

Modeling the Evolution of Influenza in Human Population

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Goal

To devise models of evolutionary branching and extinction under frequency-dependent selection with no separation of ecological and evolutionary timescales and to develop a model of evolution of human influenza A virus as a typical instance of such systems.

Background and motivation

Influenza is a common respiratory disease caused by an RNA virus from the family Orthomyxoviridae. Despite decades of intensive research, influenza remains one of the most important causes of mortality and morbidity in humans (Earn et al., 2002). The influenza virus is classified into three subtypes, A, B and C, with subtype A being the most significant from the epidemiological and most interesting from the evolutionary and ecological points of view. One of the peculiarities of influenza A is the fact that ecological and evolutionary timescales are about the same. Complicated interactions between the rapidly changing virus and the human immune system result at the level of the whole population in a rather unusual phylogenetic pattern (Fitch et al., 1997; Grenfell et al., 2004): even though at each point in time the virus shows substantial diversity, only one of the variants survives in the long run resulting in a phylogenetic tree with a single trunk. It is still unclear what combination of factors underpins this kind of evolution.

Many attempts have been made to describe the persistence of the virus in the human population from the purely epidemiological point of view (see, for example, Lin et al., 2003; Andreasen et al., 1997), but only a few models incorporated the evolution of the virus (Ferguson et al., 2003). Although these evolutionary models yield qualitatively correct phylogenetic trees, they are complicated and based on assumptions of debatable validity. In order to understand the mechanisms underlying the remarkable persistence and peculiar single-trunk evolution of influenza, simpler models with fewer assumptions are necessary.

The recently developed adaptive dynamics theory is a good candidate framework for constructing such a model. However, so far adaptive dynamics models have considered mostly systems that allowed separation of ecological and evolutionary timescales (Dieckmann & Law, 1996), which is not the case in the human-influenza system and many other real ecological systems. It is a challenge to relax this assumption and to start investigating rapidly evolving systems such as those formed by complex interactions between pathogens and their hosts.

Research questions

This research aims at elucidating the conditions that are necessary and sufficient for a model to produce the single-trunk phylogenetic tree characteristic to influenza. In other words, what are the essential features of the real host-pathogen system that result in the kind of evolution we observe?

Methods and work plan

As mentioned above, the evolutionary dynamics of influenza is characterized by two key features: (a) relatively large diversity at each time point and (b) survival of only one variant in the long run. In other words, evolutionary branching happens constantly but almost all of the branches die out relatively quickly. Previous work suggests that under some conditions adaptive dynamics models can give rise to evolutionary branching (Geritz et al., 1997; Dieckmann & Doebeli, 1999) and evolutionary extinction (Ferrière, 2000). These conditions however are not satisfied in the human-influenza system. Therefore the research plan is the following.

I will try to devise a model of the human-influenza system in which competition between different virus variants for susceptible hosts plays an analogous role as the resource competition (Roughgarden, 1976) in the previous adaptive dynamics models (Dieckmann & Doebeli, 1999). As the first step in utilizing this analogy we need to find a suitable description of our system: we need to understand, on the one hand, what viral traits should be considered and, on the other hand, how to describe the host immune system. The later “remembers” all viral variants that the host individual has been infected with in the past and provides protection against them and closely related variants in the future, thus locally depleting the pool of susceptibles with respect to these variants.

Once a suitable description is found and the model is constructed it is necessary to assess its quality. One of the ways to do so is through the comparison of phylogenetic trees generated by the model with the real ones using appropriate metrics on the space of trees. If the phylogenetic patterns are similar it would be interesting to understand the mechanism underlying the single trunk phylogeny in the human-influenza system.

Relevance and link to ADN’s research plan

In this project we aim at extending the applicability of adaptive dynamics theory to rapidly evolving complex host-pathogen systems, of which influenza A is an example. Thus, this research falls naturally into ADN’s research focus on *Foundations of Adaptive Dynamics*, and is also linked to ADN’s research focus on *Virulence Management*.

Expected output and publications

This work is expected to be published in a jointly authored paper and will be included as a chapter in my PhD thesis.

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