BIOLOGICAL EVOLUTION AND THE GENOTYPE-PHENOTYPE MAP

Populations of living organisms are made up of individuals that vary in their genetic information, what we know as ***genotype***. Each genotype translates into a series of observable characteristics, known as ***phenotype***. Classical models of evolutionary theory assume that individuals reproduce more or less effectively according to their phenotype, and in the reproductive process they undergo mutations that, as a consequence, produce offspring that do not have exactly the same genotype as their parents.

The first evolutionary models had no information about the structure of the genotype space, nor how populations could move on it by mutations. Recent work has explored the evolutionary dynamics of genotype spaces on which a network structure is imposed, in which genotypes are the nodes of the network and mutations are links between nodes (Aguirre et al. 2018, Manrubia et al. 2021). These studies have shown that the network structure of genotype space fundamentally alters the predictions of evolutionary models.

Our research project is thus focused on studying evolutionary dynamics on genotype networks from a computational perspective. The following research projects are offered:

1) EVOLUTION SIMULATOR

Evolutionary experiments with bacteria or viruses are able to study a large number of generations in relatively short time. However, there is a major limitation of these studies, in the ability to observe the genotypic structure of the population at any given time. This limits the ability to observe all genetic changes in the population and to be able to test predictions of evolutionary theory.

The project will consist of developing an agent-based evolution simulator that implements population dynamics in toyLIFE, (Catalán et al. 2018, 2020), a computational model which includes organisms with ``toy" versions of genes, proteins and metabolites, and in whose cells regulatory and metabolic networks emerge as a result of simple laws of interaction between elements. The simulator will attempt to replicate real experimental designs used in evolutionary experiments with bacteria, so that the results of the simulations can be compared with published experiments.

2) EXIT TIMES FROM A PHENOTYPE

As a result of naive modeling of the evolutionary process, which includes no information on how phenotypes are connected in evolutionary space, mutations between phenotypes have traditionally been modeled as a Poisson process. Recent results (Manrubia and Cuesta, 2015) have shown that, if we consider the evolutionary dynamics in the genotype network of all the genotypes compatible with a given phenotype, the evolutionary process at the phenotypic level is no longer Markovian, and the exit times from a phenotype cease to be exponential.

The objective of this project is to study the distribution of transition times between phenotypes in the computational model toyLIFE (Catalán et al. 2020), so that we can delve into the effects that the network structure at the genotype level has on phenotypic dynamics.

3) EVOLUTION IN ALTERNATING ENVIRONMENTS

The aim of this line of work is to explore the evolution of populations subjected to alternating environments to study the conditions that promote their extinction. The underlying motivation for this work is the development of sequential antibiotic therapies, in which several antibiotics are

administered to the patient in a sequential sequentially (one after the other), in order to eliminate the bacterial population causing the infection.

Numerical simulations of populations evolving in networks of genotypes under alternating antibiotic treatment show that populations can get stuck in regions of these genotype networks where they cannot evolve resistance to new antibiotics (Catalán et al. 2017).

A first systematic approach to this problem would be the generation of several genotype networks (for which simple generative models exist, such as the so-called rough Mount Fuji, or the NK model), which would vary in a series of topological parameters, and then simulate the evolution of populations on them. To do this, we will take as a starting point a recent work by Kevin Wood's group (Maltas et al. 2021) and we will implement the appropriate population dynamics to study this phenomenon.

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