Contrats doctoraux 2026

Titre du projet de thèse : Thermodynamic Efficiency and Trade-off principles in Cellular Metabolism

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Résumé du projet de thèse (en 20 lignes maximum) :

To maintain their organization far from thermodynamic equilibrium, living systems ground their functioning in metabolism, which plays a central role in the efficient management of energy and matter flows [1]. Metabolic networks convert nutrients into energy and biomass while ensuring an optimal allocation of resources in steady-state conditions. They must also remain sufficiently flexible and tightly regulated to anticipate and respond to environmental fluctuations, particularly regarding nutrient availability. Behaviors such as overflow metabolism — in which sugars are only partially oxidized in nutrient-rich conditions [2,3] — or diauxic shifts, marked by a latency/lag phase between two nutrient uptake regimes [4], illustrate the inherent trade-offs underlying the metabolic functioning of living cells.
This thesis project aims to investigate how kinetic and thermodynamic constraints shape the diversity and optimality of metabolic strategies [5], and how they account for specific properties — including the apparent inefficiency — associated with overflow metabolism or latency. The student will develop models of metabolic networks using tools from nonequilibrium thermodynamics, network theory, and data analysis.
This project is part of an experimental collaboration with the Toulouse Biotechnology Institute, which works on bacterial and yeast model species [6]. The study of these questions is relevant both to the physical principles underlying living systems and to applications such as bioprocess optimization or understanding the metabolic adaptations of cancer cells.

[1] Yang et al (2021) Physical bioenergetics: Energy fluxes, budgets, and constraints in cells. *PNAS*, *118*, e2026786118
[2] Basan et al (2015) Overflow metabolism in Escherichia coli results from efficient proteome allocation. *Nature*, *528*, 99-104.
[3] Gosselin et al (2025) Overflow metabolism in bacterial, yeast, and mammalian cells: different names, same game. Mol Syst Biol 21: 1419 - 1433
[4] Basan et al (2020) A universal trade-off between growth and lag in fluctuating environments. *Nature*, *584*, 470-474.
[5] Pfeuty (2024) Free-energy transduction mechanisms shape the flux space of metabolic networks. *Biophysical J*, *123*, 3600-3611.

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[6]Millard et al (2021) Control and regulation of acetate overflow in Escherichia coli. *Elife*, *10*, e63661

Date de recrutement envisagée : 09/01/2026

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Remarques/commentaires supplémentaires :