The infinitesimal model

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The infinitesimal model

- includes selection, recombination, mutation, drift, gene flow
- applies when alleles have small effects on traits
- does *not* require
    - that traits are additive
    - that allele frequencies change infinitesimally

History

- blending inheritance (Fleeming Jenkin, 1867, Davis, 1871)
- Galton: offspring follow a Gaussian; variance independent of parents
- "law of ancestral heredity"
- Pearson (~1900) formalised Galton's statistical description
- Fisher (1918) showed that Galton's observations are consistent with many freely recombining genes of small effect
- Quantitative genetics developed in obscurity …

- Re-connected with evolutionary biology (Robertson, Lande, Bulmer …)

- Robertson (1960): limit to selection on standing variation

Defining the model

For convenience, neglect non-genetic variance, and (for now) assume additivity and haploidy

Offspring of unrelated parents $z_1,\ z_2\ \sim \mathcal{N}\left(\frac{z_1+z_2}{2},\ \frac{V_0}{2}\right)$

With random mating and no selection, population $\to \mathcal{N}(\bar{z},\ V_0)$

Mating between related parents gives variation *segregation variance* $\frac{V_0}{2}\left(1 - F_{i,j}\right)$ where $F_{i,j}$ is the probability of identity by descent.

$$\mathtt{F_{i,j}} = \sum\nolimits_{\mathtt{k,l}} \mathtt{P_{i,k}}\,\mathtt{P_{j,l}}\,\mathtt{F_{k,l}} \quad (\mathtt{i} \neq \mathtt{j}),\ \mathtt{F_{i,i}} = 1$$

where $P_{i,k}$ defines the *pedigree*

Mutation adds $\frac{V_m}{2}$ to the segregation variance, and changes the mean by $\mu(\delta - \bar{z})$.

Is the "infinitesimal model" be consistent with Mendelian genetics?
Offspring from extreme phenotypes must have *low* variance
Actual phenotypes occupy a narrow range relative to the possible range
Each phenotype corresponds to *diverse* genotypes

Robertson's limit to selection from standing variation

$\Delta \bar{z} = \beta \sum_{t=0}^{\infty} V_{a,t} = \beta V_{a,0} \sum_{t=0}^{\infty} \left(1 - \frac{1}{N}\right)^t = N \beta V_{a,0}$

This also holds with epistasis if $V_{a,0}$ is replaced by the total variance, $V_{g,0}$

Robertson derived this by another route. Initial allele frequency p_i, fixation probability $u[p_i]$

$\Delta \bar{z} = \sum_i \alpha_i (u[p_i] - p_i)$

Assuming weak selection:

$u[p_i] - p_i \sim p_i(1 - p_i)\, N \beta \alpha_i$

$\Delta \bar{z} = N \beta \sum_i \alpha_i^2\, p_i(1 - p_i) = \mathrm{N}\beta V_{a,0}$

