

Adaptation dynamics of polygenic traits

Kavita Jain

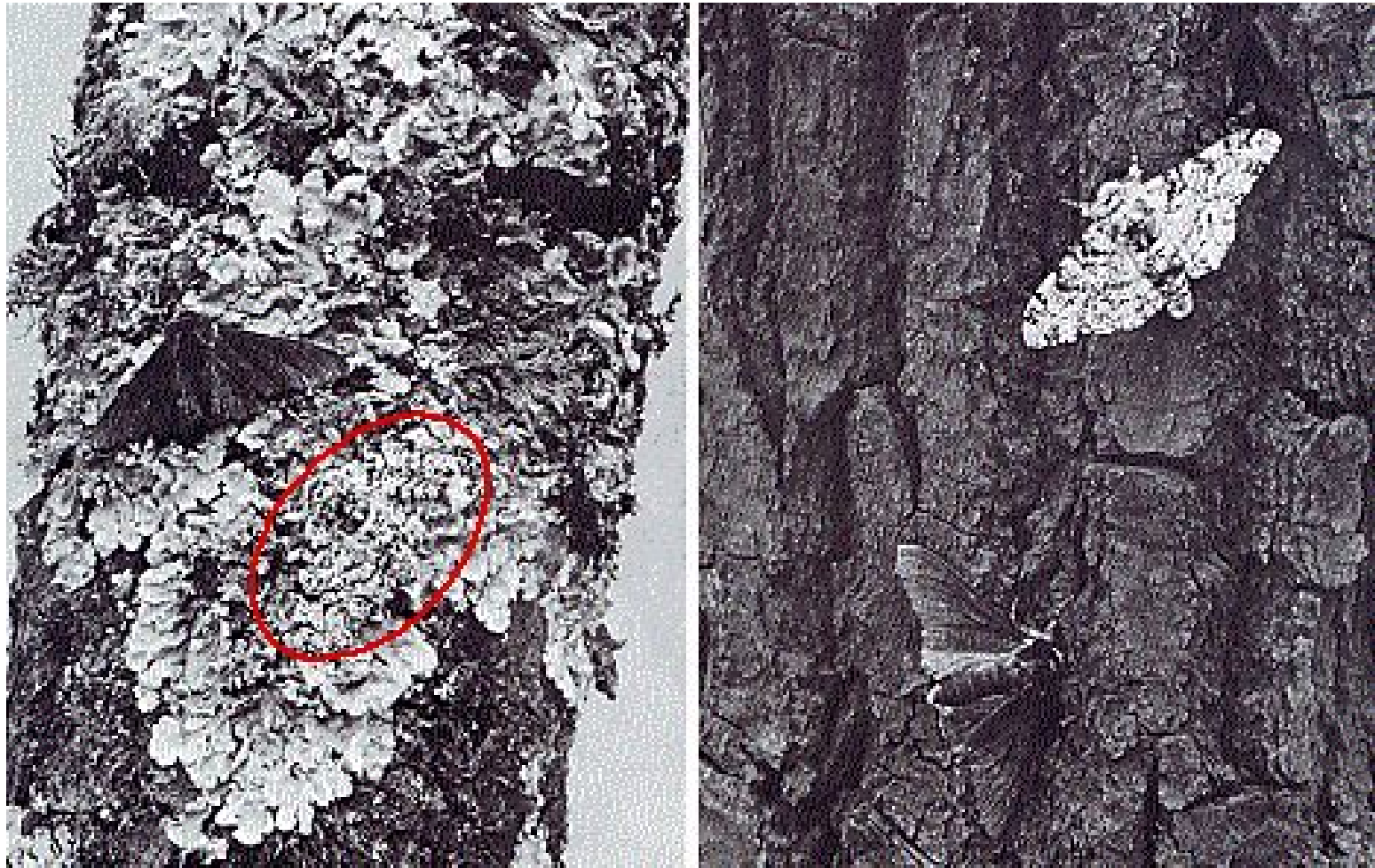
JNCASR, Bangalore

With Wolfgang Stephan (Berlin/LMU Munich)

G3: Genes | Genomes | Genetics (2015)

`arXiv:1610.05478`

The story of peppered moth (review by Cook & Saccheri 2013)



Monogenic adaptation

Frequency (color, t) ?



