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Title of the internship: Modeling cell membrane crowding with Random Sequential Adsorption

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:

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. To study these questions, we use mathematical modeling, combining analytical and numerical techniques with stochastic simulations. We also exchange frequently and collaborate with experimentalists to inform our models' development.

Description of the internship project:

Cell membranes are composed of a double layer of phospholipids, separating their inner content from the external medium, and are embedded with a myriad of proteins [1]. These proteins can function as enzymes catalyzing chemical reactions, as signaling structures, or as cellular gatekeepers, thus being essential for nutrient uptake and ionic balance. Most of them are specifically designed for unique processes; for example, proteins that transport glucose do not uptake acetate, and vice versa. Consequently, cell fitness in different environments largely depends on its membrane proteins. To overcome such dependency, one could imagine a cell producing every type of protein, thus being prepared to face any environmental condition — but this is not observed. In fact, because the membrane has a finite size, there is a maximal number of proteins that can be placed on it, and deciding which proteins should be produced is not a trivial decision for the cell. Indeed, cell membranes are highly crowded, with occupation fractions by proteins and other molecular machineries estimated to vary widely from 25% to 80% [2]. This crowding phenomenon, in turn, affects the efficiency of essential cellular processes, making its characterization a particularly relevant task in order to understand cellular physiology and even evolution.

Although membrane protein packing is the result of a variety of biochemical processes, a simple mathematical framework, known as Random Sequential Adsorption (RSA), can be used as a baseline model to describe it [3], [4] . In this model, a sequence of attempts to randomly allocate objects on a surface without overlap is performed, yielding an average occupation fraction that depends on geometrical parameters. Since distinct transmembrane proteins cannot occupy the same position on a cell membrane, RSA provides a suitable null mechanism to study membrane occupation in different cell geometries. In this project, we investigate an RSA dynamics with desorption, asking whether its simplifying assumptions can feasibly describe observed occupation fractions.

Expected results / deliverables of the internship:

At the end of the internship, the student is expected to have learned how to perform stochastic simulations, a widely used technique in mathematical biology. The primary goal of this project is to determine the occupation fraction as a function of different parameters (such as the cell and protein geometries and adsorption/desorption rates), and a critical analysis of the obtained results in the context of cell biology is also expected.

Interdisciplinarity and disciplines involved:

This project relies on stochastic processes theory, computational simulations, and cell biology.

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References

[1] B. Alberts, A. Johnson, J. Lewis, M. Raff, K. Roberts, and P. Walter, *Molecular Biology of the Cell*, 4th ed. Garland Science, 2002.

[2] M. Löwe, M. Kalacheva, A. J. Boersma, and A. Kedrov, "The more the merrier: effects of macromolecular crowding on the structure and dynamics of biological membranes," *FEBS J.*, vol. 287, no. 23, pp. 5039–5067, 2020, doi: 10.1111/febs.15429.

[3] J. Talbot, G. Tarjus, P. R. Van Tassel, and P. Viot, "From car parking to protein adsorption: an overview of sequential adsorption processes," *Colloids Surf. Physicochem. Eng. Asp.*, vol. 165, no. 1, pp. 287–324, May 2000, doi: 10.1016/S0927-7757(99)00409-4.

[4] P. Kubala, P. Batys, J. Barbasz, P. Weroński, and M. Cieśla, "Random sequential adsorption: An efficient tool for investigating the deposition of macromolecules and colloidal particles," *Adv. Colloid Interface Sci.*, vol. 306, p. 102692, Aug. 2022, doi: 10.1016/j.cis.2022.102692.