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Robust inference of selection against maladaptive gene flow

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Selection against gene flow

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 - ▶ Local adaptation
 - ▶ Admixture, secondary contact, hybridisation

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 - ▶ At closely linked neutral sites (e.g. Petry 1983)
 - ▶ At other selected sites (e.g. Bürger & Akerman 2011)
- Heterogeneity in divergence along the genome
 - ▶ Parapatric European rabbit species (Carneiro *et al.* 2009)
 - ▶ *M. musculus* hybrid zone in Europe (Geraldès *et al.* 2011)

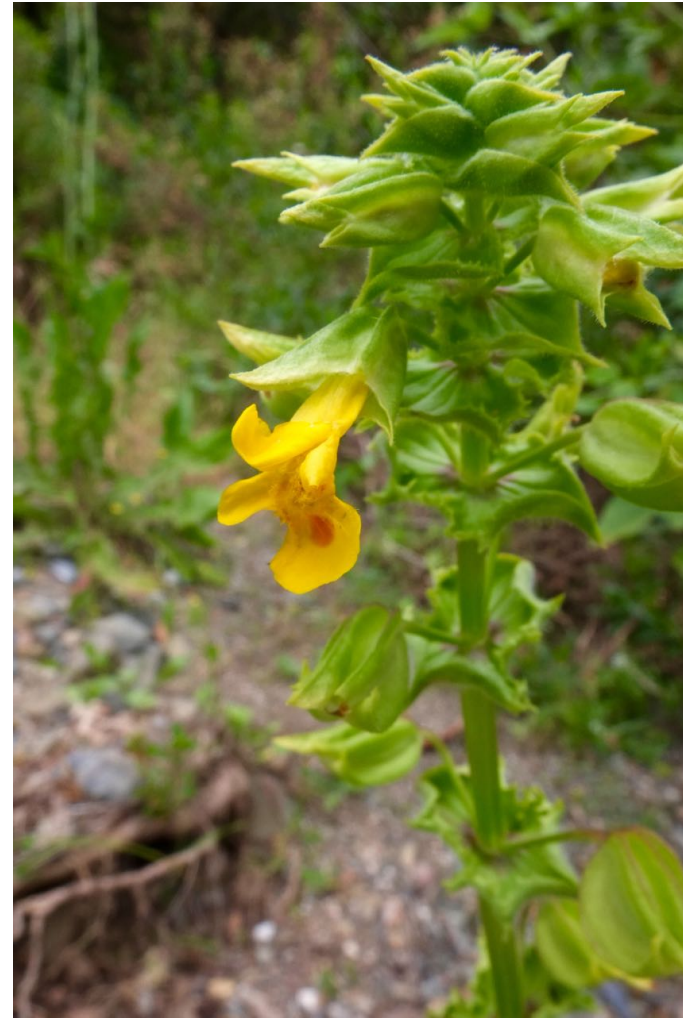
Mimulus guttatus and a selfing sister species

