

Towards a Digital Twin of the Gut Microbiota: Multiscale Modeling and Host Interaction

Eleonora PASTREMOLI, INRAE - Jouy-en-Josas

Béatrice LAROCHE, INRAE - Jouy-en-Josas

Lorenzo SALA, INRAE - Jouy-en-Josas

The human gut microbiota plays a crucial role in many physiological processes and its imbalance is linked to various diseases. Understanding the complex interactions between host and microbiota is therefore essential to advancing knowledge in health and disease.

In this work, I present a multiscale computational framework that couples a two-dimensional colon model [4, 3] based on the assumption of axisymmetry with a one-dimensional crypt model [1, 2] to simulate host–microbiota interactions.

The colon model is based on a strongly coupled system of partial differential equations (PDEs), including advection–diffusion–reaction (ADR) equations for solid and dissolved components and the Stokes equation to model intestinal transport.

This system is discretized and solved using the FEniCSx finite element library.

The crypt model, in contrast, is governed by a degenerate parabolic equation that describes cell migration along the crypt axis.

The two models are coupled through the imposition of biologically motivated boundary conditions at the interface between the crypt and colon domains. In this region, the finite element mesh of the colon domain is locally refined to accurately capture the exchange of fluxes and preserve numerical stability across scales.

To enhance biological realism, I introduced a double mucus layer structure : a protective Inner Mucus layer and a softer Outer Mucus layer where bacterial populations can accumulate.

Additionally, a more anatomically realistic 3D colon geometry was implemented, including haustral folds, which affect flow and metabolite distribution.

These developments lay the groundwork for future applications, including the integration of patient-specific data in a digital twin framework.

- [1] L. Darrigade, M. Haghebaert, C. Cherbuy, S. Labarthe, B. Laroche. *A pdmp model of the epithelial cell turn-over in the intestinal crypt including microbiota-derived regulations*. Journal of Mathematical Biology, **84**(7), 60, 2022.
- [2] M. Haghebaert, B. Laroche, L. Sala, S. Mondot, J. Doré. *A mechanistic modelling approach of the host–microbiota interactions to investigate beneficial symbiotic resilience in the human gut*. Journal of the Royal Society Interface, **21**(215), 20230756, 2024.
- [3] S. Labarthe, B. Polizzi, T. Phan, T. Goudon, M. Ribot, B. Laroche. *A mathematical model to investigate the key drivers of the biogeography of the colon microbiota*. Journal of theoretical biology, **462**, 552–581, 2019.
- [4] R. Muñoz-Tamayo, B. Laroche, E. Walter, J. Doré, M. Leclerc. *Mathematical modelling of carbohydrate degradation by human colonic microbiota*. Journal of theoretical biology, **266**(1), 189–201, 2010.