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Environmental seasonality drives digital populations towards stable cross-feeding

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Abstract

Stable bacterial cross-feeding interactions, where one strain feeds on the waste of the other, are important to understand, as they can be a first step towards bacterial speciation. Their emergence is commonly observed in laboratory experiments using Escherichia coli as a model organism. Yet it is not clear how cross-feeding interactions can resist the invasion of a fitter mutant when the environment contains a single resource since there seems to be a single ecological niche. Here, we used digital organisms to tackle this question, allowing for detailed and fast investigations, and providing a way to disentangle generic evolutionary mechanisms from specificities associated with E. coli. Digital organisms with evolvable genomes and metabolic networks compete for resources in conditions mimicking laboratory evolution experiments. In chemostat simulations, although cross-feeding interactions regularly emerged, selective sweeps regularly purged the population of its diversity. By contrast, batch culture allowed for much more stable cross-feeding interactions, because it includes seasons and thus distinct temporal niches, thereby favoring the adaptive diversification of proto-species.

Introduction

Metabolic cross-feeding interactions between microbial strains are common in nature, and emerge during evolution experiments in the laboratory, even in homogeneous environments providing a single carbon source (Rosenzweig et al., 1994; Rozen and Lenski, 2000). In sympatry, when the environment is well-mixed, the reasons why emerging cross-feeding interactions may sometimes become stable and lead to monophyletic genotypic clusters occupying specific niches – named ecotypes (Cohan, 2002) – remain unclear.

As an alternative to evolution experiments in the laboratory, we developed Evo²SIM (http://www.evoeo.eu/evo2sim-software/), a multi-scale model of in silico experimental evolution (ISEE, Hindré et al. 2012), equipped with the whole tool case of experimental setups, competition assays, phylogenetic analysis, and, most importantly, allowing for evolvable ecological interactions. Digital organisms with an evolvable genome structure encoding an evolvable metabolic network evolved for tens of thousands of generations in environments mimicking the dynamics of real controlled environments, including chemostat or batch culture, providing a single limiting resource.

By performing in silico evolution experiments, we studied the environmental conditions in which a stable cross-feeding interaction could occur. To this aim, we let populations of digital organisms evolve in three different environments:

1. Seasonal. In this environment, the organisms grow on a single resource, periodically provided each ~7 generations, the rest of the environment being rinsed at the same time. The seasonal environment mimics the single carbon source serial transfer setup of the Long Term Evolution Experiment (LTEE, Rozen and Lenski 2000);

2. Continuous. Here, the digital organisms grow on the same single resource, but continuously provided. The periodic rinse is replaced by a small degradation of the free metabolites in the environment (exogenously provided or released by the organisms). The continuous environment mimics a single carbon source chemostat setup.

3. Poisson. This environment is exactly the same as the seasonal one except that the serial passages are no more periodic. The resource is provided (and the environment is rinsed) at random times following a Poisson law.

We evolved 12 independent populations in each of the three types of environment. Importantly, the total amount of resource available is the same in the three environments.

Results

Comparison of the evolutionary outcome in the three environments shows important differences in the structure of the populations (see Fig. 1). Results show that the long-term maintenance of cross-feeding interactions is strongly favored in the seasonal environment. In this environment, half of the simulations evolved a stable cross-feeding interaction, with two monophyletic ecotypes coexisting via a negative frequency-dependent interaction. At each cycle, a first ecotype grows during the first season, feeding on the primary resource and releasing by-products, while...
the second ecotype exclusively feeds on by-products during the second season. The stable coexistence of both ecotypes is based on niche construction, followed by a negative frequency-dependent interaction, as the S and L ecotypes in the LTEE (Rozen and Lenski, 2000). According to our model, batch culture experiments seem to especially favor the evolution of stable cross-feeding polymorphisms owing to the cyclic nature of the environment that generates the conditions for the existence of at least two stable seasons: a first season is externally generated by the cyclic mechanism (thus being intrinsically stable) while the second one is generated by the replacement of the exogenously-provided nutrient by the secreted by-products through a mechanism of niche construction.

In the continuous environment, where the primary resource is constantly provided (like in a chemostat), cross-feeding interactions emerged, but were not stable because of competitive exclusion. In this case, organisms enriched their environment via their metabolic activity, such that mutants were temporarily able to feed on by-products. But the absence of seasonality precludes any possibility for the stabilization of cross-feeding interactions.

Our multi-scale model allowed us to investigate the impact of resource dynamics on the organization of genome (e.g., gene amplification) and of the metabolic network, and to dissect the precise mechanism behind the evolved robustness of the cross-feeding interaction in the seasonal environment. We also demonstrated that those results are robust to model parameters variation. Indeed, stable cross-feeding interactions emerged in the periodic environment for a wide range of parameter values, including well-mixed populations and infinite diffusion rate, while they never appeared in the continuous environment, thus reinforcing our conclusions.

As a conclusion, the stability of a cross-feeding polymorphism should only be analyzed in the light of the robustness of each ecotype against selective sweeps by other ecotypes (Cohan, 2002). This mechanism is observed in the LTEE, as well as in our model. Such complex interactions between external factors, emergent cross-feeding interactions and niche construction are therefore of primary importance to understand the evolution of microbial communities in well-mixed environments. Using a computational model of ISEE to decipher those interactions seems to be a rich complementary approach to wet experiments and mathematical modeling.

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