L’IA peut elle prédire l’antibiorésistance?

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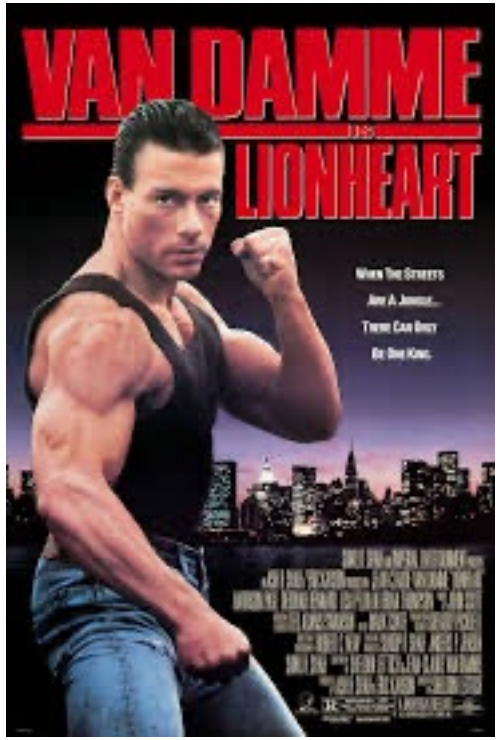
Groupe Infectiologie Digit@le

Conflit d’intérêt

Open AI



Plan

Objectives: learn AI for collaboration with AI project

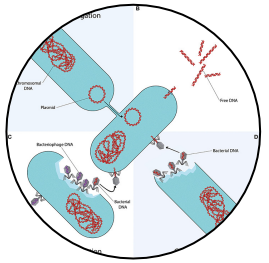
1.Antibioresistance:

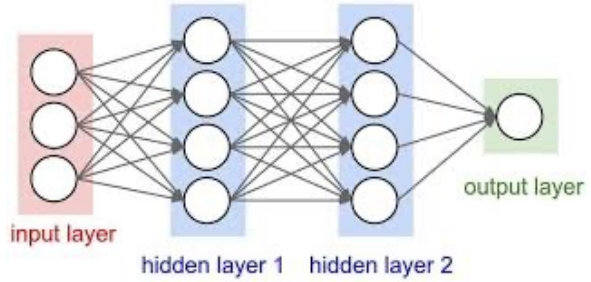
- Mecanismes
- Déterminants
- Perspectives

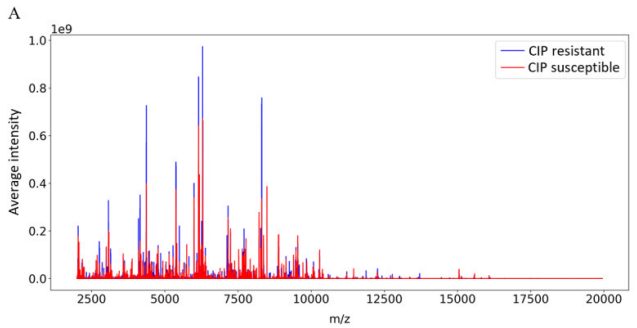
2.Intelligence artificielle

- Système expert vs Machine learning
- Machine learning traditionnel et deep learning
- Metrics