M. guttatus: outcrossing

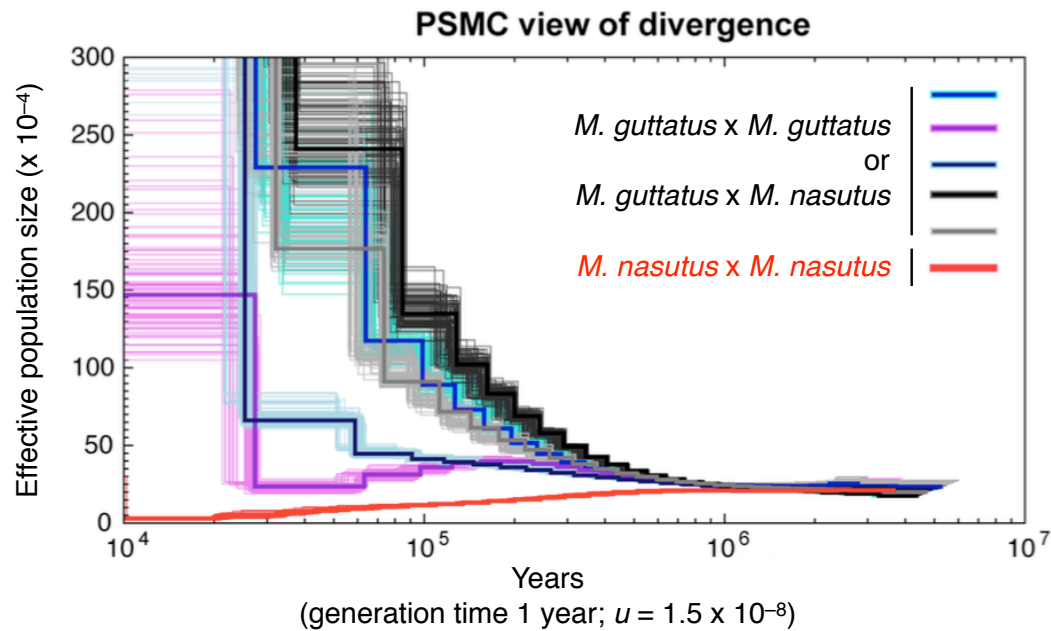


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M. nasutus: selfing



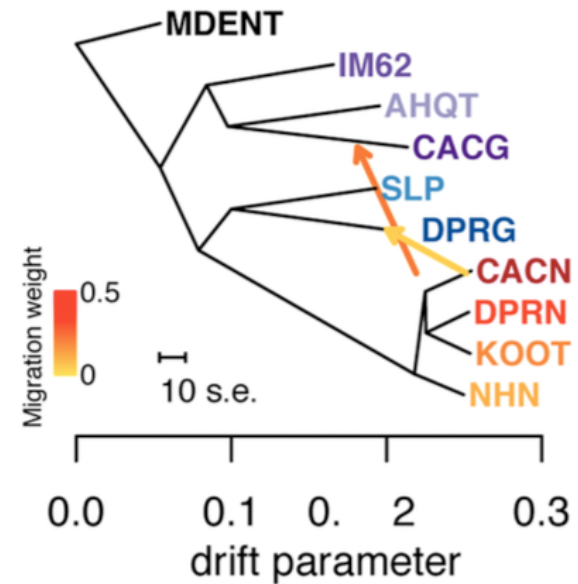
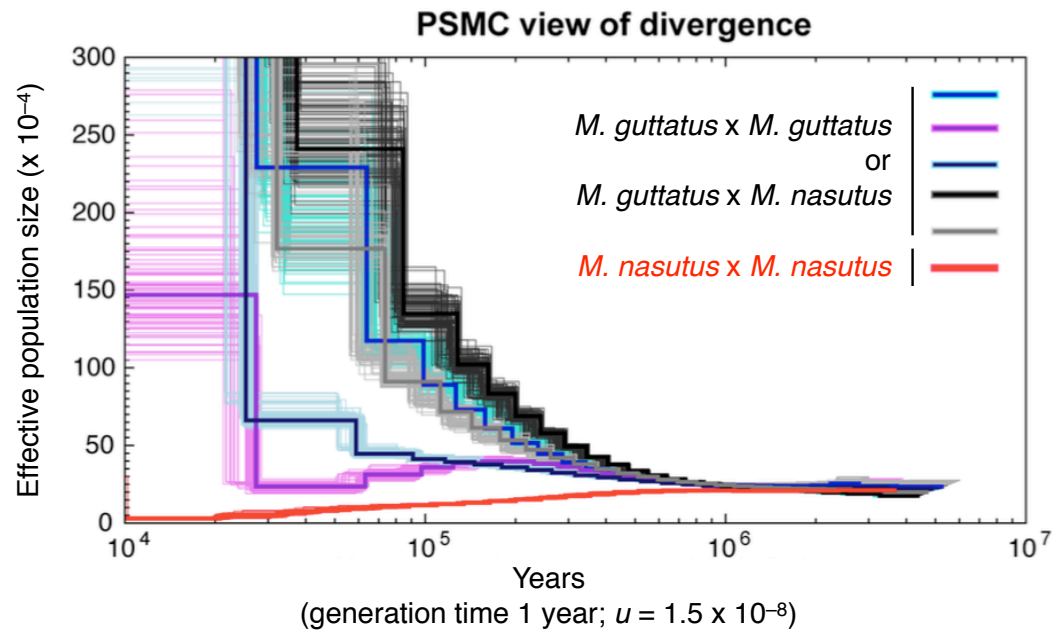
M. nasutus: Transition to selfing and decline in N_e



Split time ~ 1 Myr

Brandvain *et al.* (2014), modified

Gene flow from *M. nasutus* into *M. guttatus*



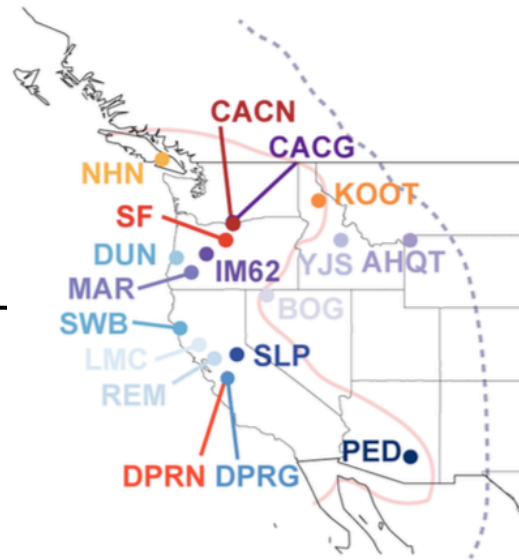
Brandvain *et al.* (2014), modified

M. guttatus: Selection against introgression?

sympatric

allopatric

North



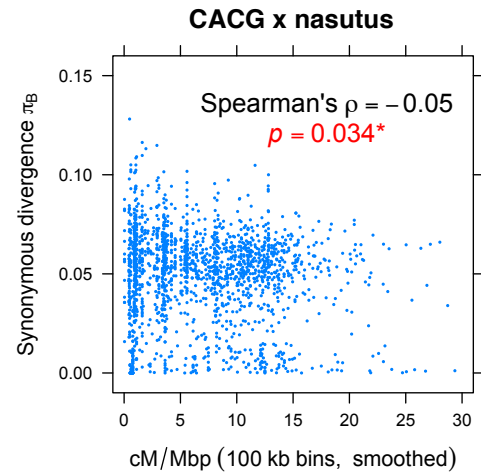
South

Brandvain *et al.* (2014),
modified

M. guttatus: Selection against introgression?

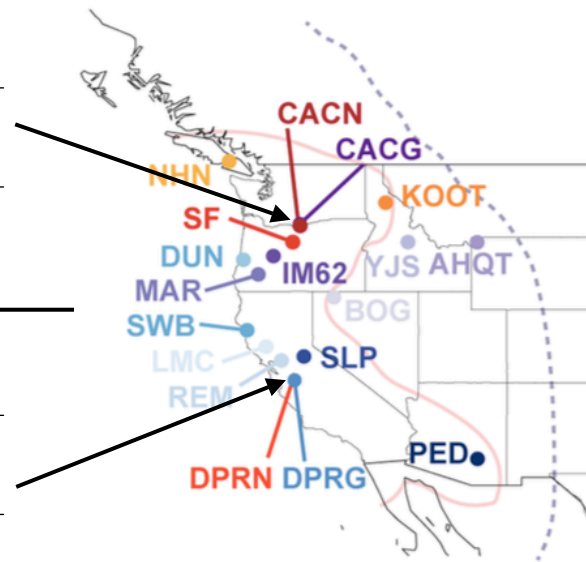
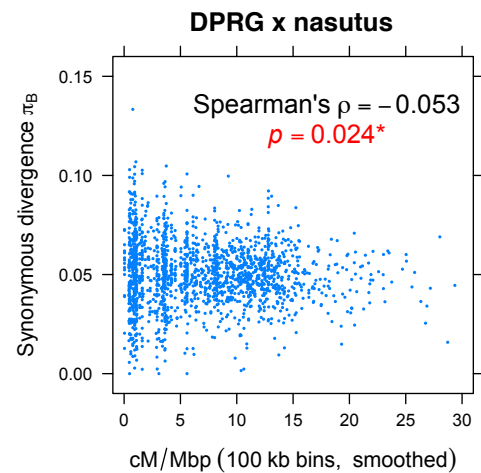
North

