

The Evolution of Evolvability: Changing Environments Promote Rapid Adaptation in Digital Organisms

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Abstract

Genetic spaces are often described in terms of fitness landscapes or genotype-to-phenotype maps, where each potential genetic sequence is associated with a set of properties and connected to other genotypes that are a single mutation away. The positions close to a genotype make up its "mutational landscape" and, in aggregate, determine the short-term evolutionary potential of a population. Populations with wider ranges of phenotypes in their mutational neighborhood tend to be more evolvable. Likewise, those with fewer phenotypic changes available in their local neighborhoods are more mutationally robust. As such, forces that alter the distribution of phenotypes available by mutation can have a profound effect on subsequent evolutionary dynamics.

We demonstrate that cyclically-changing environments can push populations toward more evolvable mutational landscapes where a wide range of alternate phenotypes are available, though purely deleterious mutations remain suppressed. We further show that populations in environments with drastic changes shift phenotypes more readily than those in environments with more benign changes. We trace this effect to repeated population bottlenecks in the harsh environments, which result in shorter coalescence times and keep populations in regions of the mutational landscape where the phenotypic shifts in question are more likely to occur.

Introduction

Fitness landscapes are a mathematical tool to map genetic sequences to expected evolutionary fitness. Many studies have examined the important role that different types of fitness landscapes play on evolutionary dynamics and outcomes, both in biological populations (Khan et al., 2011; Szendro et al., 2013; Weinreich et al., 2006; Nahum et al., 2015) and in evolutionary computation settings (Merz and Freisleben, 2000; Humeau et al., 2013; Kallel et al., 2013). However, real-world fitness landscapes are far more complex and varied than the idealized models that are used in most of these studies. Neighboring regions of real landscapes can have starkly different properties from each other based on the effects of and interactions among mutations (i.e., the mutational landscape). Examples of the type of properties that we are interested in include robustness, epistasis, and modularity, all of which are measurements of how

information is organized inside of a genome and commonly categorized as components of an organism's "genetic architecture". Isolated pockets in a landscape can often be characteristically different from the landscape as a whole due to the amount and organization of genetic information. In fact, in most natural fitness landscapes, the vast majority of neighborhoods consist entirely of non-replicating genomes with zero fitness (and thus no genetic information), making life itself appear to be a rare exception (Gavrilets, 2004).

Evolution on these convoluted landscapes is clearly limited to those regions that have non-zero fitness, with a selective pressure for fitness to increase. Beyond that, however, populations can evolve toward neighborhoods with specific local properties based on the evolutionary forces acting upon the populations. For example, high mutation rates drive populations toward neighborhoods with a higher fraction of neutral mutations in the effect dubbed survival of the flattest (Wilke et al., 2001). Similarly, sexual populations tend toward regions of the fitness landscape with more modularity (Misevic et al., 2006) and more negative epistasis (Misevic et al., 2010) than otherwise equivalent asexual populations.

Understanding these dynamics is of broad interest. It is important to evolutionary computation given the strong influence of local landscape properties on the quality of the final solutions that an evolving population is able to obtain. Its relevance to evolutionary biology is equally obvious – the local landscape that a population occupies will influence the selective forces at play in the population, creating a feedback cycle between these two important evolutionary factors (Zaman et al., 2014; Meyer et al., 2012). Disentangling such interactions is likely to provide further insights into fundamental evolutionary dynamics. Computational artificial life systems have the advantage of being able to bridge these two realms: they have unconstrained evolutionary dynamics similar to natural systems, while maintaining the ability to rapidly perform experiments and collect any data we need about populations or their local landscapes.

Evolvability and Genetic Architecture

Evolvability refers to a series of distinct but overlapping concepts that are generally concerned with adaptation, variation, and/or novelty generation (Pigliucci, 2008). For the purposes of this paper, we will focus on evolvability as the capability of genomes to generate adaptive variation in response to mutation. This kind of evolvability depends primarily on the organization and interrelation of information in the genome; that is, the genetic architecture, and the resulting genotype-to-phenotype map (Gunter P. Wagner and Altenberg, 1996). An example of evolvable architecture can be found in some bacterial genomes that contain highly mutable genome regions, called contingency loci. Small sets of insertions or deletions to these regions create transcription frameshifts that alter the expression of nearby coding regions, thus allowing populations to easily switch phenotypes via minor mutations. Contingency loci are most often seen in the genomes of pathogens, which are subject to frequent environmental shifts caused by the host immune system (Bayliss et al., 2001). Thus, these populations are able to produce large amounts of heritable variation despite the reduction in population diversity resulting from population bottlenecks.

