MULTILOCUS MODELS, SELECTION, AND GENETIC DRIFT

Denis Roze
Institute of Evolutionary Biology
University of Edinburgh

MULTILOCUS POPULATION GENETICS

When do multilocus processes matter?

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- Interference between loci → rates of adaptation

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- Evolution of genetic systems and life-cycles

MULTILOCUS POPULATION GENETICS

When do multilocus processes matter?

- Interference between loci → rates of adaptation
- Evolution of genetic systems and life-cycles
  - mutation
  - recombination
  - sex
  - mating systems (e.g., selfing vs outcrossing)
  - mate choice
  - ploidy levels

  ...

MULTILOCUS POPULATION GENETICS

When do multilocus processes matter?

- Interference between loci → rates of adaptation
- Evolution of genetic systems and life-cycles
- Speciation

MULTILOCUS POPULATION GENETICS

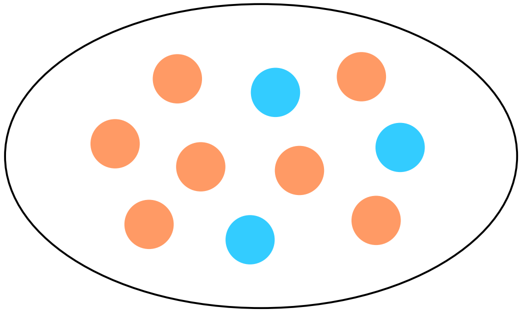
When do multilocus processes matter?

Genetic drift

MULTILOCUS POPULATION GENETICS

When do multilocus processes matter?

Genetic drift



Finite population size

MULTILOCUS POPULATION GENETICS

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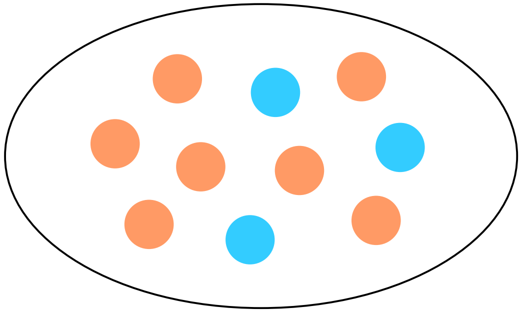

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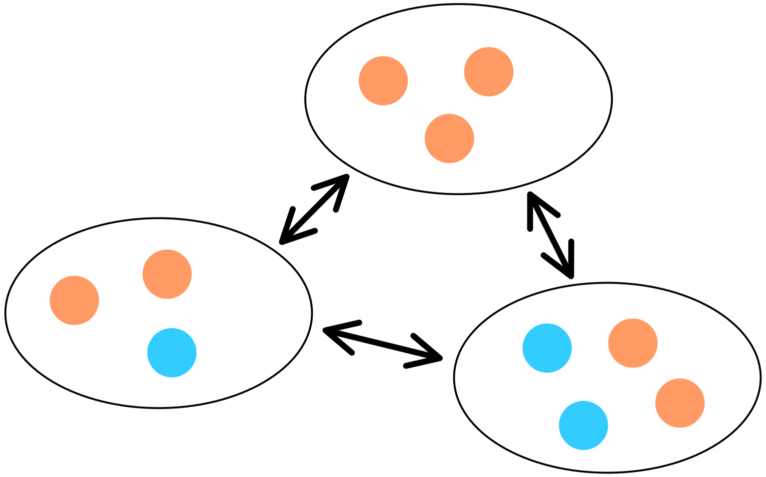

Population structure,
« local drift »

MULTILOCUS POPULATION GENETICS

When do multilocus processes matter?

Genetic drift

A general formalism?

A MULTILOCUS FORMALISM

Barton & Turelli 1991, Kirkpatrick et al 2002

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- Description of populations in terms of allele frequencies and genetic associations

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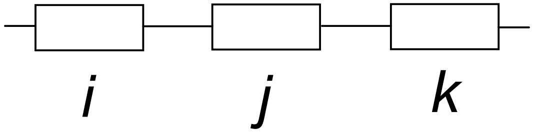
Ex: 3 biallelic loci, haploid



$$p_i\,,\ p_j\,,\ p_k\,,\ D_{ij}\,,\ D_{ik}\,,\ D_{jk}\,,\ D_{ijk}$$

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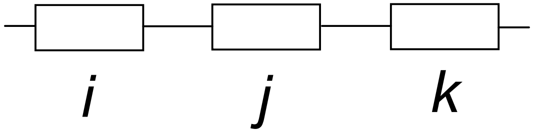

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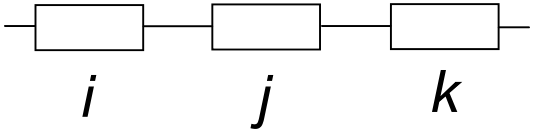

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- Recursions

Selection: $$p_i' = p_i + \sum_U a_U D_{Ui}$$

$$D_X' = D_X + \sum_U a_U \left(D_{UX} - D_U D_X \right)$$

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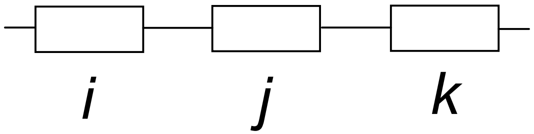

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$$D_X{}' = D_X + \sum_U a_U \left(D_{UX} - D_U D_X \right)$$

Recombination: $$D_X{}'' = \sum_{S+T=X} r_{S,T} D_S{}' D_T{}'$$

A MULTILOCUS FORMALISM

Barton & Turelli 1991, Kirkpatrick et al 2002

- Description of populations in terms of allele frequencies and genetic associations

- Recursions

  → exact recursions

  → general results in terms of a_U and $r_{S,T}$ coefficients

  → can be extended to diploidy, non-random mating, structured populations (infinite demes)....

