Answer to reviews of « The genetic architecture of local adaptation in a cline »

Dear recommander of PCI Evolutionary Biology,

Many thanks to you and two anonymous reviewers for your time and effort in reviewing the former version of our manuscript. We carefully accounted for the different issues that were raised in this round of review, and modified the manuscript to address them. We explain our modifications with explicit reference to the new manuscript in our point-by point answers (in bold below).

We hope that our answers and modifications will match your expectation and look forward hearing from you about this revised version of our manuscript.

Yours sincerely,

On behalf of co-authors, Fabien Laroche

· Recommender's comments

Around equation (4). I think it would be useful to specify that patches are large (to ignore random fluctuations within patches and consquences of kin competition) and that selection is soft (i.e. competition occurs within patches before dispersal).

The reviewer is correct that we make these assumptions. We agree that the life cycle description in methods was not sufficiently detailed. We now provide more details at ll. 175-199. In particular we specify that the life cycle corresponds to a soft selection regime ll. 198-199. We also indicate that we assume large population sizes within patches to derive equation (4) ll. 295-296.

l. 271-282 I found this section difficult to follow. Going to box 2 in Lenormand 2002 indeed helped, however I think it would be better if the manuscript did not rely so much on explanations given in another paper. One recommendation would be to express k and alpha in terms of parameters of the current model (in a way that is sufficiently general that it can apply to both fintess functions). This would help understanding the verbal definitions of k and alpha.

Expressions of k and alpha were indeed given separately in each fitness functions, without an overarching formal definition in the context of our study. We now give generic expressions of k and alpha along with the definitions (see new equations 7a,b).

l. 288 and eq. (5) I guess the argument for invasion here is that second order effects can dominate first order effects. Spelling this argument out explicitly would be helful. Also, how do you ensure that you can still ignore third order effects?

This step needed clarification. In the previous version of our manuscript, we presented an expansion of the fitness of the mutant to order two in phenotypic effect size (former eq. 5) because in some of the situations studied later in the text (Gaussian fitness with resident phenotype at z*=0), the selection gradient becomes flat and the evolutionary dynamics thus becomes driven by terms of order 2. It was convenient to deal with all the situations of interest with a single expression. When expanding along the phenotypic effect size, it is guaranteed that the effect of order 3 or higher can be neglected, as a consequence of Taylor-Young formula.

Having said that, these comments of the associate editor actually applieds on our conclusion in former equation (8), now equation (9), later in our analysis. There, we simultaneously considered two limits : epsilon → 0 which allows us to use the Taylor-Young expansion in equation (5), but also l/(sigma x sqrt(m)) → +Infty which is necessary to make order 1 and order 2 commensurate in equation (5). However, we had no argument to ensure that this second limit would not also make higher order terms in the Taylor Young expansion commensurate with order 1. In that sense, equation (9) has to be considered as an approximation, as it is now clearly explained l340-341. This approximation seems quite good, as simulations show a threshold of invasion of large effect mutations close to this value (figs. 5A, 6A ; also mentioned l461-462, 484-485).

l. 292 I recommend presenting the equation for k out of line, with its own reference. It may also be usful to write eq. 8 as a condition on pocket size l as later, many arguments are based on critical pocket sizes allowing for the invasion of locally adapted alleles (e.g Fig 5 and 7). The same holds for eq. 9.

We now systematically provide the specific formulation of k and alpha using an out of line format for Laplace (eqs. 8a,b) and Gauss (eqs. 12a,b) cases. We also systematically separate the results for Gauss and Laplace fitness functions : (i) the position on Nagylaki's chart obtained from k and alpha (fig. 4) and (ii) the condition on l for mutant to invade (eqs. 10,13).

l. 348 Could you please define Q_A and \bar{z} more precisely?

