



# L'IA peut elle prédire l'antibiorésistance?

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Maladies infectieuses, CH de Vannes

SPILF

# Conflits d'intérêt



Open AI



**Groupe  
Infectiologie  
Digit@le**

# Plan

Objectives: learn AI for collaboration with AI project

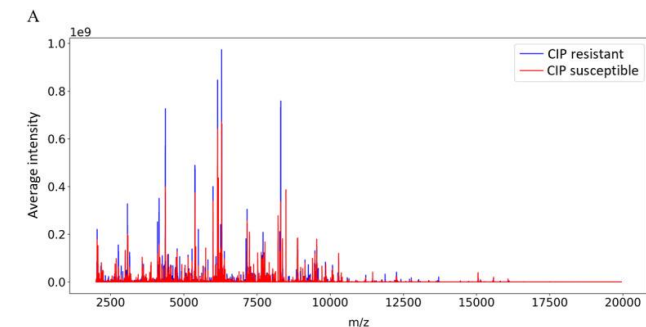
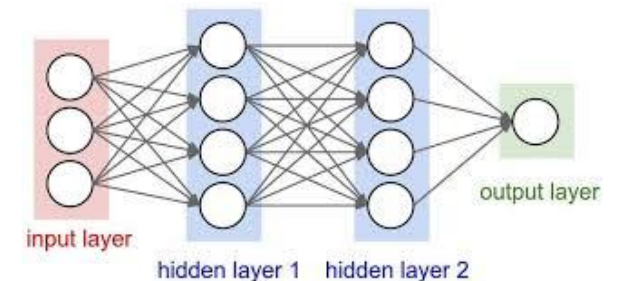
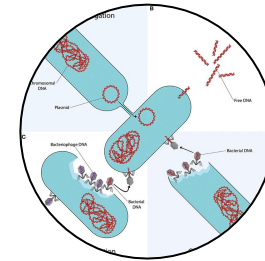
## 1. Antibioresistance:

- Mécanismes
- Déterminants
- Perspectives

## 2. Intelligence artificielle

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

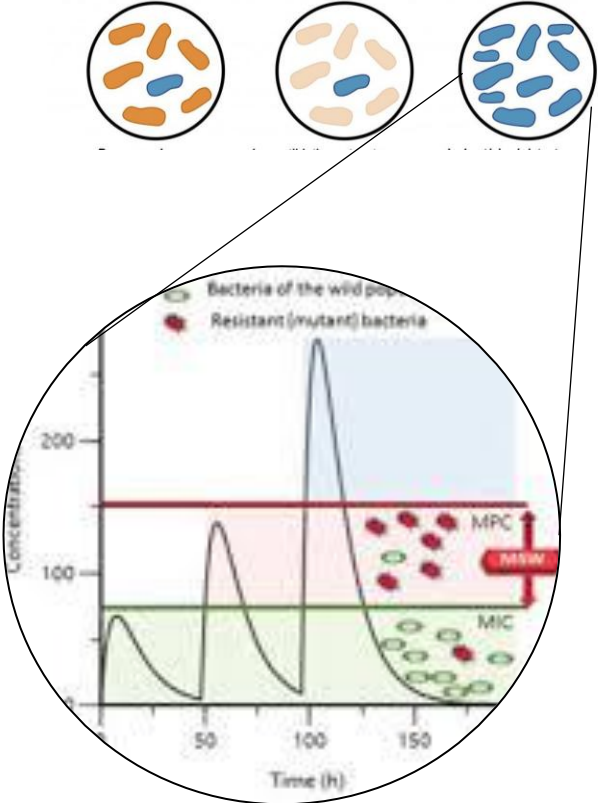
## 3. 4 exemples d'utilisation de l'IA pour prédiction de l'antibiorésistance



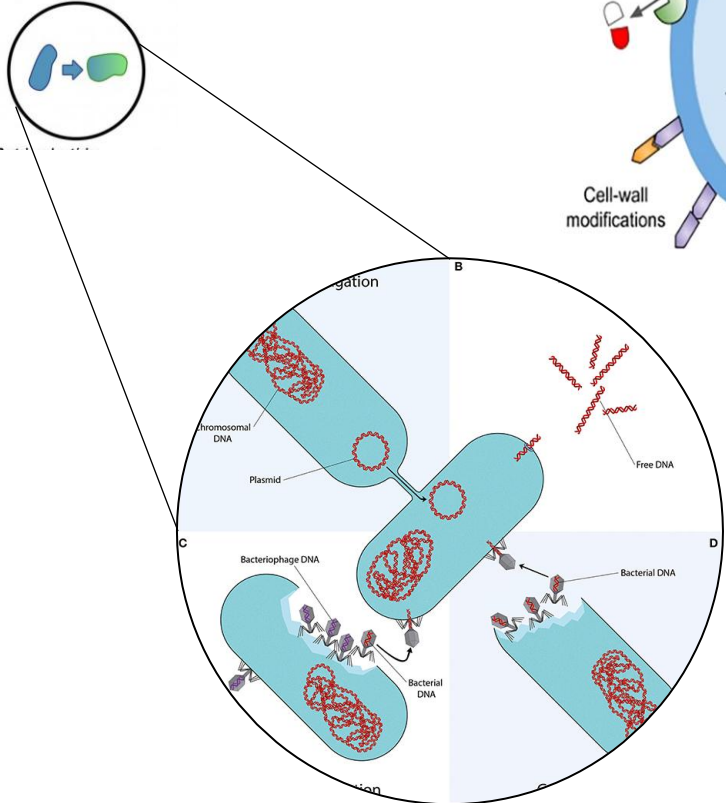
# Mécanismes de l'antibiorésistance



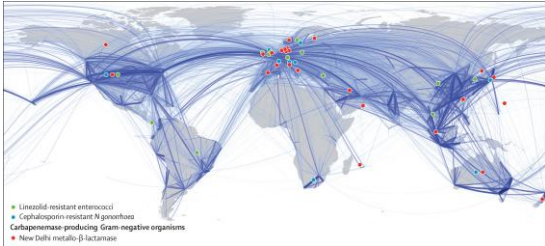
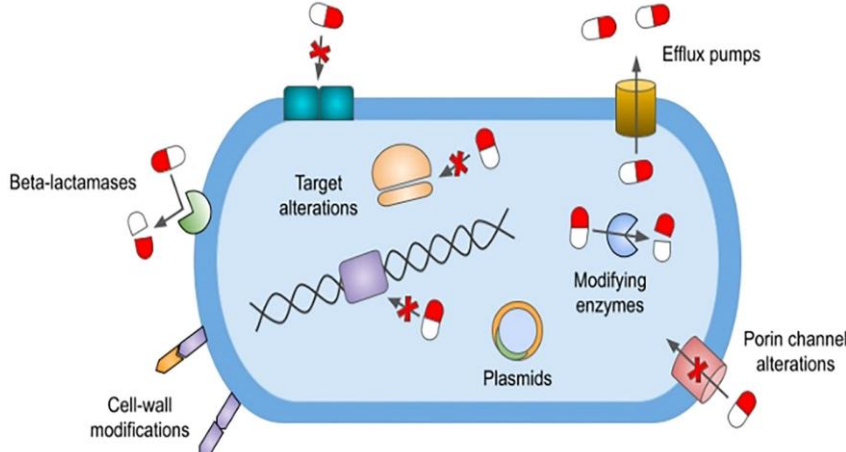
## Amplification vertical horizontal



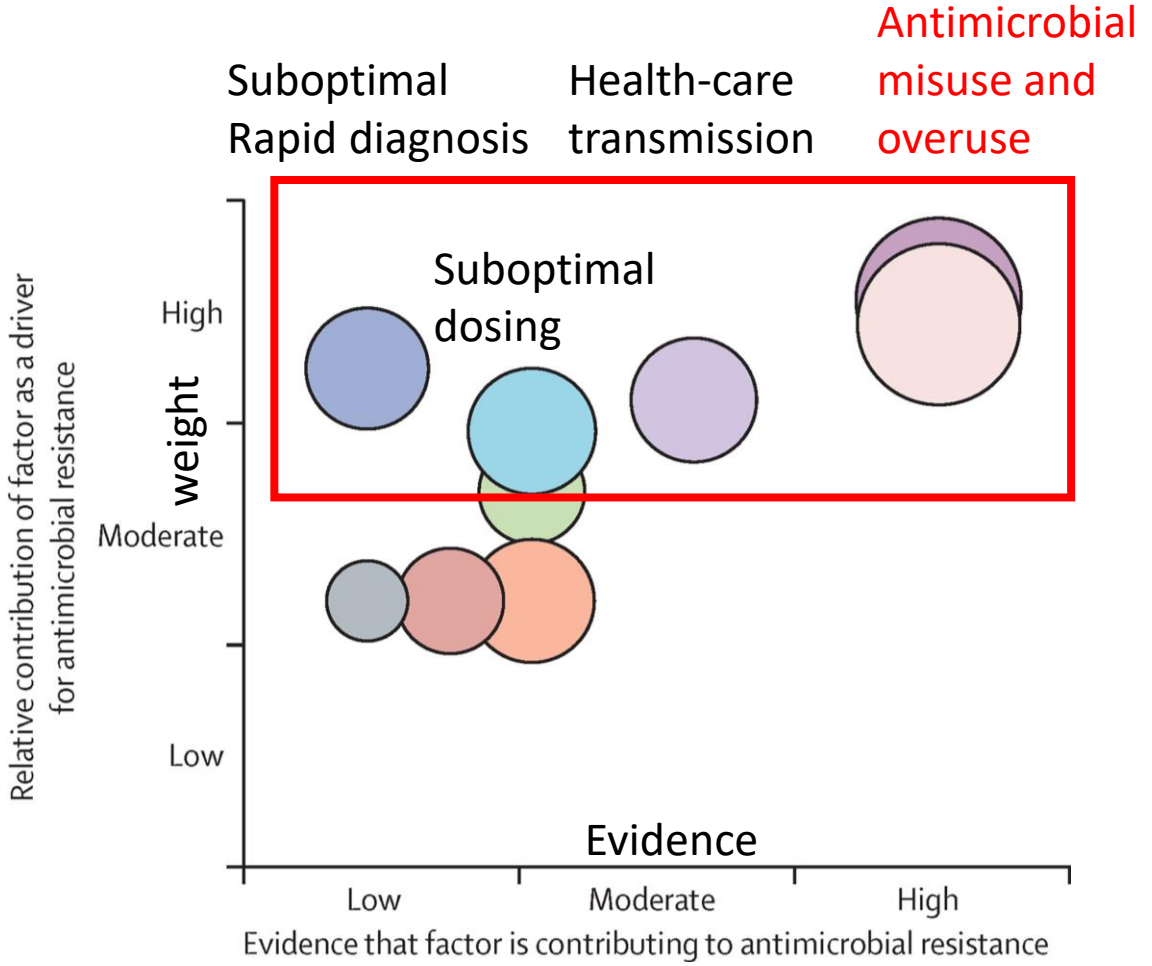
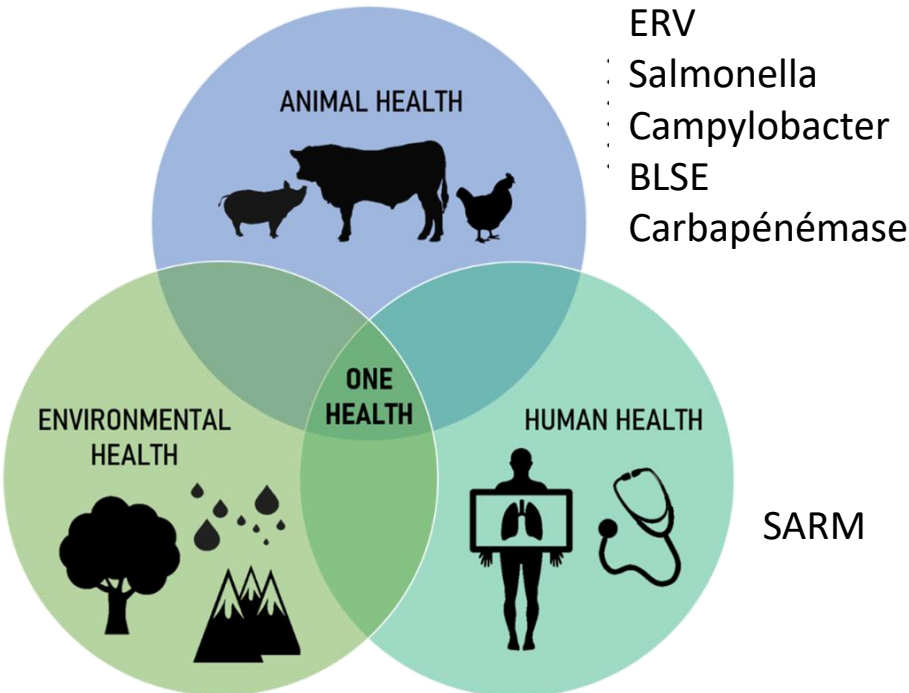
Mutant selective windows



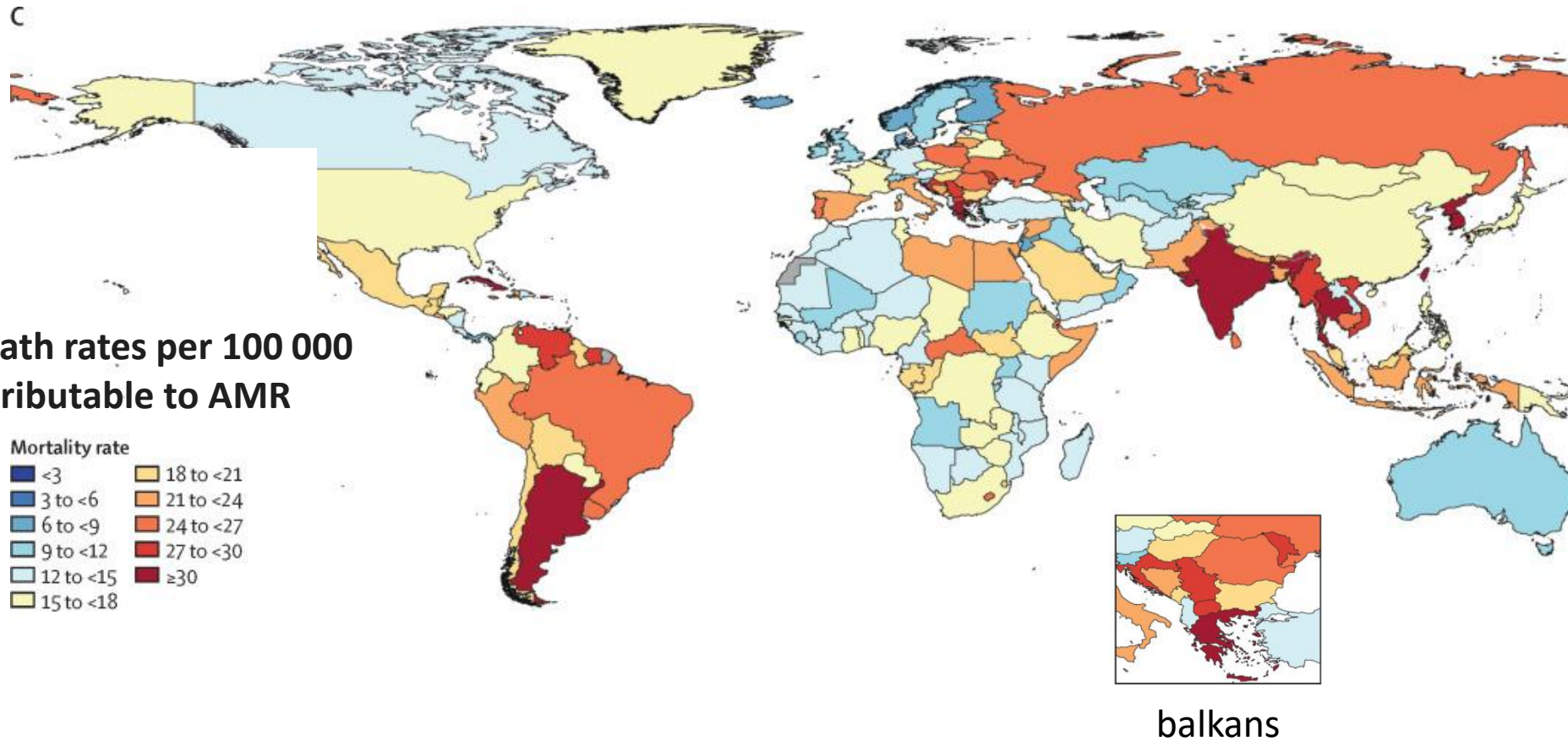
Horizontal gene transfer



# Déterminants de l'antibiorésistance



# 92 millions de morts évitables d'ici 2050



## Critical group



Enterobacterales  
carbapenem-resistant



Enterobacterales  
third-generation  
cephalosporin-resistant



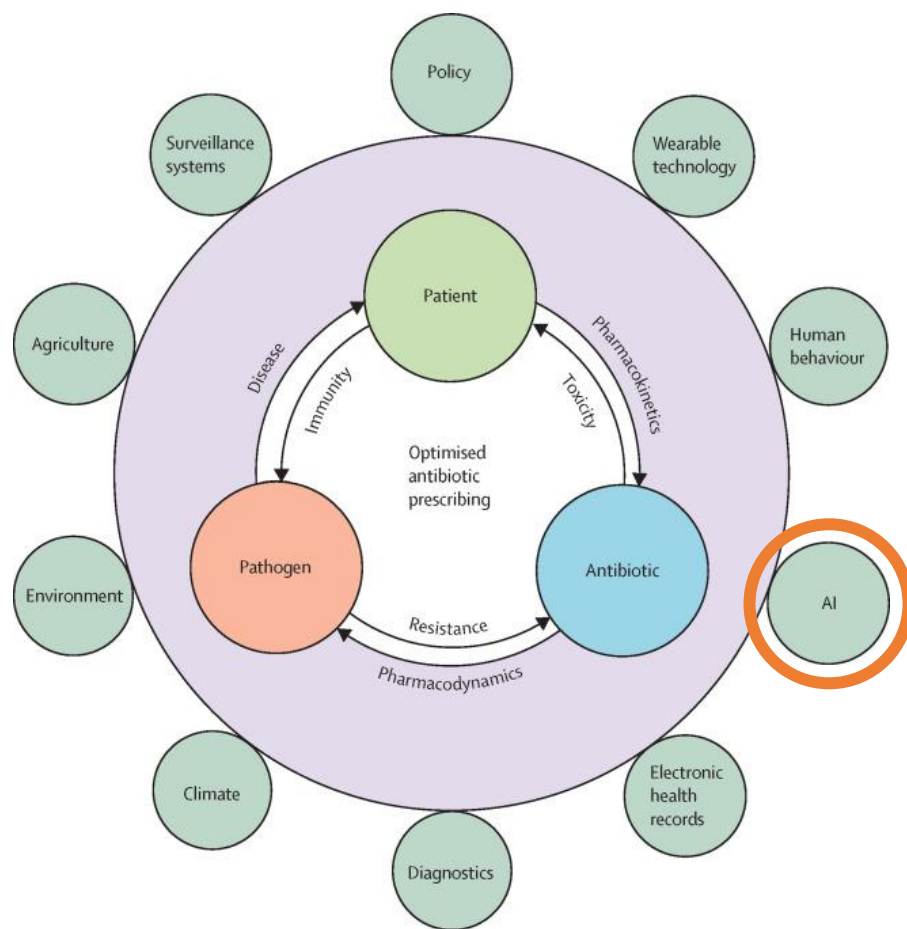
*Acinetobacter  
baumannii*  
carbapenem-resistant



*Mycobacterium  
tuberculosis*,  
rifampicin-  
resistant<sup>a</sup>

<sup>a</sup>RR-TB was included after an independent analysis with parallel criteria and subsequent application of an adapted MCDA matrix.

# L'IA pour lutter contre l'antibiorésistance?



## Drug discovery

### Accelerating antimicrobial peptide design: Leveraging deep learning for rapid discovery

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

## 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 <sup>1</sup>, Giulia Micheli <sup>1 2</sup>, Leila Lefevre <sup>1</sup>, Cécile Guyonnet <sup>3 4</sup>, Claire Poyart <sup>3 4</sup>, Etienne Canoui <sup>1</sup>, Martin Belan <sup>1 5</sup>, Caroline Charlier <sup>1 5 6 7</sup>

## Chatbot

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

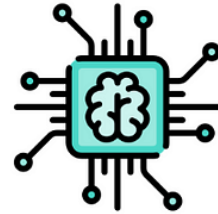
### Google AI has better bedside manner than human doctors – and makes better diagnoses

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*

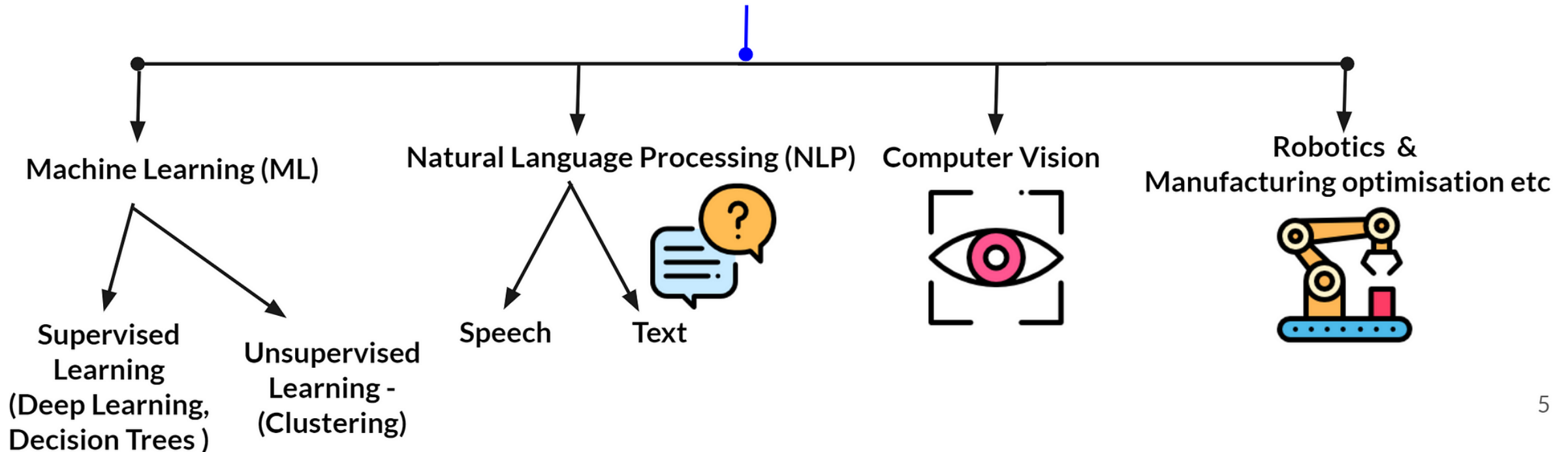
# Artificial Intelligence (AI)



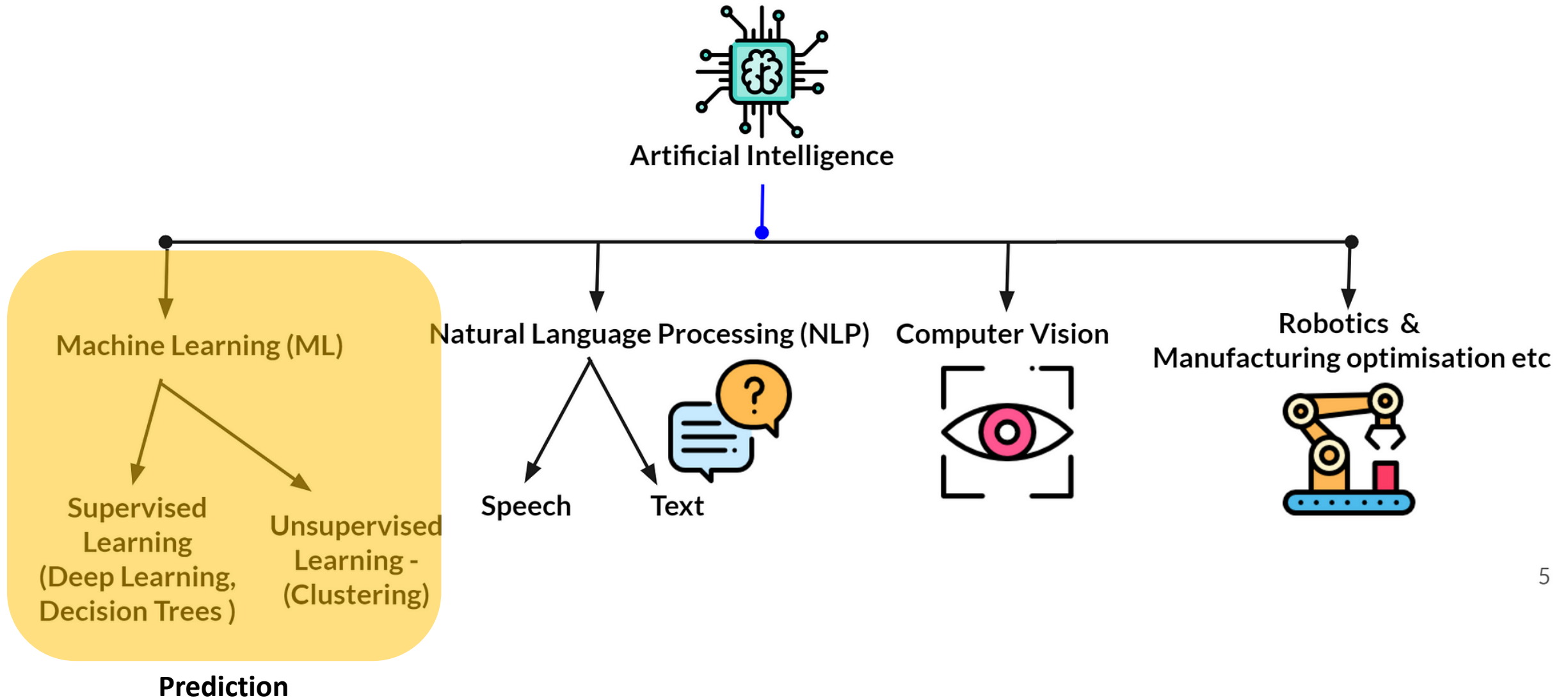
Artificial Intelligence

IA = branch of computer science that aims to create systems capable of performing tasks that typically require human intelligence »

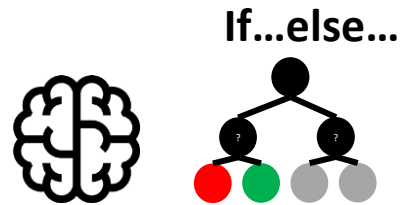
Applications : problem-solving, decision-making, perception, understanding natural language...



