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Computational design of hepatitis C vaccines using maximum entropy models and population dynamics GREGORY HART, ANDREW FERGUSON, Univ of Illinois - Urbana — Hepatitis C virus (HCV) afflicts 170 million people and kills 350,000 annually. Vaccination offers the most realistic and cost effective hope of controlling this epidemic. Despite 20 years of research, no vaccine is available. A major obstacle is the virus' extreme genetic variability and rapid mutational escape from immune pressure. Improvements in the vaccine design process are urgently needed. Coupling data mining with spin glass models and maximum entropy inference, we have developed a computational approach to translate sequence databases into empirical fitness landscapes. These landscapes explicitly connect viral genotype to phenotypic fitness and reveal vulnerable targets that can be exploited to rationally design immunogens. Viewing these landscapes as the mutational "playing field" over which the virus is constrained to evolve, we have integrated them with agent-based models of the viral mutational and host immune response dynamics, establishing a data-driven immune simulator of HCV infection. We have employed this simulator to perform in silico screening of HCV immunogens. By systematically identifying a small number of promising vaccine candidates, these models can accelerate the search for a vaccine by massively reducing the experimental search space.

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