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Using phages to control the gut microbiome: a mathematical modeling approach

Duration and available dates for the internship:

7 weeks to 6 months, starting in January 2025 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:

Phages are viruses that infect bacteria. They are among the most abundant and diverse microorganisms on Earth (1). They can be found everywhere, from oceanic waters to mammals' guts; wherever bacteria live, phages are likely to be found. Since their discovery at the beginning of the 20th century, their use as an alternative to antibiotics has shown promising results. Because phages can target specific bacteria and replicate in their presence, they constitute a powerful tool in fighting against diseases in the era of ever-increasing antibiotics resistance. However, the eco-evolutionary mechanisms that govern phage-bacteria interactions are still not fully understood, especially in the gut, where the phage-to-bacteria ratio is much higher than in other studied environments, like the ocean. The present internship project proposes the development of a mathematical model, based on (2), of phage-bacteria interactions in the gut environment, aimed to understand under which conditions (replication, adsorption and outflow rates, carrying capacity) phage therapy is a feasible control method of bacterial infections in the gut.

Expected results / deliverables of the internship:

At the end of the internship, the student is expected to have learned how to analyze, analytically and numerically, sets of differential equations which are frequently used to model ecological dynamics. The development and analysis of a model of phage-bacteria interaction in the gut is the primary product of this internship and the characterization of a feasible controlled state within the proposed model is the final goal.

Interdisciplinarity and disciplines involved:

This project is based on dynamical systems techniques applied to the ecology of phages and bacteria in the gut environment. Therefore, aspects of phage biology and of the gut microbiome, the analysis of non-linear differential equations and numerical integration methods are involved in the development of the proposed project.

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References

1. *Mutualistic interplay between bacteriophages and bacteria in the human gut.* **Shkoporov, A. N., Turkington, C. J., & Hill, C.** 12, 2022, Nature Reviews Microbiology, Vol. 20, pp. 737-749.
2. *Modeling the synergistic elimination of bacteria by phage and the innate immune system.* **Leung, Chung Yin (Joey) and Weitz, Joshua S.** 2017, Journal of Theoretical Biology, Vol. 429, pp. 241-252.