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A MULTISCALE COMPUTATIONAL FRAMEWORK FOR GUT MICROBIOTA-HOST INTERACTIONS

Eleonora Pastremoli, Béatrice Laroche, Lorenzo Sala

MaIAGE, Université Paris-Saclay, INRAE, Jouy-en-Josas, France
eleonora.pastremoli@inrae.fr

Introduction

The gut microbiota:

- plays a vital role in **physiological processes**
 - imbalance is linked to numerous **diseases**
 - hosts more than **500 bacterial species**.
- Understanding interactions between **host** and **gut microbiota** is crucial.

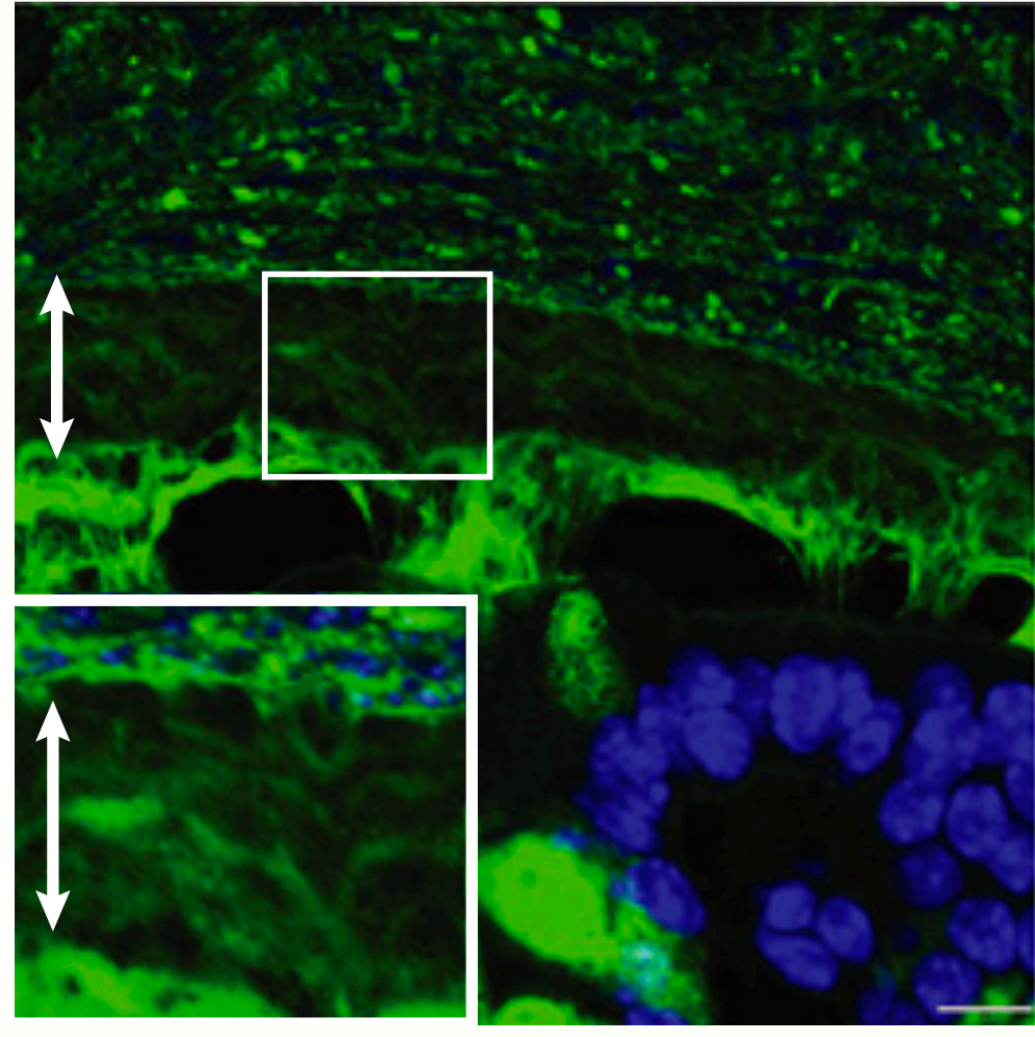


Figure 1: Taken from: Jakobsson, Hedvig E et al. "The composition of the gut microbiota shapes the colon mucus barrier." *EMBO reports* vol. 16,2 (2015).

