The non-perturbative phenomenon for the Crow Kimura model with stochastic resetting

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We consider the Crow Kimura model, modified via stochastic resetting. There are two principally different situations: First, when due to resetting the system jumps to the low fitness state, everything is rather simple in this case, we have a solution which is a slight modification of the standard Crow-Kimura model case. When there is resetting to the high-fitness state, there is a non-perturbative phenomenon via the resetting probability – even a minimal resetting probability drastically changes the solution. We found two subphases in this phase.

I. INTRODUCTION

Stochastic resetting is one of the important directions of modern statistical physics \cite{1}. The resetting research started a couple of decades ago while looking at birth-death processes \cite{2,4} and nowadays has numerous applications \cite{1} in fields such as ecology \cite{5}, biomedicine \cite{6} and population genetics related models \cite{7,8,9,10}. As has been observed in the latter works, the main equation of statistical physics of random resetting processes have been derived already in population genetics literature \cite{12}, while considering the continuous version of \cite{11}.

The idea of resetting search is very simple. If we are looking for some lost object, then after starting the stochastic search from some initial position, and failing in our search process, we renew our search returning back to the starting position. It is interesting that such strategies are very successful both in nature and in computer algorithms, i.e. in case of simulated annealing.

In the standard random walks, one looks at a linear master equation for the probability distribution, which can be considered as a discrete space version of the diffusion equation. There are random walks which are sometimes accompanied with jumps into a special state. In case of an absorbing state, the resetting brings to the faster relaxation to the absorbing state, which has many practical applications.

On the other hand, we have a problem of nonequilibrium statistical physics, which is solvable. The resetting acts against reaching equilibrium.

While the equilibrium statistical mechanics already has been successfully applied to the evolution phenomenon in static conditions, we assume that the nonequilibrium statistical physics approach is a much more adequate language to describe the living matter than the equilibrium statistical physics. There have been several relating stochastic resetting with evolution and ecology, working with continuous differential equations. In resetting problems one works with diffusion or the Fokker Planck equation, which are linear differential equations in continuous space. On the contrary, in Crow-Kimura \cite{13,17} and Eigen \cite{13,14} models of evolution with an infinitely large population, we work with the nonlinear equations, where now we have selective forces in addition to diffusion, and a discrete set of types. The Crow-Kimura model is related to the discrete time version of the Eigen model, the latter is similar to the branching processes \cite{13}. The Wright Fisher model, which is the main model of population genetics, is related to the Crow-Kimira model. So by solving the Crow-Kimura model with resetting, we can extend later our results to the other models of population genetics. The advantage of the Crow-Kimura model is that it is simpler case for the analytical investigation of evolutionary dynamics.

The vast majority of the stochastic resetting investigations are for Markovian models. Here we introduced the concept of resetting for the models with fitness. In the case of evolution with a large population, the dynamics is affected by two forces, namely selection and mutation. Without mutations, the population is focused on the state with maximum fitness, while a nonzero mutation distributes the population around the state with the high fitness.

It is interesting to study how the situation changes in our case with resetting, similar to \cite{7,12}. In the latter works, one looks at many alleles in the same locus, approximating the situation by the continuous space. We will formulate the Crow-Kimura model with resetting, and look two different situations when resetting is into a state with the non-high fitness, and the case of resetting to the high-fitness state. So we work in a discrete space of types, which is more adequate to the biological reality. We will identify two different statistical physics phases.

II. THE MODEL

A. The standard Crow-Kimura model

While for the continuous time random walk probabilities we have the diffusion equation for the probability distribution,

$$\frac{dP(x, t)}{dt} = D \frac{d^2P(x, t)}{dx^2}$$

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for the resetting case with a resetting rate \( \epsilon \) to the position \( X_r \), the equation is modified into

\[
\frac{dP(x, t)}{dt} = D \frac{d^2 P(x, t)}{dx^2} - \epsilon P(x, t) + \epsilon \delta(x - X_r). \tag{1}
\]

Consider now the Crow-Kimura model. We have a genome as a chain of letters taking values \( \pm \) with length \( L \), thus we have \( 2^L \) sequences. We denote different sequences via an index \( 0 \leq i \leq 2^L - 1 \). The Hamming distance \( d(i, j) \) between two sequences is the number of differences in the signs.

