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Evaluation of information processing capacity of bacterial metabolism through regression problem solving

BioRetroSynth and Ekinocs teams

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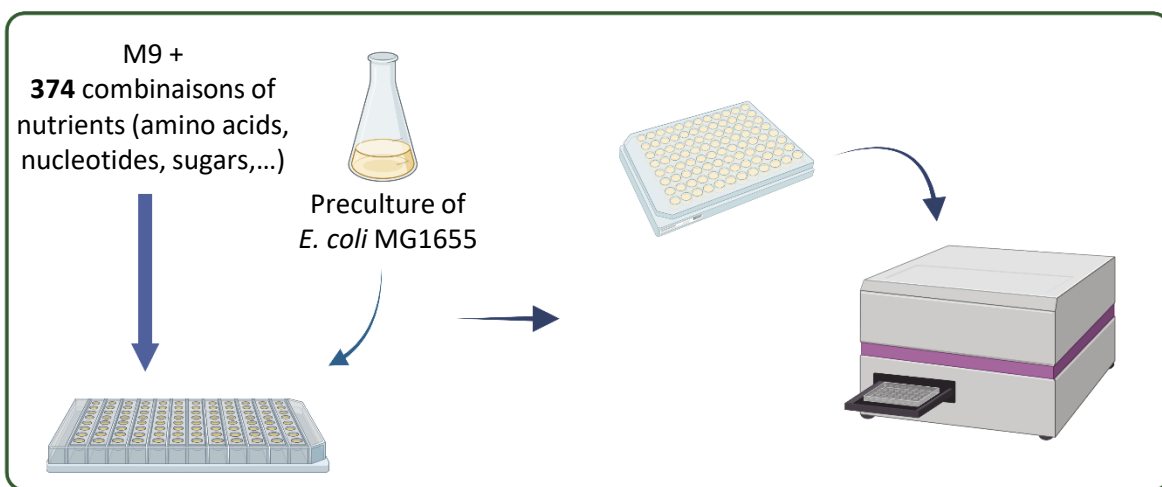
** co-last author

Context

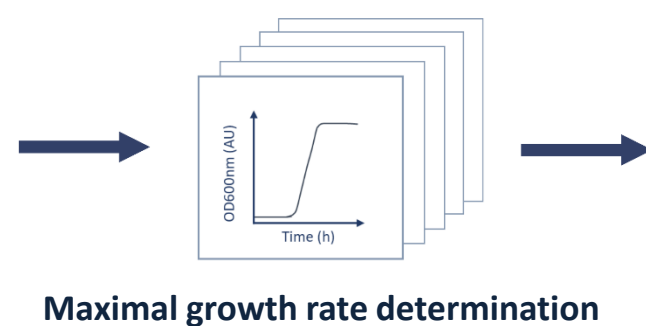
- Bacteria can **sense chemical variations** in their growth medium and **adapt their metabolism** accordingly^[1].
- Bacterial metabolism can therefore be compared to an **algorithm** taking as inputs the media composition and yielding as outputs metabolic fluxes describing a metabolic phenotype^[2].
- Our lab has focused on the perspective of metabolism as an information processing unit and previously developed a hybrid modelling method, the AMN for **Artificial Metabolic Networks**^[3] (see QRcode), which is able to **predict the maximal growth rate** and other metabolic fluxes from a **medium composition**.

➤ At present, we would like to go one step further and assess the capacity of *E. coli*'s metabolism by solving regression problems of increasing complexity.

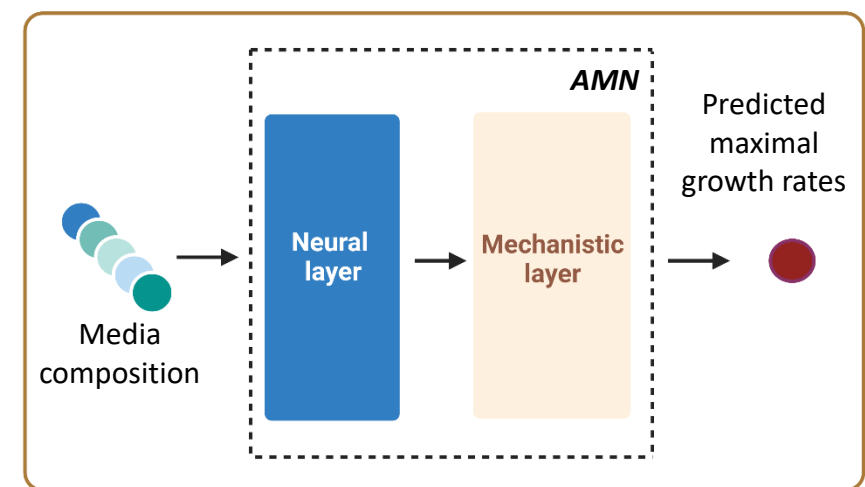
Construction of a metabolic model of *E. coli*



