VELO team meeting
22/01/2026

Thesis Overview

Inductive logic programming for the identification of markers predisposing to hospital-acquired pneumonia

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HOMI-LUNG

Homi-Lung is a European project deciphering the causal relationship between cardiovascular and respiratory diseases progression and the immune and microbiome alterations observed during and after pneumonia.

Funded by the European Union

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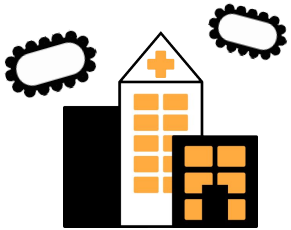
Homi-Lung – Hospital-acquired pneumonia (HAP)



Nosocomial respiratory infection acquired in hospital settings, more than 48h after hospital admission. Includes ventilator-associated pneumonia.

- **0.5%–1.7% of patients admitted in hospitals**
- **10%–20% mortality rate**
  nearly fatal for vulnerable patients with comorbidities (organ transplant, immunodeficiency)
- **Culture-based diagnostics, systematic uses of antibiotics, commensal bacterium mistook for pathogens…**
  HAP complexity can't be fully assessed without an integrative reasoning

*Lower-left lobe with hypoxemia from a Pneumococcus infection

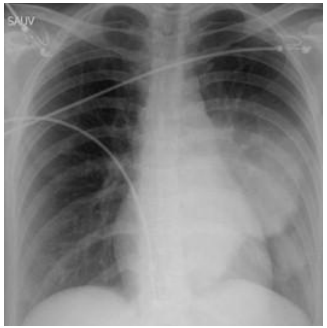


*Figure 1, from C. Beigelman-Aubry et al, Diagnostic and Interventional Imaging, 2012

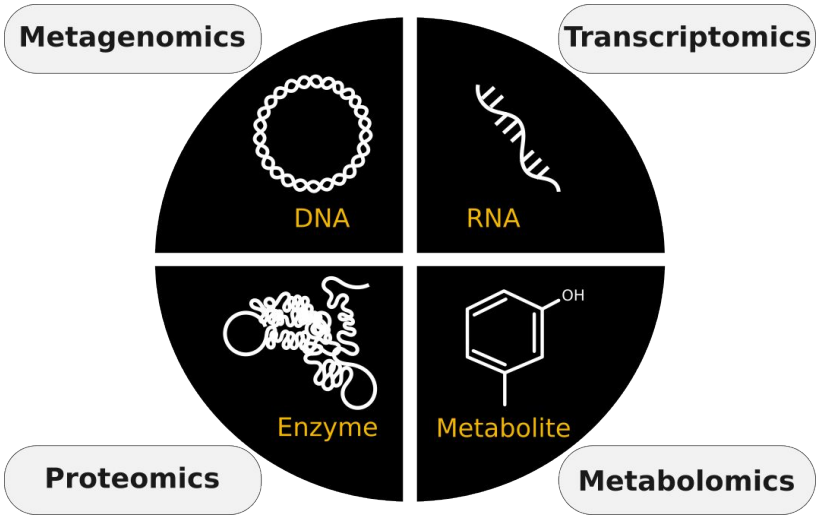
Homi-Lung – Project context

> *By integrating ecology, immunity, and time, HAP management can move from a reactive chase of pathogens to a proactive, personalised strategy, one that not only improves survival but also preserves resilience in the critically ill.*
> *Martin-Loaches I., J Crit Care 2026*

- **New paradigm focused on ecology and risk assessment**
- **Concept of *lungs interactome***
  Molecular, cellular and microbial interactions network of the host lung cells, virus, commensal and pathogenic bacteria
- **<u>Characterise key interactions in HAP patients lungs interactome</u>**

Homi-Lung – Data

- **From *HAP patients* and *healthy patients*** (expected in the following weeks :D)
- **Plasma, bronchoalveolar lavage samples**