The quantity Q_A is the proportion of the change in trait values z(t)-z(0) of individuals at the center of habitat 2 that is caused by large alleles A. This is now explicitly stated before each expression lines 391-392, 398-399, 409-410. \bar{z} was not used in the rest of the study so we simply removed the corresponding sentence.

Figure 6. There seems to be a mismatch between references in the main text to A and B and the figure legend. e.g. line 415, 6A is referred for Laplace but legend says it is Laplace.

Indeed, we modified the labels and the order of panels in what is now figure 7.

l. 533. Please provide references for those "previous models".

Many references are actually given later in the text, we mention it here (l577-578)

Appendix.

Eq. A1. This linearized form for evolution in patch structured populations has been used in previous models (e.g. models of dispersal evolution by Lee Altenberg, see also Reinhard Burger's textbook). It would be useful to refer to those.

We thank the associate editor for pointing these references. We now refer to Karlin (1976) book chapter when introducing the linearized mutant dynamics in main text (l. 297). This chapter is one of the reference underpinning Lee Altenberg's work about the general reduction principle, and it is focused on the question of dispersal-selection interaction in heterogneous environment. We also refer to this chapter in p.1 of appendix A.

Eq. A3 Please explain what \bar{s} is

We now make it clear in appendix A (p. 1) that the s_i are selection gradients in patches and \bar{s} is now defined in equation (A3) as the arithmetic mean of the s_i across demes.

Below Eq. A4. I found the explanation of what was being done a bit confusing. Why not say that you use Fourier analysis to solve eq. A4? Also refer to some works that have already used the regularity of lattice or stepping stone models (e.g. Francois Rousset's 2004 book)

We agreed that this analysis of periodic kernel is a classic and needed more references to previous works. We now explicitly refer to Fourier analysis below equation A4 and refer to the appendix of chapter 3 in Rousset (2004) for further technical details.

Eq. between (A7) and (A8) please make sure the notation for entries of the matrix pi is the same throughout.

We now consistently use bold capital letter when referring to the entire matrix and capital letter with normal font and two indices when referring to one entry of the matrix.

Below that equation, explain how you get lambda$_2$

We agree that showing more steps in the derivation is useful. We now add more details about the derivations between equations A7 and A8.

End of that same page, please define s_1 and s_2 separately.

We defined s_1 and s_2 separately (Appendix A p. 4).

Top of before last page (page with equation A9). Please epxlain how you derived that first equation (with n \sigma_k on the right hand side).

We now explicitly derive the Fourier transform of the centered vector of selection coefficients s_0 (eq. A9), which we understood was the missing step in our presentation.

Review by anonymous reviewer, 02 Aug 2022 18:49

Laroche and Lenormand present an argument that shows the conditions for the concentrated architecture of alleles involved in local adaptation may be more permissive than previously thought, by analysing it in the context of a spatially explicit model. They also consider the impact of varying the shape of the fitness function. The manuscript explains the differing effects of two different shapes well, as well as the reasons the analytical methods may differ from the simulated results. I believe this work makes a valuable contribution to our understanding of the evolution of aggregated architecture.

My main concern with the manuscript is that I found parts of the methods and results are unclear or inaccessible, which made it difficult to follow and reproduce. In particular:

I suggest making the arrival to Equation 2 more understandable. I expect this is not a technique many readers (myself included) will be familiar with.

We added more intuitive background before introducing equation (2) l254-272. We added details about the computation of the spectral density through Fourier transform, briefly explaining how it relates to the pattern of aggregation. We also, in line with reviewer 2 request, add more explanation about why a square signal allocate more weight to low frequencies than random noise. We also clarified that equation (2) computes the weighted mean of spatial frequencies along the chromosome, with weights proportional to the spectral density.

I am unfamiliar with and expect most readers to be also be unfamiliar with, the delta notation introduced in Equation 5 which isn't explained in text. If I had to guess, it's the partial derivative with respect to the second variable, and then z substituted back in? The notation is used extensively throughout so I believe it would be well worth explaining this or using alternative, more standard, notation. I struggled to work it out initially, because lambda(z,z) looks like it should equal 1.