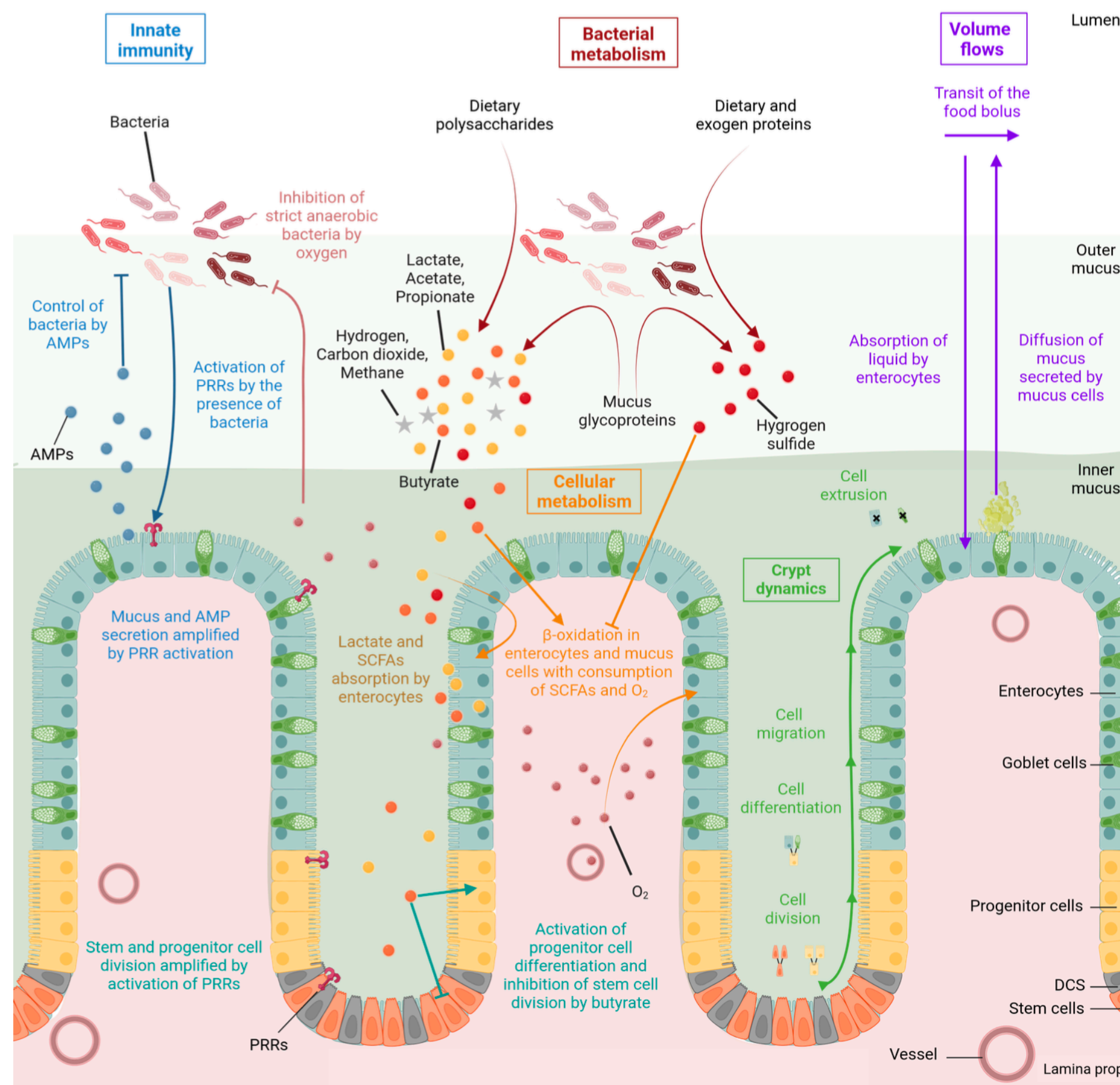
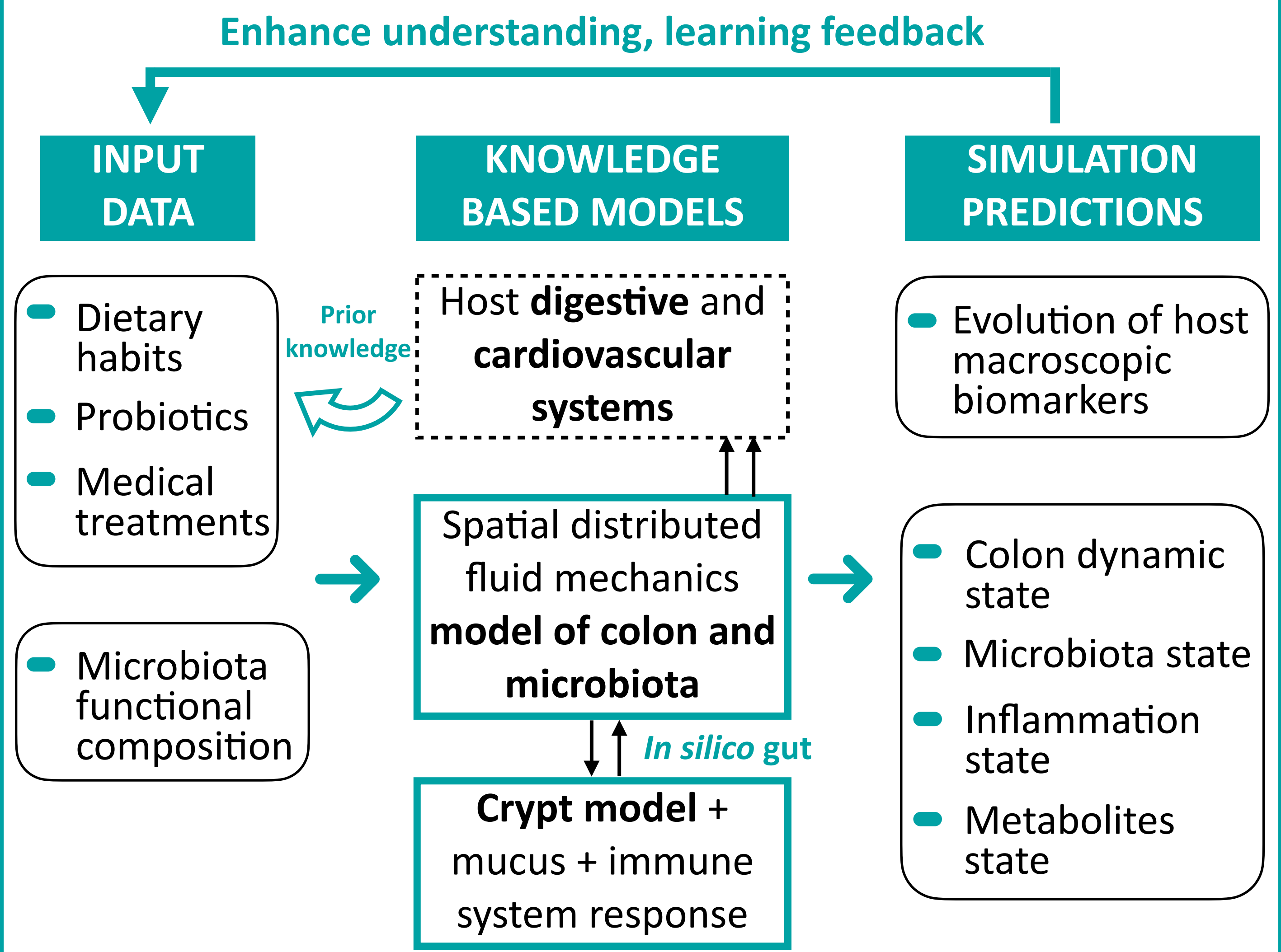