3. 4 exemples d'utilisation de l'IA pour prédiction de l'antibiorésistance



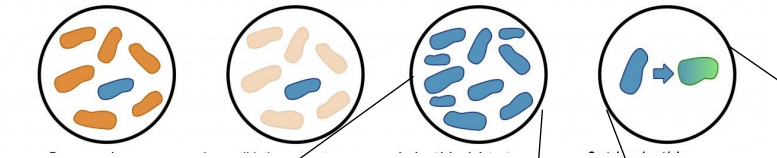


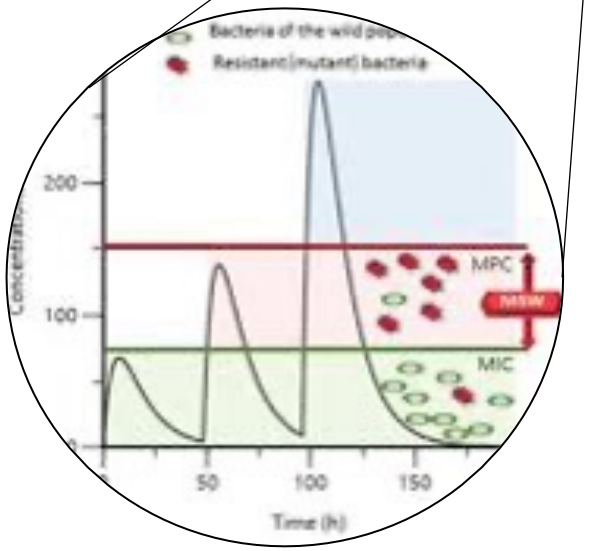


Mécanismes de l’antibiorésistance

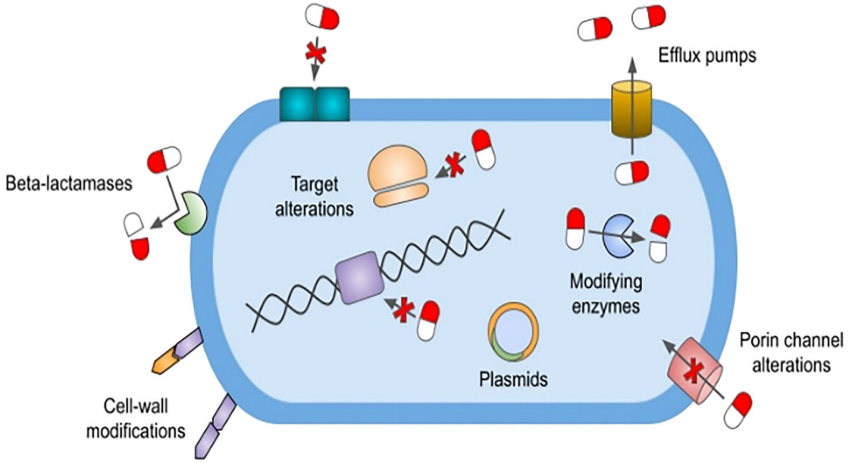
Amplification

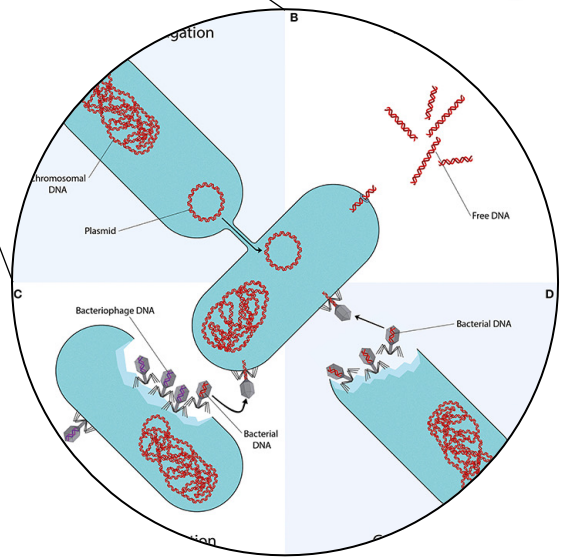
vertical horizontal



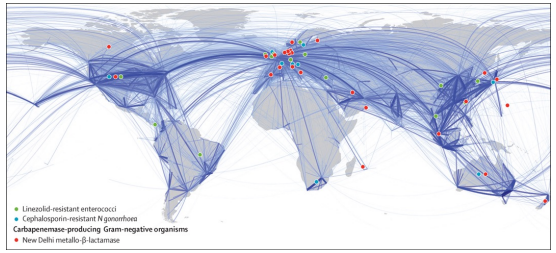


Mutant selective windows

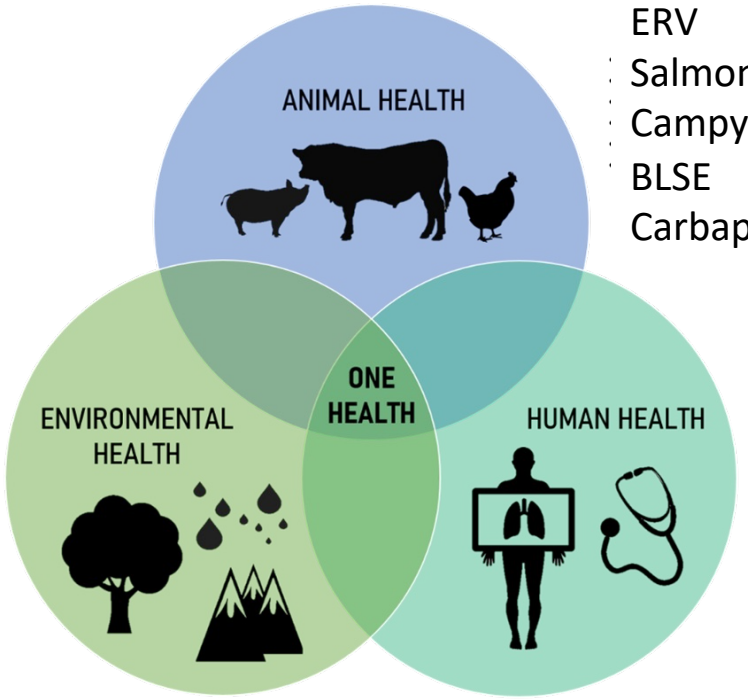




Horizontal gene transfer



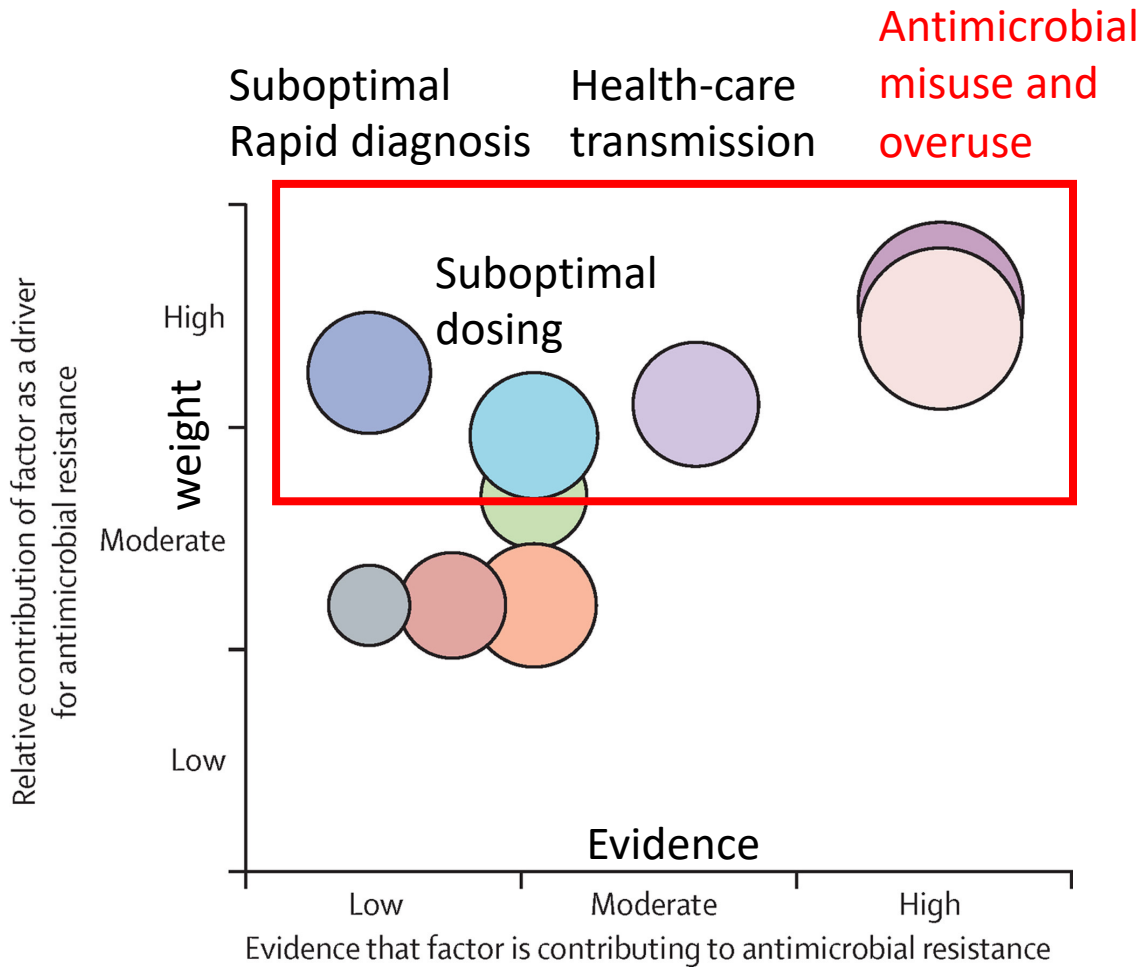
Déterminants de l'antibiorésistance



ERV
Salmonella
Campylobacter
BLSE
Carbapénémase

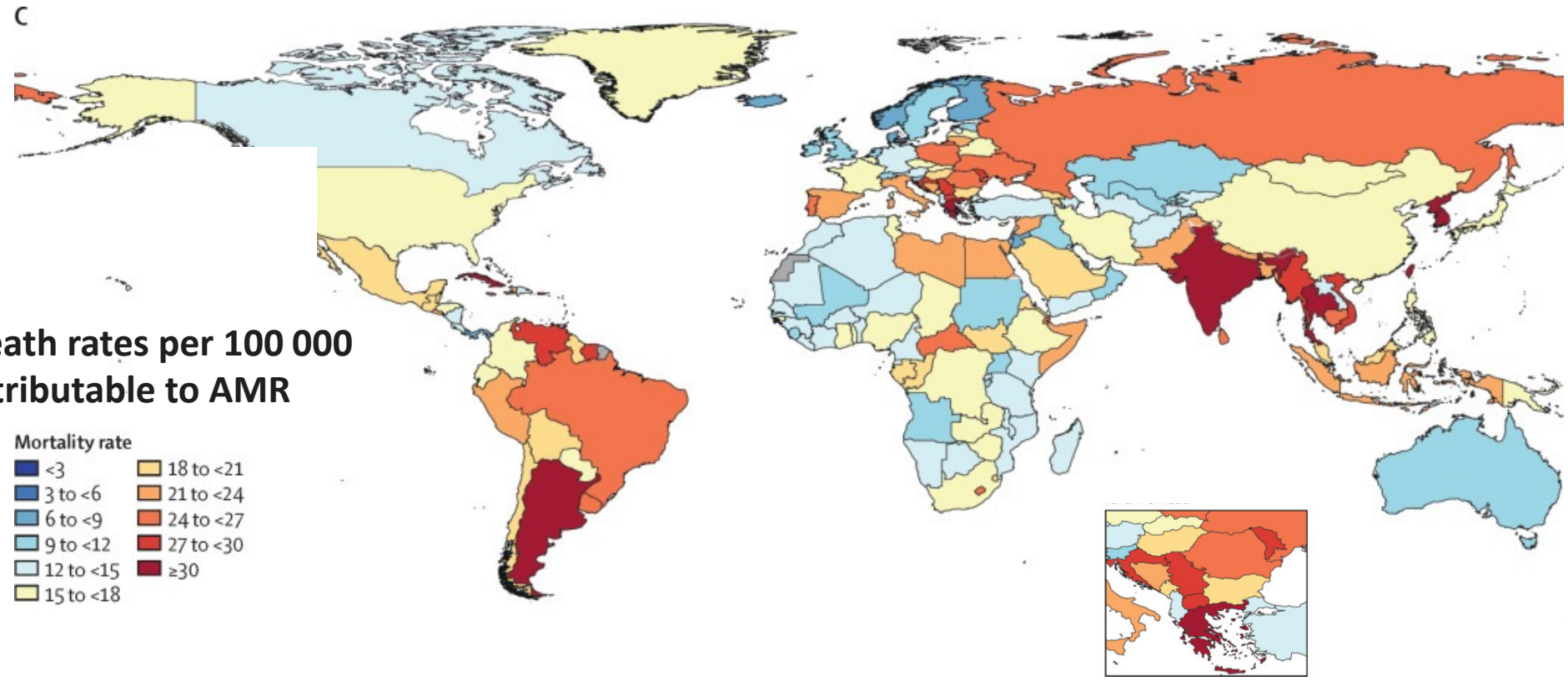
Aspergillus
Vorico R

SARM



Understanding the mechanismes and drivers of antimicrobial resistance, Lancet 2016

92 millions de morts évitables d'ici 2050



balkans

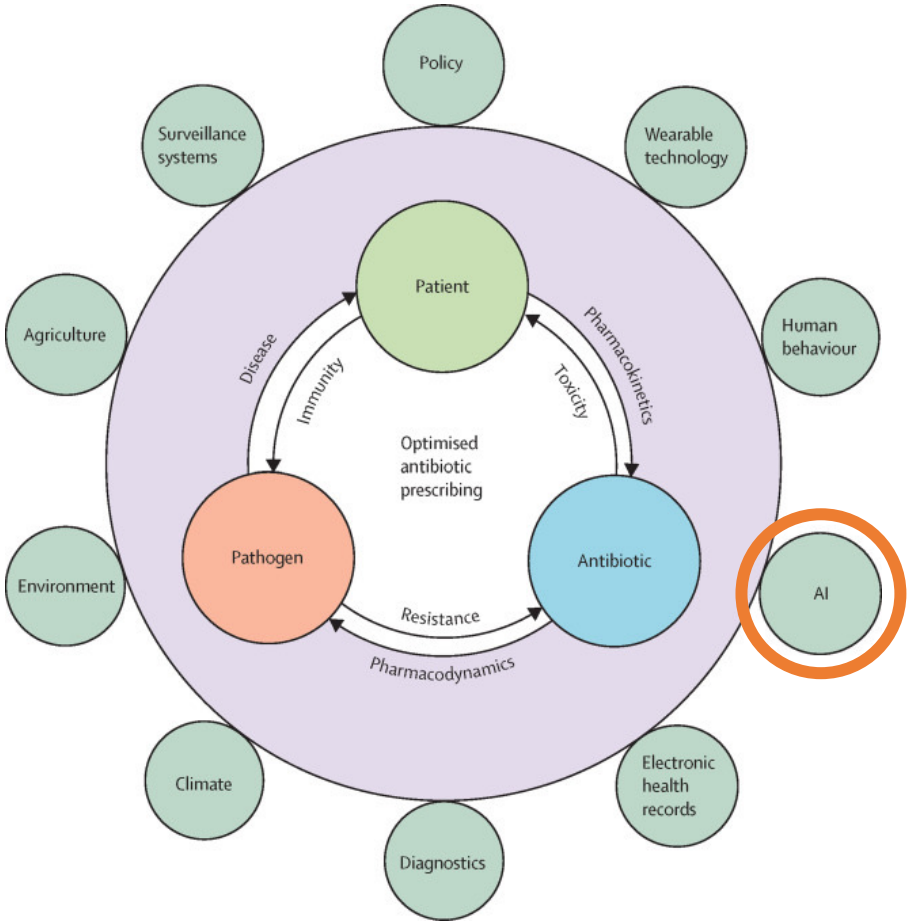
Critical group

- Enterobacterales carbapenem-resistant
- Enterobacterales third-generation cephalosporin-resistant
- *Acinetobacter baumannii* carbapenem-resistant
- *Mycobacterium tuberculosis*, rifampicin-resistant[a]

[a]RR-TB was included after an independent analysis with parallel criteria and subsequent application of an adapted MCDA matrix.

GBD 2021 Antimicrobial Resistance Collaborators *Lancet 202*

L'IA pour lutter contre l'antibiorésistance?



Drug discovery

Accelerating antimicrobial peptide design: Leveraging deep learning for rapid discovery

Ahmad M Al-Omari [1], Yazan H Akkam [2], Ala'a Zyout [1], Shayma'a Younis [1], Shefa M Tawalbeh [1], Khaled Al-Sawalmeh [3], Amjed Al Fahoum [1], Jonathan Arnold [4]

Aide à prescription

> Clin Infect Dis. 2024 Apr 10;78(4):825-832. doi: 10.1093/cid/ciad632.

Can Chatbot Artificial Intelligence Replace Infectious Diseases Physicians in the Management of Bloodstream Infections? A Prospective Cohort Study

Alexis Maillard [1], Giulia Micheli [1 2], Leila Lefevre [1], Cécile Guyonnet [3 4], Claire Poyart [3 4], Etienne Canouï [1], Martin Belan [1 5], Caroline Charlier [1 5 6 7]

Chatbot

> Nature. 2024 Jan;625(7996):643-644. doi: 10.1038/d41586-024-00099-4.

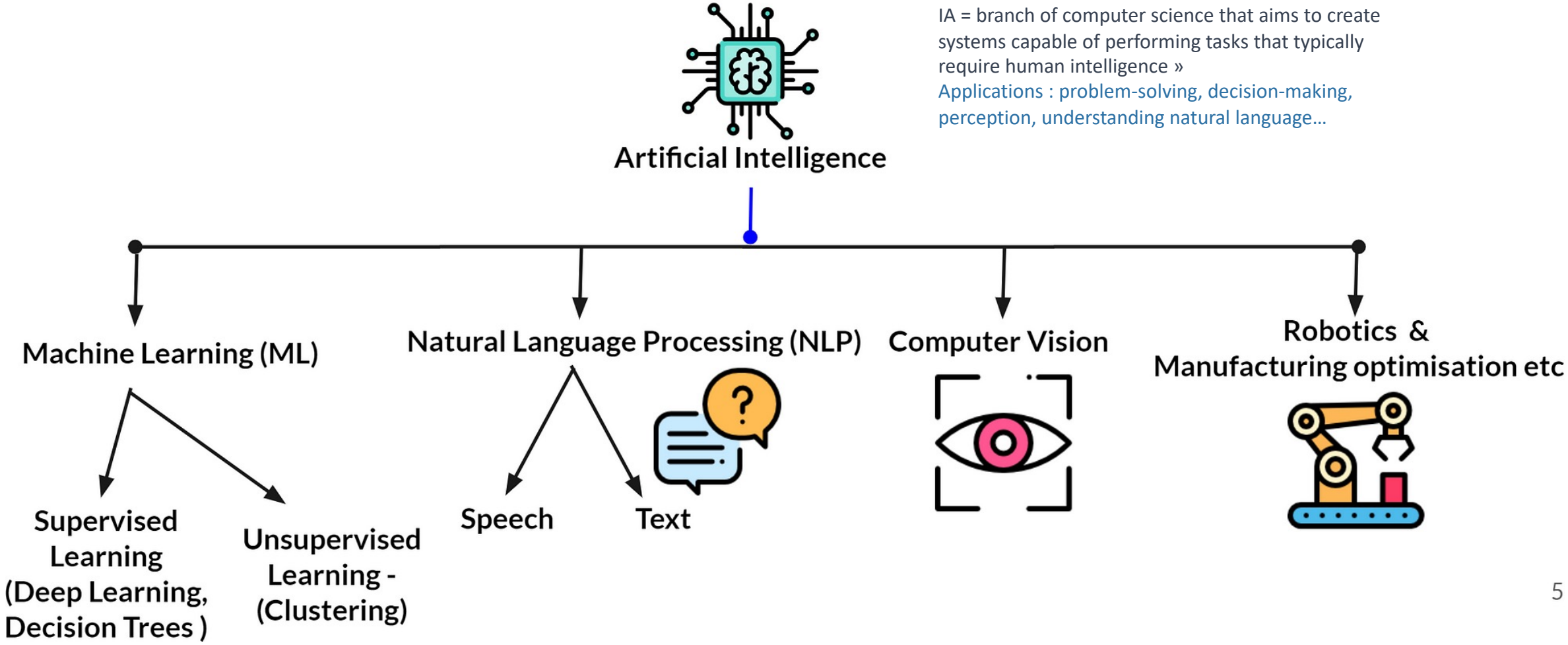
Google AI has better bedside manner than human doctors – and makes better diagnoses

