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Title of the internship: Membrane crowding and the evolution of optimal proteome allocation

Duration and available dates for the internship: 8 weeks to 6 months, starting in January 2026 at the earliest

Short description of the host team (5 lines):

Our group's research focuses on understanding the eco-evolutionary dynamics governing the composition of the gut microbiota. We are currently particularly interested in the mechanisms that allow the maintenance of the microbial community diversity, a key indicator of health [1], [2], [3]. To study these questions, we use mathematical modeling, combining analytical and numerical techniques with stochastic simulations. We also exchange frequently and collaborate with experimenters to inform our models' development.

Description of the internship project (10 lines):

Natural selection favours organisms that are better at reproduction and survival. In order to reproduce, organisms need to synthesize molecules (*e.g.,* proteins). Synthesis requires in turn both energy and building blocks. These building blocks can either be produced through metabolism, or they can be taken up from the environment [4]. But in which cases should a cell choose one over the other solution in order to maximise its fitness? Such a choice crucially depends on: 1) which nutrients are present in the environment, and with which temporal pattern, and 2) the relative costs of uptake versus *de novo* production. Since uptake from the environment only requires the synthesis of transporter proteins, it should always be favoured when the environment is rich enough to sustain the cell's needs. However, membranes are densely packed and hence the available membrane space is limited [5], [6]. This implies the existence of an environment-dependent tipping point where the cell should switch from uptake to *de novo* production. **Here, we propose to derive a rule that governs this proteome allocation choice and to study how this may create opportunities for the evolution of microbial diversity.**

Expected results / deliverables of the internship (5 lines):

During this internship, the intern will develop an ODE model (similar to [7]) in order to expand previous results [4] by accounting for the existence of multiple resources in the environment. Notably, the student will introduce the constraint of a limited membrane space in the model and test how it affects the optimal allocation between uptake and *de novo* synthesis. Analytical approximations may first be studied to gain a better understanding of the problem, before relying on numerical simulations for more realistic scenarios. It is thus expected that the student will have a strong mathematical background and the ability to develop numerical models (e.g., using R or Python).

Interdisciplinarity and disciplines involved (5 lines)

This work is at the crossroads of evolutionary ecology, biochemistry and cell biology. The student will develop mathematical models derived from first principles to help bridge the gap between these fields. Depending on her/his background, the student will thus combine an evolutionary approach with applied maths (eg., game theory) and one or several different fields including systems biology and ecology. As the internship is based in a microbiology lab, the intern will also benefit from the feedback of experimenters specialised in cell biology.

Contact: florence.bansept@univ-amu.fr and florian.labourel@univ-amu.fr

References

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[3] V. M. Marquioni, A.-C. Hofacker, J. V. Villavicencio, et F. Bansept, « Optimizing microbial intake helps to maintain the gut microbiome diversity », *bioRxiv*, p. 2025.03.05.641598, janv. 2025, doi: 10.1101/2025.03.05.641598.
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[5] M. Löwe, M. Kalacheva, A. J. Boersma, et A. Kedrov, « The more the merrier: effects of macromolecular crowding on the structure and dynamics of biological membranes », *FEBS J.*, vol. 287, n° 23, p. 5039-5067, déc. 2020, doi: 10.1111/febs.15429.
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[7] F. J. F. Labourel, V. Daubin, F. Menu, et E. Rajon, « Proteome allocation and the evolution of metabolic cross-feeding », *Evolution*, vol. 78, n° 5, p. 849-859, mai 2024, doi: 10.1093/evolut/qpae008.