MR and Selection plans

# Working group

* Monthly meetings
* George to present in April
* Mark Beaumont, Dan Lawson, Santi Rodriguez, Charlie Hatcher

# Review article

* Identify the link between models for natural selection and models for MR
* Role of pleiotropy - pleiotropy robust MR methods
* Measuring fitness in humans - fitness is a phenotype (e.g. Nick Barton’s work on number of generations before contribution is fixed - HUNT, ALSPAC, Icelandic studies)
* Time scale captured in this way
  + Lactase persistence - allele is 2.5k years old (george to send)
* SLiM to run some simulations to look at these
* Dynastic effects - parental effects on offspring fertility - non-transmitted allele (george to send - <https://journals.plos.org/plosgenetics/article/comments?id=10.1371/journal.pgen.1008222>)

Analysis plan

library(systemfit)

dat <- data.frame(x=x, y=y, g=g)

systemfit(y ~ x, inst = ~ g, data=dat, method = “2SLS”)

# Analytical project

## Whole genome approach

Fitness = y

Trait = x

Use MR to estimate s = beta coefficient of MR estimate of y ~ x

Univariate: Delta(p) = s \* h^2

Multivariate: Delta(P) = S %\*% sigma^2\_g

### Simulations

1. Null model = create traits with no genetic correlation, expect delta(p) = delta(P)
2. Allow positive and negative genetic correlations, expect delta(p) != delta(P) - what scenarios limit the evolvability
3. Forward in time - check that delta(P) is a good estimate of what actually happens using SLiM. This might be a good way to evaluate the MR method for estimating S

### Analysis

Now estimate s using MR, sigma^2\_g using LDSC, for a set of traits

## Per locus approach

* What if genetic correlation is low because the shared causal variants are in a mixture directions - how does this affect the breeder’s equation
* Take height SNPs
* Look for colocalisation
* Estimate the genotype-phenotype map for those SNPs against the traits and the traits against fitness
* What is the evolvability of height under this genotype-phenotype map?

### Selective sweeps

* Expect selection signatures to be small at each locus because they all have small effects, but perhaps large signature across all loci
* For each locus estimate the selection coefficient, and then ask if heterogeneity can be explained by pleiotropy at the locus

China selective sweep:

<https://www.biorxiv.org/content/10.1101/2020.11.16.385401v1.full.pdf>

Clare to setup skeleton document of the paper