sympatric



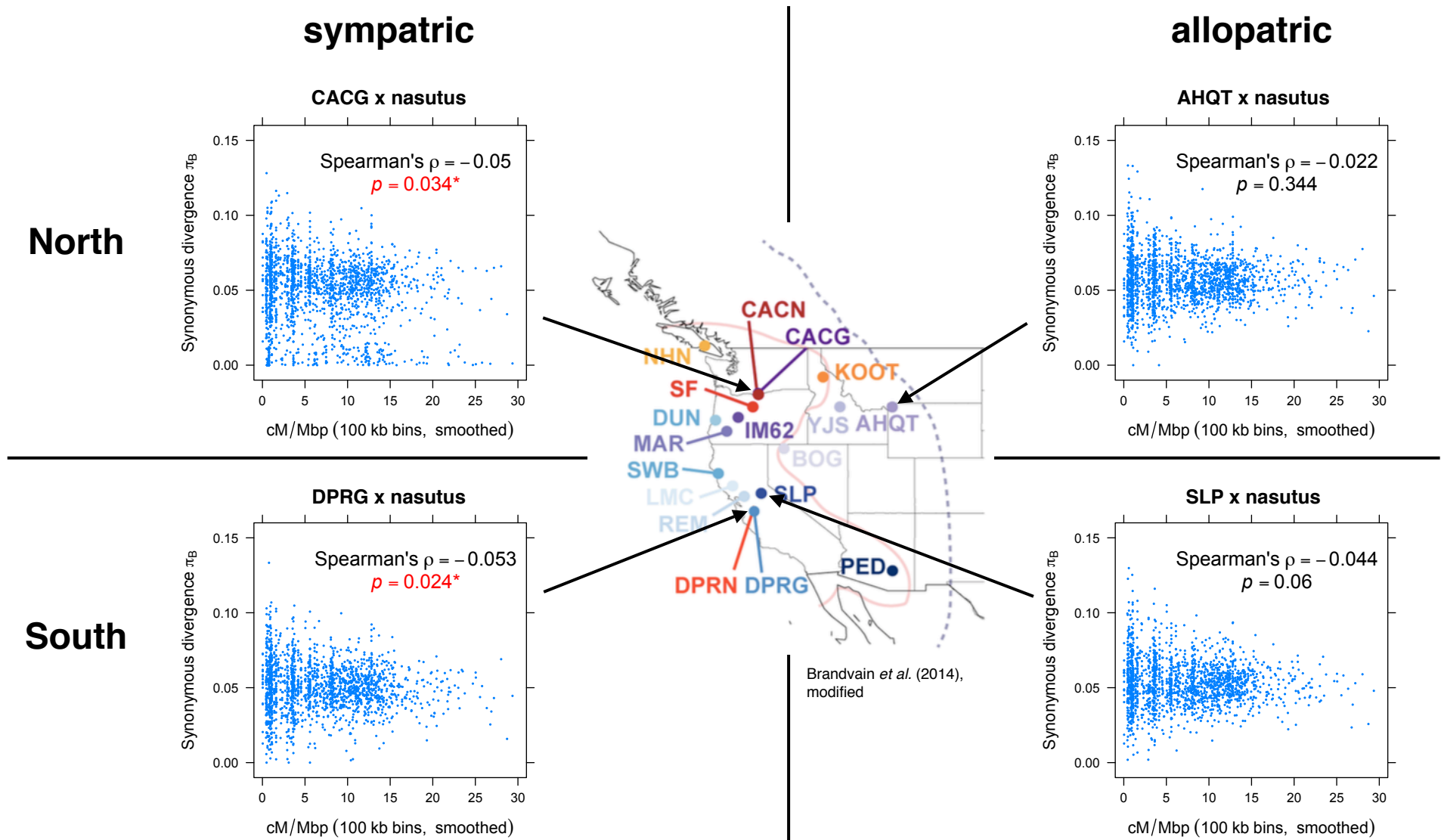
allopatric

South



Brandvain *et al.* (2014),
modified

Sympatry: π_B negatively correlated with recombination



Questions

- How strong is selection?
- When did it start?
- What is the level of neutral gene flow?

A definition

MSP = “migration–selection polymorphism”

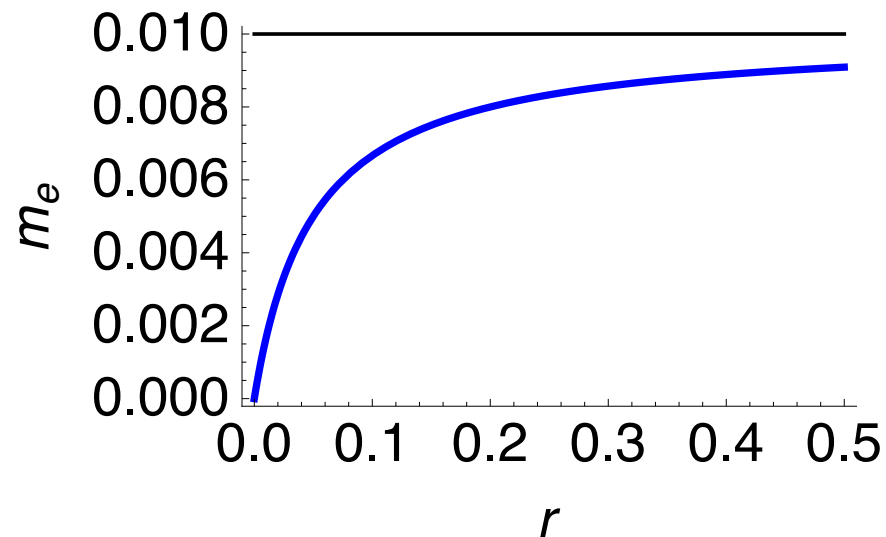
A locus at which allele frequencies have reached the migration–selection equilibrium

Approach

Effective migration rate

- Petry (1983): one migration–selection polymorphism (MSP)