A MULTILOCUS FORMALISM

Barton & Turelli 1991, Kirkpatrick et al 2002

- Description of populations in terms of allele frequencies and genetic associations
- Recursions
- *Quasi-linkage equilibrium* approximation

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  Separation of timescales, when selection is weak relative to recombination

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- Description of populations in terms of allele frequencies and genetic associations

- Recursions

- *Quasi-linkage equilibrium* approximation

  Separation of timescales, when selection is weak relative to recombination

  Recursions in terms of allele frequencies only

A MULTILOCUS FORMALISM

Example: two biallelic loci *i* and *j* , haploidy

A MULTILOCUS FORMALISM

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Fitnesses:

00	1
01	$1+s$
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11	$(1+s)^2+e$

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$$\longrightarrow$$

$$a_i \approx s + e p_j$$

$$a_j \approx s + e p_i$$

$$a_{ij} \approx e$$

A MULTILOCUS FORMALISM

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Quasi-linkage equilibrium:

$$\Delta p_i \approx a_i p_i q_i$$

$$\Delta D_{ij} \approx -r_{ij} D_{ij} + \left(1 - r_{ij}\right) a_{ij} p_i q_i p_j q_j$$

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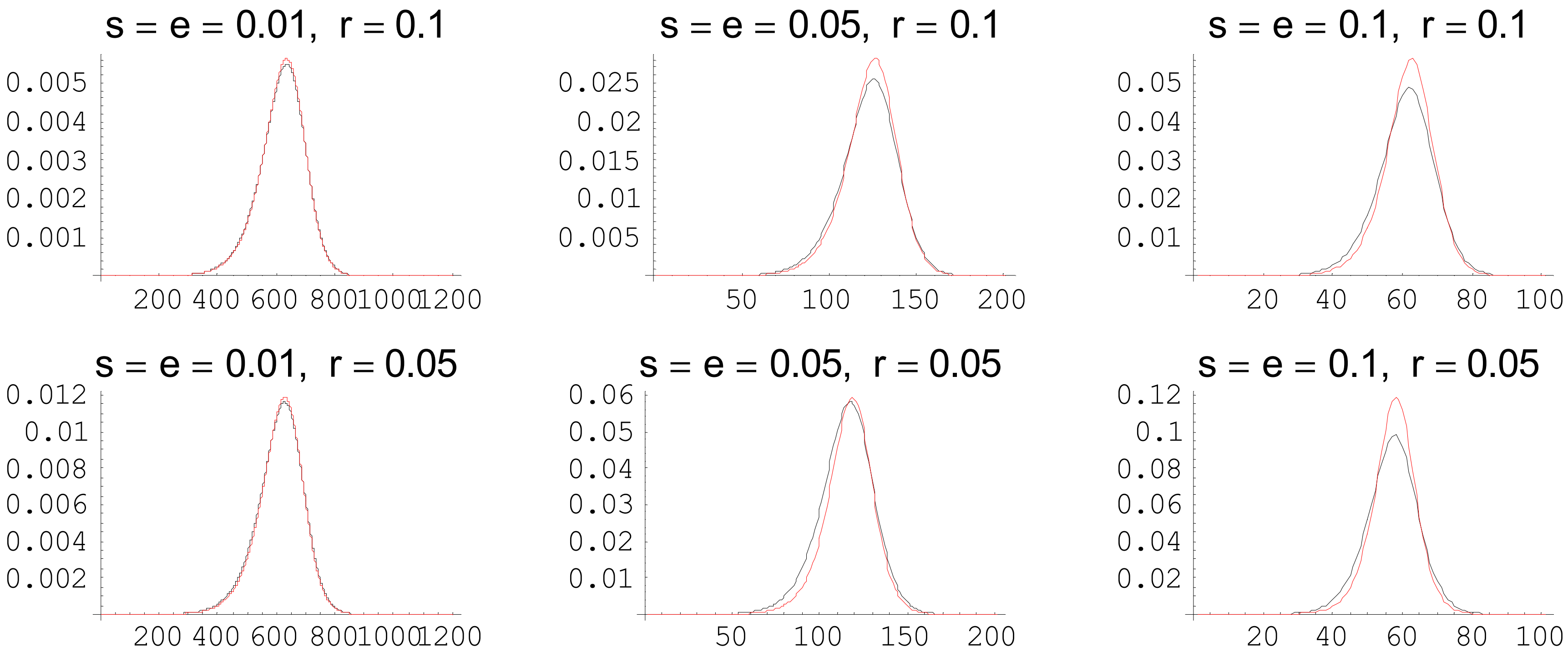
$$\Delta D_{ij} \approx -r_{ij} D_{ij} + (1-r_{ij}) a_{ij} p_i q_i p_j q_j$$

$$\longrightarrow \quad D_{ij} \approx a_{ij} \left(1/r_{ij} - 1\right) p_i q_i p_j q_j$$

A MULTILOCUS FORMALISM

Example: two biallelic loci *i* and *j* , haploidy



s = e = 0.01, r = 0.1

s = e = 0.05, r = 0.1

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INCLUDING GENETIC DRIFT

INCLUDING GENETIC DRIFT

Find appropriate variables

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Find appropriate variables

Complete system of recursions?

INCLUDING GENETIC DRIFT

Find appropriate variables

Complete system of recursions?

Which approximations can be used?

INCLUDING GENETIC DRIFT

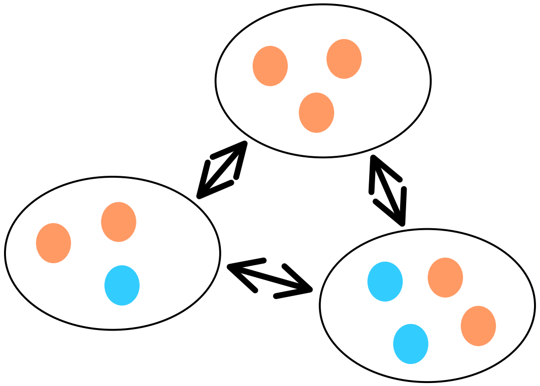
Find appropriate variables

Complete system of recursions?

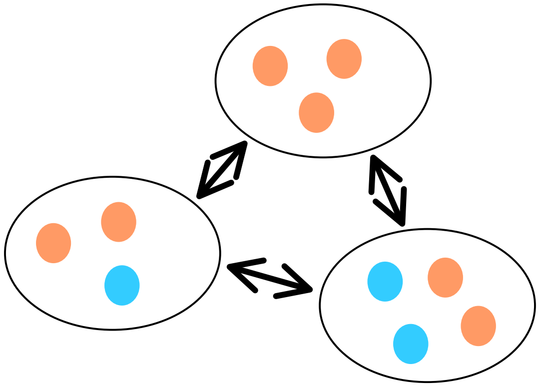
Which approximations can be used?

General framework?