Figure 2: Taken from [3].

Objective

Aim: establish a **computational framework** that integrates models at different scales to simulate host-gut microbiota symbiosis.



Model

COLON MODEL

- Using the **FEniCSx** library, I have enriched an existing macro-scale model of the colon [1,4].

Mass conservation

$$\partial_t f_i - \text{div}(\sigma \nabla f_i) + \text{div}(f_i u) = F_i$$

$$(-\sigma \nabla f_i + f_i u) \cdot n = \gamma_{f_i}$$

Stokes model for the average fluid motion

$$\nabla p - \text{div} \left(\frac{\mu(f)}{2} (\nabla u + \nabla u^T) \right) = 0$$

$$\begin{cases} u \cdot n = \sum_{i \in I_c} \gamma_{f_i} + U_{\text{per},r} \\ u \cdot n_z = U_{\text{per},z} \\ u \cdot n_\theta = 0 \end{cases}$$

$$\mu(f) = \max(\mu_m(f_m(x, z, t)), \mu_l(f_l(x, z, t)))$$

$$\mu_m(f_m) = \mu_{m,\min} + (\mu_{m,\max} - \mu_{m,\min}) \frac{f_{m,\text{hr}}^{f_m}}{f_{m,\text{hr}}^{f_m} + f_{m,\text{hr}}^{f_m}}$$

$$\mu_l(f_l) = \mu_{l,\max} - (\mu_{l,\max} - \mu_{l,\min}) \frac{f_{l,\text{hr}}^{f_l}}{f_{l,\text{hr}}^{f_l} + f_{l,\text{hr}}^{f_l}}$$

Figure 3: Adapted from [1].

- I incorporated a newly identified **Hard Mucus layer** into the model.