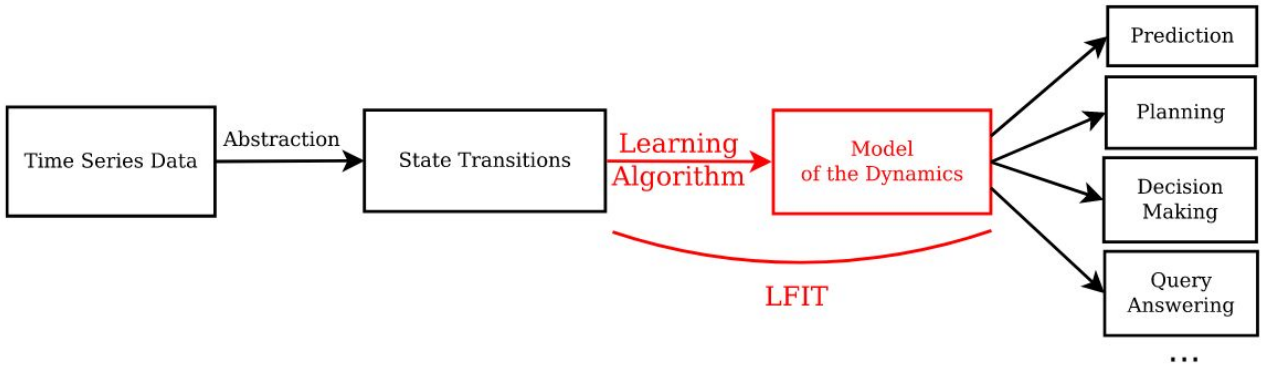


Multi-omics

- **Clinical** age, sex, comorbidity, …
- **(Meta)genomics** bacterial 16S, taxa, relative abundance
- **(Meta)transcriptomics** RNAseq
- **Proteomics**, **lipidome**, **metabolome**

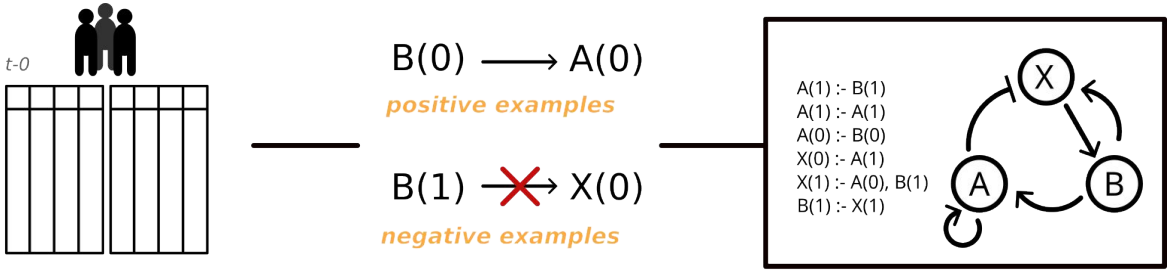
⚠ Noisy, highly dimensional, incomplete observations…

LFIT – Learning From Interpretation Transition

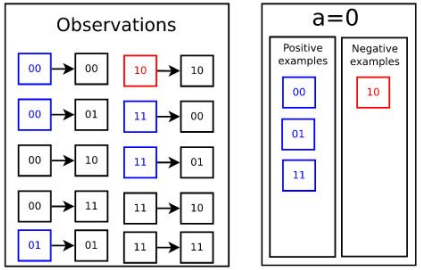


"Assuming a discretization of time series data of a system as state transitions, we propose a method to automatically model the system dynamics" Figure 1 from T. Ribeiro, M. Folschette, M. Magnin, and K. Inoue, "Learning any memory-less discrete semantics for dynamical systems represented by logic programs," Machine Learning, 2021

LFIT – Learning From Interpretation Transition



Inductive logic programming global framework, from clinical data to a set of logical rules and its representative Boolean network

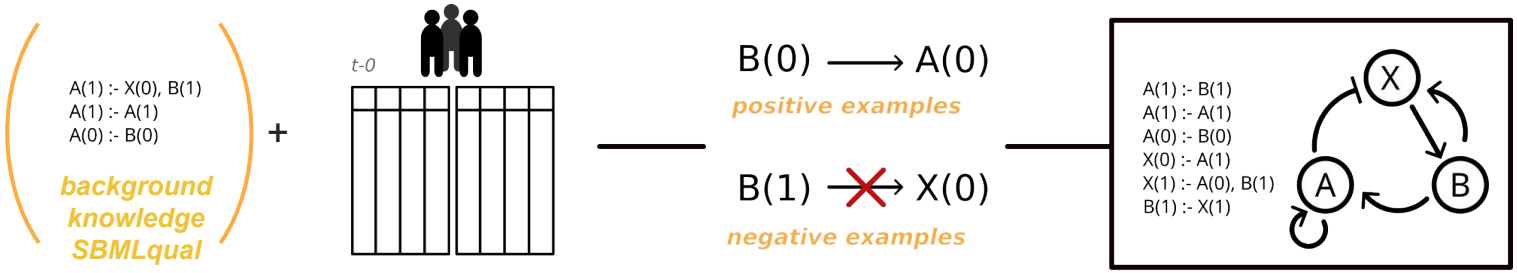


*Preprocessing of the general semantics state transition into positive/negative example of occurrence of variable a_t^0

- ***Main algorithm***
  - GULA
  - PRIDE
- **From biological observation and background knowledge, learn relational structure and rules**
- **Infer and model explainable mechanisms hypothesis**
  does not only focus on prediction of a given target, but extract hypothesis about relationships and their interdependence