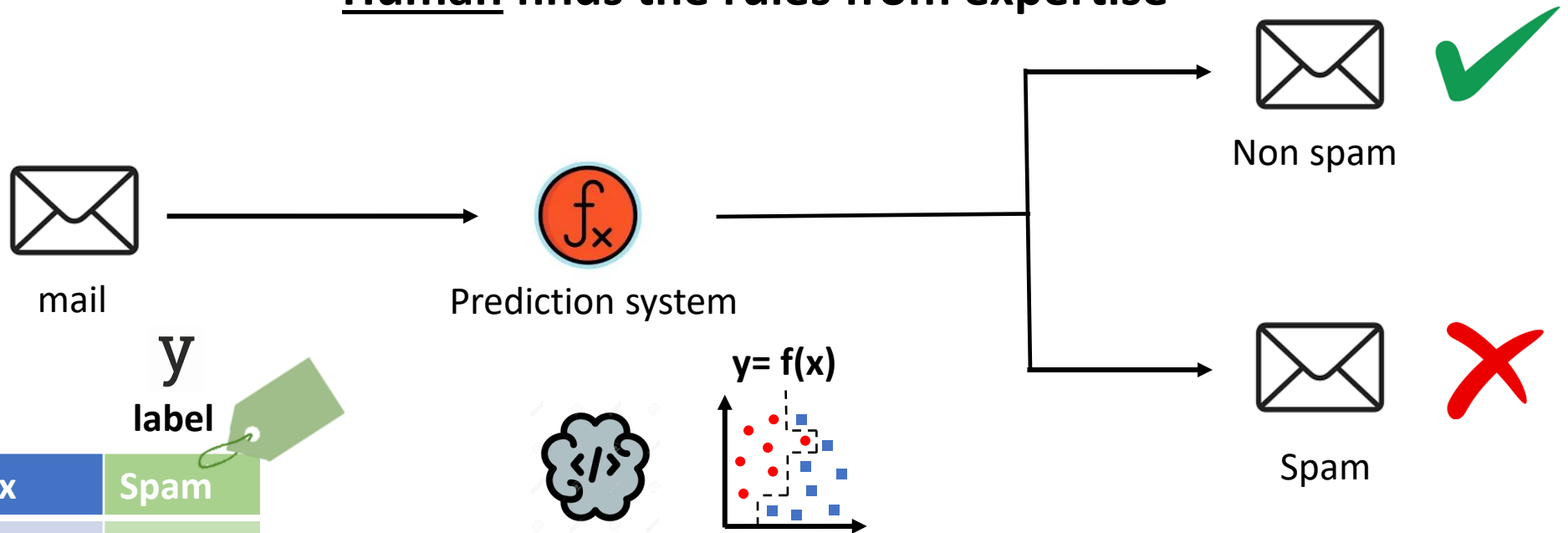
# Artificial Intelligence (AI)



# Expert system $\neq$ Machine Learning



Human finds the rules from expertise

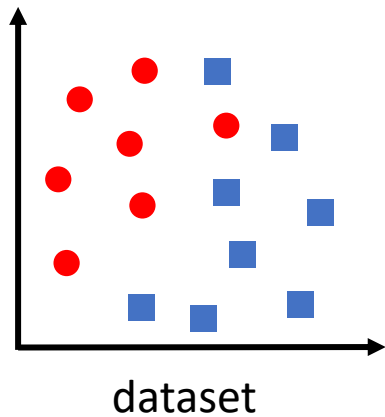



$x$ features			$y$ label
sender	ortho	sex	Spam
1	1	1	yes
0	0	0	no
1	0	1	yes

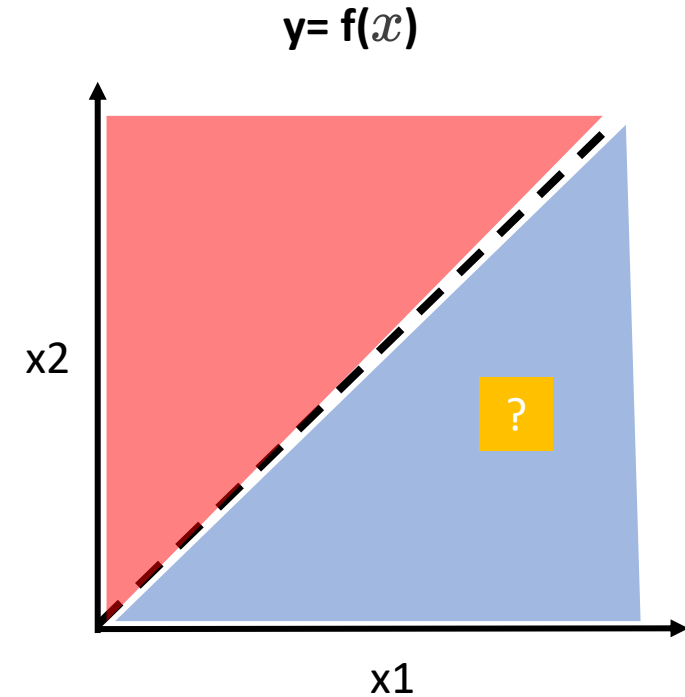
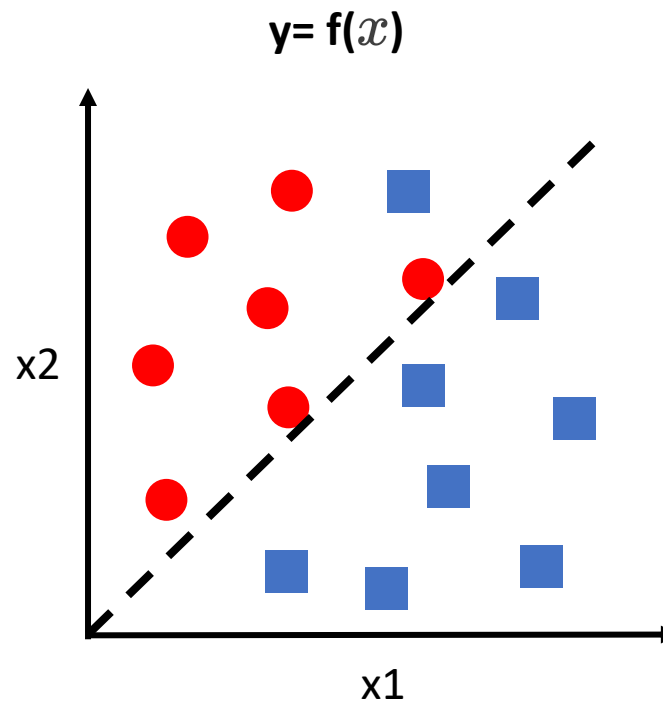
Machine Learn pattern from data

# Machine learning: Training then Testing

● ■ Catégorie: Spam, Fraudeur bancaire, Maladie...



  
ML model

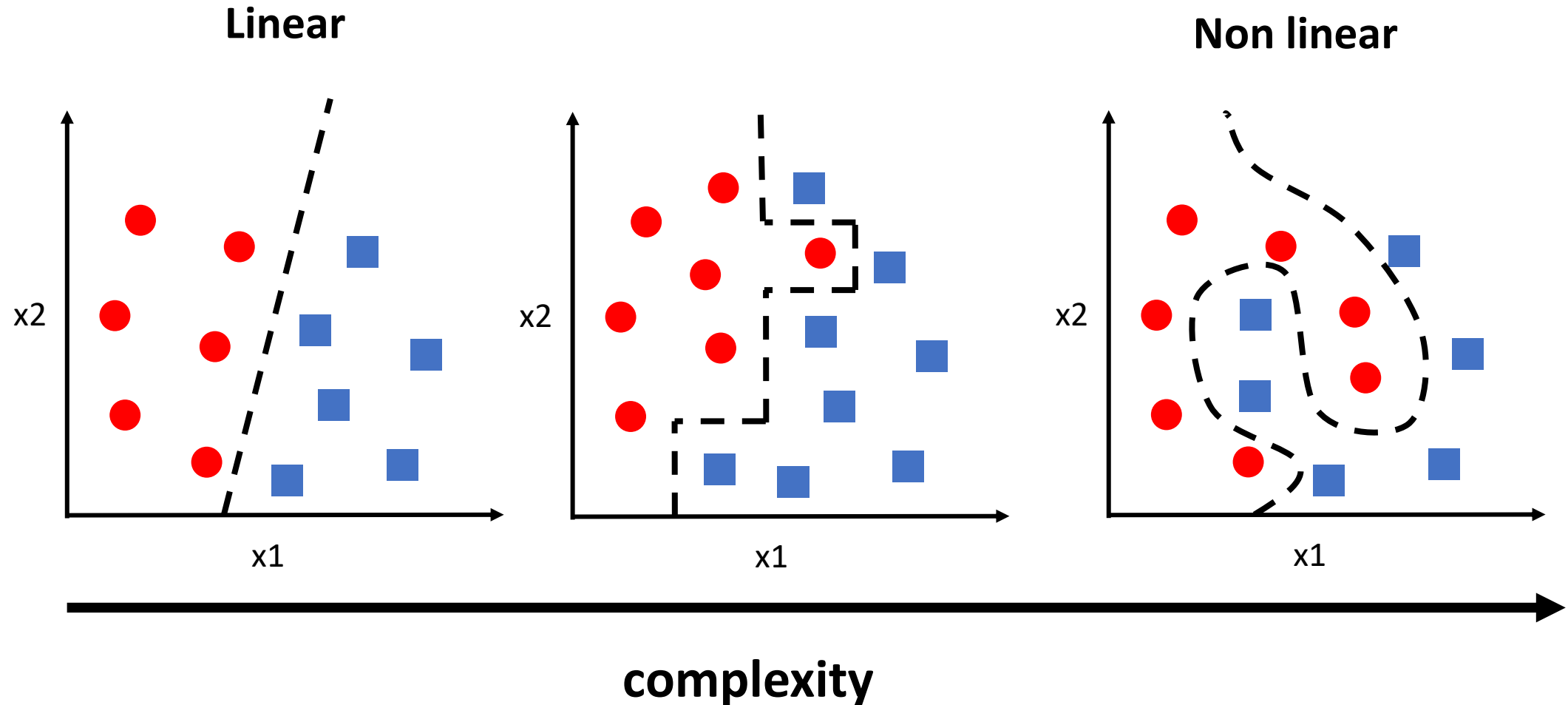


1.training

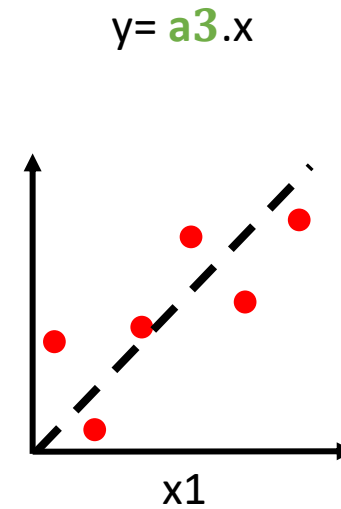
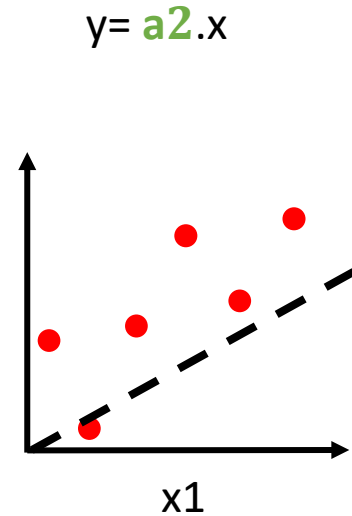
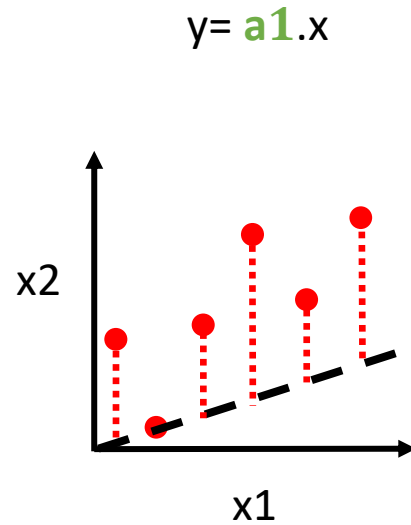


2. Testing

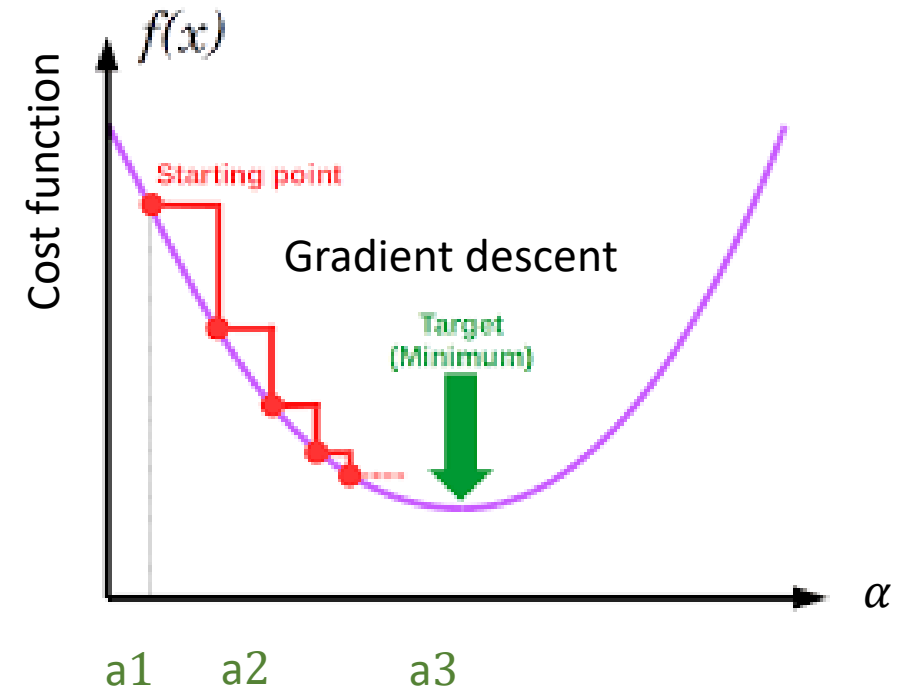
# Prediction= finding a mathematical pattern



# Machine Learning & Auto correction mechanism

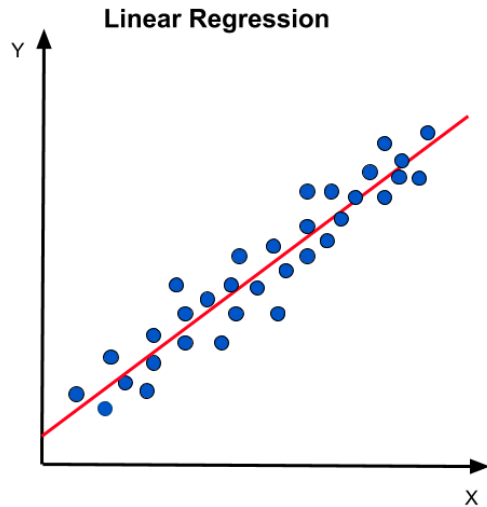
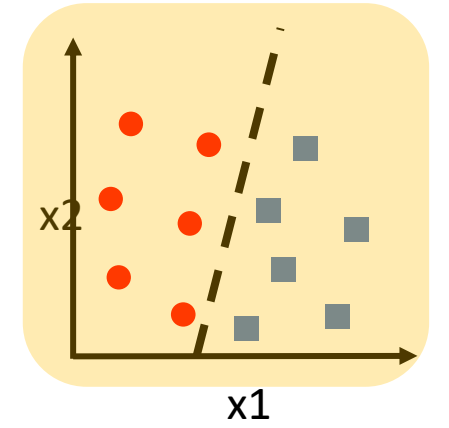


$a_3$

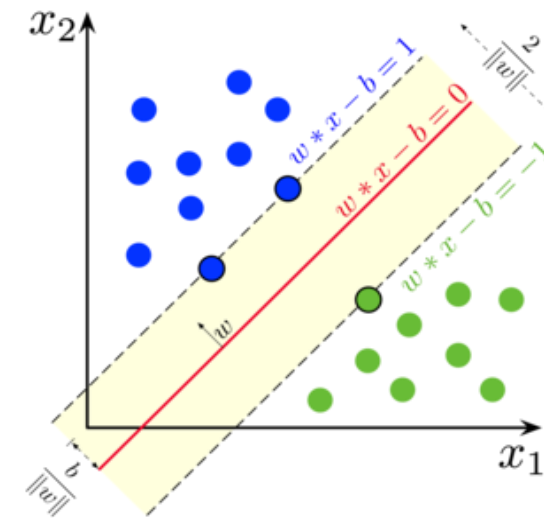


« Weights optimization »

# Traditional ML: linear algorithms

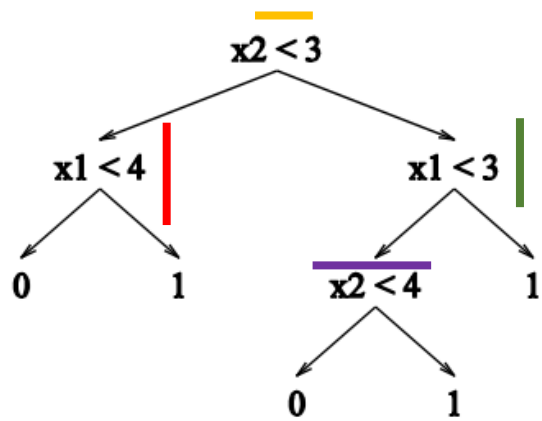


Linear/logistic regression

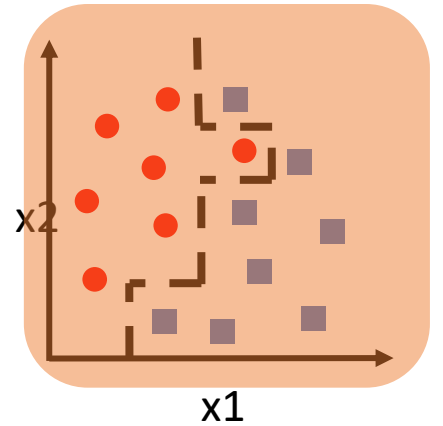
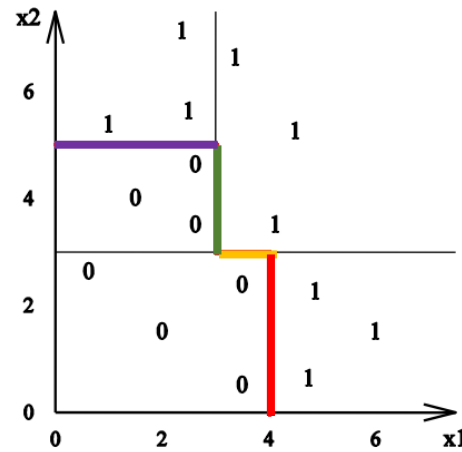


Support Vector Machine  
SVM

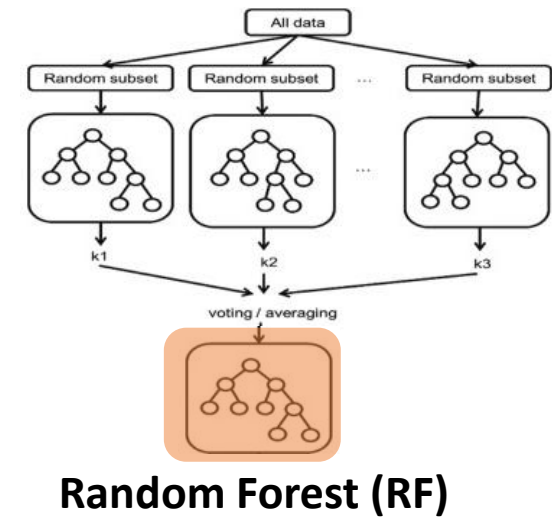
# Traditional ML: Decision Tree



Decision tree

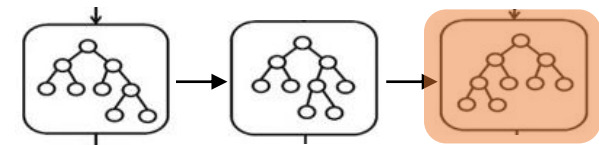


$\mu$



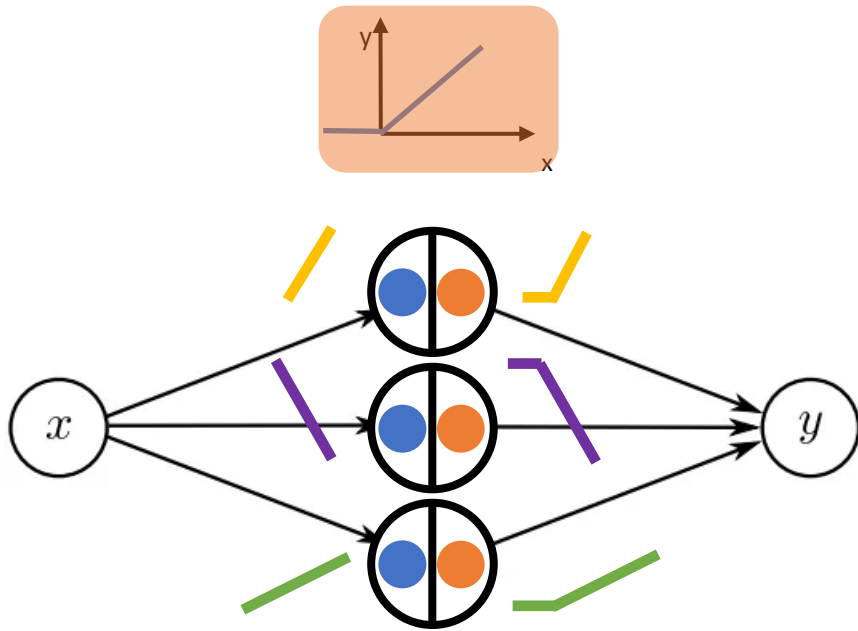
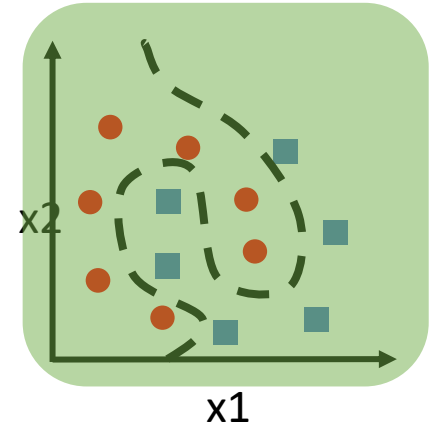
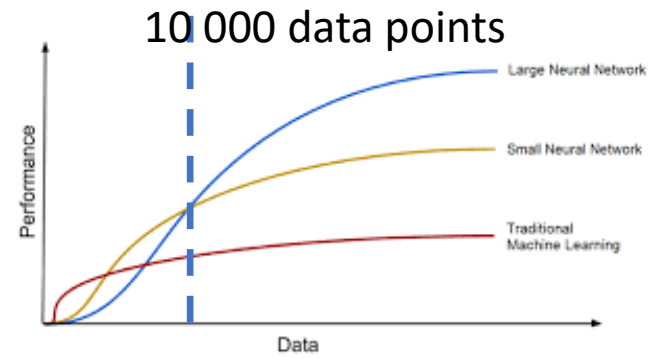
Random Forest (RF)

$\nearrow$

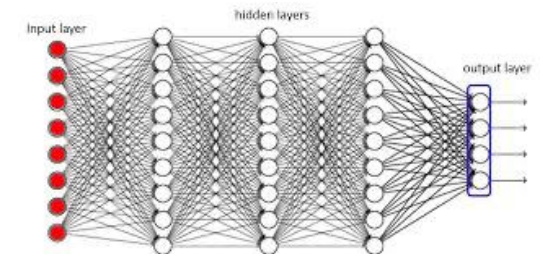
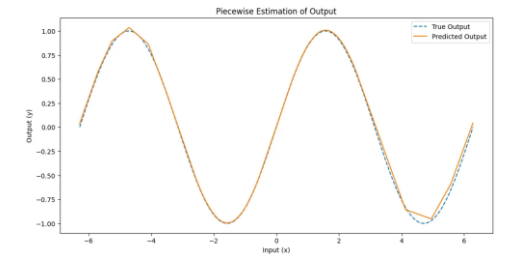
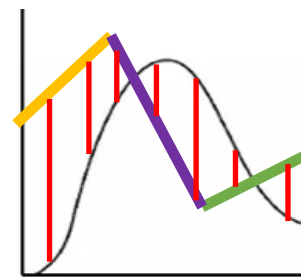


eXtrem Gradient Boosting (XGBoost)

# Deep Learning



Neural network



# Comparaison critique des modèles IA

Modèle	Avantages techniques	Limites	Applicabilité clinique
<b>XGBoost</b>	<ul style="list-style-type: none"><li>- Excellente performance en régression et classification- Gère les données manquantes-</li><li>Rapide et interprétable (feature importance)</li></ul>	<ul style="list-style-type: none"><li>- Moins performant sur des données très petites-</li><li>Peut surajuster sans régularisation</li></ul>	<ul style="list-style-type: none"><li>✓ Très adapté à la prédiction de l'AUC et de la dose initiale à partir de peu de variables</li></ul>
<b>Random Forest</b>	<ul style="list-style-type: none"><li>- Stable et robuste face au bruit-</li><li>Moins sensible à l'overfitting que XGBoost</li></ul>	<ul style="list-style-type: none"><li>- Moins précis que XGBoost dans des tâches complexes-</li><li>Moins facilement interprétable</li></ul>	<ul style="list-style-type: none"><li>✓ Bon choix pour les premières itérations de modèles cliniques</li></ul>
<b>Réseaux de neurones</b>	<ul style="list-style-type: none"><li>- Capable de modéliser des relations très complexes-</li><li>Bon sur grands jeux de données</li></ul>	<ul style="list-style-type: none"><li>- « Boîte noire » difficile à expliquer-</li><li>Risque d'overfitting important-</li><li>Long entraînement</li></ul>	<ul style="list-style-type: none"><li>⚠ Moins adapté à la pratique clinique sans système d'explication intégré</li></ul>
<b>Modèles empilés</b>	<ul style="list-style-type: none"><li>- Combine les forces de plusieurs algorithmes-</li><li>Très performants</li></ul>	<ul style="list-style-type: none"><li>- Complexes à mettre en œuvre-</li><li>Peu transparents-</li><li>Plus longs à entraîner et à valider</li></ul>	<ul style="list-style-type: none"><li>✓ Potentiel fort pour outils automatisés, mais encore difficilement utilisables au lit du patient</li></ul>

# 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

	<b>Resistant (+)</b>	<b>Sensible (-)</b>
<b>Predicton</b>		
<b>R (+)</b>	True Positive	False positive
<b>S (-)</b>	False negative	True Negative

“How reliable is a positive/negative result?”

• **PPV (Precision)**

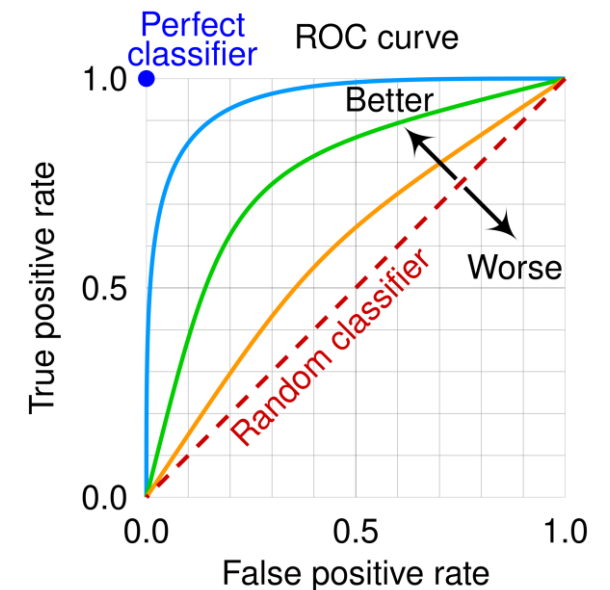
• **NPV**

• **Sensitivity(Recall):**    • **Specificity**

• **Accuracy:** “overall prediction?”

• **F1 Score (harmonic mean of precision & recall):** >0.8: good

“balance resistant cases and false alarms?”



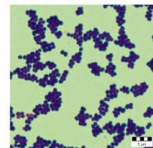
# Les modèles de machine learning ont montré une bonne performance globale :

<b>Indicateur</b>	<b>Effet moyen pondéré (IC 95%)</b>
Aire sous la courbe (AUC)	72,3 [70,4 – 74,1]
Exactitude (Accuracy)	75,0 [73,4 – 76,6]
Sensibilité	76,9 [71,9 – 81,9]
Spécificité	73,8 [67,9 – 79,7]
Valeur prédictive négative	79,9 [76,5 – 83,3]
Valeur prédictive positive	69,4 [60,2 – 78,6]

# AMR prediction: 4 examples



<1d



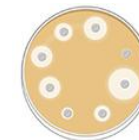
<5d



<1d

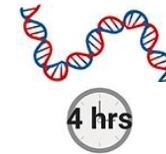


<48h

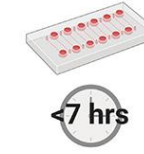


#4 AST

GeneXpert, BioFire  
Betalactatest



Vitek, phoenix



Données épidémioclinico-bio

Liquide biologique

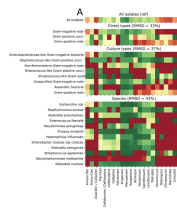
Examen direct

Cultures

Identification

Antibiogramme

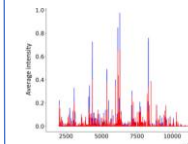
#1: Epidemio



#2 Imaging



#3 Maldi-TOF



Genomic surveillance

BK  
acinetobacter  
...