Mutational Landscapes Properties of genetic architectures such as evolvability and robustness are determined by the shape of the resulting mutational landscape (Andreas Wagner, 2008). Robust genetic architectures that can tolerate more mutations without altering their phenotype reside in mutational landscapes that connect to more neutral mutants. Similarly, architectures that more easily switch phenotypes in response to mutation without substantial reduction in fitness, reside in more evolvable regions of genotype-space.

It is worth noting that not all regions of the mutational landscape are equally accessible. Some genome regions may be more resistant to mutation than others (Lee et al., 2012), thereby altering the probabilities of mutations occurring that lead into certain regions of the mutational landscape. This kind of differential probability may therefore moderate a population's diffusion through the mutational landscape. Further, in regions of the landscape where there are fewer available mutations that provide potentially adaptive traits, response to selection is likely to be weaker than in regions where there are many adaptive variants available within a few mutational steps (Alberch, 1991; Carter et al., 2005).

Changing environments create more paths to different kinds of phenotypes

Directional selection acts to change the composition of phenotypes and genotypes in a population (Wright, 1931). This change moves the population across the mutational landscape to local regions of higher fitness. As populations ar-

rive at a fitness peak, they tend to cluster there, and the accumulation of new phenotype-altering mutations decreases (Wright, 1964; Kauffman and Levin, 1987). In changing environments, however, the direction of selection is not fixed. Instead, as the environment changes, populations are driven to explore new regions of the mutational landscape (Kash-tan et al., 2007; Connelly et al., 2015). As they proceed, populations accumulate and carry with them the history of prior explorations and adaptations, and use them as raw material for new adaptation (McClintock, 1993). Indeed, earlier work has shown that changing environments promote evolvability in many contexts, without compromising robustness (Crombach and Hogeweg, 2008; Wilke et al., 2001). Strength of selection is also an important component of this exploration, since the harshness of the environment drives the speed with which organisms adapt to new conditions (Goddard et al., 2005).

In this paper, we show how changing environments not only drive exploration of the mutational landscape, but also create populations whose genetic architectures are qualitatively different than those from populations evolved in static environmental conditions. In particular, we show that populations evolved under harsh cyclically-changing environments have many more changes along their phylogenetic histories than those evolved in static or benign changing environments. They also individually contain large reservoirs of pseudogene-like vestigial loci that were acquired and deactivated through repeated adaptation and fixation cycles. As a result, populations evolved in these harsh cyclically-changing environments are low in standing neutral diversity at the population level, but they still connect with many more phenotypically-interesting regions of the mutational landscape than more diverse populations evolved in static or benign environments.

Digital Evolution

Digital Evolution is a sub-field of Artificial Life that focuses on studying evolutionary dynamics using self-replicating computer programs as model organisms (McKinley et al., 2008). Unlike theoretical simulations, digital organisms self-replicate, mutate, and compete with their peers for resources and space in which to reproduce. Because populations of digital organisms have a source of variation, inheritance of genetic material across generations, and are subject to selective pressures, they undergo evolution by natural selection.

Digital organisms do not suffer from many of the drawbacks of experimentation on natural organisms. Three of the advantages of digital organisms are particularly relevant for our study. First, the rates of reproduction in digital systems are much faster than in even the most rapidly-reproducing physical organisms; we can get generations in seconds, rather than the hours for the fastest biological organisms (Ryan, 1953; Lenski et al., 1991), or the days

or even weeks needed for complex multicellular organisms (Anderson et al., 2010; Stearns et al., 2000). Second, using digital organisms allows us to tightly control and verify experimental conditions. For example, in physical organisms, factors such as mutation rate can generally only be measured after the fact, or coarsely altered through mutagens. In digital organisms, however, we can not only control mutation rates with fine-grained precision, but also types and probabilities of different types mutations (e.g., point mutations, insertions, deletions). Further, we are also able to track and replay the evolutionary history of every organism at any point in time to verify that unusual or unexpected results do not represent measurement error. This ability to exactly replicate evolutionary results at an individual organism level is firmly out of reach for experiments with physical organisms. Finally, we can precisely and exhaustively map the mutational landscape of a digital organism, and identify the role of every site in its genome (Ofria and Adami, 2002); this is not feasible in even the simplest physical organisms. All of these factors make digital organisms ideal for studying the effects of changing environments on the mutational landscape.