We now use a more standard, fractional notation throughout the text.

L267-268: I understand the parameters s_i and t_i as far as “this is what pops out the exponential when we differentiate w_i”, but a placing within a biological context (if they have one) would improve the accessibility of the paper. The names chosen make them look like selection coefficients.

The s_i are selection gradients within patches, we indicate this l 310 of main text and in Appendix A (p1).

Some justification of the simulation parameters used would improve the manuscript. For example, the juvenile migration rate is 0.5; I don’t have much expertise of models with limited dispersal, but this seems an incredibly high value.

We added a new paragraph l218-235 to justify our choices of parameter values.

Other points:

Main text needs proof reading throughout.

We carefully proof-read the manuscript.

Figures: Legends and within-figure text require proofreading. Perhaps merge Figures 5 and 7 for easy comparison without flicking between figures, and so they can share a legend.

It is true that the reader has to navigate back and forth to compare those figures. Having a single figure would be too large given that each of them already has 4 panels, but we changed the ordering so that they will remain in close proximity in the formatted version (now figures 5 and 6).

I suggest keeping a consistent order Laplace/Gauss or Gauss/Laplace across figure panels (and throughout the manuscript) for ease of comparison.

As mentioned in our answer to the recommender, we modified order of panels in figure 6 to be consistent with the rest of the manuscript. In addition, in figures 5-7, we recalled the fitness shape is used in each panel, next to the panel index. More generally, we systematically presented the Laplace case before the Gauss case in main text. The only exception was for section « Contribution of small and large effect mutations to local adaptation » because the logic there was to follow an increasing size of habitat 2. This made us talking about Gauss case first because it leads to a smaller swamping limit than in the Laplace case.

Figure 4 L812: Can you include what it is you want the reader to find in the text in the legend?

We now precisely refer to equations (11), (12a), (12b) in the legend of figure 4.

Table 1: Main text uses “n” for number of patches, rather than “X” as in table.

Thanks for pointing out. We corrected it.

L236-237: Citation missing for this invasion approximation?

We now refer to Haldane (1927) at l. 382.

Reviewed by anonymous reviewer, 14 Aug 2022 11:31

“The genetic architecture of local adaptation in a cline” addresses how adaptation to a new habitat occurs at a quantitative trait. The model assumes several patches organised in a circle, a proportion of which are in the “ancestral” habitat and another in the “new” habitat, each habitat having it’s own phenotypic optimum. Migration occurs between the patches at a fixed rate. The authors explore how the fitness function, the size of the second habitat, and migration influence the strength of mutations (strong or weak) that are recruited during the adaptation process, and how these mutations are

distributed along the genome (clustered within the same genomic region or not). Their main findings are that clustering of mutations is indeed favoured in a large range of parameter values.

The paper is well thought out and well written, I enjoyed reading it, despite my limited understanding of the underlying mathematics in the analytical part of the model. I find the approach quite elegant, with a relatively "simple" scenario to answer a very complex question. I mean this in a very positive sense – the authors have proposed a model with but a few parameters and found a way to analyse and present the results in an intuitive way. The comments I have are minor and should be quite easy to see to.

Comments:

Abstract:

line 23: "spatially continuous space" seems awkward … "continuous space" would seem sufficient, unless I have missed something. But on that note, I had understood the patches to be discrete, which could lead to some confusion on the use of "continuous space", but I can't think of a better way to phrase it. Maybe a "continuous habitat space/range"?

We now explicitly refer to « circular stepping-stone » in the abstract (l. 24), which is a keyword synthesizing both the spatially-explicit aspect and the existence of discrete patch.

Introduction:

line 107: rewording suggested "At one extreme, if a single mutation that confers perfect adaptation can occur, indirect…"

Corrected.

line 146: "1-dimensional" → "one-dimesional"

Corrected.

