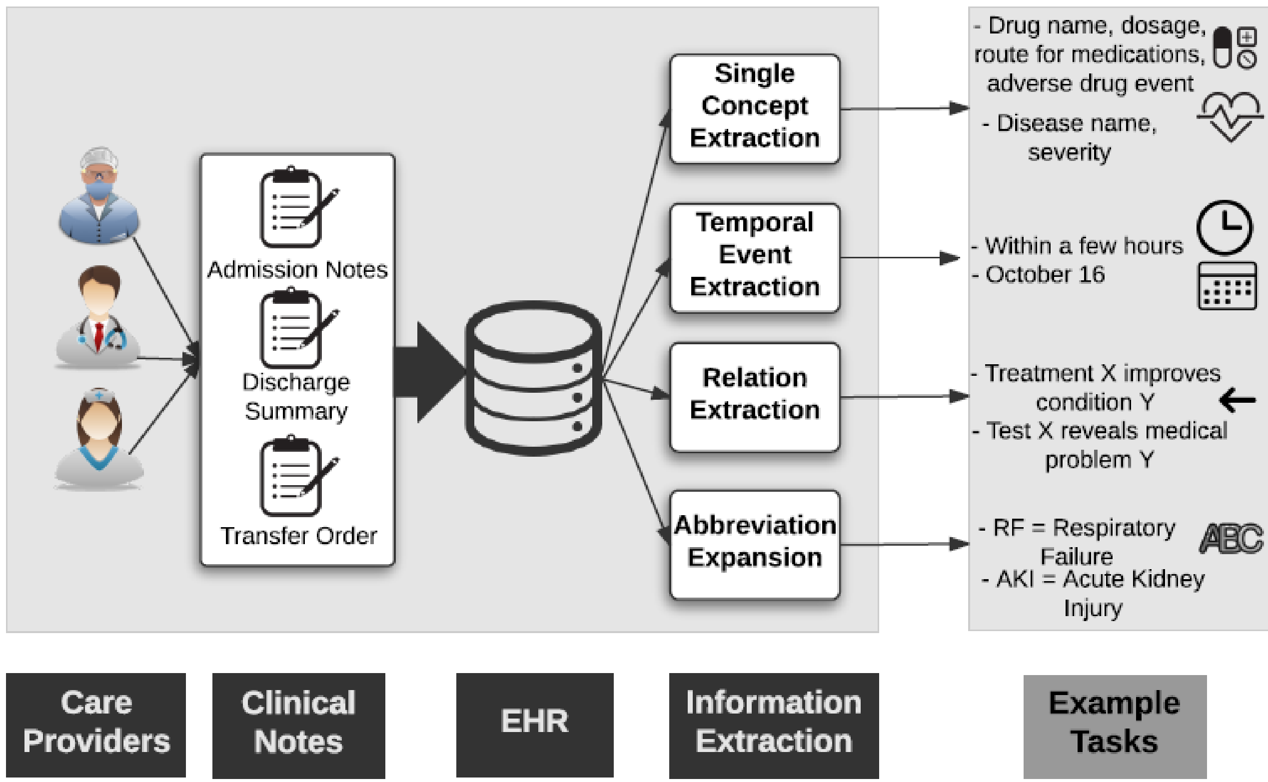


Fig. 7. EHR Information Extraction (IE) and example tasks.

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

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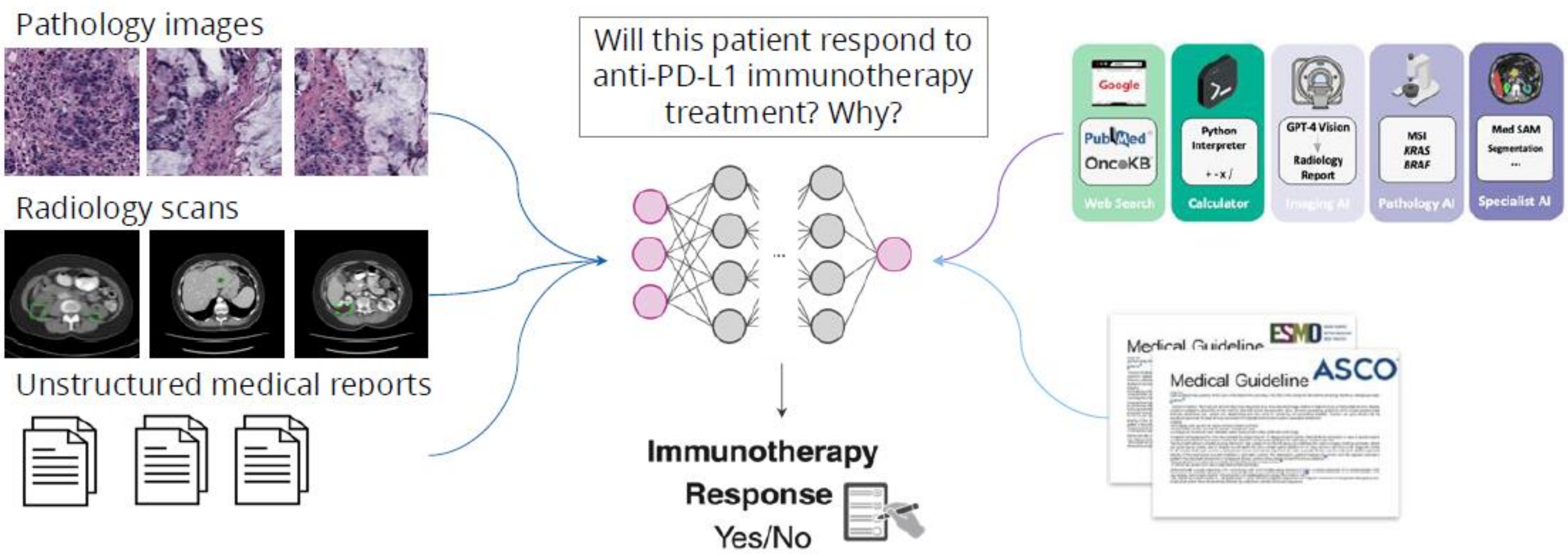
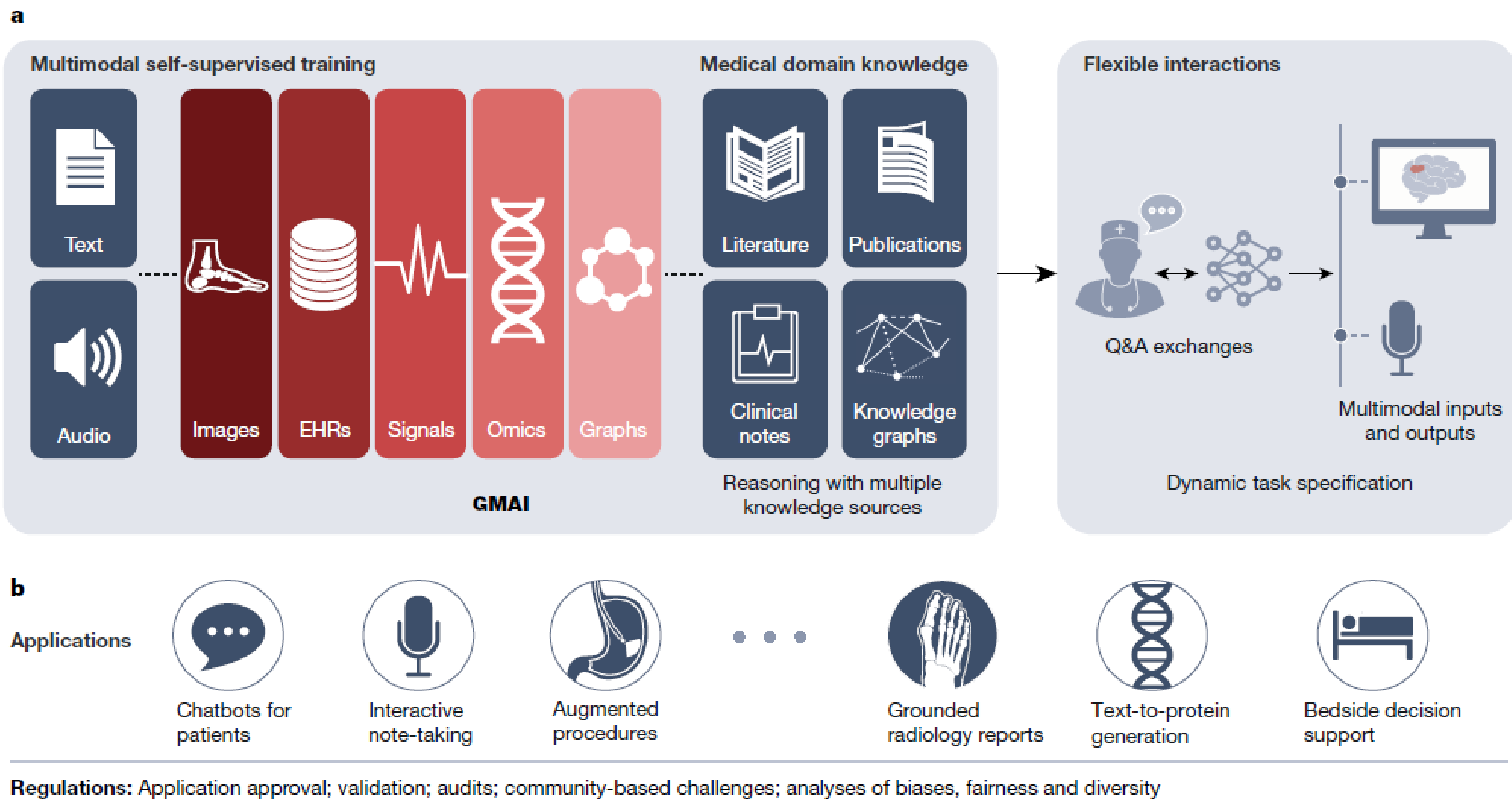
IA pour prise de décision

