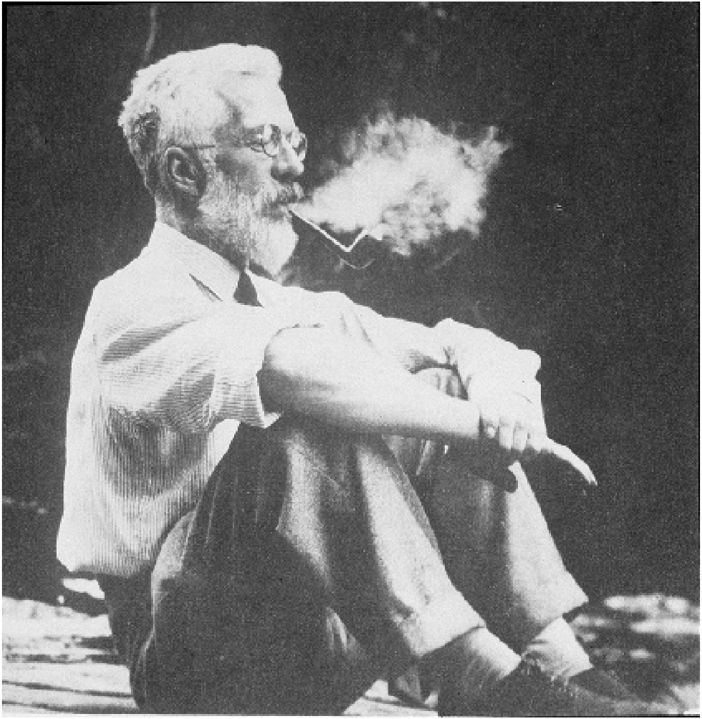
Adaptation and the cost of complexity (Orr 2000)

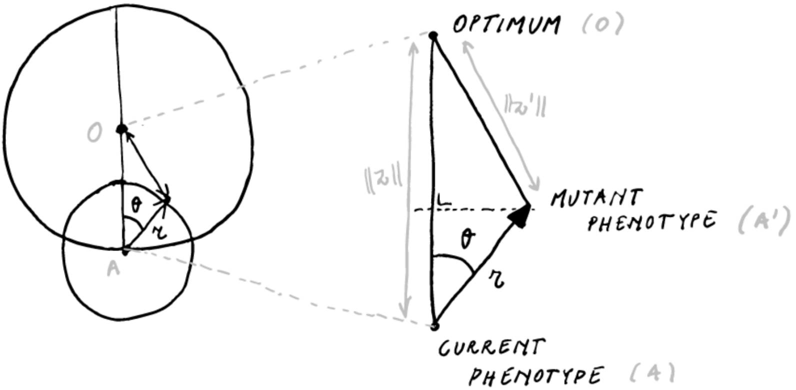
Arthur Zwaenepoel

January 2021

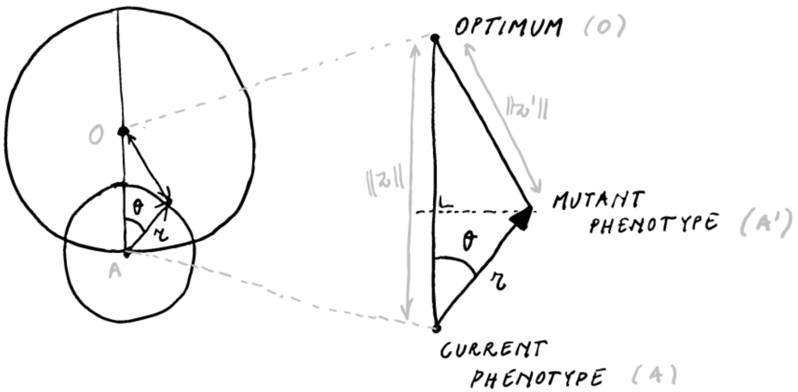
1. Fisher's geometric model (FGM)
2. Orr's model of evolution based on FGM
3. Cost of complexity