Color-gene relationship

(Bowater 1914; ...; van't Hof et al. 2016)

Gene	Color
+/+	Dark
+/-	Dark
-/-	Light



Frequency (gene, t) ? ↗

Population genetics model

(Punnett/Norton 1915; Haldane 1924)

Gene	Fitness	Frequency
+	s_+	p_+
-	s_-	p_-

$$\dot{p}_+ = s_+p_+ - (s_+p_+ + s_-p_-)p_+$$

Fitter one takes over in time

$$\sim |s_+ - s_-|^{-1}$$

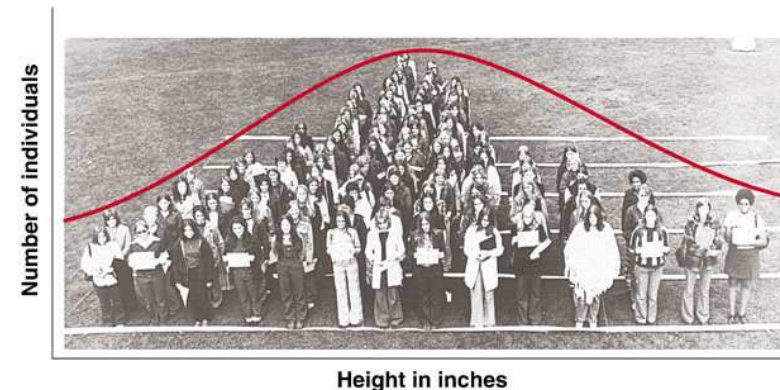
Polygenic traits

Many traits of interest vary continuously (e.g., human height)

(Nilsson-Ehle 1909, East 1910)

Genotype	Effect	Phenotype
+ + + +	$\sum_i (+\gamma_i)$	very tall
{ + - + - }	$\sum_i (\pm\gamma_i)$	intermediate
- - - -	$\sum_i (-\gamma_i)$	very short

Tobin/Dusheck, Asking About Life, 2/e
Figure 16.6



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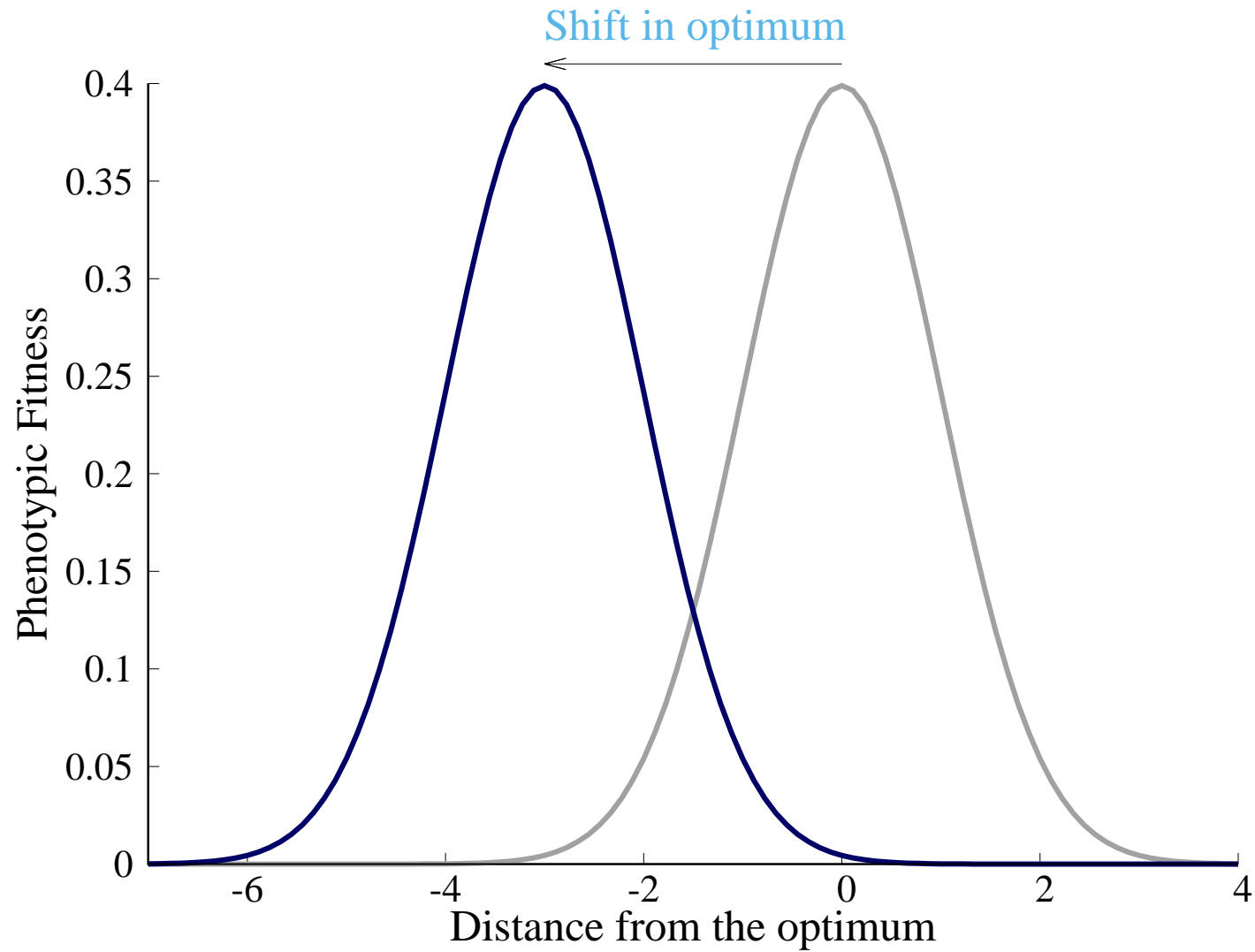
Distribution of heights is normal (central limit theorem)