Time evolution of volume fraction of Hard Mucus:

$$\partial_t f_{hm} - \text{div}(\sigma_{hm} \nabla f_{hm}) + \text{div}(f_{hm} u_{hm}) = 0 \quad \text{in } \Omega$$

Boundary conditions:

$$\begin{cases} (-\sigma_{hm} \nabla f_{hm} + f_{hm} u_{hm}) \cdot n = 0 & \text{on } \Gamma_{in} \\ (-\sigma_{hm} \nabla f_{hm} + f_{hm} u_{hm}) \cdot n = -0.2 \cdot q_m \cdot N_{crypt} \cdot \overline{N}_{gc} & \text{on } \Gamma_m \\ (-\sigma_{hm} \nabla f_{hm} + f_{hm} u_{hm}) \cdot n = 0 & \text{on } \Gamma_{out} \end{cases}$$

where N_{crypt} : crypt density per surface unit,

$$u_{hm} = \begin{bmatrix} U_a \\ 0 \end{bmatrix},$$

$$U_a = \begin{cases} \frac{B-A}{R_{gut} - r_0} \cdot r + A & \text{if } r < R_{gut} - r_0 \\ 0 & \text{if } r \geq R_{gut} - r_0 \end{cases}$$

CRYPT MODEL

- I coupled this enriched model with a pre-existing **crypt model** [2, 3].

Migration of cell type $\ell \in \{sc, dcs, pc, gc, ent\}$:

$$\partial_t \rho_\ell - W \partial_z (\varphi(z) \rho_\ell \partial_z \rho) = H_\ell(\rho_{sc}, \rho_{pc}, D \times \rho, z),$$

$$\rho_\ell(0, t) = \rho_\ell^{bot},$$

$$\partial_z \rho_\ell(Z_{max}, t) = 0.$$

Evolution of chemical $i \in \{but, O_2\}$:

$$\partial_t c_i - \sigma_i \partial_{zz} c_i = -s_i K_i(c_{O_2}, c_{but}, \rho_{ent}, \rho_{gc})$$

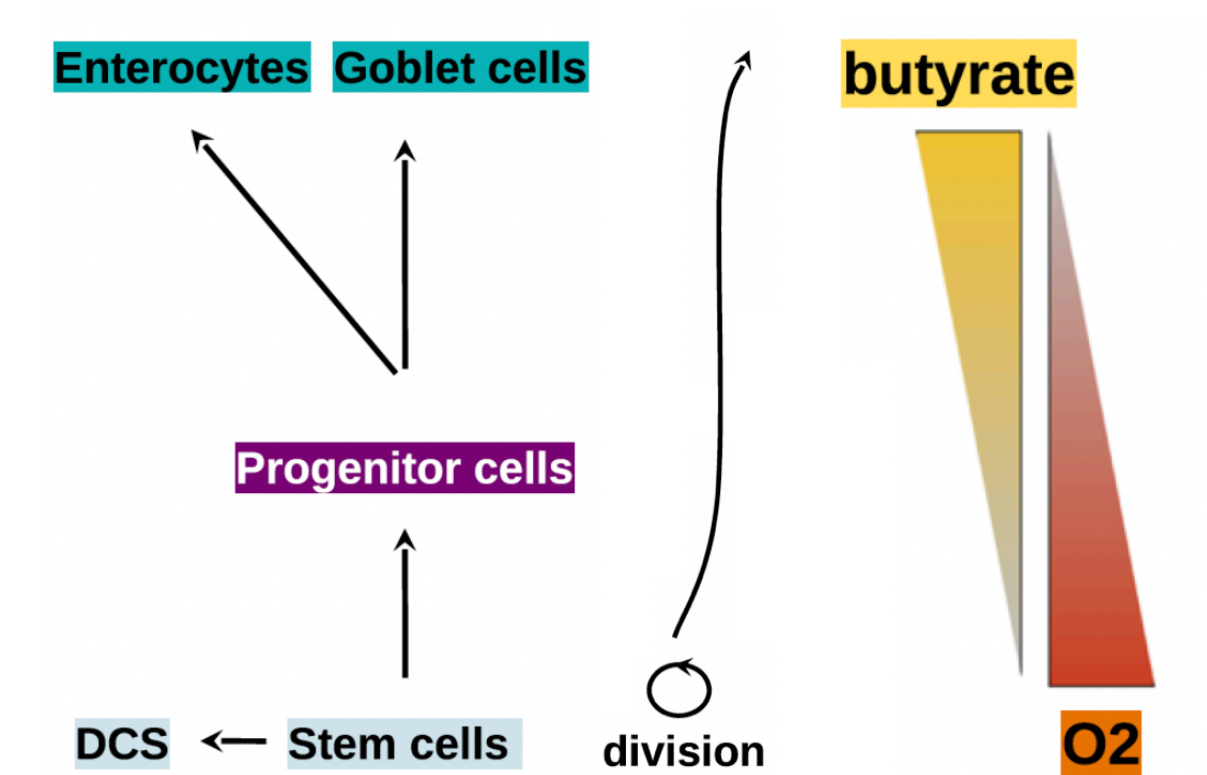


Figure 4: Taken from [2].

