

Biophysics and bioinformatics of influenza virus reassortment

The rapid evolution of influenza virus presents a significant threat to public health. Unlike many other pathogens, the flu virus has a segmented genome consisting of 8 independent RNA molecules. This feature enables genetic reassortment (segment mixing) if a host is co-infected by more than one strain at once. Molecular details and biological significance of reassortment and the related problem of packaging of the genome segments in the virions remain poorly understood.

In this talk, I will present a biophysical model of reassortment, and show how selection for proper genome packaging leads to a self-repulsion pattern of RNA-RNA interactions, confirmed experimentally. I will then discuss next-generation sequencing approaches to study reassortment between two strains of human influenza in vitro, and demonstrate that specific, reproducible combinations of genome segments emerge during experimental evolution. Changes of the fitness landscape during reassortment lead to significant epistatic effects, so the fitness of individual mutants may be different in the reassortment context compared to pure strains. Finally, I will present a general linear programming approach for estimating haplotype frequencies from population-averaged data, and discuss how natural selection favors specific segment flu segment combinations.