POPULATION STRUCTURE AND LOCAL DRIFT



POPULATION STRUCTURE AND LOCAL DRIFT



Drift generated by finite deme size and local competition

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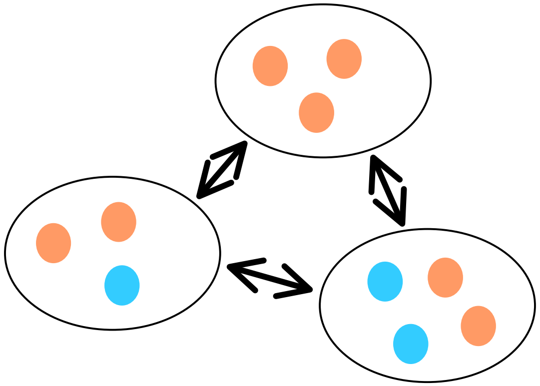
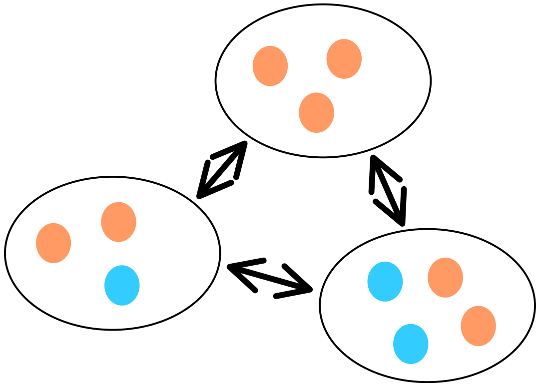


Drift generated by finite deme size and local competition

Infinite number of demes: deterministic model

POPULATION STRUCTURE AND LOCAL DRIFT



Drift generated by finite deme size and local competition

Infinite number of demes: deterministic model

Possible variables: moments of allele frequencies and genetic associations (averages and variances across demes, higher-order moments)

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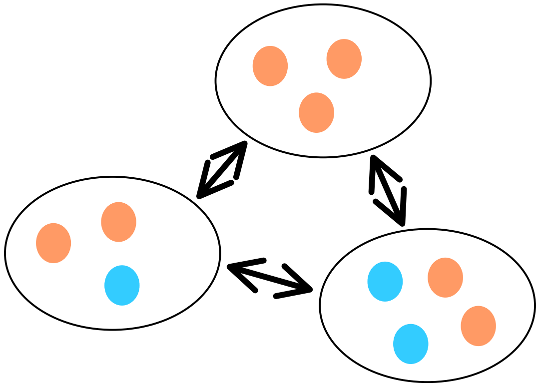


Drift generated by finite deme size and local competition

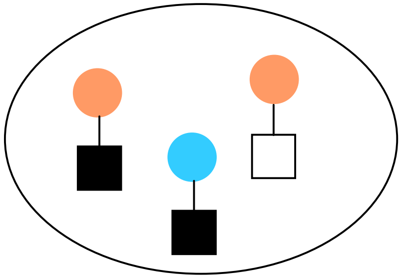
Infinite number of demes: deterministic model

Possible variables: moments of allele frequencies and genetic associations (averages and variances across demes, higher-order moments)

These moments can also be represented by associations between genes present in different individuals from the same deme (link with concept of IBD)

POPULATION STRUCTURE AND LOCAL DRIFT

Example: infinite island model



POPULATION STRUCTURE AND LOCAL DRIFT

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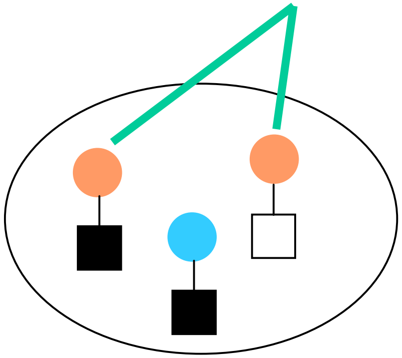
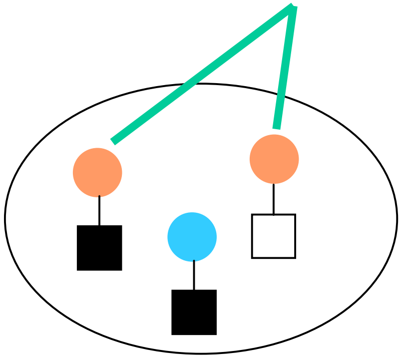


Association between two genes sampled with replacement at locus *i*:

$$D_{i/i} = \overline{p_{i(d)}^{2}} - p_{i}^{2}$$

POPULATION STRUCTURE AND LOCAL DRIFT

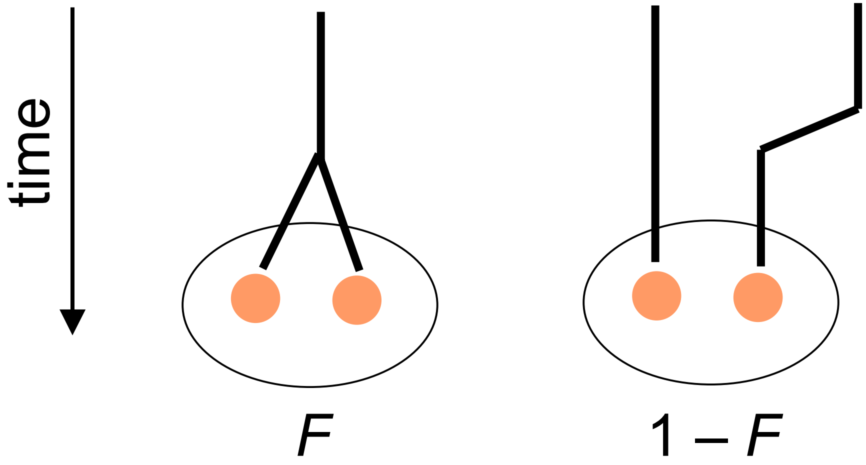
Example: infinite island model



Association between two genes sampled with replacement at locus *i*:

$$D_{i/i} = \overline{p^2_{i(d)}} - p_i^2$$

Equilibrium value in the neutral case:

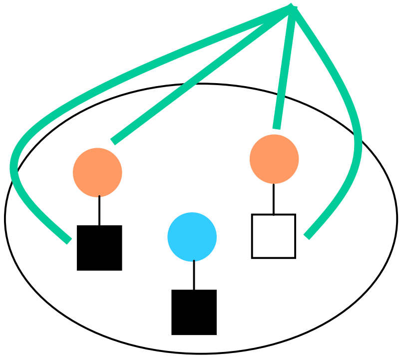


$$\overline{p^2_{i(d)}} = F\,p_i + \left(1 - F\right) p_i^2$$
$$= p_i^2 + F\,p_i q_i$$

$$D_{i/i} = F\,p_i q_i$$

POPULATION STRUCTURE AND LOCAL DRIFT

Example: infinite island model



Association between four genes sampled in two individuals:

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POPULATION STRUCTURE AND LOCAL DRIFT

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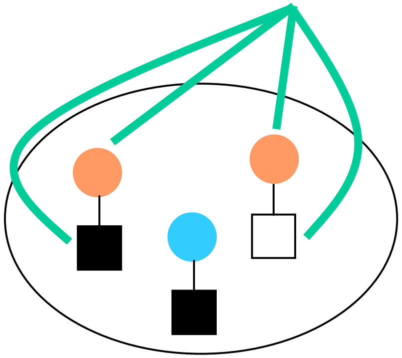

Association between four genes sampled in two individuals:

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Neutral equilibrium: $D_{ij/ij} = \phi p_i q_i p_j q_j$

probability that the two pairs of genes are IBD

POPULATION STRUCTURE AND LOCAL DRIFT

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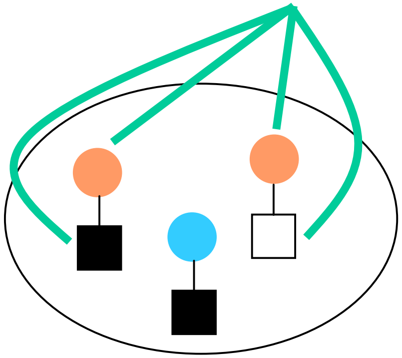

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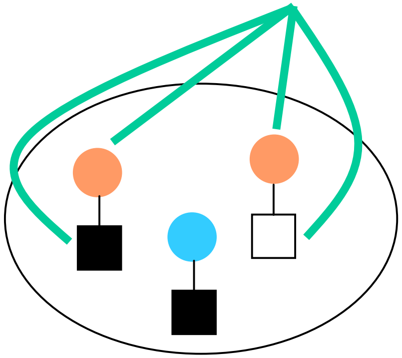

Association between four genes sampled in two individuals:

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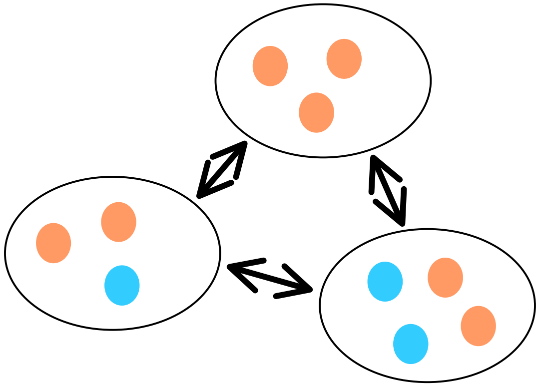
Selection: not possible to obtain complete sets of recursions

Quasi-equilibrium approximation: under weak selection (relative to migration and recombination), all associations are close to their neutral equilibrium value, and equilibrate fast

POPULATION STRUCTURE AND LOCAL DRIFT

Single-locus example, soft selection



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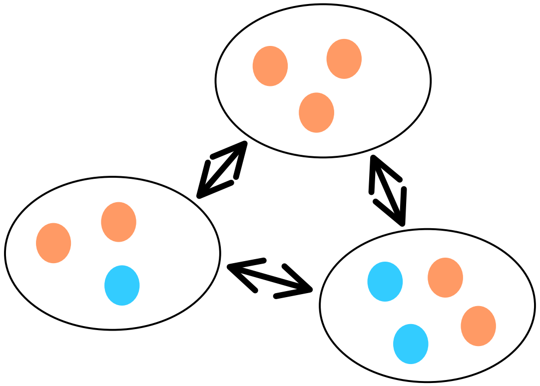

$$\Delta p_i = \overline{\frac{(1+s)\,p_{i(d)}}{1+s\,p_{i(d)}}} - p_i$$

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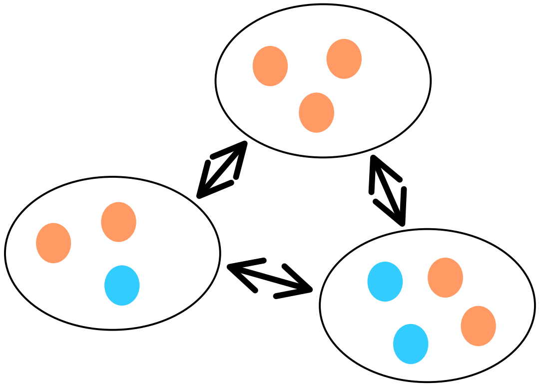

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Weak selection:

$$\Delta p_i = s\left(p_i - \overline{p^2_{i(d)}}\right) + o(s)$$

$$= s\left(p_i q_i - D_{i/i}\right) + o(s)$$

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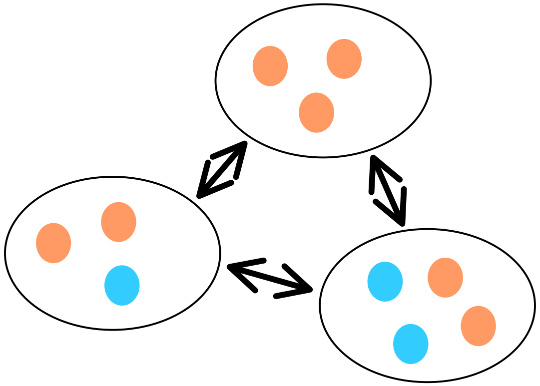

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Quasi-equilibrium:

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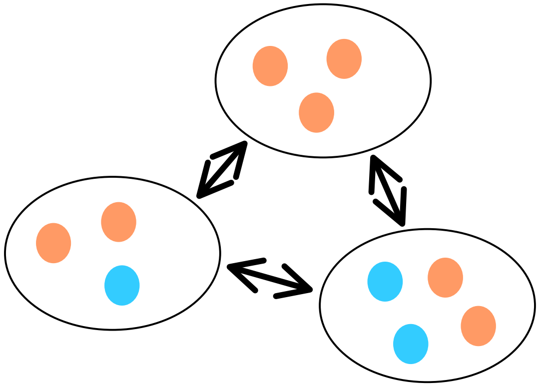

Quasi-equilibrium:

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Possible to express associations at quasi-equilibrium, to leading order in selection coefficients