Results

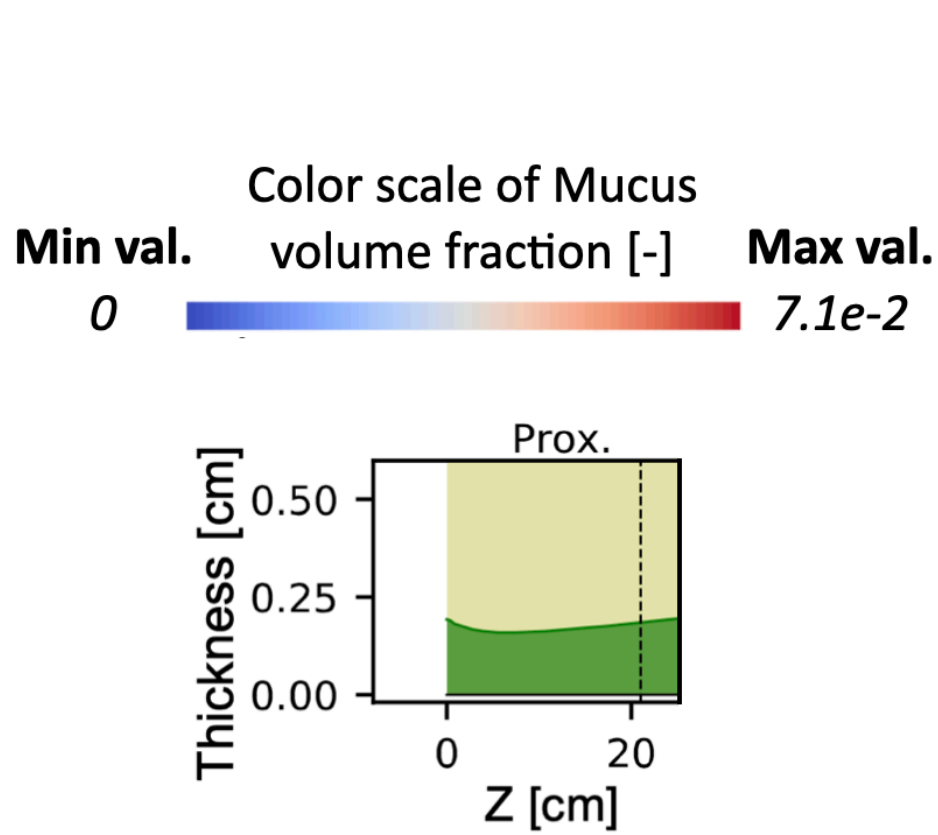


Figure 5: Taken from [1]. Spatial distribution of the mucus in the pre-existing model of the colon.