# ML article reading guidelines

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

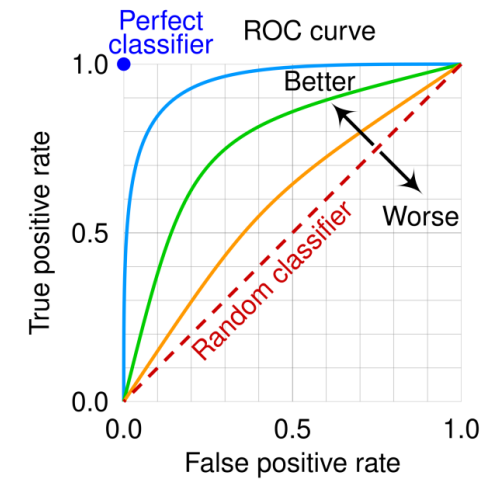
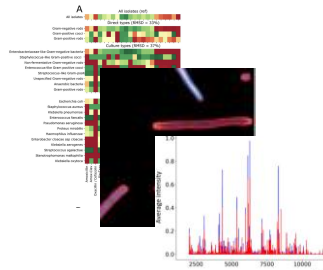
label = f(Features)



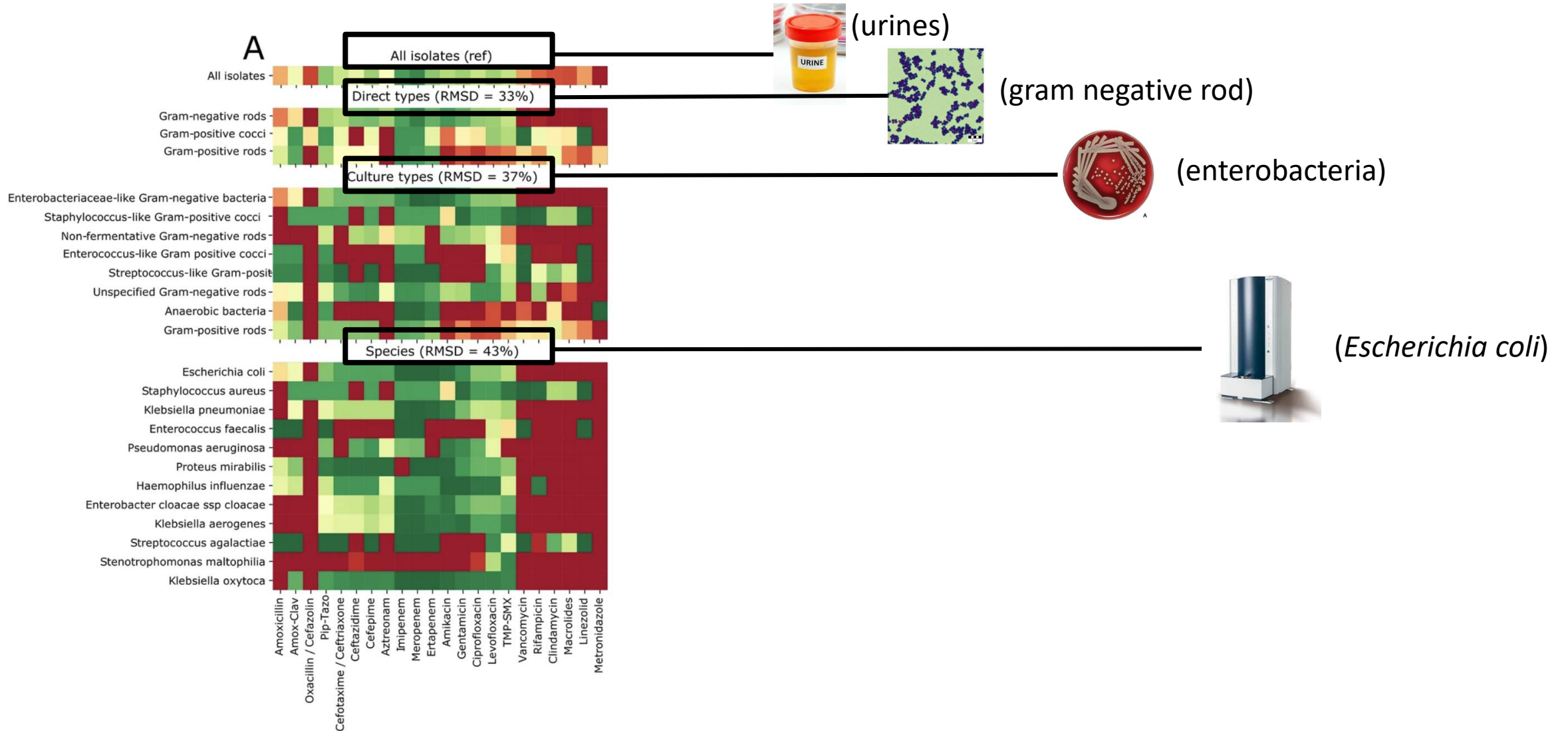
Key findings



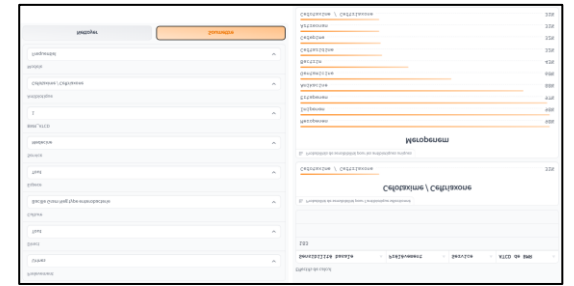
- Expert system
- ML
- deepLearning
- LLM



# Exemple #1: Epidemiological data



# #1 Objective & Methods

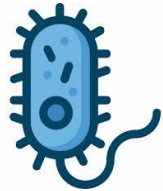


$y$

$x$

$f ( )$

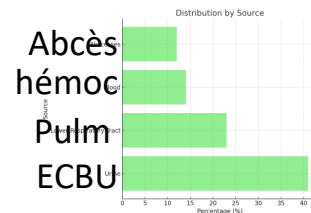
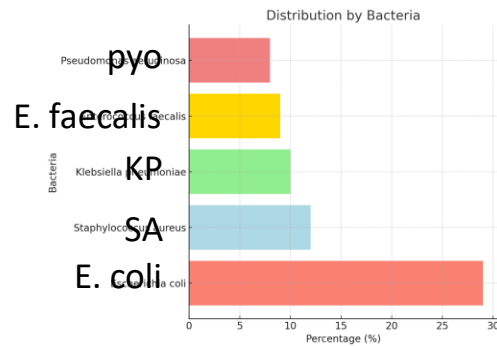
AMR prediction for:



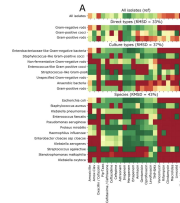
12 species



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

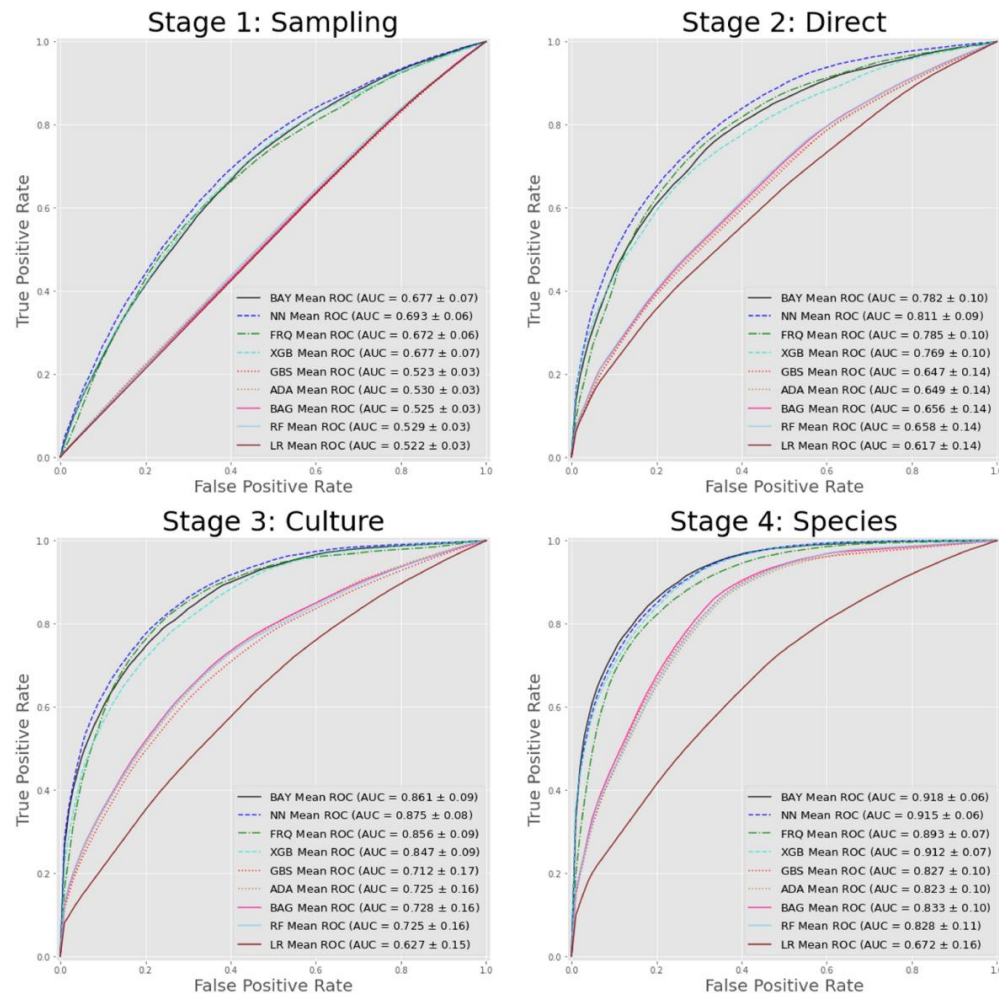
Logistic regression

Random forest  
XGBoost  
ADA, GBS

Neural network



# #1 Key findings



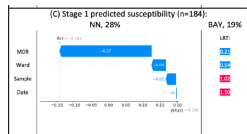
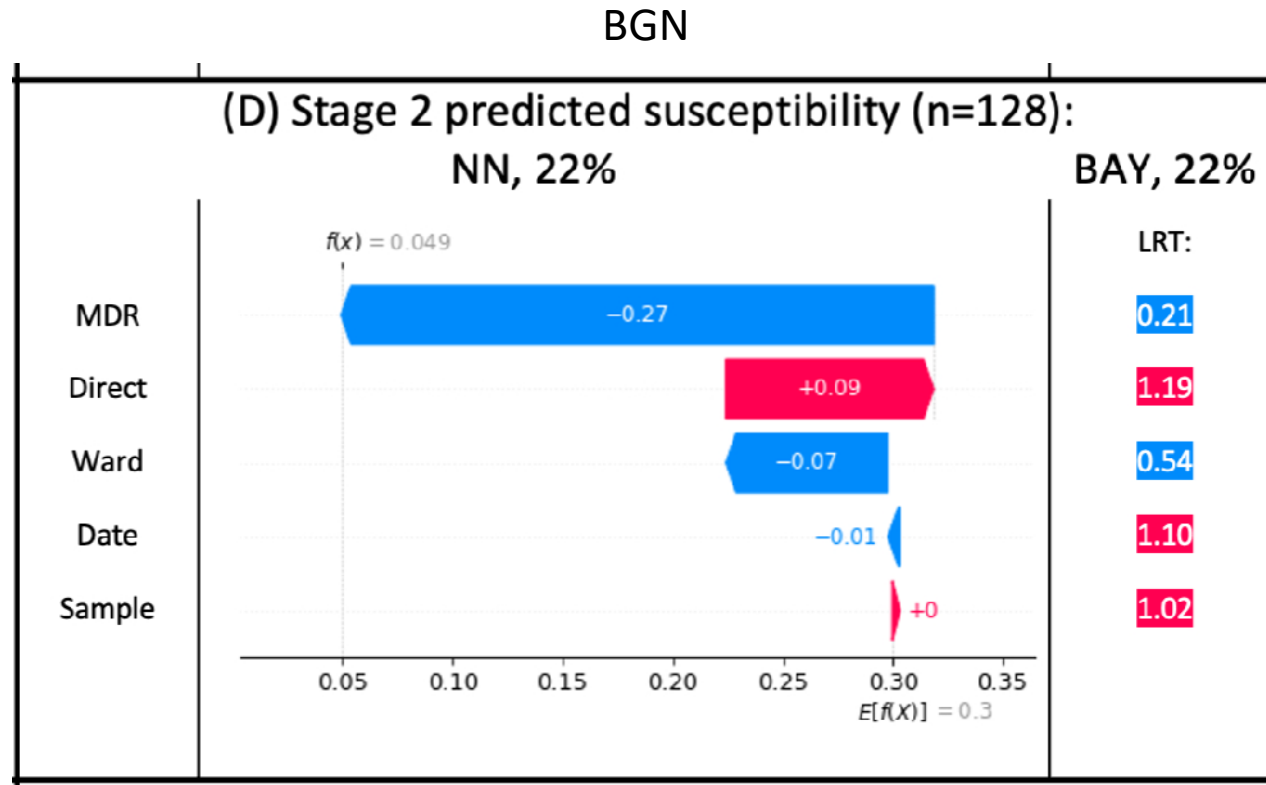
- Prediction quality improve with stage of analysis
- **Bayesian and neural net win the competition**

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

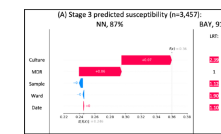


Récidive de PNA  
avec portage  
BLSE

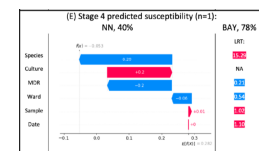


1.Sampling

2.Direct Examination

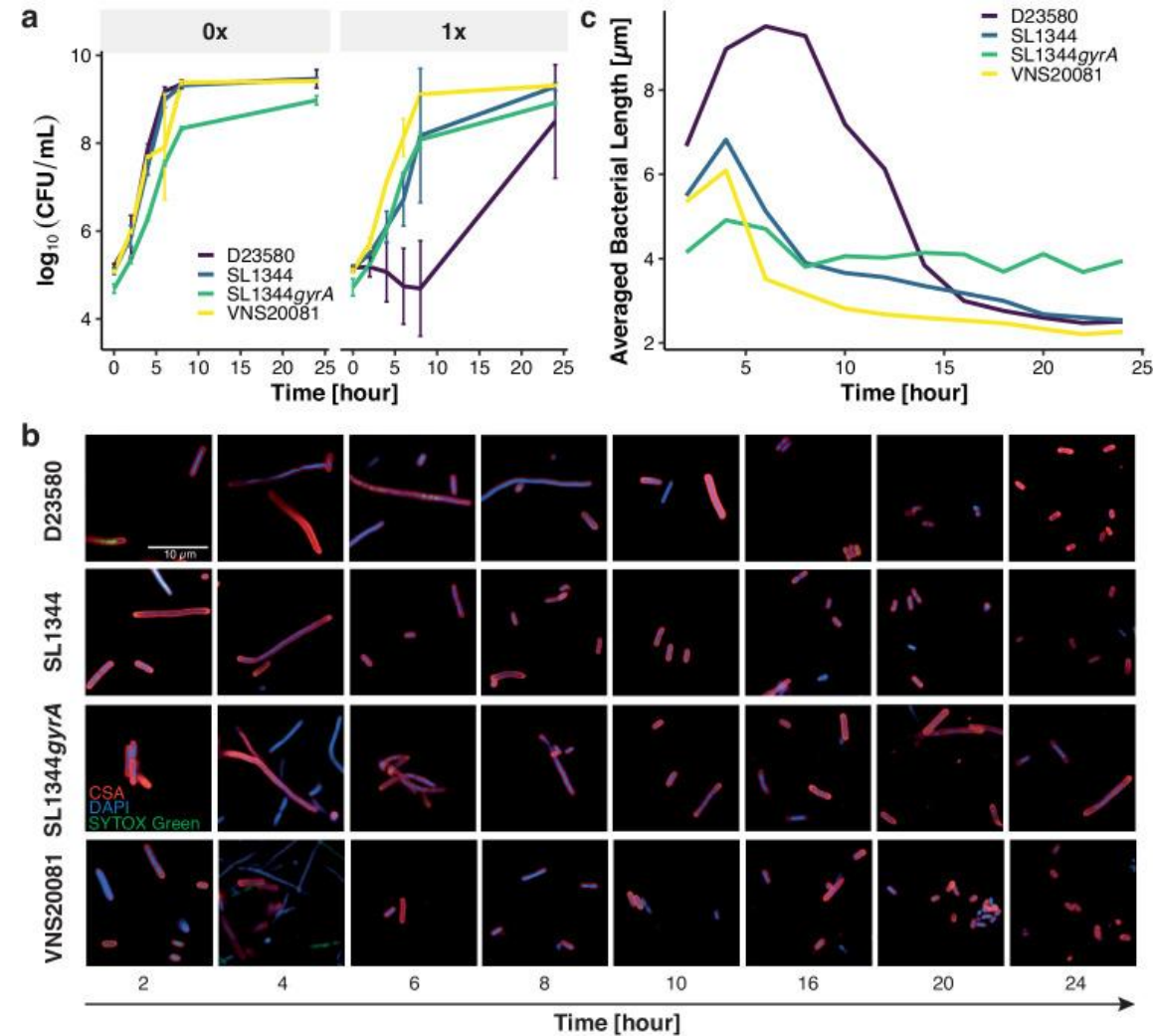


3.Cultures

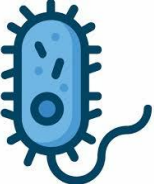




4.MALDI\_TOF

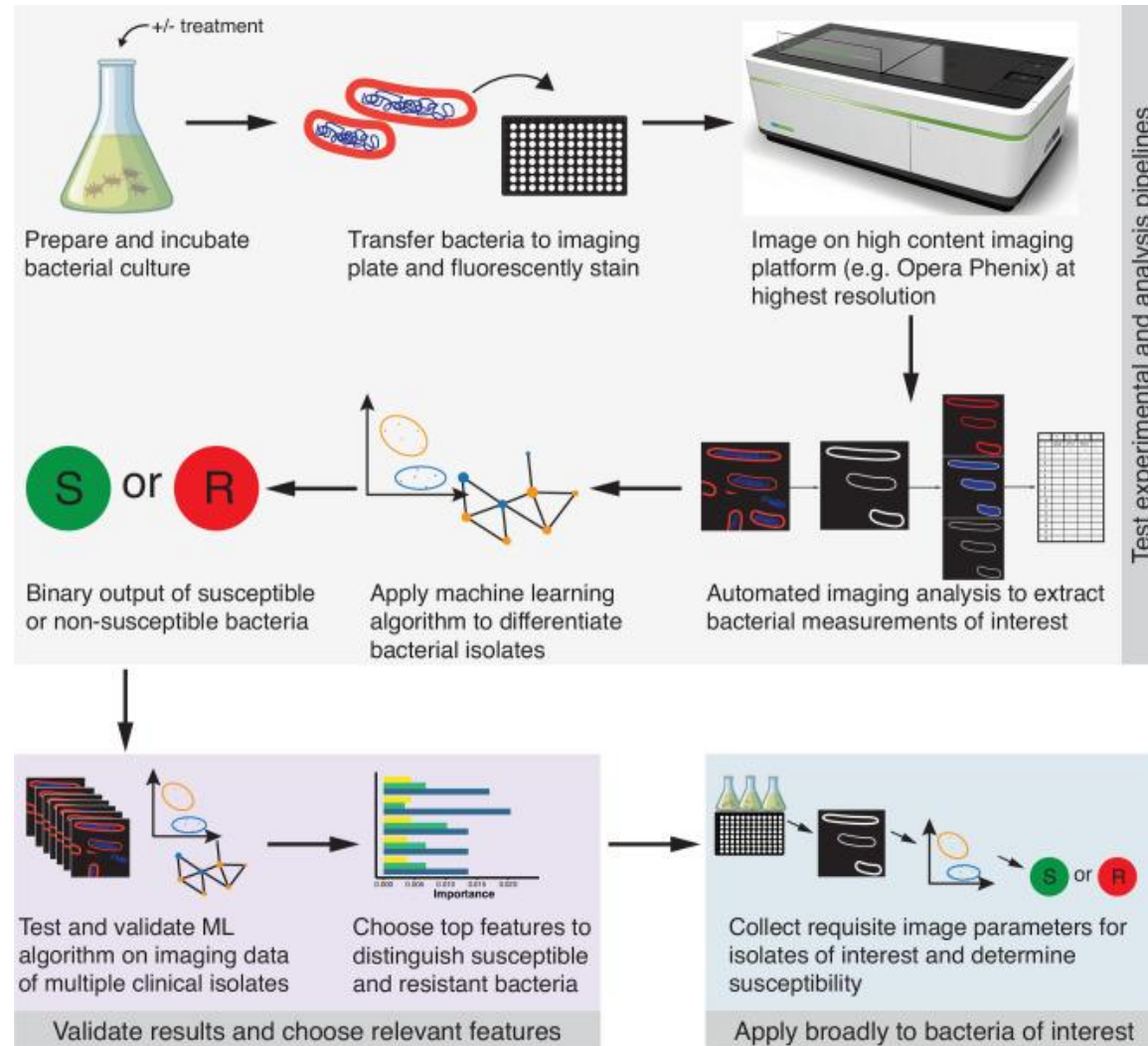
# Example #2: Imaging data



# #2: Objective & Methods

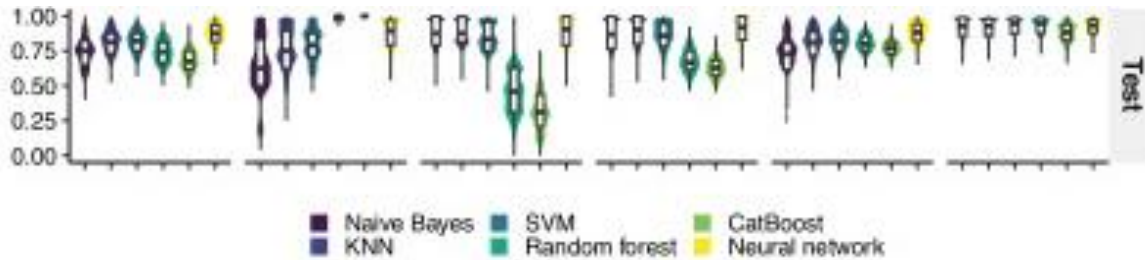
$y$	$x$	$f ( )$
<p>AMR prediction for:</p>  <p><i>Salmonella typhi</i></p>  <p>Ciprofloxacin</p>	<p>4 S. Typhimurium isolates 4 C° of ciprofloxacin 24h 1681 High-content imaging (HCI) :</p>  <p>65 features: morphological, intensity, and texture features for each individual bacterial cell</p>	<p>Bayes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

# #2: Workflow





# #2 Key findings



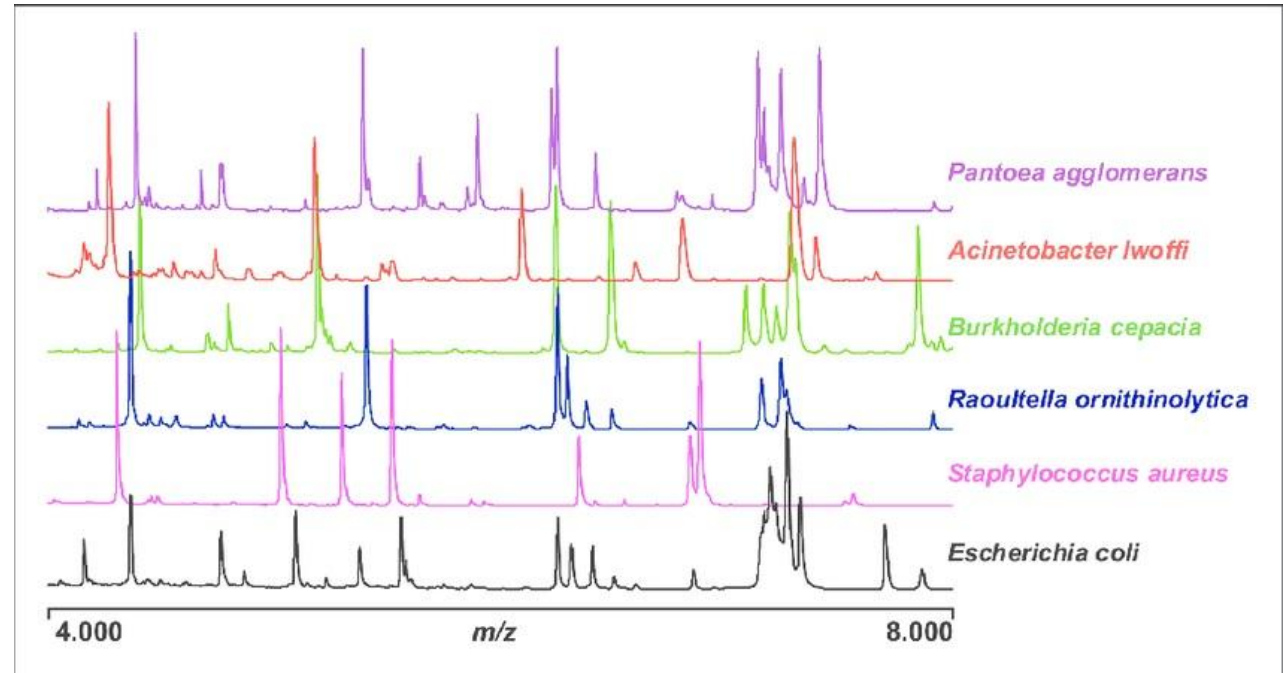
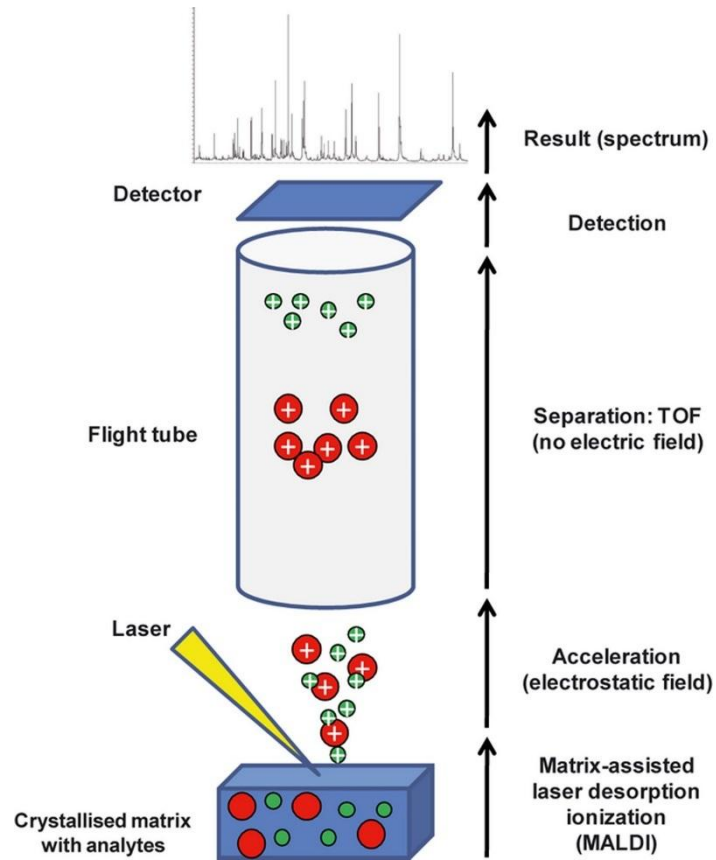
Method	Test set					
	Accuracy	Sensitivity	Specificity	Precision	F1 score	AUC
Naïve Bayes	0.74±0.13	0.63±0.24	0.87±0.15	0.85±0.15	0.69±0.20	0.91±0.10
KNN	0.81±0.11	0.74±0.20	0.88±0.11	0.88±0.12	0.78±0.15	0.91±0.08
SVM	0.81±0.09	0.78±0.14	0.84±0.12	0.85±0.11	0.81±0.11	0.92±0.09
Random forest	0.74±0.09	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**

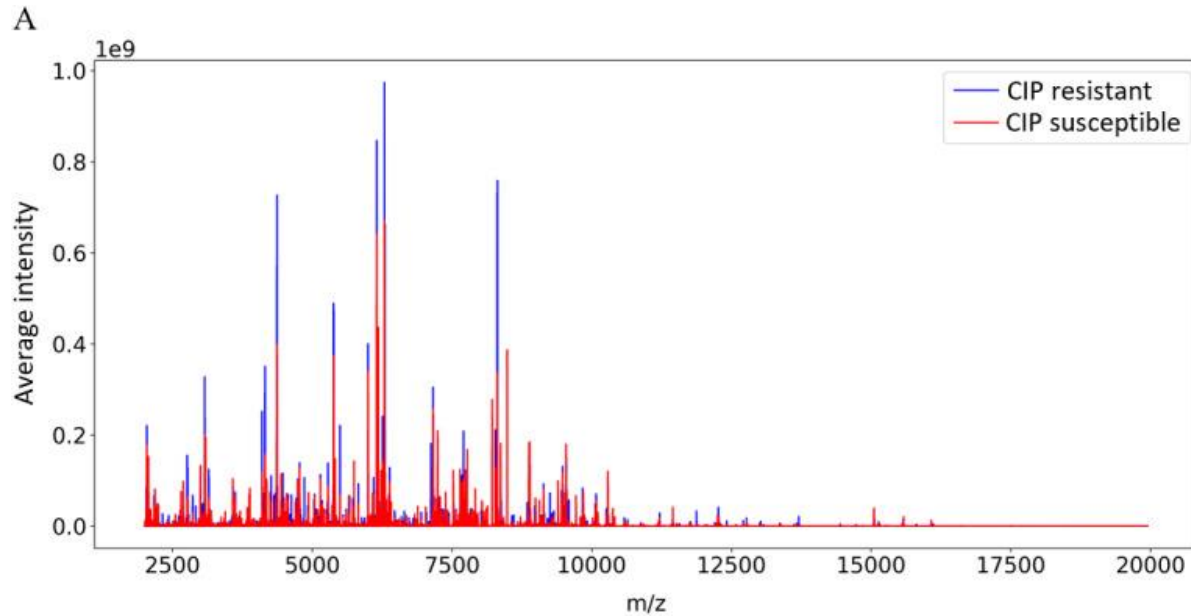
### Mécanistic hypothesis:

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

# Exemple #3: proteomic data from MALDI-TOF



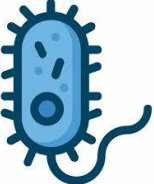

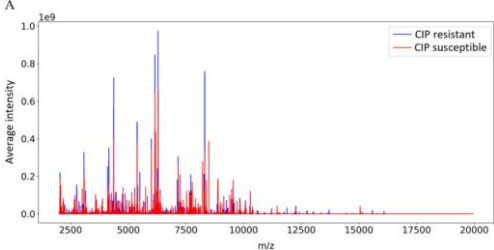
# #3 MALDI\_TOF & AMR prediction



Differential mass spectrometry profiles for CIP resistance in *Klebsiella pneumoniae*.

m/z: mass-to-charge

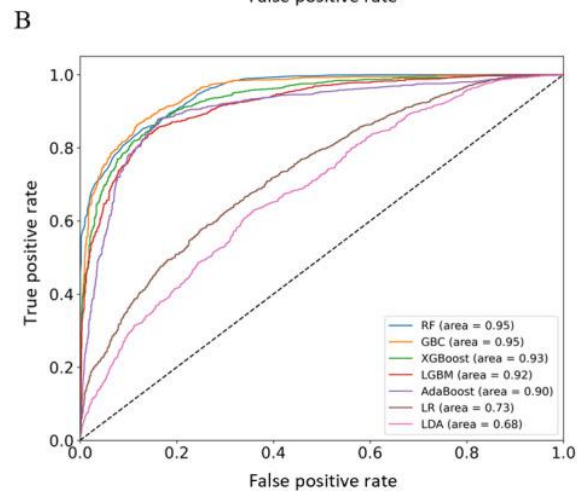
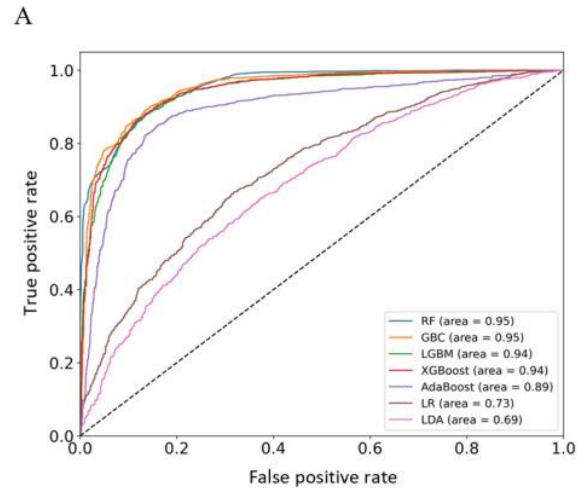
# #3 Objective and Methods

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



# #3 Key findings

## ROC curve



## Levofloxacin resistance prediction

Models	Training AUC <sup>a</sup>	Testing AUC	Accuracy	Sensitivity	Specificity	PPV <sup>b</sup>	NPV <sup>c</sup>	F <sub>1</sub> -score
RF <sup>d</sup>	0.99	0.95	0.86	0.89	0.82	0.86	0.86	0.87
GBC <sup>e</sup>	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 <sup>f</sup>	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 <sup>g</sup>	0.77	0.73	0.66	0.74	0.57	0.68	0.64	0.70
LDA <sup>h</sup>	0.72	0.68	0.64	0.81	0.43	0.63	0.65	0.71

Random Forest and XGBoost achieved the best performances

# #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.

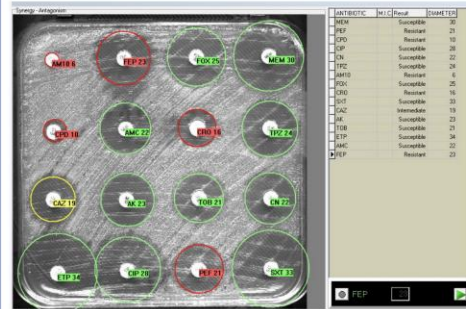
Using document from EUCAST.org  
- EUCAST breakpoint table v13.1  
- Expert rules

**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

**EUCAST GPT Expert**  
Based on the information provided for Sample 2.81 and the image analysis, here's the output for *Escherichia coli* considering the EUCAST guidelines:

**Sample 2.81 - *Escherichia coli* Resistance Mechanisms Analysis**

Resistance Mechanism	Detected (Observed)	Likelihood Analysis	Recommendation on Confirmation Tests
None	No	Unlikely	N/A
ESBL production	Yes	Very likely	Confirmatory tests recommended: double synergy test (DOST), combined disk test if or molecular tests (PCR)
AmpC production	No	Unlikely	N/A
Carbapenemase production	No	Very unlikely	N/A

**Argumentation:**

- **None:** The resistance pattern does not support the absence of resistance mechanisms as there is resistance to several antibiotics including broad spectrum cephalosporins.
- **ESBL production:** Resistance to carbapenems (CPD) and amoxicillin/clavulanic acid (AMC) while retaining susceptibility to meropenem (MEM) and ceftazidime (FOX) is indicative of ESBL production. ESBL-producing organisms typically show reduced susceptibility to cephalosporins but remain susceptible to carbapenems and colistin.
- **AmpC production:** Susceptibility to ceftazidime (FOX) indicates that AmpC production is unlikely, as organisms with AmpC typically have reduced susceptibility to ceftazidime.
- **Carbapenemase production:** The pronounced susceptibility to meropenem (MEM) suggests that carbapenemase production is very unlikely, as resistance or reduced susceptibility to carbapenems would be expected if carbapenemase enzymes were present.