Mariana Lenharo

PMID: 38216763 DOI: 10.1038/d41586-024-00099-4

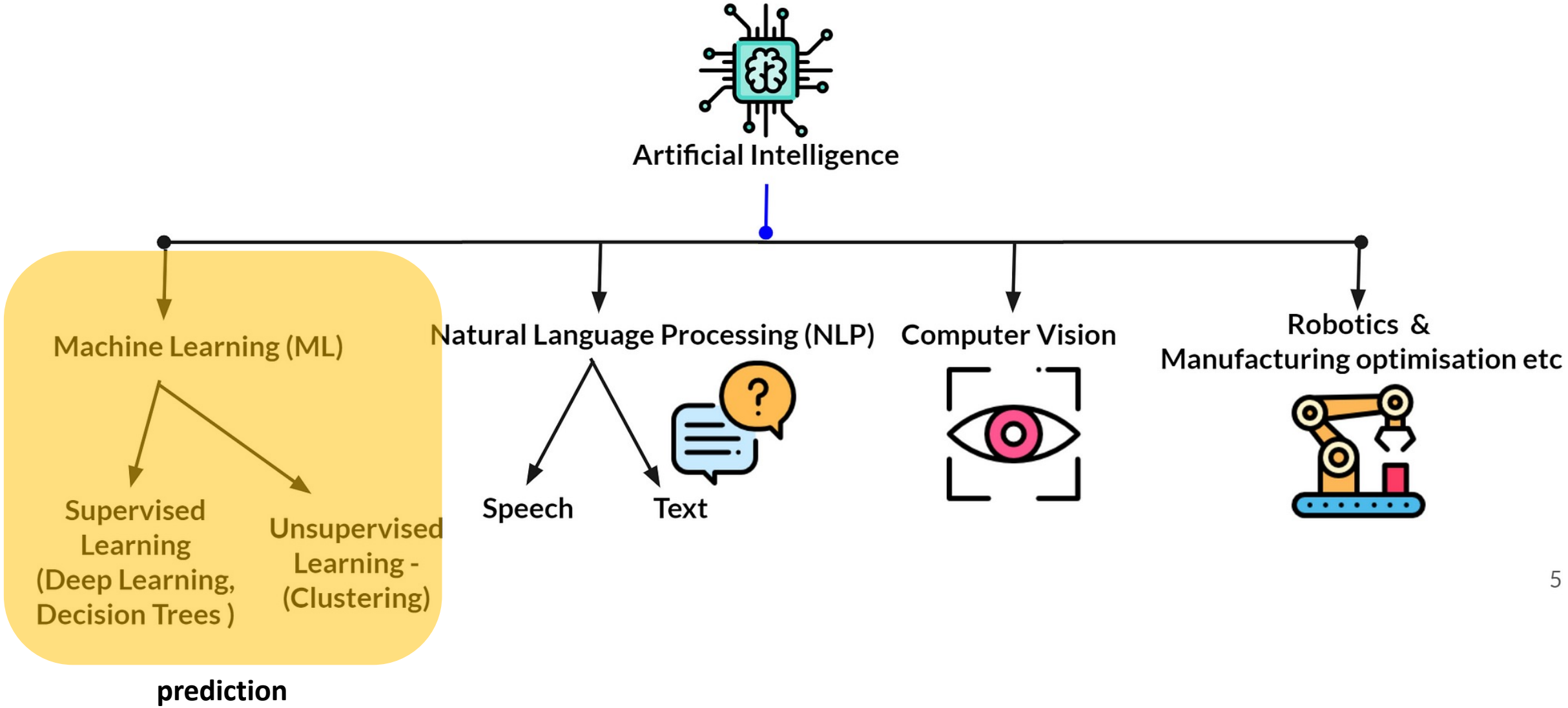
Using digital health technologies to optimise antimicrobial use globally.The lancet digital health 2024

Artificial Intelligence (AI)

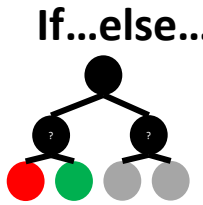


IA = branch of computer science that aims to create systems capable of performing tasks that typically require human intelligence »
Applications : problem-solving, decision-making, perception, understanding natural language…

Artificial Intelligence (AI)



