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Guiding the evolution to catch the virus: An in silico study of affinity maturation against rapidly mutating antigen SHENSHEN WANG, MIT, DENNIS BURTON, The Scripps Research Institute, MEHRAN KARDAR, ARUP CHAKRABORTY, MIT — The immune system comprises an intricate and evolving collection of cells and molecules that enables a defense against pathogenic agents. Its workings present a rich source of physical problems that impact human health. One intriguing example is the process of affinity maturation (AM) through which an antibody (Ab)—a component of the host immune system—evolves to more efficiently bind an antigen (Ag)—a unique part of a foreign pathogen such as a virus. Sufficiently strong binding to the Ag enables recognition and neutralization. A major challenge is to contain a diversifying mixture of Ag variants, that arise in natural infection, from evading Ab neutralization. This entails a thorough understanding of AM against multiple Ag species and mutating Ag. During AM, Ab-encoding cells undergo cycles of mutation and selection, a process reminiscent of Darwinian evolution yet occurring in real time. We first cast affinity-dependent selection into an extreme value problem and show how the binding characteristics scale with Ag diversity. We then develop an agent-based residue-resolved computational model of AM which allows us to track the evolutionary trajectories of individual cells. This dynamic model not only reveals significant stochastic effects associated with the relatively small and highly dynamic population size, it also uncovers the markedly distinct maturation outcomes if designed Ag variants are presented in different temporal procedures. Insights thus obtained would guide rational design of vaccination protocols.

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