**Confirmation Tests Recommendation:**  
Given the very likely presence of ESBL, confirmatory testing should be pursued. EUCAST recommends using phenotypic confirmatory tests like DOST or CD1 to confirm ESBL production, or molecular tests like PCR for specific gene detection.

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

	<b>Human experts<sup>a</sup></b>	<b>EUCAST-GPT-expert<sup>b</sup></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)
Feasibility	#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)

# Freins actuels à la mise en œuvre clinique

## Problème

Données d'entraînement peu représentatives

Manque d'explicabilité (surtout pour NN)

Intégration technique difficile

Validation prospective limitée

## Conséquences

Risque de biais (ex. patients âgés, multi-comorbidités, contextes à faibles ressources)

Difficulté pour les cliniciens de faire confiance aux recommandations

Manque d'interopérabilité avec les logiciels hospitaliers (ex. DPI, LIMS)

Données souvent issues de simulations ou de bases rétrospectives, faible validation clinique

## Solutions envisagées



Développement de jeux de données multicentriques et multiethniques

Intégration de méthodes explicatives (SHAP, LIME, arbres de décision)

Normalisation des formats, API universelles

Essais randomisés en vraie vie, validation externe systématique

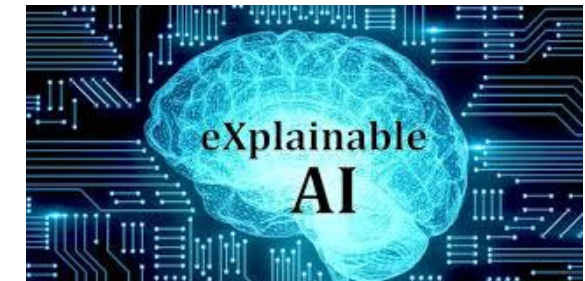
# Artificial intelligence in antimicrobial stewardship: a systematic review and meta-analysis of predictive performance and diagnostic accuracy

	
<p>2000- 2024. Observational, cohort, or retrospective studies focusing on the application of AI/ML in AMS.</p> <p>3,458 retrieved articles 80 studies met the inclusion criteria.</p>	<ul style="list-style-type: none"><li>• AUC [ES: 72.28 (70.42-74.14)]</li><li>• accuracy [ES: 74.97 (73.35-76.58)]</li><li>• sensitivity [ES: 76.89; (71.90-81.89)]</li><li>• specificity [ES: 73.77; (67.87-79.67)]</li><li>• NPV [ES:79.92 (76.54-83.31)]</li><li>• PPV [ES: 69.41 (60.19-78.63)]</li></ul> <p>ES: mean pooled effect size (ES)</p>

# Conclusion:

## L'IA peut elle prédire l'antibiorésistance?

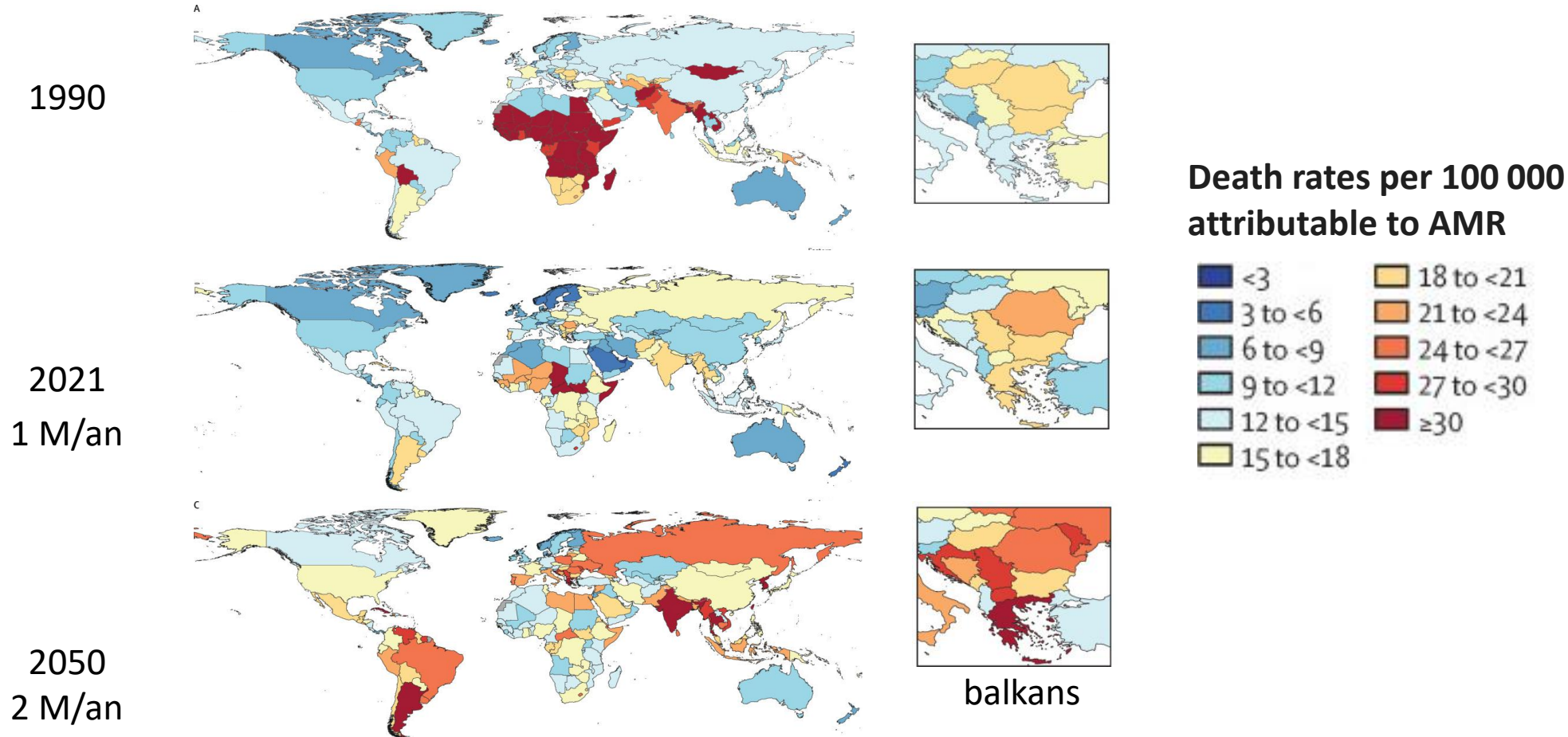
- L'IA peut tout prédire .... si accès à big data
- Pertinence?
  - Santé animale > humaine | Ville & Hôpital | aide à prescription > aide à prédiction
  - Timing % prescription d'antibiotique?
    - +++ si épargne prescription antibiotique
    - ++ si épargne large spectre
    - + si gain 24 heures 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



## Critical group



Enterobacteriales  
carbapenem-resistant



Enterobacteriales  
third-generation  
cephalosporin-resistant



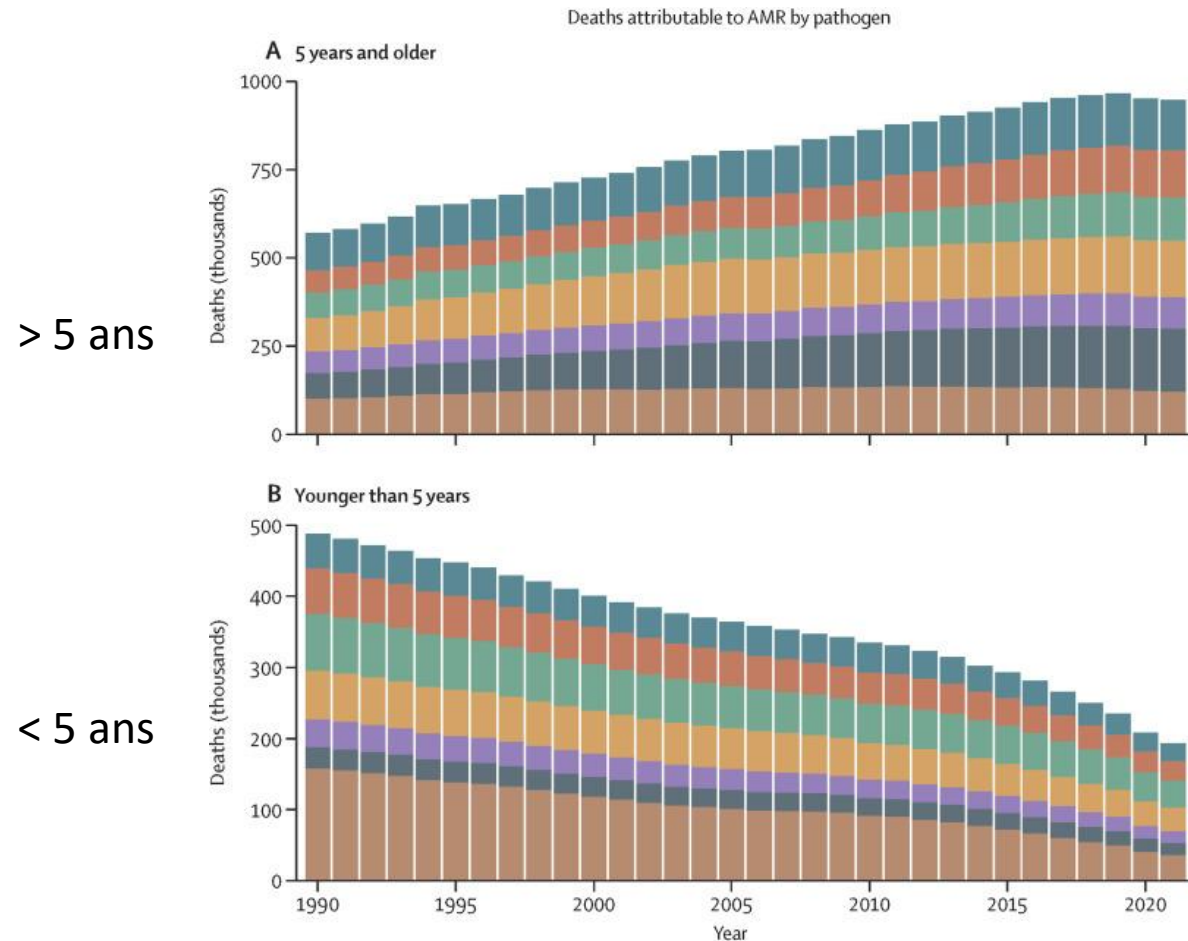
*Acinetobacter  
baumannii*  
carbapenem-resistant



*Mycobacterium  
tuberculosis*,  
rifampicin-  
resistant<sup>a</sup>

<sup>a</sup>RR-TB was included after an independent analysis with parallel criteria and subsequent application of an adapted MCDA matrix.

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



> 5 ans

< 5 ans

## Pathogen

*Acinetobacter baumannii*

*Escherichia coli*

*Klebsiella pneumoniae*

Other AMR bacteria

*Pseudomonas aeruginosa*

*Staphylococcus aureus*

*Streptococcus pneumoniae*

## Critical group



Enterobacterales  
carbapenem-resistant



Enterobacterales  
third-generation  
cephalosporin-resistant



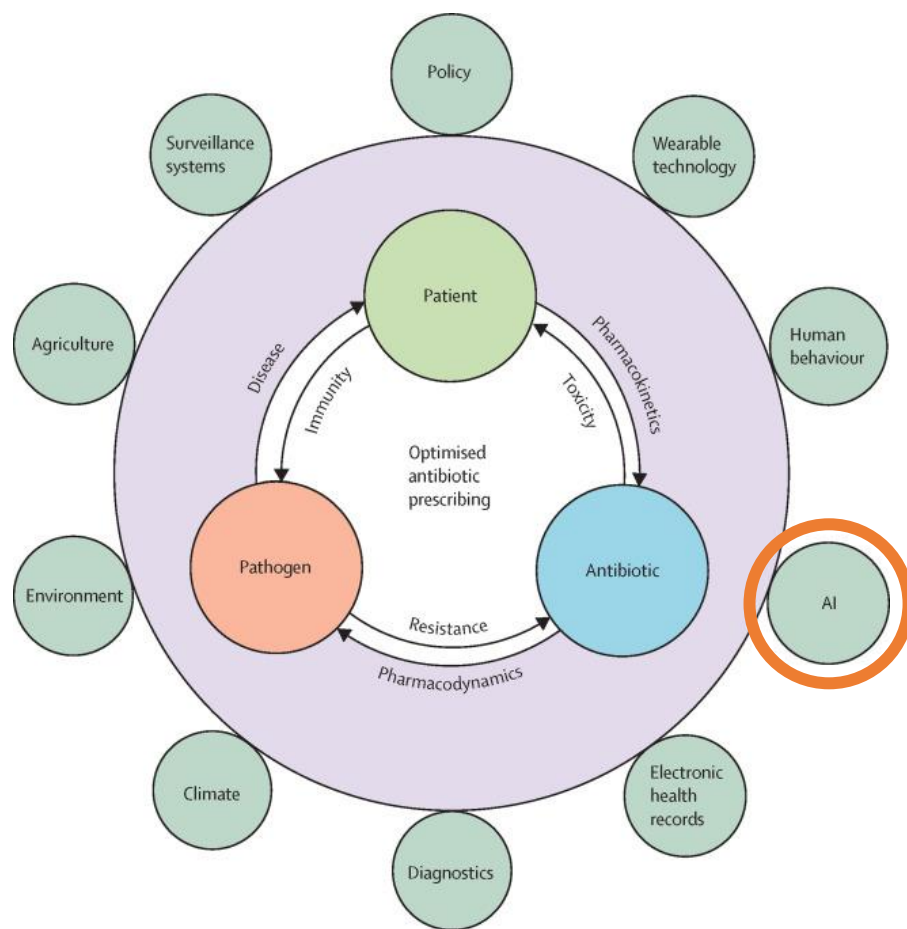
*Acinetobacter  
baumannii*  
carbapenem-resistant



*Mycobacterium  
tuberculosis*,  
rifampicin-  
resistant\*

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

# L'IA pour lutter contre l'antibiorésistance?



## Drug discovery

### Accelerating antimicrobial peptide design: Leveraging deep learning for rapid discovery

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

## 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 <sup>1</sup>, Giulia Micheli <sup>1 2</sup>, Leila Lefevre <sup>1</sup>, Cécile Guyonnet <sup>3 4</sup>, Claire Poyart <sup>3 4</sup>, Etienne Canoui <sup>1</sup>, Martin Belan <sup>1 5</sup>, Caroline Charlier <sup>1 5 6 7</sup>

## Chatbot

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

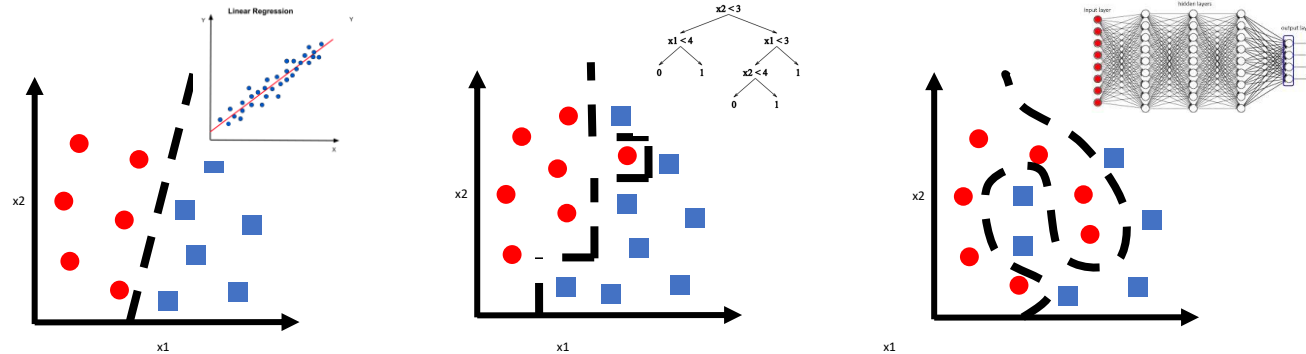
### Google AI has better bedside manner than human doctors – and makes better diagnoses

Mariana Lenharo

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

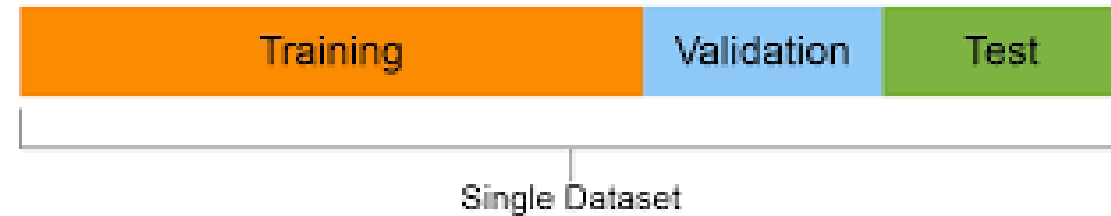
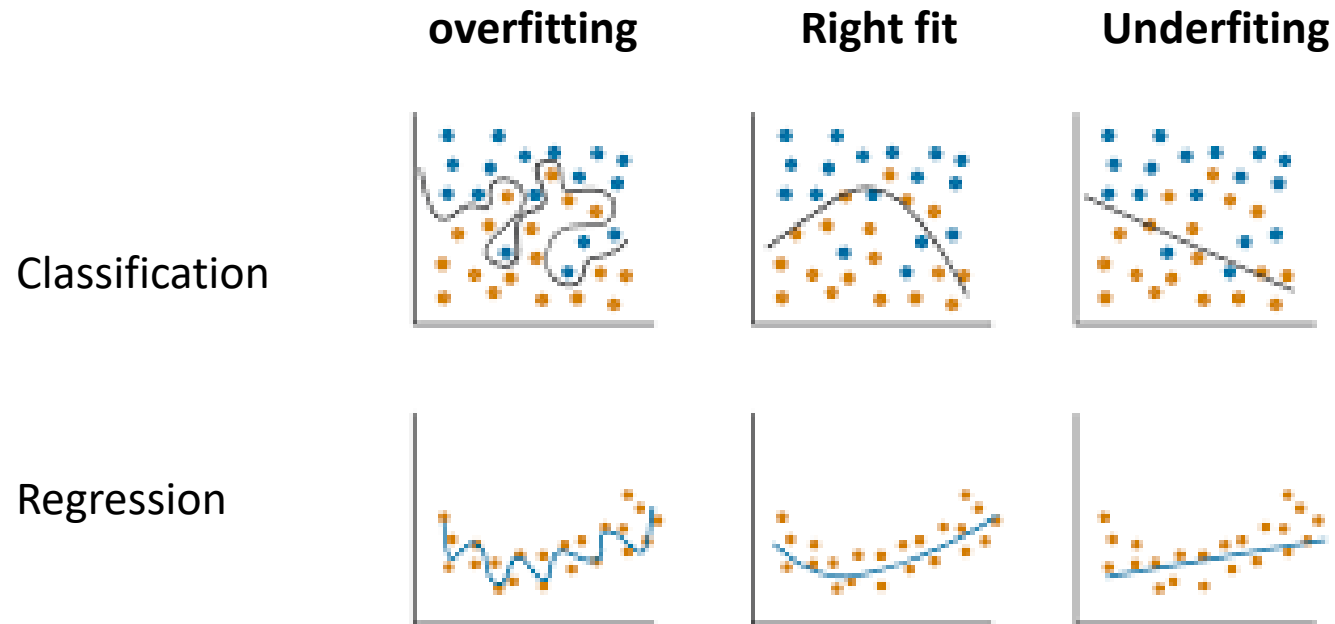
*Using digital health technologies to optimise antimicrobial use globally. The lancet digital health 2024*

# Different ML flavours



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

# Overfitting concept



# #1 Pros & Cons



	✓	✗
Quality	Data curation steps	Demographics, ATCD & history of antibiotic ttt
Feasibility	Simple (historical laboratory data)	Bayesian model update difficult
Explainability	Yes	
Relevance	Stages of prediction Multi pathogens/antibio	

## #2 Pros & Cons



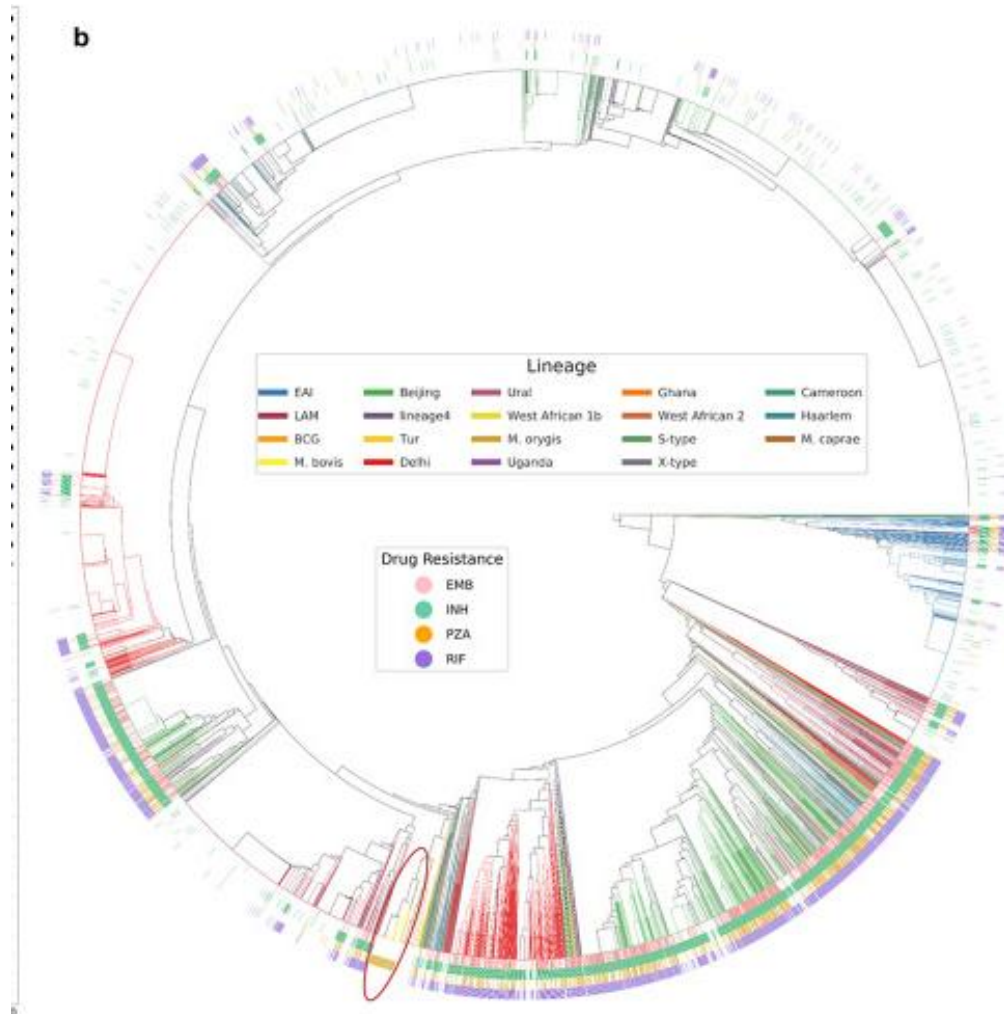
	✓	✗
Quality		
Feasibility		Complex and expensive
Explainability	'white-box' machine learning classifiers	
Relevance	No need for antibiotic exposure Earlier than rapid AST	Salmonella typhi only Extrapolation to other BGN?

# #3 Pros & Cons



	✓	✗
Quality		No Deep learning No clinical or epidemio data
Feasibility	++	
Explainability		no
Relevance	1-2 days gain of AMR prediction compare to traditional AST	Limited to KP, CIP and LEV

# Example # 4: genomic data



Visualization of isolate identification from detected genetic information, lineage and DST.

