

Molecular Evolution in Time-Dependent Environments

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Abstract. The quasispecies theory is studied for dynamic replication landscapes. A meaningful asymptotic quasispecies is defined for periodic time dependencies. The quasispecies' composition is constantly changing over the oscillation period. The error threshold moves towards the position of the time averaged landscape for high oscillation frequencies and follows the landscape closely for low oscillation frequencies.

The quasispecies theory, put forward by Eigen in 1971 [1], and subsequently studied by Eigen, Schuster, McCaskill and coworkers [2, 3, 4], is nowadays one of the classical theories of self-replicating entities. Its prediction of an error threshold, above which the self-replication ceases to produce useful offspring, has important implications for the origin of life. The error threshold effectively limits the amount of information the entities can carry, thus placing an upper bound on the complexity self-reproducing information carriers can achieve without sophisticated error correction mechanisms.

Although completely static environments are unrealistic in any case apart from experiments in perfectly controlled flow reactors, the quasispecies theory has so far been considered mainly in static replication landscapes. Nevertheless, even under fixed environmental conditions can the replication rates of RNA molecules, for example, change because of changing concentrations of template and replica [5]. Jones [6, 7] has studied underlying time-dependencies which are identical for all sequences. Contrasting to that, we want to focus on replication landscapes with individual time-dependency for each sequence. One of the reasons for the neglect of individually changing replication coefficients in earlier work is probably the fact that for arbitrary temporal changes an asymptotic quasispecies cannot be defined. However, a meaningful definition is at hand for time-periodic replication landscapes, as we are going to show below.

We start from the discretized form of Eigen's evolution equation [8], linearized with the appropriate transformation [9, 10]. Due to space limitations, we cannot repeat the arguments leading to that equation here. For details about this calculation, the reader is referred to [4]. We use the same notations as are used there. Additionally, we define the error rate $R = 1 - q$, which gives the probability that a single symbol is copied erroneously. The string length will be denoted by l throughout this paper.

The vector of the unnormalized sequence concentrations $\mathbf{y}(t)$ evolves according to

$$\mathbf{y}(t + \Delta t) = \left[\Delta t \mathbf{W}(t) + \mathbf{1} \right] \mathbf{y}(t). \quad (1)$$

Here, $\mathbf{W}(t)$ is the replication matrix $\mathbf{W}(t) = \mathbf{Q}\mathbf{A}(t) - \mathbf{D}(t)$. We assume the matrix $\mathbf{W}(t)$ is periodic with period $T = n\Delta t$, $n \in \mathbb{N}$, with some chosen discretization time step $\Delta t \ll T$. After iteration of Eq. (1), we obtain for $t' = t + \zeta\Delta t$, $\zeta \in \mathbb{N}$

$$\mathbf{y}(t') = \mathcal{T} \left\{ \prod_{\nu=0}^{\zeta-1} \left[\Delta t \mathbf{W}(t + \nu\Delta t) + \mathbf{1} \right] \right\} \mathbf{y}(t). \quad (2)$$

where $\mathcal{T}\{\cdot\}$ stresses that the product has to be evaluated in the time order given by the iteration. With the definition of the matrix (or operator)

$$X := \mathcal{T} \left\{ \prod_{\nu=0}^{n-1} \left[\Delta t \mathbf{W}(\nu\Delta t) + \mathbf{1} \right] \right\}. \quad (3)$$

which maps $\mathbf{y}(0)$ onto $\mathbf{y}(T)$, we are now able to write down the solution of the discretized differential equation Eq. (1) for the initial condition $\mathbf{y}(0)$ as

$$\mathbf{y}(t) = \mathcal{T} \left\{ \prod_{\nu=0}^{\zeta-1} \left[\Delta t \mathbf{W}(\nu\Delta t) + \mathbf{1} \right] \right\} X^m \mathbf{y}(0). \quad (4)$$

where the time t has been subdivided into $t = mT + \zeta\Delta t$, with $\zeta < n$ and $m, \zeta \in \mathbb{N}$.

If we observe the system in time steps of the period length T , the system appears to evolve in a static replication landscape, which is defined by X . The asymptotic steady state for the oscillation phase $\zeta = 0$ is therefore given by the normalized Perron eigenvector ϕ_0 of X [11]. For $0 < \zeta < n$, the steady states are found by application of $\mathcal{T}\{\dots\}$ from Eq. (4) to ϕ_0 and subsequent normalization.