But, how does height evolve?

Status of the subject

- Much of the work in the last century when few genes under selection
- When thousands of genes are simultaneously under selection:
 - remains poorly understood (joint evolution)
 - many diseases are polygenic, lot of data is becoming available

Dynamical response to a sudden shift (Jain & Stephan 2015, 2016)



Deterministic model (de Vladar & Barton, 2014)

The frequency at the i th gene evolves according to

$$\begin{aligned}\dot{p}_i &= \frac{p_i q_i}{2} \frac{\partial \ln \bar{w}}{\partial p_i} + \text{Mutation term} \\ &= \underbrace{s \gamma_i p_i (1 - p_i) (z_{\text{opt}} - \bar{z})}_{\text{DIRECTIONAL}} + \underbrace{\frac{s \gamma_i^2}{2} p_i q_i (p_i - q_i)}_{\text{FIXATION}} + \underbrace{\mu (q_i - p_i)}_{\text{MUTATION}}\end{aligned}$$

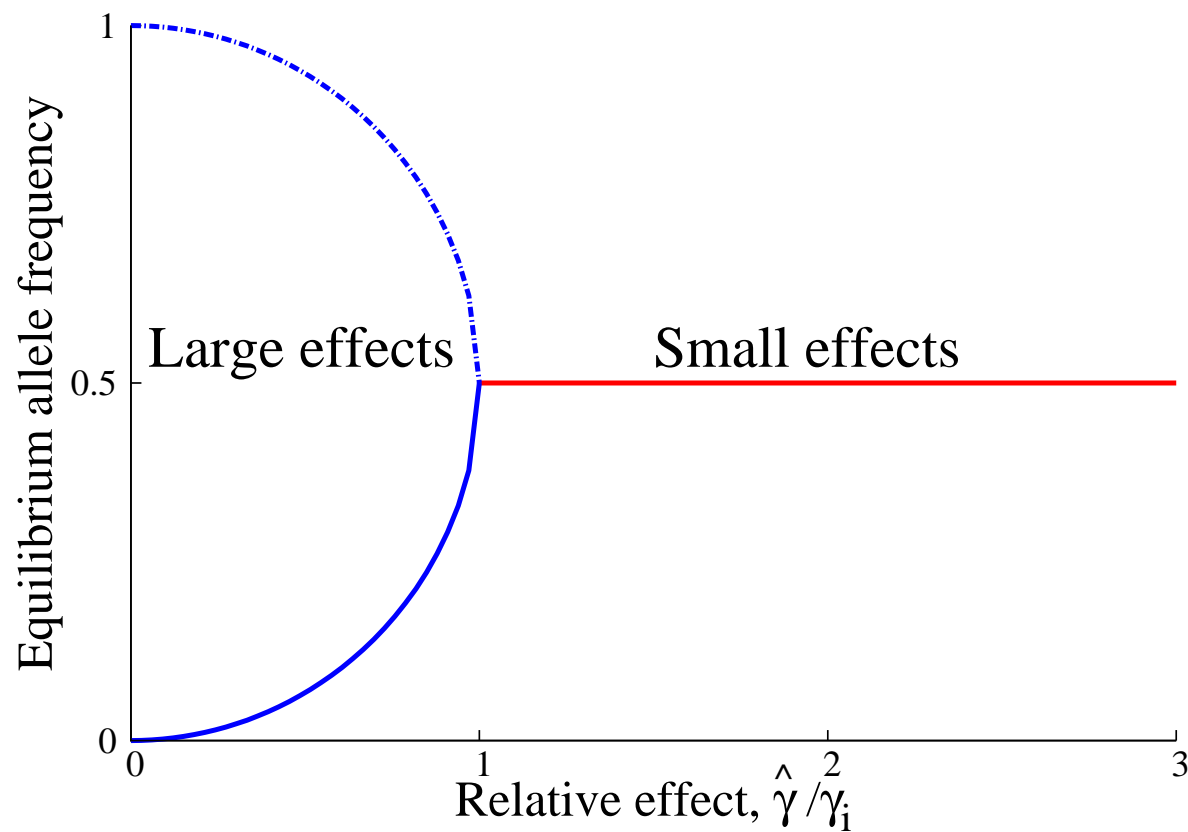
where the mean phenotype depends on all frequencies,

