Dissecting the dynamics of epigenetic changes in phenotype-structured populations exposed to fluctuating environments

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HIGHLIGHTS

- We present a PDE model of adaptive dynamics in a phenotype-structured population.
- The fitness landscape evolves in time due to environmental oscillations.
- We establish the existence of periodic solutions with a Gaussian profile.
- We study the effects of different ecological mechanisms as drivers of adaptation.
- The results of our study are applicable to a broad range of asexual populations.

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ABSTRACT

An enduring puzzle in evolutionary biology is to understand how individuals and populations adapt to fluctuating environments. Here we present an integro-differential model of adaptive dynamics in a phenotype-structured population whose fitness landscape evolves in time due to periodic environmental oscillations. The analytical tractability of our model allows for a systematic investigation of the relative contributions of heritable variations in gene expression, environmental changes and natural selection as drivers of phenotypic adaptation. We show that environmental fluctuations can induce the population to enter an unstable and fluctuation-driven epigenetic state. We demonstrate that this can trigger the emergence of oscillations in the size of the population, and we establish a full characterisation of such oscillations. Moreover, the results of our analyses provide a formal basis for the claim that higher rates of epimutations can bring about higher levels of intrapopulation heterogeneity, whilst intense selection pressures can deplete variation in the phenotypic pool of asexual populations. Finally, our work illustrates how the dynamics of the population size is led by a strong synergism between the rate of phenotypic variation and the frequency of environmental oscillations, and identifies possible ecological conditions that promote the maximisation of the population size in fluctuating environments.

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1. Introduction

Evolution can be thought of as a complex and dynamic interplay between hereditary phenotypic modifications, environmental change and natural selection. In this framework, it is largely an open question in evolutionary biology how individuals and populations adapt to fluctuating environments.

Previous theoretical and experimental work involving asexual populations has shed some light on the way phenotypic diversity can evolve in the presence of environmental fluctuations (Acar et al., 2008; Avery, 2006; Casadesus and Low, 2006; Dubnau and Losick, 2006; Gander et al., 2007; Kussell et al., 2005; Kussell and Leibler, 2005; Lachmann and Jablonka, 1996; Thattai and van Oudenaarden, 2004; Wolf et al., 2005). With the aim of dissecting the relative contributions of phenotypic variation, environmental oscillations and natural selection as drivers of phenotypic adaptation, here we formulate and analyse an integro-differential model of adaptive dynamics in a phenotype-structured population embedded in a changing environment. Models of this type can be derived from stochastic

individual-based models in the limit of large numbers of individuals (Champagnat et al., 2006, 2001), and they have been proven to constitute a suitable conceptual apparatus to study evolutionary processes in population dynamics (Bouin and Calvez, 2014; Bouin et al., 2012; Chisholm et al., 2015a; Delitala et al., 2013; Delitala and Lorenzi, 2012; Lavi et al., 2014; Lorz et al., 2013; Stiehl et al., 2014).

We focus on the ecological scenario where a population has a fitness landscape with one single peak, the location of which undergoes periodic oscillations in time. Due to random epimutation events (which change the way genes are expressed), individuals within this population undergo stochastic variation in phenotype (Brock et al., 2009; Sharma et al., 2010; Gupta et al., 2011; Pisco et al., 2013). We assume that small (large) epimutations correspond to small (large) phenotypic changes, and noting that small epimutations occur at a much higher frequency than large epimutations (Becker et al., 2011), we model the effects of heritable variations in gene expression by means of a diffusion operator, along the lines of Lorz et al. (2011), Mirrahimi et al. (2015), and Perthame and Barles (2008). Moreover, in order to take into account the fact that epimutations can be inherently biased towards particular variants (Arthur and Farrow, 1999; Donoghue and Ree, 2000; Laland et al., 2014; Wallace, 2002), we follow the modelling strategy presented in Chisholm et al. (2015a,b) and include a drift operator in our model.

From the mathematical point of view, our work follows earlier papers on the analysis of integro-differential equations that arise in models of adaptive evolution of phenotype-structured populations (Lorz et al., 2011; Mirrahimi et al., 2015; Perthame and Barles, 2008; Calsina et al., 2013; Desvillettes et al., 2008; Raoul, 2011). These papers are devoted to the study of solutions of such equations when the rate of diffusion across the phenotypic space is small or tends to zero. The main novelty of our work is that we do not impose any smallness assumptions on the diffusion rate. We also allow the presence of a drift term in the governing equation. In this setting, we are able to establish the existence of periodic solutions with a Gaussian profile, without any specific assumptions concerning the nature of the periodic variation in the trait associated with the maximum of the fitness landscape.