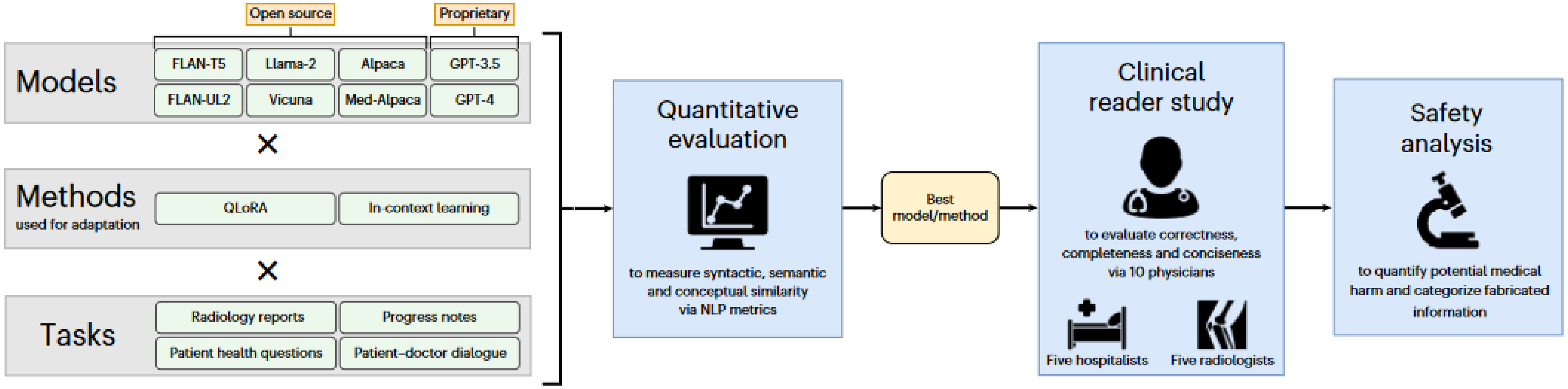


Jakob Kather
Ferber et al., arXiv (2024)

Generalist medical AI



Moor et al., Nature 2023



Radiology reports

Example 1: The model performed *better* because the medical expert made a laterality mistake (red).

Input:
The patient is s/p left frontal craniotomy. A small amount of intracranial gas is seen posterior to the surgical intervention, which could represent postoperative changes. Extensive edema is seen in the left frontal lobe at the site of presumed surgery. Additionally multiple foci of hemorrhage are seen in the region of the left frontal lobe. Midline shift to the right is seen in the frontal region. The ventricles, cisterns, and sulci are unremarkable, without effacement. Comparison with prior studies from outside institution would be helpful in further evaluation of these findings.

Summary (medical expert):
1. Left frontal craniotomy. 2. Frontal midline shift to the right. 3. Extensive left frontal lobe edema. 4. Multiple foci of hemorrhage in the right frontal lobe.

Summary (best model):
Postoperative changes following left frontal craniotomy with intracranial gas, extensive edema, and multiple foci of hemorrhage in the left frontal lobe. Midline shift to the right is noted.

Example 2: The model performed *worse* because it was less concise, i.e. included non-important information (green).

Input:
Right frontoparietal craniotomy again identified, with decreasing pneumocephalus and small amount of subdural fluid. There is persistent mild leftward shift of approximately 2–3 mm, not significantly changed from prior study. Size and configuration of the ventricles is unchanged from prior study. There is no new hemorrhage. Multiple facial fractures, better evaluated on prior dedicated maxillofacial CT. Increasing opacification is seen in the ethmoid and sphenoid sinuses. Large right subgaleal hematoma again identified.

Summary (medical expert):
Postoperative changes in the right frontoparietal region identified, with decreasing pneumocephalus. No new hemorrhage. Persistent mild leftward shift, not significantly changed from prior.

Summary (best model):
Stable post-craniotomy changes with decreasing pneumocephalus and persistent mild leftward shift. No new hemorrhage. Increasing opacification of ethmoid and sphenoid sinuses. Large right subgaleal hematoma unchanged.

Reader scores:

Attribute	Average	Example 1	Example 2
Completeness	2.8	5	−1
Correctness	1.7	8	0
Conciseness	0	0	−4

Color key:

Blue: Correct; exists in input + expert + model
Purple: Correct; exists in input + expert only
Green: Correct; exists in input + model only
Orange: Incoherent or filler
Red: Incorrect

