# Quantifying the Statistical Power in the Inference of the Evolution of the Distribution of Fitness Effects in Canine Lineages
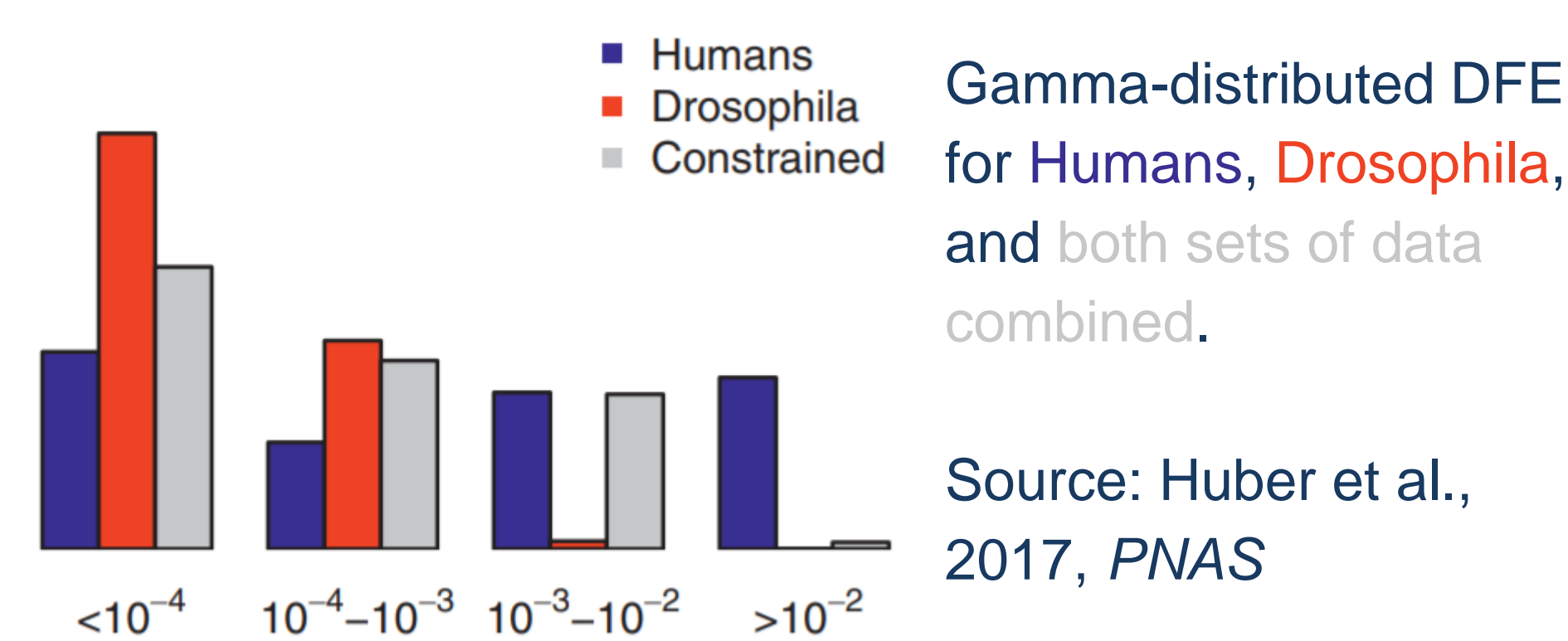
