# Understanding genetic variance, load, and inbreeding depression with selfing

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# A recommendation – based on reviews by Frédéric Guillaume and an anonymous reviewer – of

Abu Awad D, Roze D. 2017. Effects of partial selfing on the equilibrium genetic variance, mutation load and inbreeding depression under stabilizing selection. bioRxiv, 180000, ver. 4 of 17th November 2017. doi: 10.1101/180000

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A classic problem in evolutionary biology is to understand the genetic variance in fitness. The simplest hypothesis is that variation exists, even in well-adapted populations, as a result of the balance between mutational input and selective elimination. This variation causes a reduction in mean fitness, known as the mutation load. Though mutation load is difficult to quantify empirically, indirect evidence of segregating genetic variation in fitness is often readily obtained by comparing the fitness of inbred and outbred offspring, i.e., by measuring inbreeding depression. Mutation-selection balance models have been studied as a means of understanding the genetic variance in fitness, mutation load, and inbreeding depression. Since their inception, such models have increased in sophistication, allowing us to ask these questions under more realistic and varied scenarios. The new theoretical work by Abu Awad and Roze [1] is a substantial step forward in understanding how arbitrary levels of self-fertilization affect variation, load and inbreeding depression under mutation-selection balance.

It has never been entirely clear how selfing should affect these population genetic properties in a multi-locus model. From the single-locus perspective, selfing increases homozygosity, which allows for more efficient purging leading to a prediction of less variance and lower load. On the other hand, selfing directly and indirectly affects several types of multilocus associations, which tend to make selection less efficient. Though this is certainly not the first study to consider mutation-selection balance in species with selfing (e.g., [2-5]), it is perhaps the most biologically realistic. The authors consider a model where n traits are under



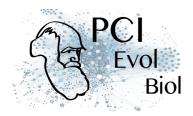
stabilizing selection and where each locus affects an arbitrary subset of these traits. As others have argued [6-7], this type of fitness landscape model "naturally" gives rise to dominance and epistatic effects. Abu Awad and Roze [1] thoroughly investigate this model both with analytical approximations and stochastic simulations (incorporating the effects of drift).

Their analysis reveals three major parameter regimes. The first regime occurs under low mutation rates, when segregating deleterious alleles are sufficiently rare across the genome that multi-locus genetic associations (disequilibria) can be ignored. As expected, in this regime, increased selfing facilitates purging, thereby leading to less standing genetic variation, lower load and less inbreeding depression.

In the second regime, mutation rates are higher and segregating deleterious alleles are more common. Though the effects of multilocus genetic associations cannot be ignored, Abu Awad and Roze [1] show that a good approximation can be obtained by considering only two-locus associations (ignoring the multitude of higher order associations). This is where the sophistication of their analysis yields the greatest insights. Their analysis shows that two different types of interlocus associations are important. First, selfing directly generates identity disequilibrium (correlation in homozygosity between two loci) that occurs because individuals produced through outbreeding tend to be heterozygous across multiple loci whereas individuals produced by selfing tend to be homozygous across multiple loci. These correlations reduce the efficiency of selection when deleterious effects are partially recessive [5]. Second, selfing indirectly affects traditional linkage disequilibrium. Epistatic selection resulting from the fitness landscape generates negative linkage disequilibrium between alleles at different loci that cause the same direction of deviation in a trait from its optimum. Because selfing reduces the effective rate of recombination, linkage disequilibrium reaches higher levels. Because selection tends to generate compensatory combinations of alleles, partially masking their deleterious effects, these associations also make purging less efficient. Their analysis shows the strength of the effect from identity disequilibrium scales with U, the genome-wide rate of deleterious mutations, but the effect of linkage disequilibrium scales with U/n because with more traits (higher n) two randomly chosen alleles are less likely to affect the same trait and so be subject to epistatic selection. Together, the effects of multilocus associations increase the load and can, in some cases, cause the load to increase as selfing increases from moderate to high levels.

However, their analytical approximations become inaccurate under conditions when the number of epistatically interacting segregating mutations (proportional to U/n) becomes large relative to the effective recombination rate (dependent on outcrossing and recombination rates). In this third regime, higher order genetic associations become important. In the limit of no recombination, model behaves as if the whole genome is a single locus with a very large number of alleles, becoming equivalent to previous studies [2-3].

The study by Abu Awad and Roze [1] helps us better understand the "simplest" explanation for genetic variance in fitness – mutation-selection balance – in a model of considerable complexity involving multiple traits under stabilizing selection, which 'naturally' allows for pleiotropy and epistasis. Their model tends to confirm the classic prediction of lower variation in fitness, less load, and inbreeding depression in species with higher levels of selfing. However, their careful analysis provides a clearer picture of how (and by how much) epistasis and selfing affect key population genetic properties.



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### **Appendix**

Reviews by Fédéric Guillaume and an anonymous referee: http://dx.doi.org/10.24072/pci.evolbiol.100041