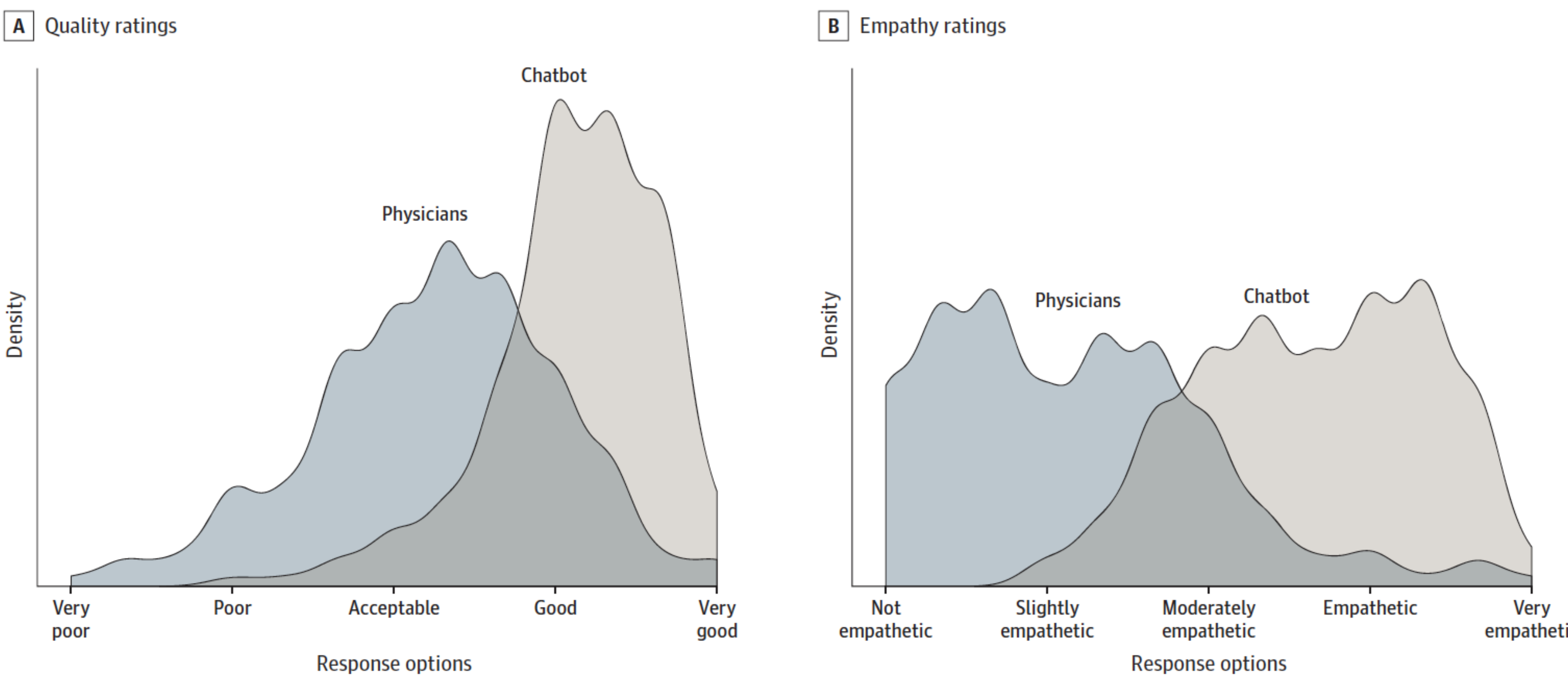
Van Veen et al., Nature Medicine 2024

JAMA Internal Medicine | Original Investigation

Comparing Physician and Artificial Intelligence Chatbot Responses to Patient Questions Posted to a Public Social Media Forum

John W. Ayers, PhD, MA; Adam Poliak, PhD; Mark Dredze, PhD; Eric C. Leas, PhD, MPH; Zechariah Zhu, BS; Jessica B. Kelley, MSN; Dennis J. Faix, MD; Aaron M. Goodman, MD; Christopher A. Longhurst, MD, MS; Michael Hogarth, MD; Davey M. Smith, MD, MAS

Figure. Distribution of Average Quality and Empathy Ratings for Chatbot and Physician Responses to Patient Questions



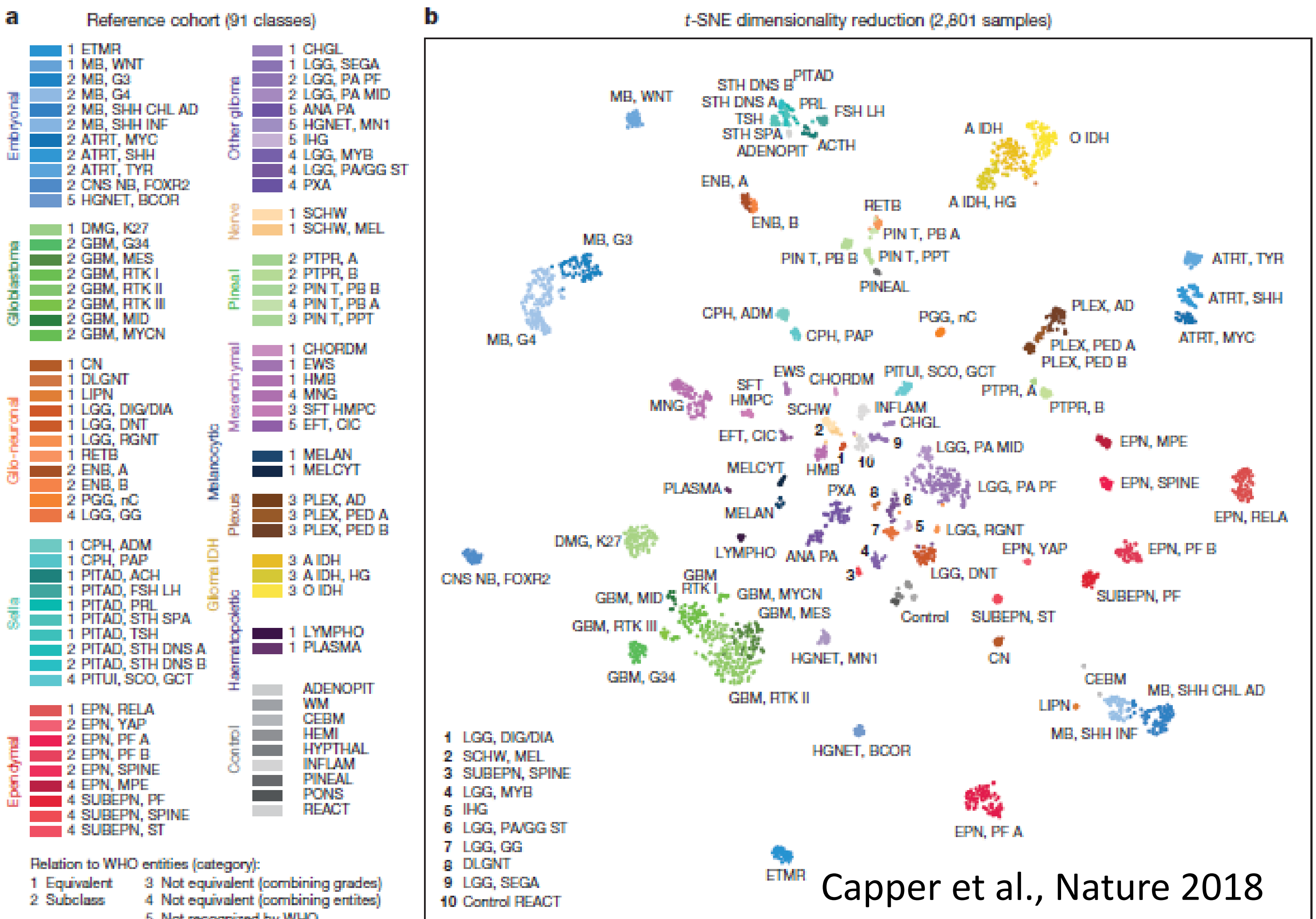
Kernel density plots are shown for the average across 3 independent licensed health care professional evaluators using principles of crowd evaluation. A, The overall quality metric is shown. B, The overall empathy metric is shown.