Let us now study quantitatively the effects a periodic replication landscape has on the prominent quasispecies. As the first step into that direction, we start from the Swetina-Schuster landscape [12] and introduce small oscillations in the master sequence's replication coefficient A_0 . For reasons of simplicity, we set all decay constants equal $D_i(t) = D$, because then they drop out of Eq. (1) during the foregoing linearization.

We will write the time-dependent replication coefficient $A_0(t)$ as

$$A_0(t) = A_{0,S} \exp[\epsilon f(t)], \quad (5)$$

where $A_{0,S}$ is the replication coefficient in the static landscape, $f(t)$ is a T -periodic function and ϵ is the oscillation amplitude. For $\epsilon = 0$ the corresponding static landscape is reached. The other replication coefficients are equal $A_1 = \dots = A_l = A$ and constant. We will choose A so small that the condition $A \ll$

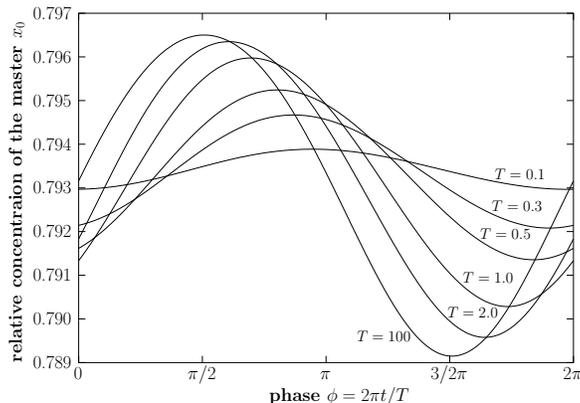


Fig. 1. The steady state oscillations of the master sequence in cyclically changing environments with different oscillation periods T . Parameters used are $l = 2$, $A_{0,S} = e^{2.4}$, $A_1(t) = A_2(t) = 1$, $\epsilon = 0.2$.

$A_0(t)$ is satisfied for all t and $\epsilon \ll 1$. This assures that we see a clear transition from the static case to the dynamic case, and additionally, that the changes in the master sequence's abundance can be directly related to the changes in $A_0(t)$.

One of the simplest forms the function $f(t)$ in Eq. (5) can take on is

$$f(t) = \sin(\omega t) \quad \text{with} \quad \omega = 2\pi/T. \quad (6)$$

In the following, we will shortly discuss the influences of different frequencies ω and amplitudes ϵ for this time dependency.

As response to the oscillation of the replication coefficients, a modified oscillation is found in the concentration x_0 of the Master sequence (Fig 1). For increasing frequency ω , the amplitude of the x_0 oscillation decreases and a phase shift strengthens. This behaviour is due to the finite time a reaction system as described by Eigen's equation needs to settle into equilibrium. In constant environments, the asymptotic species distribution is approached in exponential time, with the relaxation time scale τ set by the difference between the largest and the second-largest eigenvalue of W . For the oscillating environments the relaxation time needs to be compared to the period T . If $T \gg \tau$, the system is virtually in equilibrium for arbitrary (asymptotic) times t , whereas for $T \approx \tau$ the changes cannot be tracked anymore and phase shift as well as amplitude damping of the response sets in. For $T \ll \tau$ the response amplitude gets fully damped and the system gets identical to one with the time-averaged replication coefficients. Interpreting the A_0 and x_0 time-dependence as input and output signal, the system acts as a low pass analog filter, in analogy to observations made in population genetics models with dynamic fitness landscapes [13, 14, 15, 16]. Moreover, for small ϵ , the filter works linear, which means that a sinusoidal oscillation is found in x_0 , whereas this linearity is quickly destroyed for increasing ϵ ¹.

¹ Details on this analysis can be found in [17].