Methods

Avida Digital Evolution Platform

We used Avida (Lenski et al., 2003) to examine the effects of cyclic changing environments on the genomes of evolved digital organisms. Avida is a software platform for performing evolution experiments with digital organisms in a virtual world.

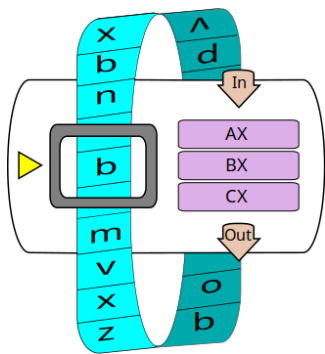


Figure 1: **An example virtual CPU from Avida**, with a circular genome (blue), three registers (purple), input and output handlers (tan), and an instruction pointer (yellow) indicating the next instruction to be executed.

An Avida organism is composed of a circular genome of assembly-like computer instructions that are executed in a virtual CPU (Figure 1). Populations of these organisms are placed in a toroidal world in individual cells where they are allowed to execute, reproduce, compete for space, mutate, and evolve.

Organisms in Avida are self-replicating, and experience mutation. The genome in the initial default organism contains all of the instructions necessary for reproduction. However, the instructions are not copied into an offspring with perfect fidelity. By default, the reproductive copy instruction is faulty, meaning that it will probabilistically introduce errors (mutations) into the offspring genomes. These offspring organisms carry and execute the mutations to their genomes, and in turn pass them on, along with new mutations, to their own offspring (i.e., variation in the systems is heritable).

Avida worlds can be space- or resource-constrained. Avida allows the experimenter to configure many aspects of the environment, thus subjecting the organisms to various kinds of selective pressures. In many cases, these environments will include resources that can be metabolized by performing specific functions or activities, resulting in a boost to execution speed that gives the organisms a competitive advantage. However, even without explicit external pressures, organisms still experience an implicit pressure to execute more quickly and efficiently. The organisms that run fastest are typically able to also reproduce fastest, and thus outcompete their peers for space.

Thus, because populations have a source of variation, inheritance, and experience selection, evolution by natural selection is an inevitable consequence. Further, because the Avida genome instruction set is Turing-complete¹, populations may evolve potentially infinite complexity of behavior (Ofria et al., 2002).

Avida is available for download without cost from <http://avida.devosoft.org/>, and specific versions along with data-files to reproduce the experiments described in this paper may be found at <https://github.com/voidptr/avida> and <https://github.com/voidptr/alife2016>.

Experimental Design

We subjected a total of 150 replicate populations of digital organisms to two different treatments of two-phase cyclical changing environments, plus a static control. The environment cycles between equal-length periods of reward and punishment. Each cycle extends for 1000 updates, or roughly 30 generations. In the static control, there is no cycle. Rather, the rewards remain constant. The complete experiment extends for 200 cycles, or 200,000 updates, approximately 6,000 generations.

We structured the environment to provide large rewards to organisms for performing two challenging bit-wise logical tasks: XOR and EQU. XOR is rewarded with a CPU speed (and thus fitness) multiple of 8, while EQU is rewarded with a CPU speed multiple of 32. In the harsh treatment, as the cycle progresses, the XOR reward remains constant, while

¹The Avida instruction set is a super-set of the Tierra instruction set, which has been shown to be Turing-complete (Maley, 1994).

the EQU reward cycles between a 32-fold bonus and a correspondingly harsh 32-fold penalty (i.e., CPU speed is divided by 32 when EQU is performed in the off cycle). The benign treatment is identical to the harsh treatment, except that the reward merely goes away in the off-cycle as opposed to incurring a severe penalty.

We identify EQU as the *Fluctuating Task*. XOR, because it is rewarded continuously, is the *Backbone Task*, and is used as a background for comparing the separation or intertwining of functional genetic components in the evolution of EQU. Further, the 4-fold difference in reward level between XOR and EQU encourages the evolution and maintenance of EQU when possible.