# #4: Objective & Methods



objective

Tuberculosis drug resistance from genome sequence data using traditional machine learning algorithms and CNN



data



10,575 MTB isolates from sequence read archive database : WGS

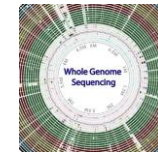
282 features selected

rpoB.S450L

katG.T463L

...

phenotypic drug susceptibility test (DST) data from CRyPTIC Consortium and the 100,000 Genomes project in an excel file



Random Forest  
Logistic regression  
CNN  
MyKrobe



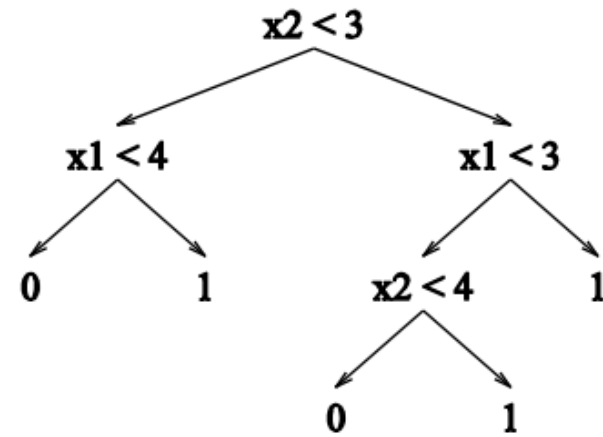
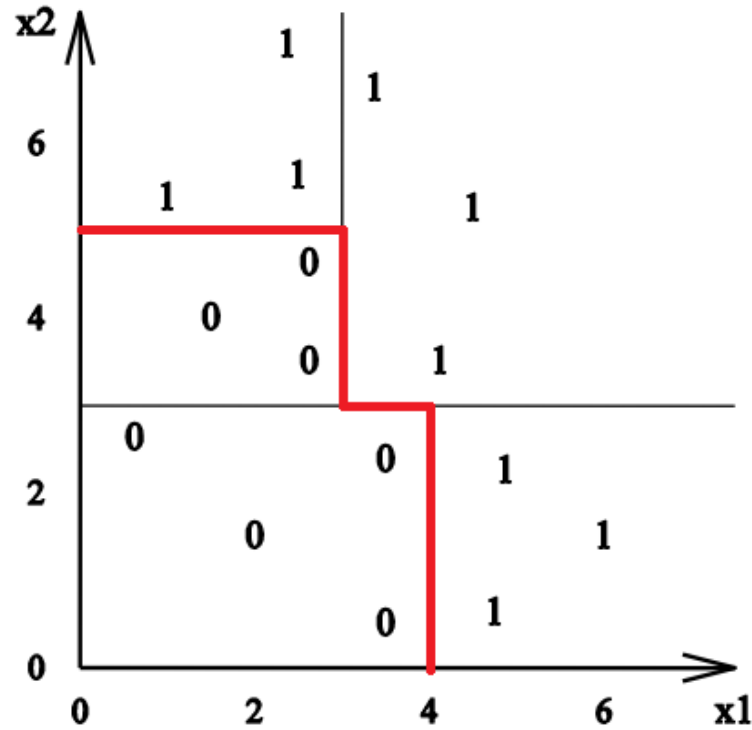
# #4 Key findings, implication & limits

Methods	Precision (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	F1 (%)	G-mean (%)
<b>First-line</b>						
<b>INH</b>						
RF	95.2	98.7	91.7	96.1	97.0	95.1
LR	94.3	99.2	90.0	95.7	96.7	94.5
CNN	95.5	99.0	90.5	96.2	97.2	94.7
Mykrobe	92.9	99.2	95.3	96.2	95.9	97.2
<b>PZA</b>						
RF	92.3	96.4	53.6	90.1	94.3	71.9
LR	93.0	95.5	58.0	90.0	94.2	74.4
CNN	93.2	96.5	56.1	90.5	94.8	73.6
Mykrobe	91.1	95.1	60.9	87.3	93.1	76.1
<b>RIF</b>						
RF	94.3	97.0	88.6	94.1	95.6	92.7
LR	93.5	98.3	86.6	94.3	95.8	92.3
CNN	94.4	98.1	87.5	94.6	96.2	92.7
Mykrobe	92.4	95.0	92.3	92.5	93.7	93.6
<b>EMB</b>						
RF	92.9	94.4	70.8	89.7	93.6	81.8
LR	93.1	93.4	72.1	89.2	93.3	82.1
CNN	93.1	94.5	71.7	90.0	93.8	82.3
Mykrobe	92.2	72.4	85.3	76.3	81.1	78.6

- Deep learning (CNN) first> expert system (Mykrobe)
- No ROC AUC
- Limited to TB resistance surveillance>clinical practice

trash

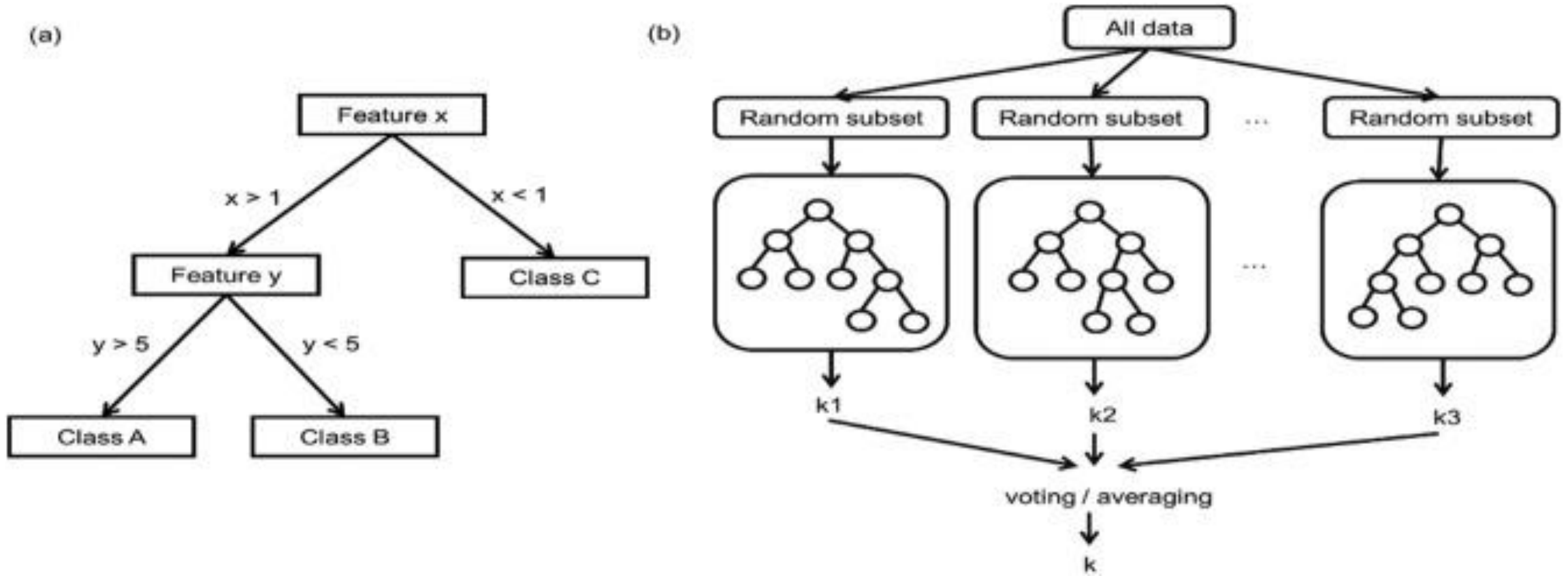
# Random forest space splitting



$$\begin{aligned}
 obj^{(t)} &= \sum_{i=1}^n l(y_i, \hat{y}_i^{(t)}) + \sum_{i=1}^t \Omega(f_i) \\
 &= \sum_{i=1}^n l(y_i, \hat{y}_i^{(t-1)} + f_t(x_i)) + \Omega(f_t) + \text{constant}
 \end{aligned}$$

$$\begin{aligned}
 obj^{(t)} &= \sum_{i=1}^n (y_i - (\hat{y}_i^{(t-1)} + f_t(x_i)))^2 + \sum_{i=1}^t \Omega(f_i) \\
 &= \sum_{i=1}^n [2(\hat{y}_i^{(t-1)} - y_i)f_t(x_i) + f_t(x_i)^2] + \Omega(f_t) + \text{constant}
 \end{aligned}$$

# Random forest



(A) A simple [decision tree](#) model that divides a dataset into three classes based on two features. (B) Schematic diagram of random forest algorithm.

# Support Vector Machine

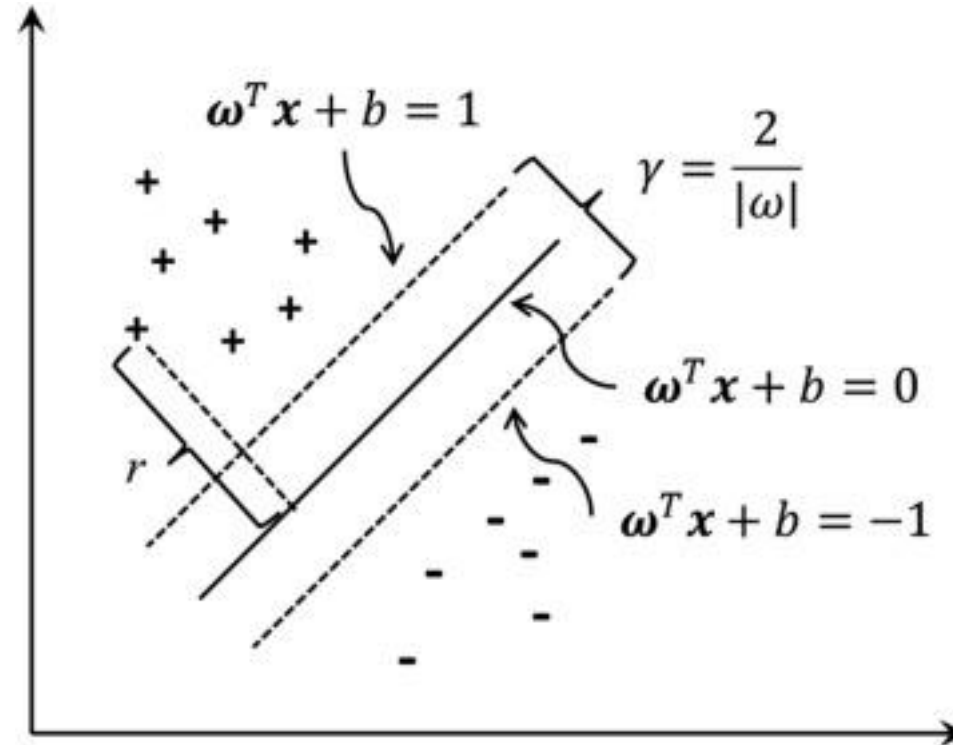
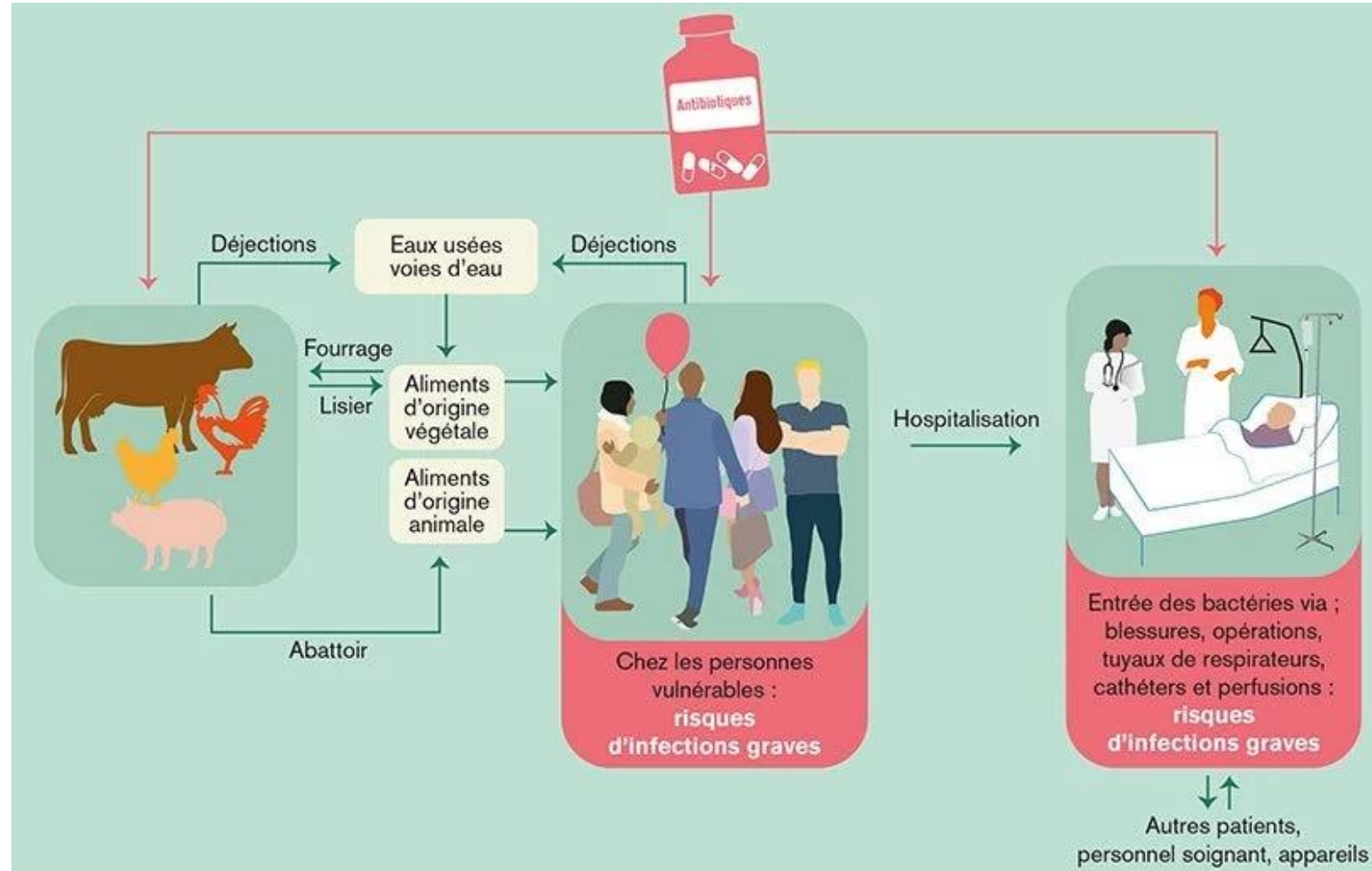
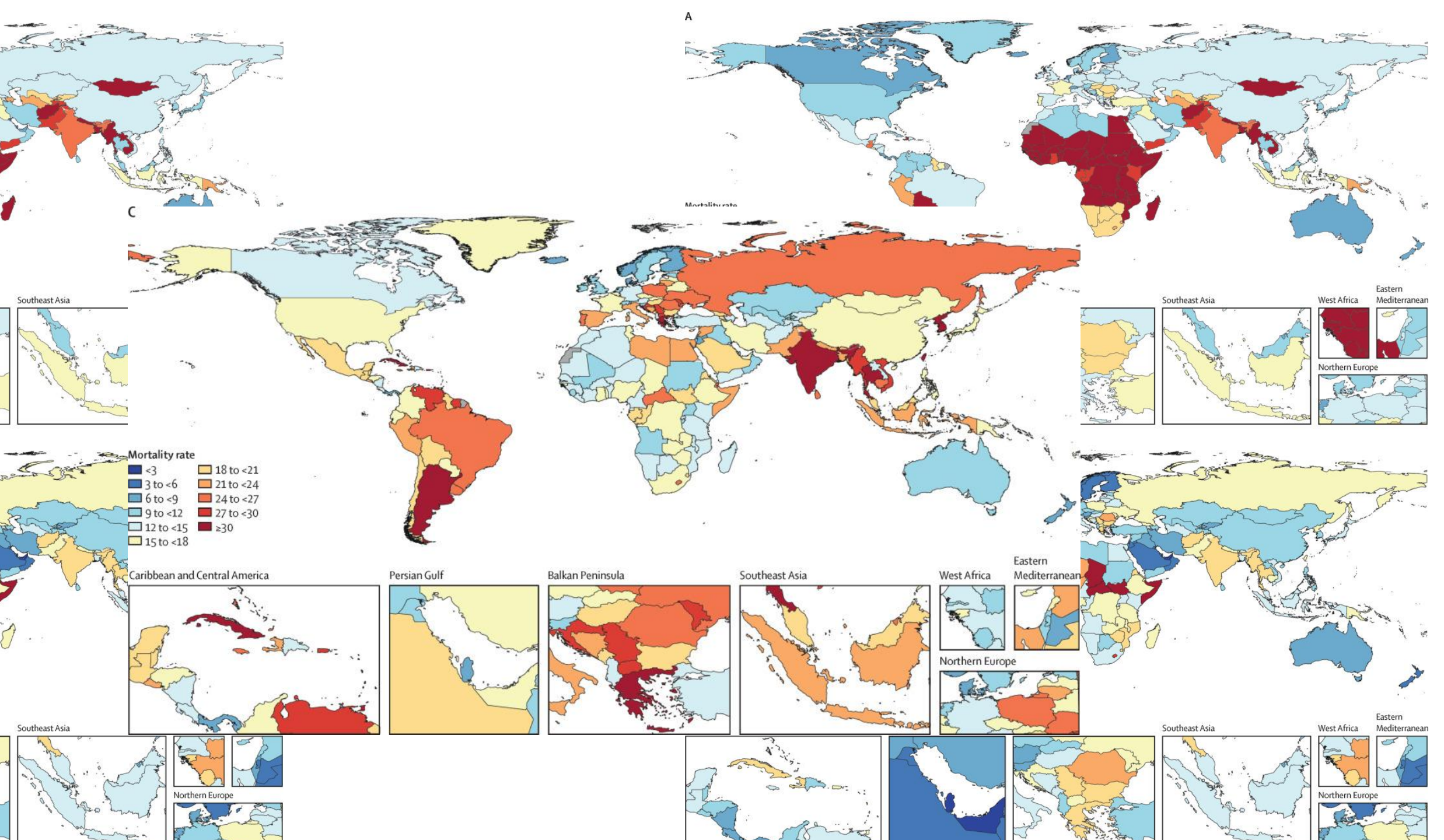
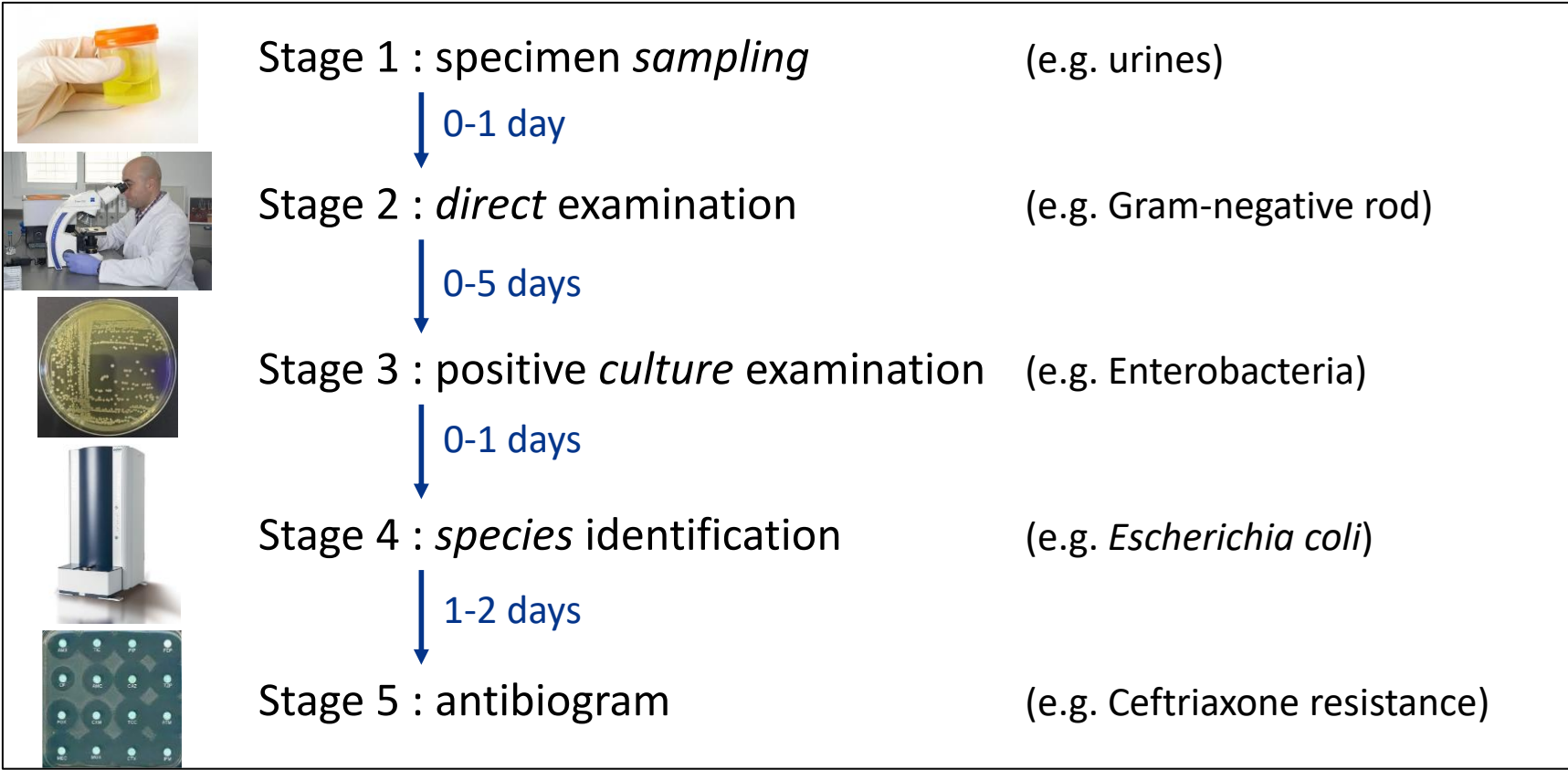


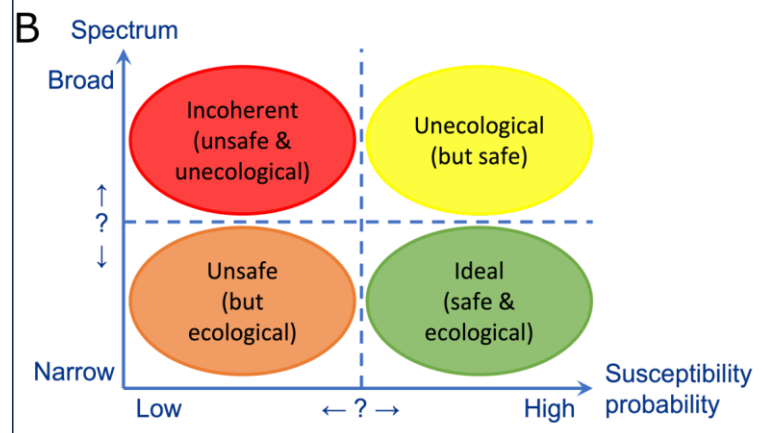
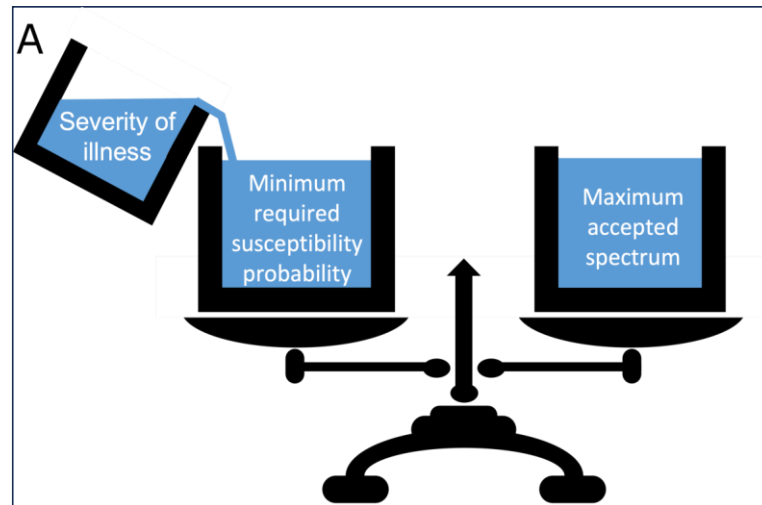
Fig. 2. A simple [support vector machine](#) that divides a dataset into two classes

# One Health

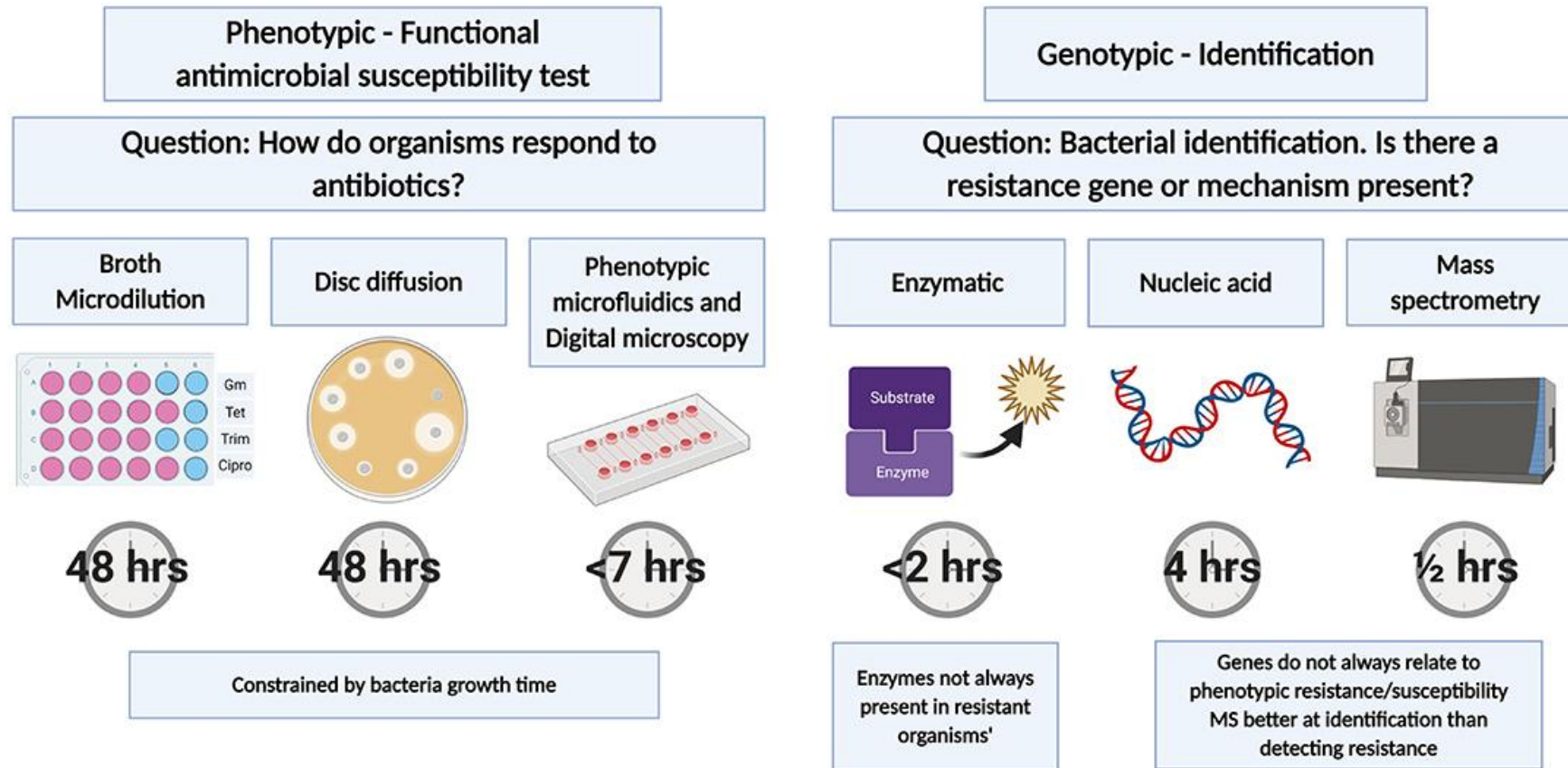




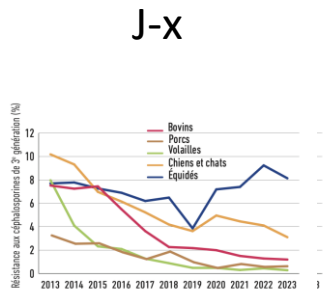




# AMR prediction best timing?



# AMR prediction: un marché en expansion



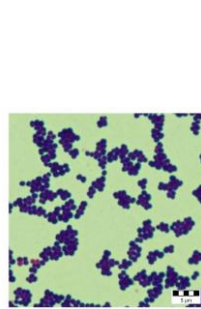
Données épidémi



Données clinico-bio



Liquide biologique



Examen direct



Cultures



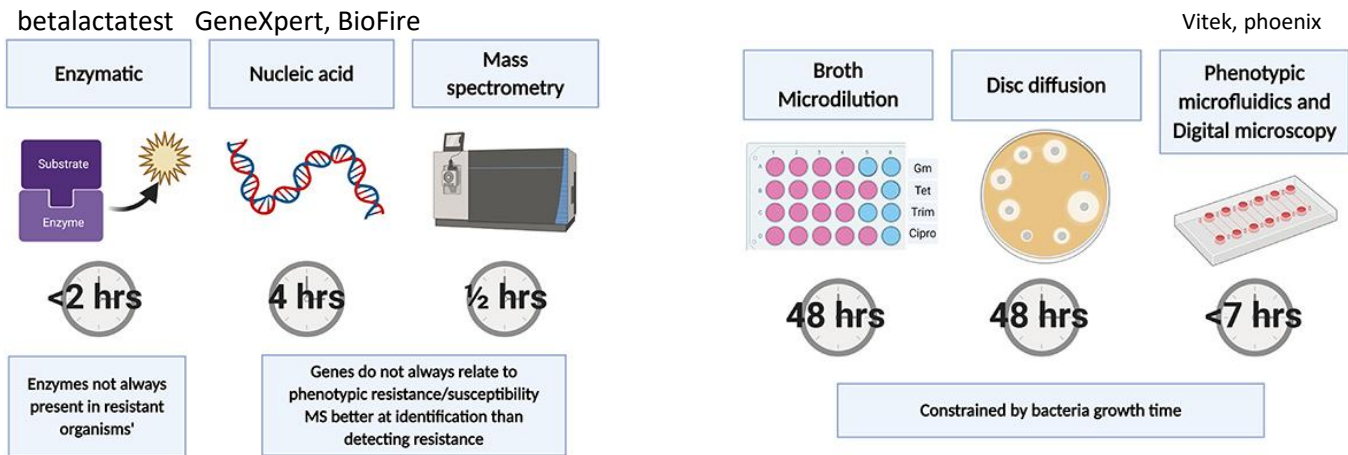
Identification



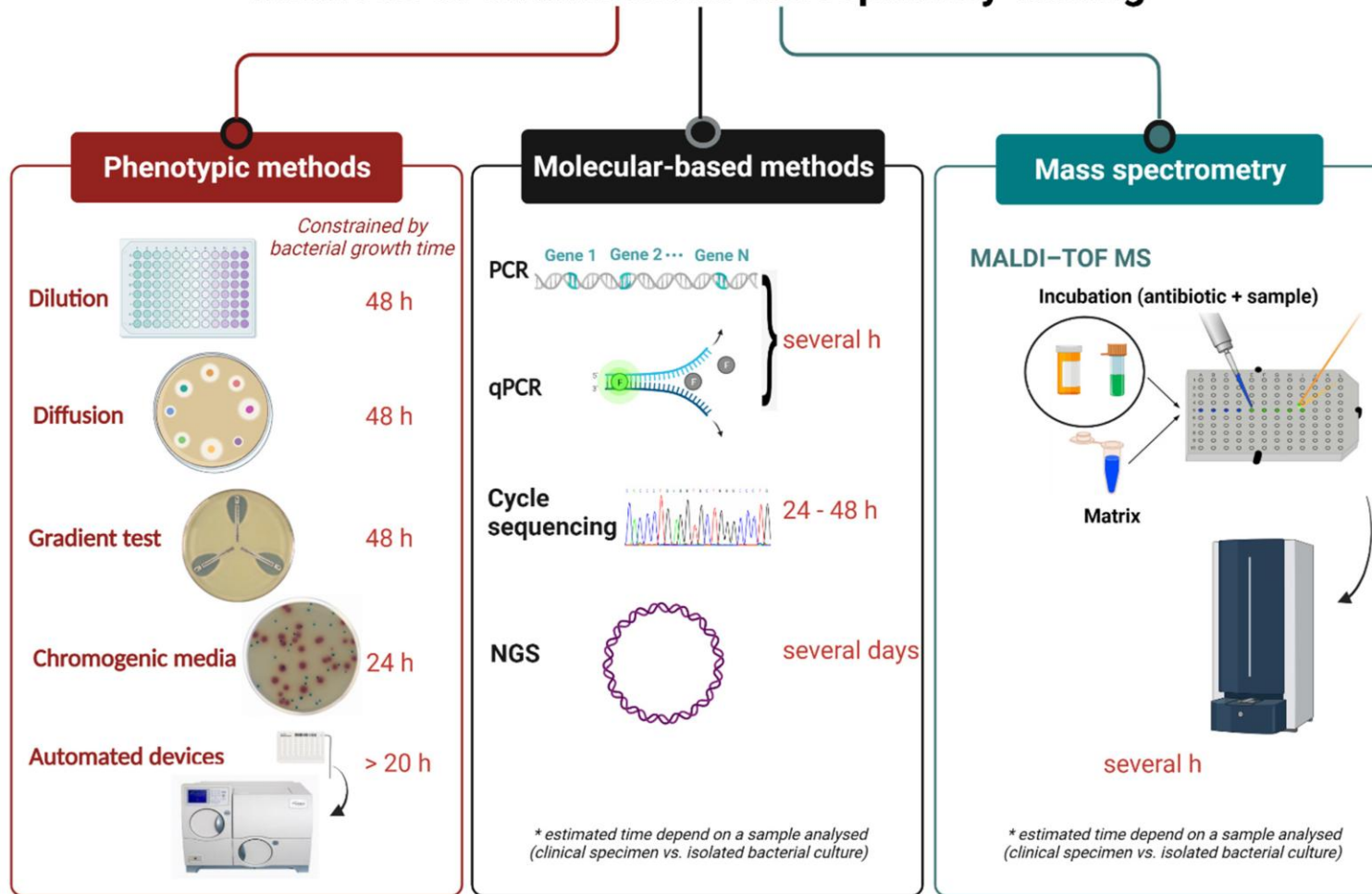
Antibiogramme

Antibiothérapie probabiliste

Désescalade



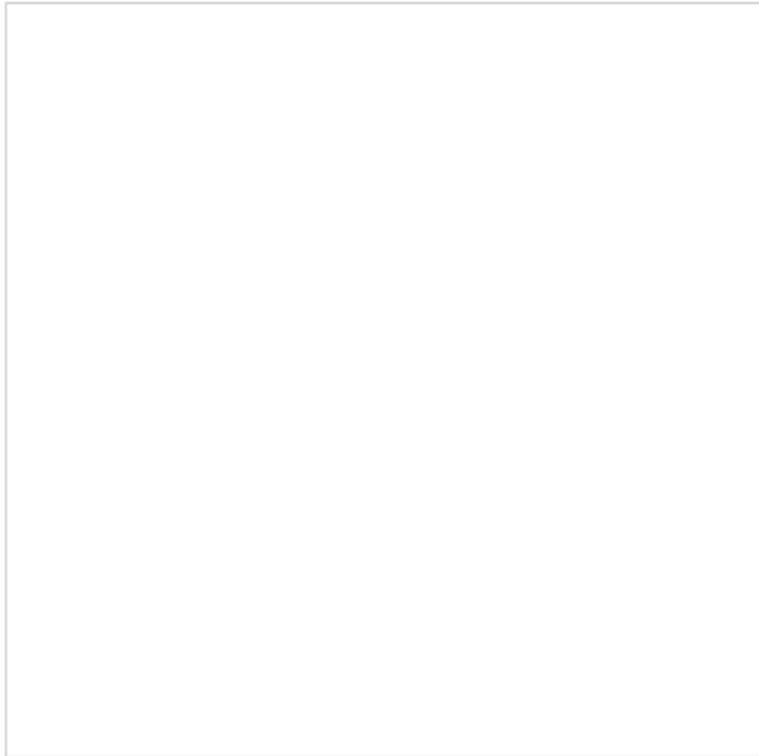
# Methods of antimicrobial susceptibility testing



