A lineage-dependent molecular clock with anomalous diffusion models SARS-CoV-2 evolution in humans

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Abstract

The evolution of SARS-CoV-2 in humans has been monitored at an unprecedented level due to the public health crisis, yet the stochastic dynamics underlying such a process is dubious. Under the most simple scenario, the number of mutations over time $m(t)$ can be modeled as the following Langevin SDE

$$\frac{dm(t)}{dt} = \kappa + \xi(t)$$

where κ is the evolution rate and $\xi(t)$ is an integrative noise source whose properties shape the evolutionary motion. Most of the state-of-the art methods for phylogenetic analyses implicitly assume that the integrative noise source $\xi(t)$ is gaussian and has $\langle \xi(t) \rangle = 0$ and $\langle \xi(t)\xi(s) \rangle = \delta(t-s)$ as mean and correlation functions respectively. This description yields that the second central moment is linear with time ($\langle \Delta m^2(t) \rangle \propto t$) and gives rise to the molecular clock hypothesis, which states that the rate of genetic mutations in DNA is relatively constant over time, which is widely accepted and used in the field of phylogenetics.

In this work, considering the number of acquired mutations as the displacement of the viral particle from the origin, we performed biostatistical analyses from numerous whole genome sequences on the basis of a time-dependent probabilistic mathematical model. We showed that a model with constant variant-dependent evolution rate and nonlinear mutational variance with time (i.e., anomalous diffusion, characterized by a gaussian integrative noise source $\xi(t)$ with $\langle \xi(t) \rangle = 0$ and $\langle \xi(t)\xi(s) \rangle = \alpha(\alpha-1)|t-s|^{\alpha-2}$ as mean and correlation functions) explained the SARS-CoV-2 evolutionary motion in humans during the first 120 weeks of pandemic in UK. In particular, we found subdiffusion patterns ($\alpha < 1$) for the Primal, Alpha, and Omicron variants, while a weak superdiffusion ($\alpha > 1$) pattern for the Delta variant. Our findings indicate that non-Brownian evolutionary motions occur in nature, thereby providing novel insight for viral phylodynamics.

References

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