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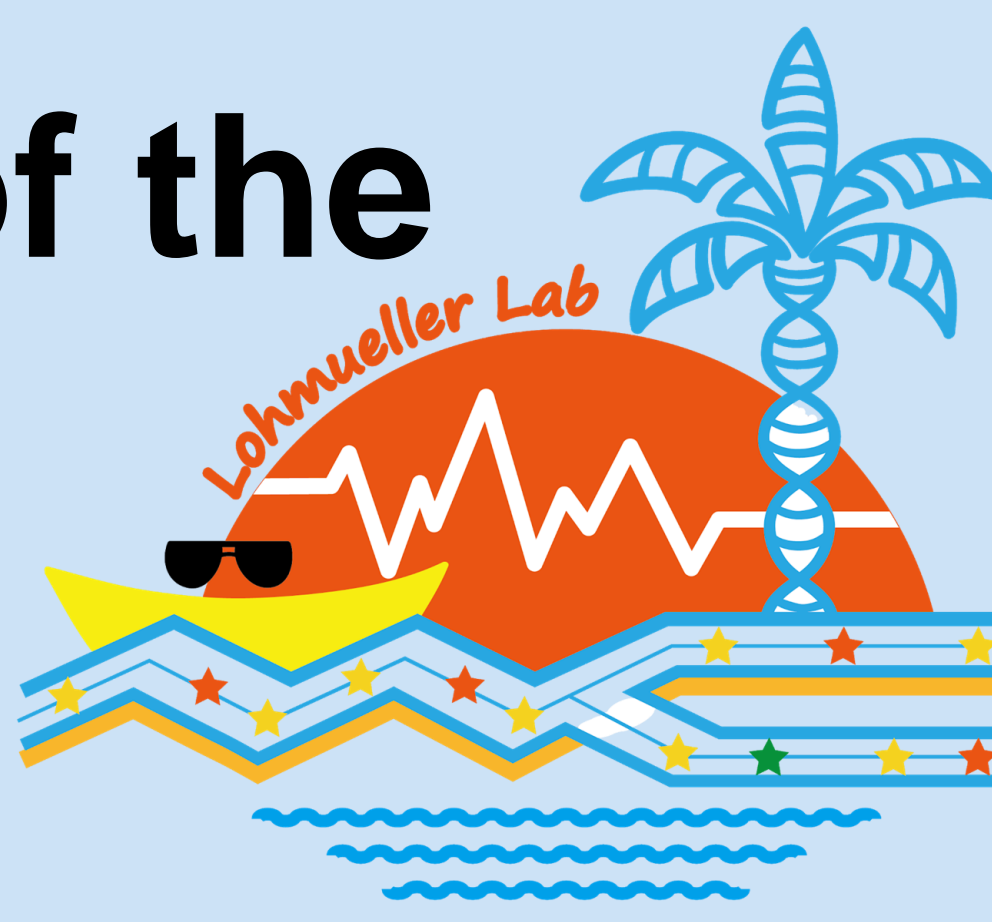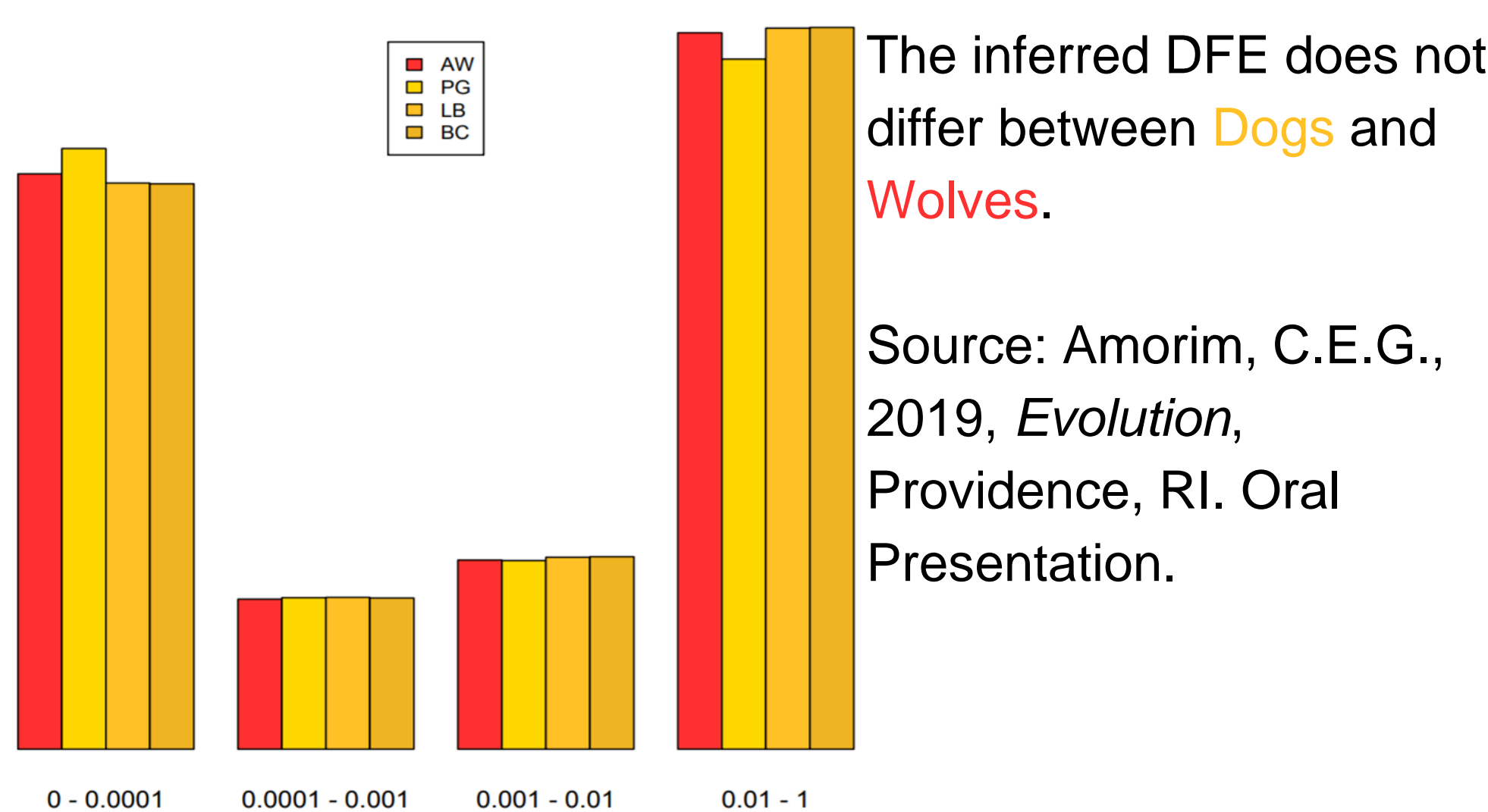
Introduction

