1 Summary

Tomasini & Peischl apply the key findings of one of their recent papers to ask which features control the probability of evolutionary rescue in a non-uniformly deteriorated habitat. In concordance with other papers in the literature, they find that p_{rescue} is maximized at intermediate migration rates which act to balance the migration-positive effects of the non-deteriorated population as a source and the migration-negative effects of gene swamping. They describe conditions when a small amount of gene flow is detrimental for evolutionary rescue, and examine how choices of asymmetry in population size, migration rates and density regulation can be important in driving these relationships.

Overall, I enjoyed reading this paper, and it got me thinking excitedly about the many directions the authors could explore in the future. I especially liked their handling of the non-instantaneous growth dynamics/density regulation. However, I felt that the authors could do a better job contextualizing their findings with existing literature, and helping the reader understand their key findings.

2 Major Comments

2.1 Better delineate the differences from Uecker et al 2014

This paper could do a better job emphasizing what differentiates itself from previously written literature, namely Uecker's Am Nat paper (minor - my saved reference for that Am Nat paper is 2014, not 2013. Worth double checking?). This paper seems like it's addressing fundamentally the same questions, and little time is spent on what exactly makes it different. For example, in the sentence contextualizing their paper, the authors write

> Although both theoretical and experimental advances have been made to understand the role of dispersal in metapopulation models of evolutionary rescue, the interactions between **the speed and the severity of environmental change**, and the amount and mode of dispersal are not well understood.

However, this is from the abstract of Uecker:

> Specifically, we study the influence of population structure and density-dependent competition **as well as the speed and severity of environmental change**. We also determine the relative contribution of standing genetic variation and new mutations to evolutionary rescue.

What parts of the speed and severity of environmental change is Uecker's paper not understanding that remain to be elucidated? I ask this not to be difficult, but because it's genuinely unclear to me from the introduction and

context. The paper presents a model similar to Uecker's, which finds similar qualitative behavior with respect to intermediate migration rates. Again, while the authors are doing something different than Uecker et al 2014, it would be useful to readers to state it much more explicitly: "We make certain simplifications of Uecker's model (two demes, time homogeneity to compute fixation probabilities) in order to explore additional phenomena Uecker et al did not consider: namely, 1) when does a small amount of migration facilitate gene flow? 2) How does asymmetry of migration rates and population sizes among demes impact fixation probabilities? 3) etc. "

2.2 Understanding of dP_{dn}/dm at $m = 0$

One of the major contributions of this paper is equation $(11)/(12)/(16)$ - effectively all the dP_{dn}/dm equations. They delineate **when** a small amount of gene flow should enhance the probability of evolutionary rescue above a situation with no gene flow. My primary issue here is not when, but **why**. I feel like I did not understand where this result came from - the supplemental material in Appendix B was too brief, and the intuitive explanation could also use more exposition. For example, I am having a difficult time grasping why θ is important - is it because the amount of migrants from the non-deteriorated deme is proportional the θ, but the amount of migrants lost to migration is mostly independent of θ as long as it's not too small?

This leads me to a more fundamental question: how exactly would a small amount of migration from/to a non-deteriorated environment not facilitate rescue? Is there an intuitive argument that can be made here about where mutants are coming from that could help us better understand equation 12?

Put another way: what are the major costs of migration? Moving mutants from the deteriorated environment out of that environment. What are the benefits of migration? Adding new WT individuals to the population in the deteriorated environment so it declines less slowly **and** (maybe?) adding in mutants migrating from the new population. How many mutants are lost before θ to migration? How many mutants are gained directly via migration before θ? How many mutants are gained due to a larger WT population that can then mutate before θ? As long as the mutants gained (via mutation then migration or migration then mutation) are greater than the mutants lost, gene flow should help, and presumably this should work out to be what you computed in equation 12. Can the authors frame the question as mutants gained/lost instead/in addition to just taking the derivative with respect to m?

For example, the authors' discussion of equation 20 is very clear, and provides a practical foothold as to why this inequality leads to diverging behavior. Given how central equations $11/12/16$ are, it would be very helpful to the reader to provide a similar argument, if possible.

2.3 Time homogeneity assumption seems to be a major shortcoming

Comparison between stochastic simulations and analytics suggests that for certain ranges of m, the analytics don't really describe the behavior of stochastic simulations. The authors were fairly upfront about the time homogeneity assumption being an issue, which I appreciated. However, there were two things related to this that I would have liked to have seen addressed:

2.3.1 Crash point for p_{rescue}?

A feature in common between all of the figures is a crash of the rescue probability at a certain migration rate. P_{rescue} then begins to increase again above that critical migration rate. What determines where this crash point occurs? Presumably it stems from the max in equations 3 and 4, but I don't feel like I have an intuitive grasp on the major factors that determine where it is. Why is it so steep on the left-hand side? Is there any combination of analytics and intuition that can help us understand the shape of this curve, that might also help us understand why this range of migration rates tends to match stochastic simulations (relatively) poorly?

2.3.2 Display of stochastic simulations

In several instances, stochastic versus analytical comparisons are put in the supplement. This makes it harder for the reader to interpret the appropriateness of modeling assumptions.

