

Predicting and controlling how microbes evolve using biophysics and population genetics

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Evolution is a unifying theme in the urgent medical and public health problems we face today including cancer, the rise of antibiotic resistance, and the spread of pathogens. But the ability to predict evolution requires (1) a quantitative description of the “fitness landscape” (the genotype-phenotype relationship) and (2) a description of the dynamics by which microbial populations explore this landscape. I will briefly introduce the conceptual and mathematical parallelism between fitness landscape in biological systems and free energy landscape in physical systems. Then, I will describe our recent work where we showed that the fitness landscape of norovirus escaping a neutralizing antibody can be projected onto two traits, the capsid folding stability and its binding affinity to the antibody. We then developed a theory based on protein biophysics and population genetics to predict how the fitness landscape might be explored. Using a droplet-based microfluidics “Evolution Chip”, we propagated millions of independent viral sub-populations, and showed that by tuning viral population size per drop, we could control the direction of viral evolution. Additionally, I will describe how this combined framework of biophysics and evolutionary biology also applies to bacterial evolution due to horizontal gene transfer.

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