The infinitesimal model assumes that selection is *weak* at each locus

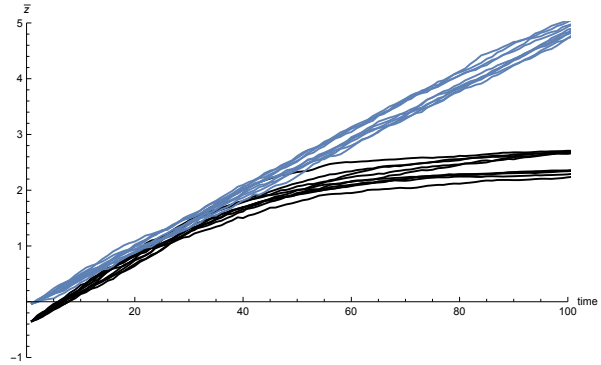
Mathematical interlude

Directional selection on an additive trait

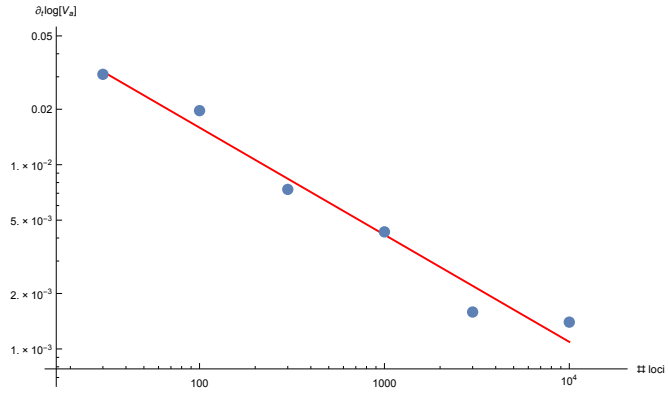
Initially, $p \sim 0.2$ at M loci; $\frac{\mathrm{var}(p)}{p(1-p)} \sim 0.2$.

Allelic effects exponential, mean $\frac{1}{\sqrt{M}}$; $V_{a,0} \sim 0.26 \; \forall \; M$

This shows the response to selection β=0.2, with N=1000; 10 replicates for 30 loci or 10^4 loci; maximum possible 2.94, 49.76 resp.

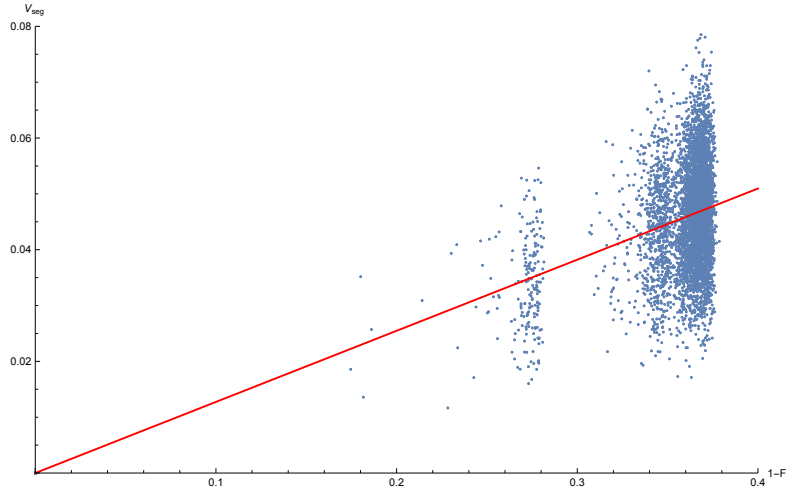


The genetic variance is lost at $\sim 1/\sqrt{M}$



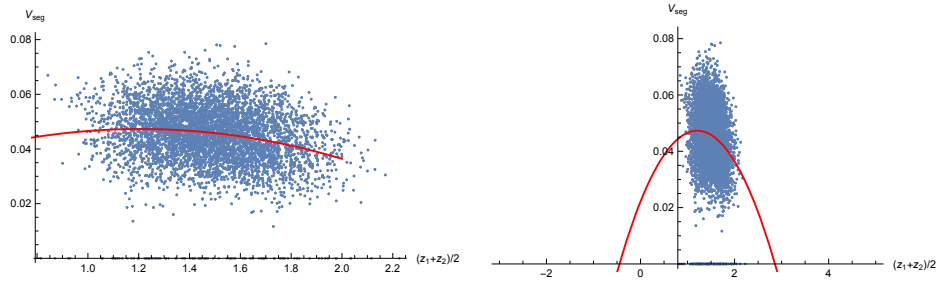
Segregation variance is proportional to 1-F

N = 100, 1000 loci, selected at β=0.1 for 100 generations:



Segregation variance hardly depends on parents' traits

The possible range is {-3.2, 4.9}



Summary

- The “infinitesimal model” describes the evolution of phenotype
- includes selection, random sampling, mutation, recombination, gene flow
- open questions (empirical and theoretical):
    - dominance, inbreeding depression …
    - can it describe long-term evolution ?
    - what shapes the genetic variance ?
- why bother finding the genes ?