For example, the extent to which the analytics do not fit the simulations at high migration rates, while stated in the text, is much more evident from the figures in the supplement. This actually makes the point that mutations arriving before θ and lasting through the epoch change are likely critically important for rescue at high migration rates - this is interesting! Looking at figure S3, for example, to my eye, $p_{rescue} = 0.75$ for $s = 0.1$, whereas the model not accounting for the switch in environments suggests that p_{rescue} should be 0.1. This unmodeled effect accounts for almost 90% of rescues among mildly deleterious alleles at high migration rates? Cvijovic et al, PNAS 2015 may be an interesting citation to check out with respect to the fate of a deleterious mutation undergoing an environmental switch and becoming beneficial.

According to Figure S4 and S5, there is interesting behavior of fixation probabilities with respect to balanced β at high m. Namely, more skew ($\beta = 0.1$) is not always greater than balanced carrying capacities in terms of p_{fix} - a behavior that is not at all predicted by the model. What causes this? The figure caption directs us to Appendix A, which talks only about the temporal inhomogeneity in selection strength.

In short, I feel like placing nearly all of the stochastic simulations in the supplement doesn't really allow most readers to understand when the model fails and masks multiple interesting departures that should be studied further

in the future. Why not replace Figure 4A/B with Figures S4A/B and overlay simulations throughout Figure 3?

2.4 Schematic?

A schematic similar to the sketch below would have helped me in reading the manuscript:
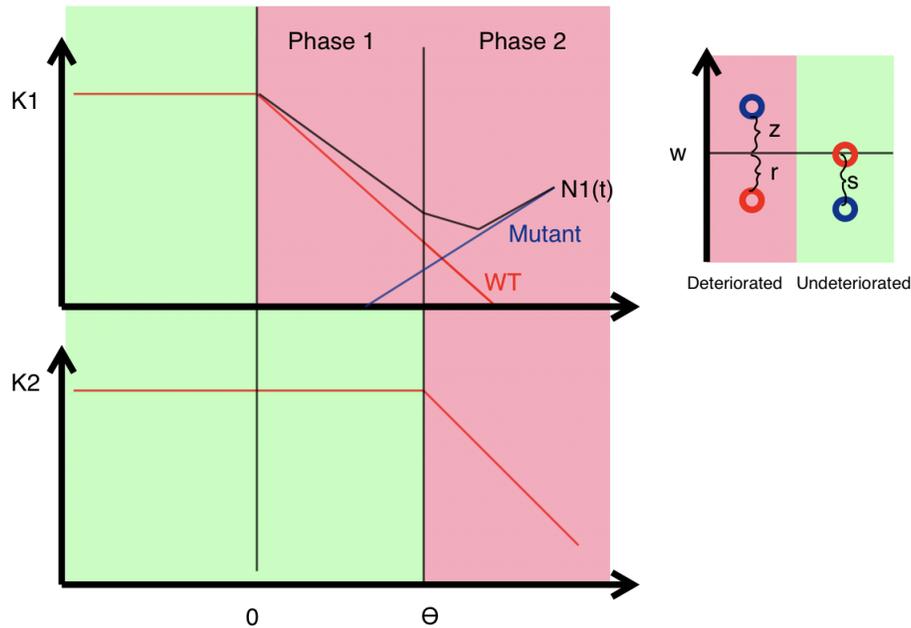
3 Minor Comments

- In some but not all plots, m goes up to 1. Is this useful to show? Limits of m could be consistent across plots.

- What are the constraints on the selection strength? Based on $p_{est} = 2z$ and description in Tomasini & Peischl 2018, selection cannot be too strong, right? Worth discussing the selective regimes in which these approximations are appropriate (the authors do a nice job discussing the importance of other parameters on their approximations).

- Line 55: form → from

- Line 103: "$m_{i,j}, i, j = 1, 2$" could be easier to parse.

- Equations 3, 4, 7: Is ")" a more conventional exclusive range delimiter than "["?

- Line 167: 20'000 → 20,000

- Line 167: The authors didn't vary K_{tot}. It's worth commenting on the how changes to K_{tot} might alter results.

- Line 172: space between migrated and followed

- Line 172: Perhaps, "a Poisson distributed number of offspring" instead of "Poisson distributed offspring"?

- Figure 2: Is f_0 assumed to be mutation-selection balance here? Mention in figure caption.

- Line 239: "not adapted to" → "not adapted"

- Line 252: Right-hand? This is confusing as written.

- Line 292: $e.g.$ → , for example,

- Line 317: gets → goes

- Line 318: Can you explain the vice versa here?

- The notation between equations 16/17 and the supplements should be consistent

- Line 331: in which population does not declines - something is off about this sentence.

- Line 338: This could do a sentence or two of interpretation in words.

- Line 358: loosing → losing

- Supplemental Line 32: It would be useful if a *Mathematica* notebook be made available.

- In general, I found the explanation in Appendix B insufficient to follow the progression.

- Equation S6 - In the natural order of reading, the reader is directed to this equation before β and ζ are introduced. It's worth redefining them here.

- Supplemental Line 44: fr → for

- Supplemental Line 45: Beverton-Holt citation?

- Supplemental Line 57: "We find that $N_2(t) \to 0$ if $t \to \infty$ if" - Not sure how to parse this.

- Supplemental Line 60: kind $\rightarrow$ kinds

- Figure S5 caption: "We can see that at $m = 0$ expectations are different than simulations" - at $m = 0$? Typo?