POPULATION STRUCTURE AND LOCAL DRIFT

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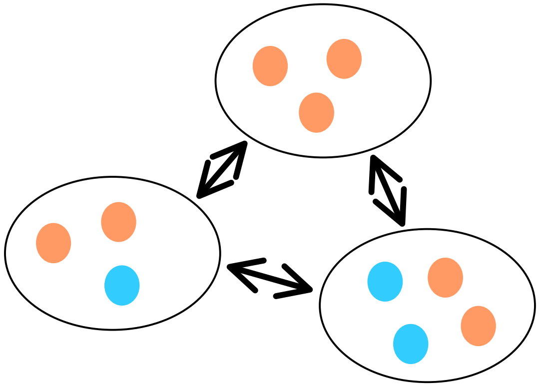

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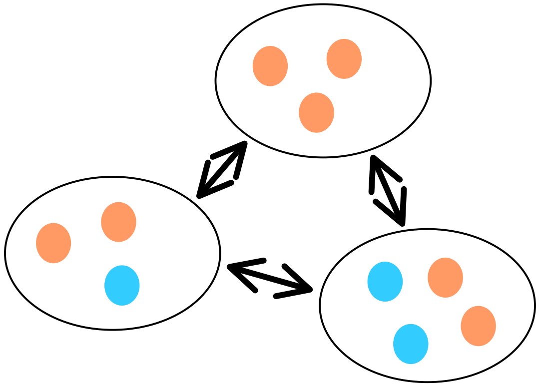

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Large deme size:

$$p_{i(d)} = p_i + \underbrace{p_{i(d)} - p_i}_{\zeta_{i(d)}}$$

(small)

POPULATION STRUCTURE AND LOCAL DRIFT

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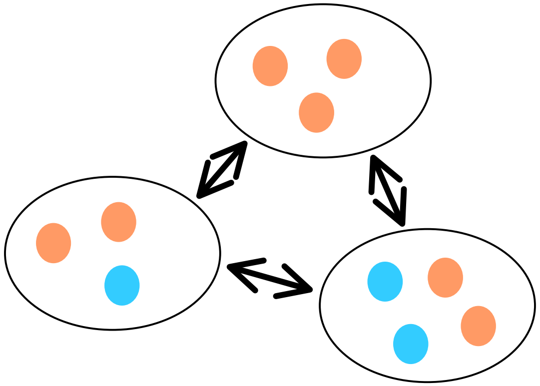

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$$\Delta p_i = \frac{s\,p_i q_i}{1+s\,p_i} - \frac{s(1+s)}{(1+s\,p_i)^3}\,\overline{\zeta^2_{i(d)}} + o\left(\zeta_i^2\right)$$

POPULATION STRUCTURE AND LOCAL DRIFT

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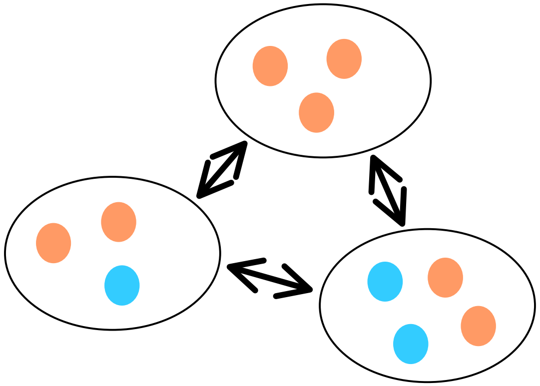

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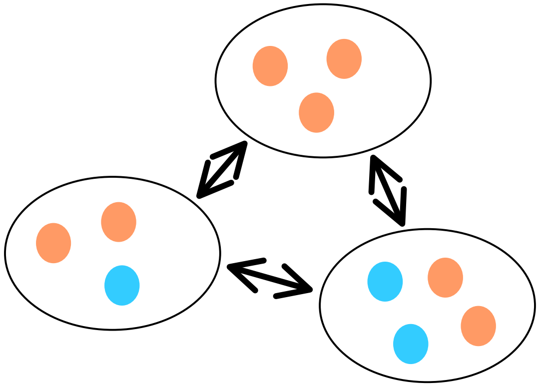

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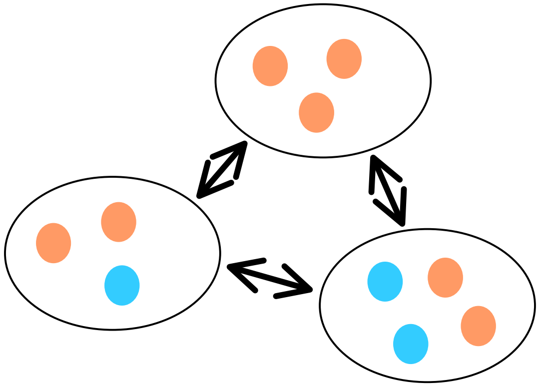

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→ need hypothesis on higher-order moments to close the system of recursions

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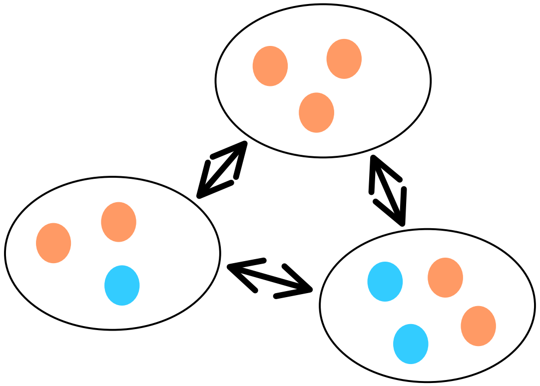

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→ need hypothesis on higher-order moments to close the system of recursions

→ method used by Barton & Otto (2005), Martin et al (2005)

INBREEDING DEPRESSION AND THE EVOLUTION OF DISPERSAL RATES

Evolution of dispersal:

INBREEDING DEPRESSION AND THE EVOLUTION OF DISPERSAL RATES

Evolution of dispersal:

- Individual selection: cost of dispersal

INBREEDING DEPRESSION AND THE EVOLUTION OF DISPERSAL RATES

Evolution of dispersal:

- Individual selection: cost of dispersal
- Kin selection: dispersal reduces competition among kin

INBREEDING DEPRESSION AND THE EVOLUTION OF DISPERSAL RATES

Evolution of dispersal:

- Individual selection
- Kin selection

$$\left.\begin{array}{l}\text{Individual selection}\\ \text{Kin selection}\end{array}\right\} \text{ESS dispersal rate} \approx \frac{1}{2Nc}$$

(infinite island model)

INBREEDING DEPRESSION AND THE EVOLUTION OF DISPERSAL RATES

Evolution of dispersal:

- Individual selection
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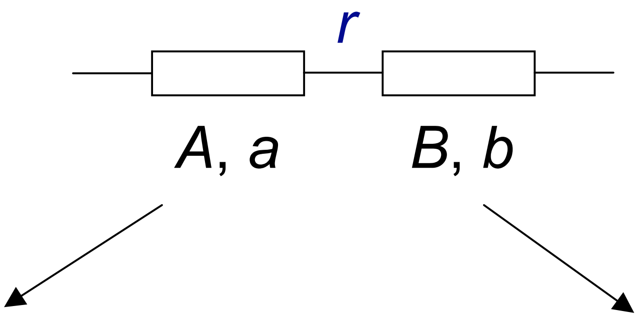
Inbreeding depression (due to recessive deleterious alleles):

→ generates heterosis (gives an advantage to migrants)

→ decreases strength of kin selection for dispersal

TWO-LOCUS MODEL

- Infinite island model, random mating within demes
- Finite deme size N
- Migration cost c



r

A, a B, b

locus 1: migration modifier

aa: m

Aa: $m + \varepsilon / 2$

AA: $m + \varepsilon$

locus 2: selected locus

bb: 1

Bb: $1 - h\,s$ (fecundities)

BB: $1 - s$

VARIABLES

Allele frequencies (in the whole metapopulation):

p_1 = freq(A) , p_2 = freq(B) $q_1 = 1 – p_1$, $q_2 = 1 – p_2$

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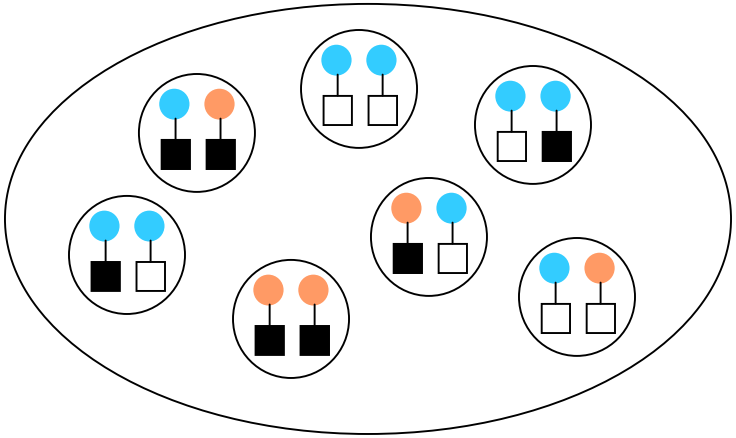

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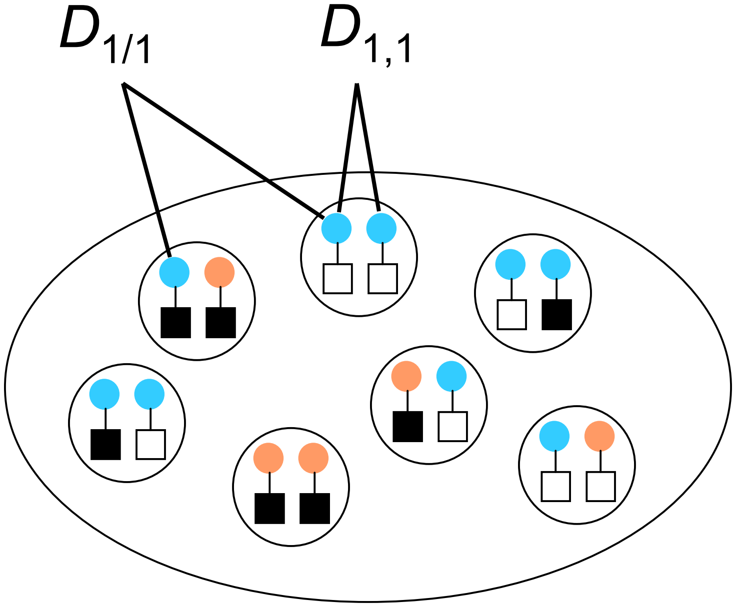

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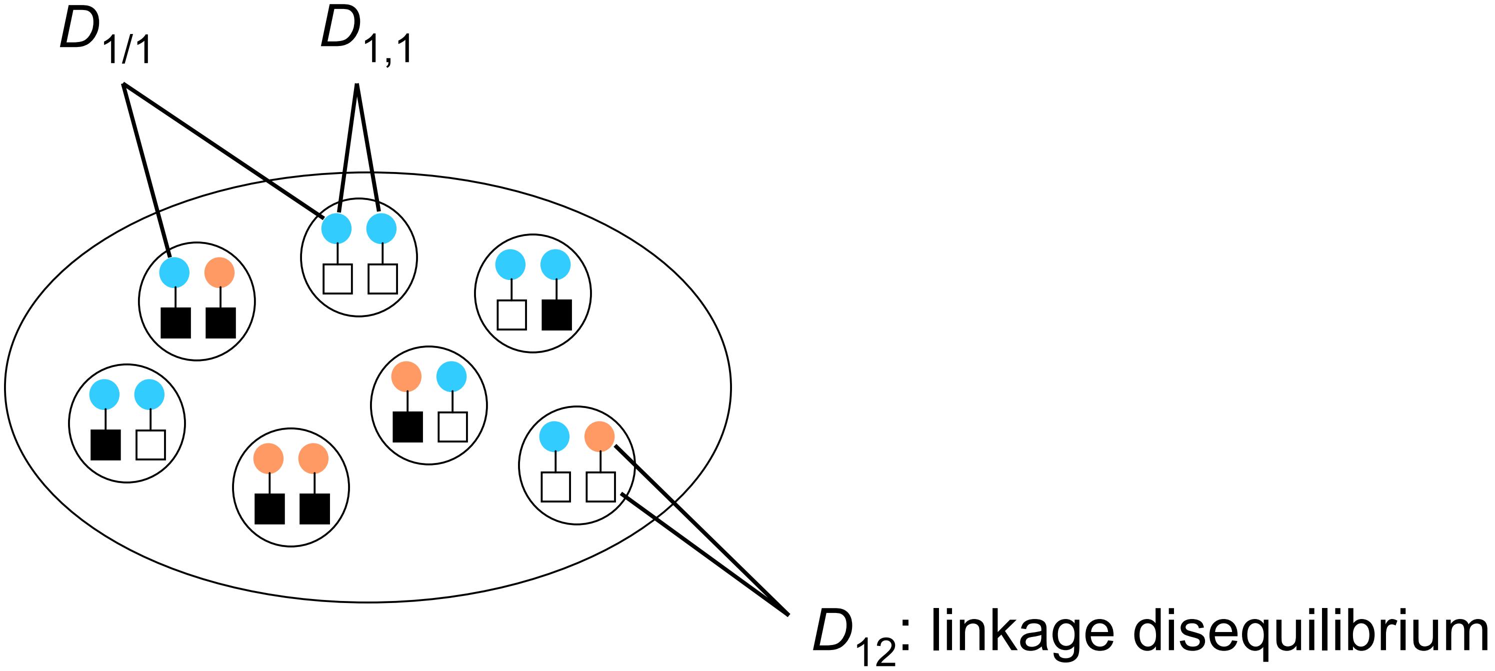