Expert system ≠ Machine Learning



Human finds the rules from expertise

mail

Prediction system

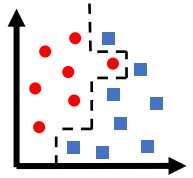
Non spam

Spam

x **features**

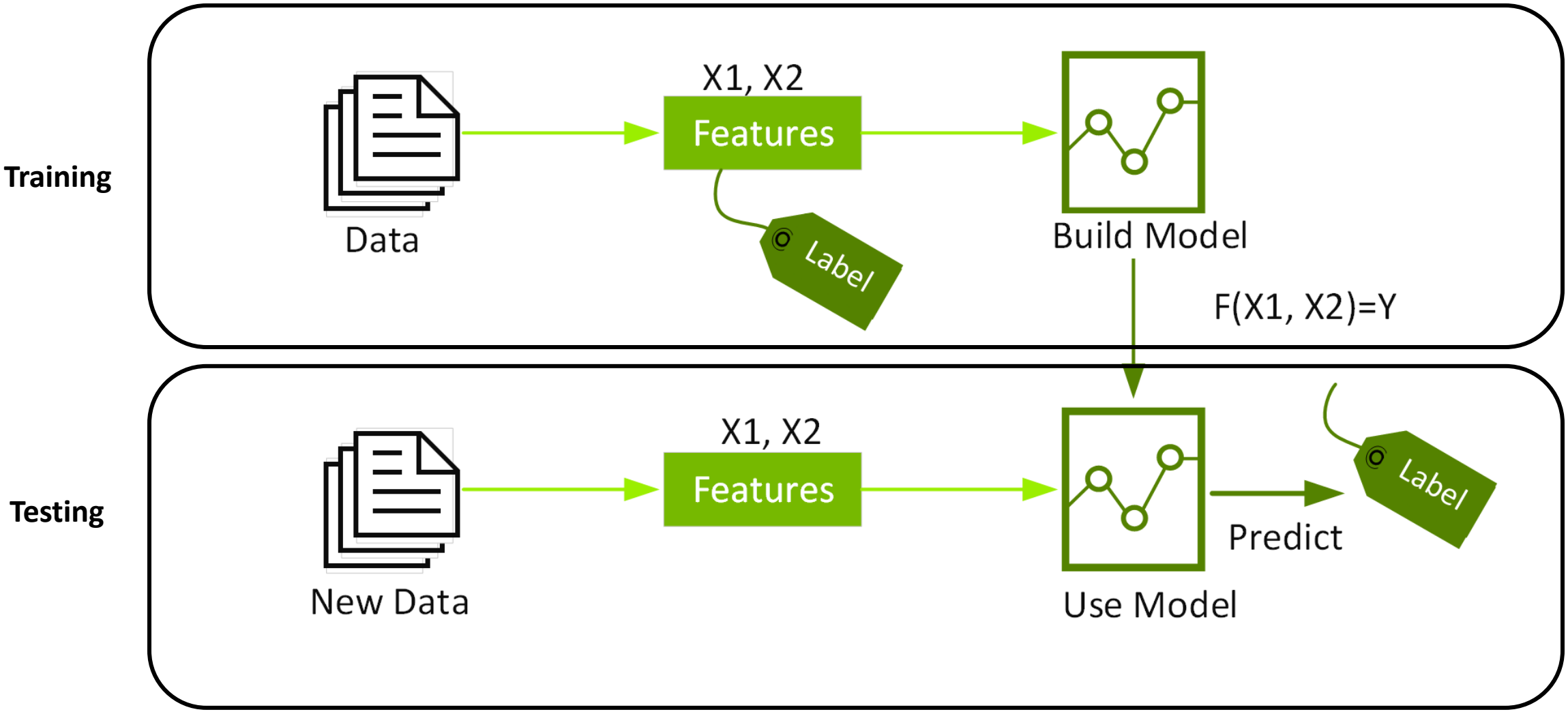
y **label**

sender	ortho	sex	Spam
1	1	1	yes
0	0	0	no
1	0	1	yes

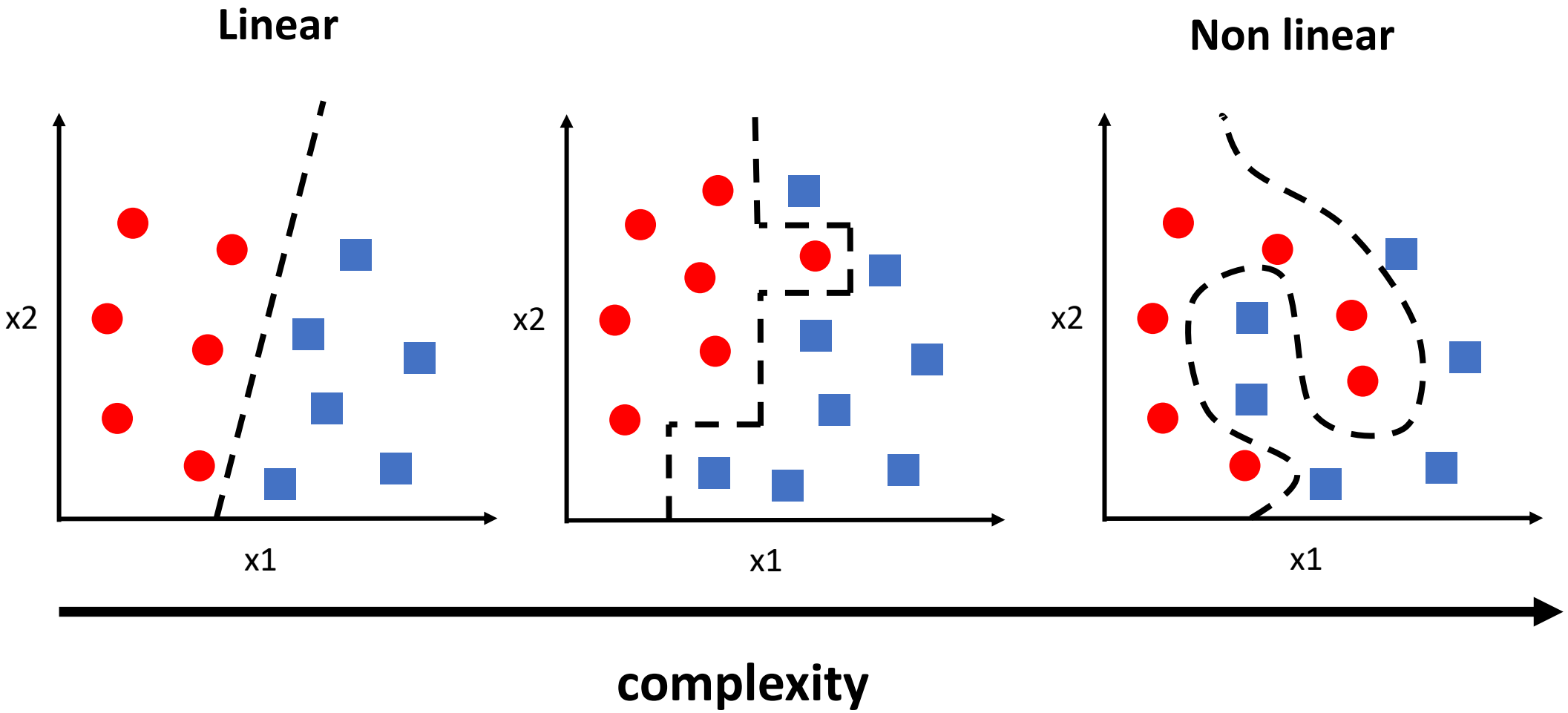


Machine Learn pattern from data

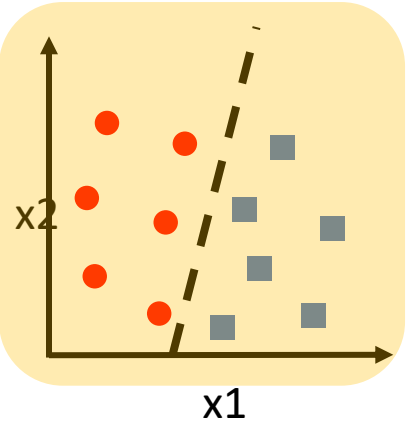
Machine learning: Training then Testing

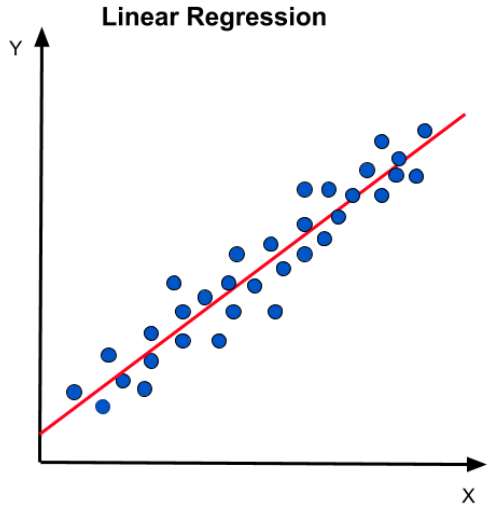


Prediction= finding a mathematical pattern

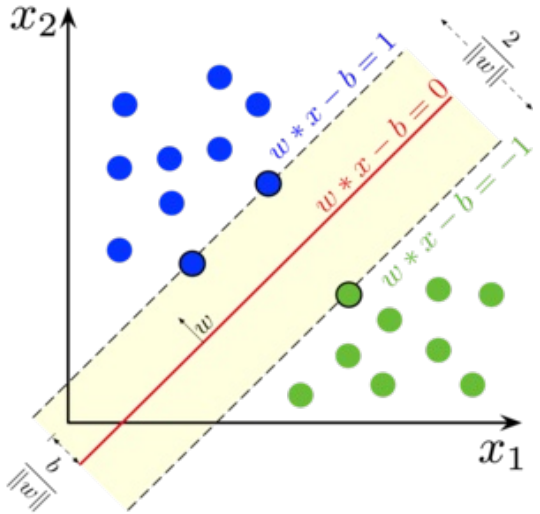


Traditionnal ML: linear algorithms



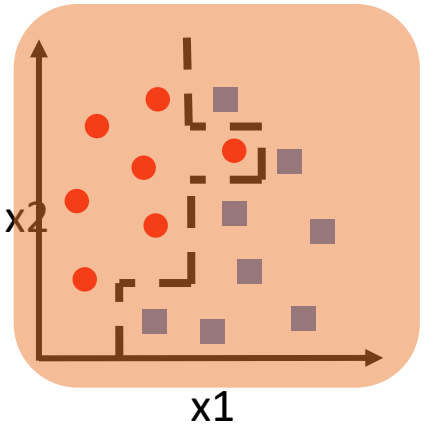


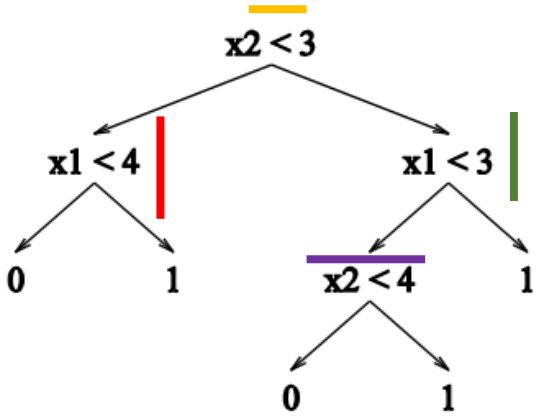
Linear/logistic regression



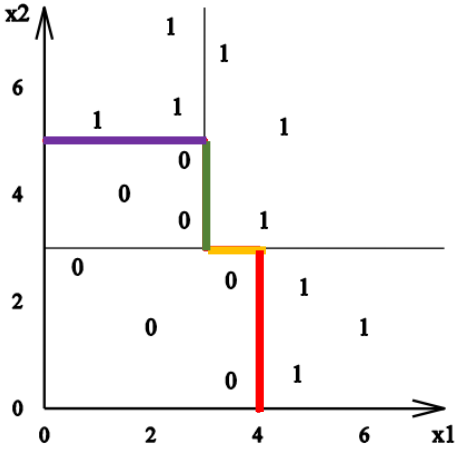
Support Vector Machine
SVM

Traditionnal ML: Decision Tree

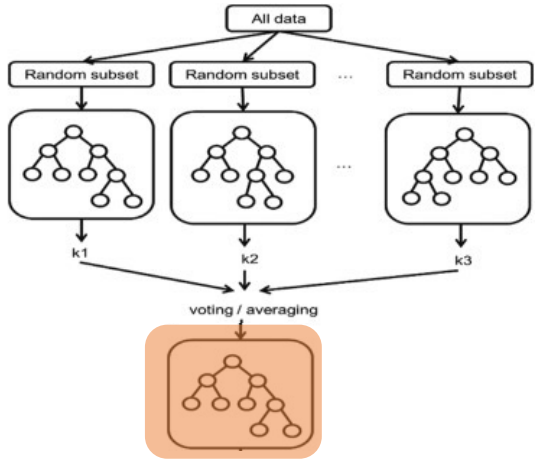




Decision tree

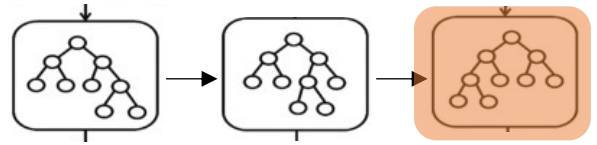


μ



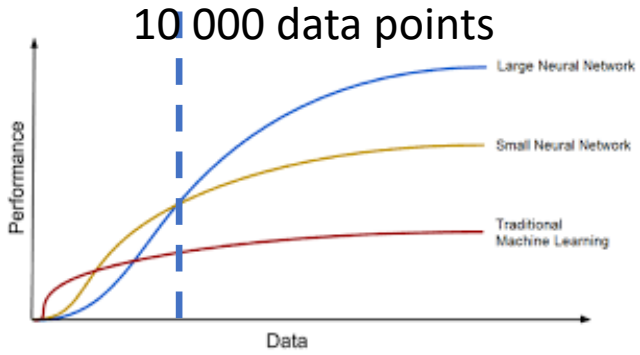
Random Forest (RF)

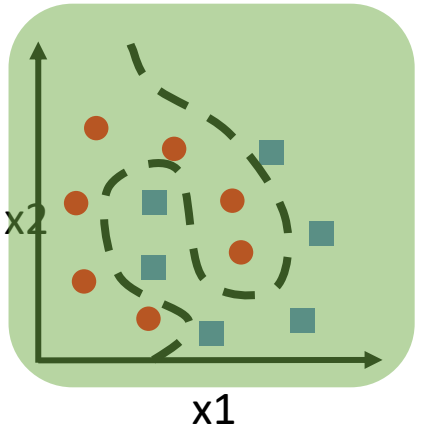
↗

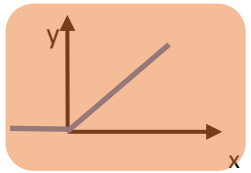


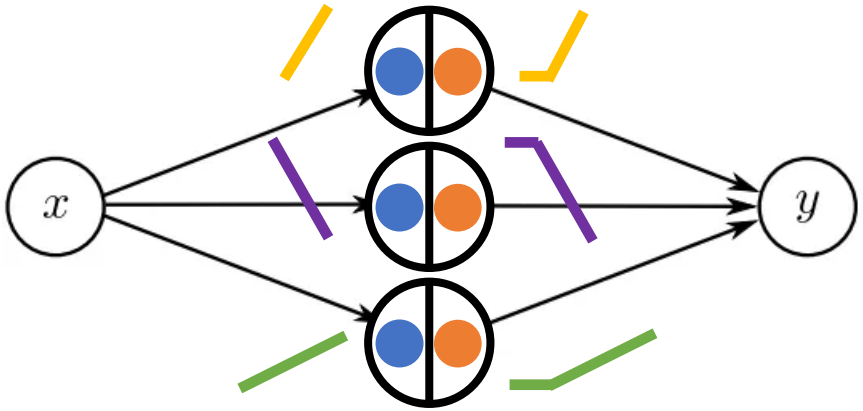
eXtrem Gradient Boosting (XGBoost)

Deep Learning

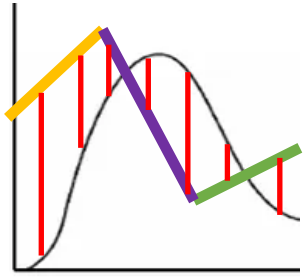








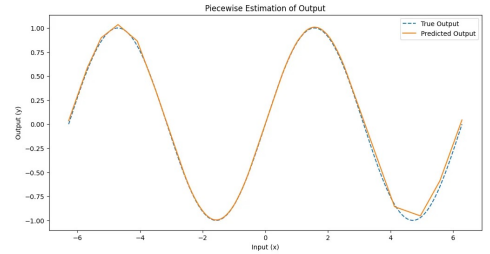
Neural network

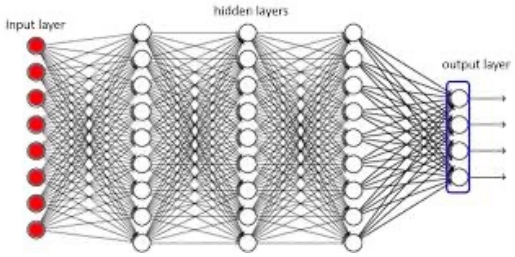


truth

prediction

errors





Large Language Model: « stochastic parrots »

User prompt

« Un, deux, trois … »

System prompt= context

« tu es un mathématicien…»

LLM

« quatre, cinq, six» P= 0.8

« partez!» P= 0.15

« Soleil!» P= 0.05

Comparing ML algo: Metrics

Truth

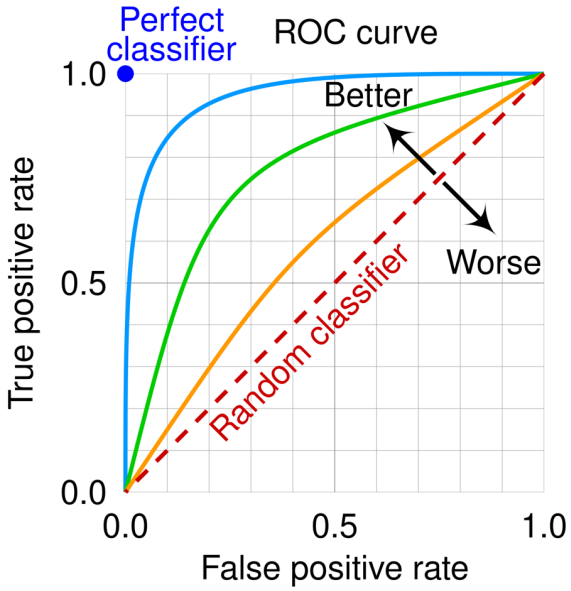
Prediciton

	Resistant (+)	**Sensible (-)**
R (+)	True Positive	False positive
S (-)	False negative	True Negative

"How reliable is a positive/negative result?"

- **PPV (Precision)**
- **NPV**

- **Sensitivity(Recall)**:
- **Specificity**



- **Accuracy**: "overall prediction?"
- **F1 Score (harmonic mean of precision & recall)**: >0.8: good

"balance resistant cases and false alarms?"

AMR prediction: 4 examples

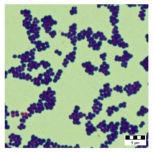
#4 AST

GeneXpert, BioFire

Betalactatest

Vitek, phoenix

<1d



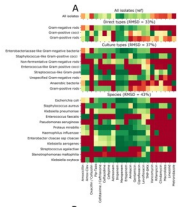
<5d

<1d

<48h

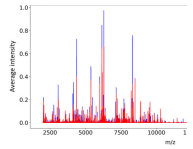
Données épidemio-clinico-bio **Liquide biologique** **Examen direct** **Cultures** **Identification** **Antibiogramme**