There is a mutation from the \( i^{th} \) to the \( j^{th} \) state with a rate \( \mu_{ij} \). The latter is nonzero only when \( d(i, j) = 1 \). We have a mutation rate \( \mu/L \) neighbors with the Hamming distance 1, also \( \mu_{ii} = -\mu \).

\[
\frac{dp(i, t)}{dt} = (r_i - \mu - R)p(i, t) + \mu \sum_j p(j, t), \tag{2}
\]

where the sum is over the neighbors with the Hamming distance \( d = 1 \), and \( R = \sum_j p(j, t)r_j \).

For the symmetric fitness case, when the fitness is a function of the total number of mutations from the \( 0^{th} \) sequence, we introduce a fitness function \( f(m) \), \( r_j = f(m), m = 1 - 2l/L, l = d(j, 0) \). The we define the total probability \( P(l, t) \) of the \( l^{th} \) Hamming class:

\[
\frac{dP(l, t)}{dt} = (f(m, t) - \mu - R)P(l, t) + \mu \frac{(l+1)}{L} P(l+1, t) + \frac{(l-1)}{L} P(l-1, t). \tag{3}
\]

The coefficients \( \frac{(l+1)}{L} \) and \( \frac{(l-1)}{L} \) arose from the combinatorics, while considering the Hamming class probabilities.

We will investigate the stochastic resetting modification of the model. While the model is formulated and investigated for the general case of function \( f(x) \), in literature three versions of fitness functions have been popular: a. the single peak case, where \( f(1) = J > 0 \) while \( f(m) = 0, m < 1 \) \[14\], b. linear fitness function \( f(x) = kx \) from population generics \[15\], c. quadratic fitness function \[16\].

B. The stochastic resetting version of the Crow-Kimura model

Consider the resetting in the Crow-Kimura model to the given configuration \( r \).

\[
\frac{dp(i, t)}{dt} = (r_i - \mu - R - \epsilon)p(i, t) + \mu \sum_j p(j, t), \tag{4}
\]

for \( i \neq r \) and for the \( r^{th} \) sequence

\[
\frac{dp(r, t)}{dt} = (r_i - \mu - R - \epsilon)p(r, t) + \mu \sum_j p(j, t) + \epsilon \sum_j p(j, t), \tag{5}
\]

Consider now the symmetric fitness case, and choose as the resetting state \( r \) the \( L^{th} \) Hamming class

\[
\frac{dP(l, t)}{dt} = (f(m, t) - \mu - \epsilon)P(l, t) + \mu \frac{(L-l+1)}{L} P(l+1, t) + \frac{(L-l-1)}{L} P(l-1, t) + \frac{\mu \epsilon}{L} P(l + 1, t), \tag{6}
\]

Thus we have a resetting to the \( L^{th} \) Hamming class.

Further we set \( \mu = 1 \), which is always possible with the rescaling of the fitness and \( \epsilon \). We denote the steady state distribution as \( \rho(l) = P(l, T), T >> 1 \).

Consider the case when \( f(m) \neq f(-m) \) and the maximum is at the peak \( m = 1 \). First we obtain \( p_L \) in the steady state. Ignoring 1/L terms, we get

\[
\rho(L) = \frac{\epsilon}{R - f(-1) + 1 + \epsilon}. \tag{7}
\]

We have done numerics (see Figures 1–3), and identified three different situations. In the first case, we have a peak at an intermediate Hamming class, and the second half-peak near the \( L^{th} \) class. In the second case, we have a single peak near the \( L^{th} \) sequence. In the third case, we have a half-peak at the \( L^{th} \) sequence.