$$m_e \approx m \left(1 + \frac{s}{r}\right)^{-1}$$



Approach

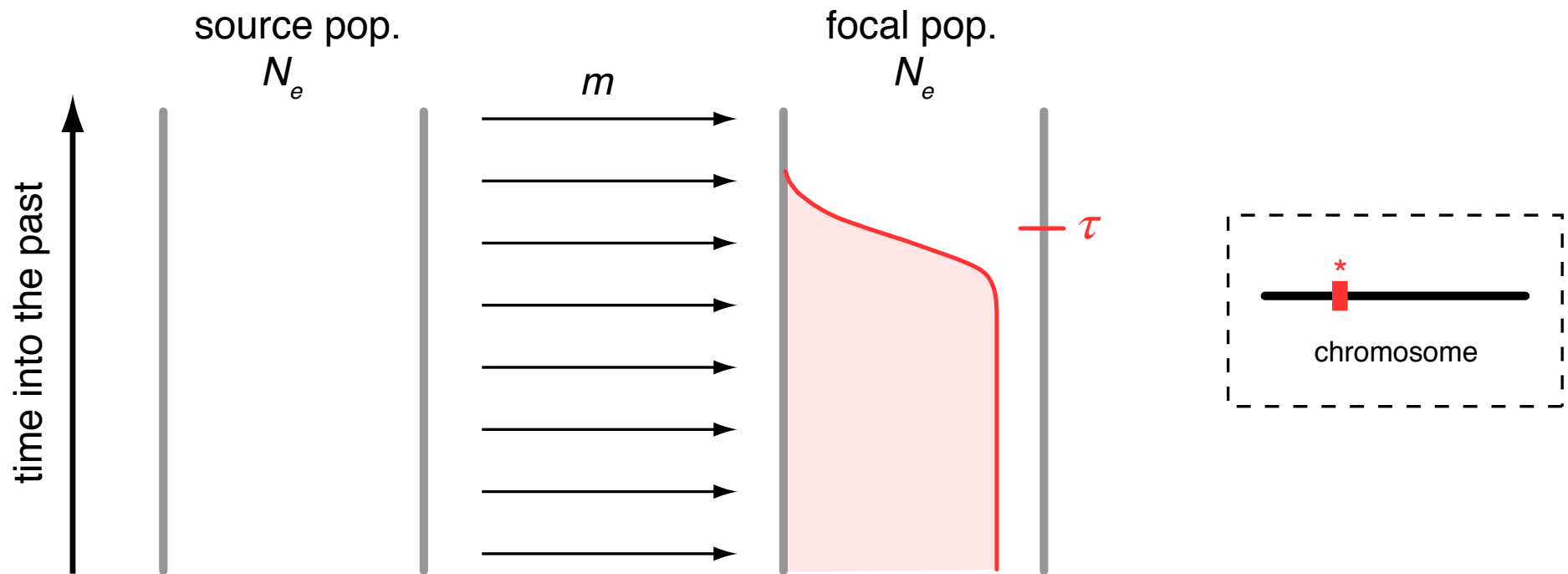
Structured coalescent

- Continent–island model of migration

$$\mathbb{E}[T_B] = 2N_c + \frac{1}{m}$$

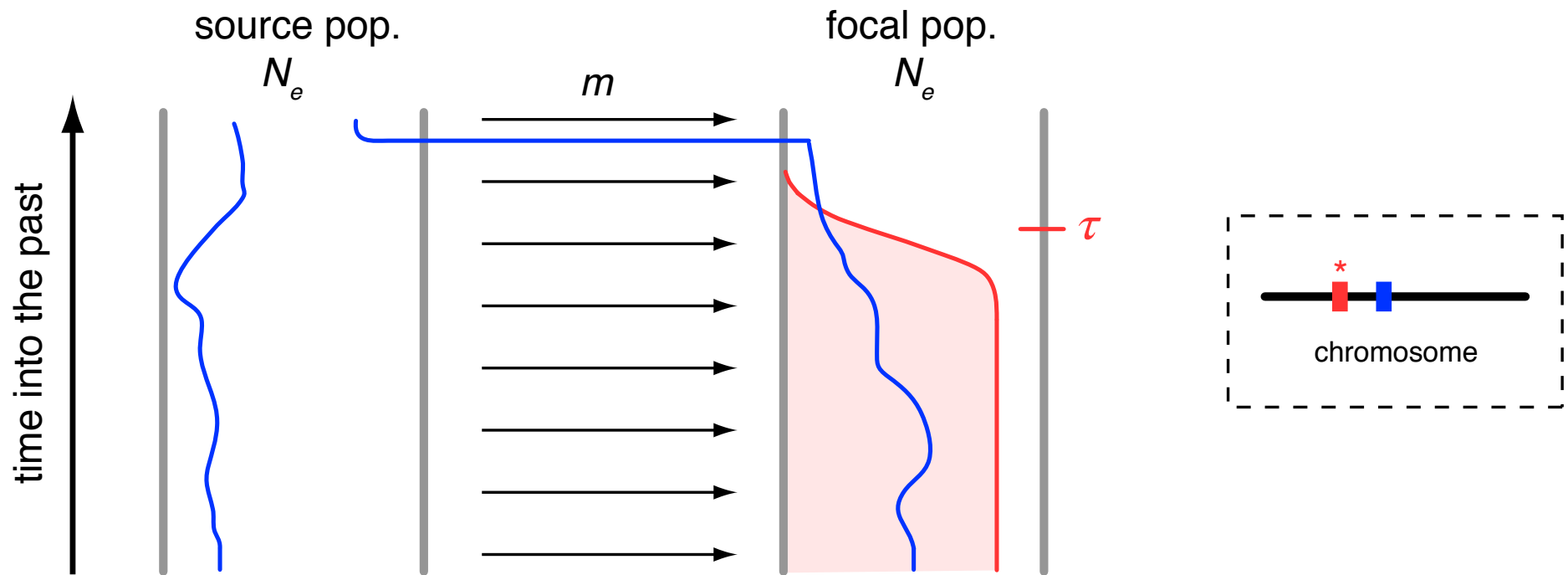
- Replace m by $m_e = f(m, s, r, l)$

Illustration: One MSP of finite age τ



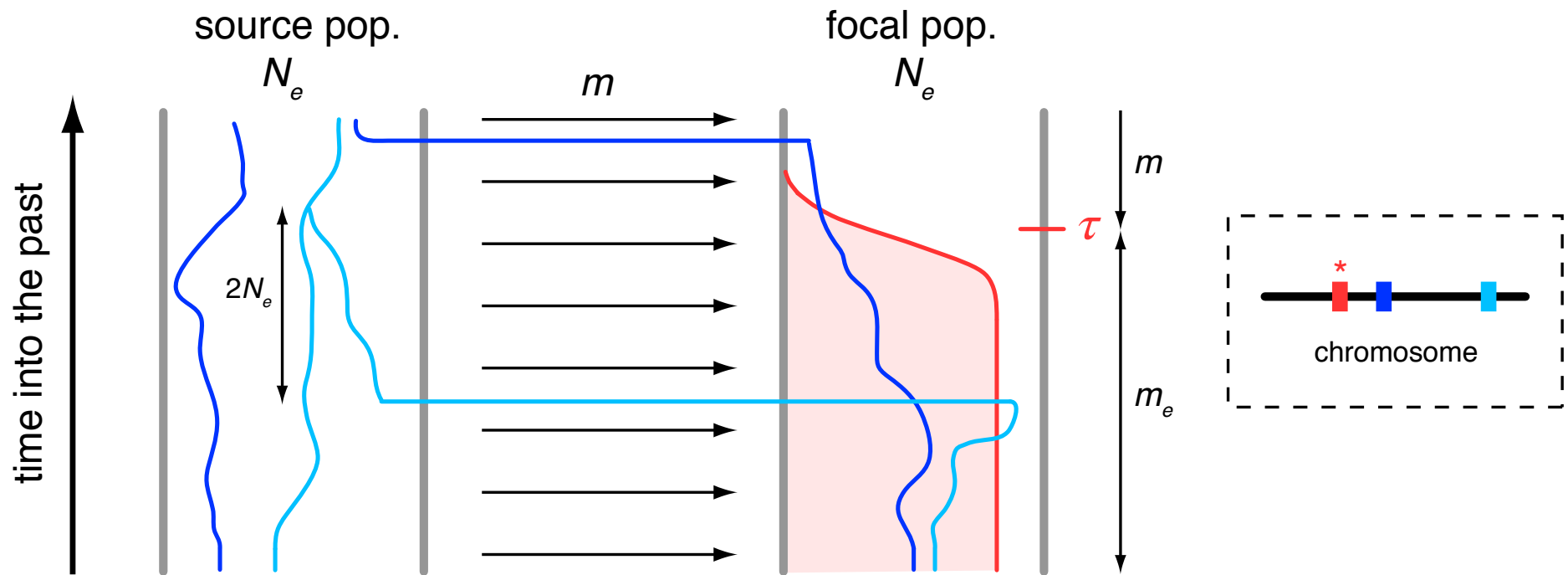
Locally beneficial mutation arose at time τ