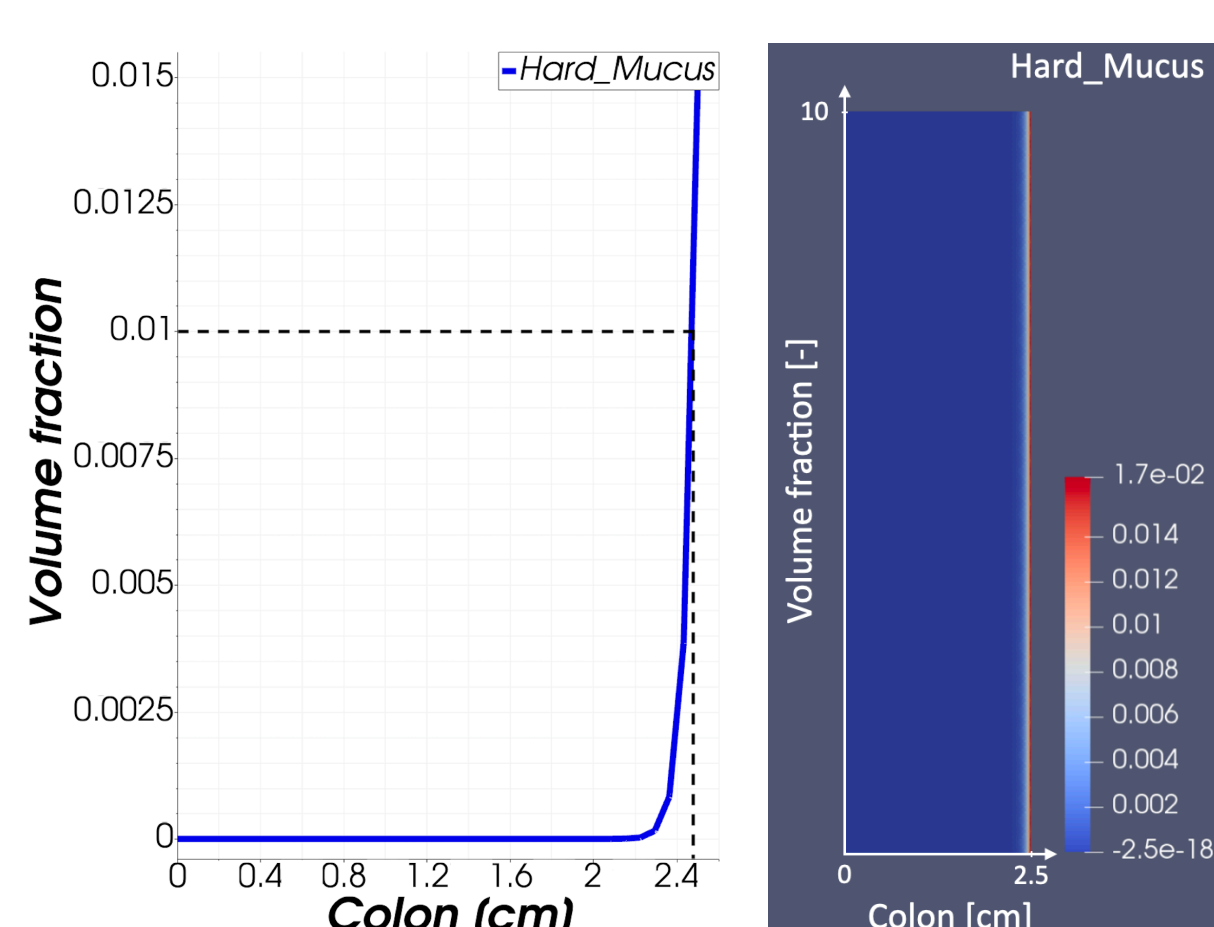


Figure 6: Hard Mucus layer thickness ~ 0.03 cm (left) and its volume fraction (right).

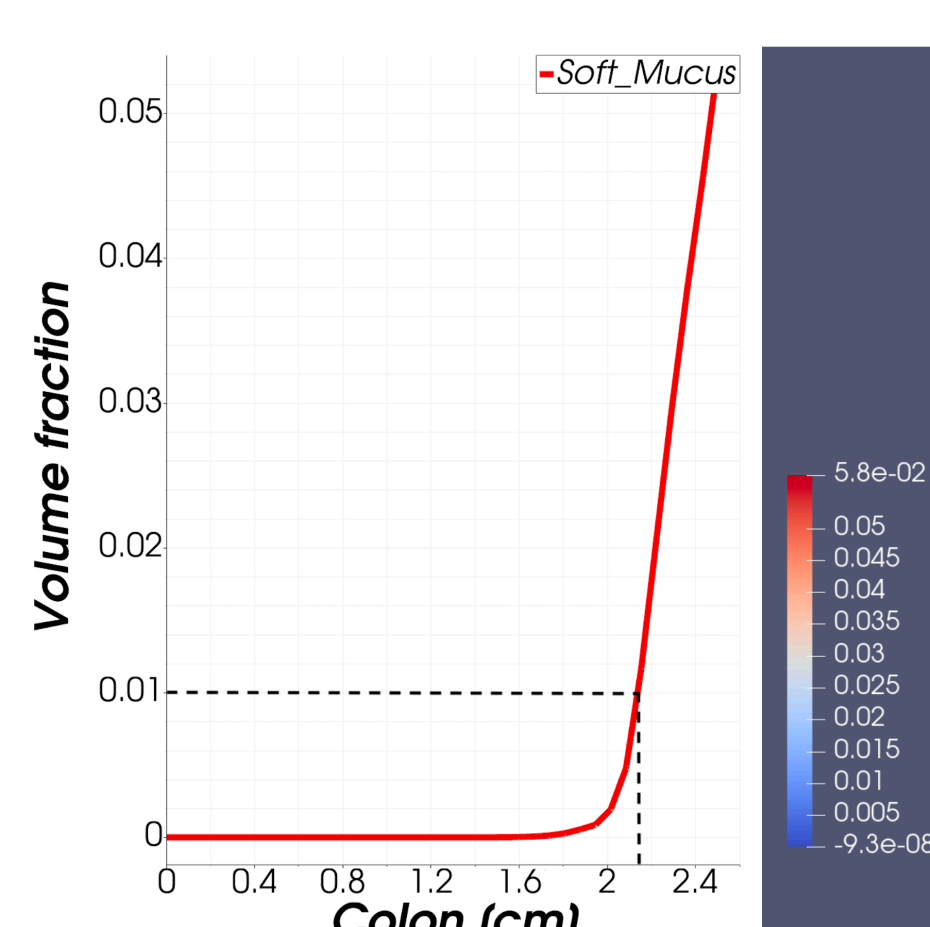


Figure 7: Soft Mucus layer thickness ~ 0.365 cm (left) and the color scale of its volume fraction.