![FIG. 1. The probability distribution via Hamming classes \( \rho(n) \). \( \epsilon = 0.2, f(x) = x, L = 100 \).](image1)

![FIG. 2. The probability distribution via Hamming classes \( \rho(n) \). \( \epsilon = 0.01, f(x) = 1.5x^2, L = 100 \).](image2)
III. THE SOLUTION OF CROW-KIMURA MODEL WITH resetting

A. The case of resetting to the low fitness state

Let us express the probability of the \( n \)-th sequence via probability of the \( L \)-th sequence:

\[
\rho(n) = \frac{\rho(L)}{R - f(1) + 1 + \epsilon}.
\]

For the Hamming classes \( \rho(L - l), l > 1 \) we get

\[
\rho(L - l) = \rho(L) \left( \frac{1}{R - f(1) + 1 + \epsilon} \right)^l.
\]

Summing the members of the geometric progression, we obtain for the \( P \), the total probability near the \( L \)-th sequence

\[
P = \frac{\epsilon}{R - f(1) + \epsilon}.
\]

There is the second peak of the distribution with the total probability of population around the peak, \( p = 1 - P \)

An ansatz [19]

\[
\rho(1) = p \exp(Lu(x))
\]

gives the Hamilton-Jacobi equation [19]

\[
\frac{\partial u}{\partial t} = f[x] - \epsilon + \frac{1 + x}{2} e^{2u'} + \frac{1 - x}{2} e^{-2u'}.
\]

We obtain the steady state distribution as

\[
R = f[x] - \epsilon + \frac{1 + x}{2} e^{2u_0'} + \frac{1 - x}{2} e^{-2u_0'} - 1,
\]

and define the mean fitness \( R \) looking at the maximum of the right hand side via \( u_0' \)

\[
R = \max[f[x] - \epsilon + \sqrt{1 - x^2} - 1]
\]

The maximum is at the point \( s \) defined via the equation

\[
R = f(s) - \epsilon
\]

while for the standard surplus

\[
S = \sum_l \rho(l)(1 - 2l/N) = ps - (1 - p).
\]

The surplus is one of the key characteristics of the population distribution, it defines the mean number of mutations as \( L(1 - S)/2 \). Our Eqs.(10), (15)-(17) are among the main results of the article. We compare our analytical results with the numerics.

We have a distribution with double peaks. For the linear fitness case \( f(x) = kx \) we get

\[
\rho(L) = \frac{\epsilon}{R + k + 1 + \epsilon},
\]

\[
R = \sqrt{k^2 + 1} - 1 - \epsilon,
\]

\[
s = \frac{\sqrt{k^2 + 1}}{k},
\]

\[
1 - p = \frac{\epsilon}{R + 1 + \epsilon}
\]

Figures 4-5 illustrate the accuracy of our analytical results for the linear fitness case.

For the single peak fitness, with the peak fitness \( J \) and fitness for other sequences, we get for the mean fitness just

\[
R = J - 1 - \epsilon.
\]
B. The case of resetting to the high fitness state with the smooth fitness function

Consider the fitness choice \( f(x) = kx^2/2 \), so that resetting is to the state with a maximal fitness. We verified numerically that now we have a single maximum for the distribution. For the \( f(x) = 1.5x^2 \), we have at \( \epsilon = 0 \) case \( R = 2/3 \).

Let us calculate the mean fitness of this phase. First we simplify Eq. (6) at steady state for the \( |L-l| \ll L \).

\[
(f(m) - 1 - \epsilon)\rho(l) + \mu\left(\frac{L-l+1}{L}\right)\rho(l+1) = 0
\]

(20)

We expand \( f(m) \approx f(-1) + f'(-1)2n/L \), where \( n = L-l \), then get an equation.

\[
(f(-1) - R - 1 - \epsilon + f'(-1)2n/L)\rho(L-n) + \frac{(n+1)}{L}\rho(L-n-1) + \frac{(L-n+1)}{L}\rho(L-n+1) = 0
\]

(21)

In the bulk approximation, we obtain

\[
\rho(L-n) = \frac{\rho(L-n+1)}{\Delta},
\]

\[
\Delta = -f(-1) + R + 1 + \epsilon
\]