$$\bar{z} = \sum_{j=1}^{\ell} \gamma_j (2p_j - 1)$$

→ Equations of motion are nonlinear and do not close

Stationary state (de Vladar & Barton, 2014)

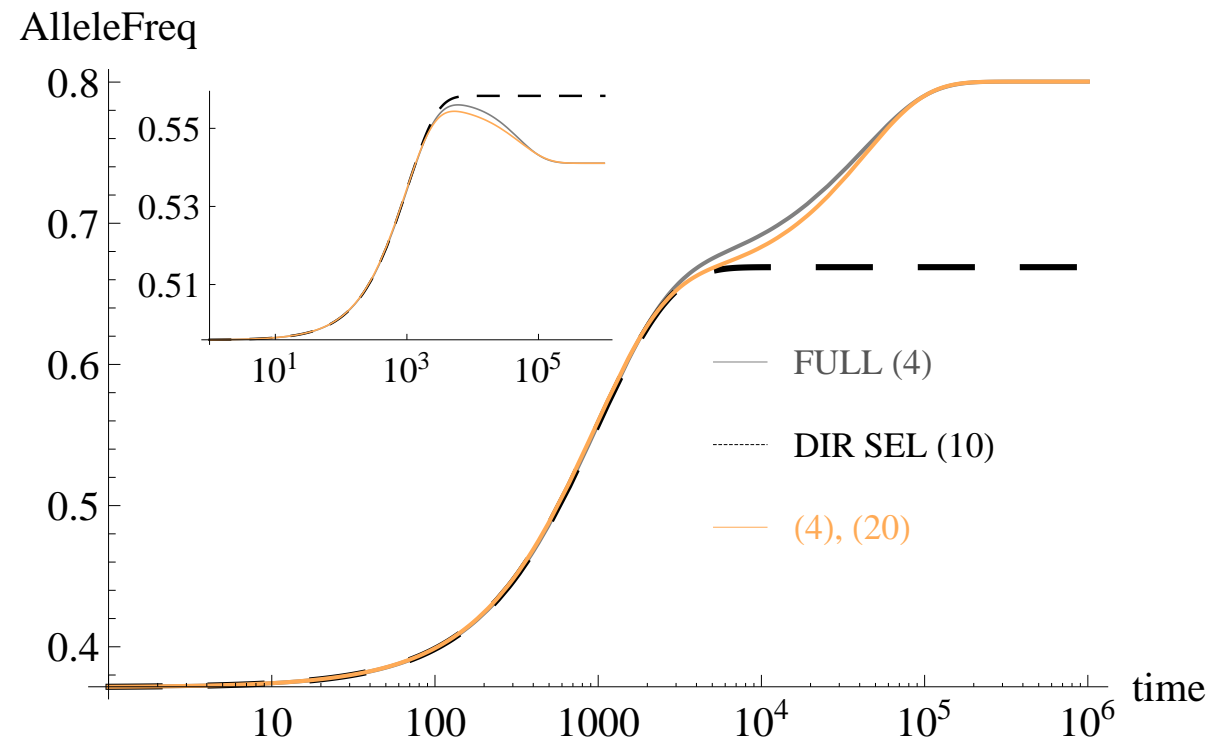
$$\text{Equilibrium frequency} = \begin{cases} \text{polymorphic} & , \gamma_i < \hat{\gamma} \\ \text{monomorphic} & , \gamma_i > \hat{\gamma} \end{cases}$$