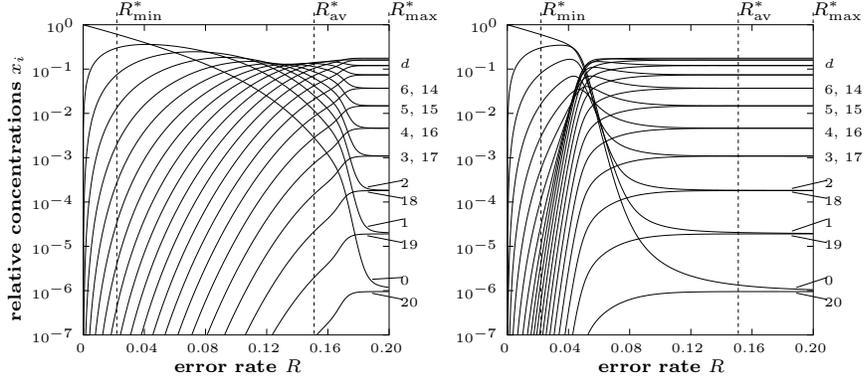


Fig. 2. The quasispecies distribution as a function of the error rate R . $A_{0,S} = e^{2.4}$, $A = 1$, $\epsilon = 2$, $T = 100$. Two different oscillation phases are shown. *left*: $\zeta = n/2$, *right*: $\zeta = 0$.

We will now focus on the influence of a time-dependency as given in Eq. (5) onto the error-threshold. In accordance with the above, we have to distinguish between different dynamic regimes. For $T \ll \tau$, a sharp error-transition occurs at R_{av}^* , which denotes the error-threshold of a system with time-averaged $\dot{A}_0 = \frac{1}{T} \int_0^T A_0(t) dt$. Contrasting to that, a moving error-transition can be found for $T \gg \tau$ at approximately $R^*(t)$, which denotes for any given t the error-threshold in a constant landscape with $\dot{A}_0 = A_0(t)$. $R^*(t)$ lies between R_{max}^* and R_{min}^* , which correspond to $\dot{A}_0 = \max_t A_0(t)$ and $\dot{A}_0 = \min_t A_0(t)$, respectively. In the intermediate cases $T \approx \tau$, the numerical simulations (see Fig. 2) show that the error-threshold $R^*(t)$ oscillates within a smaller interval than $[R_{min}^*, R_{max}^*]$.

These findings allow to draw a phase diagram as displayed in Fig. 3. For low T , we observe the standard separation into an ordered phase (below the error threshold) and a disordered phase (above the error threshold). With increasing oscillation period T , a third, new phase appears between the two. In this phase,

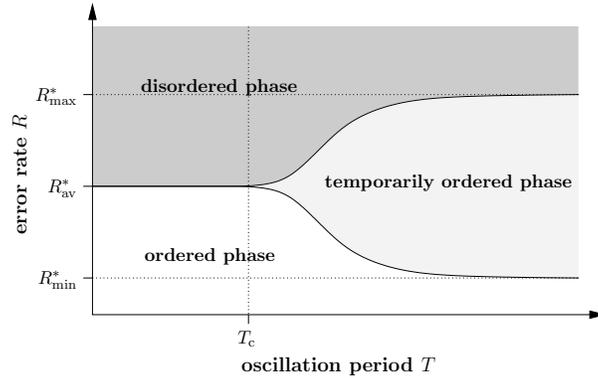


Fig. 3. Schematic phase diagram for a time-dependency like Eq. (5).

we observe—for a fixed error rate R —an alternation between a fully developed quasispecies and a completely disordered system. The population seems to be moving back and forth over the error threshold. Therefore, we call this new phase the temporarily ordered phase. Since a similar phase diagram can be expected for any periodic landscape with finite R_{av}^* and $R_{\text{min}}^* \neq R_{\text{max}}^*$, we believe that such observations could also be made in typical AL simulations such as Tierra or Avida [18] provided with the appropriate replication landscape. The temporarily ordered phase would for a finite population in a rugged landscape have the effect of causing a random drift over the landscape at some times and a localization around a local master sequence at other times.

Upon completing this work, we became aware of Ref [19], in which a different approach towards dynamic replication landscapes is given, using a stochastic time dependency in the landscape. The results presented there cannot directly be related to our findings here, because the equivalent to R_{av}^* vanishes in [19], while the equivalents to R_{max}^* and R_{min}^* take on the same finite value. This leads to a different phase diagram than the one we observe here.

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