For all of the experiments described in this section, we held the individual genomes at a fixed length of 121² instructions instructions, but mutated the new genome after each successful replication event at a substitution probability of 0.00075 per site. We configured the Avida world to have local interactions on a toroidal grid that is 60 cells by 60 cells (3600 cells in total), and we seeded the initial populations with an ancestor that was previously evolved to perform XOR and EQU under a static reward. The genetic architecture for performing XOR and EQU is tightly intertwined in this ancestral organism, as it was evolved with no selective pressure for modularity.

Results and Discussion

Our experiments demonstrate that digital organisms that were evolved in cyclic changing environments differ substantially from those evolved in static environments in a number of ways. These differences include the number of mutations that fix in the lineage from the ancestor (the “phylogenetic depth”), key metrics of their genetic architecture, and the presence of reservoirs of pseudogenes that change the nearby mutational landscape.

Evolutionary History and Population Structure Evolution in the harsh changing environment resulted in populations with substantially higher phylogenetic depth as compared to those evolved in static or benign environments. At each environmental shift, adaptive mutations rapidly swept and fixed in the populations. (Figure 2)

The populations evolved in the control and benign environments displayed much more genetic diversity compared to those evolved in the harsh cyclic environment, which underwent what was effectively a bottleneck at each cycle shift. Because a selective sweep reduces current diversity within a population, the smaller number of sweeps in the benign and control treatments led populations in them to

²As part of the initial exploratory protocol, we hand-wrote an organism with separated sections that performed XOR and EQU. In order to compare the hand-written organism with a sample of evolved organisms, we matched their genome lengths, which were 121 instructions.

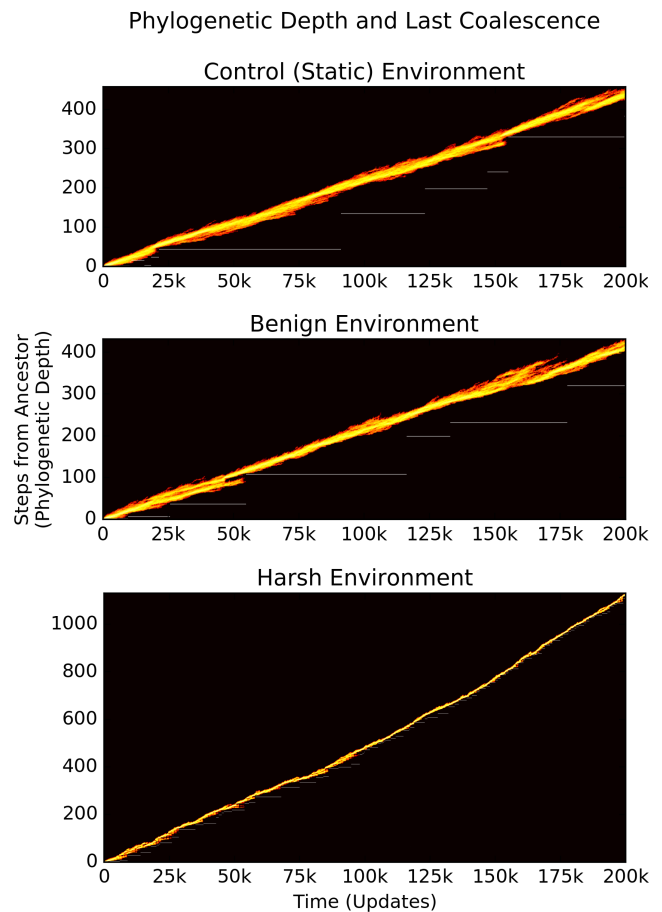


Figure 2: **Phylogenetic depth of representative populations** evolved in each of the three treatments. White horizontal lines mark the depth of the most recent common ancestor, and discontinuities in this line indicate that the most recent common ancestor has changed, and thus that a sweep occurred. The control treatments had a mean of 18 sweeps (STD=9.05), the benign treatments had a mean of 21 (STD=19.05), and the harsh treatments had a mean of 88 sweeps (STD=23.37). Note the difference in scales between y-axes: the control-evolved population has a maximum depth of 400 mutational steps from ancestor, while the harsh-evolved has upward of 1100.

have higher standing diversity for most of their evolutionary history than those populations from the harsh changing environment. Despite this higher standing diversity in the benign and control treatments, regions of low diversity are still evident in the genomes of these populations, implying purifying selection on the traits encoded at these sites (see Figure 3).

