

**From:** Graham Coop [gmcoop@ucdavis.edu](mailto:gmcoop@ucdavis.edu)   
**Subject:** Fwd: Thank you for reviewing 55813  
**Date:** 3 December 2014 15:05  
**To:** Simon Aeschbacher [saeschbacher@ucdavis.edu](mailto:saeschbacher@ucdavis.edu)

GC

----- Forwarded message -----

**From:** The American Naturalist <[am@editorialmanager.com](mailto:am@editorialmanager.com)>  
**Date:** Wed, Dec 3, 2014 at 2:52 PM  
**Subject:** Thank you for reviewing 55813  
**To:** Graham Coop <[gmcoop@ucdavis.edu](mailto:gmcoop@ucdavis.edu)>

Dear Dr. Coop,

Thank you for reviewing the article "Local adaptation by small-effect alleles" by Sam Yeaman. As you can see in the decision letter below, we requested a revision before making a final decision on the manuscript.

Attachments are available in the Editorial Manager system if you log into the system with your reviewer role.

Please keep all comments, including your own, confidential. Thank you very much for participating in our review process. The integrity of The American Naturalist depends on the efforts of devoted individuals such as yourself, and we appreciate your contribution.

The American Naturalist

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**To:** "Sam Yeaman" [yeaman@zoology.ubc.ca](mailto:yeaman@zoology.ubc.ca)  
**From:** "The American Naturalist" [amnat@press.uchicago.edu](mailto:amnat@press.uchicago.edu)  
**Subject:** Decision on Manuscript 55813  
Dear Sam,

I've read your paper with great interest, and I like it a lot. I'm very glad that it will be part of this special issue.

Both reviewers have a lot of comments that can help the presentation of the paper a lot, I think. In addition, I'll add some thoughts from my reading below.

Thanks for writing for this issue. I think this is a very useful contribution, and with some revision it will be a very highly cited item, I think.

Thanks,  
Mike

67: will have → may have

88 and later: I agree strongly with Flo that these acronyms (SPA and SRA) hinder rather than aid communication. You don't actually use them very much, and they add quite a bit of cognitive load to reading the paper. (Acronyms in general add difficulty, but in this case the two only differ by one pen stroke making the P into an R.) Please just spell them out when these come into the text or figures.

97: adaptation would be unstable: I don't agree. The adaptation can be stable even if the genetic basis of that adaptation is transient.

111-112: "This increased fitness" --- this should have "locally" in there somewhere

166 (approximately) -- I think that this overstates the population genetics result. This critical migration is when you might lose strong differentiation, but it doesn't tell you that there is no differentiation in allele frequency between the sites. There is still expected to be some subtle difference in allele frequency on average. Perhaps if this were brought out sooner it would make the conclusions more understandable.

195-197: This sentence didn't make sense to me.

222-3: I'm slightly worried about the consequences of using  $r = 1/2$ . Can you defend this choice better in the paper?

Top of page 12: It seems worth mentioning that the quantitative match between the theory and the figure is poor.

280 individual's → individuals'

Figure 6: "monogenic" and "oligogenic" printed with the e moved to far to the right for me. Check this figure?

MS #55813  
Author: Sam Yeaman

xx

Reviewer #1: please see attached .pdf for complete review which begins as follows:

"The author investigates the role of many loci in maintaining local adaptation in the face of migrational swamping. The paper illustrates

the importance of statistical linkage disequilibrium (or between-population covariance in allelic effects among loci) and recurrent mutation in maintaining local adaptation if selection coefficients at individual contributing loci are so small that these could not be maintained in a single-locus model. The genetic architecture of local adaptation in such scenarios is transient, with individual beneficial mutations constantly establishing via recurrent mutation, and going extinct after some time due to genetic drift and migration. Individual loci show low population divergence, but overall, local adaptation is maintained. This is in stark contrast to the case where individual mutations are strongly selected, survive much longer in the face of gene flow, and hence contribute to much more stable architectures."