Illustration: One MSP of finite age τ



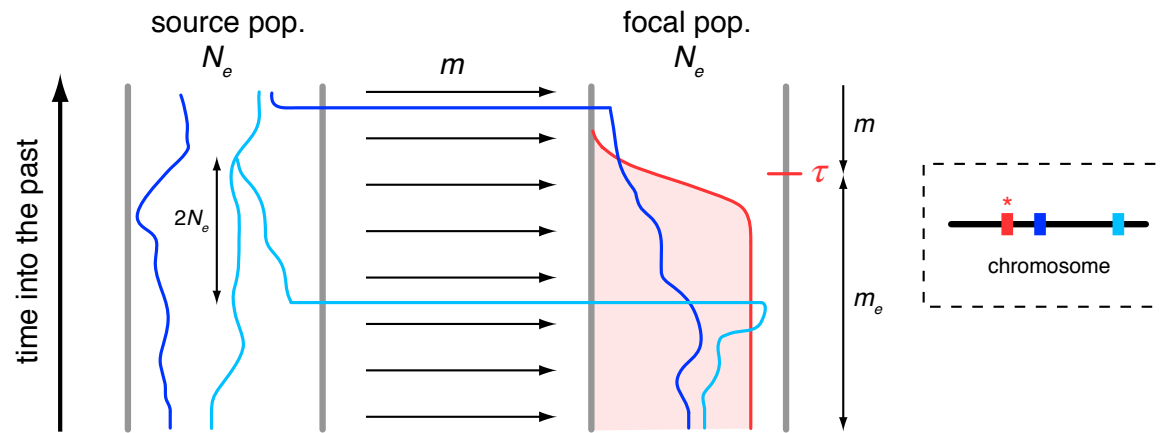
Trajectory of a tightly linked pair of neutral lineages

Illustration: One MSP of finite age τ



Trajectory of a loosely linked pair of neutral lineages

Expected coalescence time T_B



$$\mathbb{E}[T_B] = \int_0^\tau (t + 2N_e) m_e e^{-m_e t} dt + e^{-m_e \tau} \int_0^\infty (\tau + s + 2N_e) m e^{-m s} ds$$

Expectation over the genomic context

$$\begin{aligned}\mathbb{E}_L [\mathbb{E} [T_B]] &= \int_1^\Lambda \mathbb{E} [T_B] f_L(l; \nu) dl \\ &= g(N_e, m, s, \nu, \tau, r)\end{aligned}$$

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PDF of distance between neutral and selected site

Baseline migration rate

Selection coefficient

Density of MSPs

Age of MSP

Per-base pair recombination rate

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$$\mathbb{E}_L [\pi_B] = 2u \mathbb{E}_L [\mathbb{E} [T_B]]$$

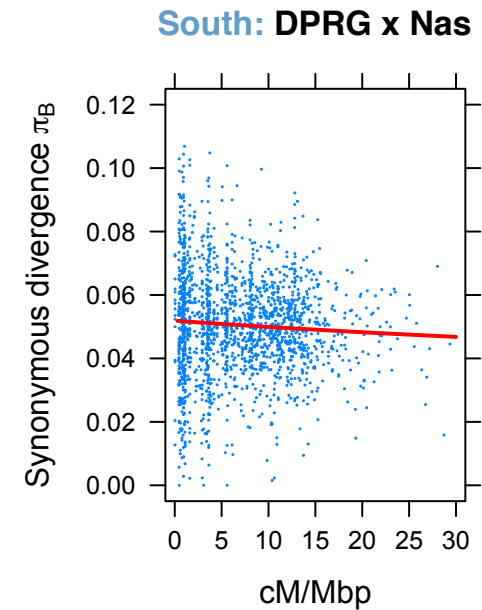
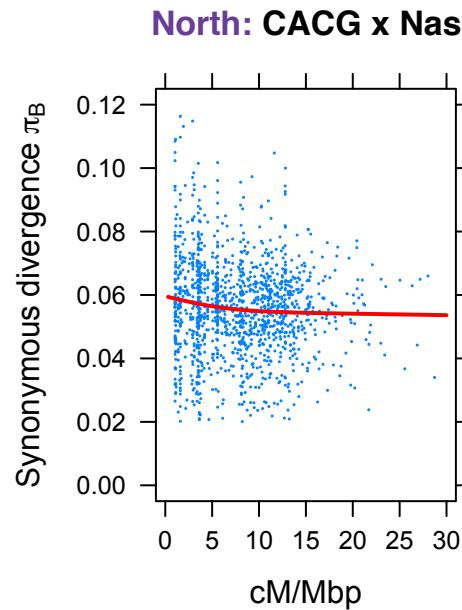
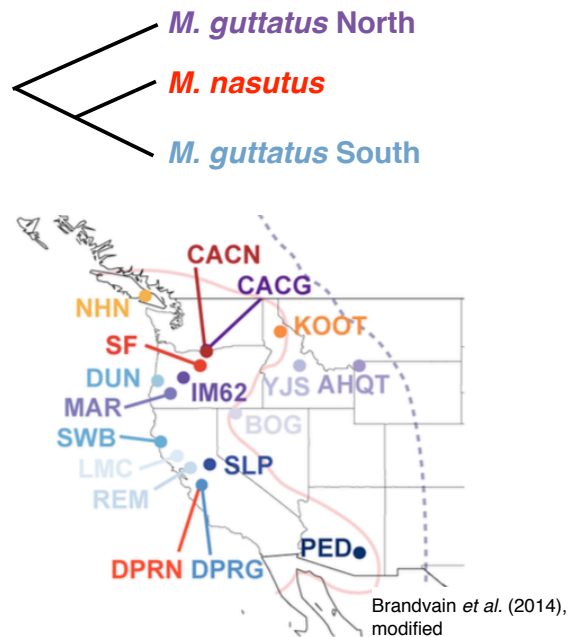
Analytical approximation for one MSP of finite age

Suggestive of a compound parameter **selection density**:

$$\sigma := s \nu \quad [\text{selection / base pair}].$$

Selection against introgression into *M. guttatus*

$N_{nas} \approx 1.7 \times 10^5$ (Brandvain *et al.* 2014), $u = 1.5 \times 10^{-8}$ (Koch *et al.* 2001)



Baseline migration Nm :

1.47 per gen.