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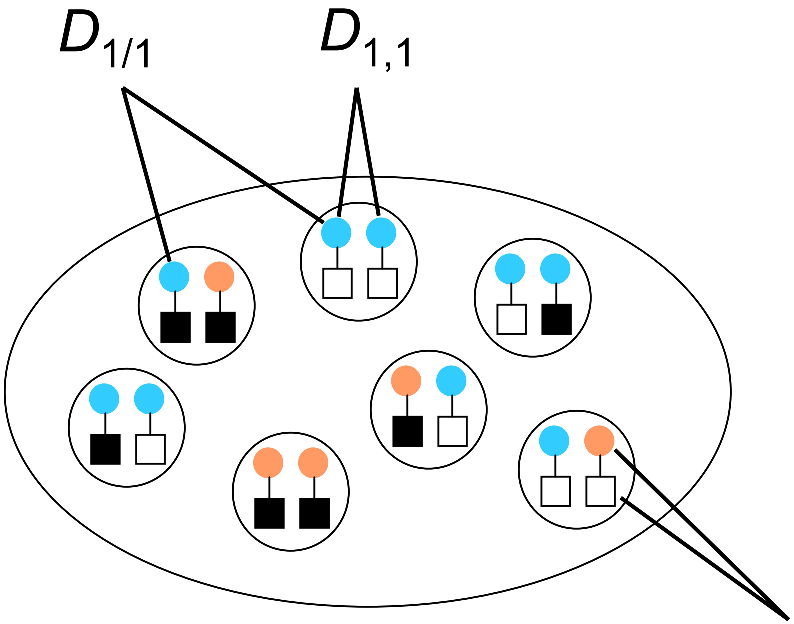

Neutrality:

$D_{1,1} = F_{IT}\, p_1 q_1$

$D_{1/1} = F_{ST}\, p_1 q_1$

Random mating within demes:

$$F_{IT} = F_{ST} = F \approx \frac{1}{1+4Nm(1-c)}$$

D_{12}: linkage disequilibrium

LIFE-CYCLE

- Reproduction within demes: differences in fecundity according to genotype at locus 2

- Dispersal: differences in dispersal rates according to genotype at locus 1

CHANGE IN FREQUENCY OF THE MODIFIER

During reproduction:

$$\Delta_{\mathrm{S}} p_1 = -s\left(1-2h\right)\left(1-\frac{1}{N}\right)\left(D_{12,2}-D_{1/2,2}\right)+o\left(s\right)$$

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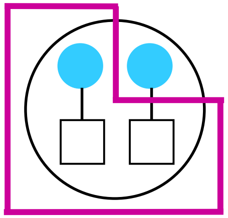

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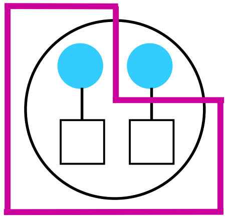

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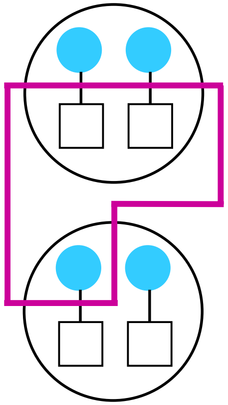

$D_{1/2,2} < 0$:
individuals in deme with higher frequency of allele *A* are less homozygous at locus 2

CHANGE IN FREQUENCY OF THE MODIFIER

During dispersal:

$$\Delta_{\mathrm{M}} p_1 = \frac{\varepsilon}{2(1-cm)}\left[-c\,p_1 q_1 + 2\left(\frac{1-m}{1-cm}-c\right)D_{1/1}\right]+o(\varepsilon)$$

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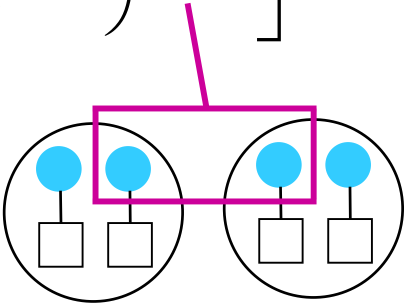

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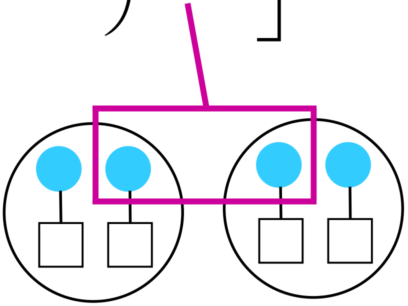

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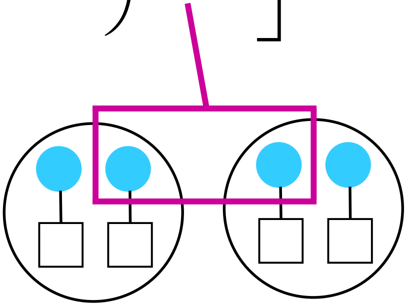

$s = 0$ → $D_{1/1} = F\,p_1 q_1 + O\left(\varepsilon\right)$

$s \neq 0$ → $D_{1/1}$ is affected by s → term in $\varepsilon\, s$

APPROXIMATE SOLUTIONS

m small, *N* large

Change in frequency of the modifier during reproduction:

$$\Delta_{\mathrm{S}} p_1 \approx \varepsilon s\left(1-2h\right)\frac{1-c}{r}\frac{1+2\left(1-c\right)Nm}{\left[1+4\left(1-c\right)Nm\right]^2} p_1 q_1 p_2 q_2$$

Change in frequency of the modifier during dispersal:

$$\Delta_{\mathrm{M}} p_1 \approx \left(\Delta_{\mathrm{M}} p_1\right)_{s=0} - \varepsilon s\left(1-2h\right)\frac{2\left(1-c\right)\left(2-c\right)Nm\left(1+r\right)}{r\left[1+4\left(1-c\right)Nm\right]^3} p_1 q_1 p_2 q_2$$

