Available online at www.sciencedirect.com

SCIENCE DIRECT®

BioSystems 81 (2005) 31–41

BioSystems

www.elsevier.com/locate/biosystems

RNA viruses as complex adaptive systems

Santiago F. Elena[a,*], Rafael Sanjuán[b]

[a] *Instituto de Biología Molecular y Celular de Plantas, CSIC-UPV, 46022 Valencia, Spain*
[b] *Institut Cavanilles de Biodiversitat i Biologia Evolutiva, Universitat de València, 46071 Valencia, Spain*

Received 10 June 2004; received in revised form 3 February 2005; accepted 3 February 2005

Abstract

RNA viruses have high mutation rates and so their populations exist as dynamic and complex mutant distributions. It has been consistently observed that when challenged with a new environment, viral populations adapt following hyperbolic-like kinetics: adaptation is initially very rapid, but then slows down as fitness reaches an asymptotic value. These adaptive dynamics have been explained in terms of populations moving towards the top of peaks on rugged fitness landscapes. Fitness fluctuations of varying magnitude are observed during adaptation. Often the presence of fluctuations in the evolution of physical systems indicates some form of self-organization, or where many components of the system are simultaneously involved. Here we analyze data from several in vitro evolution experiments carried out with vesicular stomatitis virus (VSV) looking for the signature of criticality and scaling. Long-range fitness correlations have been detected during the adaptive process. We also found that the magnitude of fitness fluctuations, far from being trivial, conform to a Weibull probability distribution function, suggesting that viral adaptation belongs to a broad category of phenomena previously documented in other fields and related with emergence.

Keywords: Adaptation; Complex systems; Experimental evolution; Fitness; Vesicular stomatitis RNA virus; Self-organized criticality; Weibull pdf

1. Introduction

The dynamics of adaptation of RNA viruses to a handful of in vitro conditions have been explored during the recent years (Novella et al., 1995, 1999a, 1999b; Elena et al., 1998; Miralles et al., 2000). In general, all these studies converge into a common picture of viral adaptation: a first instance of rapid fitness increase followed by a deceleration in the rate of adaptation as the viral population reaches an adaptive peak that represents an optimal solution for the environment (Elena et al., 2000; Elena and Lenski, 2003). Over the long-term, fitness trajectories might seem smooth and continuous. However, if they are measured with sufficient temporal resolution, then fluctuations in the magnitude of fitness become evident. Naïvely, we can assume that these fluctuations are trivial, i.e., they reflect pure error variance and, hence, distribute as normal deviates. In statistical physics, by contrast, the presence of fluctuations in an evolving system

* Corresponding author. Tel.: +34 963 877 895; fax: +34 963 877 859.
E-mail address: sfelena@ibmcp.upv.es (S.F. Elena).

0303-2647/$ – see front matter © 2005 Published by Elsevier Ireland Ltd.
doi:10.1016/j.biosystems.2005.02.001

can be seen as the manifestation of some sort of self-organizing phenomena (Bak et al., 1987). The common feature of self-organization towards critical points is the presence of the so-called scaling or power laws of the form $f(s) = Ks^{-c}$, where s stands for the amplitude of the fluctuation, K is a normalizing constant and $c > 0$ is called the critical exponent (Bak et al., 1988; Jensen, 1998; Solé et al., 1999a). Values of $0 < c < 2$ are indicative of a self-similar behavior. This law is a characteristic of fractal objects because changes of scale do not modify the statistical behavior of the system. In other words, a power law probability distribution function (pdf) is when there is the same proportion of smaller and larger events, regardless of the value within the power law range.

Self-organization is not a new concept in evolutionary biology and ecology (Kauffman, 1993; Solé et al., 1999b; Camazine et al., 2001). Complex phenomena have been described in situations such as the patterns of punctuated equilibrium caused by the fixation of beneficial mutations (Adami, 1995; Bak and Boettcher, 1997; Chaudhuri and Bose, 1999), the magnitude of extinction events (Solé and Manrubia, 1996; Solé et al., 1997), ecosystems stability (Solé and Montoya, 2001; Solé et al., 2001), the fractal structure of taxonomic trees (Newman, 1997), rainforest dynamics (Solé and Manrubia, 1995), or social behavior in ant swarm raids (Solé et al., 1993). A possible reason for the widespread presence of self-similar fluctuations in such different processes was proposed by Bak et al. (1987) and is known as self-organized criticality (SOC). SOC is defined as the spontaneous evolution of large complex systems, formed by many interacting parts, towards a critical state that is robust to perturbations and whose macroscopic behavior is predictable to the extent that it follows the power laws.

RNA viruses have been proposed as paradigms of complex adaptive systems (Solé et al., 1999a; Domingo, 2002; Solé and Goodwin, 2000). RNA virus exists as complex and highly dynamic mixtures of genotypes. New mutations constantly arise as a consequence of the high mutation rate of virus-encoded RNA-polymerases lacking proofreading mechanisms (Drake et al., 1998; Drake and Holland, 1999). The frequency of each genotype in the population is determined by the balance between mutation rate and selection. It has been argued that due to these properties, the unit of selection is not the single genome but the entire population (the so-called quasispecies) (Domingo, 2002). A prediction of the quasispecies theory is the existence of a critical state named the error threshold (Eigen, 1971; Eigen et al., 1988) which is determined by the maximum mutation rate compatible with the integrity of the message encoded in the genome. Beyond this point, the population undergoes error catastrophe and will go extinct. Available data support the prediction that RNA viral populations replicate near the error threshold (Holland et al., 1990; Domingo, 2000; Crotty et al., 2001). In a recent study, Lázaro et al. (2003) looked for the existence of power laws in the distribution of fluctuations in population size during a long-term evolution experiment in which several lineages of foot-and-mouth disease virus (FMDV) were subjected to 50 consecutive bottleneck passages of a single individual. These authors observed that fluctuations in population size rather than being trivially explained by a Normal distribution fitted a Weibull pdf. The Weibull pdf is more flexible than the power law (still having two parameters) and it can be used to explain frequently observed deviations from the pure power law (Laherrère and Sornette, 1998).

Here we are interested in the existence of self-organizing behavior associated with the adaptation of vesicular stomatitis virus (VSV) to constant environments. To do so, data from several long-term evolution experiments were collected and we explored which one of several alternative probability distributions better explained the observed fluctuations.

2. Materials and methods

2.1. Data

The long-term evolution fitness data used in the present study were collected from four previously published reports (Table 1). All experiments were carried out by regular dilution transfers of viral populations, and different genotypes of VSV were used in each experiment. Fitness relative to a non-evolved congenic strain was determined by head-to-head competition experiments at different time points during the evolution experiments. Fitness values are reported as differences in Malthusian parameters (i.e., selection rate constants). We only considered for our study those time-series that contained $\geq$10 data points.