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Modelling influenza re-infection dynamics to quantify the roles of innate and adaptive immunity

Abstract: Qualitative results of experiments in which ferrets were exposed to two influenza strains within a short time (1-14 days) suggest that innate immunity mediates cross-protection between strains through delaying a second infection, while cross-reactivity in the cellular adaptive immune response may shorten a second infection. Here I will describe the development of an influenza viral dynamics model designed to explain these experimental observations. Because of the many parameters required for a model to describe all major immune components, we have taken an incremental approach to development, analysis and ultimately application to data.

We begin by noting that a priori it is unclear whether the quantitative contribution of each immune component to cross-protection can be recovered from application of a viral dynamics model to sequential infection data. Moreover, we should ask if such data can be used to discriminate between proposed alternative models for immune mechanisms.

I will report on a simulation-estimation study, conducted under a Bayesian framework, to investigate whether the relative contribution of innate and adaptive immune responses can be recovered from sequential infection data. We found that within the

simulation-estimation framework, a model fitted to sequential infection data accurately captures the timing and extent of cross-protection; attributes such cross-protection to the correct broad components of the immune response; and captures the timing and role of each immune component in controlling a primary infection.

Our results confirm that the application of viral dynamics models to data from sequential infection studies should provide a rich source of information for quantifying the effect of each immune component in controlling infection, although further work is required in the inference framework to deal with stochastic extinction effects and host-to-host heterogeneity. Our findings improve the understanding of cross-protection on short timescales, and provide a new avenue to resolve discrepancies between existing models for a primary (single) infection.