*Figure 6, from T. Ribeiro et al, Machine Learning, 2021

LFIT – Learning From Interpretation Transition



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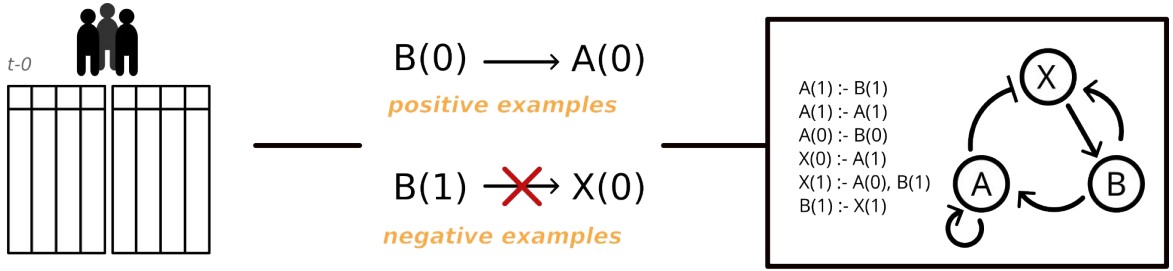
LFIT – … and the lung interactome



Characterize misunderstood relationships between biological elements and processes of the pulmonary system

A naive approach, nonetheless guided by prior knowledge on relevant features and host / bacterial mechanisms

Probabilistic logic programming (PLP)

LFIT learn structures and rules… but

- Noisy omics measurements
- Partial, context-dependent mechanisms
- Multiple plausible explanations

Sato's *Distribution Semantics*

T. Sato, "A Statistical Learning Method for Logic Programs with Distribution Semantics," L. S. Sterling, Ed., The MIT Press, 1995

- uncertainty of facts, rules are deterministic
- queries are probabilistic inference

```
0.6 :: infected(p1).
0.6 :: infected(p2).
0.7 :: virulent(b1).

pneumonia(P) :- infected(P), virulent(b1).
```

$$P(q) := \sum_{\substack{F' \subseteq F \\ \exists\theta\, F' \cup R \models q\theta}} P_F(F')$$

$$= \sum_{\substack{F' \subseteq F \\ \exists\theta\, F' \cup R \models q\theta}} \prod_{f_i \in F'} p_i \cdot \prod_{f_i \in F \setminus F'} (1 - p_i) \,.$$

q: *query*
R: *logical rules*
F: *probabilistic facts*
F' true facts
F' / F false facts

PLP – PRISM and ProbLog

PRISM (Sato and Kameya, 1997), and ProbLog (De Raedt, 2007)

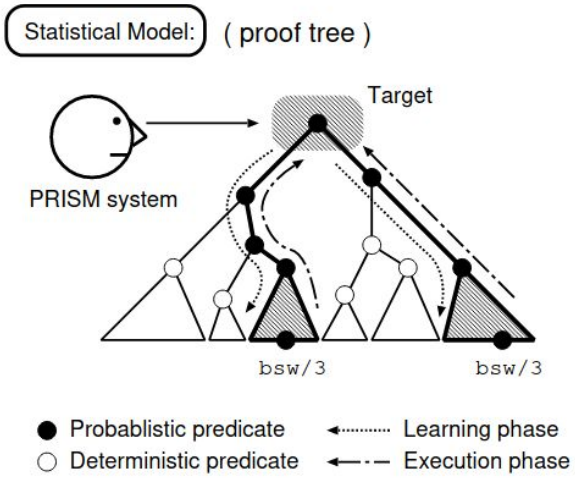
- adopt distribution semantics
- make the probability space explicit

PRISM

- **No overlapping proofs**
- **uses of *random switches***

```
gene(P,a):- bsw(1,P,1).
  % Sample binary_switch_1,
  % and if it is on, give gene a. Else
gene(P,b):- bsw(1,P,0),bsw(2,P,1).
  % sample binary_switch_2. If it is on,
gene(P,o):- bsw(1,P,0),bsw(2,P,0).
  %  give gene b. Else give gene o.
```

*Random switches in a blood type program



**A PRISM program

*Bloodtype exemple, from T. Sato, 1995
** PRISM program figure from T. Sato, 1995

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ProbLog

- **Accept overlapping proof**
- **Boolean monotone DNF**
- **Binary Decision Diagrams**

*Bloodtype exemple, from T. Sato, 1995

```
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  % Sample binary_switch_1,
  % and if it is on, give gene a. Else
gene(P,b):- bsw(1,P,0),bsw(2,P,1).
  % sample binary_switch_2. If it is on,
gene(P,o):- bsw(1,P,0),bsw(2,P,0).
  %  give gene b. Else give gene o.
```

*Random switches in a blood type program

```
0.3::road(r1)
0.9::road(r2)
path :- road(r1)
path :- road(r2)
```

A simple ProbLog program with overlapping proof

Aims and potential issues

Apply LFIT to homi-lungs data

- Identify discrepancies between healthy and HAP patients
- Characterize explainable relationships between clinical features and HAPs
- Evaluate interpretability of rules and structure
- Link with prior knowledge about relevant HAP actors

Bridge LFIT and probabilistic logic programs

- Link logical rules inference to PLP
- Support uncertain biological facts to assess new patients