The distribution of fitness effects (DFE), which describes the impact and effect of all new mutations in a population, plays a fundamental role in shaping evolutionary genetics[1]. Previous work on inferring the DFE has shown that distantly related species have distinct DFEs[2]. However, the timescales and conditions under which the DFE evolves remain unclear.

Gamma-distributed DFE for Humans, Drosophila, and both sets of data combined.

Source: Huber et al., 2017, *PNAS*

Domestic dogs and wolves provide a system in which to understand how the DFE evolves over recent timescales, as these populations have recently diverged. However, using genomic resequencing data from arctic wolves and breed dogs, no detectable difference in the inferred DFE was found.

The inferred DFE does not differ between Dogs and Wolves.

Source: Amorim, C.E.G., 2019, *Evolution*, Providence, RI. Oral Presentation.

We sought to determine if current state-of-the-art methods for DFE inference had sufficient statistical power to detect a change in the DFE between wolf and dog populations.

We performed forward population genetics simulations modeling wolf and dog evolution, and compared the inferred DFE and demographic parameters of simulated and empirical data.
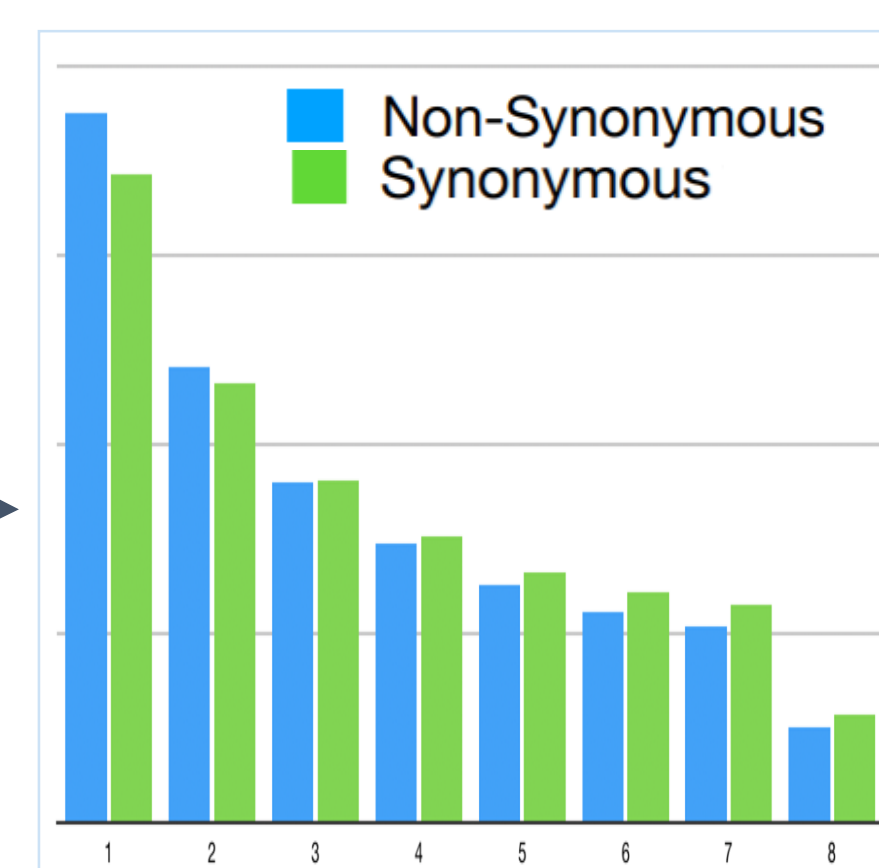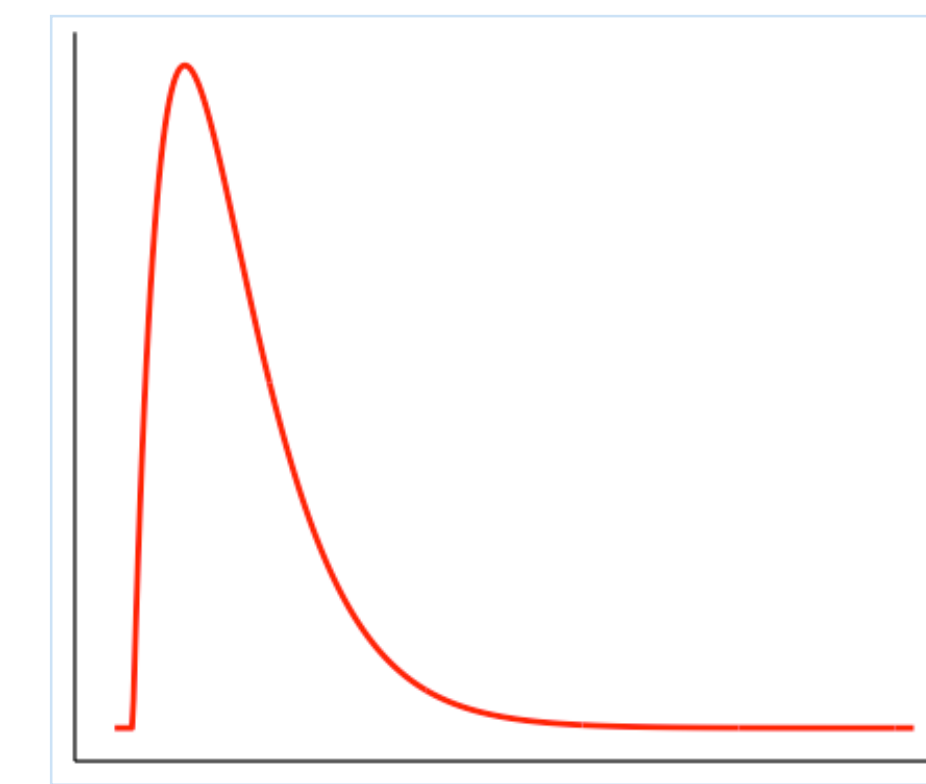
Demographic Model
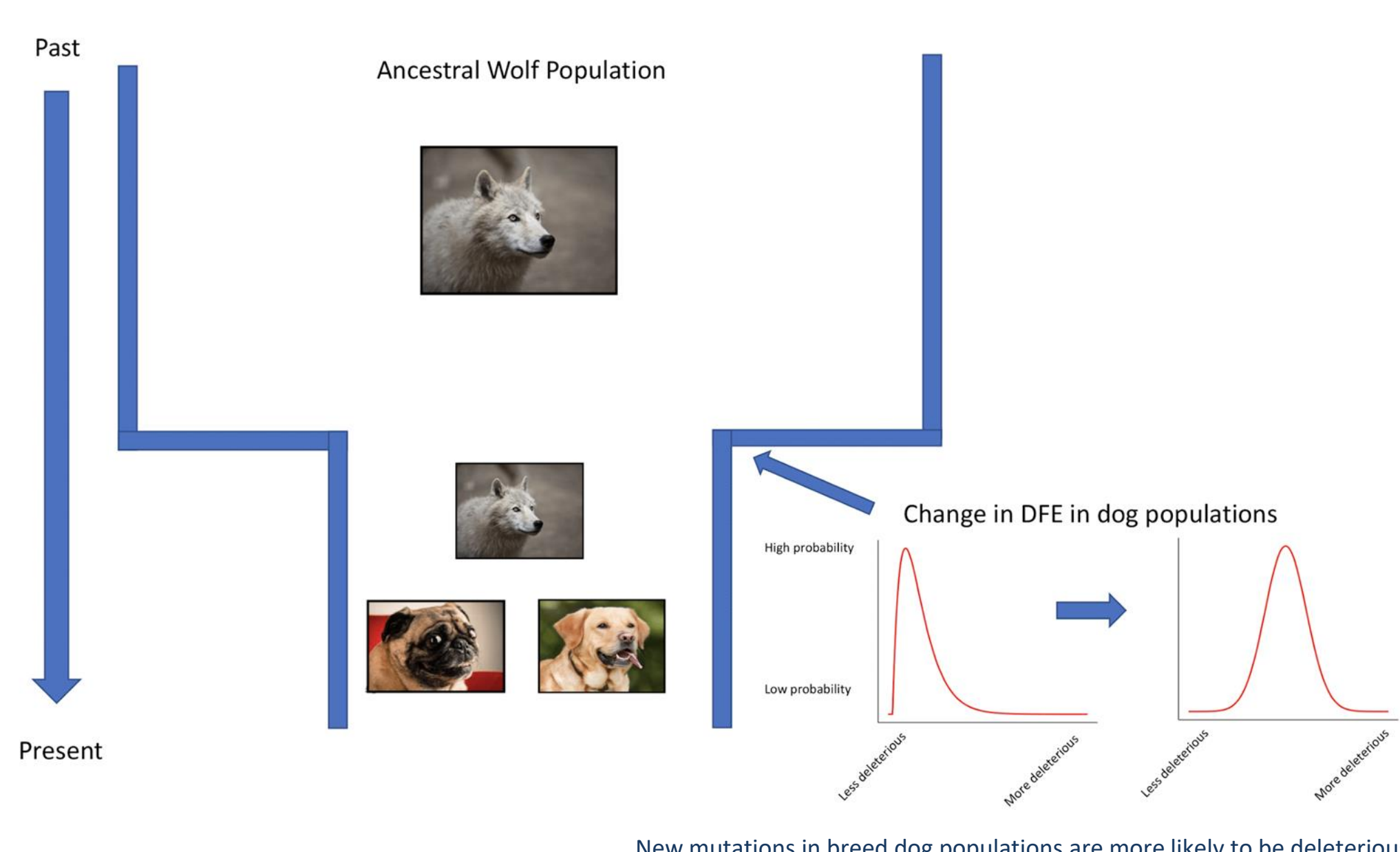
Methods and Models
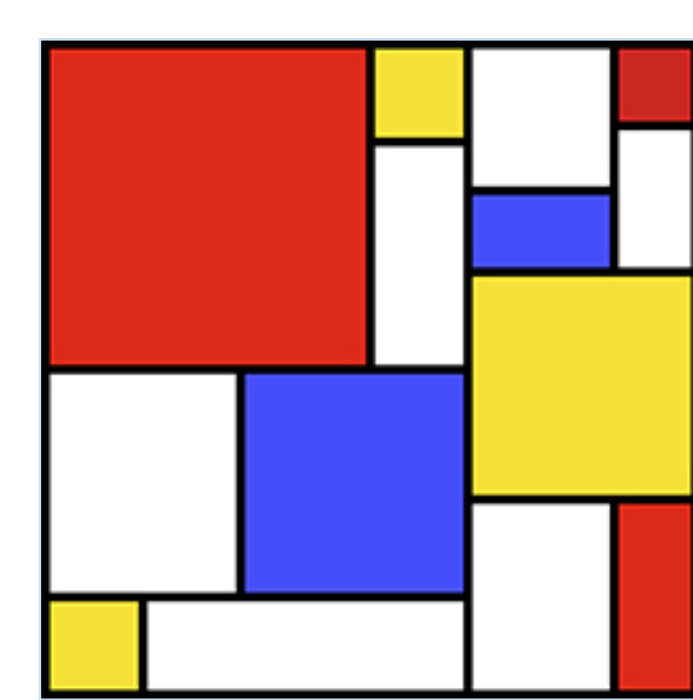
Simulate canine evolution though `SLiM`, generate Variant Call Format (VCF) data.