#1: Epidemio



#2 Imaging

#3 Maldi-TOF



Genomic

surveillance

BK

acinetobacter

…

ML article reading guidelines

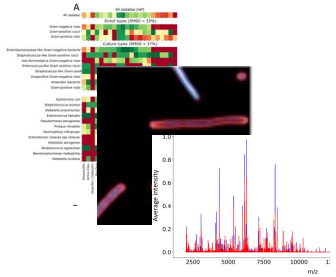
$$\hat{y} = f(x)$$

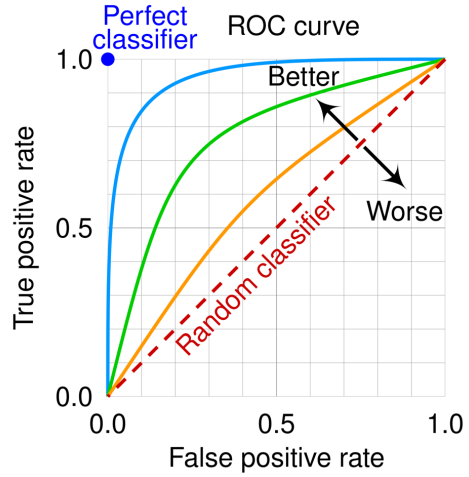
label

Features

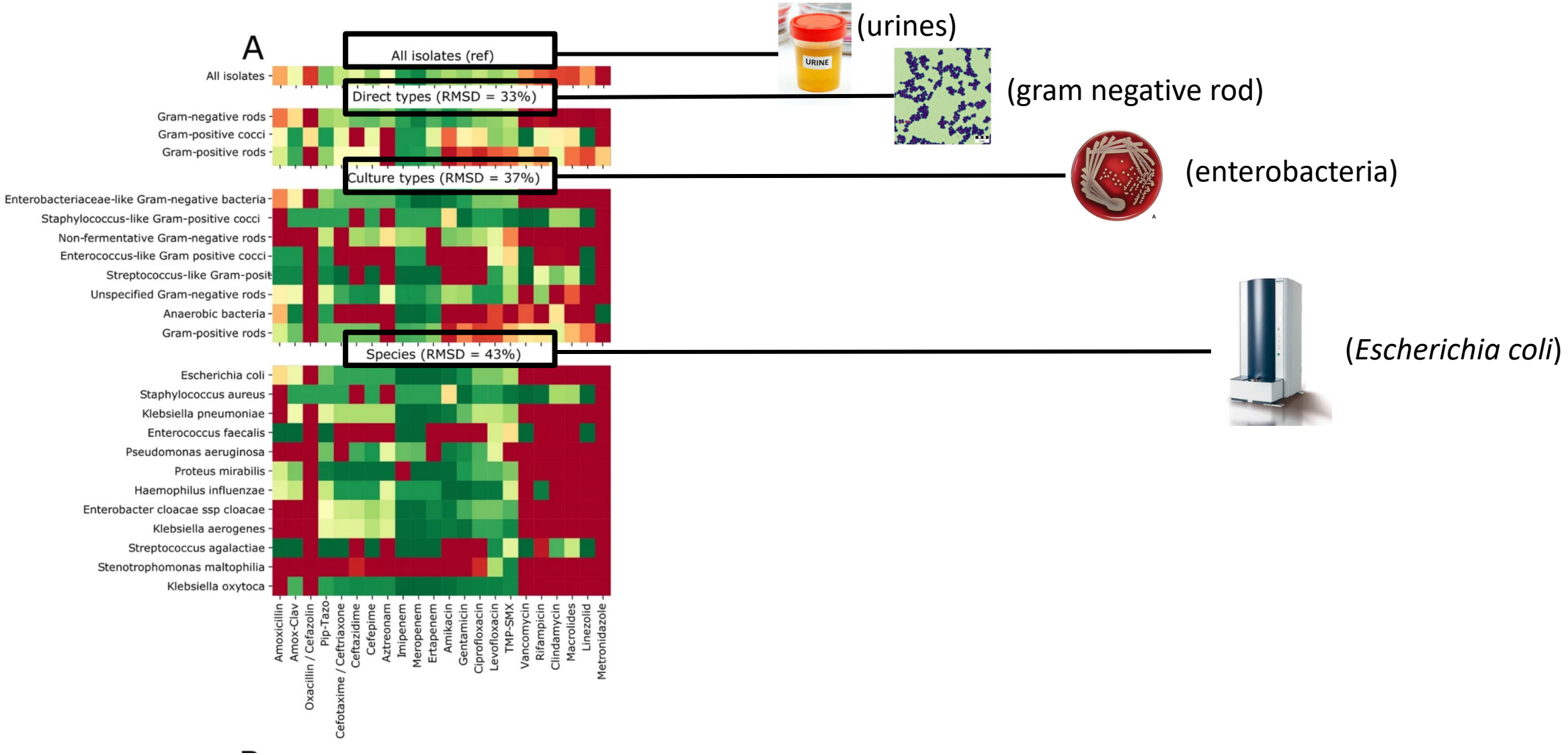
Key findings

- Expert system
- ML
- deepLearning
- LLM

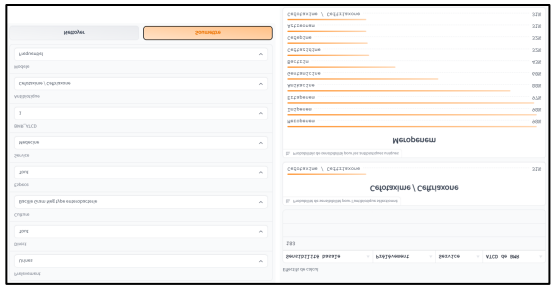


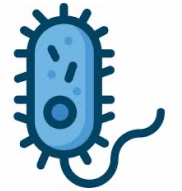
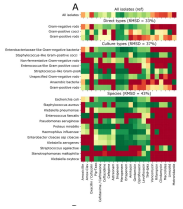


Exemple #1: Epidemiological data

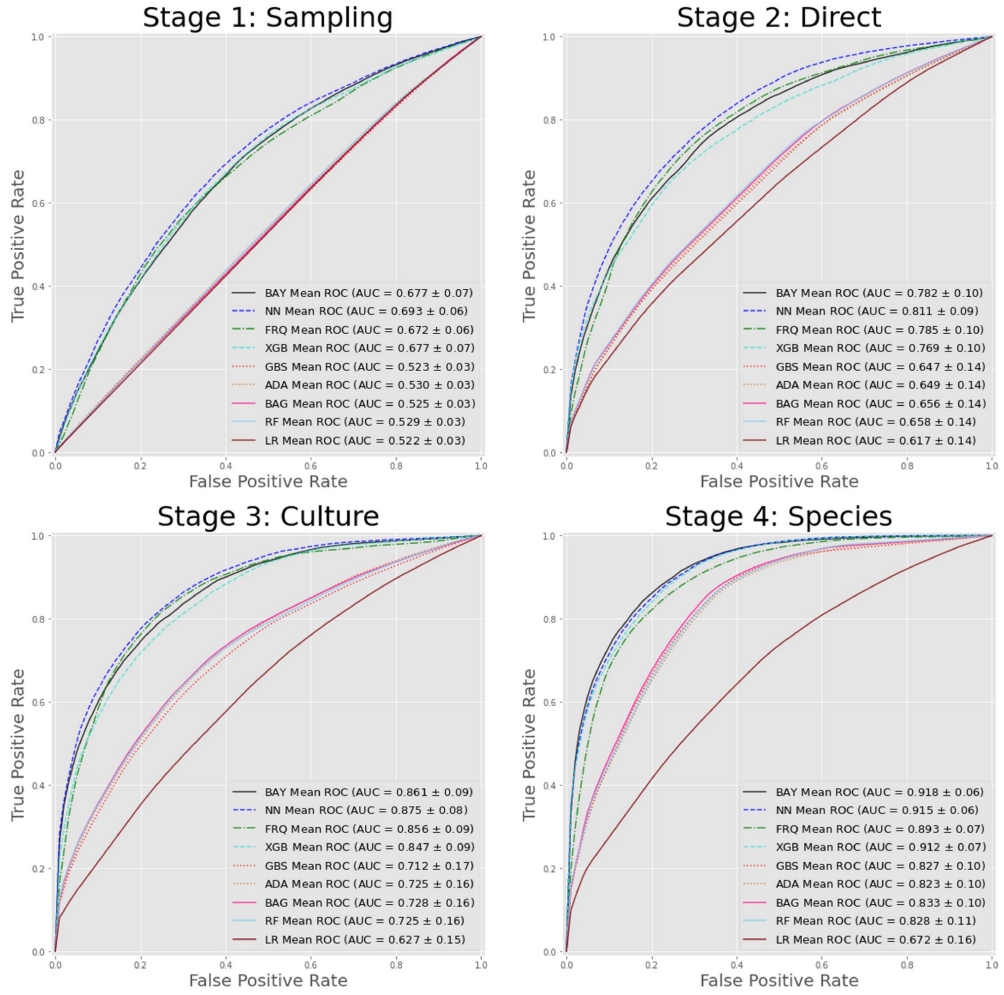


#1 Objective & Methods



y	x	f ( )
AMR prediction for:  12 species  22 ATB	• 2014- 2020, Hôpital Européen Marseille • 13,166 patients 30,975 antibiograms  • Historical bacterial ecology, Stage, Ward, BMR past history, period	Bayes/frequency based inference Logistic regression Random forest XGBoost ADA, GBS Neural network

#1 Key findings



- Prediction quality improve with stage of analysis
- **Bayesian and neural net win** the competition

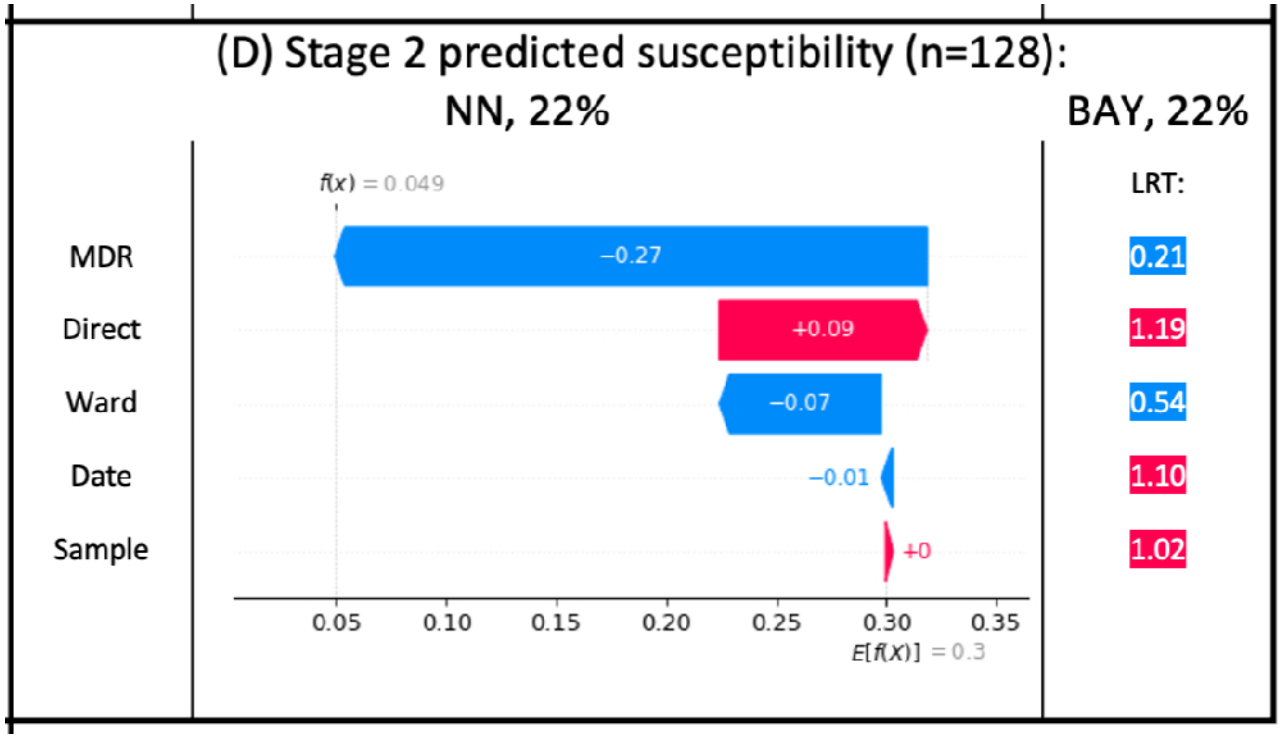
Model	Stage 1 "sampling"	Stage 2 "Direct"	Stage 3 "Culture"	Stage 4 "Species"	Overall mean
	All isolates of the 2020 validation dataset				
BAY	0.677	0.782	0.861	0.918	0.809
NN	0.693	0.811	0.875	0.915	0.823
FRQ	0.672	0.785	0.856	0.893	0.802
XGB	0.677	0.769	0.847	0.912	0.801
GBS	0.523	0.647	0.712	0.827	0.677
ADA	0.530	0.649	0.725	0.823	0.682
BAG	0.525	0.656	0.728	0.833	0.686
RF	0.529	0.658	0.725	0.828	0.685
LR	0.522	0.617	0.627	0.672	0.610
Overall mean	0.594	0.708	0.773	0.847	0.731

