Focusing antibody responses against distraction and loss in diversity[1] SHENSHEN WANG[2], MEHRAN KARDAR, ARUP CHAKRABORTY, Massachusetts Institute of Technology — Pathogens are complex and evolving fast. They have developed full ranges of disguises to divert immune responses and often manage to escape recognition and thereby outpace natural immunity. A prominent example is the scarce and staggered development of broadly neutralizing antibodies against highly mutable viruses. It remains unclear under what evolutionary conditions these exceptional antibodies could emerge and dominate the response. To address this challenge, we construct an individual-based stochastic model of the Darwinian evolution of antibody-producing immune cells. We consider complexity of viral epitopes, vary seeding diversity of the immune cell population, and allow a time varying population size and extinction – new aspects essential for designing a realistic vaccine. We show that various temporal statistics of antigenic environments would select distinct evolutionary paths that lead to predominantly non-neutralizing, strain-specific or broadly neutralizing antibody responses. We suggest strategies to focus antibody responses on the targeted vulnerability of the virus and confer selective advantage to cross-reactive lineages. This implies a new step toward an effective vaccine against rapidly mutating complex pathogens.

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