in $\mathbb{R}^2$

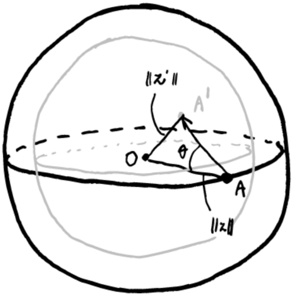


$$\Delta z(\theta) \approx r\cos\theta - \frac{r^2}{2\|z\|}$$



$$\begin{cases} \Delta z(\theta) \approx r\cos\theta - \frac{r^2}{2\|z\|} \\ \theta \sim \mathrm{Uniform}(0, 2\pi) \end{cases} \implies P_{\text{adaptive}} = P\{\Delta z(\theta) > 0\}$$

in $\mathbb{R}^3$

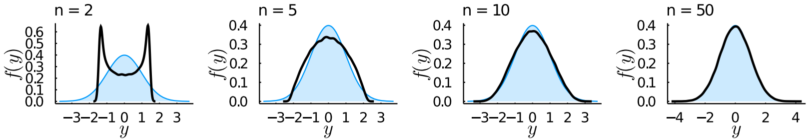


$$\begin{cases} \Delta z(\theta) \approx r\cos\theta - \frac{r^2}{2\|z\|} \\ \theta \sim ??? \end{cases} \implies P_{\text{adaptive}} = P\{\Delta z(\theta) > 0\})$$

in $\mathbb{R}^n$?

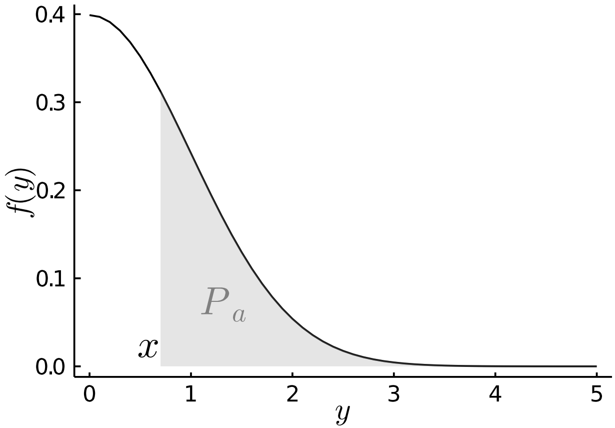
$$y = \sqrt{n}\cos\theta$$

For $n \gg$, it turns out that $y \sim \mathrm{Normal}(0,1)$



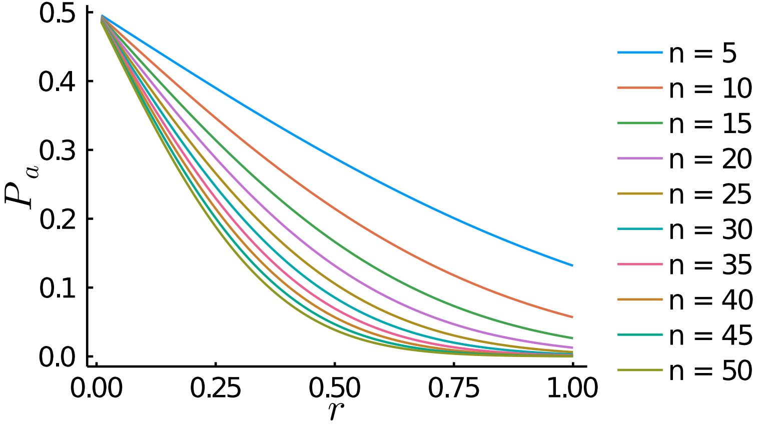
$$\Delta z(y) \approx \frac{r}{\sqrt{n}}\left(y - \frac{r\sqrt{n}}{2\|z\|}\right)$$

