Tuning Evolution Towards Generalists by Resonant Environmental Cycling

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***Short Abstract* —Some evolutionary conditions result in `generalists' that are well-adapted to a common aspect of environments in evolutionary history and can thus deal with unseen environments. Such `generalists' can be hard to evolve if they are less fit or are entropically disfavored. We show that time-dependent evolutionary protocols, such as environmental cycling on an intermediate timescale or a chirp can select for generalists in spite of high fitness or entropic costs. These time-dependent strategies can be successful even when all static protocols fail. We show the regimes of the landscape ruggedness, selection pressure, and other parameters in which time-dependent protocols can discover generalist solutions.**

***Keywords* — changing environments, immunology models, population genetics models**

I. Purpose

UNDERSTANDING the conditions under which a system is able to generalize the experience of past challenges to solve novel challenges is a theme at the heart of diverse fields, ranging from statistical learning theory to evolutionary biology. Arriving at such a generalist solution is especially difficult since `specialist' solutions might be entropically favored or generally outperform (i.e., have higher fitness) any generalist solution. In addition, this task can be made more difficult by the ruggedness of the fitness landscape, as the system may become trapped in a local well and fail to successfully evolve a solution to the environment.

The emergence of generalists has been linked to the idea of changing environments. Simplified models[1] of evolutionary dynamics in low-dimensional spaces have indicated that environmental cycling at a specific frequency could select (or `localize') a population at a `generalist' phenotype or genotypes. Such emergence of generalists has also been thought about in the context of modularity[2,3].

Recent experiments in immunology have provided a quantitative handle on such questions. The observed emergence of broadly neutralizing antibodies (bnAbs) suggests that by exposing the germinal center to a variety of mutants of a given antigen, the immune system can develop antibodies that succeed against mutants not previously seen in spite of the fact that these antibodies are not entropically favored. In addition, epistatic interaction between the sites increases the difficulty of the problem by enhancing degeneracies of antibodies[4]. Discovery of bnAbs is promoted by switching between antigens, rather than simultaneous presentation of multiple strains of antigen [5].

These examples raise critical questions about exactly what circumstances make the emergence of generalists difficult and necessitate temporal strategies.

II. Methods and Results

The works above suggest three critical parameters to be studied: the switching rate of the environment, the cost of the generalist strategy relative to specialized strategies, and the ruggedness of the fitness landscapes. We performed Wright-Fisher simulations and varied the above parameters.

We find that generalists can emerge in static environments only if their fitness cost (relative to specialists) is below a critical value. For larger fitness costs, static environments or rapid cycling of environments cannot produce generalists. In parts of this regime, we find that cycling through different environments favors the emergence of generalists. However, the timescale of environmental cycling must be tuned to match the timescale of the evolutionary dynamics itself, set by the mutation rate, population size and selection pressure. If the environmental cycling is faster or slower, we do not recover generalists. We summarize our results in the form of a phase diagram.

References

[1] Kussell, Edo, Leibler, Stanislas, Grosberg, Alexander. (2006) Polymer-Population Mapping and Localization in the Space of Phenotypes. *Physical Review Letters.* **97,** 068101.

[2] Lorenz, Dirk M., Jeng, Alice, Deem, Michael W. (2011) The Emergence of Modularity in Biological Systems. *Physics of Life Reviews.* **8**. 129-160.

[3] Kashtan, Nadav, Alon, Uri. (2005) Spontaneous Evolution of Modularity and Network Motifs. *Proceedings of the National Academy of Science*. **102(39)**. 13773-13778.

[4] Adams, Rhys M., Kinney, Justin B., Walczak, Aleksandra, Mora, Thierry. (2017) Physical Epistatic Landscape of Binding Affinity. arxiv:1712.04000v1.

[5] Wang, Shenshen, Mata-Fink, Jordi, et al. (2015) Manipulating the Selection Forces during Affinity Maturation to Generate Cross-Reactive HIV Antibodies. *Cell.* **160,** 785-797.

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