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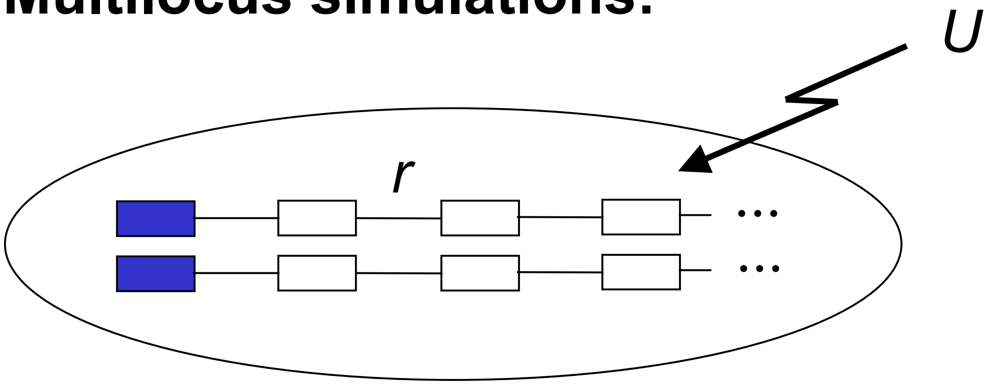
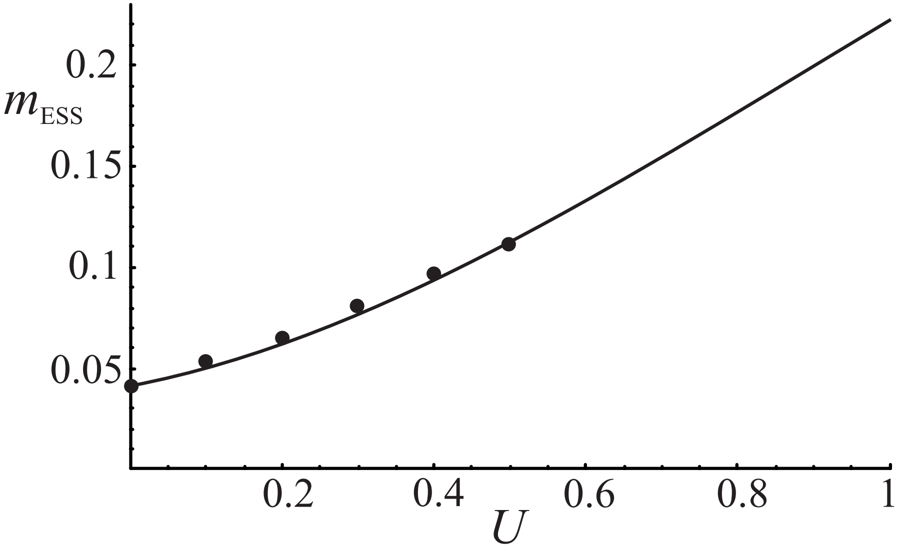
→ two different effects of inbreeding depression, of opposite sign

ESS DISPERSAL RATE

Multilocus simulations:



s, h constant



c = 0.4, N = 30

h = 0.1, s = 0.01

R = 10

ESS DISPERSAL RATE

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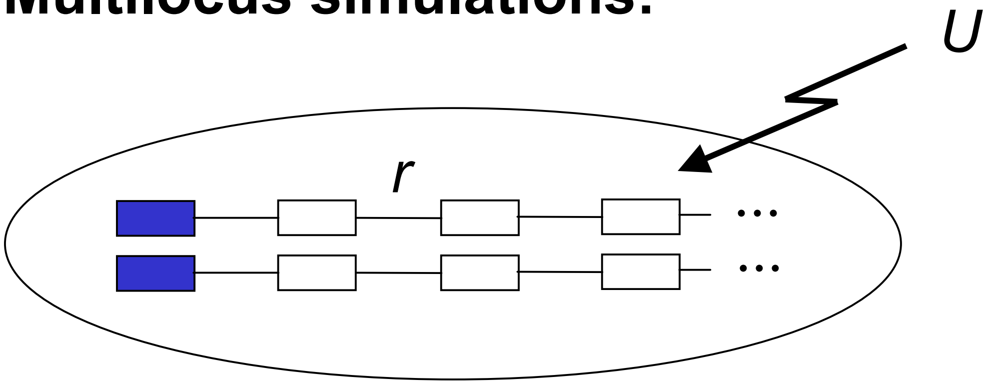

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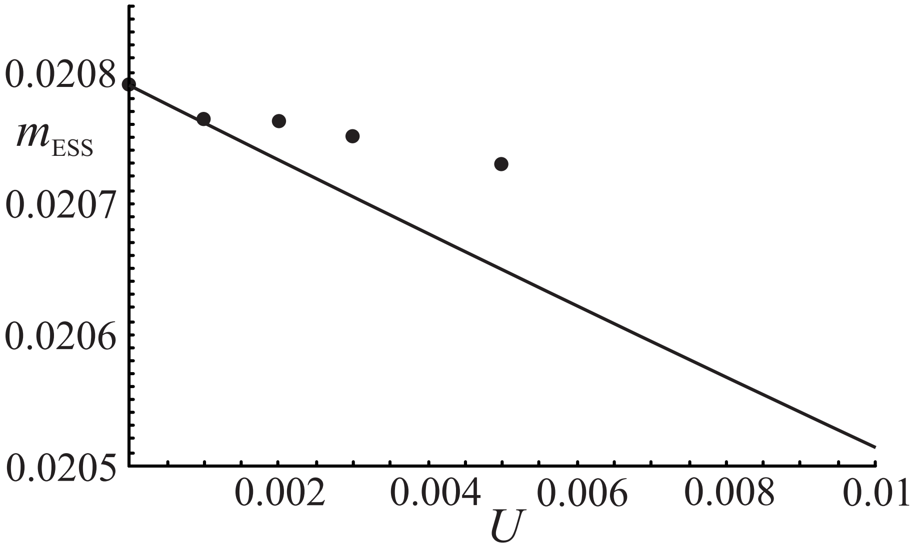

$c = 0.8$, $N = 30$

$h = 0.1$, $s = 0.001$

$R = 10$

CONCLUSION

Multilocus models, selection and drift

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Not possible to derive complete systems of recursions

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- weak selection / quasi-equilibrium
- weak effects of drift / moment closure

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Approximations:

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Becomes tedious when associations between more than a few loci do matter...