Genetic Architecture The selective shifts in both benign and harsh changing environments result in qualitatively dif-

Population Entropy by Site and Genotype

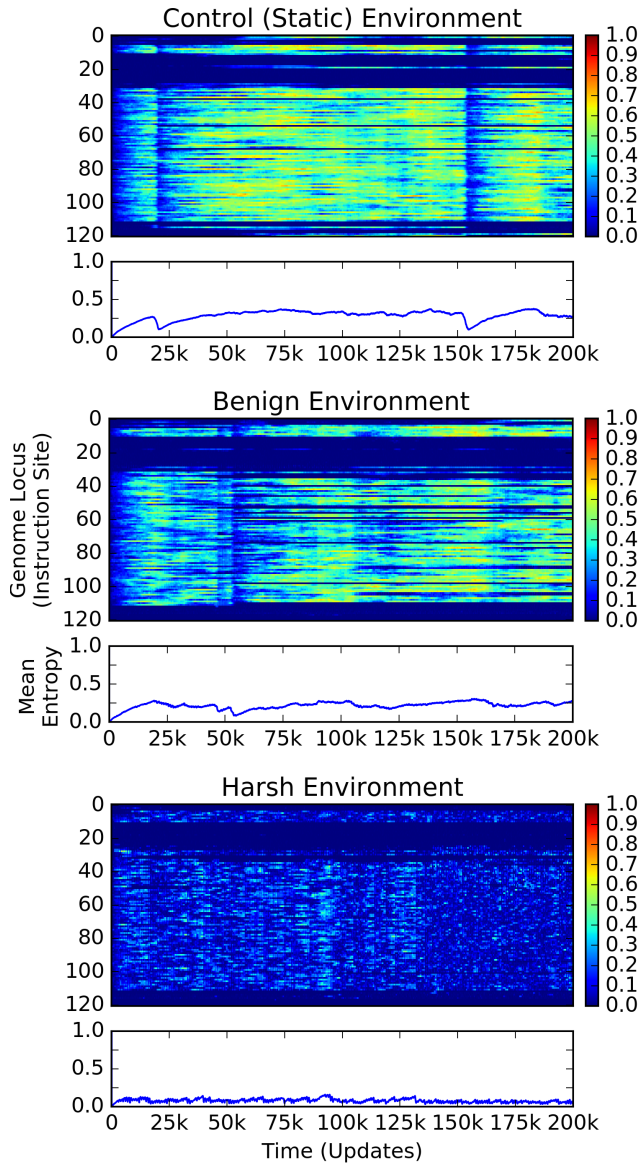
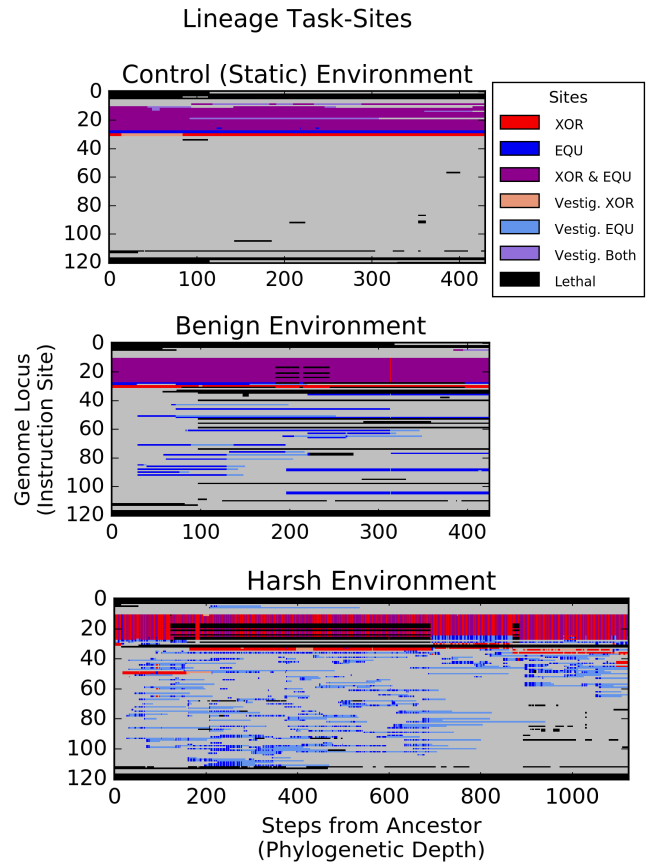