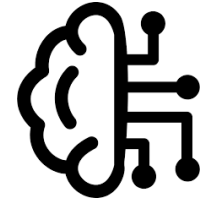
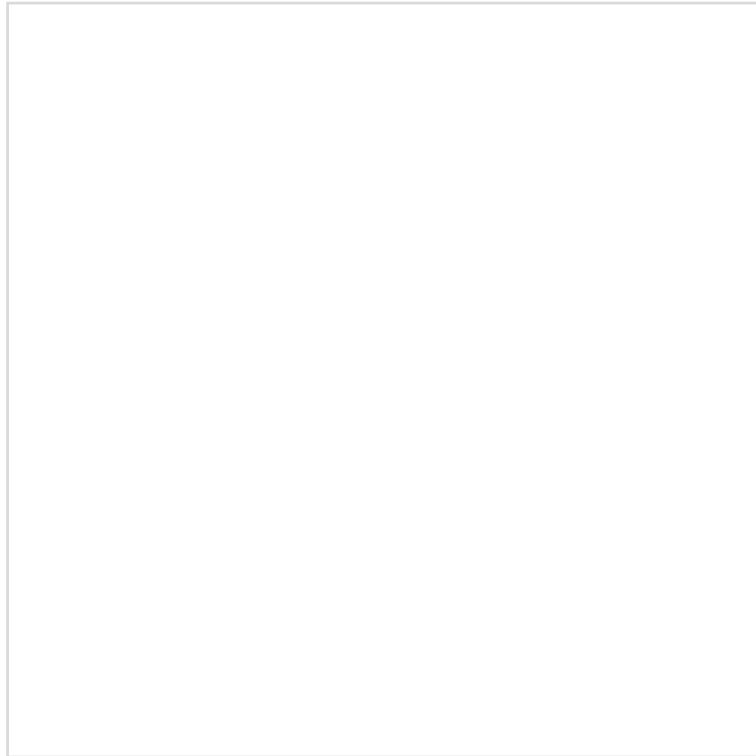
# Example: XXX



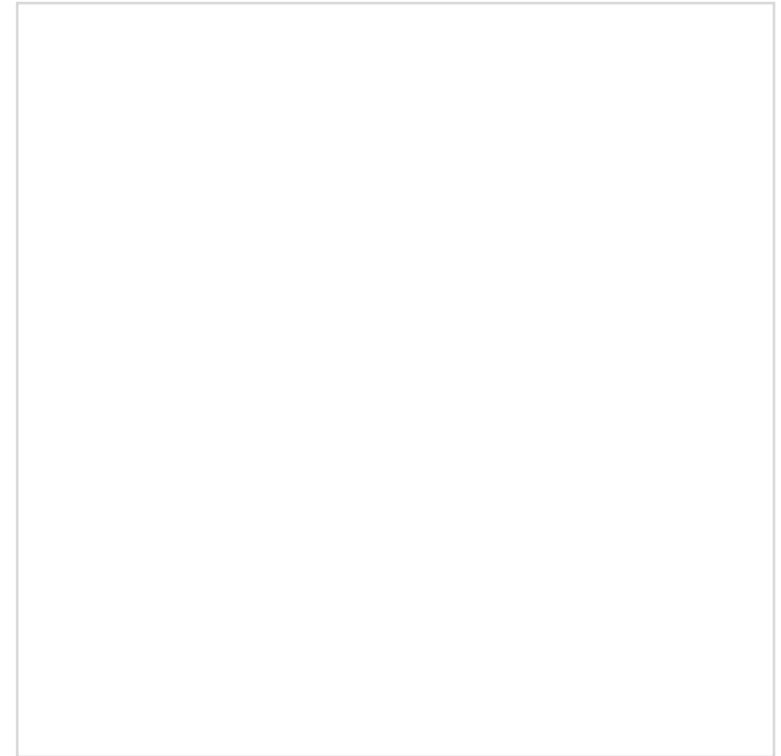
objective



data



ML algorithm



# Exemple: epidemiological data

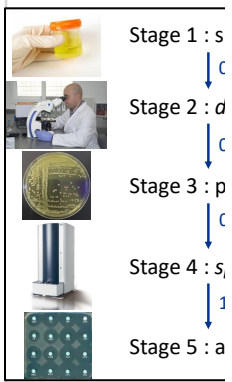


objective

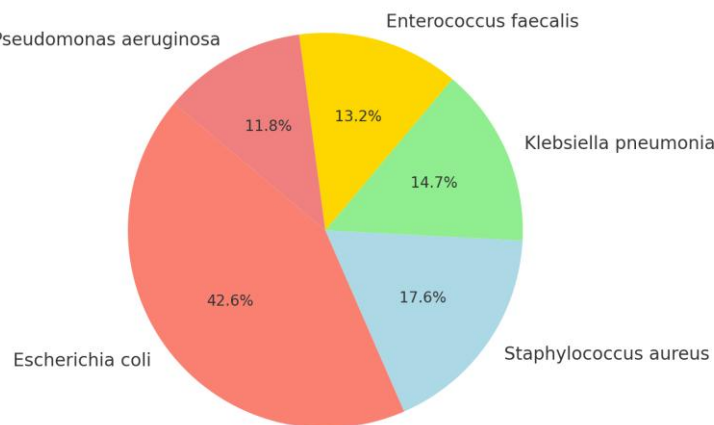


data

Prediction of antibiotic resistance at 4 different stages prior to the antibiogram from historical bacterial ecology data



Distribution by Bacteria

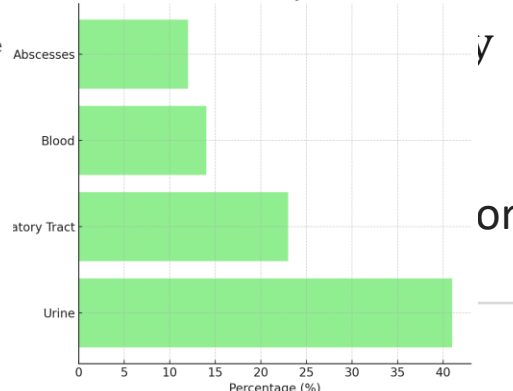


30,975 antibiograms

Ward, BMR past history, date

Jan2014 to Dec 2020,  
Hôpital Européen Marseille .  
13,166 patients from 6  
different types of wards.

Distribution by Source



Emergency room (25%),  
critical care (24%), surgery  
(20%) or medicine (19%).

urine (41%), lower  
respiratory tract (23%), blood  
(14%) or abscesses (12%)

*Escherichia coli* (29%), *Staphylococcus*

# Example: XXX



Key findings

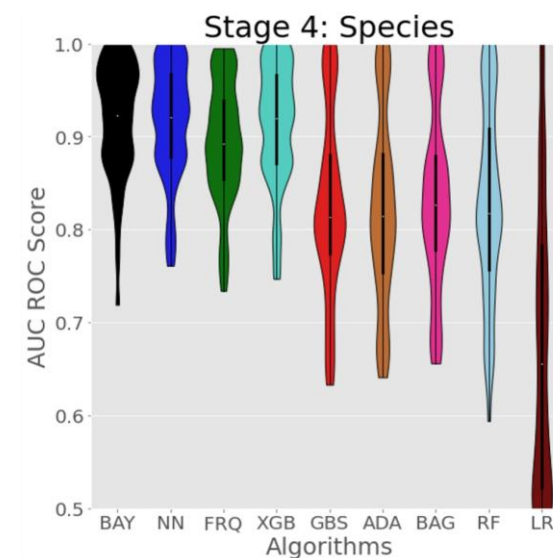
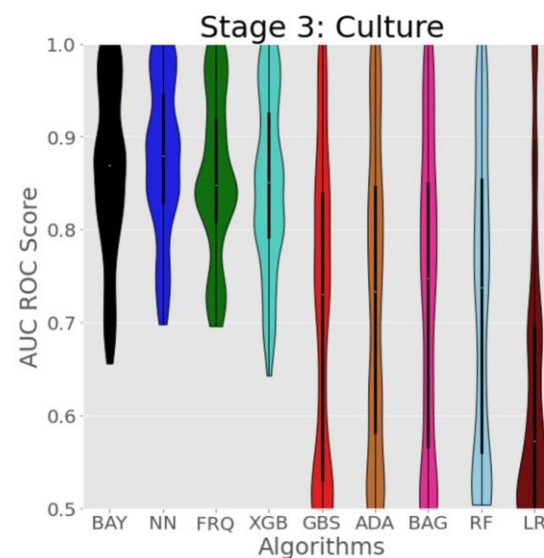
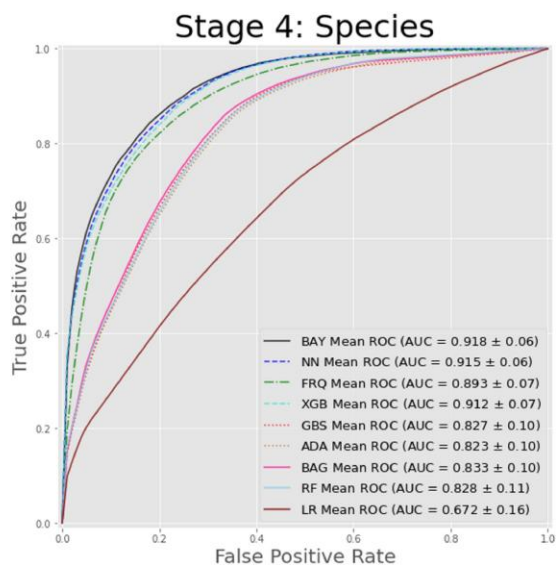
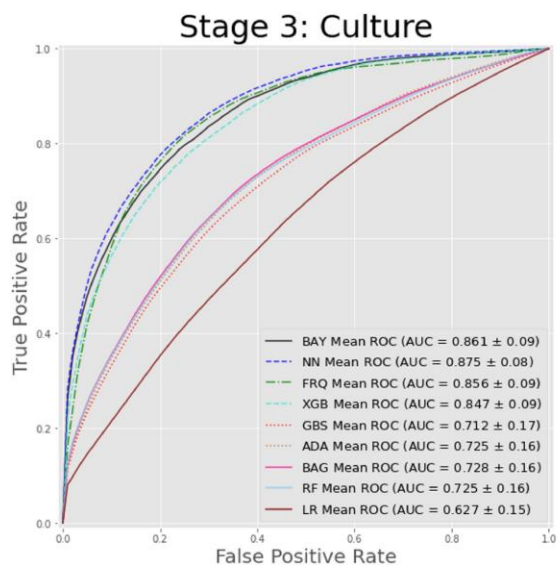
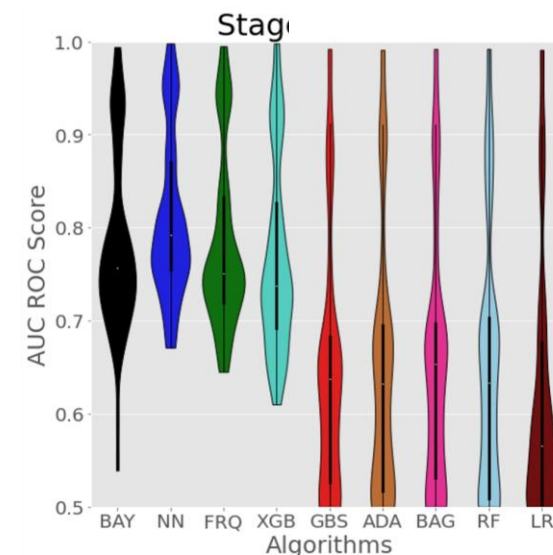
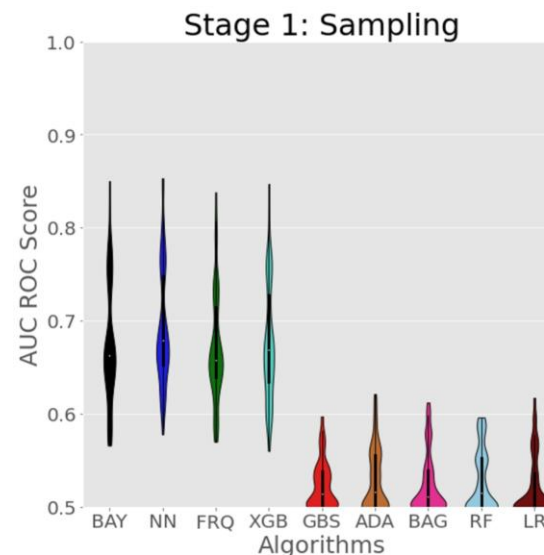
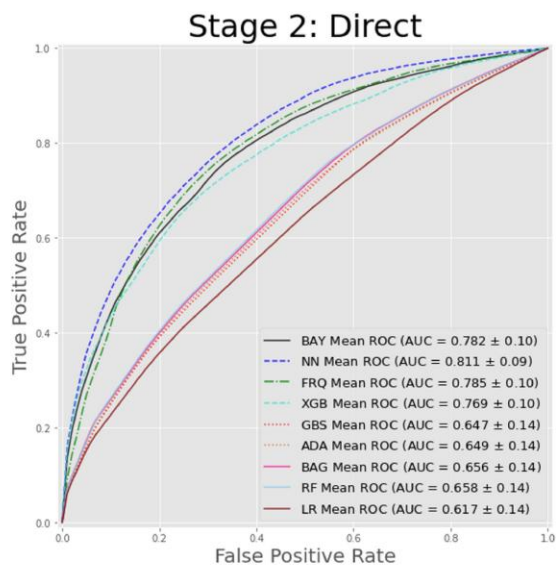
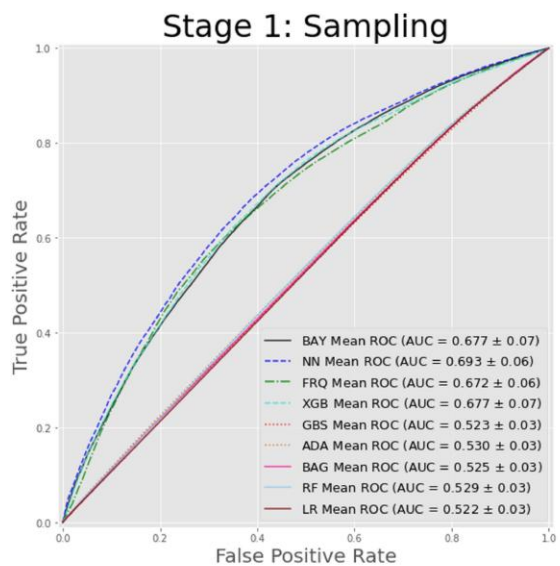


Clinical implications

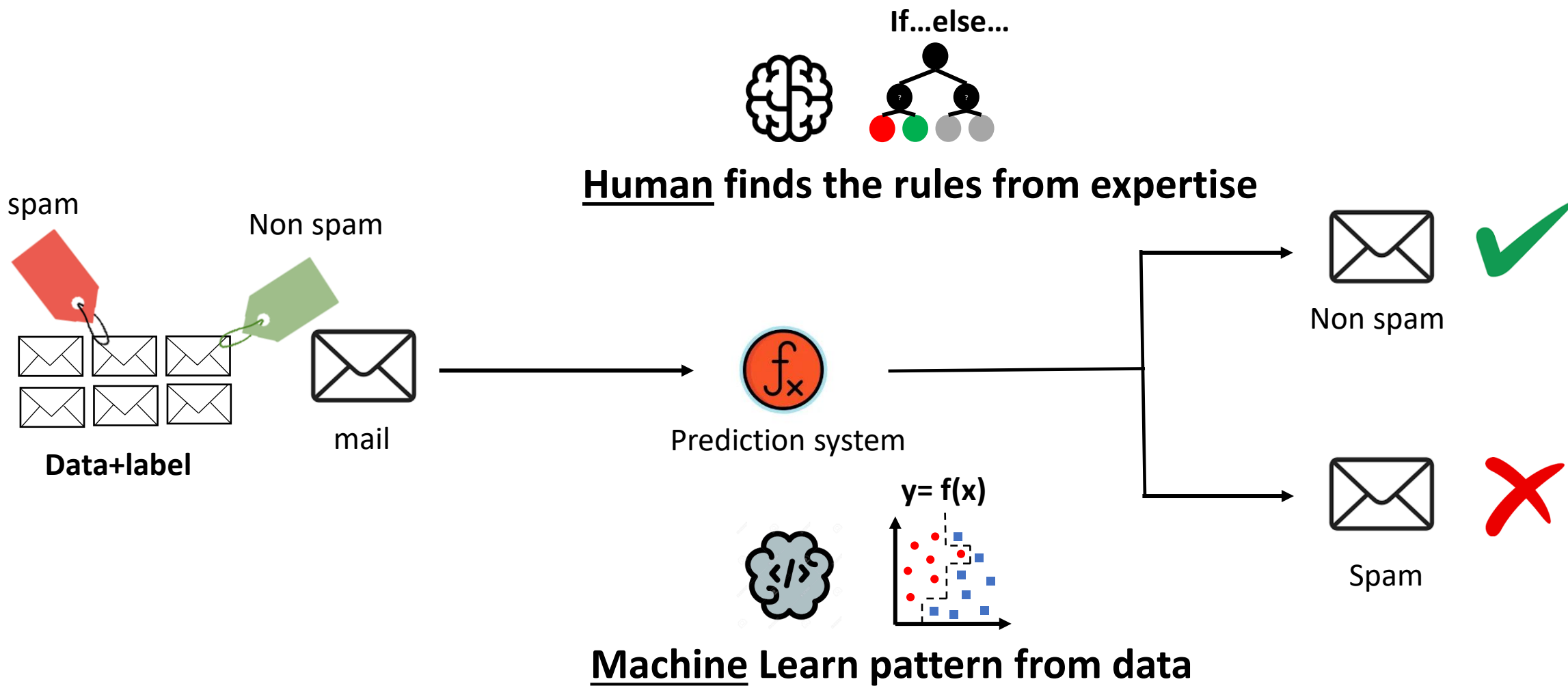


Limits

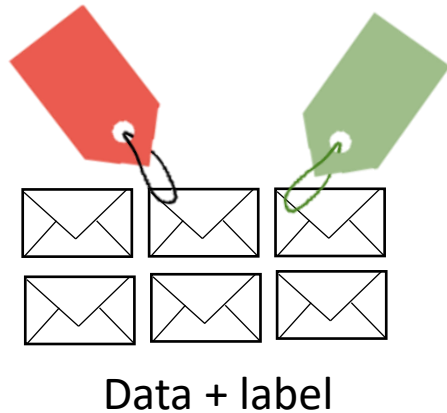
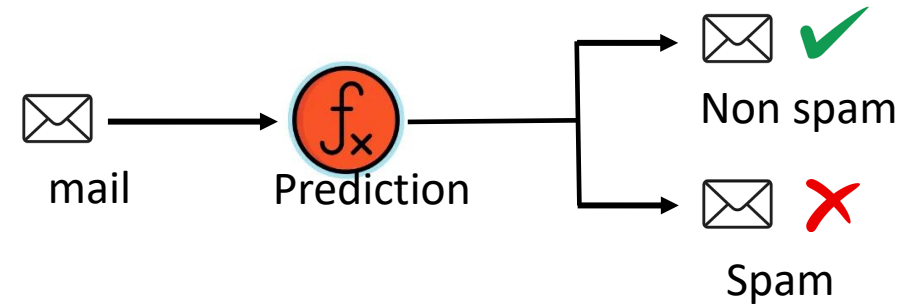
# Epidemiological data: Key findings



# Expert system $\neq$ Machine Learning



# Expert system ≠ Machine Learning

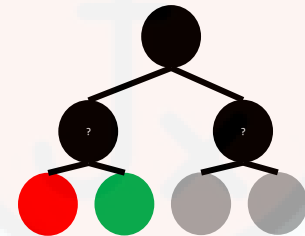


Experience



Human finds the rules from data during past experiences

If...else...

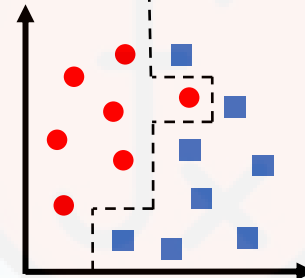


Training



Machine learns pattern from data during training

$y = f(x)$



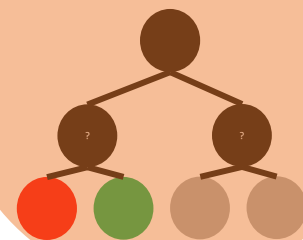
# Expert system $\neq$ Machine Learning

Experience



Human finds the rules from data during past experiences

If...else...

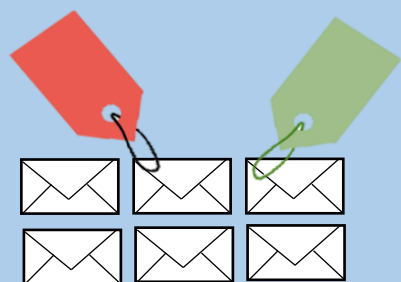
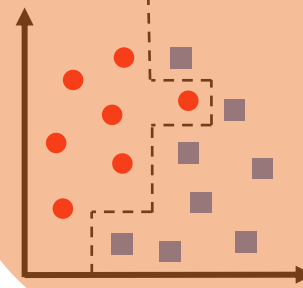


Training



Machine learns pattern from data during training

$y = f(x)$



Data + label



New mail



Prediction

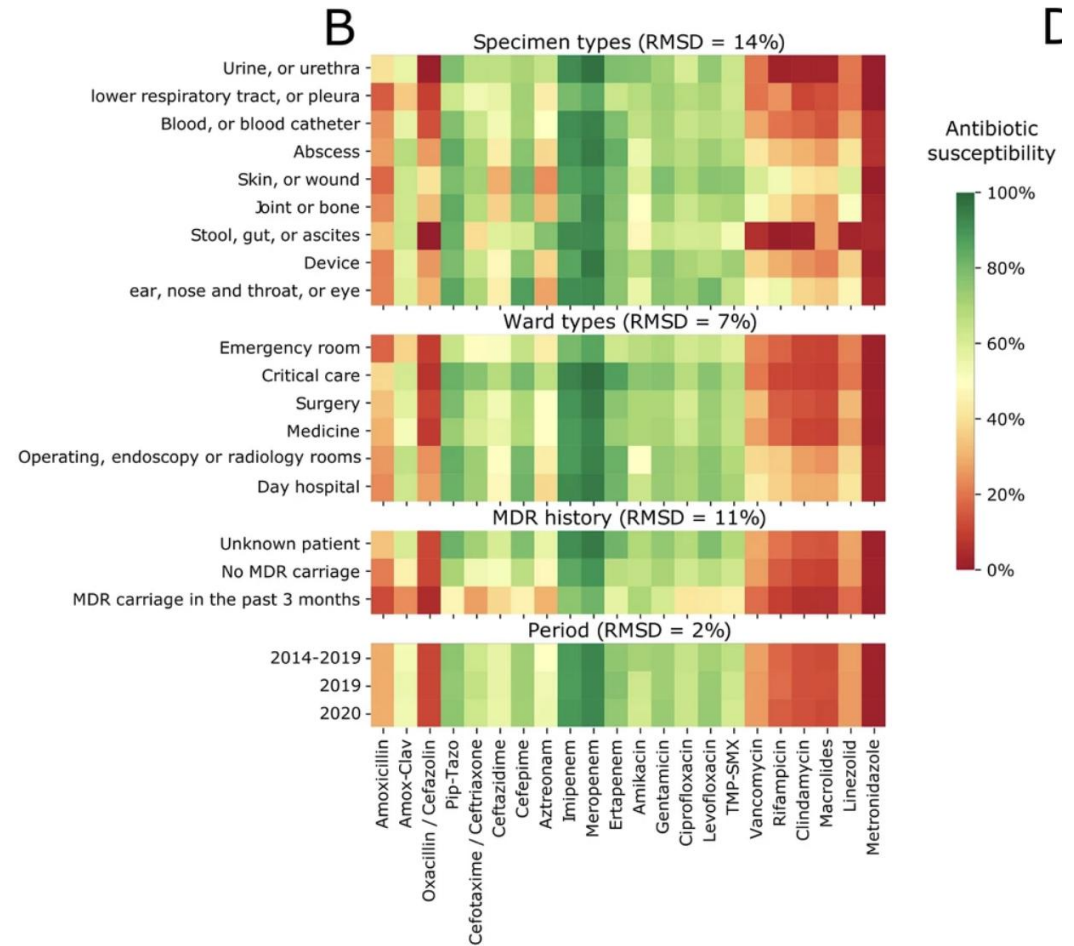
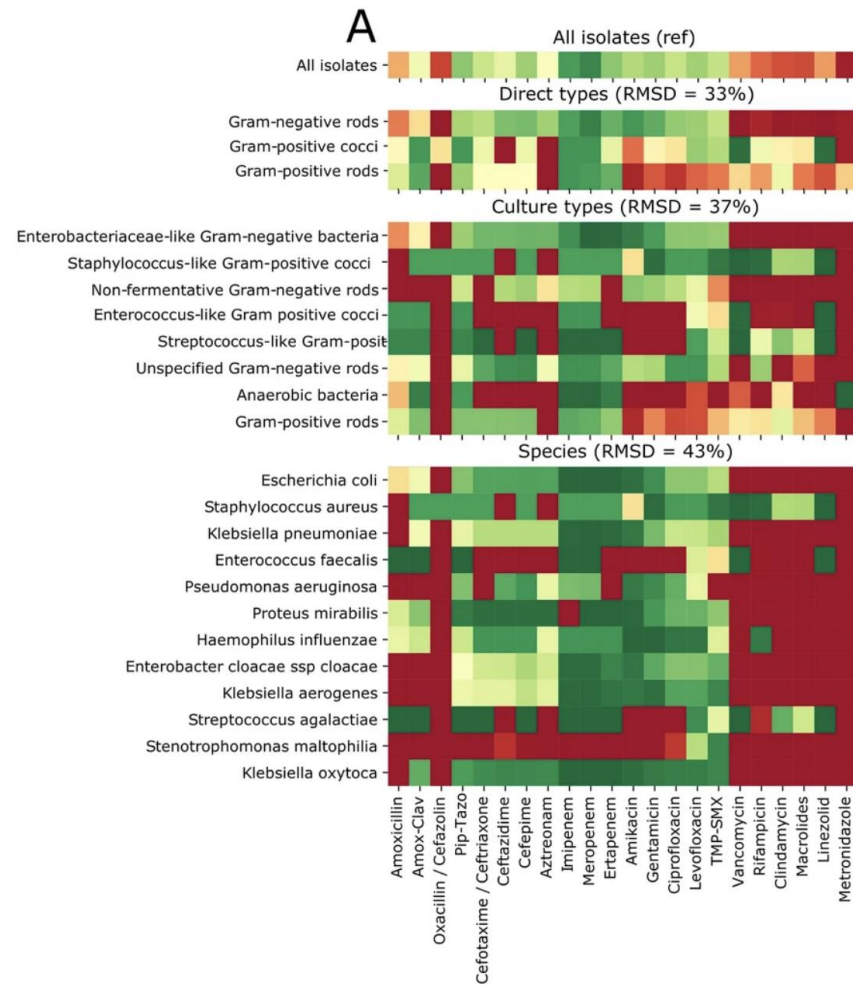