2.85 per gen.

Age of mutation τ :

1.1 Myr

1.1 Myr

Selection density $\sigma = s\nu$:

0.023 per kb

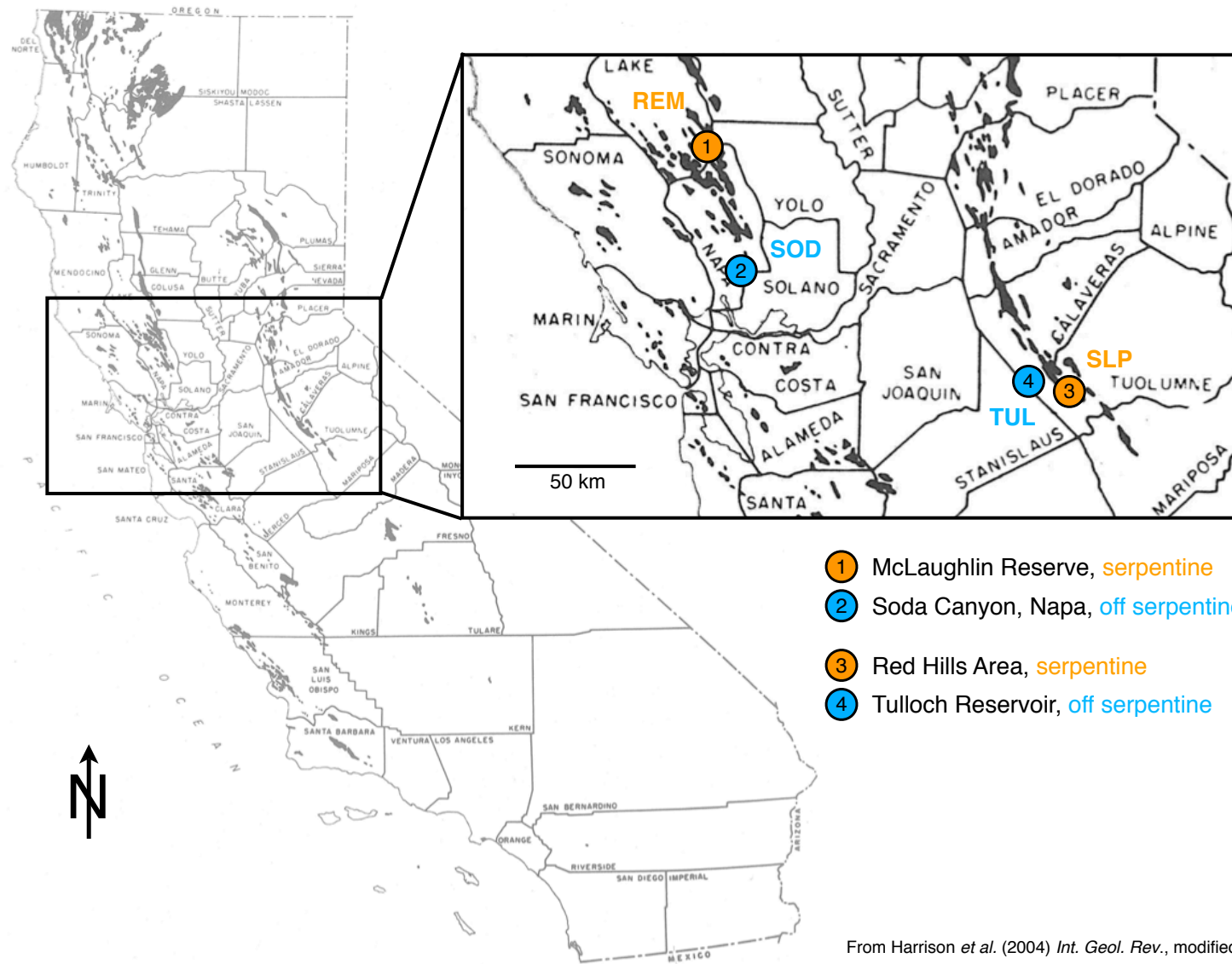
0.16 per kb

Serpentine outcrops in California

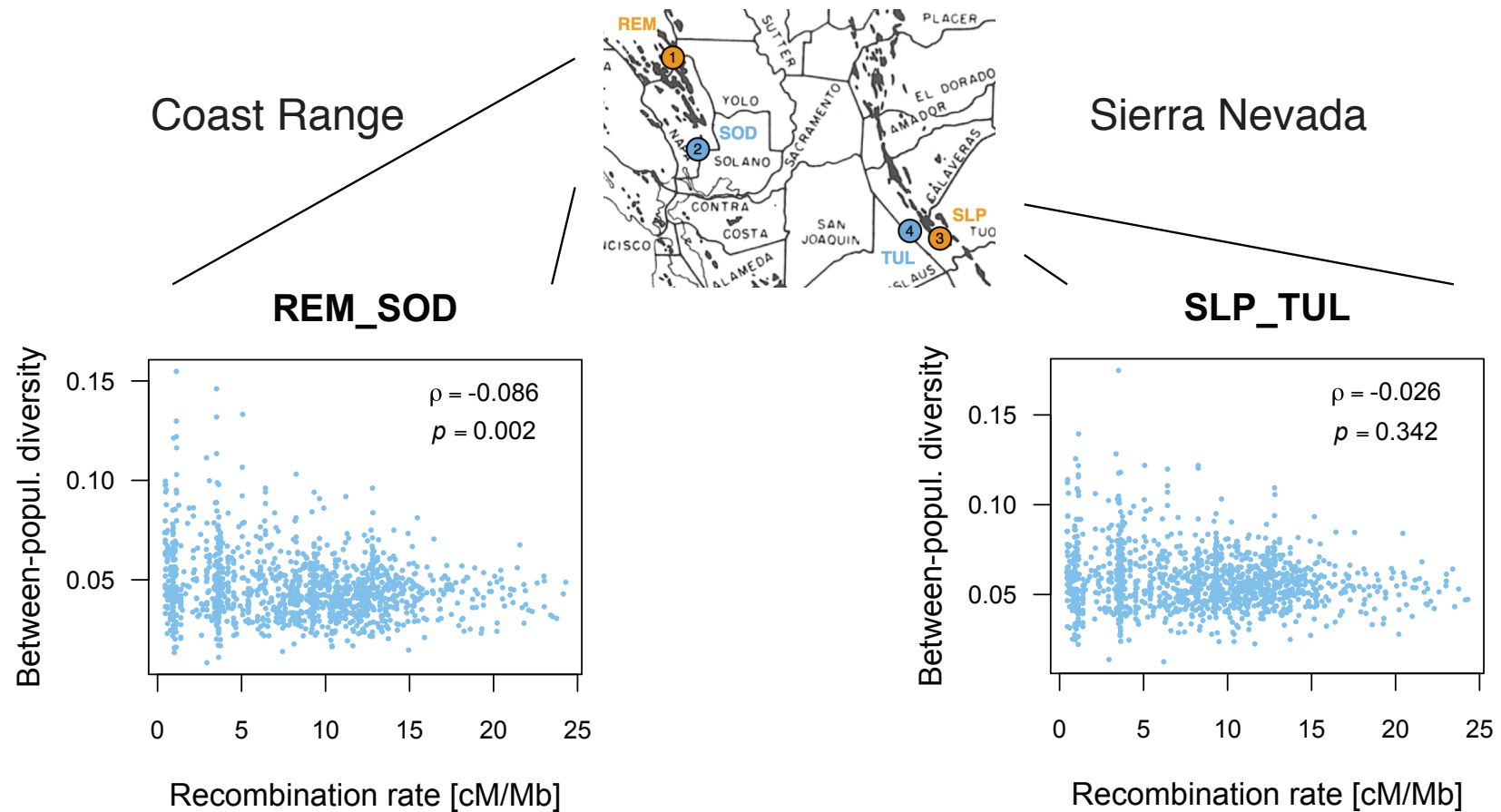


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Two on/off-serpentine population pairs