IA en génomique et transcriptomique du cancer

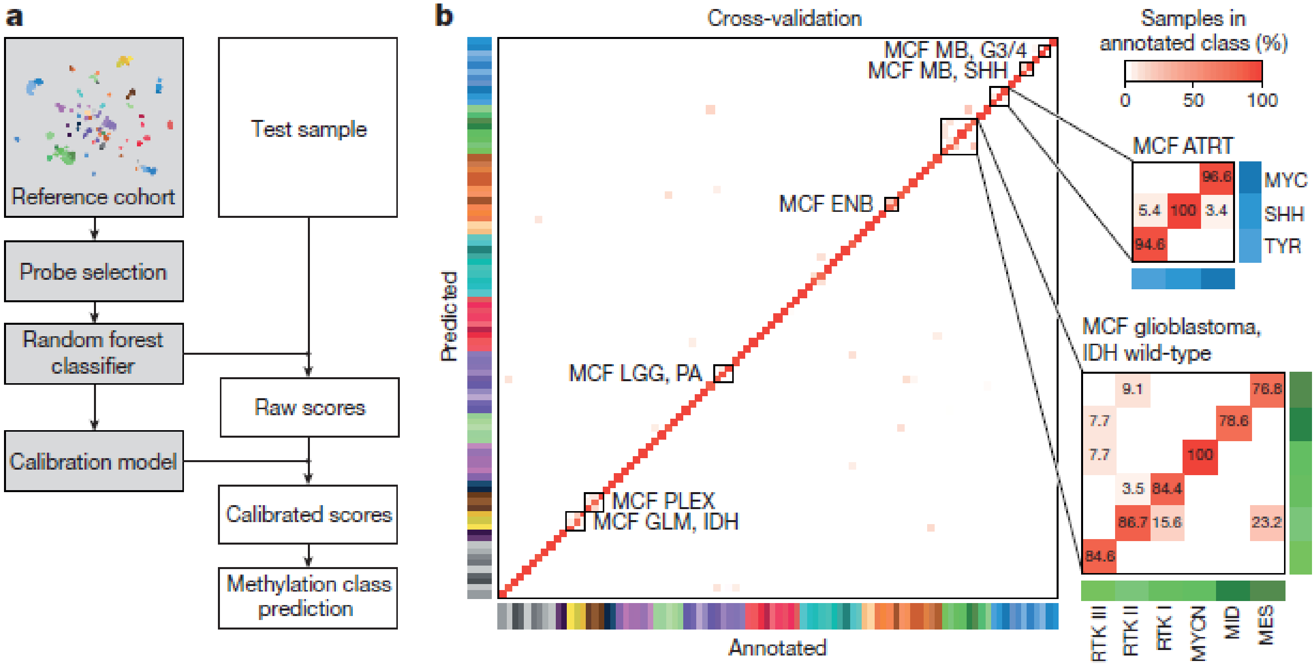
ARTICLE

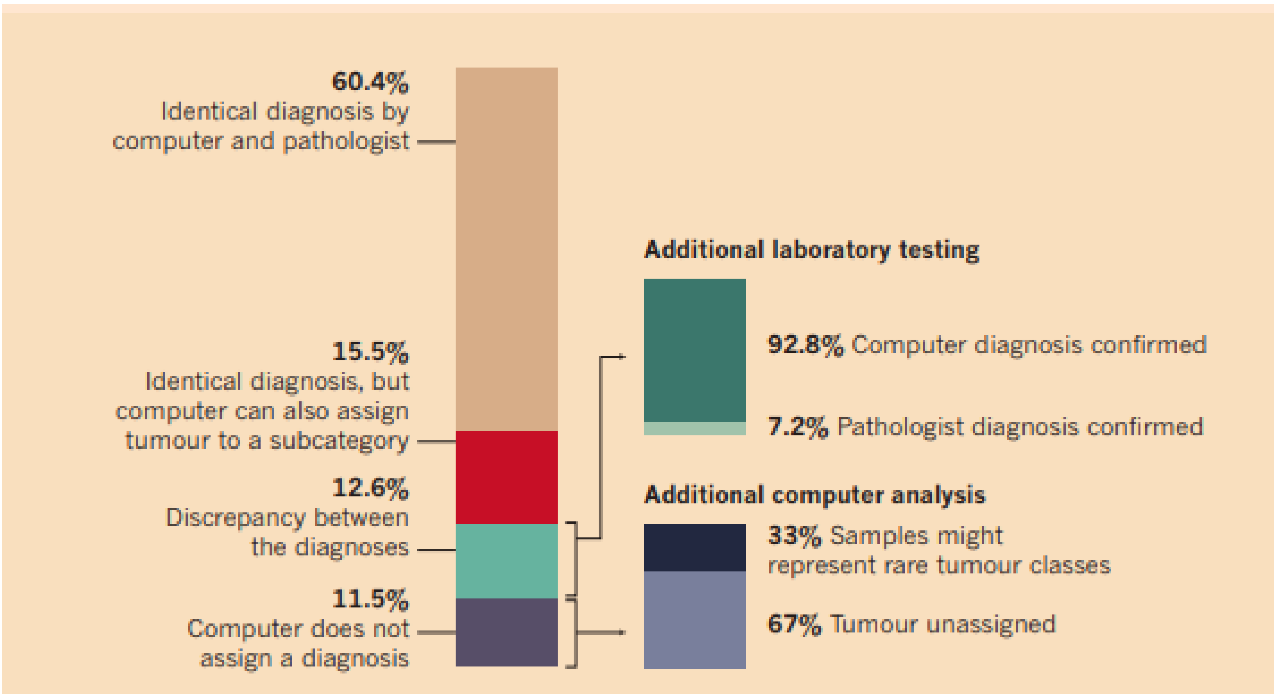
doi:10.1038/nature26000

DNA methylation-based classification of central nervous system tumours

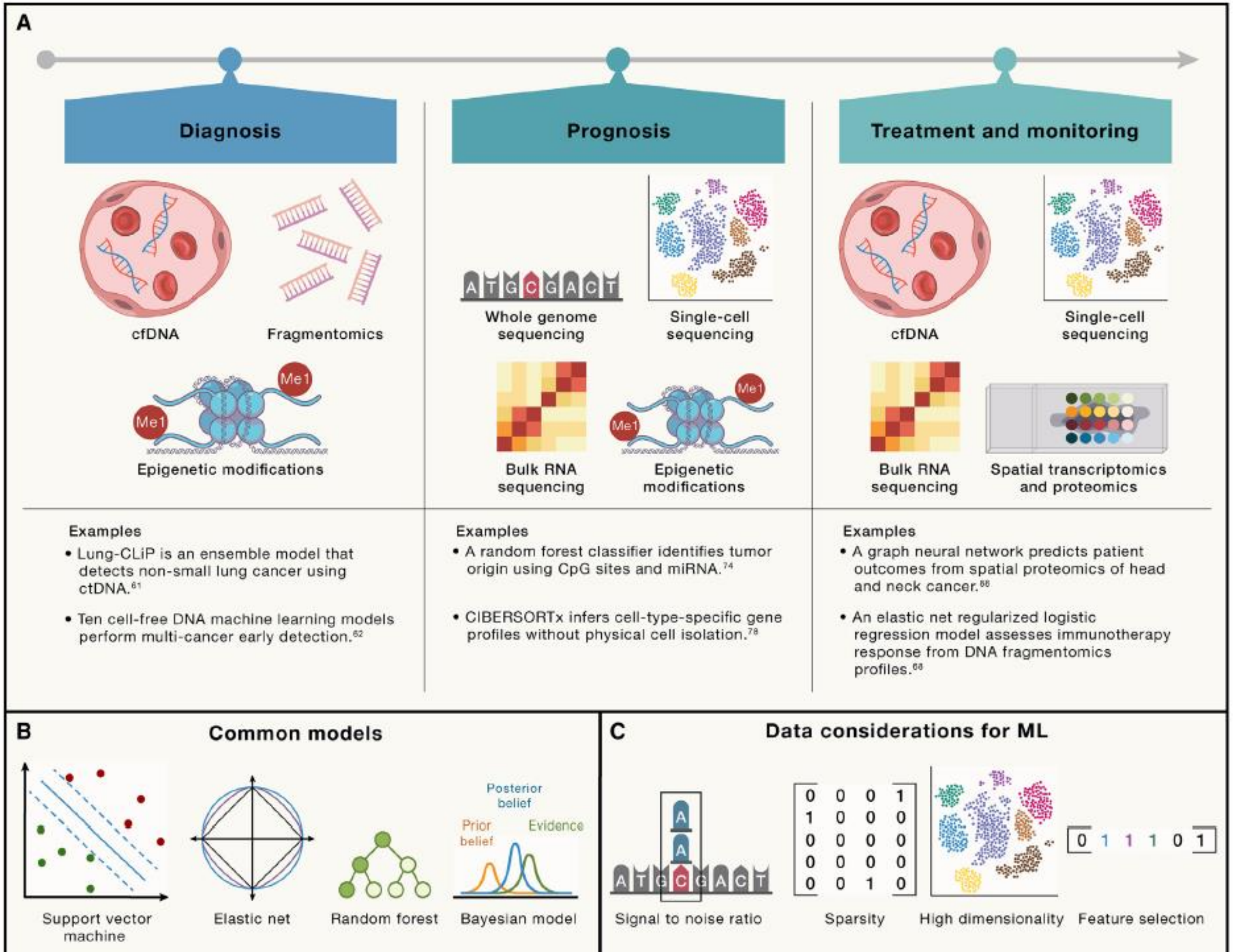


Capper et al., Nature 2018



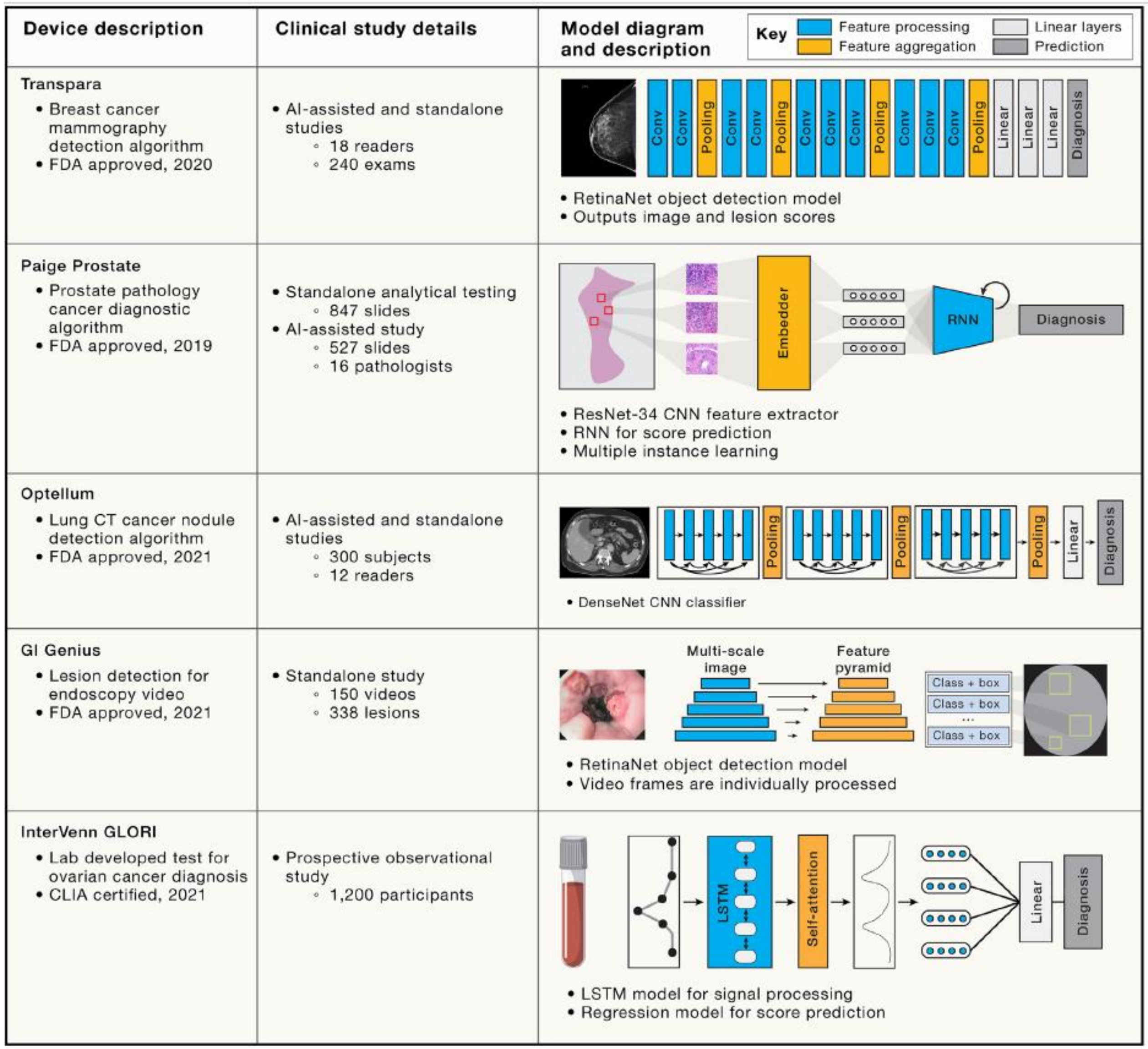


Capper et al., Nature 2018



Swanson et al., Cell 2023

Quelques algorithmes déjà approuvés pour la pratique clinique



Device description	Clinical study details	Model diagram and description
Transpara • Breast cancer mammography detection algorithm • FDA approved, 2020	• AI-assisted and standalone studies ◦ 18 readers ◦ 240 exams	• RetinaNet object detection model • Outputs image and lesion scores
Paige Prostate • Prostate pathology cancer diagnostic algorithm • FDA approved, 2019	• Standalone analytical testing ◦ 847 slides • AI-assisted study ◦ 527 slides ◦ 16 pathologists	• ResNet-34 CNN feature extractor • RNN for score prediction • Multiple instance learning
Optellum • Lung CT cancer nodule detection algorithm • FDA approved, 2021	• AI-assisted and standalone studies ◦ 300 subjects ◦ 12 readers	• DenseNet CNN classifier
GI Genius • Lesion detection for endoscopy video • FDA approved, 2021	• Standalone study ◦ 150 videos ◦ 338 lesions	• RetinaNet object detection model • Video frames are individually processed