Figure 3: **Population Per-site Entropy over time.** Each vertical slice represents the per-site entropy of the population at each update, both by genetic locus (upper), and overall population mean (lower). Hotter colors (upper) indicate greater diversity at this locus. Mean population entropy indicates the relative diversity of the population at any given time, while the per-site entropy shows where in the genomes the population diversity is located.

ferent architectural styles from the static control environment. The task arrangements evolved under both experimental treatments are much more scattered than in the control. The bulk of the sites responsible for performing the fluctuating task (EQU) were separated from the backbone task (XOR), except for a core region of overlap, which represent portions of the tasks that are shared between XOR and EQU. (Figure 4)

Figure 4: **Varying genetic architecture of XOR and EQU over time** for the final dominant genotype in a randomly selected replicate. Proceeding from the left of each figure, each vertical slice along the X-axis represents an ancestor of the final dominant. The Y-axis represents the tasks coded for at each genome locus. Sites in **red** are active sites that code for the XOR task only, sites in **blue** are active sites for the EQU task only, and **purple** sites code for both XOR and EQU. Knockouts to the sites in black are lethal to the organism. Sites in the lighter colors (tan, light blue, lavender) represent vestigial sites for XOR only, EQU only, or both tasks, respectively. As we proceed from left to right, we can see the evolutionary history of the final dominant genotype.



In contrast, the architecture of XOR and EQU remain tightly intertwined in the control, and site positions do not change significantly over the course of the experiment. In the benign treatment, many more regions that perform the fluctuating task (XOR) are scattered throughout the genome, but site positions remain relatively static throughout the run after an initial adaptive phase. In the harsh treatment, not

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only are the active sites scattered, but the positions of active sites change and proliferate wildly.

Interestingly, populations evolved in both the benign and harsh treatments also show development of a large reservoir of formerly functional, now vestigial, sites; that is, sites that were previously active in performing a task, but were disabled by a mutation elsewhere and are now neutral. However, these vestigial pseudogene-like sites appear to be important for allowing the organisms to quickly re-adapt as the fluctuations in the environment restore the previously-rewarded functions. (Figure 5)

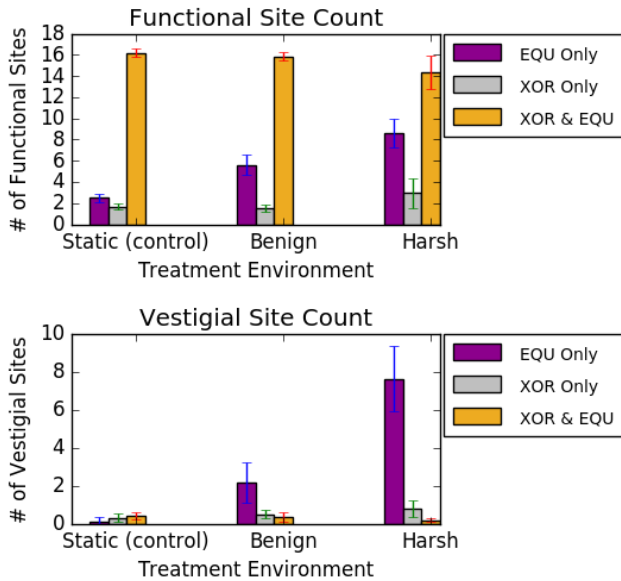


Figure 5: **Number of functional and vestigial sites by treatment.** The harsh environment has a significantly larger number of vestigial sites for the fluctuating (EQU) task compared to the benign treatment or control, while having a comparable number of functional sites (One-Way ANOVA $F(2,132) = 54.35$, $p << 0.0001$).

Nearby mutational landscape In order to identify the role that these pseudogene-like structures play, we performed a survey of the single-step mutational landscape surrounding the last common ancestor of each replicate population. This landscape contained approximately 3,200 distinct mutants in each of the 50 replicates per treatment, for a total of almost 500,000 mutants surveyed. We found that the availability of reservoirs of vestigial sites shifted the treatment-evolved organisms' position in genotype space such that, compared to the control-evolved organisms, a task lost due to mutation more often remains one or two mutational steps away. In this way, the treatment organisms have an advantage over organisms from the control runs in terms of the short-term evolvability of the fluctuating task. (Figures 6 and 7)

