Evolution towards critical fluctuations in a system of accidental pathogens

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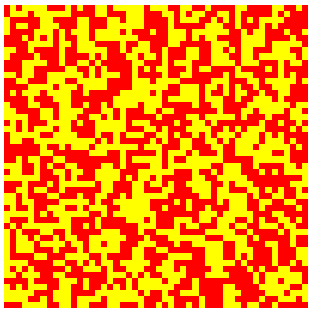

Figure 1:
From random initial conditions the Kimura/voter model quickly aggregates areas of one or the other species (population I yellow, Y red).

Abstract

We investigate the by now so called SJ model [1] not only in its simples formulation as recently used, but an extended version, the SJ model version II. In this we find the system to evolve to low pathogenicity causing large critical fluctuations without tuning the control parameter, a self-organization of critcality.

1 Introduction

Already Kimura suggested a model with two populations replacing each other with equal probability, a neutral model for evolution, leading eventually to fixation of on or the other population. Kimura's model was later reinvented in a different context, called the voter model, and more rigorously investigated mathematically. However, in relevant evolutionary systems selection can play a role next to pure mutation as described by the neutral theory. Hence near-neutrality becomes an important research area. We propose a model to describe accidental pathogens, with a paradigmatic empirical system of bacterial meningitis, which includes mutations between different strains of the bacteria, and via epidemiological interaction of the hosts and pathogens also selection.
The model shows in its easiest version of two strains I and Y critical fluctuations with power law $3/2$ for outbreak sizes. This version has recently been demonstrated to be in the universality class of the Kimura/voter model [1], and is now coined the SJ-model (Stollenwerk-Jansen model) [1]. This universality class is characteristic for two absorbing states, fixation of one or the other strain I or Y. All systems in such a universality class share the same critical exponents.
In a second version with infinitely many strains evolution of the system towards a critical state is observed, leaving most pathogens with only minor pathogenicity, i.e. probability to cause disease. This model is a valid candidate for a self-organized critical (SOC) system [2], since it has infinitetly many absorbing states, like the for SOC paradigmatic sand-pile models. We call this the SJ model version II.

2 The Kimura/voter model

Two species I and Y can replace each other with transition rates ι, respectively υ

$$I_i + Y_j \xrightarrow{\upsilon} Y_i + Y_j$$
$$Y_i + I_j \xrightarrow{\iota} I_i + I_j$$

on a lattice with N sites i etc., at lattice site $i \in \{1, \ldots, N\}$ an type $Y_i = 1$, or not $Y_i = 0$, hence $I_i := 1 - Y_i = 1$, stochastic dynamics given for variables $Y_i \in \{0, 1\}$ by the master equation

$$\begin{aligned}
&\frac{d}{dt}\, p(Y_1, Y_2, \ldots, Y_N, t) \\
&= \sum_{i=1}^{N} \upsilon \left(\sum_{j=1}^{N} J_{ij} Y_j \right) Y_i \; p(Y_1, \ldots, 1-Y_i, \ldots, t) \\
&\quad + \sum_{i=1}^{N} \iota \left(\sum_{j=1}^{N} J_{ij} (1-Y_j) \right) (1-Y_i) \; p(\ldots, 1-Y_i, \ldots) \\
&\quad - \sum_{i=1}^{N} \left[\upsilon \left(\sum_{j=1}^{N} J_{ij} Y_j \right) (1-Y_i) \right. \\
&\quad \left. + \iota \left(\sum_{j=1}^{N} J_{ij} (1-Y_j) \right) Y_i \right] \\
&\qquad \cdot p(Y_1, \ldots, Y_i, \ldots, Y_N, t)
\end{aligned}$$

with adjacency matrix $J_{ij} \in \{0, 1\}$.

3 Properties

In mean field approximation [3] we obtain the simple ODE

$$\frac{d}{dt} \langle Y \rangle = (\upsilon - \iota) \frac{Q}{N} \langle Y \rangle \, (N - \langle Y \rangle)$$

which is exactly neutral for $\upsilon = \iota$, hence $\frac{d}{dt} \langle Y \rangle = 0$.
The model has mean field exponent $\tau = 3/2$ for the "out-break size", here e.g. the distribution of Y introduced into a completely I filled environment, when getting extinct again for $\varepsilon := \iota - \upsilon \to 0$, see [1]. In spatial simulations one can observe that an intitially random distribution of the 2 populations, Fig. 1, shows after a transient the for critical systems typical percolation structure at $\varepsilon = 0$, Fig. 2.

4 Bacterial meningitis

Neisseria meningitidis, a bacterium which can cause meningitis and septicaemia, often lives a commensal with its human host and is unnoticed by the host. Only rarely the bacterium enters the blood stream and then causes major dammage to the host, an evolutionary cul de sac for the bacterium. The rarer a mutant of this commensal comits this accidental mistake the more often it will be found in the host population, hence strains with low and near to none pathogenicity will dominate at the population level, but still occasionally cause disease outbreaks [4].

