

# Review of: "Evolution of new variants of SARS-CoV-2 during the pandemic: mutation-limited or selection-limited?"

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Potential competing interests: No potential competing interests to declare.

1. How was the probability of generating a new variant at a given time determined, and what factors influenced this probability? Were any assumptions made regarding the acquisition of immunity to each variant and the presence of cross-immunity in the simulations?
2. Can the authors explain how do the incidence curves for different variants compare in terms of their peak levels and durations? It will be beneficial to observe how the incidence curves for different variants compare.
3. According to the study the authors suggest that the observed patterns of variant origins and incidence levels do not align with the predictions of the mutation-limited hypothesis. As stated in page 13, most variants have originated at low levels of incidence, contrary to the general prediction of mutation-limited hypotheses. But, Sangeet et al 2022 (<https://pubs.acs.org/doi/10.1021/acs.jpcb.2c04574>), recently showed that during the transition/emergence of a new variant the mutational entropy/activity increases. But according to the current study, the authors reject the mutation-limited hypothesis. Can the authors comment if mutation-limited hypothesis should be totally neglected or can it be considered in certain cases?
4. I suggest the authors could comment on the rejection of mutation-limited hypothesis with some exceptions while citing the following references:  
*"Ghanchi et al 2021, Higher Entropy Observed in SARS-CoV-2 Genomes from the First COVID-19 Wave in Pakistan. PLoS One 2021, 16 (8), e0256451"*  
*"Mullick et al 2021, Understanding mutation hotspots for the SARS-CoV-2 spike protein using Shannon Entropy and K-means clustering"*  
*"Sangeet et al 2022, Quantifying Mutational Response to Track the Evolution of SARS-CoV-2 Spike Variants: Introducing a Statistical-Mechanics-Guided Machine Learning Method"*
5. Are there any specific factors or conditions that contribute to the origin of variants at low levels of incidence?
6. Some minor changes: In figure1 it should be "variant" instead of "varinat".