InterVenn GLORI • Lab developed test for ovarian cancer diagnosis • CLIA certified, 2021	• Prospective observational study ◦ 1,200 participants	• LSTM model for signal processing • Regression model for score prediction

Swanson et al., Cell 2023

Quelques commentaires

- L'IA peut potentiellement être utilisée dans **toutes les questions en médecine auxquelles il est possible de répondre avec des données** : prédiction du diagnostic, pronostic, réponse au traitement...
- Dès qu'il y a **suffisamment de bonnes données** pour entraîner un algorithme
- La génomique et la transcriptomique sont bien adaptées à l'IA (nombre élevé de dimensions, « big data »), en particulier avec les techniques récentes (unicellulaire)
- Mais **peut souffrir d'un faible nombre d'échantillons** (« fat data »)

Conclusions et perspectives

- L'IA apporte une **aide précieuse** pour le cerveau humain, notamment avec les *big data*
- L'IA **ne remplace pas l'humain**
- Nécessité de valider les algorithmes et montrer un bénéfice en **vie réelle**
- Problème de l'**interprétabilité**

IA : Challenges et perspectives

Génération des modèles → Evaluation des modèles → Utilisation en routine

- **Big data « utiles »**
- qualité/homogénéité/ représentabilité
- **Sources de données et aspects juridiques**
- Stockage des données

- **Par qui, quand et comment?**
- **Robustesse/ vraie vie**
- Autorité de régulation

- **Formation des médecins**
- **Aspect user-friendly**
- **IA « explicable »**
- **Data scientists**