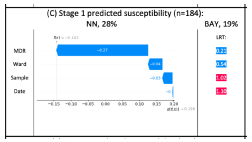
#1 Explainable AI? C3G S prediction

Résistance Sensibilité

BGN

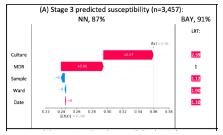
Récidive de PNA
avec portage
BLSE



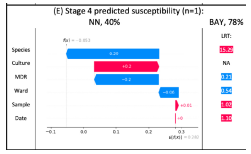


1.Sampling

2.Direct Examination

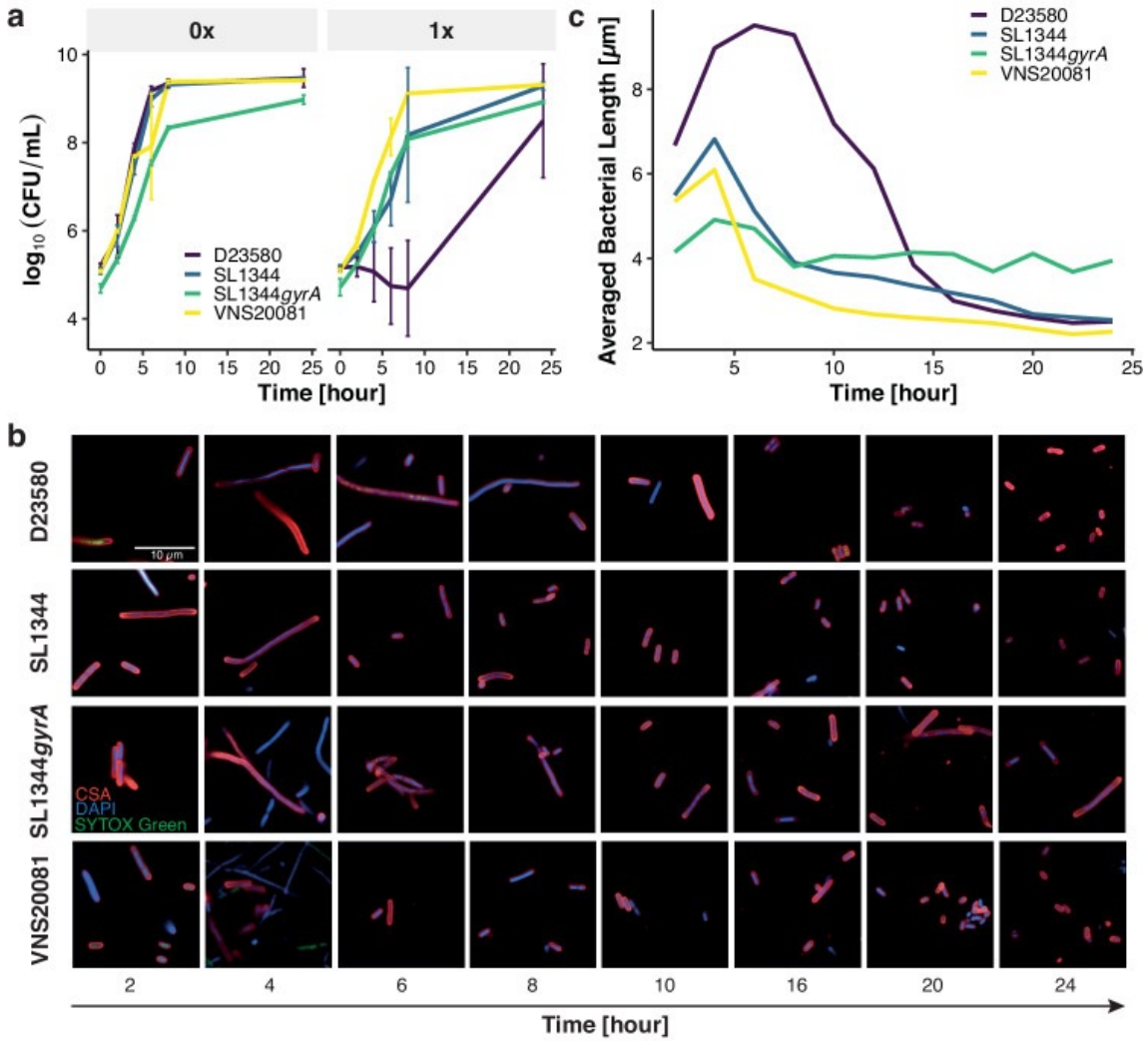


3.Cultures



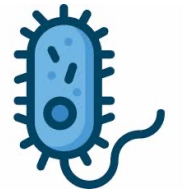
4.MALDI_TOF

Exemple #2: Imaging data



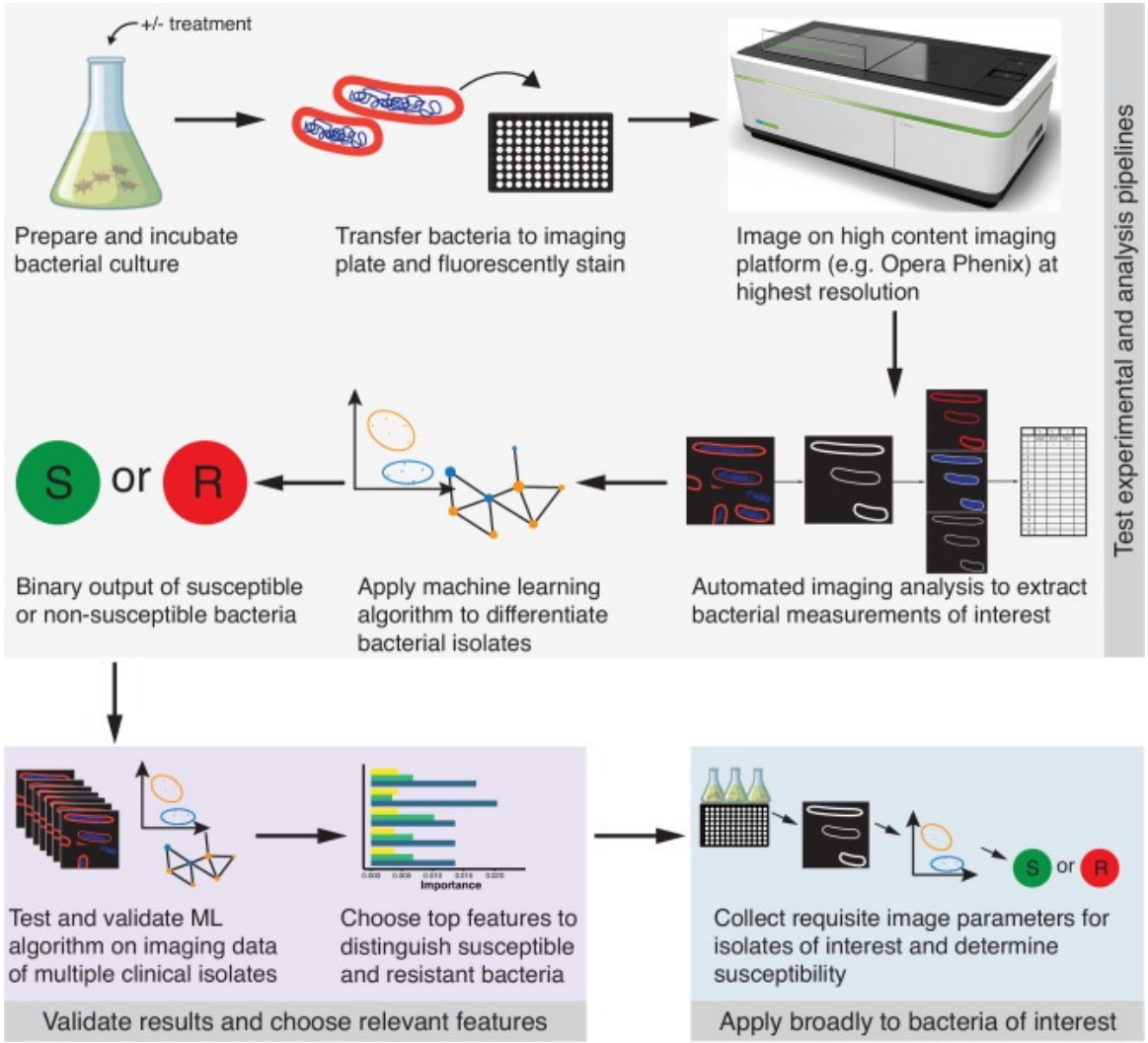
Tuan-Anh Tran, Nat Commun, 2024 Jun

#2: Objective & Methods

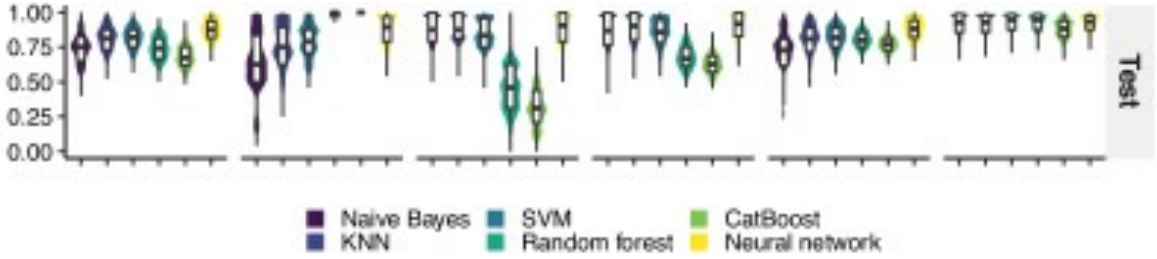
y	x	f ( )
AMR prediction for:  ***Salmonella typhi***  **Ciprofloxacin**	4 S. Typhimurium isolates 4 C° of ciprofloxacin 24h 1681 High-content imaging (HCI) :  65 features: morphological, intensity, and texture features for each individual bacterial cell	Bayes KNN SVM Random Forest CatBoost Neural network

Tuan-Anh Tran, Nat Commun, 2024 Jun

#2: Workflow


+/- treatment
Prepare and incubate bacterial culture
Transfer bacteria to imaging plate and fluorescently stain
Image on high content imaging platform (e.g. Opera Phenix) at highest resolution
Test experimental and analysis pipelines
S or R
Binary output of susceptible or non-susceptible bacteria
Apply machine learning algorithm to differentiate bacterial isolates
Automated imaging analysis to extract bacterial measurements of interest
Importance
Test and validate ML algorithm on imaging data of multiple clinical isolates
Choose top features to distinguish susceptible and resistant bacteria
Validate results and choose relevant features
S or R
Collect requisite image parameters for isolates of interest and determine susceptibility
Apply broadly to bacteria of interest

#2 Key findings

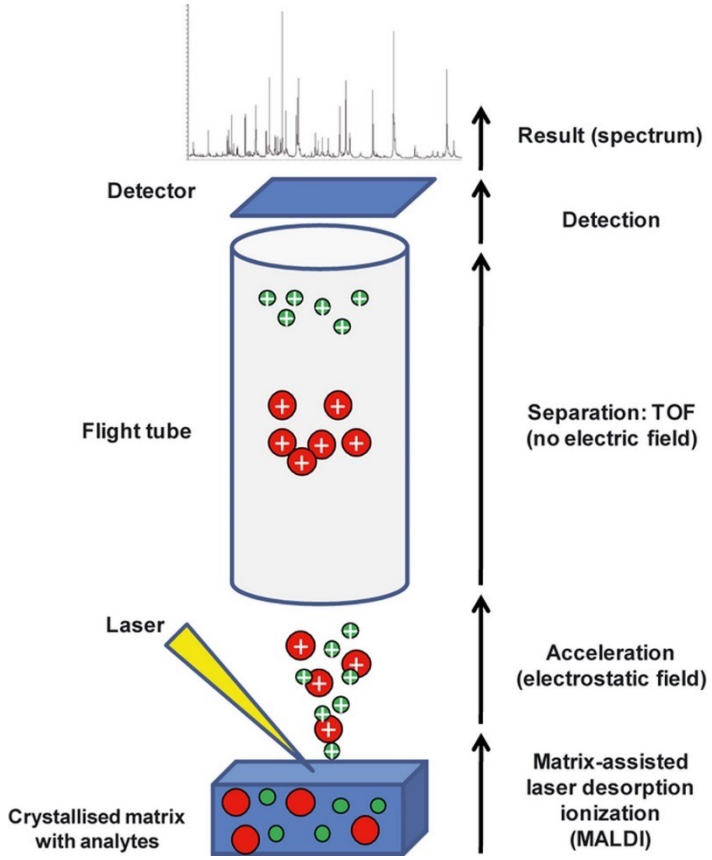


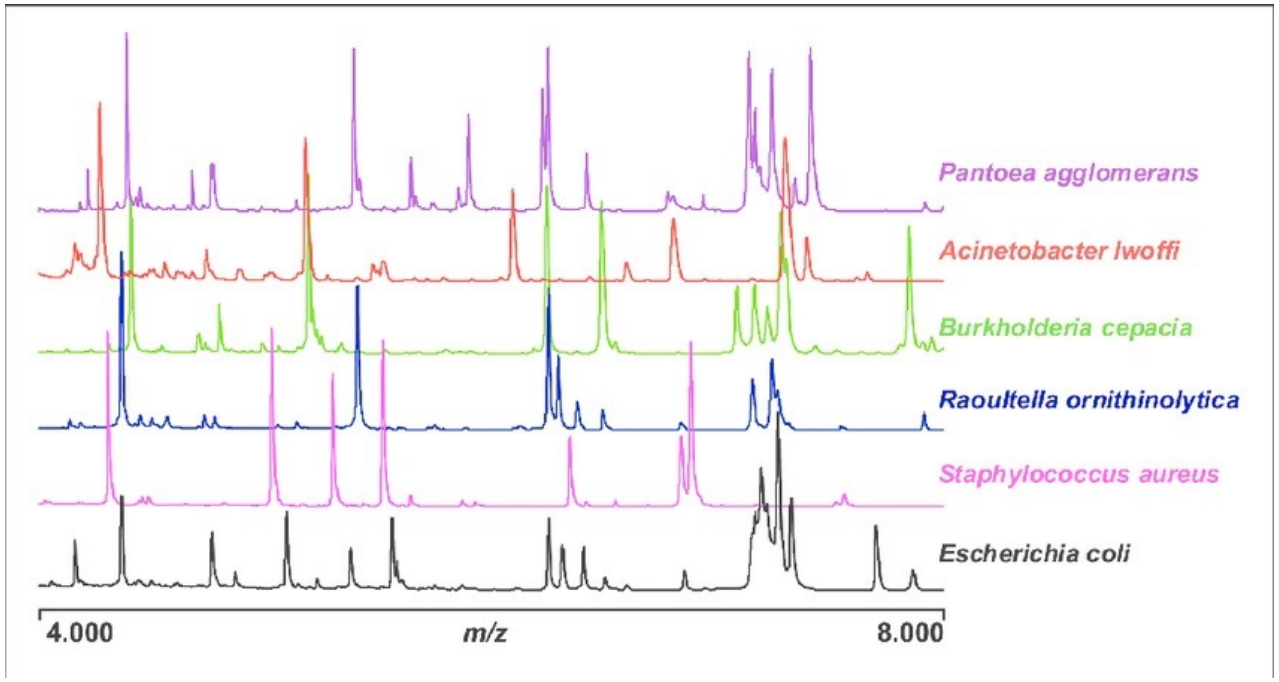
	Test set					
Method	Accuracy	Sensitivity	Specificity	Precision	F1 score	AUC
Naïve Bayes	0.74±0.13	0.63±0.24	0.87±0.15	0.85±0.15	0.69±0.20	0.91±0.10
KNN	0.81±0.11	0.74±0.20	0.88±0.11	0.88±0.12	0.78±0.15	0.91±0.08
SVM	0.81±0.09	0.78±0.14	0.84±0.12	0.85±0.11	0.81±0.11	0.92±0.09
Random forest	0.74±0.09	0.99±0.03	0.46±0.18	0.68±0.10	0.80±0.07	0.92±0.07
CatBoost	0.68±0.09	1.00±0.02	0.32±0.16	0.63±0.08	0.77±0.06	0.88±0.08
Neural network	0.87±0.08	0.87±0.12	0.88±0.12	0.90±0.10	0.87±0.08	0.91±0.07

