Hi everyone, I’m Nick, and today I’ll be talking to you about my research into simulating the evolution and adaptation of polygenic traits.

The allure of adaptation comes from the power of Darwin’s theory to explain natural diversity both within and between populations. Evolutionary study is often focused on natural selection and its role in shaping the forms of diversity around us. For instance, the beak shape of Darwin’s finches conforming to their diet provides a classic example of natural selection leading to adaptation.

As intuitive as it is to focus on the ability of populations to adapt to new situations, populations are seldom perfectly adapted. Trait values are rarely optimal, populations decline, and extinctions are commonplace. It seems unlikely that populations would ever be able to perfectly match their phenotypic optimum.

This leads us to the concept of maladaptation, where populations maintain a stable phenotype some distance away from a phenotypic optimum. For example, here a population hovers around a phenotype described by two polygenic traits, with selection keeping it from hovering too far away. However, new mutation, and genetic drift keep the population from being precisely at the optimum.

This behaviour seems common in nature: a 2007 literature review by Estes and Arnold found 64% of the studied populations were maladapted to some degree.

Despite this, maladaptation is rarely studied. Over 4600 papers featuring the keyword ‘adaptation’ were published in Nature research journals in 2019. The keyword ‘maladaptation’ was mentioned in just 45.

The prevalence of maladaptation in nature raises interesting questions into the essence of evolution: what does it take to be adapted?

Quantitative genetic models attempt to explain adaptation to phenotypic optima using stabilising selection on polygenic traits, where intermediate trait values lead to peak fitness. Here we see the ancestral population, shown in red, become less variable, narrowing its range of phenotypes until we reach the derived population, in blue.

Driving adaptation is the heritable variability within a population, the additive genetic variance of a trait, or VA. Theory predicts that increased VA allows for more rapid responses to selection, because the larger the range of phenotypes in the population, the higher the chance that one of them becomes adaptive after an event spurs on a selective pressure.

During adaptation, VA is expected to decline, as populations become more homogeneous as more and more individuals reach the optimum phenotype.

So here we’ve seen a paradox: populations need VA to make the move towards an optimum (gesture to orange arrow), but being variable when hovering around an optimum (hovering blue line) means populations are maladapted to a degree.

In other words, there is a trade-off between adaptability and adaptedness. The nature of this trade-off depends on how variance is maintained in populations, and the genetic architectures underpinning important traits in those populations.

VA is maintained in populations by a balance between incoming mutation introducing new variation, and the forces of drift and selection which drive allele fixations or losses. Ignoring drift for now, which results in random fixations or losses of alleles, quantitative genetic models aim to simulate this balance between selection and mutation based on one of two major assumptions.

Gaussian models assume weak selection relative to mutation rates, resulting in higher levels of standing genetic variation.

House-of-Cards models on the other hand assume strong selection and relatively low mutation rates, leading to lower standing genetic variation. However, genetic aspects of the traits themselves can also influence the maintenance of variation in populations.

Quantitative genetics aims to tease apart nature from nurture: the genetic (point) and environmental effects (point) contributing to a phenotype. To do this, we can define a trait’s genetic architecture, which consists of the genetic characteristics defining G in this equation.

The genetic architecture of a trait defines its characteristics – the number of genes affecting it, their locations within the genome, and their strength of allelic effects (POINT TO EACH ON FIGURE). Here I explore the effect of additive effect distributions (those creating Va) on equilibrium variance after adaptation.

Now with a firmer view on how adaptation is driven in quantitative traits, we can reform our question:

Is there a specific genetic architecture or balance of evolutionary forces that facilitate movement towards a phenotypic optimum, and being able to hover around it over time?

I investigated this with a computational approach, using the forward population genetics software SLiM. I simulated populations hovering around a phenotypic optimum for 100,000 generations.

Populations had eight traits with equal effects on fitness, which I combined to a ‘mega-trait’ for simplicity. I explored a six dimensional ‘parameter space’ using Latin hypercube sampling to efficiently sample the entire range of parameter combinations.

Parameters included: additive effect size variance, or alpha, which describes the variability in mutational effects on traits.

Pleiotropy rate, which describes how often pleiotropic mutations that affect all eight traits (as opposed to just one) arise.

Mutational correlation, which describes how correlated the effects of pleiotropic mutations are on all traits.

Recombination rate, which is a genome wide rate

Mutation rate, which describes the ratio of mutations which affect traits versus those which do not.

And selection strength, describing the strength of stabilising selection across all traits.