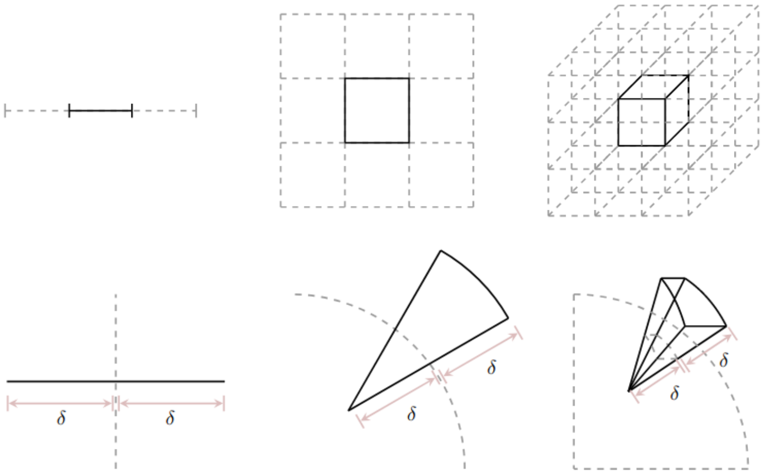
So $y \sim \mathrm{Normal}(0, 1)$ and $\Delta z(y) > 0$ if $y > \frac{r\sqrt{n}}{2\|z\|}$



where $x = \frac{r\sqrt{n}}{2\|z\|}$

The first cost of complexity




δ
δ
δ
δ
δ
δ

From FGM to Orr

To build a complete evolutionary model of adaptation around FGM we need

1. a mutation *process*

$$N\mu$$

2. a relationship between phenotype and *fitness*

$$w(\mathbf{z}) = \exp(-\|z\|^2)$$

Simplifying assumptions:

1. Every mutation is either fixed or lost before the next one occurs
2. Deleterious mutations do not fix

The distance moved to the optimum

$$\mathbb{E}[\Delta z(\delta t)] = \mathbb{E}[\Delta z|\text{fix}] \times \underbrace{P[\text{fix}|\text{adv}]}_{\Pi} \times \underbrace{P[\text{adv}|\text{mut in } \delta t]}_{P_a} \times \underbrace{P[\text{mut in } \delta t]}_{(N\mu)\delta t}$$

$$\mathbb{E}[\Delta z(\delta t)] = \mathbb{E}[\Delta z|\text{fix}] \times \underbrace{P[\text{fix}|\text{adv}]}_{\Pi} \times \underbrace{P[\text{adv}|\text{mut in } \delta t]}_{P_a} \times \underbrace{P[\text{mut in } \delta t]}_{(N\mu)\delta t}$$

The rate of phenotypic change

$$\begin{aligned}
\frac{d\|z(t)\|}{dt} &= \lim_{\delta t \to 0} \frac{\|z(t+\delta t)\| - \|z(t)\|}{\delta t} \\
&= \lim_{\delta t \to 0} \frac{(\|z(t)\| - \mathbb{E}[\Delta z(\delta t)]) - \|z(t)\|}{\delta t} \\
&= \lim_{\delta t \to 0} \frac{-\mathbb{E}[\Delta z(\delta t)]}{\delta t} \\
&= -(N\mu) \times \Pi \times P_a \times \mathbb{E}[\Delta z|\text{fix}]
\end{aligned}$$

Or if we rescale time

$$\frac{d\|z(t)\|}{dt} = -\Pi \times P_a \times \mathbb{E}[\Delta z|\text{fix}]$$

Challenge:

Express Π and $\mathbb{E}[\Delta z|\text{fix}]$ in terms of z, r, n and θ

The probability of fixation of an advantageous mutation

$\Pi \approx 2s$ we know from popgen theory where

$$\frac{1+s}{1} = \frac{w(z')}{w(z)}$$

we can find $s \approx \|z(t)\| \mathbb{E}[\Delta z|\text{adv}]$

$$\frac{d\|z(t)\|}{dt} = -2\|z(t)\| \times P_a \times \mathbb{E}[\Delta z|\text{adv}] \times \mathbb{E}[\Delta z|\text{fix}]$$