(22)

Thus Eq. (20) gives

\[
(f(-1) - R - 1 - \epsilon + f'(-1)2n/L)\rho(L-n) + \frac{(n+1)}{L}\rho(L-n-1) + \frac{(L-n+1)}{L}\rho(L-n+1).
\]

(23)

Then

\[
\rho(L-n) = \rho(L-n+1)/(\Delta - \frac{(n+1)}{L}\Delta + \frac{(n-1)}{L}\Delta - kn)
\]

(24)

where \( k = f'(1)/2L \). We should look at an infinite product

\[
\rho(L-n) = \rho(L)\prod_{m=0}^{\infty}1/\Delta - \frac{(n+1)}{L}\Delta + \frac{(n-1)}{L}\Delta - kn,
\]

(25)

then calculate the sum

\[
\tilde{P}(R) = \sum_{n=0}^{\infty}\rho(L-n).
\]

(26)

Using the equation

\[
F(a, b) = \sum_{n=0}^{\infty}\prod_{m=0}^{n} \frac{1}{\alpha + mn} = e^{1/b}\left(\frac{1}{b}\right)^{-\frac{a}{b}}\left(\Gamma\left(\frac{a+1}{b}\right) - \Gamma\left(\frac{a}{b} + 1,\frac{1}{b}\right)\right) + \frac{1}{a},
\]

we then derive an expression for the mean fitness \( R \).

\[
F(a, b) = R,
\]

\[
a = \Delta - \frac{1}{2\Delta} - \frac{2}{\Delta},
\]

\[
b = k - \frac{1}{2\Delta} + \frac{2}{\Delta}
\]

(28)

We calculate \( R \) using the last equation and gave the comparison with numerics in fig 6. We verified that both cases on Figures 2,3 are given by the same Eq. (28).

C. The case of resetting to the high fitness state with single peak fitness function

Consider now the single peak fitness case, when the resetting sequence coincides with the peak sequence. We modify Eq. (6), considering the resetting to the 0-th Hamming class. We have a fitness \( J \) for the peak sequence, and 0 fitness for other sequences. Ignoring the \( O(1/L) \) terms, we get

\[
\rho(0)R = (J - 1)\rho(0) + \epsilon(1 - \rho(0)),
\]

\[
R = J\rho(0)
\]

(29)

Then we derive the following equation for the mean fitness in the steady state

\[
R = \frac{J - 1 + \epsilon + \sqrt{(J - 1 + \epsilon)^2 + 4J\epsilon}}{2J}
\]

(30)

IV. CONCLUSION

Random walk models with stochastic resetting are on the focus of the modern statistical physics, and have numerous
applications. While there have been some resetting related results in population genetics, till now the quasispecies models have not been investigated in case of stochastic resetting. We formulated the resetting version of the Crow-Kimura model Eq. (6), then investigated the model both numerically and analytically. It is astonishing funny that stochastic resetting arose for the first time just in population genetics [12], so our work returns back the research process to the origins. We identify two statistical physics phases in our model. The first one given by Eqs. (10),(15)-(17) is not too hard mathematical problem, this phase in the case when the resetting sequence is an ordinary sequence with a non-highest fitness. Our analytics is well confirmed by numeric, see figures (4)-(5). When we choose as the resetting sequence the sequence with the fitness peak, the situation is becoming highly non-trivial, the solution is given by hypergeometric function Eq. (28). We met a highly non-perturbative phenomenon. Even the $\sim 10^{-6}$ resetting probability brings to 100% change of the mean fitness. Eqs. (6),(7) illustrate the accuracy of our analytical results.

It will be interesting to look the equivalents of our findings in other stochastic resetting models, as the driving forces in random walks resemble our fitness in case of evolution models. Here we looked at the most direct mapping of resetting mechanism from the random walks to evolution. An alternative approach should be to look at the evolution models with reservoirs - there is a two-habitat model [20, 21] with some transitions between them, and second, reservoir habitat where the mutations are suppressed by strong selection forces.

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