XX

Reviewer #2:

This manuscript investigates how the sizes of the effects of alleles underlying a quantitative trait influence whether the local mean values of this trait will differ when it is subjected to divergent selection. This work unites and reconciles seemingly contradictory predictions of quantitative genetic and population genetic models: on the one hand, population genetics models predict that alleles being only weakly beneficial (alleles of small effect) locally will be "swamped" by migration, while on the other hand, quantitative genetic models, typically assuming that the effects of all alleles are very small, predict that divergence can occur provided there is enough standing genetic variation ( $V_G$ ). The outputs of numerical simulations provide an answer to this conundrum, showing the strong differences in the architecture of the trait when alleles have small vs. large effects, but also the influence of genetic redundancy (when the same trait can be produced by many different combinations of alleles) and per locus mutation rate. The simulations confirm that divergence (phenotypic differentiation) can occur even with small-effect alleles, but that at the level of individual loci, differentiation is only transient, while statistical associations between loci can be strong.

This is a clear, well-written and very interesting study, especially in the context of the current (-omic) efforts to identify the genetic architecture of local adaptation. The facts that divergence can build up even when loci have very small effects, and that statistical associations between loci are key, are not exactly new findings, and previous work of Latta and LeCorre & Kremer is duly acknowledged in this manuscript; what is new, however, is the thorough investigation of the effects of further details of the architecture (e.g., the effect of genetic redundancy), the clear presentation of the "problem" in the introduction, and the explanation of the consequences of these findings for the detection of the genetic architecture of local adaptation, using genomic data.

The following comments are meant to help improve the presentation of the work.

== General comments ==

- The opening question of the manuscript, "How does migration-selection balance shape the genetic architecture of local adaptation" can be a bit confusing, unless what is meant by "genetic architecture" is precisely defined. The effects of the alleles that underlie the trait can be considered as components of genetic architecture, but in this study, the effects are rather considered as "genetic constraints" (l. 370), that are fixed. With the opening question, one could expect these effects to evolve themselves, so a quick clarification, in the introduction, of what these terms mean, would be welcome!

- The discussion of the importance of linkage disequilibrium / statistical associations is not always clear. Different terms are used ("LD", "statistical LD", "allelic covariances" (between populations/within populations)), but (l.470-471) "allelic covariances are equivalent to LD". Also, it is somehow assumed that the reader is very familiar with the work of LeCorre and Kremer. For instance, around l. 342,  $\theta_B$  is not clearly defined (and, incidentally, the notation is a bit confusing given that  $\theta$  already refers to the local optima). I think that it would be really useful to clearly (i.e. with equations if needed, as in Latta 2003) define these concepts of within population/between population covariances (and LD?), since they are so central to the explanation of the results.

- I found some of the figures a bit unclear, mainly because I had to read the legend in detail to know whether the panel was about swamping prone or swamping resistant alleles (and sometimes even read again the legend of another figure, e.g., for Fig2). The figures would be more helpful if this key piece of information was more easily accessible (e.g., in the title of the figures) or if there were an associated color/pch code or if the grouping of the panels reflected this (e.g. in Fig 1, it would be better to have panels B and C next to each other).

- I feel that there is a simple explanation for the difference between the predictions of the quantitative genetic and population genetic models, that is hinted at, but could be more clearly described... Namely, it is the fact that only one mutation is considered in the population genetic model (comparing  $Z=4$   $\alpha$  to  $Z=0$ ), while a large  $V_G$  in the quantitative genetic model means that  $|Z|$  will probably go much beyond  $4\alpha$ ... or am I missing something?

- The discussion is already quite long, but maybe it could be useful to add a few lines to warn people doing simulations that their assumptions (e.g., number and sizes of the alleles) can have a huge impact (e.g., reiterating the remark made around line 250 that some researchers focus on cases with  $n_{tot} > n_{opt}$ ).