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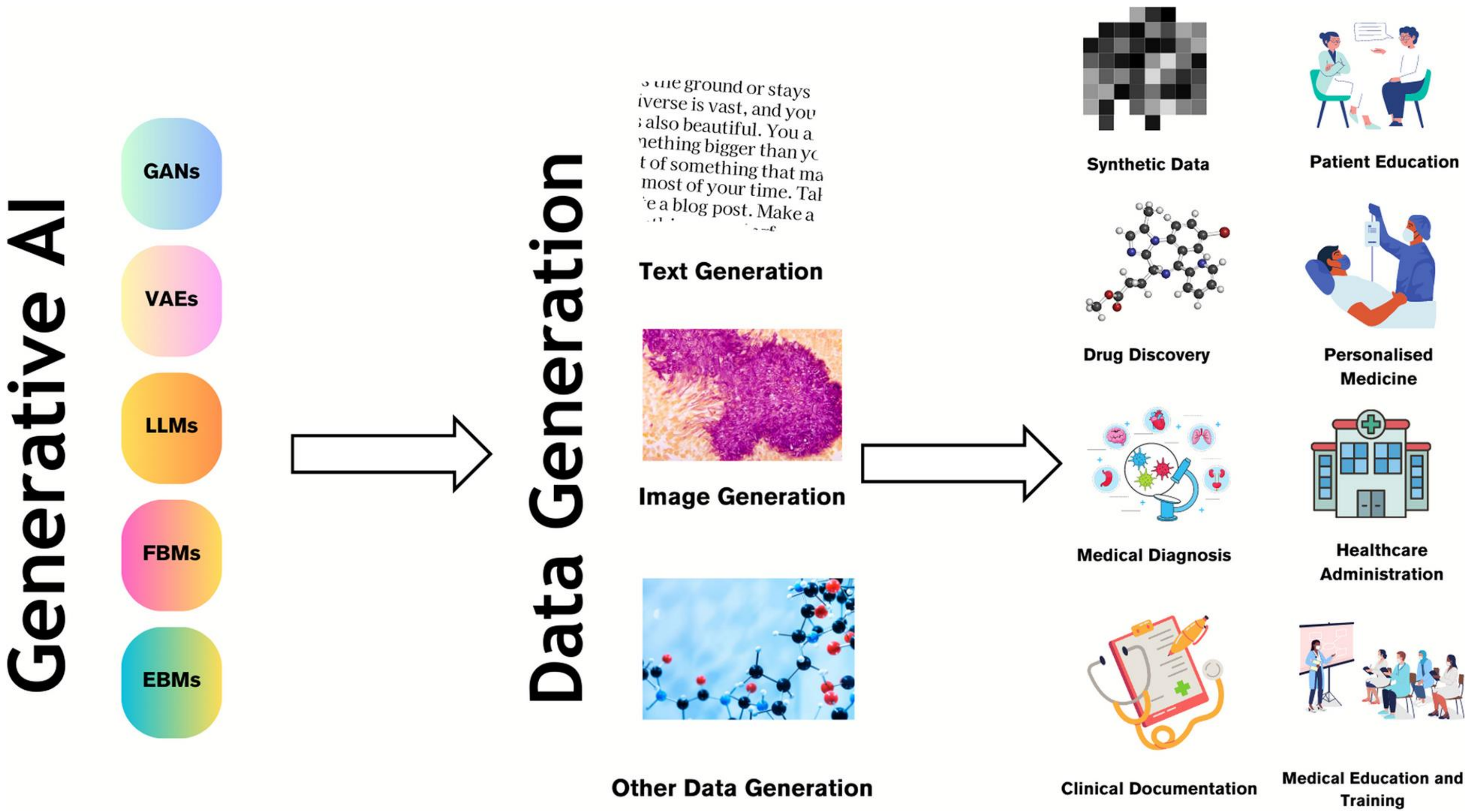
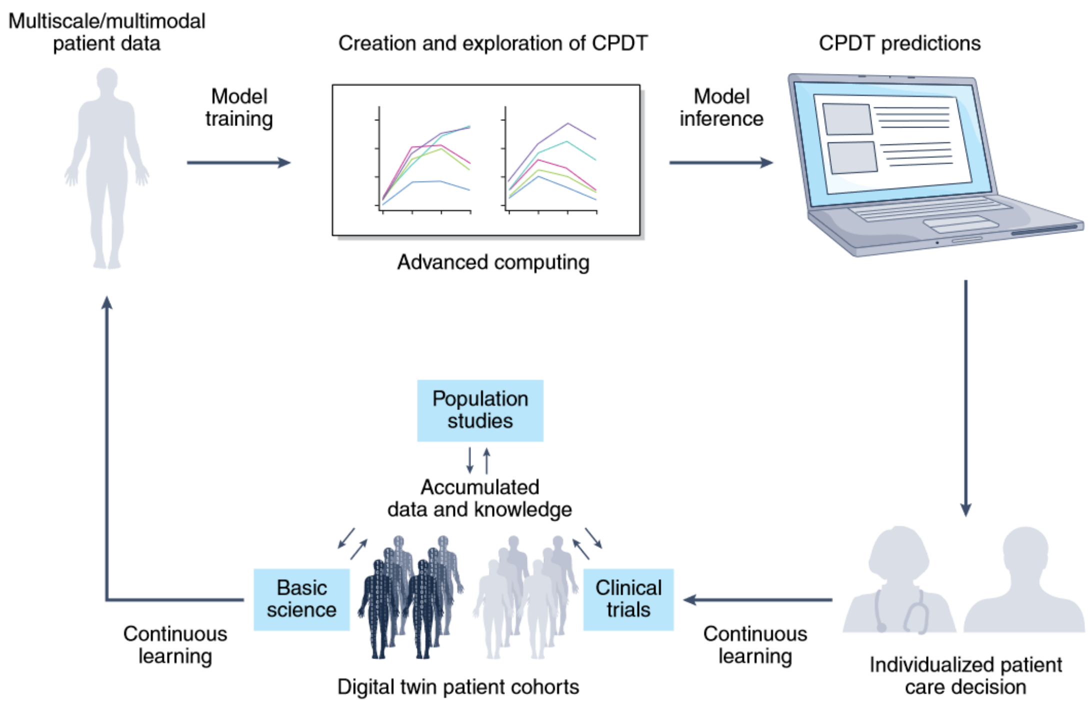
IA générative



Reddy, Impl Sci (2024)

The Cancer Patient Digital Twin (CPDT)

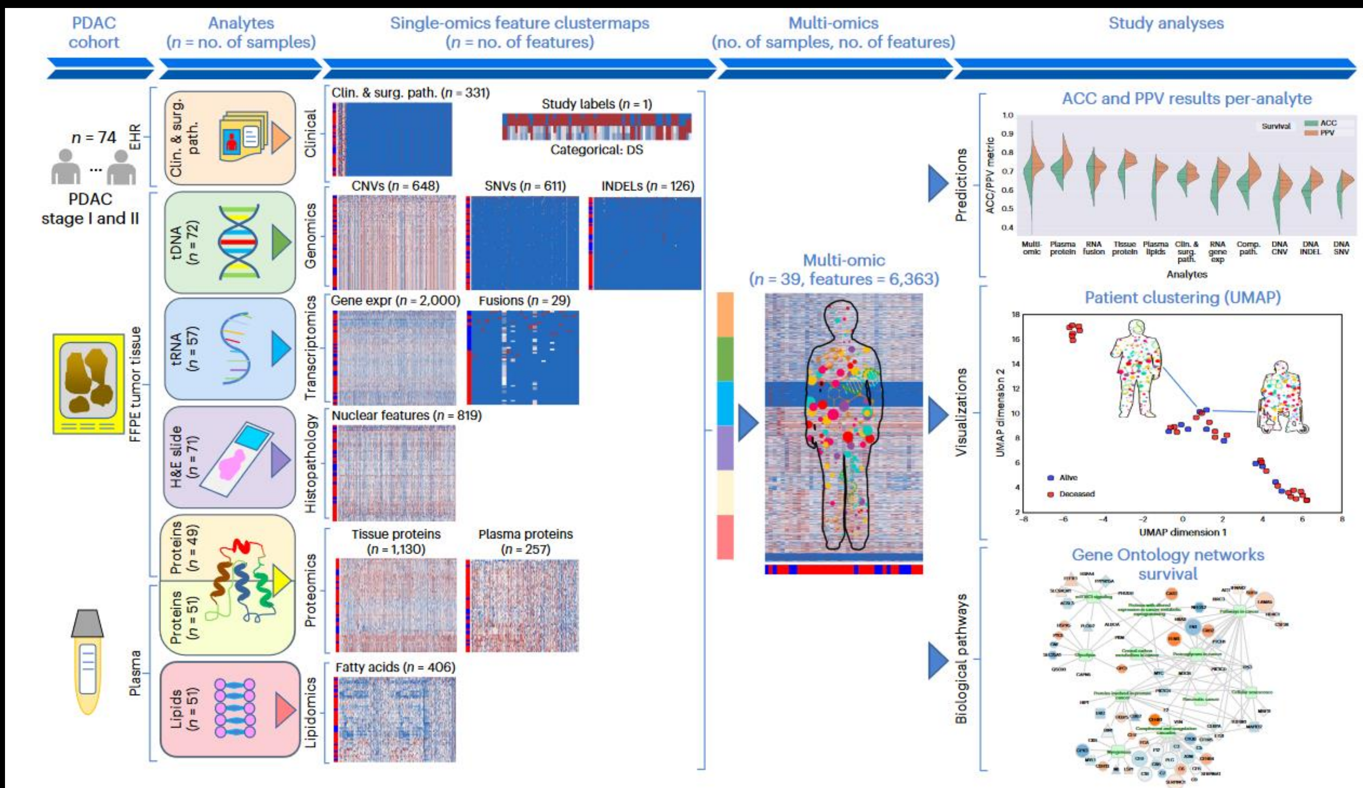


Cycling between:
- Training on patient data
- Learning from accumulated data/knowledge

