# Population genetics of adaptation

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# Spreading of beneficial mutations

# Population

Branching process: Birth rate I+s. Death rate I

Fixation probability: ~s Sweep time: ~ ln(Ns) / s

## Interference between beneficial mutations



Small population: sequential innovations, rate of evolution  $\sim sNU_b$ 

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Large populations: competing mutations



## Interference between beneficial mutations



## Recombination accelerates evolution



Small population: sequential innovations

Large populations: competing mutations

Recombination can combine competing mutations and accelerate adaptation -BUT BY HOW MUCH?



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# "Path integral"



$$\partial_t P(x,t) = (x - \bar{x}(t))P(x,t) + r \left[ \int \frac{dx_1 dx_2}{\sqrt{\pi\sigma}} e^{-\frac{(x - \frac{x_1 + x_2}{2})^2}{\sigma^2}} P(x_1,t)P(x_2,t) - P(x,t) \right]$$

-

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Selection
Recombination

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Selection Recombination



$$P(x,t) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{-\frac{(x-\bar{x}(t))^2}{2\sigma^2}}$$
$$\frac{\partial}{\partial t}\bar{x}(t) = \sigma^2$$

$$\partial_{t}P(x,t) = (x - \bar{x}(t))P(x,t) + r \left[ \int \frac{dx_{1}dx_{2}}{\sqrt{\pi\sigma}} e^{-\frac{(x - \frac{x_{1} + x_{2}}{\sigma})^{2}}{\sigma^{2}}} P(x_{1},t)P(x_{2},t) - P(x,t) \right]$$
Selection
Recombination
$$\int_{0.4}^{0.4} \frac{v = \sigma^{2}}{\sigma^{2}} \int_{0.2}^{0.4} \frac{v = \sigma^{2}}{\sigma^{2}} \int_{0.2}^{0} \frac{1}{\sigma^{2}} e^{-\frac{(x - \bar{x}(t))^{2}}{2\sigma^{2}}} \frac{\partial}{\partial t} \bar{x}(t) = \sigma^{2}$$
New mutations:
$$\frac{\partial}{\partial t} \bar{x}(t) = \sigma^{2} = NU_{b}sp_{fix}(s, r, \sigma)$$

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# Stochastic dynamics of novel mutations



# Stochastic dynamics of novel mutations



birth rate :  $B = 1 + s + x - \bar{x}(t)$ 

death rate : D = 1

$$w(x,t-dt) = w(x,t)(1 - dt(B + D + r)) + dtB(1 - (1 - w)^2) + dt r \int K_{xy}w(y,t)$$

## Stochastic dynamics of novel mutations



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comoving frame :  $x \to x - \bar{x}(t)$ 

$$\sigma^2 \partial_x w(x) = r \int_y K_{x,y} w(y) + (x + s - r) w(x) - w(x)^2$$

## Asymptotic solutions



## Asymptotic solutions



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## Self-consistent solution

$$\frac{\partial}{\partial t}\bar{x}(t) = \sigma^2 = NU_b sp_{fix}(s, r, \sigma)$$

$$\frac{\partial}{\partial t}\bar{x}(t) = \begin{cases} 2s^2 \left(\frac{r}{s}\right)^2 \frac{\log NU_b}{\ln^2 r/s} & 1 \ll \frac{r^2}{s^2} \ll NU_b/\ln NU_b \\ NU_b s^2 \left(1 - \frac{4NU_b s^2}{r^2} + \dots\right) & \frac{r^2}{s^2} \gg 4NU_b \end{cases}$$

In large populations, recombination is limiting adaptation
In small population, the supply of mutations is limiting

# The more recombination, the better?

Genetic interactions

# So far: Fitness = # beneficial mutations



Genetic interactions

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# Genetic interactions (Epistasis)

$$F(g) = \sum_{i} f_i s_i$$
  $g = \{s_1, \dots, s_L\}$   $s_i = \pm 1$ 

# Genetic interactions (Epistasis)

$$F(g) = \sum_{i} f_i s_i + \sum_{i < j} f_{ij} s_i s_j + \sum_{i < j < k} f_{ijk} s_i s_j s_k + \cdots$$

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# Allele vs genotype selection





# Epistasis models

# Random epistasis model

$$F(g) = \sigma \left[ h \sum_{i} f_{i} s_{i} + \sqrt{1 - h^{2}} \xi(g) \right]$$

Gaussian distributed random number drawn  $\xi(g)$ once and fixed for each genotype

# Pairwise epistasis model

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 $\sum_i f_i^2 = 1 \qquad \sum_i f_i^2 = 1 \qquad \mbox{Gaussian distributed} \\ \mbox{coefficients}$ 

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Gaussian distributed coefficients

# Correlations between loci:



# Dynamics of selection



## Dynamics of selection



## The time it takes to loose genetic diversity

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## Dynamics of selection

## The time it takes to loose genetic diversity



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# Self-consistency Condition

$$\partial_t P(A, E; t) = (F - \overline{F} - r) P(A, E; t) + r \rho(E) \vartheta(A)$$

- *E* of recombinants is a random from a Gaussian  $\rho(E)$ .
- A of recombinants is the marginal of P(A,E)



## The success of selection



# Selection on interacting clusters



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# Collaborators



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