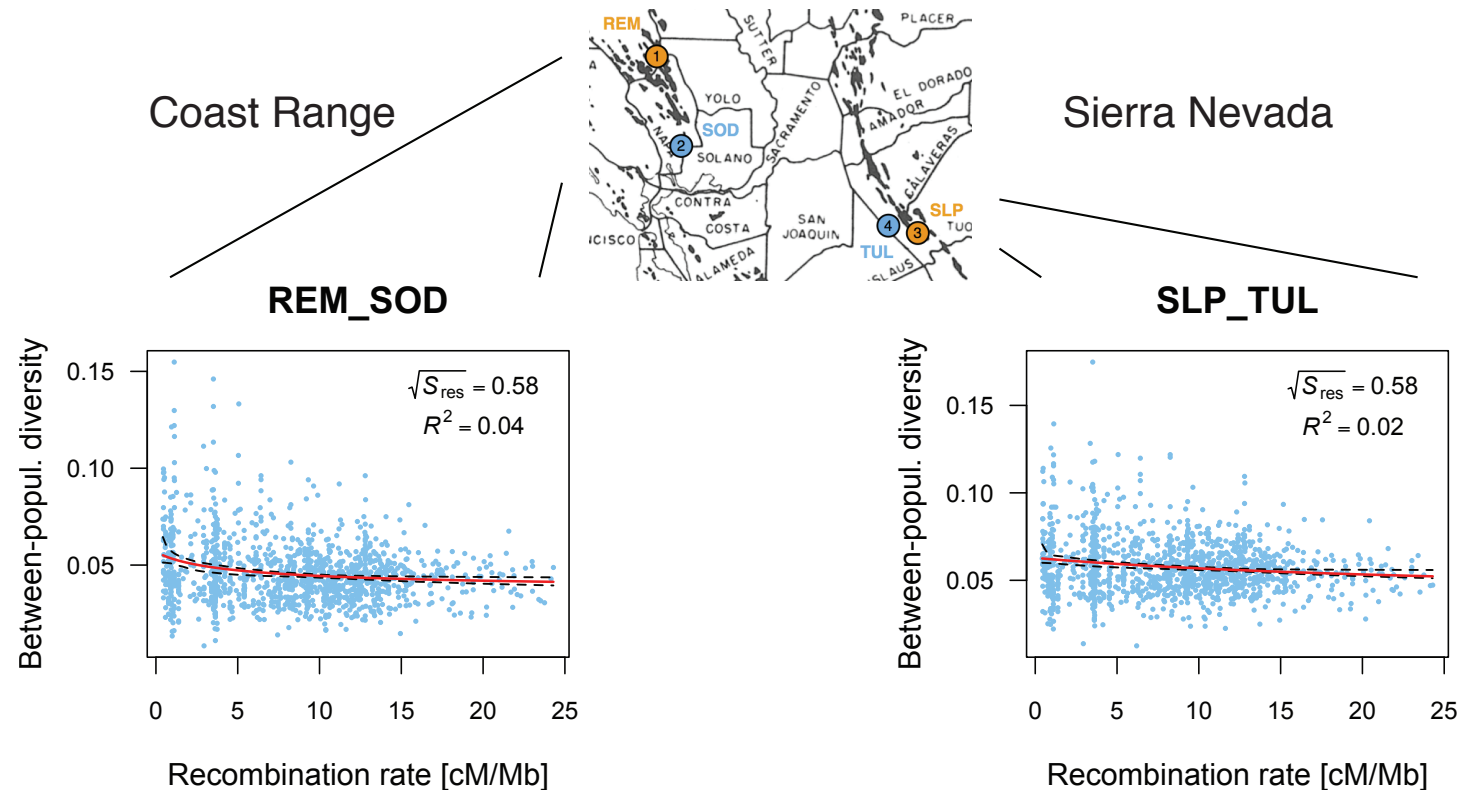


Significantly negative correlation between diversity and recombination in the Coast Range



Selection against substantial gene flow

$$N_{\text{REM}} \approx 2.3 \times 10^6; N_{\text{SOD}} \approx 2.0 \times 10^6; N_{\text{SLP}} \approx 2.2 \times 10^6; N_{\text{TUL}} \approx 2.4 \times 10^6; u \approx 4.1 \times 10^{-9}$$