Spam  
87%



Non spam

# Épidémiologie Marseillaise



# WHO: Les pathogènes prioritaires



# Hémoculture positive



## BioFire Blood Culture IDentification 2 (BCID2) Panel

Type d'échantillon: hémoculture positive (200 µL)



1 test

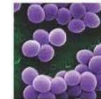
43 cibles

1h15



### Bactéries Gram -

**Complexe Acinetobacter calcoaceticus- baumannii**  
**Bacteroides fragilis**  
**Enterobacterales**  
*Enterobacter cloacae* cp.  
*Escherichia coli*  
***Klebsiella aerogenes***  
*Klebsiella oxytoca*  
*Groupe Klebsiella pneumoniae*  
*Proteus*  
***Salmonella***  
*Serratia marcescens*  
*Haemophilus influenzae*  
*Neisseria meningitidis*  
*Pseudomonas aeruginosa*  
***Stenotrophomonas maltophilia***



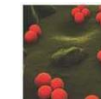
### Bactéries Gram +

*Enterococcus faecalis*  
***Enterococcus faecium***  
*Listeria monocytogenes*  
**Staphylococcus**  
*Staphylococcus aureus*  
***Staphylococcus epidermidis***  
***Staphylococcus lugdunensis***  
**Streptococcus**  
*Streptococcus agalactiae*  
*Streptococcus pneumoniae*  
*Streptococcus pyogenes*



### Levures

*Candida albicans*  
***Candida auris***  
*Candida glabrata*  
*Candida krusei*  
*Candida parapsilosis*  
*Candida tropicalis*  
***Cryptococcus neoformans/gattii***



### Gènes de résistance aux antibiotiques

#### Carbapénémases

**IMP**  
**KPC**  
**NDM**  
**OXA-48-like**  
**VIM**

#### Résistance à la colistine

***mcr-1***

#### BLSE

**CTX-M**

#### Résistance à la pénicilline

*mecA/C*  
***mecA/C* et *MREJ* (SARM)**

#### Résistance à la vancomycine

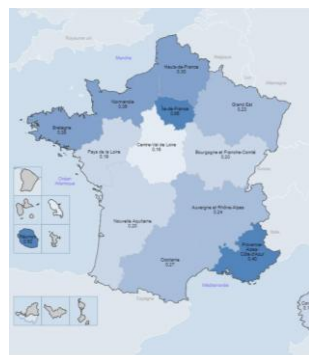
*vanA/B*

**Nouvelles cibles sur BioFire BCID2 Panel**  
**Identification spécifique sur BioFire BCID2 Panel**

# Discussion microbiologiste

- Hémoculture positive
- genXpert 30-40€ <2h: SA vs Scoag neg? MetiR? Carbapénemase? BK? RpoB?
- Betalacta test (4-5h): BLSE (y compris carbapenemase). Pas ampC
- Antibiogramme rapide pour hémocultures: 50€ (<5-7h)
- FilmARRAY 120€ <2h: PCR multiplex, identification, resistance (SARM, BLSE, AmpC, carbapenemase)

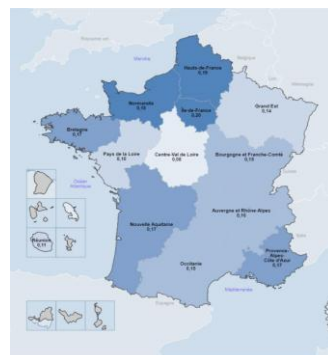
# En France, en 2023



E coli BLSE



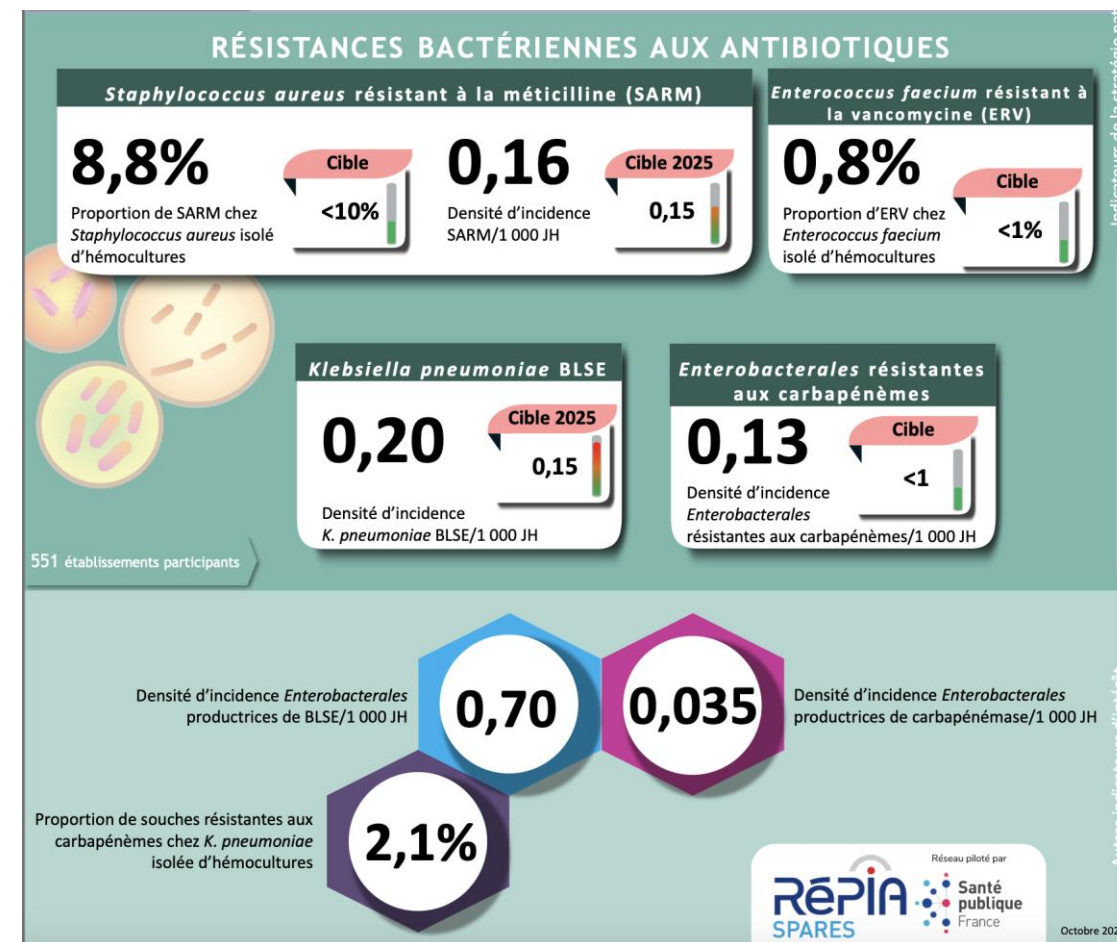
KP BLSE



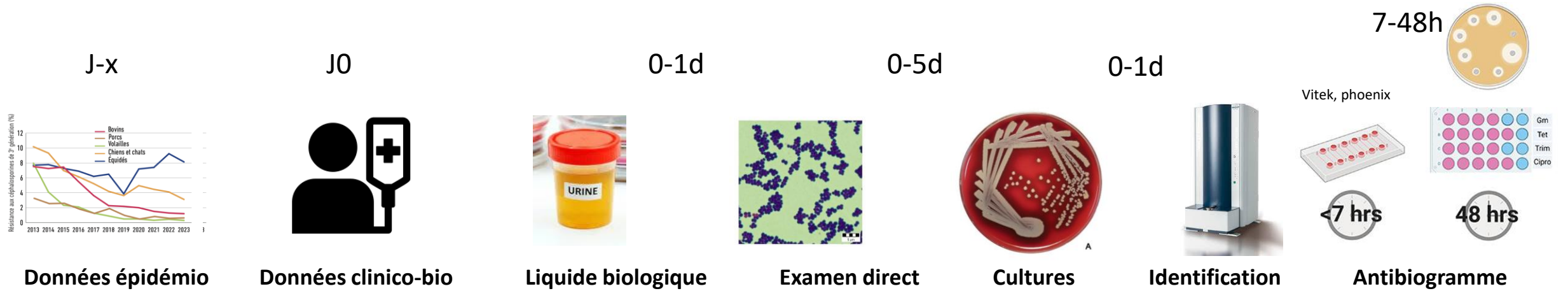
SARM



Densité d'incidence pour 1 000 JH en établissement de santé

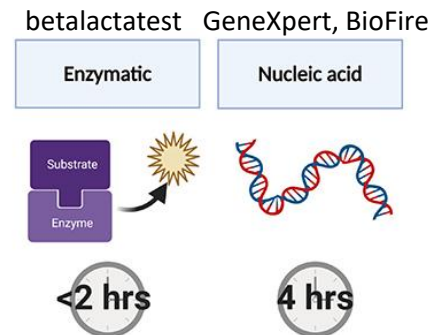


# AMR prediction: un marché en expansion



Antibiothérapie probabiliste

Désescalade



**Gènes de résistance aux antibiotiques**

**Carbapénémases**

**<2h**

- IMP
- KPC
- NDM
- OXA-48-like
- VIM

Résistance à la colistine

*mcr-1*

BLSE

CTX-M

Résistance à la métilline

*mecA/C*

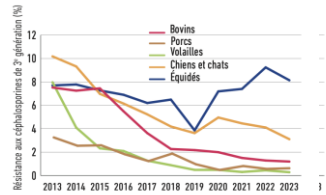
*mecA/C* et MREJ (SARM)

Résistance à la vancomycine

*vanA/B*

# AMR prediction: 4 examples

J-x



Données épidémi

J0



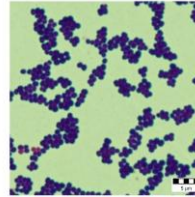
Données clinico-bio

0-1d



Liquide biologique

0-5d



Examen direct

0-1d



Cultures



Identification

7-48h



Antibiogramme

#1: Epidemio

#2 Imaging

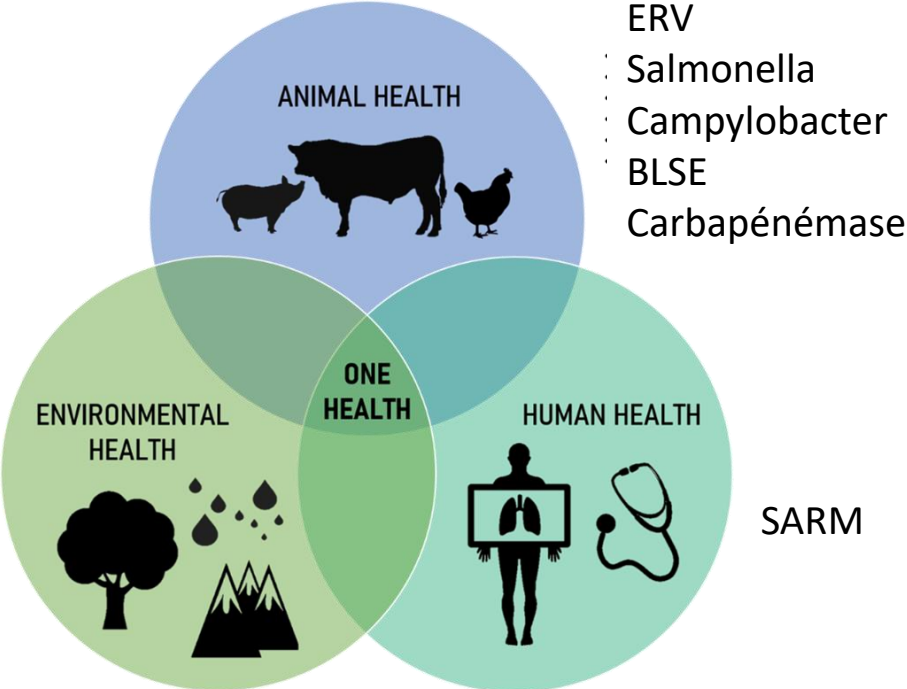
#3 Maldi-TOF

#4 Genomic

surveillance

BK  
acinetobacter  
...

# Déterminants de l'antibiorésistance



## CAUSES OF ANTIBIOTIC RESISTANCE

**HANDLE ANTIBIOTICS WITH CARE**

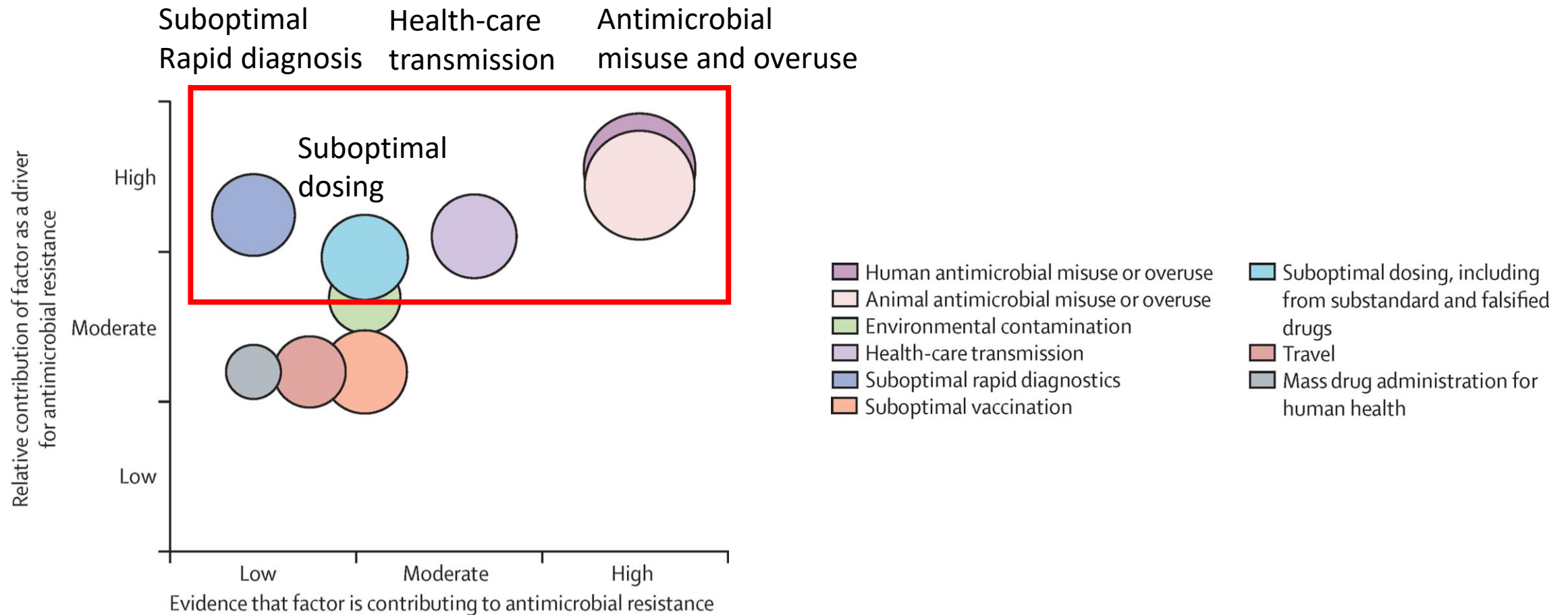
Antibiotic resistance happens when bacteria change and become resistant to the antibiotics used to treat the infections they cause.

- Over-prescribing of antibiotics
- Patients not finishing their treatment
- Over-use of antibiotics in livestock and fish farming
- Poor infection control in hospitals and clinics
- Lack of hygiene and poor sanitation
- Lack of new antibiotics being developed

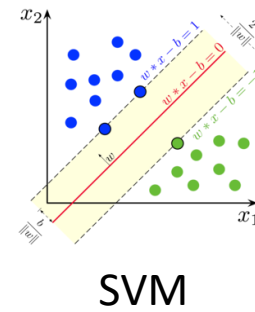
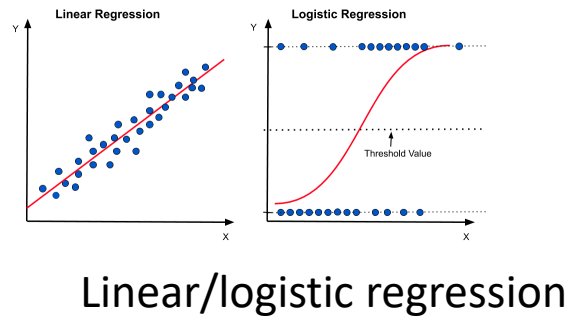
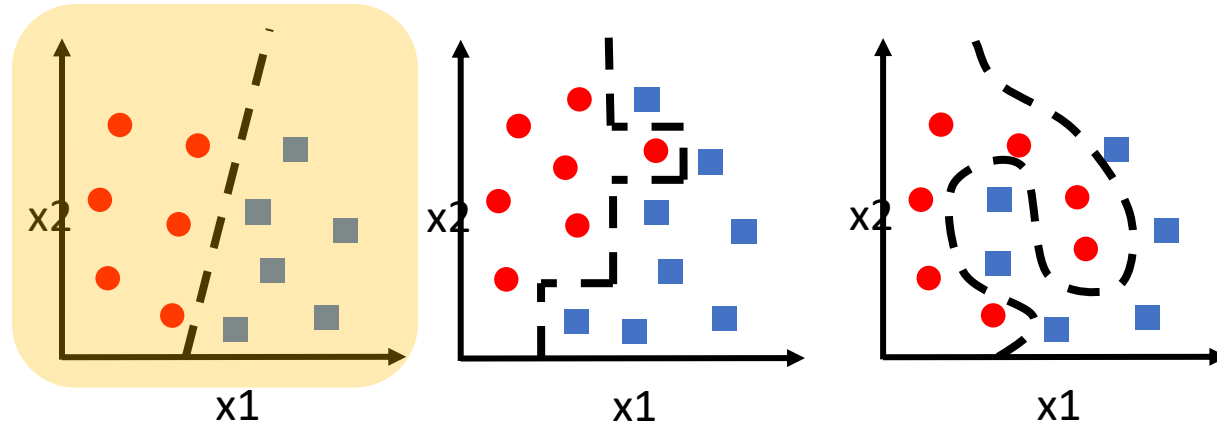
[www.who.int/drugresistance](http://www.who.int/drugresistance)  
**#AntibioticResistance**

World Health Organization

# AMR: Les coupables



# Traditional ML: linear algorithms



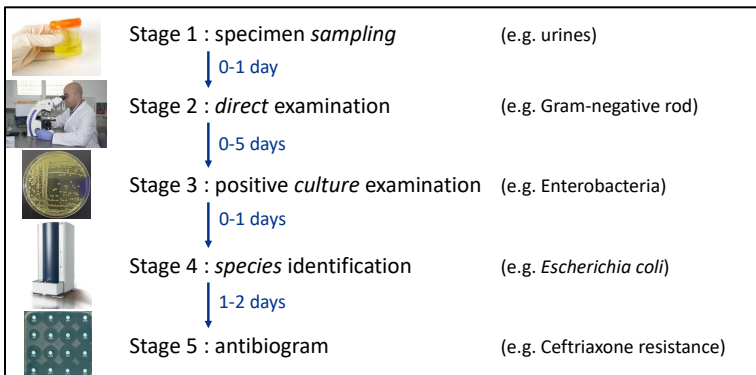
# #1 Objective & Methods



objective

AMR prediction

4 different stages from historical bacterial ecology data

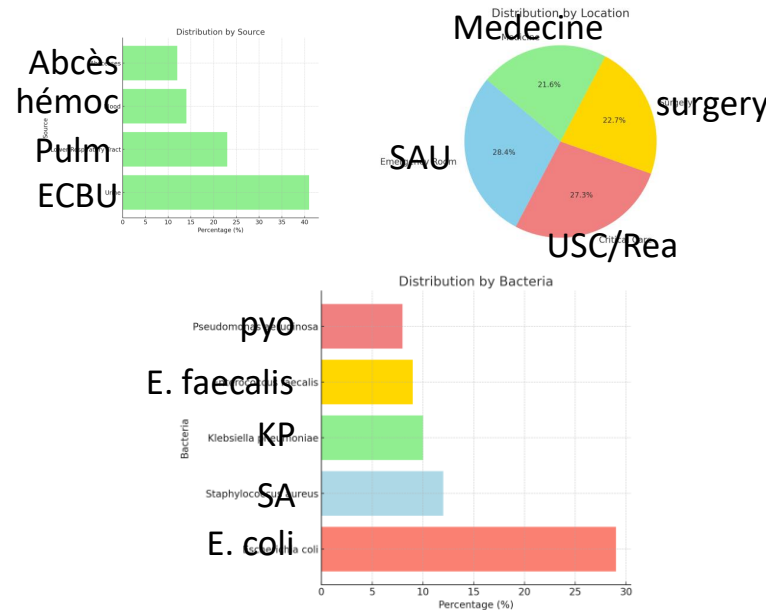


data

Jan2014 to Dec 2020, Hôpital Européen  
Marseille . 13,166 patients



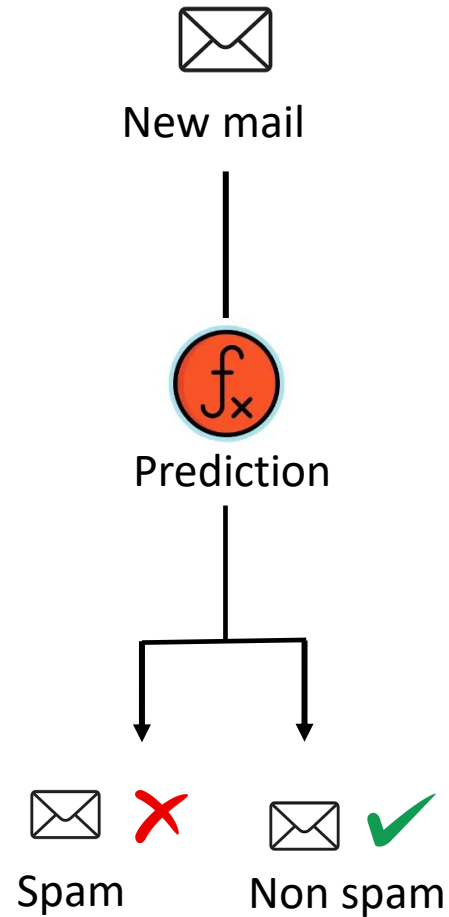
30,975 antibiograms  
Ward, BMR past history, date



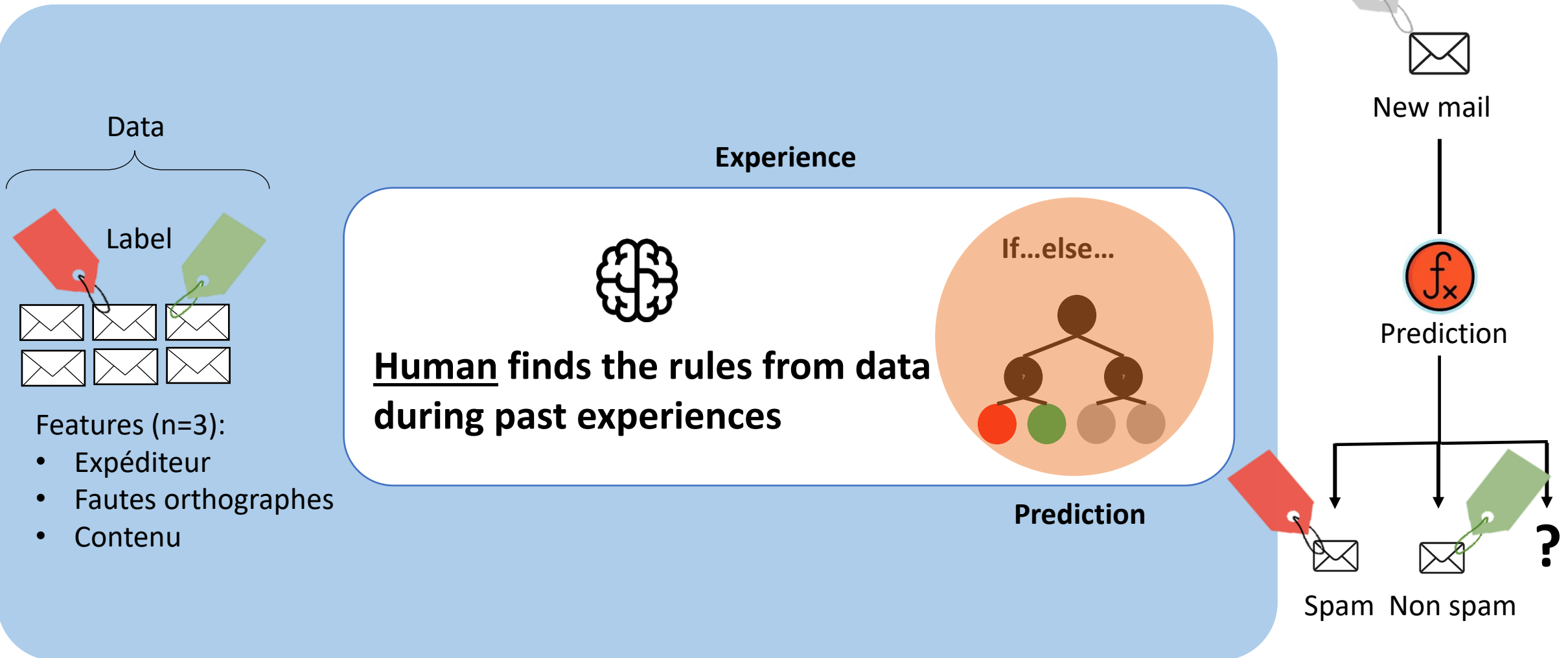
Antibiotic sensitivity testing

VITEK® 2 system  
(bioMérieux France) or  
diffusion techniques

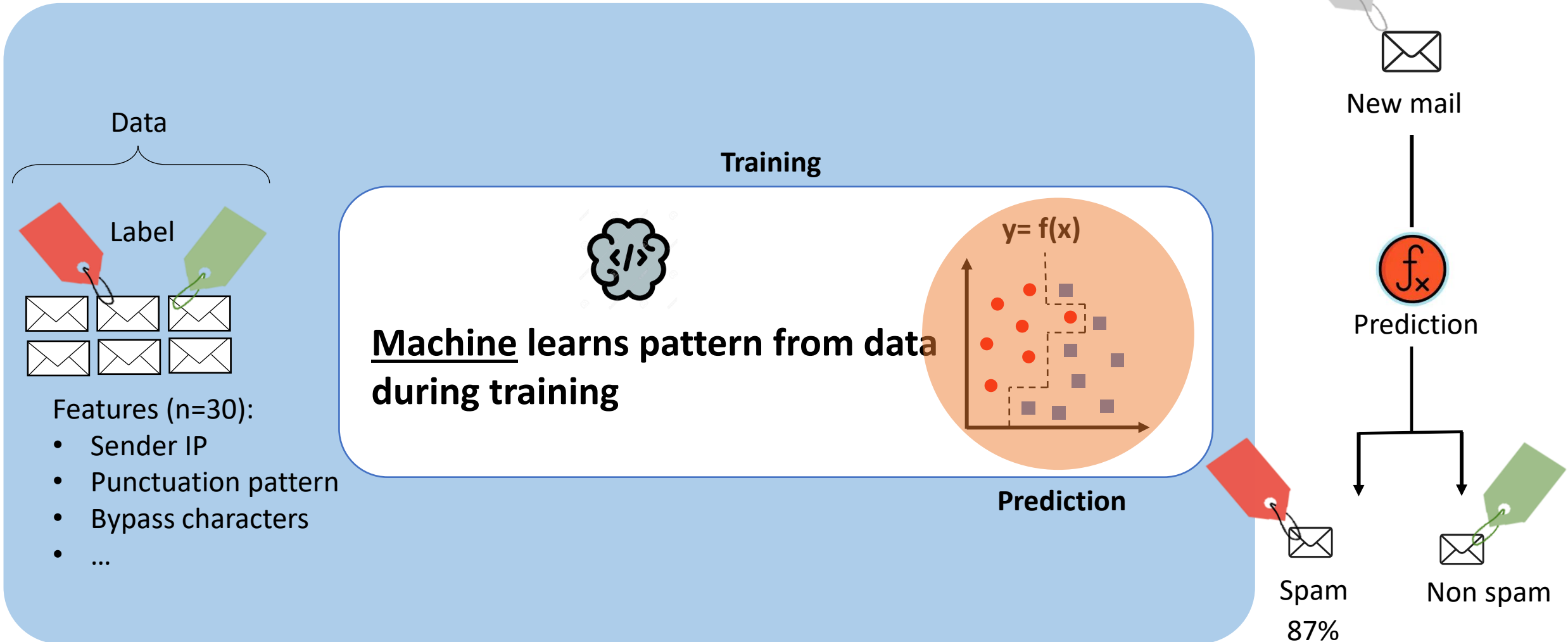
# Expert system $\neq$ Machine Learning



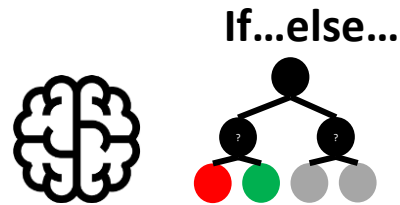
# Expert system



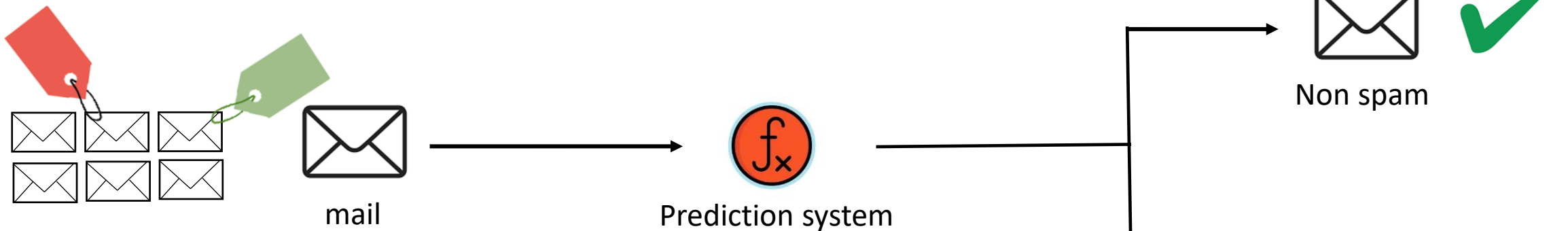
# Machine Learning



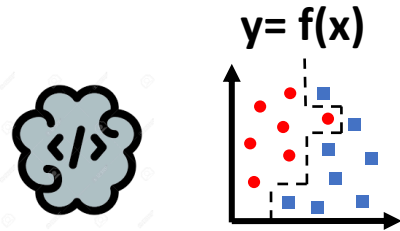
# Expert system $\neq$ Machine Learning



Human finds the rules from expertise

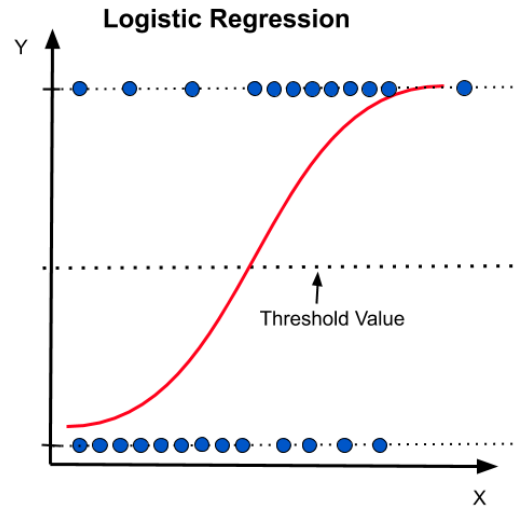
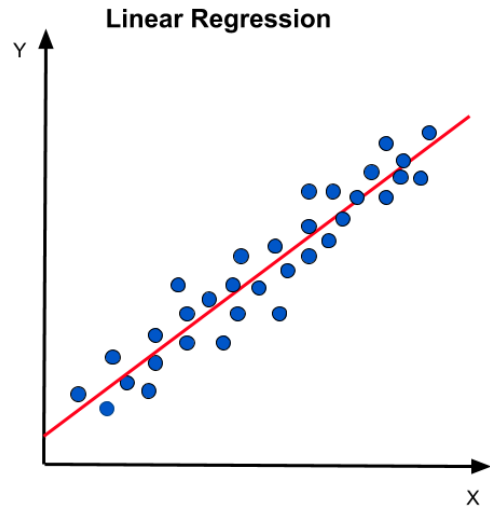
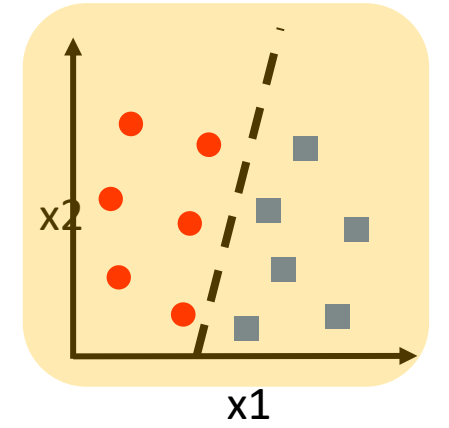