Given VCF data, use `easySFS` to generate nonsynonymous and synonymous site frequency spectra.
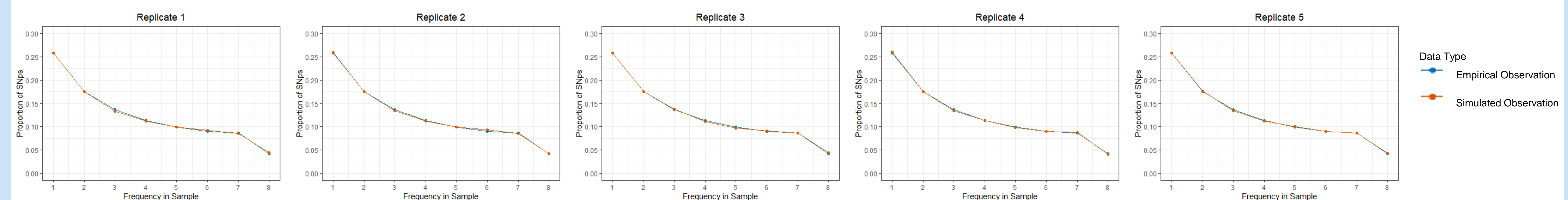
Given site frequency spectra, use `dadi` to infer population demographic parameters, and `fitdadi` to infer the gamma-distributed DFE from demographic parameters.
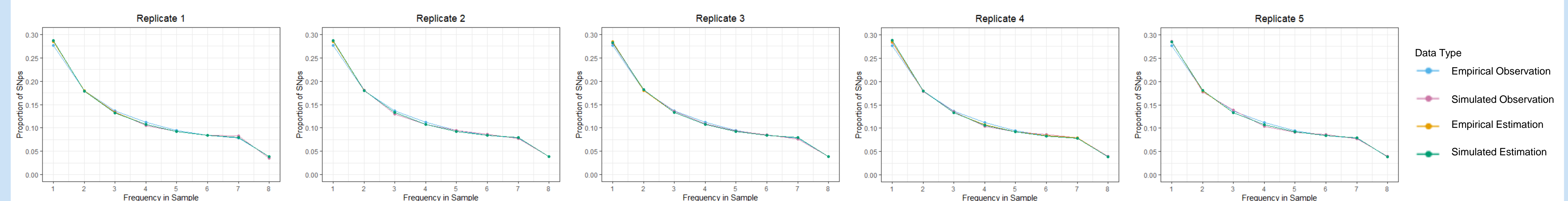
Compare the inferred DFE from simulated and empirical data.
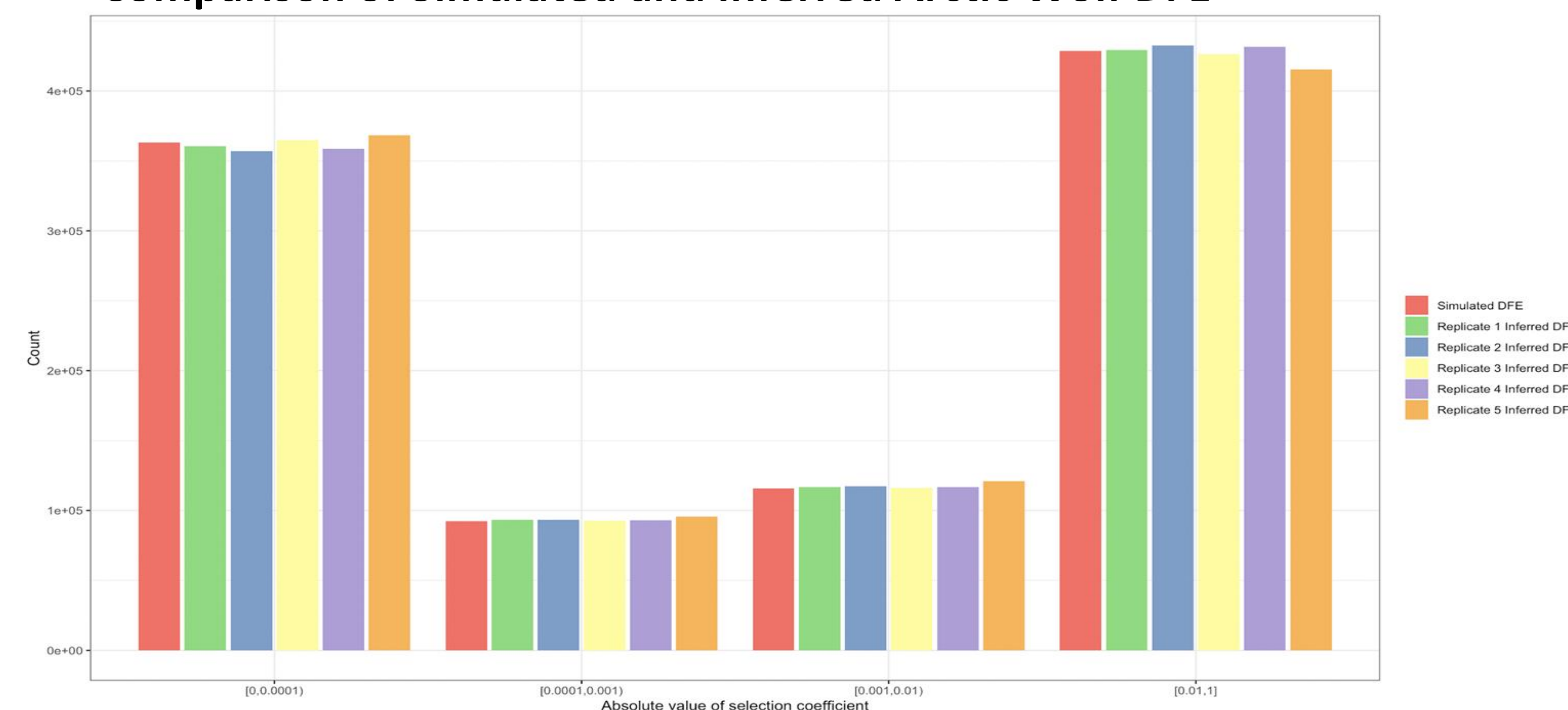
Results