-> **Individualized patient care for precision medicine**

Hernandez-Boussard et al., Nat Med (2021)

EXAMPLE 1: MOLECULAR TWIN FOR PANCREATIC CA



Advanced machine learning for integration of multiomic data

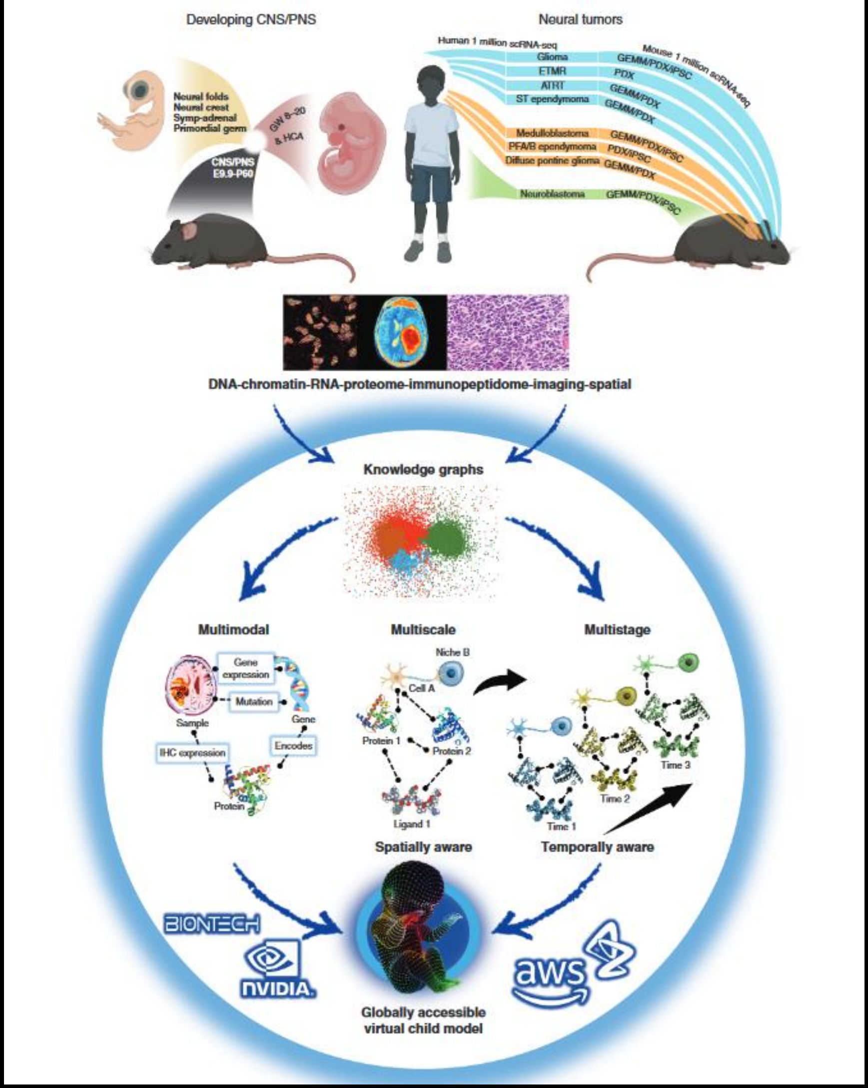
-> **Prediction of disease survival and biomarker discovery**

Osipov et al., Nat Cancer (2024)

EXAMPLE 2:
THE VIRTUAL CHILD

- Large-scale academic-industrial project
- Model at **the cellular level** development of pediatric tumors
- Ability to run **virtual clinical trials**

Gilbertson et al., Cancer Discov (2024)



MEDITWIN

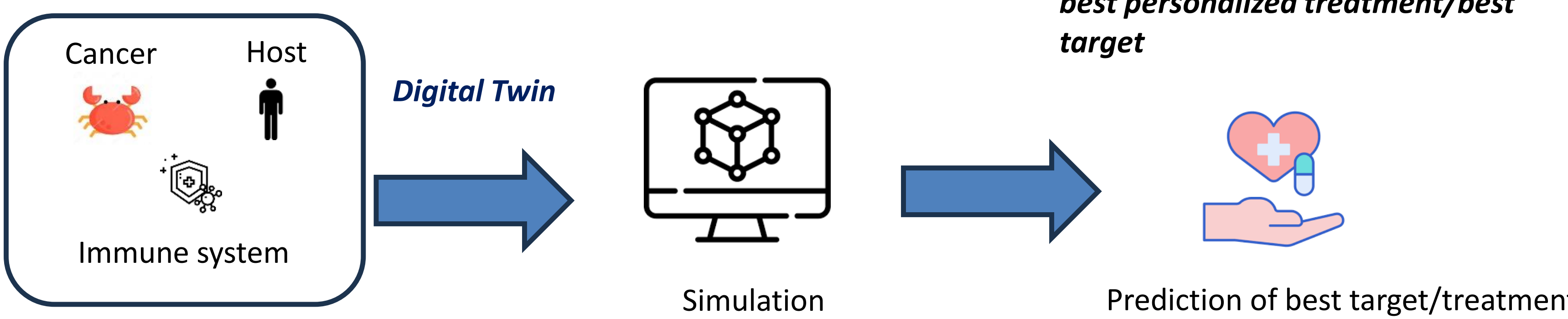
MEDITWIN: large-scale academic-industrial consortium (including IHU) for creation of digital twins in oncology, cardiology, neurology...

WP3: Precision Medicine for Oncology
(PRISM, Dassault Systèmes)

