Evolution of RNA Genomes from a Quasispecies Perspective

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References:

OBSERVATION

Viruses are biological systems that have played an important role in the early evolution of life, in the generation of living genetic diversity and the evolution of contemporary cellular systems [1]. However, the evolution of viruses itself is a complex issue of study due to its controversial nature: their dependency of the cells to replicate, a “simple” genomic composition and a huge diversity of mutation rates and mechanisms developed to infect almost any living cell on Earth.

In 1977, Manfred Eigen and Peter Schuster proposed the quasispecies model (see Equation 1) [2], which has been applied to understand the evolution of RNA viruses, among other genetic phenomena such as the early steps in the origin of life. In general terms, quasispecies are clouds of genotypes (i.e. master sequences) that appear in a population at mutation-selection balance. Thus, viruses when modeled as quasispecies can be conceived as a distribution of replicating, small and mutant genomic sequences which reach an equilibrium state of infinite size by processes of high mutation rate and fitness-selection from a finite initial population [3].

In this work, we have created a genetic algorithm (Figure 2) that incorporate additional biological “realism” into the basic models in order to assess the evolution of Human immunodeficiency virus 1 (HIV-1) as quasispecies. Therefore, we are evaluating the impact of the genome size, effective population size and differential mutational fitness on our evolutionary dynamics. From our modeling, we are able to measure the most novel properties of quasispecies [4]:

a) Eigen limit or error threshold, a mutation rate below which populations equilibrate in a traditional mutation-selection balance and whereby the favored genotype can maintain the replication of information despite high mutation rates (Figure 3C).

b) Error catastrophe, the phase transition above the mutation rate whereby the loss of the favored genotype or viral identity is carry out through frequent deleterious mutations (Figure 3B and 3D).

c) Extinction catastrophe, the complete loss of the genotypes of the viral population through lethal mutations (Figure 3A).

METHODOLOGY

Estimation of a MUTATIONAL FITNESS for HIV-1 (strain HXB2 ID: K03455)

In order to calculate a mutational fitness (positive, negative or neutral selection) for the functional regions and codons in HIV-1 genome, we perform the following steps:

2. Redundancy analysis: Final data set of 124 viral genomes.

RESULTS

Estimate the Selection in viral genome by:

5. Codons

6. Functional regions

CONCLUSION

Our main contribution to the quasispecies model is to consider the evolutionary impact of purifying selection on the viral fitness. Based on our mutational fitness approach, it is possible to observe that a high proportion of negative mutations in the viral genomes (Fig. 7 and 6) can drive the evolutionary dynamic of HIV-1 to reach the quasispecies thresholds and faster.

Figure 1

Figure 2

Figure 3

Figure 4

Figure 5

Figure 6

Figure 7

Figure 8