- Machine learning classifiers can distinguish between ciprofloxacin susceptible and resistant isolates without ciprofloxacin exposure
- **Neural network win**

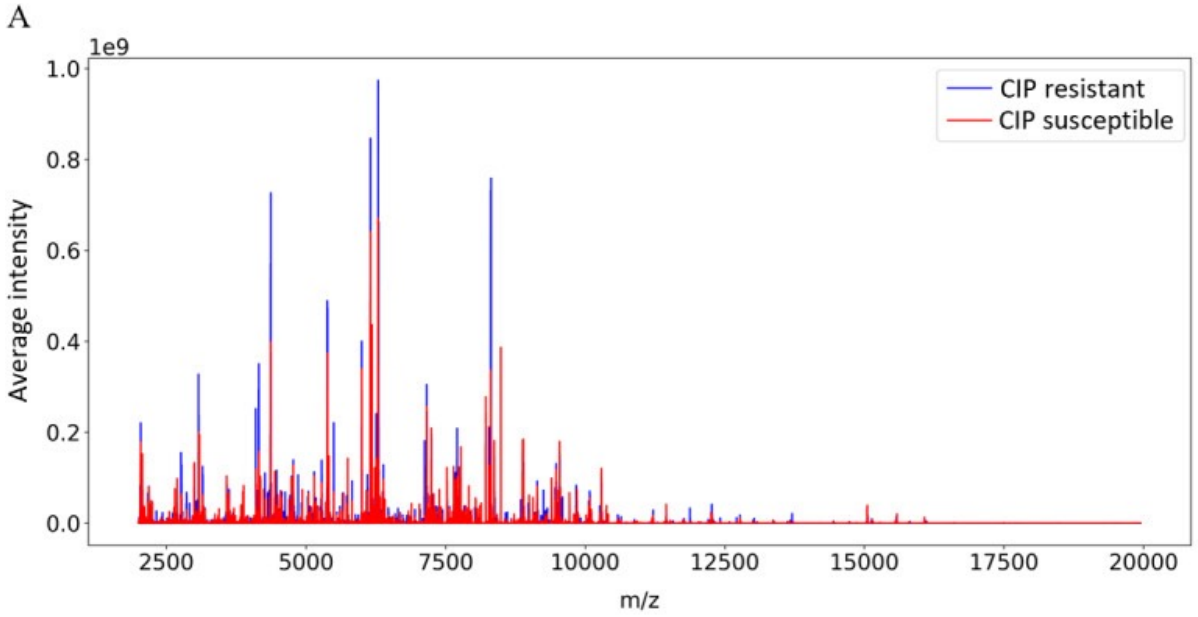
Mécanistic hypothesis:
DNA gyrase mutations may interact with other cellular pathways, which ultimately impact directly on cellular morphology.

Exemple #3: proteomic data from MALDI-TOF





#3 MALDI_TOF & AMR prediction

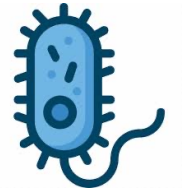
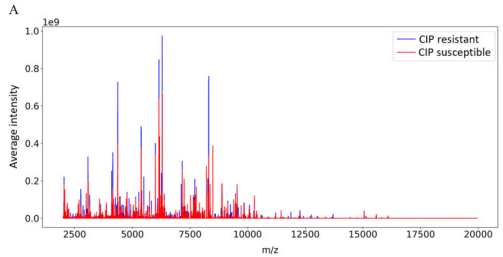


Differential mass spectrometry profiles for CIP resistance in Klebsiella pneumoniae.

.

m/z: mass-to-charge

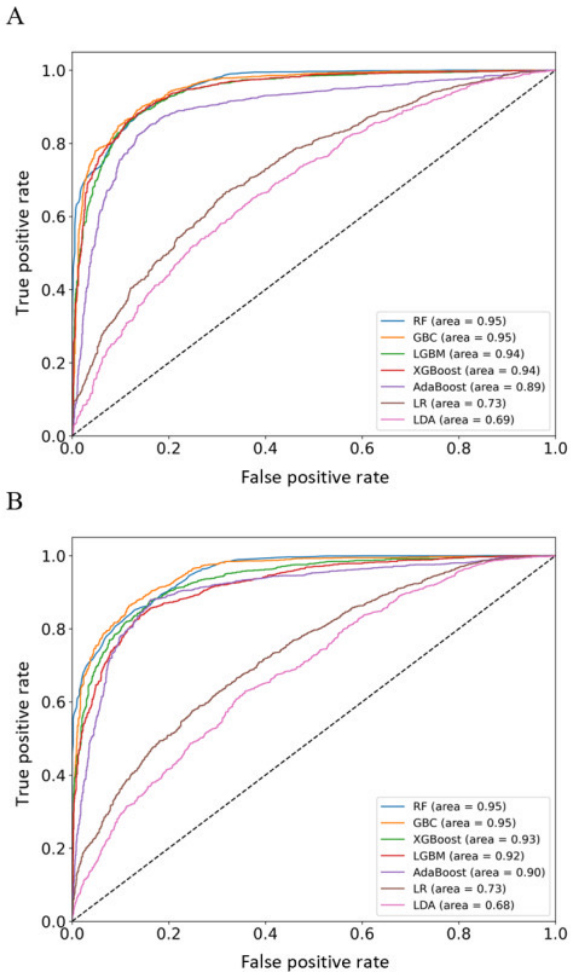
#3 Objective and Methods

y	x	$f(\ )$
AMR Prediction for:  ***Klebsiella pneumoniae***  **Ciprofloxacin/Levo**	January 2021 to December 2023 4 hospitals Taipei city 11,996 KP isolates.  MALDI-TOF Mass spectrometry profiles ~ 15 000 features	Logistic regression. LDA: linear discriminant analysis. Random forest. XGBoost GBC: gradient boosting classifier. LGBM: light gradient boosting machine.

J Med Internet Res. 2024 Nov

#3 Key findings

ROC curve



Levofloxacin resistance prediction

Models	Training AUC[a]	Testing AUC	Accuracy	Sensitivity	Specificity	PPV[b]	NPV[c]	F_1-score
RF[d]	0.99	0.95	0.86	0.89	0.82	0.86	0.86	0.87
GBC[e]	0.99	0.95	0.87	0.88	0.86	0.89	0.85	0.88
XGBoost	0.99	0.93	0.85	0.86	0.85	0.87	0.83	0.86
LGBM[f]	0.99	0.92	0.85	0.84	0.85	0.87	0.82	0.86
AdaBoost	0.99	0.90	0.85	0.85	0.84	0.87	0.83	0.86
LR[g]	0.77	0.73	0.66	0.74	0.57	0.68	0.64	0.70
LDA[h]	0.72	0.68	0.64	0.81	0.43	0.63	0.65	0.71

Random Forest and XGBoost achieved the best perfomances

#4 LLM & AST interpretation

Step 1: Generation of a GPT powered generative AI agent.

EUCAST GPT Expert

Expert on EUCAST standards and general antimicrobial susceptibility

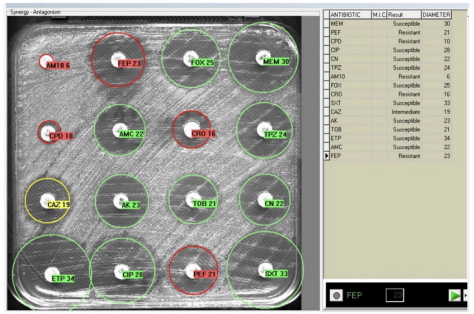
Step 2: Acquisition of knowledge.

Using document from EUCAST.org
- EUCAST breakpoint table v13.1
- Expert rules

Step 3: Within model testing.

Checked with few examples. Improving rules for obvious mistakes e.g. list of species with chromosomal AmpC.

Step 4: Input for prompt.



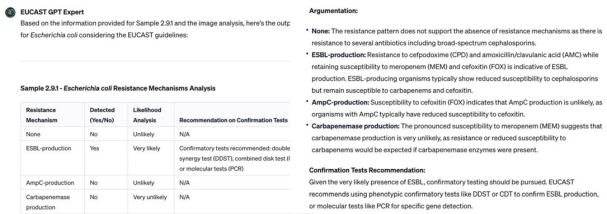
+ same image without measurement circles.

+ Table with measured inhibition zones

Step 5: Standardized prompting.

Ask for:
(i) Interpretation of image and table;
(ii) Provide output table with 4 categories: “None”, “ESBL”, “AmpC”, and “Carbapenemase”;
(iii) recommended confirmation;
(iv) and short argumentation text.

Step 5: Output analysis



Output table Argumentation

Step 6: Calculation of output performance e.g., sensitivity and specificity.

#4 LLM & AST interpretation

TABLE 1 Sensitivity and specificity of human experts and the customized EUCAST-GPT-expert

	Human experts[a]	EUCAST-GPT-expert[b]
ESBL		
Sensitivity	98.0% (91.8–100)	95.4% (94.5–96.3)
Specificity	99.1% (97.1–100)	69.2% (63.8–85.7)
AmpC		
Sensitivity	96.8% (93.3–100)	96.9% (87.5–96.9)
Specificity	97.1% (95.9–97.7)	86.3% (84.1–91.8)
Carbapenemases		
Sensitivity	95.5% (90.9–100)	100% (90.9–100)
Specificity	98.5% (98.5–98.5)	98.8% (98.8–98.8)

Pros & Cons

#1: epidemio 4 stages
#2: imaging
#3: MALDI TOF
#4 AST interpretation

	✔	✘
Quality	Data cleaning (#1)	No Clinical ATB data No Deep learning (#3)
Feasibilty	#1, #3, #4	#2
Explainability	#1, #3, #4 (SHAP)	#2
Relevance	Fast prediction: #1>#2>#3 Number species/ATB (#1, #4)	#4>WGS (5d) Limited to species/ATB (#2, #3)

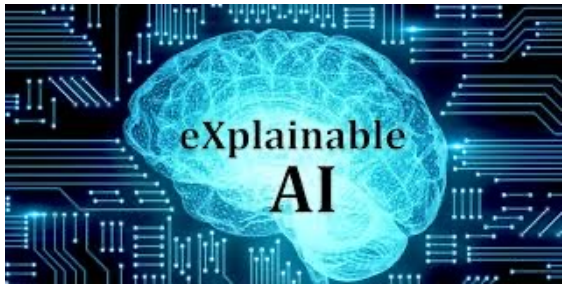
Artificial intelligence in antimicrobial stewardship: a systematic review and meta-analysis of predictive performance and diagnostic accuracy

	
2000- 2024. Observational, cohort, or retrospective studies focusing on the application of AI/ML in AMS. 3,458 retrieved articles 80 studies met the inclusion criteria.	• AUC [ES: 72.28 (70.42-74.14)] • accuracy [ES: 74.97 (73.35-76.58)] • sensitivity [ES: 76.89; (71.90-81.89)] • specificity [ES: 73.77; (67.87-79.67)] • NPV [ES:79.92 (76.54-83.31)] • PPV [ES: 69.41 (60.19-78.63)] ES: mean pooled effect size (ES)

Eur J Clin Microbiol Infect Dis 2025

Conclusion:
L'IA peut elle prédire l'antibiorésistance?