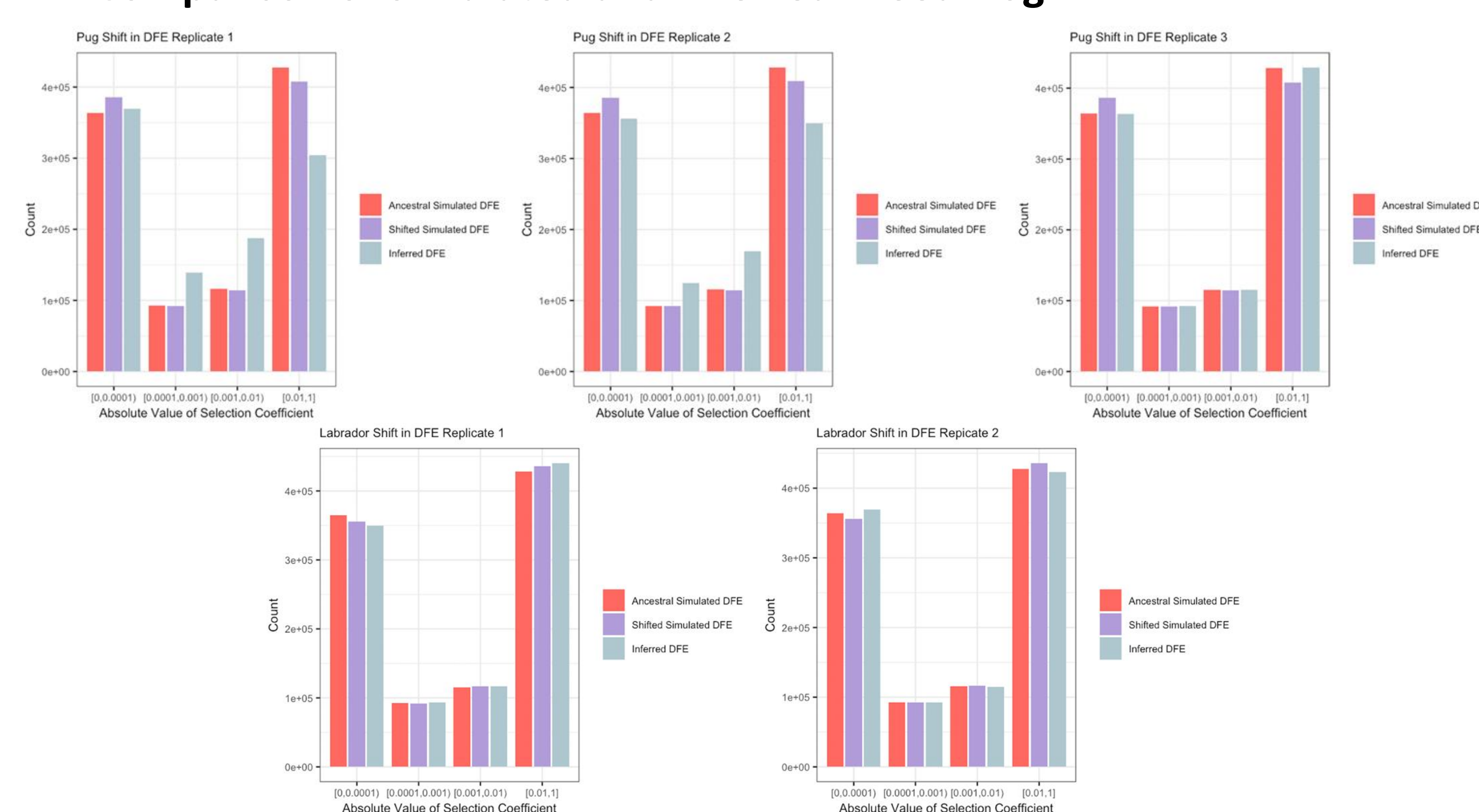### Comparison of Simulated and Empirical Synonymous Proportional Site Frequency Spectra

Comparison of Simulated and Empirical Nonsynonymous Proportional Site Frequency Spectra

Comparison of Simulated and Inferred Arctic Wolf DFE

Comparison of Simulated and Inferred Breed Dog DFE

Conclusions and Future Directions

- Our simulations successfully replicated Arctic Wolf nonsynonymous and synonymous site frequency spectra.
- From these spectra, we accurately inferred the ancestral Arctic Wolf DFE.
- When simulating a shift in DFE, we find that it is easier to detect the changes present from Wolf to Pug than from Wolf to Labrador.
- Our findings reflect that the DFE in Pug populations are more diverged from the ancestral DFE than the DFE of Labrador populations.
- Next, we seek to develop a statistical framework to test changes in DFE.

Acknowledgements

References

1. Loewe L, Hill WG (2010) The population genetics of mutations: Good, bad and indifferent. *Philos Trans R Soc Lond B Biol Sci* 365:1153–1167.
2. Huber, C. D., B. Y. Kim, C. D. Marsden, and K. E. Lohmueller, (2016) Determining the factors driving selective effects of new nonsynonymous mutations. *Proceedings of the National Academy of Sciences* 114(17), 4465-4470.