Methods

As a non-mathematician, some notions were difficult to follow. I am quite aware that it is impossible for me, and readers such as myself, to gain detailed knowledge of the whole process behind the derivations (I have given up on trying to understand the Fourier transform in sufficient detail), but some hints on how it works could be useful. My greatest challenge (that can be remedied), which I think should be explained by adding a line or two is the measure of aggregation (starting line 224). It was not initially intuitive to me as to why a square signal would translate as a "low frequency signal". Is it because these approaches based on spectral analyses are temporal? Hence a square signal in a spatial context, concentrated only on a part of the genome, would be translated as a weak temporal signal?

A low frequency signal is usually shown as a Sin wave with long period (hence low frequency which is the inverse of the period). For instance, the sound spectrum covered by the human voice ranges from 60 Hz (or vibrations per second, i.e. low frequency) for the lowest and deepest bass to about 1,200 Hz for the highest rising sopranos. In our case, if you imagine that all loci are aggregated it looks like 111110000 (which looks like a long period signal if it was repeated indefinitely, i.e. low frequency). If the loci were 'anti-agregated', it would look like 1010101010, i.e. a short period signal. In practice, this analogy is not entirely accurate since we do not necessarily have 50% of 1. But in all cases, decomposing the spectrum will show a peak at low frequency for an aggregated signal irrespectively of this proportion. The weighed metrics we use allow gauging whether the pattern of loci on the chromosome is biased towards bass, and this bias toward bass is measured relative to a white noise baseline, where 0 and 1 are randomly permuted.

As we mentioned above in our answers to reviewer 1, we now add more qualitative explanations to our metrics based on spectral analysis of aggregation l254-269.

line 220: Out of curiosity: why the choice of the last 75% of simulation time? is it an arbitrary choice?

In fact, we just follow long term simulation until we are sure that for a long period of time we are in a stationnary regime for the mean phenotype. In practice, we used 400 000 generations, which proved sufficient to have at least 75% of the simulation time during this stationnary regime. So, in effect, there is little arbitrariness here. We are just mentionning that we used sufficiently long simulation according to the dynamics of mean phenotype. We changed the text to better explain this at ll. 242-252.

lines 267-268: It would be appropriate to specify that w' and w'' (lines 267-268) are first and second derivations of (if I understood correctly) the Fourier transform.

We now explicitly refer to a selection gradient when introducing w'/w at l. 310, which makes it clear that the notation ' stands for a derivative.

line 276: "characteristic length" (sensu Slatkin 1973) – can more information be given? I'm not sure what this means., since it is crucial to the understanding of k (which I have only been able to understand in a very superficial way)

We now provide a generic expression of k and alpha now given in equation (7a,b). We also explain in plain words what this compound parameter means in the preceding paragraph (l321-327).

Results

line 327: Missing "." before "Hence"

Corrected.

Figures: I was very grateful for Figures 1-4, thank you! They made the understanding of the model intuitive.

Thank you for this positive feedback.

Figure 5 is a bit information heavy, and the dotted lines may need to be made more visible (thicker?). I suggest that the vertical line be removed completely from panels A and C, as they are not very visible, make it a bit difficult to follow what is on those panels and are in any case represented on panels B and D. This will also aid in shortening the legend, which as is, was slightly confusing to read.

We made fig. 5 and previous fig. 7 (now 6) simpler, removing unused elements, and we used thicker lines.

Discussion

line 519: rewording "the optimal value"

Corrected.

General: There are some small residual language mistakes that are easily corrected. I had started a detailed correction, but then realised it was too time consuming and could more easily and efficiently be done by having someone directly make the changes in the document. There are small recurring mistakes, such are missing or too many s's and the's, as well as "same … than" ("same … as" – "different … than"). Some are also present in the appendices.

Yes, this point was also raised by reviewer 1. As mentioned earlier, we carefully proof-read this revised version of the manuscript.