

Two neat “genetic architecture hacks”:

### Effective migration rates with complete divergence

For  $L$  divergently selected loci with selection and dominance coefficients  $s_i$  and  $h_i$ ,  $i = 1, \dots, L$ , where the two populations are near complete fixation for their respective locally beneficial allele, we get, at position  $x$  in the genome, the following expression for  $m_e$ :

$$m_e(x) = m \times \exp \left( - \sum_{i=1}^L \frac{s_i h_i}{m + r(x, x_i) + s_i h_i} \right)$$

This will be a reasonable approximation as long as  $N_e s h \gg m$  and  $N_e s h \gg 1$ , so that selection is much stronger than both drift and migration.

This can be obtained by considering the reproductive value of a migrant individual in the resident background, or by an *ad hoc* extrapolation of two-locus theory to the multi-locus setting, see Barton and Bengtsson (1986), Aeschbacher et al. (2017), Sachdeva (2022), Zwaenepoel, Sachdeva, and Fraïsse (2024).

### Effective population size under BGS

In the “background selection regime” (see Good et al. (2014)), we can use the following expression (Hudson and Kaplan 1994):

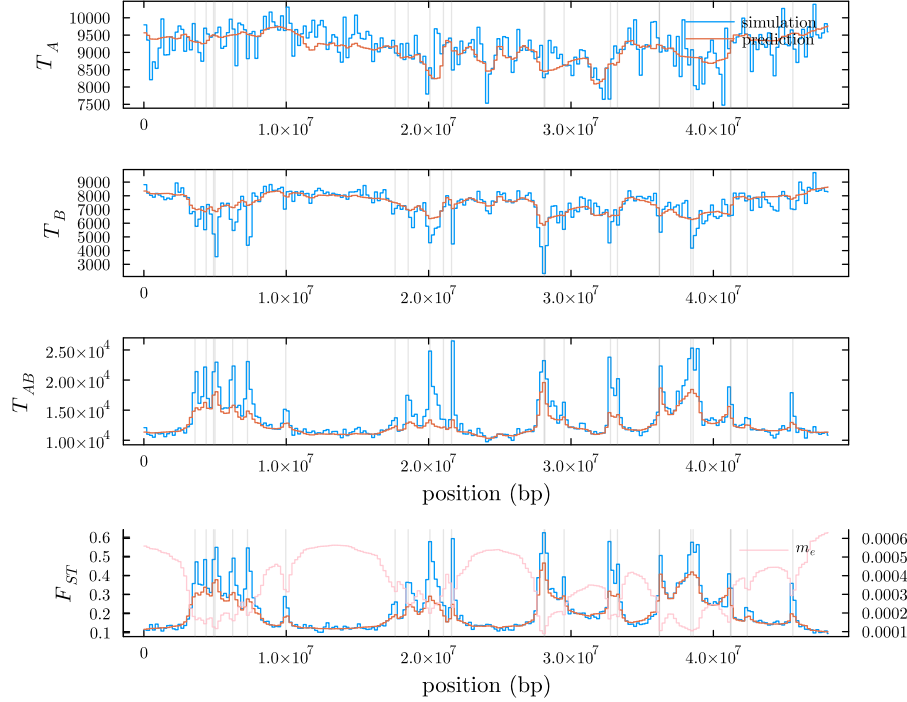
$$N_e(x) = N \times \exp \left( - \sum_{i=1}^G \frac{u_i}{s_i \left( 1 + r(x, x_i) \frac{(1-s_i)}{s_i} \right)^2} \right)$$

Where there are  $G$  sites with recurrent deleterious mutations at rate  $u_i$  and (haploid) selection coefficient  $s_i$ ,  $i = 1, \dots, G$ . This should hold more or less whenever it provides reasonable  $N_e$ ’s – see Good et al. (2014), Buffalo and Kern (2024).

This can be derived, more or less, from the structured coalescent, where the different subpopulations are deleterious backgrounds, see Hudson and Kaplan (1994), Charlesworth, Nordborg, and Charlesworth (1997), Nordborg (1997), Charlesworth and Charlesworth (2010), Good et al. (2014), Santiago and Caballero (1995), Santiago and Caballero (1998), Santiago and Caballero (2016), Buffalo and Kern (2024).

### How well do they work?

Zwaenepoel, Sachdeva, and Fraïsse (2024) showed that the  $m_e$  theory can predict equilibrium allele frequencies at selected loci very accurately when linkage between selected loci is not too tight. To what extent the theory allows to



**Figure 1:** Predictions based on  $m_e$  and BGS theory for forward simulations using SLiM.

predict genome-wide *neutral* divergence/differentiation was not studied in depth. In particular, predictions very close to barrier loci are not expected to be accurate.

In addition, it is not clear how BGS and divergent selection interact. In the regime where the Hudson & Kaplan theory applies with respect to BGS, can we account for both processes by rescaling  $N$  and  $m$  in the neutral theory? This remains to be studied in depth.

It would be interesting to study these questions systematically, focusing on the regimes with near-complete divergence and HK-like BGS.

## References

- Aeschbacher, Simon, Jessica P Selby, John H Willis, and Graham Coop. 2017. “Population-Genomic Inference of the Strength and Timing of Selection Against Gene Flow.” *Proceedings of the National Academy of Sciences* 114 (27): 7061–66.
- Barton, Nicholas H., and Bengt Olle Bengtsson. 1986. “The Barrier to Genetic Exchange Between Hybridising Populations.” *Heredity* 57 (3): 357–76.
- Buffalo, Vince, and Andrew D Kern. 2024. “A Quantitative Genetic Model of

- Background Selection in Humans.” *Plos Genetics* 20 (3): e1011144.
- Charlesworth, Brian, and Deborah Charlesworth. 2010. *Elements of Evolutionary Genetics*. Vol. 42. Springer.
- Charlesworth, Brian, Magnus Nordborg, and Deborah Charlesworth. 1997. “The Effects of Local Selection, Balanced Polymorphism and Background Selection on Equilibrium Patterns of Genetic Diversity in Subdivided Populations.” *Genetics Research* 70 (2): 155–74.
- Good, Benjamin H, Aleksandra M Walczak, Richard A Neher, and Michael M Desai. 2014. “Genetic Diversity in the Interference Selection Limit.” *PLoS Genetics* 10 (3): e1004222.
- Hudson, Richard R, and Norman L Kaplan. 1994. “Gene Trees with Background Selection.” In *Non-Neutral Evolution: Theories and Molecular Data*, 140–53. Springer.
- Nordborg, Magnus. 1997. “Structured Coalescent Processes on Different Time Scales.” *Genetics* 146 (4): 1501–14.
- Sachdeva, Himani. 2022. “Reproductive Isolation via Polygenic Local Adaptation in Sub-Divided Populations: Effect of Linkage Disequilibria and Drift.” *PLoS Genetics* 18 (9): e1010297.
- Santiago, Enrique, and Armando Caballero. 1995. “Effective Size of Populations Under Selection.” *Genetics* 139 (2): 1013–30.
- . 1998. “Effective Size and Polymorphism of Linked Neutral Loci in Populations Under Directional Selection.” *Genetics* 149 (4): 2105–17.
- . 2016. “Joint Prediction of the Effective Population Size and the Rate of Fixation of Deleterious Mutations.” *Genetics* 204 (3): 1267–79.
- Zwaenepoel, Arthur, Himani Sachdeva, and Christelle Fraïsse. 2024. “The Genetic Architecture of Polygenic Local Adaptation and Its Role in Shaping Barriers to Gene Flow.” *Genetics*, iyae140.