Crossing valleys in multipeaked adaptive landscapes

Aided by fluctuations in the environment

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Abstract — **We resurrected the adaptive landscape between a suboptimal and the optimal wild type *lac* repressor in *E. coli* by systematically mutating two amino acids in the repressor and four base pairs in the operator, which govern the specificity of their binding. We assayed the repression, the repressor-operator binding in the absence of the inducer IPTG, and expression, unbinding, in the presence of IPTG by measuring the expression level of the downstream reporter LacZ. We find that both constant environment adaptive landscapes, in the respective absence or presence of IPTG, are multipeaked. Mutations that increase the binding ability in the absence of IPTG are often detrimental in the other environment, and vice versa. These so- called trade-ffs allow an evolving population to follow trajectories that fix beneficial mutations one-by-one in alternating environments, thereby overcoming constraints in both constant environments.**

***Keywords* — Experimental evolution, *lac* repressor, trade-off, constraint.**

I. Introduction

The evolutionary implications of multiple fitness peaks have been debated ever since Wright introduced this idea in the 1930's [1]. Central to the effects of multiple fitness peaks are the limitations they impose on the adaptive process. For single-peaked landscapes, optimal phenotypes can evolve rapidly by fixing one adaptive point mutation after the other. In contrast, such mutational trajectories can become trapped at sub-optima on multipeaked fitness landscapes. Mutations conferring fitness losses are then essential for access to the global optimum, thus preventing evolution by fixing positively selected mutations one-by-one. Adaptive landscapes have been mapped experimentally by systematically constructing neighbouring genotypes that differ by one mutation, and assaying their phenotype or fitness in one constant environment. These efforts have so far recovered single fitness peaks [2-4]. Empirical observations of multipeaked adaptive landscapes are scarce, though various studies have found indications for their existence [5-7]. Also, since evolution occurs in heterogeneous environments it is important to understand the shapes of adaptive landscapes and their correlations between the environments to draw their evolutionary consequences.

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II. Results

We find the landscapes describing the *lac* repressor-controlled repression and expression to be highly rugged in the constant environments: all measured mutational trajectories with substitutions in the two amino acids in the *lac* repressor binding site and four base pairs in the operator DNA, contain valleys. These valleys persist in both environments, both in the presence or absence of inducer IPTG.

Negative correlations between the landscapes in both environments reveal that mutations beneficial in one environment, eg in the presence of IPTG, act to the detriment in the other environment, eg in the absence of IPTG. This correlation is responsible for many tradeoffs in the individual trajectories. These tradeoffs allow the adaptive fixation of mutations; valleys can be crossed by the one-by-one fixation of mutations by alternating between the two constant environment landscapes. This provides for continuous hill climbing trajectories.

Computations using Markov chain modelling show that these results are robust to alterations in dwelling time per environment and environmental fluctuation rate, within the boundaries of the strong selection- weak mutation regime.

III. Conclusion

The multipeaked landscapes functionally underlain by the *lac* repressor binding and unbinding to the operator DNA are multipeaked, both in the presence or absence of inducer IPTG. Due to the negative correlations between the constant environment landscapes, there are many tradeoffs between the environments in the individual trajectories. We show that these tradeoffs not only constrain evolution in fluctuating environments, as thought to many generations of evolutionary biologists, but instead aid adaptive progress by allowing valleys to be crossed by the one-by one fixation of mutations.

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