After some tedious math... [where $x = \frac{r\sqrt{n}}{2\|z(t)\|}$]

$$\frac{d\|z(t)\|}{dt} \approx -\frac{2\|z(t)\|r^2}{n\sqrt{2\pi}} \int_x^\infty (y-x)^2 \exp(-y^2/2) dy$$

After some tedious math... [where $x = \frac{r\sqrt{n}}{2\|z(t)\|}$]

$$\frac{d\|z(t)\|}{dt} \approx -\frac{2\|z(t)\|r^2}{n\sqrt{2\pi}} \int_x^\infty (y-x)^2 \exp(-y^2/2) dy$$

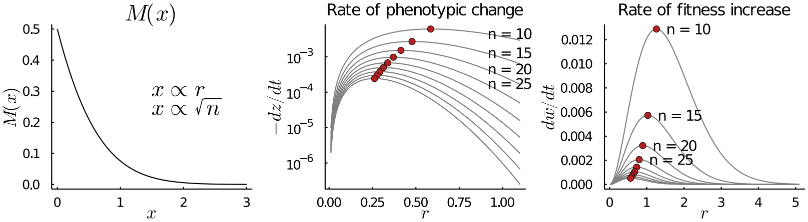
$$\frac{d\|z(t)\|}{dt} \approx -\frac{2r^2}{n} M(x) \|z(t)\|$$

The rate of phenotypic change

$$\frac{d\|z(t)\|}{dt} \approx -\frac{2r^2}{n} M(x)\|z(t)\|$$

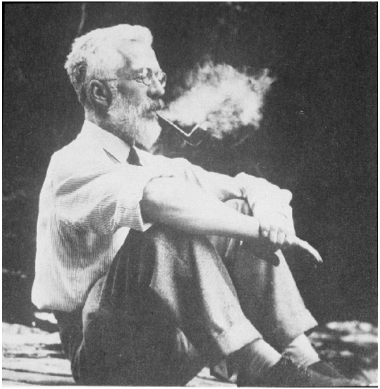
The rate of adaptation

$$\frac{dw(t)}{dt} \approx -\frac{4r^2}{n} M(x) w(t) \log w(t)$$



The rate of adaptation is highest for intermediate r

1. Probability that a mutation is advantageous *decreases* with r
2. Probability that an advantageous mutation is fixed in the population *increases* with r (i.e. $\propto \mathbb{E}[\Delta z|\mathrm{adv}]$)



vs.

The three-fold cost of complexity

For a **given**

- mutation effect size r
- current distance to the optimum $\|z(t)\|$

we get

$$
\begin{aligned}
&P_{\text{advantageous}} && \text{decreases with } n && (1)\\
&\mathbb{E}[\Delta z|\text{adv}] && \text{decreases with } n && (2)\\
&\mathbb{E}[\Delta z|\text{fix}] && \text{decreases with } n && (3)
\end{aligned}
$$

$$
\frac{d\|z(t)\|}{dt} = -2\|z(t)\| \times P_a \times \mathbb{E}[\Delta z|\text{adv}] \times \mathbb{E}[\Delta z|\text{fix}]
$$

"The purpose of models is not to fit the data but to sharpen the question."

Samuel Karlin

Welch & Waxman (2003) Modularity & the cost of complexity

1. r as a random variable from a broad range of distribution
2. r scaling differently with n
3. Parcellar complexity (mutations affecting only a subset of traits)

All leave the cost of complexity more or less intact

Wagner *et al.* (2008) examined 70 skeletal traits in mice

1. Most QTLs affect a relatively small number of traits (50% of QTLs affect $< 7/70$ traits)
2. A substitution at a QTL has an effect on each trait that increases with the number of traits that are affected