Exploiting the analytical tractability of the model, we perform a systematic investigation of the ways in which the presence of a time-varying environment, the evolution of the epigenetic state, the level of phenotypic diversity and the size of the population are shaped by the rate of epimutations, the degree of bias in the generation of novel phenotypic variants, the strength of natural selection, and the frequency of environmental oscillations. The generality of this model makes the results of our study applicable to a broad range of asexual populations evolving in fluctuating environments.

2. The model

We study evolutionary dynamics in a well-mixed population that is structured by a phenotypic trait $x \in \mathbb{R}$. Individuals inside the population proliferate through asexual reproduction, die due to competition for limited resources, and undergo epimutations. To reduce biological complexity to its essence, we make the *prima facie* assumption that stochastic variations in gene expression yield infinitesimally small phenotypic modifications. Moreover, we let the environment evolve independently of the population (Ashcroft et al., 2014). Despite these simplifications, the model captures a wide spectrum of ecological scenarios.

The phenotype distribution of the population at time $t \geq 0$ is characterised by the population density $c(x, t) \geq 0$, which evolves

through the following integro-differential equation:

$$\frac{\partial c}{\partial t} + \alpha \frac{\partial c}{\partial x} = \beta \frac{\partial^2 c}{\partial x^2} + R(x, t, \varrho(t)) c, \tag{2.1}$$

with

$$\varrho(t) = \int_{-\infty}^{\infty} c(x, t)\, dx, \tag{2.2}$$

$$c(x, t) \to 0 \quad \text{as } x \to \pm\infty \tag{2.3}$$

and

$$c(x, 0) \in L^1 \cap L^\infty(\mathbb{R}), \quad c(x, 0) \geq 0 \text{ a.e. on } \mathbb{R}. \tag{2.4}$$

It is natural to characterise the population's phenotype distribution in terms of its mean $\mu(t)$ and standard deviation $\sigma(t)$, given in the usual way by

$$\mu(t) = \frac{1}{\varrho(t)} \int_{-\infty}^{\infty} x\, c(x, t)\, dx, \tag{2.5}$$

$$\sigma^2(t) = \frac{1}{\varrho(t)} \int_{-\infty}^{\infty} x^2 c(x, t)\, dx - \mu(t)^2. \tag{2.6}$$

If the distribution $c(x, t)$ is unimodal and reasonably symmetric, the mean phenotype will be close to the most prevalent phenotype, which has greater direct biological interest.

In Eq. (2.1), the diffusion term models the effects of heritable variations in gene expression, which occur at the average rate $\beta \in \mathbb{R}_+$. The drift term accounts for the fact that epimutations can be more likely to produce phenotypic variations in certain directions, since the process leading to the introduction of novel phenotypic variants may be not purely random (Arthur and Farrow, 1999; Donoghue and Ree, 2000; Laland et al., 2014; Wallace, 2002). The sign of the parameter $\alpha \in \mathbb{R}$ models the direction of bias, and the absolute value of α measures the degree of bias. Natural selection is driven here by the fitness function $R(x, t, \varrho(t))$, which models the net proliferation rate of individuals with phenotypic trait x at time t, given the total population size $\varrho(t)$. Throughout this paper, we make use of the following definition:

$$R(x, t, \varrho(t)) := b(x, t) - \kappa \varrho(t). \tag{2.7}$$

The above definition relies on the idea that a higher total population corresponds to less available resources; therefore, we let individuals inside the population die at rate $\kappa \varrho(t)$, where the parameter $\kappa \in \mathbb{R}_+$ models the average rate of death due to intra-population competition. Moreover, we let individuals with phenotypic trait x at time t proliferate or die at rate $b(x, t)$. Since we focus on a population with a single-peaked fitness landscape, we assume that the function b is strictly concave in its first argument at each time instant t. In particular, we focus on the case where

$$b(x, t) := \gamma - \epsilon [x - \varphi(t)]^2, \tag{2.8}$$

where $\gamma \in \mathbb{R}_+$, $\epsilon \in \mathbb{R}_+$ and for some $T > 0$

$$\varphi : [0, \infty) \to \mathbb{R}, \quad \varphi(t) = \varphi(t + T). \tag{2.9}$$

The parameter γ and the coefficient ϵ provide a measure of the strength of natural selection. Definition 2.8 mimics the effects of a fluctuating environment that induces the phenotypic trait associated with the maximum of the fitness landscape to change over time with period T.

3. Analysis of the model

Subject to a single condition below [the inequality (3.5)], there is a solution $c(x, t) = C(x, t) \geq 0$ of the problem (2.1)–(2.4), where

(i) $C(x, t)$ is periodic with period T;