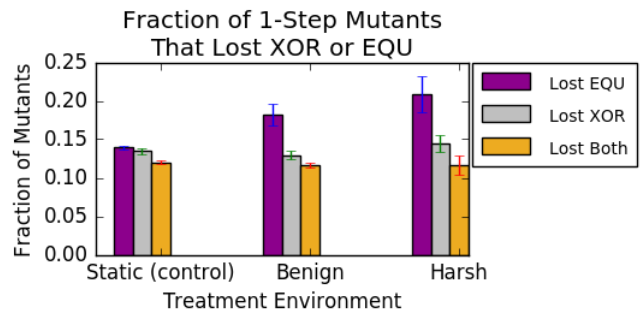


Figure 6: **A survey of the single-step mutational neighborhood** around organisms that performed the fluctuating task. Note that in both the benign and harsh treatments, there were significantly more mutants that lost the EQU task as compared to the control (Wilcoxon Rank Sum Test: $Z = -6.59$ and -6.70 respectively, $p << 0.0001$). This result indicates that it was easier for the organisms in both treatments to turn off the EQU task in response to one mutation.

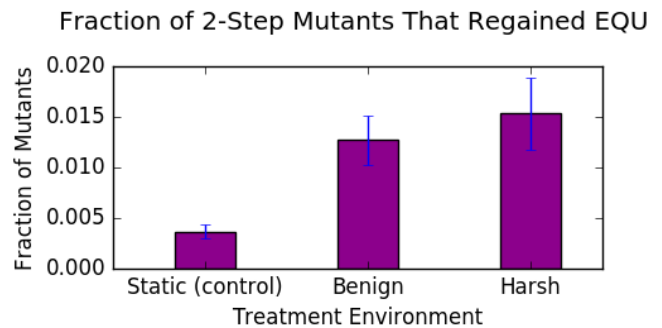


Figure 7: **A survey of the two-step mutational neighborhood** of the organisms that lost EQU function in the one-step survey. We found that in both the harsh and benign treatments, there were significantly more organisms that regained function in response to mutation than the control. (Wilcoxon Rank Sum Test: $Z = -6.11$ and -7.38 respectively, $p << 0.0001$). This result indicates that it was easier for the organisms in both treatment environments to regain the task in response to one additional mutation.

Conclusion

In cyclic changing environments, the direction of selection shifts frequently, and periodically drives populations to not only explore new regions of the genetic landscape, but also to carry with them the genetic heritage of previous environmental adaptations. Thus, the resulting populations are not only adapted to the local temporarily static environment, but also to the meta-environment of cyclic change. Because of their mutational history, and the paths that led them to their current region of genotype space, the genomes contain vestigial fragments of genetic material that were adapted to prior

environments. As this exploration proceeds, more mutations accumulate in the population, and each of these creates a link to a new region of the mutational landscape. As these links accumulate, they form a reservoir of mobility for the population to quickly shift to new phenotypes as dictated by shifting selective forces. In this way, the accumulation of vestigial or pseudogene-like regions acts as an adaptation to the larger pattern of changing selective forces.

By contrast, in static (non-changing) environments, the majority of neutral mutations do not connect to as many phenotypically-interesting regions of genotype-space. There are far fewer pseudogenes-like regions available that could regain functionality should conditions change. Thus, populations evolved in static environments are less evolvable in the short-term.

Limitations of Changing Environments and Future Directions

Changing environments produce unique sets of selective pressures that promote more rapid exploration of genotype space, while also building useful reservoirs of partial functionality that may be co-opted in the evolution of more complex structures. These features make changing environments useful for both their explanatory power in natural evolution, and as practical tools in the Artificial Life toolkit. Ultimately, however, cyclic changing environments only re-tread existing phenotypic ground, and though genotypic exploration is wider and faster than under purely directional or stabilizing selection, the space explored remains limited to the scope of the phenotypes that are being selected for.

Even so, there must certainly exist other methods of exploring genotype space that do not suffer from these limitations. For example, perhaps repeated bottlenecking of populations could promote faster traversal of the fitness landscape in quasi-random directions. Another alternative may be randomly changing environments, rather than cyclic, which might produce a broader exploration of the wider genotype space. Finally, perhaps these kinds of environments could be coupled with dynamically increasing open-ended complexity goals.

Understanding the mechanisms by which different types of environments alter fitness landscapes is vital to developing an understanding of the forces that promote evolvability and increase complexity. Cyclic changing environments provide one view into these dynamics, but we must explore further to find other mechanisms for exploring and exploiting genotype space.

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