A Multi-Scale Epidemic Model of *Salmonella* infection with Heterogeneous Shedding

Simon Labarthe*, Béatrice Laroche*, Bastien Polizzi**, Magali Ribot†
*INRA, **Fields Institute & University of Waterloo, †Univ. Orléans

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1 General description

Salmonella infection is the most common vector of collective food poisoning in the developed world. As such, deciphering the mechanisms of infection in humans and animals is a fundamental step towards the design of efficient epidemiological policies against Salmonella zoonoses, in order to reduce the burden on agrifood industry and healthcare systems.

Salmonella, in the form of various strains, are pathogens that colonize and infect the digestive tract of chickens, pigs or humans (food poisoning, typhoid fever). In this type of epidemic, it has been shown that the ability to excrete the pathogen in the environment (water, food, excreta) and thus to contaminate other individuals varies from one individual to another. Some individuals, called super-excretors (or super-shedders), are permanent carriers of the pathogen without being affected and are responsible for most of the spread. This super-excretor phenotype, still poorly defined, is in all probability the result of interactions between the host's immune response, the pathogen and the commensal intestinal flora.

Recent studies [1] have identified key interactions between *Salmonella Typhimurium* and its host during infection. In the host's gut, pathogenic virulence factors promote the inflammation of the epithelium. The inflammatory process modifies the nutritional environment of the gut lumen which disturbs the ecological equilibrium of the microbiota and creates new niches that are targeted by the pathogen. The induced inflammation provides to the pathogen a competitive advantage, which can be sufficient to promote its proliferation and its transmission to another host.

The aim of the project is to develop multiscale models of heterogeneous pathogen transmission, from the intra-host level (interaction dynamic between commensal microbiota, pathogen and immune response) to between-host scale. The models

will be designed to allow assessment of the efficiency and/or cost-effectiveness of different intervention strategies. In particular, assessment of intervention strategies targeting super-shedders and based on probiotic and/or prebiotic treatments is of interest, as well as combinations of such strategies with biosecurity measures based on hygiene and movement restriction.

The model will therefore be composed of two systems coupled together :

- an ODE system which describes the interaction between bacteria, pathogen and immune system response in the host gut,
- a structured population model, describing the infected individuals through a function that depends on time, space but also on the bacteria load, the pathogen load and the immune system response.

We expect the ODE system to present a bistable behavior, with two stable stationary solutions corresponding respectively to a healthy host and to a super-excretor. Some ideas of such kinds of models may be found in [2, 3].

The structure population model can take several forms according to the size of the population : advection-diffusion equations if we consider large populations, kinetic equations, deterministic individual-based models or stochastic individual-based population models, in the case of small populations. The links between all these models can also be explored in a further step.

Finally, some efficient numerical schemes should be found and implemented in order to understand the properties of the solutions of the models, and, possibly, to compare the various mentioned models altogether.

Références

[1] M. Byndloss et al. Microbiota-activated PPAR-γ signaling inhibits dysbiotic Enterobacteriaceae expansion, Science, 6351(357), 570-575 2017.

[2] J. D. Murray. *Mathematical biology. I*, volume 17 of *Interdisciplinary Applied Mathematics*. Springer-Verlag, New York, third edition, 2002. An introduction.

[3] J. D. Murray. *Mathematical biology. II*, volume 18 of *Interdisciplinary Applied Mathematics*. Springer-Verlag, New York, third edition, 2003. Spatial models and biomedical applications.