

Dear Editor,

Thank you very much for your comments. Certainly, they will contribute to increase the clarity and potential impact of our work. Below you will find a point-by-point response to each of your suggestions. For convenience, your comments are labeled as Q# (in red) and our answers as A# (in black).

We hope you find this second revised version suitable for your final positive recommendation and publication as a *Peer Community Journal* after such a long reviewing process.

Looking forward hearing from you at your earliest convenience.

Dr. Guillaume Lafforgue
(On behalf all coauthors)

Q1. However, I am at a loss to understand how this addresses the question in the title - are you suggesting/hypothesizing that the third demographic condition [bottleneck followed by expansion] is the mechanism? Please clarify. And if this is so, how does this demography work in natural populations (I am probably missing some biology here).

A1. Yes. Our hypothesis is that population expansions after severe bottlenecks are enough to stop the deleterious effect of Muller's ratchet. As stated in the manuscript, this effect was long-ago observed in cell cultures for vesicular stomatitis virus (Novella et al. 1995; Elena et al. 1996). Reference to Novella et al. (1995) in which these observations were made is now properly cited in the text (line 93).

We have rewritten an entire paragraph of the Introduction to provide more biological details describing at which stages of the infection cycle bottlenecks may take place (lines 53 – 80).

We end up now the Discussion with a final paragraph in which we summarize our hypothesis and the extent in which our results support it.

Q2. At several places, the text is quite vague – some of this has already been pointed by reviewers but their comments have not been carefully addressed. For e.g., on l. 65, instead of one, you now write 'very small quantity' – how much? You also mention '4' on l. 330. Similarly, on l. 219, you have now changed 100% to nearly 100% - although you have not shown the data but from your data, you can quantify 'nearly'.

A2. The new paragraph in the Introduction provides numerical values to illustrate what we meant by "very small quantity".

Q3. l. 20: generation of genetic diversity - What does this mean?

A3. The unavoidable generation of mutants by error-prone replication of RNA viruses.

Q4. Although you cite the relevant experimental literature on Muller's ratchet, the theoretical contributions are largely ignored. Surely, the work on mutational meltdown is relevant to your work and merits discussion.

A4. We agree this is a good suggestion and now presented some relevant theoretical results about Muller's ratchet speed and of mutational meltdown in the Discussion (lines 386-404)..