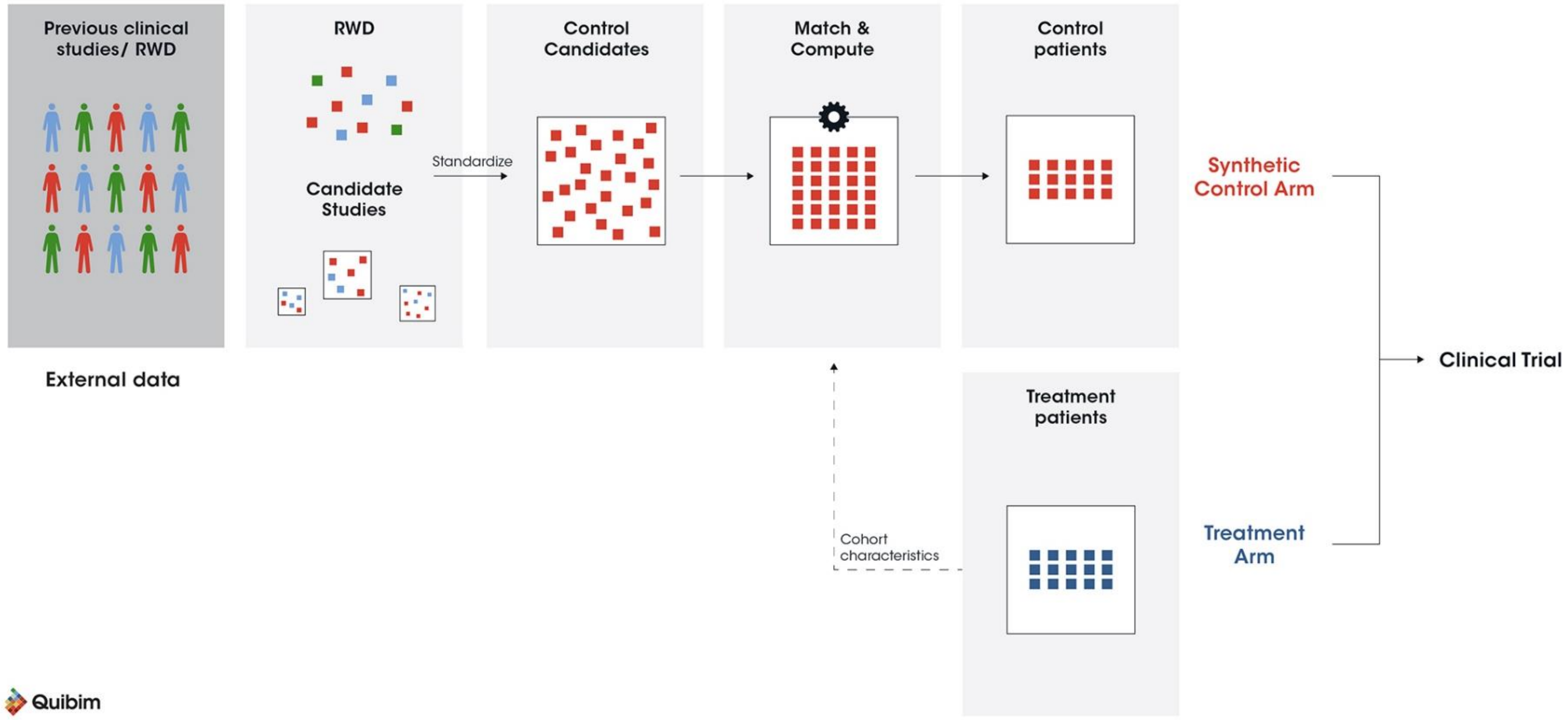
Create digital twins for cancer patients

- ***Multi-scale***
- ***Evolving in time***
- ***Integrating Cancer/Host/Immunity***

Allow simulation and prediction of best personalized treatment/best target



Bras synthétiques pour essais cliniques



SOME PERSPECTIVES

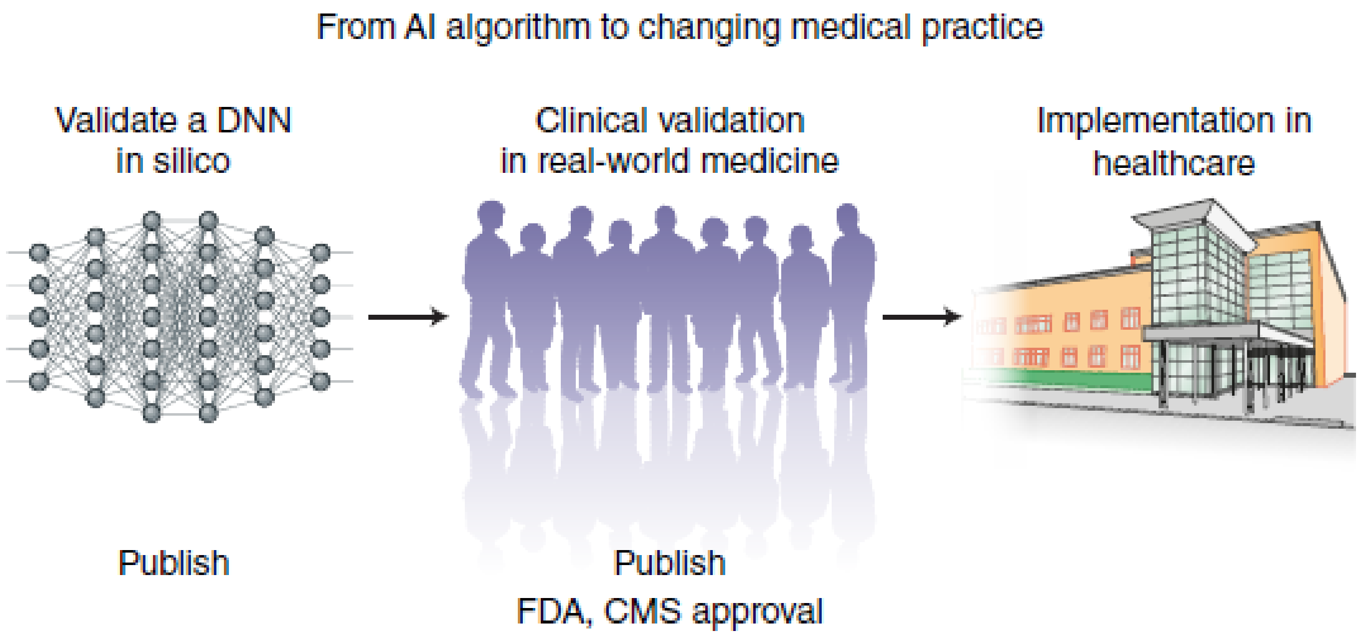
Consultation with digital twin

Synthetic data for clinical trials

Insights into biology of cancer

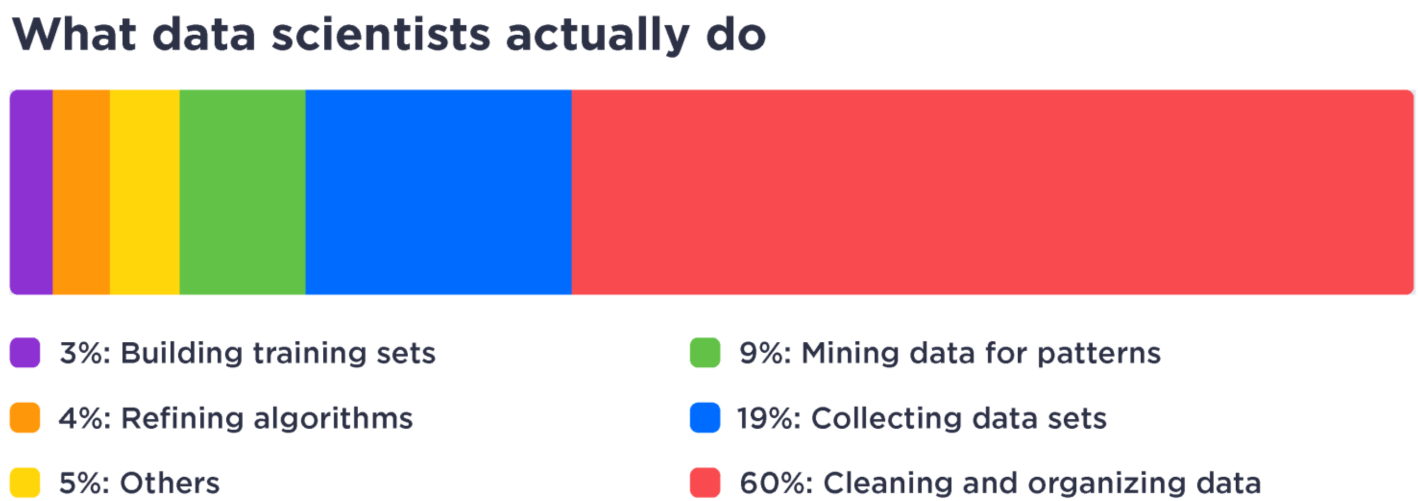
AI-generated images

Attention à ne pas sauter les étapes avant l’application en vie réelle



Validation externe !

Topol, Nat Med 2019



https://cldcvr.com/news-and-media/blog/clean-data-the-foundation-of-effective-machine-learning/

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- Inserm U981

- Les patients et leurs familles
- Les médecins et les autres soignants

MERCI POUR VOTRE ATTENTION

FONDATION
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La science pour la santé
From science to health