Effects of multiple sources of genetic drift on pathogen variation within hosts

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Changes in pathogen genetic variation within hosts alter the severity and spread of infectious diseases, with important implications for clinical disease and public health. Genetic drift may play a strong role in shaping pathogen variation, but analyses of drift in pathogens have oversimplified pathogen population dynamics, either by considering dynamics only at a single scale – such as within hosts or between hosts – or by making drastic simplifying assumptions, for example, that host immune systems can be ignored or that transmission bottlenecks are complete. Moreover, previous studies have used genetic data to infer the strength of genetic drift, whereas we test whether the genetic drift imposed by pathogen population processes can be used to explain genetic data. We first constructed and parameterized a mathematical model of gypsy moth baculovirus dynamics that allows genetic drift to act within and between hosts. We then quantified the genome-wide diversity of baculovirus populations within each of 143 field-collected gypsy moth larvae using Illumina sequencing. Finally, we determined whether the genetic drift imposed by host–pathogen population dynamics in our model explains the levels of pathogen diversity in our data. We found that when the model allows drift to act at multiple scales – including within hosts, between hosts, and between years – it can accurately reproduce the data, but when the effects of drift are simplified by neglecting transmission bottlenecks and stochastic variation in virus replication within hosts, the model fails. A de novo mutation model and a purifying selection model similarly fail to explain the data. Our results show that genetic drift can play a strong role in determining pathogen variation and that mathematical models that account for pathogen population growth at multiple scales of biological organization can be used to explain this variation.

⋆Mini-Symposium: Immuno-epidemiological models