Modeling transport of antibodies in the digestive tract

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In the digestive tract, there are commensal bacteria which are beneficial to the host, but also pathogenic bacteria that can invade. How does the host control its microbiota? One of the tools for the host is its immune system. The main effector of the adaptive immune response in the gut is a type of antibodies, secreted Immunoglobulin A (sIgA). This molecule bind very specifically a target, for instance a pattern on the surface of a bacterial strain, but once bound to bacteria, sIgA do not kill nor prevent bacteria from replicating, but can bind them together [1, 2]. This system can also be seen as a physico-chemical system, with a complex hydrodynamic flow, and spatially varying concentration of reactive molecules and their targets.

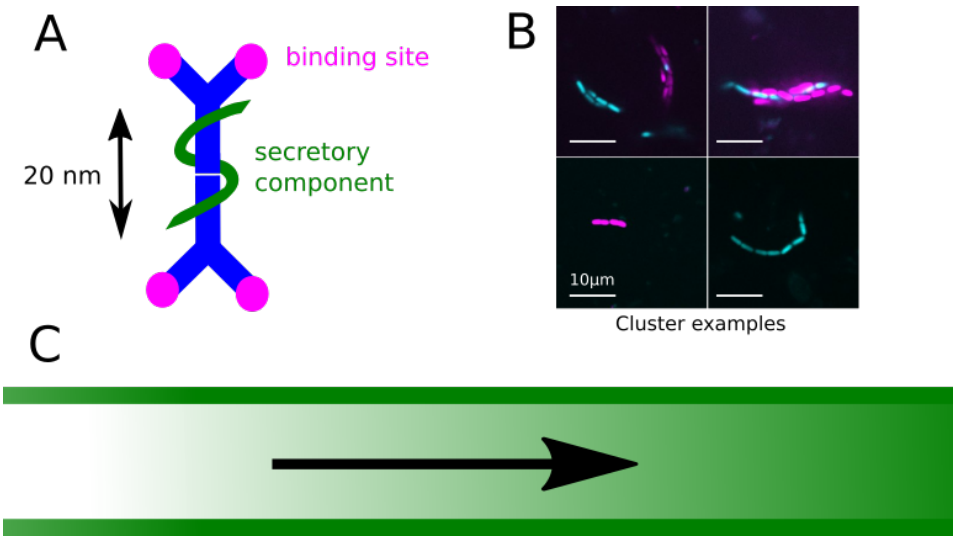

Figure 1: A. Schematic representation of an sIgA. B. Experimental microscopy images of bacterial clusters mediated by sIgA. C. Simplified 1-dimneisonal model for the digestive tract.

There are many open questions about sIgA, but they are hard to tackle quantitatively, because there is so far no spatial model of sIgA concentration along the digestive tract, taking into account how antibodies are transported from one part of the digestive tract to the next. Such a model must also take into account which proportion of antibodies are free and which proportion of antibodies are attached to their target, in particular when antibodies'target are bacteria, which concentration varies widely along the digestive tract. Our hypothesis is that the physical description of this system, a system with a flow and complex mixing, inhomogeneous antibody production, and reaction with targets, will enable to understand the profile of antibody concentration, and how they interact with bacteria.

The aim is to start building a first spatial model, representing the complex gut transport unidimensionally, with a mean velocity and an effective diffusion, representing mixing, using a combination of numerical calculations and analytical approximations.

References

[1] **Moor, K., M. Diard, M. E. Sellin, B. Felmy, S. Y. Wotzka, A. Toska, E. Bakkeren, M. Arnoldini, F. Bansept, A. D. Co, T. Völler, A. Minola, B. Fernandez-Rodriguez, G. Agatic, S. Barbieri, L. Piccoli, C. Casiraghi, D. Corti, A. Lanzavecchia, R. R. Regoes, C. Loverdo, R. Stocker, D. R. Brumley, W.-D. Hardt, and E. Slack**. 2017. High-avidity IgA protects the intestine by enchaining growing bacteria. Nature. **544**:498–502. ISSN 0028-0836.

[2] **Bansept, F., K. Moor-Schumann, M. Diard, W.-D. Hardt, E. W. Slack, and C. Loverdo**. 2019. Enchained growth and cluster dislocation: a possible mechanism for microbiota homeostasis. PLOS Computational Biology. page in press.