

The authors tackle here an interesting biological question: how a new population, of asexual organisms, can survive in a hostile environment, “the sink”, through the constant immigration of new individuals from a self-sustaining population, “the source”. Using Fisher Geometric Model and building upon their own previous work (Martin & Lenormand 2015, Martin & Roques 2016), they analytically tracked the distribution of fitness of the individuals forming the sink population, as well as the population size in “the sink”. Here, the authors focus on the deterministic dynamics of the system as opposed to Débarre et al 2013 who characterize the long-term equilibria of a similar two populations systems. In addition, they simulated Wright Fisher population to confirm the analytical results.

The authors were able to provide an analytical solution to ODE-PDE system, allowing them to characterize both the mean fitness as well as the demographics of the population. Successful trajectories can be described in terms of three phases, matching some previous experimental works. One of the most striking results is that immigration does not affect the evolutionary dynamics of the population. In addition, the authors also derived the time it takes for a population to become self sufficient (defined as surviving even in the absence of immigration), as whether establishment happens rapidly or very slowly has quite distinct biological implication. Lastly, the authors discuss their results in regards to classical measure to prevent and limit infections or pest invasions. In particular, this analytical approach allows to compare the relative effectiveness of various method, ranging from quarantine, prophylaxis or mutagenesis. Interestingly, their analytical expression captures that mutagen drugs can be more harmful than helpful when used at wrong concentrations.

General comments regarding figures 2-5:

The various panels are quite small, with the axes label and ticks barely readable. Distinguishing between solid, dashed-dotted and dotted lines require to zoom up to 400% to be able to see which line is which. The panels themselves are quite clear but they definitely need to be larger. Note also that the black line is sometimes hard to distinguish against the red ones.

Also while mentioning that figures share the same legend is a good idea, please rewrite the legend in addition to “same legend as in figure 2”.

In figure 1 legend, individuals with fitness between $\bar{r}(0)$ and 0 are called selected. This name is a bit confusing as these individuals are doomed to extinction. I'm assuming that the authors called them because in the absence of migration they will initially increase in frequency in the shrinking population.

It would be nice to discuss the new results with respect to Orr & Unckless (2008) (<https://www.journals.uchicago.edu/doi/10.1086/589460>) and Orr & Unckless (2014) (<https://doi.org/10.1371/journal.pgen.1004551>). In particular, it would be nice to mention how the results for an isolated system compared to a source-sink system.

I also would like if the authors could discuss the role of compartmentalisation within a host as discussed in the following paper: Moreno-Gamez et al 2015 (<https://doi.org/10.1073/pnas.1424184112>).

In addition to the case of lethal mutagenesis, it would be interesting if the authors could also discussed the potential dynamics of mutational meltdown (Lynch and Gabriel 1990 <https://doi.org/10.1111/j.1558-5646.1990.tb05244.x>, Matuszewski et al 2017 <https://doi.org/10.1093/ve/vex004>) and whether their analytical results can inform us on the effectiveness of such approach.

Minor comments:

l 14-15: define briefly what establishment means: formation of a self-sufficient population in the

sink

l 18: the fitness optimum in the sink and that of the source

l 23 and l 26: “beyond some mutation rate threshold” is written twice to describe different outcomes. On line 314, you describe the first behaviour as below some threshold. I assume you mean below on line 23.

l 25 : trajectory of [the] mean fitness

l 78 : define GxE

l 167 (+2) : [on] average

l 181: at → of

l 291: is larger → increases

l 293: For consistency, “the mean” should also be capitalized

Figure 2: plain lines → solid lines, dash-dot line → dashed-dotted lines
“theory given by” → “analytical predictions given by”

Figure 3: remove clearly.

Figure 4: plain → solid, dash-dot → dashed-dotted

l 348: Please rephrase. I'm confused by “when U is not too small, even far from the WSSM regime”. I don't know what the authors are trying to convey: the results hold both for medium and low values of U or only for one of the two regimes.