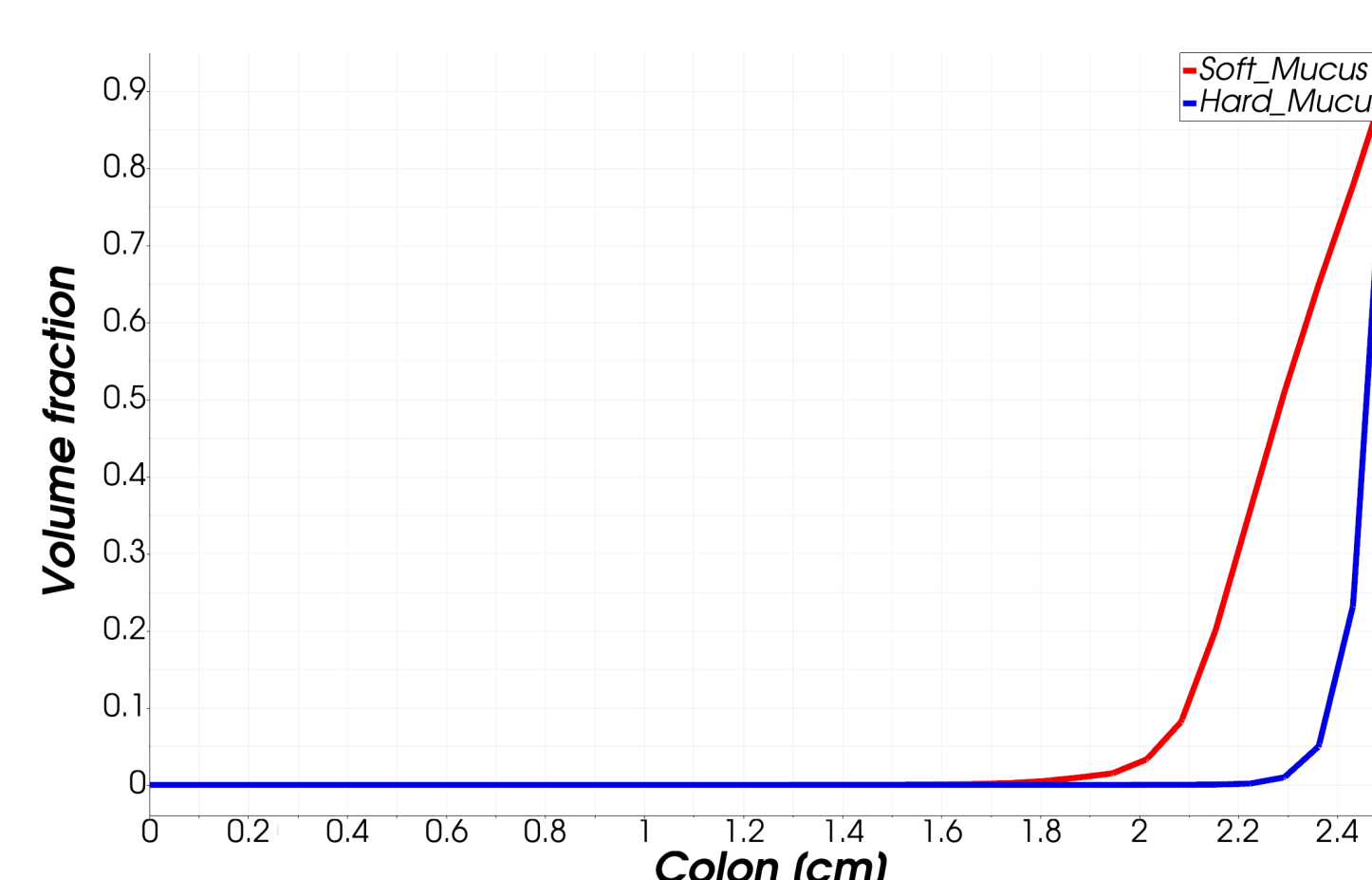


Figure 8: Comparison between Soft and Hard Mucus layer radial section normalised.