Acquisition of growth kinetics of *E. coli* MG1655 in 374 different media



Maximal growth rate determination



AMN training

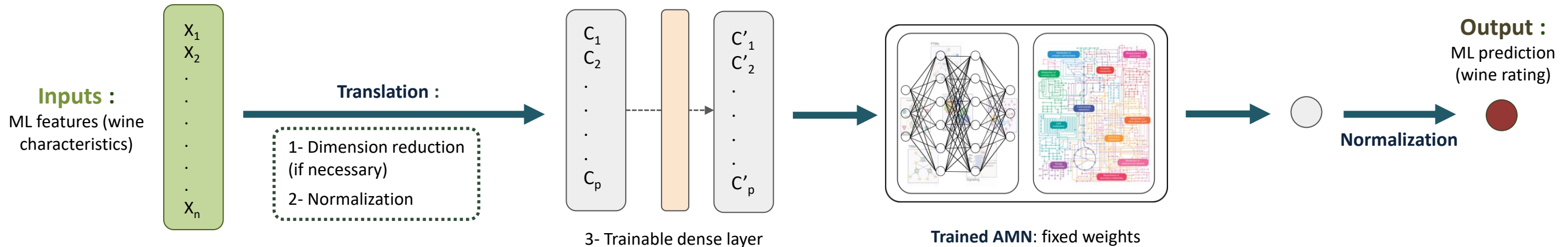
Problem-solving

Example : White wine quality dataset (score from 1 to 10)

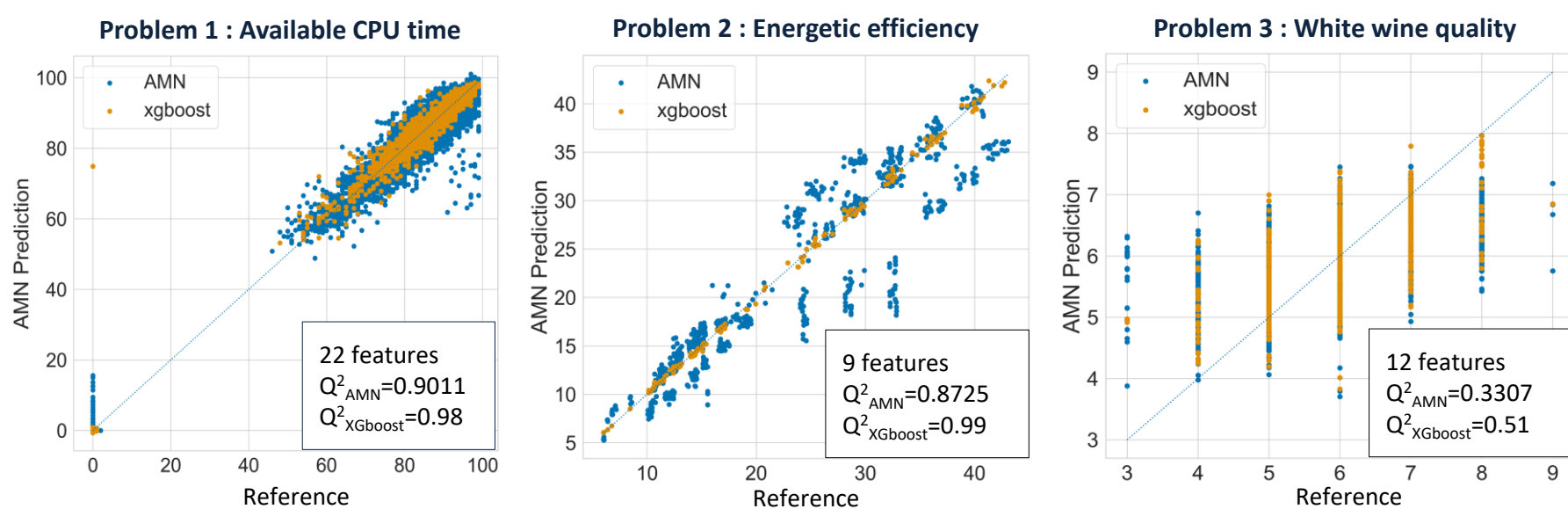
| Densité | pH | Sulfates |
|---------|------|----------|
| 0.9956 | 3.13 | 45 |

| Glucose | Pi | Ala |
|---------|------|------|
| 0.9956 | 0.43 | 0.25 |

| μ_{max} | Wine rating |
|-------------|---------------|
| 1,12 | 0,72 (7.2/10) |



Results



- The AMN model obtains satisfactory performance on regression problem, but it is less effective than XGBoost, the state of the art
- Open questions for the next steps:
 - What is the role of the trainable dense layer ?
 - What is the influence of feature pairing ?

Perspectives

- Experimental validation** : An independent test set will be converted into growth media for bacteria after training the dense layer. The maximal growth rates will be experimentally verified.
- Kinetic modelling** : The AMN is a hybrid model based on an artificial neural network (ANN) and flux-balance analysis (FBA), the latter being a stoichiometric model. Using a kinetic model will increase the number of outputs and may enable to solve more complex problems
- Computing more metabolic fluxes** : Same principle, by increasing the number of outputs, the model may be able to solve more complex problems.
- Performance on classification problems**

References

- [1] Zampieri, Mattia, Manuel Hörl, Florian Hotz, Nicola F. Müller, et Uwe Sauer. « Regulatory Mechanisms Underlying Coordination of Amino Acid and Glucose Catabolism in Escherichia Coli ». *Nature Communications* 10, n° 1 (26 juillet 2019): 3354. <https://doi.org/10.1038/s41467-019-11331-5>.
- [2] Lahoz-Beltra, Rafael, Jorge Navarro, et Pedro C. Marijuán. « Bacterial computing: a form of natural computing and its applications ». *Frontiers in Microbiology* 5 (25 mars 2014). <https://doi.org/10.3389/fmicb.2014.00101>.
- [3] Faure, Léon, Bastien Mollet, Wolfram Liebermeister, et Jean-Loup Faulon. « A Neural-Mechanistic Hybrid Approach Improving the Predictive Power of Genome-Scale Metabolic Models ». Preprint. *Systems Biology*, 11 janvier 2022. <https://doi.org/10.1101/2022.01.09.475487>.