I ran a total of 128,000 simulations with 100 replicates of 1280 parameter combinations. To explore the data, I first investigated how common adaptation was.

In my simulations I found a visible ‘dead zone’ where populations weren’t represented. The y-axis here is the distance from the phenotypic optimum, whereas the x axis shows the two model types – Gaussian, with high mutation rates and weak selection, and House-of-Cards, with low mutation rates and strong selection. I split populations that fell on either side of the dead zone into ‘adapted’ populations, shown in blue and ‘maladapted’ populations, shown in black.

Within null models with no selection treatment at all, populations very rarely reached the optimum – 0.5% of the time. Conversely, Gaussian and House-of-Cards models reached the optimum a similar amount – 15.23 and 16.1%, respectively.

But what caused these populations to break away from their maladapted cousins?

I found pleiotropy, mutational correlation, and recombination rate each had very little effect on whether populations appeared in the adapted zone. Additive effect size variance, or alpha, was extremely important. I’ll go over what alpha describes in my simulations in a bit more detail.

What alpha describes is the distribution of mutational effects. When a mutation occurs, it has some effect on the phenotype. This effect is randomly sampled from a normal distribution centered around 0. Alpha describes the standard deviation of that distribution, so larger alphas result in more variable, but also larger mutational effects on traits. Now knowing this, let’s have a look at what increasing alpha means for adaptation.

Additive effect size variance was strongly correlated with adaptive success: 36.12% of models with low alphas reached the adapted space, versus 2.29% of medium-alpha populations, and 0.19% of high alpha populations. However, additive effect size had considerably different effects on Gaussian versus House-of-Cards models.

Under House-of-Cards, where mutation is weak and selection is strong, populations tend to be more robust to increases in mutational variance, whereas under Gaussian models, populations are more susceptible to increases, with distance to the optimum tracking the mutational input closely.

Variance followed a similar pattern – House-of-Cards models had lower VA than Gaussian populations and maintained that with increased mutation rates. Given that VA is expected to inhibit adaptedness, the ability to hover around an optimum, this is expected given the Gaussian tendency to rest further from the optimum, as seen in the previous slide.

One way to visualise this is via the movement of molecules – Gaussian models are hot, erratically moving around the optimum with increasing mutational variability, whereas House of Cards models are colder and less motile, since strong selection allows for deleterious mutations to be efficiently purged, without large numbers of new mutations coming in to swamp the population.

So now that I knew Gaussian models responded differently to increasing mutational variance than House-of-Cards models, I wanted to find what was mediating this difference.

I looked at the distributions of allelic effects underpinning each model. This is the realised distribution of alleles segregating in the population. Under neutrality, this looks very similar to the distribution of mutations in general, as shown here. However, stabilising selection can influence this distribution by selecting against large effect alleles (point to ends of distribution) that drive populations away from the optimum.

I found distributions of allelic effects mirrored the impact of each model and mutational variance treatment on distance to the optimum. This figure shows the distributions of alleles across both models, with Gaussian models in general appearing more leptokurtic than House-of-Cards models at higher alpha values (point to each). In House-of-Cards models, there were no significant differences between distributions, whereas Gaussian models tended to reflect their alpha values, with higher alpha resulting in a more leptokurtic curve. This means that large effect alleles are more likely to be segregating in Gaussian populations than House-of-Cards populations.

From this, we can say that House-of-Cards models deal with deleterious alleles differently to Gaussian models. The strong selection – low mutation combo leads to efficient removal of deleterious alleles that drag populations away from the optimum.

Under Gaussian models, selection is less able to reign in these effects, so fluctuations away from the optimum are more likely as more and more mutations pile up.

Where does this matter though? These findings have implications for the environments under which different mutation-selection balances could flourish.

In environments where spatial or temporal change is rare, House-of-Cards models should be favoured: the increased stability and favours stronger adherence to the optimum over time, and so in the trade-off between adaptability and adaptedness, adaptedness is favoured.

In heterogeneous environments, Gaussian models should be favoured: increased mutation rates allow for a broader exploration of the phenotype space, and over time those explorations might become adaptive – as seen here, with the future optima, shown in orange.

There’s a lot of potential for this methodology and clearly a lot more to understand in terms of how mutation-selection equilibria interact with genetic architecture to influence adaptation. Future adjustments to models to hone our insights might include population size, fitness differences among traits for more realistic insights into correlated selection, and the number of loci contributing to traits. With enough refinement it should be possible to predict genetic architectures of natural populations by matching experimental data with a model in our hypercube sample.