== Detailed comments ==

l. 33 "variants": because of the phrasing, I was not sure whether the word referred to different forms of the same gene, or to different genes (as the next question seems to imply).

l. 65--71: This part of the paragraph is about the tension between specialists and generalists (intermediate, non locally adapted allele); but the notion is swamping is different (it does not require generalist alleles), and unless I misunderstood the model, there will not be generalist alleles in this study (although there may be generalist phenotypes). I therefore think that this part of the paragraph is a bit confusing and could be removed(?).

l. 88/90: I am not a huge fan of acronyms in general; I think that it would be clearer to spell out "swamping prone" and "swamping resistant"...

l. 113--114: Huisman, J., & Tufto, J. (2013). Modelling wild-domestic interbreeding: How selection on a quantitative trait affects gene flow

at a neutral locus. Journal of theoretical biology, 332, 42-51 , can be another useful reference.

I. 158 "V\_G is a parameter" is a bit confusing given that it is then written that V\_G is "itself affected by migration-selection balance" [= rephrase?]

I. 169 There is not need to specify a fitness function to derive eq. (2), right?

I. 180 "the Gaussian fitness function with  $\omega^2=25$ " implies that the reader knows what  $\omega$  represents (to play the devil's advocate,  $\omega$  could be the mean). The Gaussian function is written up in the supplementary information, but it could be useful to nevertheless explain what  $\omega$  is.

I. 185 I find it a bit confusing that all the analytical part uses a Gaussian fitness function (with  $(Z-\theta)^2$ ), while the simulations use a linear function (with  $|Z-\theta|$ ). Why is that the case?

(also, it may be useful to add that the parameters are such that  $w$  remains  $>0$ )

I. 239  $n_{\text{tot}}$  has not been introduced before

I. 247  $n_{\text{opt}}$  is an integer, but  $\theta/(2\alpha)$  may not [add a symbol to say you will round  $\theta/(2\alpha)$ ]

I. 249--252 maybe it would be worth adding an adjective like "locally", because at the scale of the entire population, selection is divergent.

I. 277--292 I am not sure that I understand the argument here... if there is no divergence (= same means in both habitats), what does having phenotypes beyond one local optimum tell us about what happens in the other patch type, and how would this help create divergence?

I. 328 I am not sure that it is spelt out that  $\mu$  is a per locus mutation rate (or so I imagine); it is crucial to mention it to explain why increasing  $n_{\text{tot}}$  increases V\_G (more mutations per individual)

I. 328 and following: it is actually a very interesting point that V\_G is almost not influenced by  $\Delta\theta$  when the alleles are swamping-prone... [and maybe this would also be a place to mention that the variance is not the only moment that changes with the size of the alleles!]

I. 441 I do not understand what "earlier" refers to

I. 515 but it does not challenge phenotypic definitions of local adaptation.

Figure 1CD: The dotted lines (Homgen,  $m=0.5$ ) are completely invisible.

Figure 1D: It is hard to distinguish between the two nuances of teal

Figure 3B&E: What were the values of  $n_{\text{tot}}$ ? Do the values on the vertical axis correspond to  $n_{\text{tot}}*2000$  generations? (maybe divide them by 2000?)

Figure 6: Consider changing into a double-entry table?

Supplementary materials:

[first equation] should not the denominators be  $f[Z=0]$  ?

== Typos and other details ==

I. 40 Fournier-Level (missing majuscule)

I. 50 Lythgoe (spelling)

I. 92 "with can" -- rephrase?

I. 216 The "gamma" in the equation is almost invisible

I. 230 maybe a comma is missing (too many "and"s and hard to group them)

Fig 5, legend: between ( $\theta_B$ ) [instead of  $_w$ ]

Suppl. Mat: "Guassian"

[signed, since we said we would review each other's contributions]

Flo Débarre

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