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Quantifying Selection and Diversity in Viruses by Entropy Methods, with Application to the Hemagglutinin of H3N2 Influenza

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Many viruses evolve rapidly. For example, hemagglutinin of the H3N2 influenza A virus evolves to escape antibody binding. This evolution of the H3N2 virus means that people who have previously been exposed to an influenza strain may be infected by a newly emerged virus. In this paper, we use Shannon entropy and relative entropy to measure the diversity and selection pressure by antibody in each amino acid site of H3 hemagglutinin between the 1992-1993 season and the 2009-2010 season. Shannon entropy and relative entropy are two independent state variables that we use to characterize H3N2 evolution. The entropy method estimates future H3N2 evolution and migration using currently available H3 hemagglutinin sequences. First, we show that the rate of evolution increases with the virus diversity in the current season. The Shannon entropy of the sequence in the current season predicts relative entropy between sequences in the current season and those in the next season. Second, a global migration pattern of H3N2 is assembled by comparing the relative entropy flows of sequences sampled in China, Japan, the USA, and Europe. We verify this entropy method by describing two aspects of historical H3N2 evolution. First, we identify 54 amino acid sites in hemagglutinin that have evolved in the past to evade the immune system. Second, the entropy method shows that epitopes A and B in the top of hemagglutinin evolve most vigorously to escape antibody binding. Our work provides a novel entropy-based method to predict and quantify future H3N2 evolution and to describe the evolutionary history of H3N2.

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