- L'IA peut tout prédire …. si accès à big data
- Pertinence?
  - Santé animale > humaine | Ville & Hôpital | aide à prescription> aide à prédiction
  - Timing % prescription d'antibiotique?
    - +++ si épargne prescription antibiotique
    - ++ si épargne large spectre
    - + si gain 24 heures désescalade
- Faisabilité:
  - Légale et politique: RGPD & DPI et accès données patients
  - Technique: « databases don't travel ». Combien de data scientist spécialisés en IA dans vos hôpitaux?
- Acceptabilité:
  - Effet black box IA



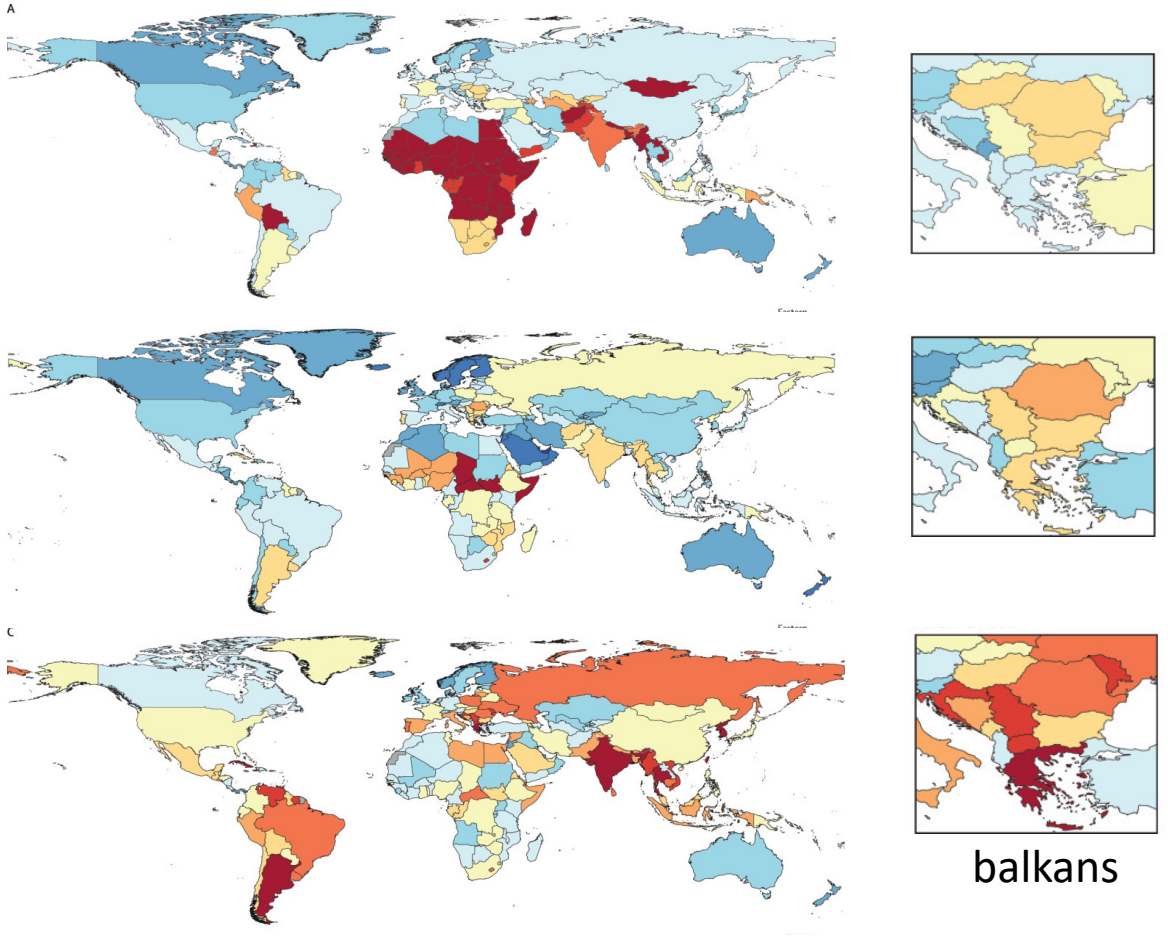
Bravo et Merci!

92 millions de morts évitables d'ici 2050

1990

2021
1 M/an

2050
2 M/an



balkans

Death rates per 100 000 attributable to AMR

<3	18 to <21
3 to <6	21 to <24
6 to <9	24 to <27
9 to <12	27 to <30
12 to <15	≥30
15 to <18	

Critical group

- Enterobacterales carbapenem-resistant
- Enterobacterales third-generation cephalosporin-resistant
- *Acinetobacter baumannii* carbapenem-resistant
- *Mycobacterium tuberculosis*, rifampicin-resistant[a]

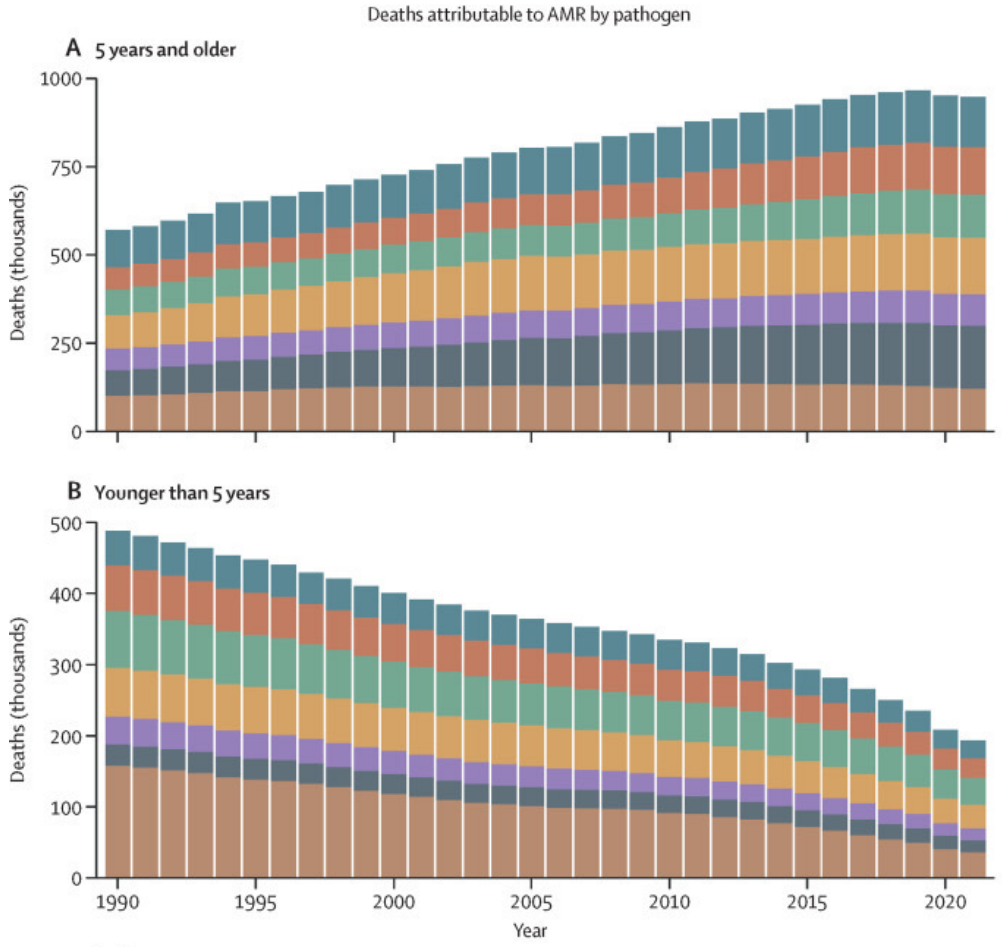
[a]RR-TB was included after an independent analysis with parallel criteria and subsequent application of an adapted MCDA matrix.

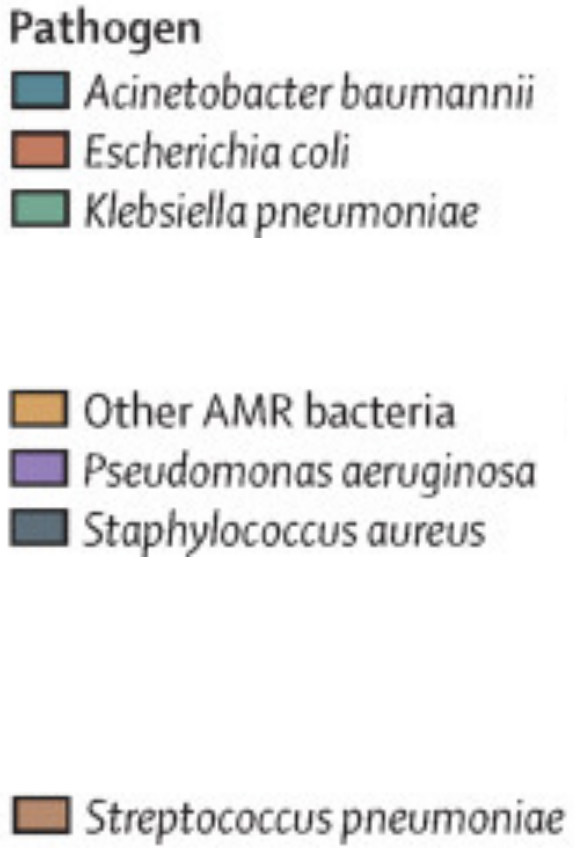
GBD 2021 Antimicrobial Resistance Collaborators *Lancet 202*

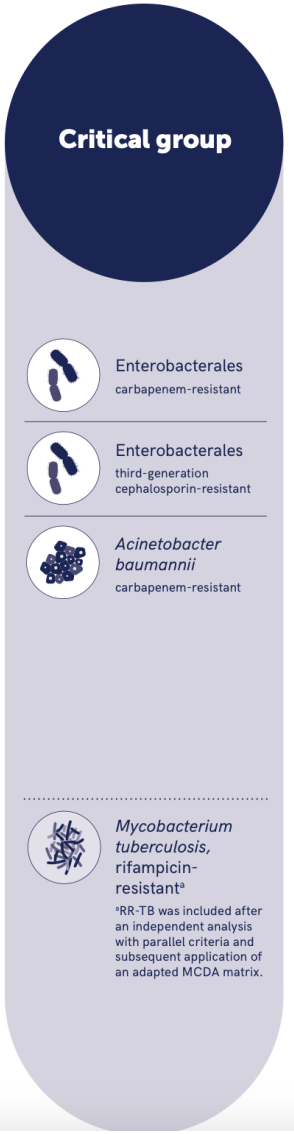
Deaths attributable to AMR by pathogen, global, 1990–2021

> 5 ans

< 5 ans

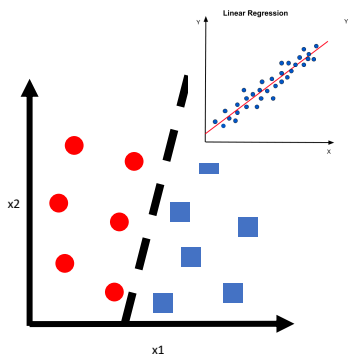


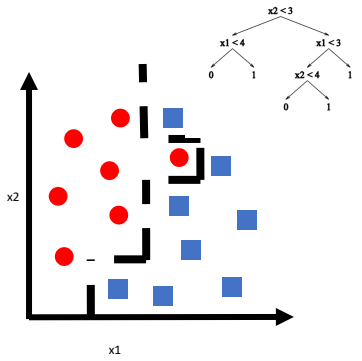


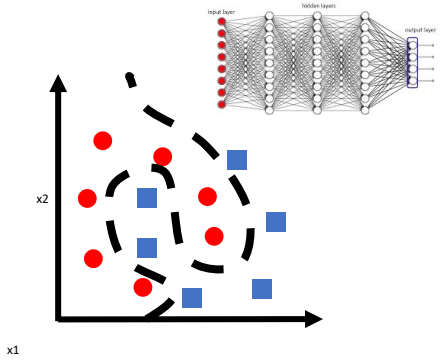


Global burden of bacterial antimicrobial resistance 1990–2021: a systematic analysis with forecasts to 2050, Lancet 2024

Different ML flavours







	Regression	Decision tree	deep learning
Use case	Structured data	Structured data	Text, image, sound
Features extraction	Manual	Manual	Automated
Performance	+	++	+++
Explainability	+++	++	+
Data points	100	1000	10 000
Overfitting risk	+	++	+++

Overfitting concept