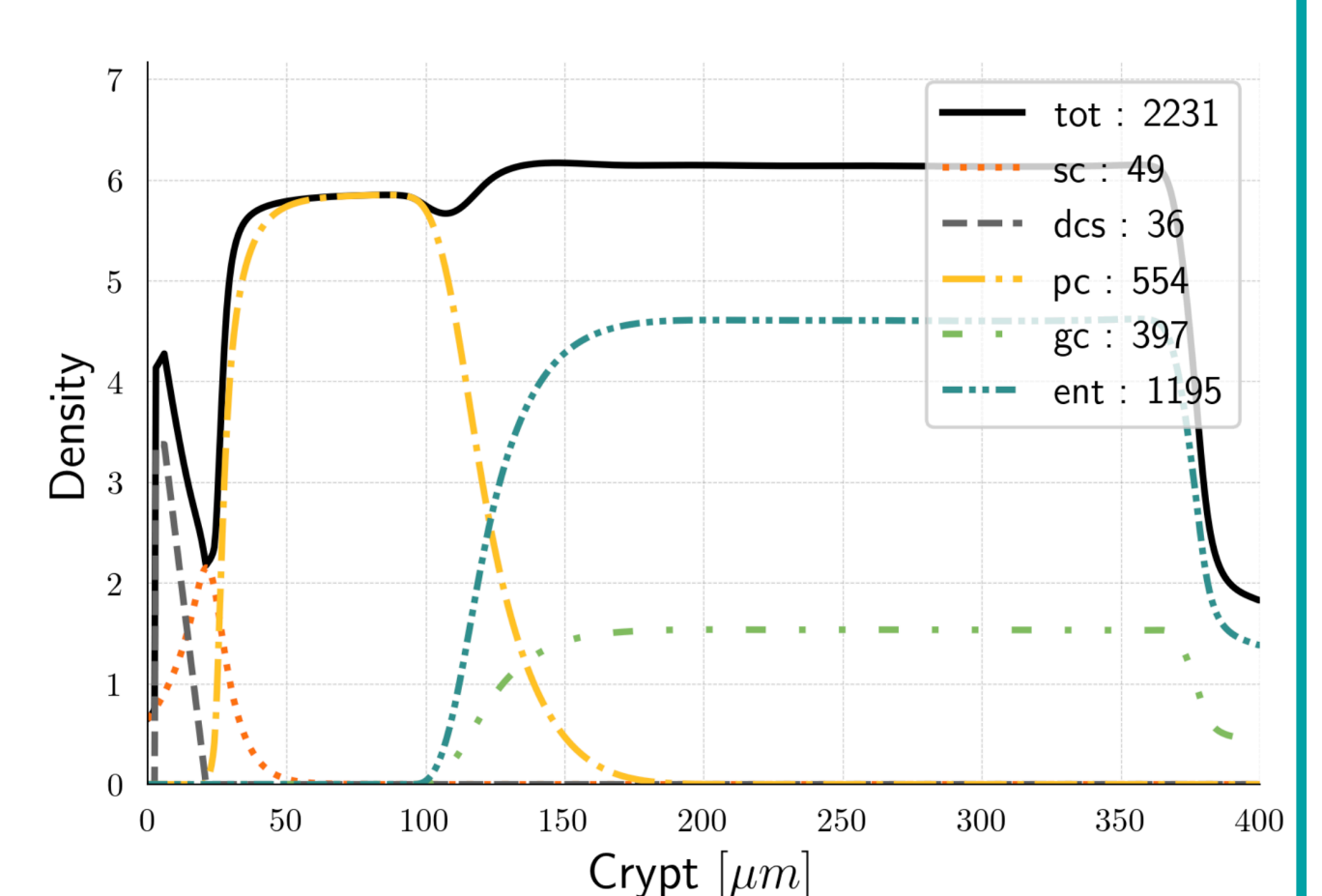


Figure 9: Taken from [3]. Cell densities along the crypt.

Conclusion and Perspectives

- The **results** obtained are **consistent** with biological knowledge and previous models.
- This framework enables the establishment of a **virtual laboratory** to test hypotheses.

Current efforts:

- Enhancing the computational efficiency by developing **MOR techniques**.
- Enabling efficient **SA, parameter estimation** and **biological data integration**.

Bibliography

- [1] Labarthe, Simon, et al. "A mathematical model to investigate the key drivers of the biogeography of the colon microbiota." *Journal of theoretical biology* 462 (2019): 552-581.
- [2] Darrigade, Léo, et al. "A PDMP model of the epithelial cell turn-over in the intestinal crypt including microbiota-derived regulations." *Journal of Mathematical Biology* 84:7 (2022): 60.
- [3] Haghebaert, Marie, et al. "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 (2024): 20230756.
- [4] Muñoz-Tamayo, Rafael, et al. "Mathematical modelling of carbohydrate degradation by human colonic microbiota." *Journal of theoretical biology* 266.1 (2010): 189-201.