features			label
sender	ortho	sex	Spam
1	1	1	yes
0	0	0	no
1	0	1	yes

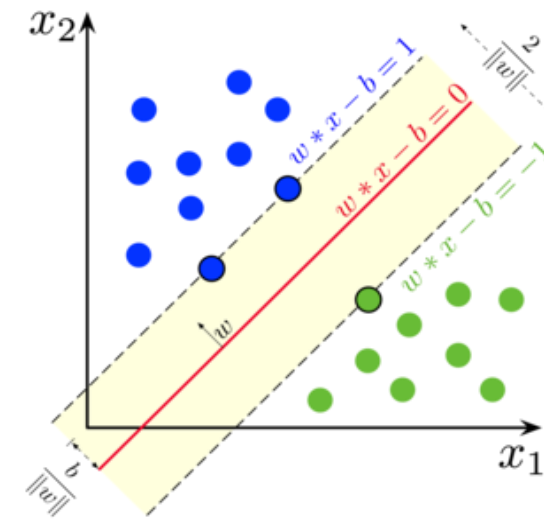


Machine Learn pattern from data

# Traditional ML: linear algorithms

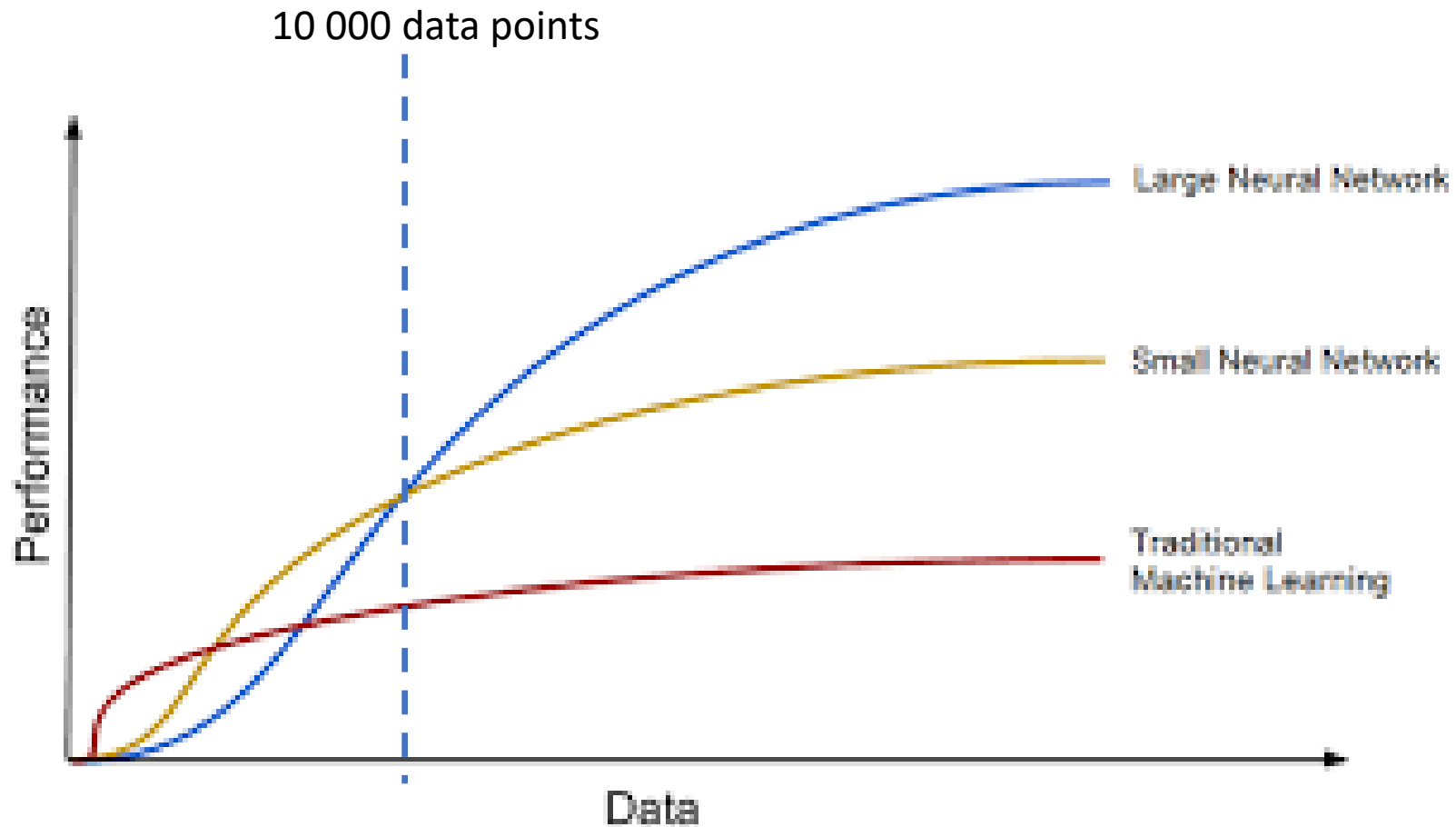


Linear/logistic regression



Support Vector Machine  
SVM

# Why is Deep Learning Hot?

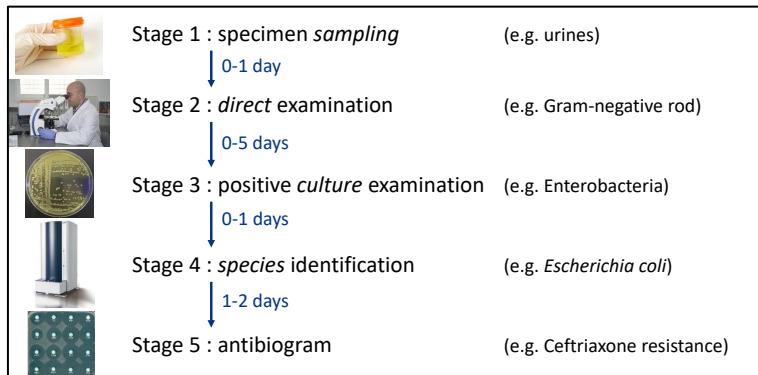


# #1 Objective & Methods



AMR prediction

4 stages from historical bacterial ecology data



2014- 2020, Hôpital Européen Marseille  
13,166 patients 30,975 antibiograms



Historical bacterial  
ecology, Stage, Ward,  
BMR past history,  
period



AST

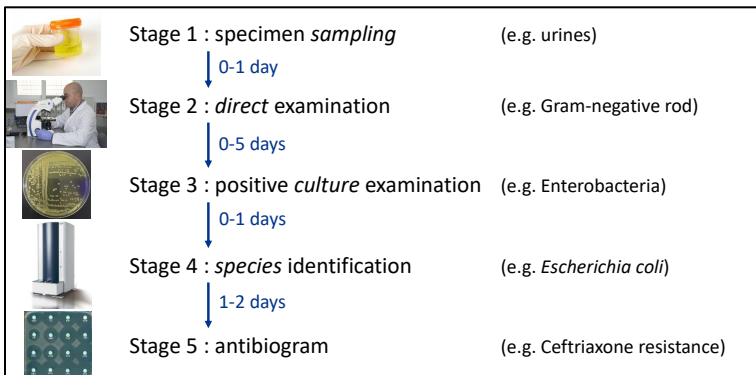
# #1 Objective & Methods



objective

AMR prediction

4 different stages from historical bacterial ecology data

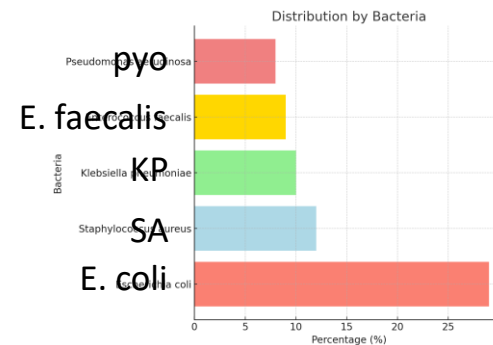
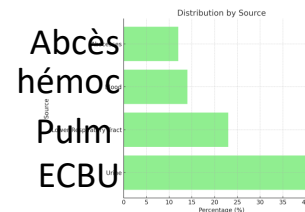


data

Jan2014 to Dec 2020, Hôpital Européen  
Marseille . 13,166 patients

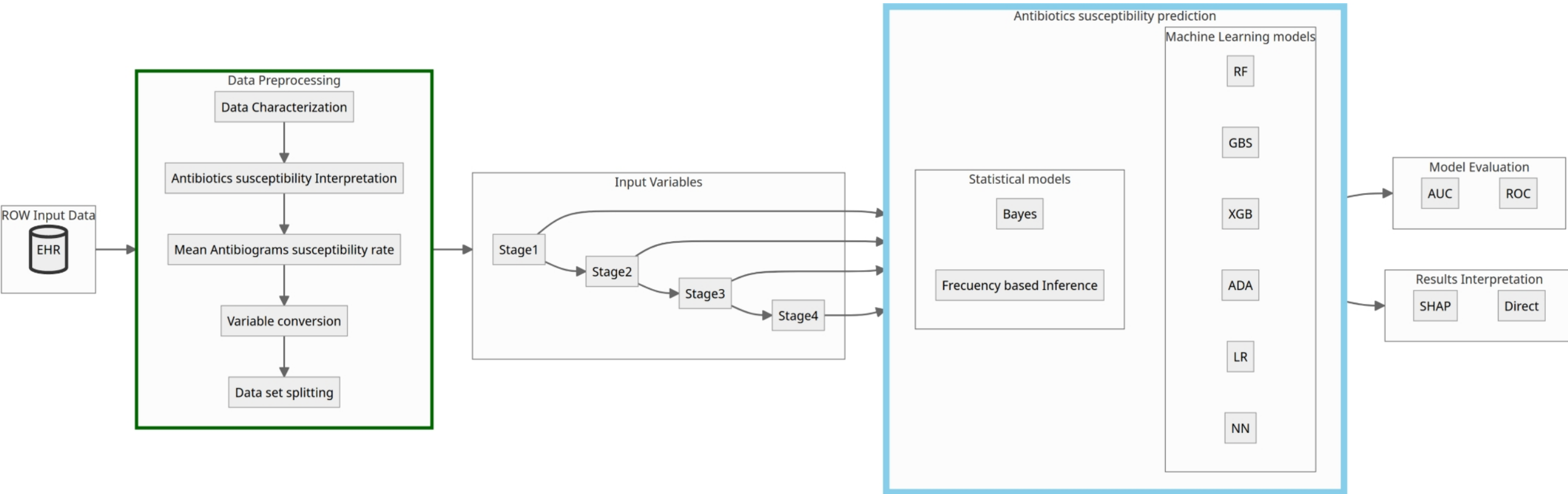


30,975 antibiograms  
Ward, BMR past history, date



VITEK® 2 system  
diffusion techniques

# #1 Machine Learning stack

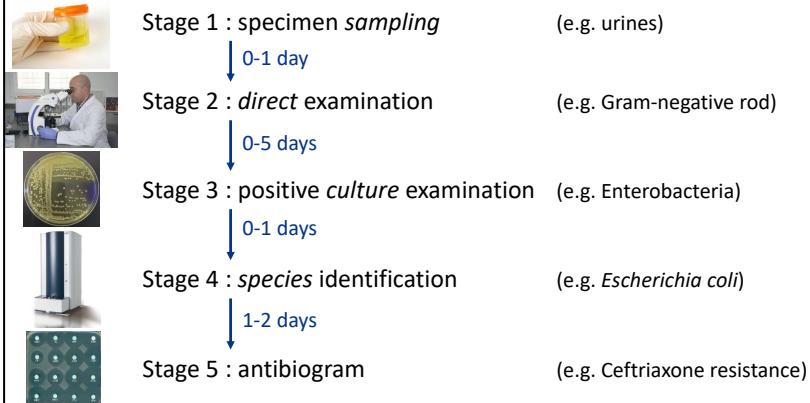


# #1 Objective & Methods



AMR prediction

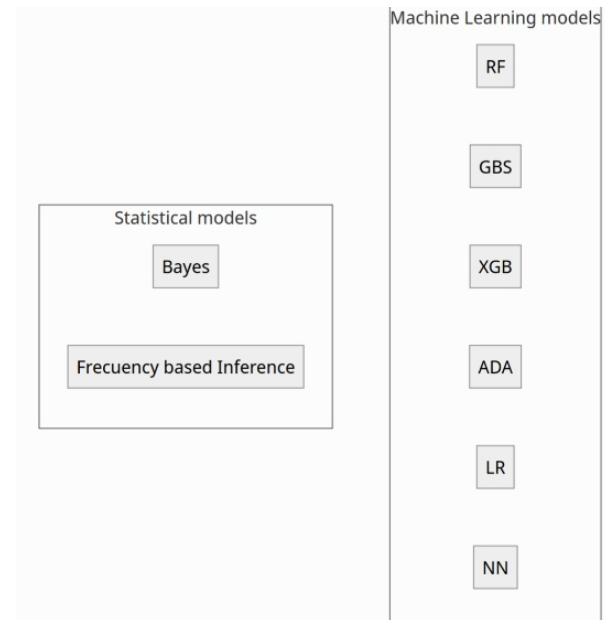
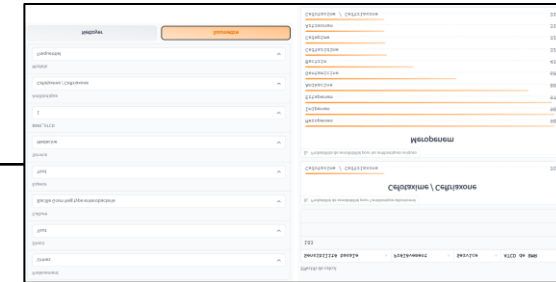
4 stages from historical bacterial ecology



- 2014- 2020, Hôpital Européen Marseille
- 13,166 patients 30,975 antibiograms

$\mathcal{X}$

- Historical bacterial ecology, Stage, Ward, BMR past history, period

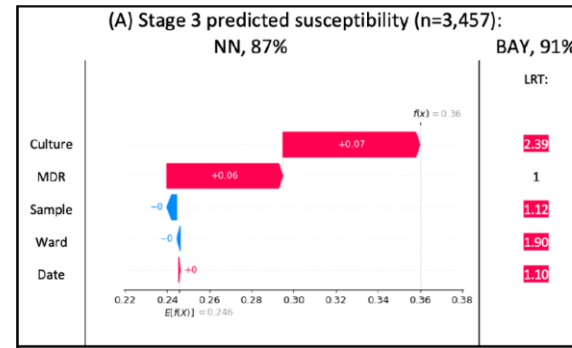


# #1 Explainable AI? C3G S prediction

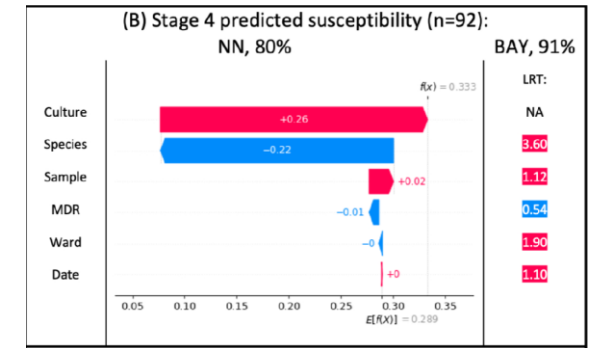


**Avril 2024:** PNA simple,  
pas BMR connu

Culture +: enterobactérie

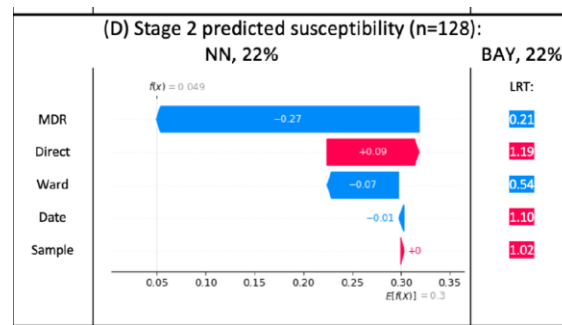
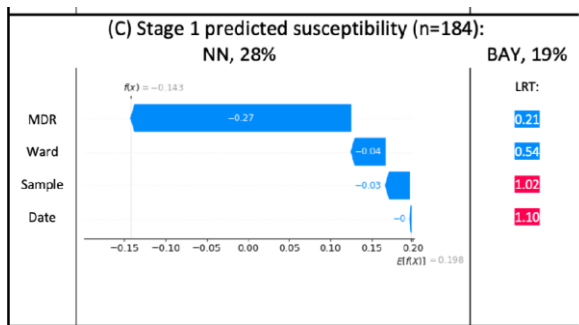


*E Coli*

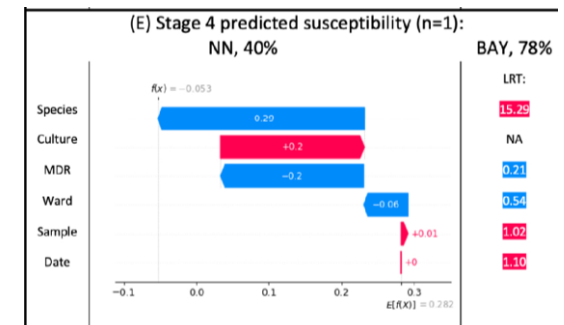


**Mai 2024:** Choc septique  
BMR connu

BGN



*Citrobacter koseri*



En fait E Coli BLSE...

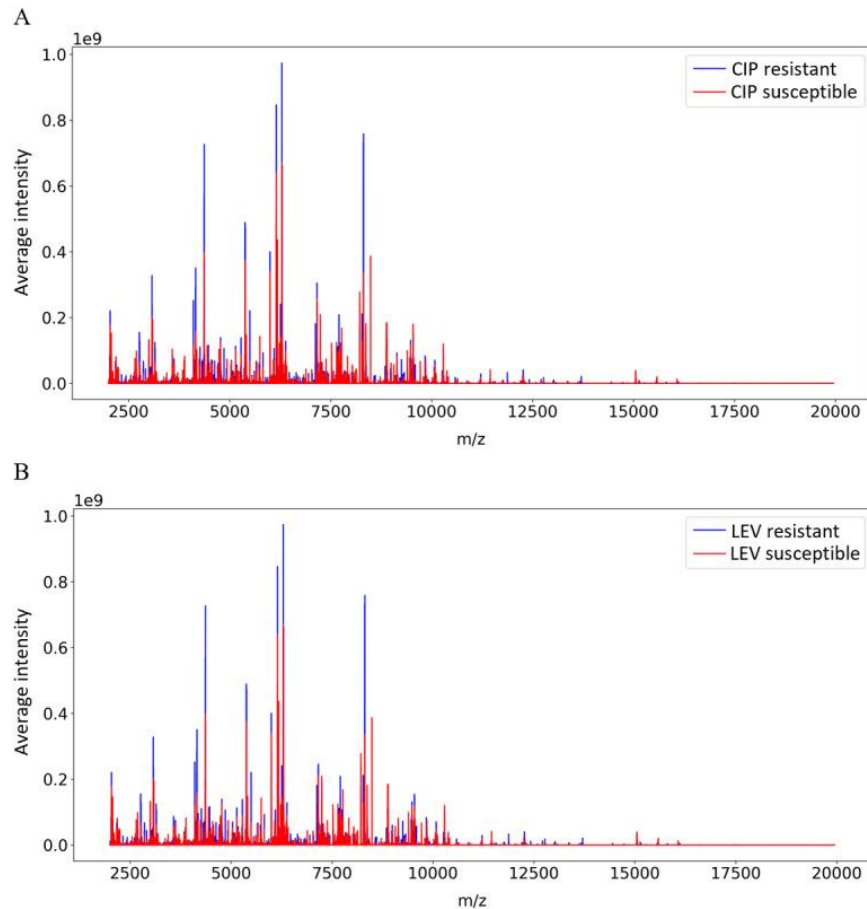
1.Sampling

2.Direct Examination

3.Cultures

4.MALDI\_TOF

# #3 MALDI\_TOF & AMR prediction

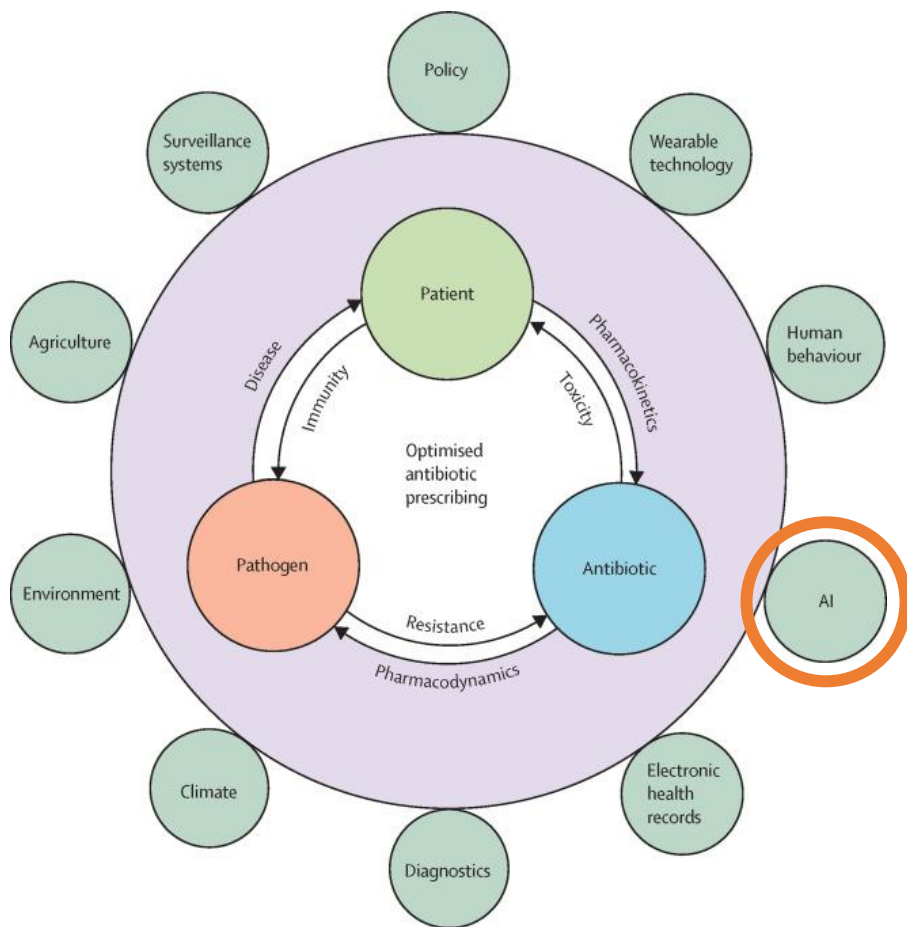


- (A) Average intensity distribution for CIP-resistant and susceptible *Klebsiella pneumoniae*.
- (B) Average intensity distribution for LEV-resistant and susceptible *Klebsiella pneumoniae*.

CIP: ciprofloxacin; LEV: levofloxacin; m/z: mass-to-charge.

Differential mass spectrometry profiles for CIP and LEV resistance in *Klebsiella pneumoniae*.

# L'IA pour lutter contre l'antibiorésistance?



Aide à prescription

Chatbot observance

Vegan

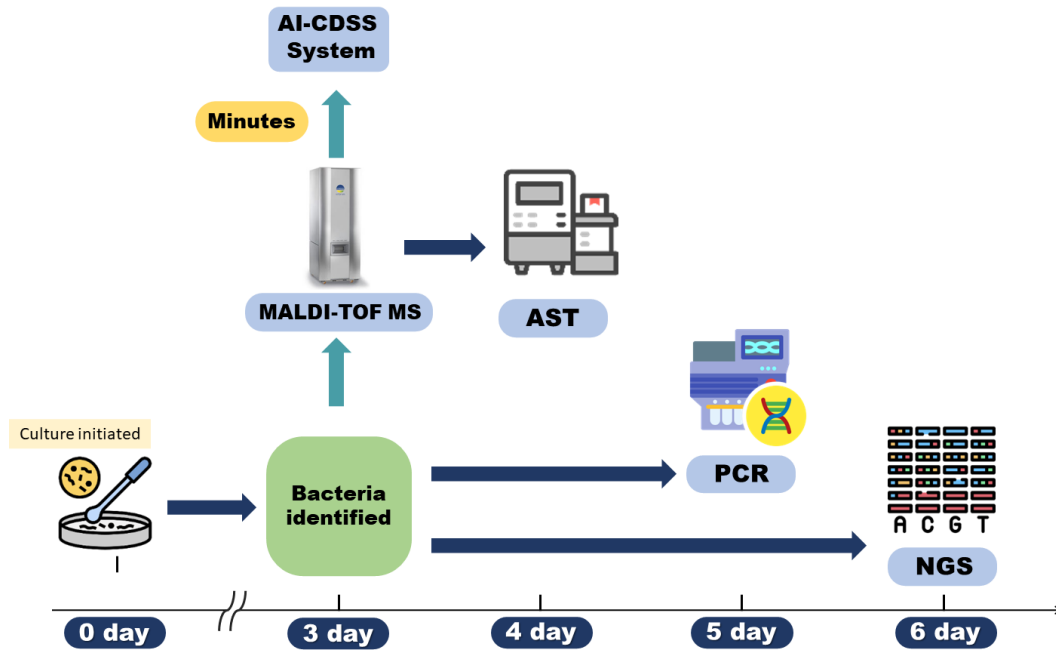


Le topic!

SHA

Drug discovery

# #3 clinical implication & limits



No Deep learning algo  
No clinical or epidemiological data  
Limited to KP, CIP and LEV

« 1-2 days gain of AMR prediction compare to traditional AST »