5 The SIRYX model

Am model for such accidental pathogens can be described as an SIR model for harmless carriage, and includes mutation to carriage Y with a bacterium with non-zero probabilty to cause a disease case X. The reaction schemes for transitions of host classes is

$$\begin{aligned}
R_i &\xrightarrow{\alpha} S_i \\
S_i + I_j &\xrightarrow{\beta-\mu} I_i + I_j \\
&\xrightarrow{\mu} Y_i + I_j \\
I_i &\xrightarrow{\gamma} R_i \\
S_i + Y_j &\xrightarrow{\beta-\nu-\varepsilon} Y_i + Y_j \\
&\xrightarrow{\nu} I_i + Y_j \\
&\xrightarrow{\varepsilon} X_i + Y_j \\
Y_i &\xrightarrow{\gamma} R_i
\end{aligned}$$

which gives a master equation formulated along the lines of the above shown Kimura/voter model with transition rates α, β, γ from the basic SIR model and in addition mutation μ, ν and pathogenicity ε.

6 Small pathogenicity, large epidemics

Model parameters: basic epidemic parameters $\alpha := 0.1$, $\beta := 0.2$ and $\gamma := 0.1$ on a fast time scale. Mutation rates $\mu = \nu := 0.0001$ on a slow time scale. Pathogenicity ε varying on an intermediate time scale, e.g. $\varepsilon := 0.05$.

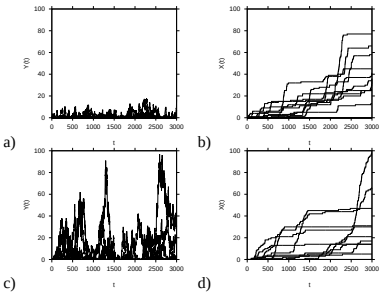

Figure 3:
For relatively large pathogenicity $\varepsilon := 0.05$ (upper two graphs) we find low numbers of mutant strains Y causing stochastic numbers of disease cases X. For 10 times smaller $\varepsilon := 0.005$ highly fluctuating numbers of mutant carriers Y cause stochastically fluctuating as many disease cases X as with much higher pathogenicity (lower two graphs).

7 Power law analytically

In a simplified model, where the SIR-subsystem is assumed in stationarity (due to its fast dynamics), we can show analytically divergence of variance and power law behaviour for the size of the epidemics $p(X)$ as soon as the pathogenicity is going to zero. For the size distribution of the epidemic we obtain power law behaviour

$$p_\varepsilon(X) := \lim_{t \to \infty} p(Y = 0, X, t) \sim X^{-\frac{3}{2}}$$

for $\varepsilon \to 0$ and large X. This was obtained by approximations to a solution with the hypergeometric function [5]. This critical exponent corresponds to the mean field exponent of the voter universality class. Also other exponents in mean field and in dimension 1 below the upper critical dimension have been found to be equal in the SIRYX model as in the voter model.

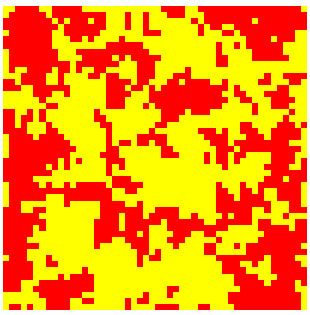

Figure 2:
Percolation clusters in the Kimura/voter model build up after longer time.
(Color coding as in Fig. 1)

8 Evolution towards criticality

Introducing strains with many different pathogenicities ε leaves the system ultimately being dominated by strains with small ε. $p(\varepsilon)$ shifts towards small ε, as time passes [6].

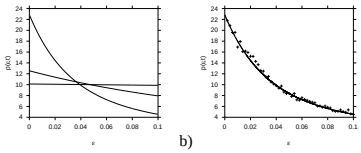

Figure 4: a) Theoretical curves for times $t = 1$, $t = 20$, $t = 100$. b) Comparison between simplified model and simulations of the SIRYX system for time $t = 100$.

In a branching process approximation we find for the distribution of pathogenicity, i.e. frequency of mutants $Y(\varepsilon)$ with certain pathogenicity ε

$$p(\varepsilon, t) = \frac{\frac{1}{\varepsilon}\left(1 - e^{-\varepsilon \frac{\gamma}{\beta} t}\right)}{\sum_{\nu=1}^{\infty} (-1)^{\nu+1} \cdot \frac{\left(\varepsilon m \frac{\gamma}{\beta} t\right)^{\nu}}{\nu \cdot \nu!}} \quad .$$

In a spatial version of the complete model, Fig. 5, this behaviour is confirmed by investigating the mean pathogenicity, Fig. 5 b), going beyond the presently studied SJ model [1] in its simplest version.

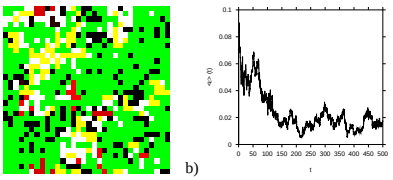

Figure 5:
a) Randomly varying pathogenicity, colored in blue to red for decreasing pathogenicity of mutants Y. The other states are S $\to$ green, I $\to$ yellow, R $\to$ white, and X $\to$ black. b) Mean value of pathogenicity ε over time.

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