Regime I: All genes participate

- frequency changes at any gene are small to moderate
- all genes participate in the process (“classic Fisherian view”)

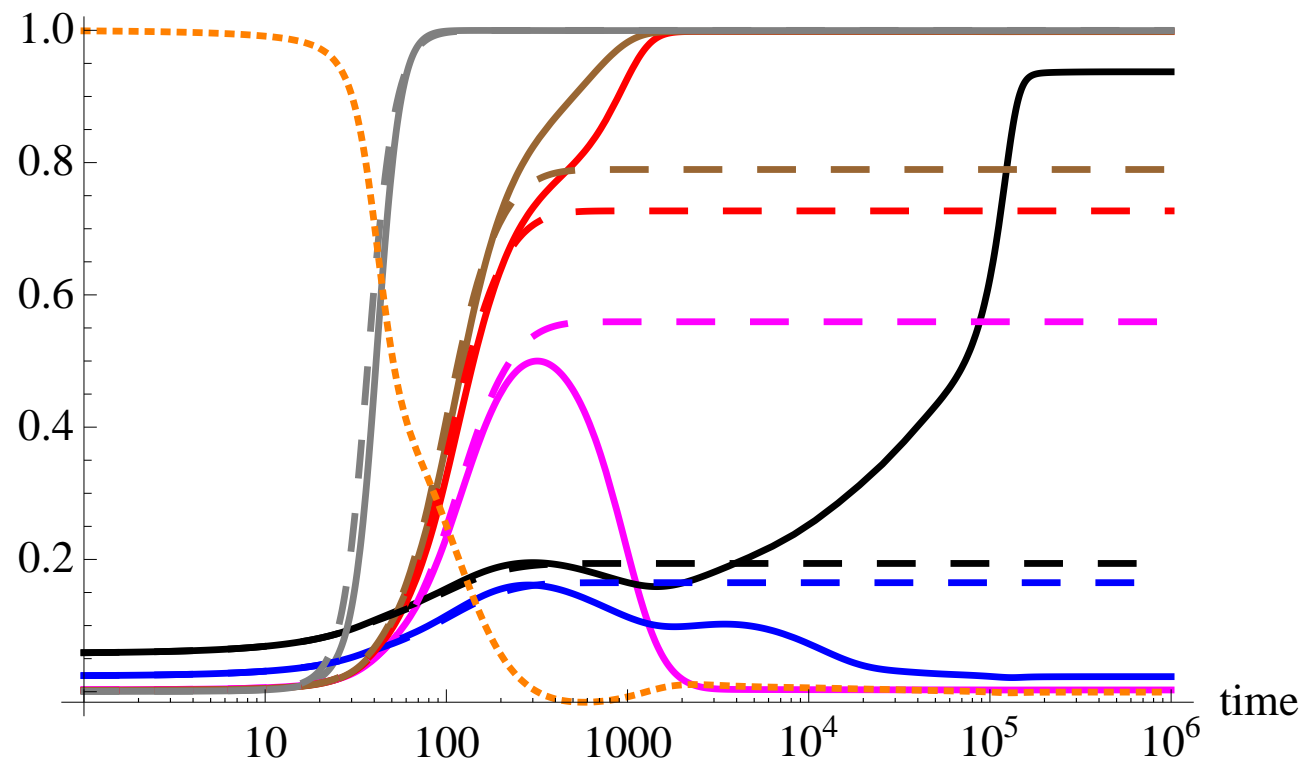
→ time scale for adaptation found



Regime II: Few genes dominate

- large changes in frequencies can occur (as in moth's case)
- only a few genes drive the adaptation process

→ Which ones? quantitative criterion found



Summary

- Described a deterministic model for adaptation of single trait
- Several biologically relevant factors not taken care of :

stochasticity; dominance; linkage; multiple traits ...

[Joint distribution $\text{Prob}(p_1, \dots, p_{1000})$?]