
Dynamics, prediction, and computation for evolutionary mechanisms in immune responses

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Abstract:

To defend against rapidly evolving pathogens, jawed vertebrates have specialized cells that evolve during each individual's lifetime. Lymphocytes (T cells and B cells) mount adaptive immune responses to pathogenic threats that would outpace defenses encoded in the host germline. Immune recognition and memory formation are somatic evolutionary processes playing out in step with rapidly evolving pathogens. Prediction and control of this complex adaptive system would have far-reaching impacts on human health, but requires us to first understand the evolutionary mechanisms that promote and constrain the establishment of immune memories and the emergence of functional responses from sequence-level dynamics.

In this talk, I'll present recent work on the evolutionary dynamics of antibody responses, using data-driven approaches from experimental evolution, phylodynamics, and genotype-phenotype mapping. I'll show how we're learning fundamental response functions that determine antibody affinity maturation, and finding a high degree of predictability in a mammalian model system. I'll present probabilistic model-driven work that lays a foundation for inferring dynamics from molecular phenotype evolution in immune cell lineage trees. I'll also discuss predictive epitope mapping for antibodies, synthesizing large protein language models, explicit spatial prediction, and antigen mutagenesis data.

Adaptive immune responses are a natural setting to study the function of evolving systems, and there is considerable scope for quantitative data-driven study of evolutionary mechanisms in this setting. It's also a special opportunity for computational evolutionary biology models to function as predictive engineering tools, and enter tight feedback loops with experimental research.

Background reading:

This review is a succinct introduction to quantitative immunology (section 8, in particular, discusses the dynamics of antibody affinity maturation):

Altan-Bonnet, Mora, and Walczak, Quantitative immunology for physicists. *Physics Reports*, Volume 849 (2020). DOI: [10.1016/j.physrep.2020.01.001](https://doi.org/10.1016/j.physrep.2020.01.001)

This review describes the “parallel replay” approach in experimental evolution:

Blount, Lenski, and Losos, Contingency and determinism in evolution: Replaying life's tape. *Science* **362**, eaam5979 (2018). DOI: [10.1126/science.aam5979](https://doi.org/10.1126/science.aam5979)

Review of the biology of germinal centers—the micro-anatomical evolutionary engines where our antibodies compete and evolve.

Victora and Nussenzweig, Germinal centers. *Annual Review of Immunology* 40:1, (2022). DOI: [10.1146/annurev-immunol-120419-022408](https://doi.org/10.1146/annurev-immunol-120419-022408)

Review of B-cell repertoire evolution (B cells are the cells that make antibodies):

Cobey, Wilson, and Matsen, The evolution within us. *Philosophical Transactions of the Royal Society B*. Volume 370, Issue 1676 (2015). DOI: [10.1098/rstb.2014.0235](https://doi.org/10.1098/rstb.2014.0235)

Summary of recent success using protein language models for antibody engineering:

Outeiral and Deane. Perfecting antibodies with language models. *Nature Biotechnology* 42 (2024). DOI: [10.1038/s41587-023-01991-6](https://doi.org/10.1038/s41587-023-01991-6)