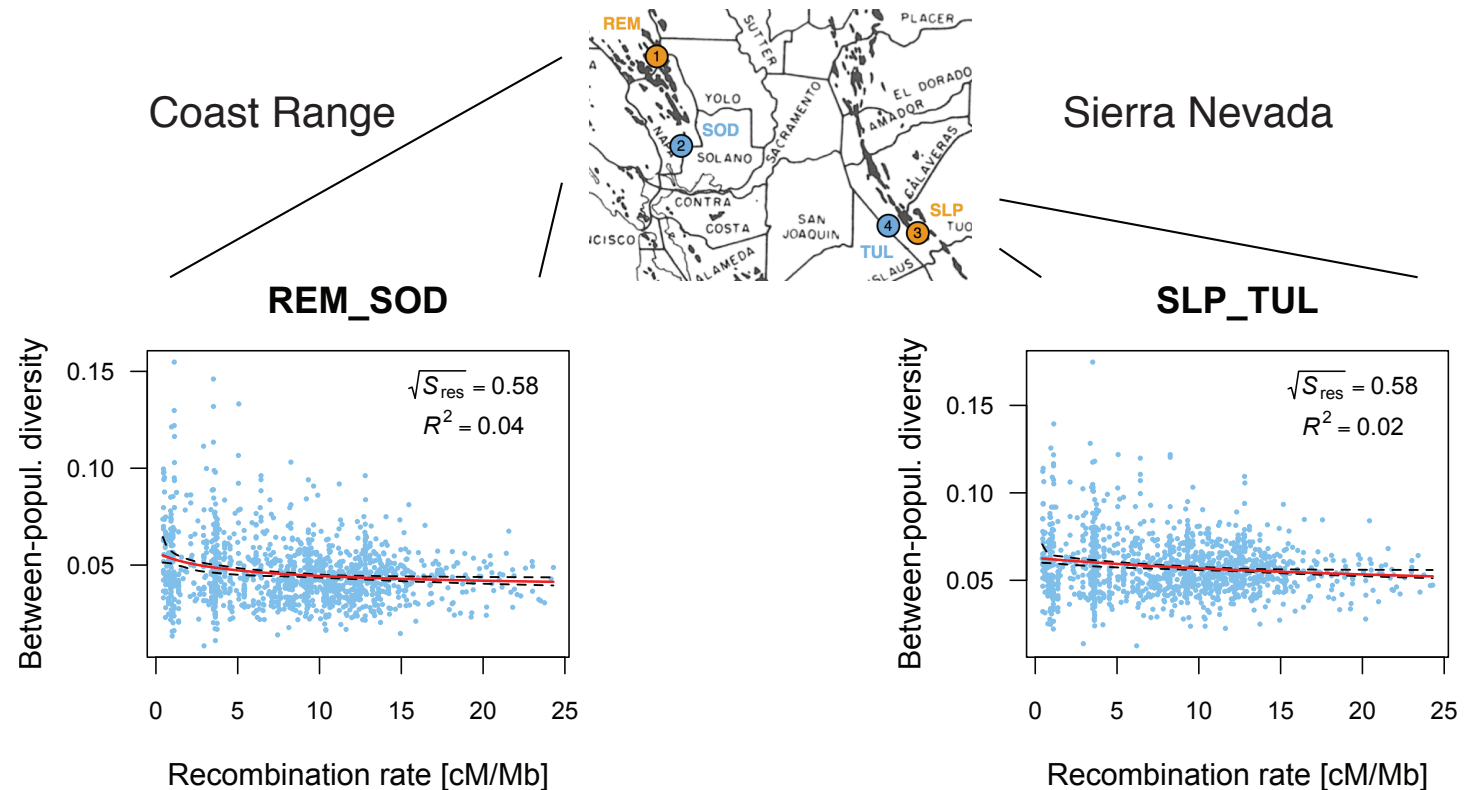


Baseline migration Nm : 4.0 per gen.
Age of mutation τ : 2.2 Myr

25.0 per gen.
2.2 Myr

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Baseline migration Nm : 4.0 per gen.

Age of mutation τ : 2.2 Myr

Selection density σ : 0.04 per Mb

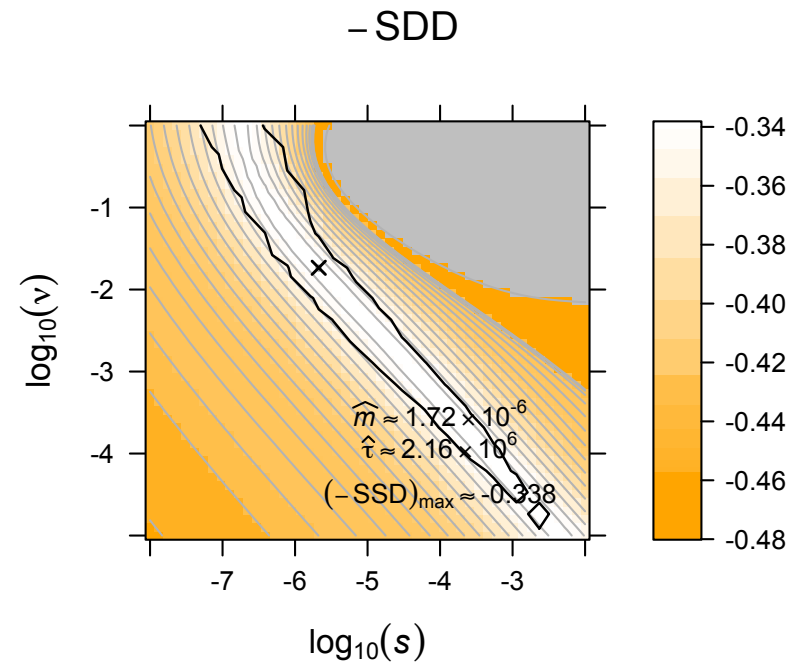
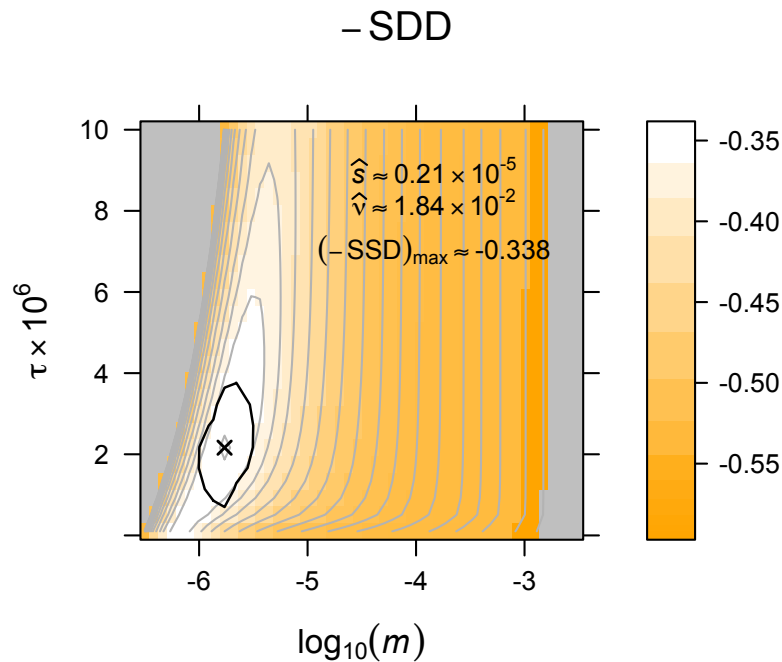
25.0 per gen.

2.2 Myr

2.2 per Mb

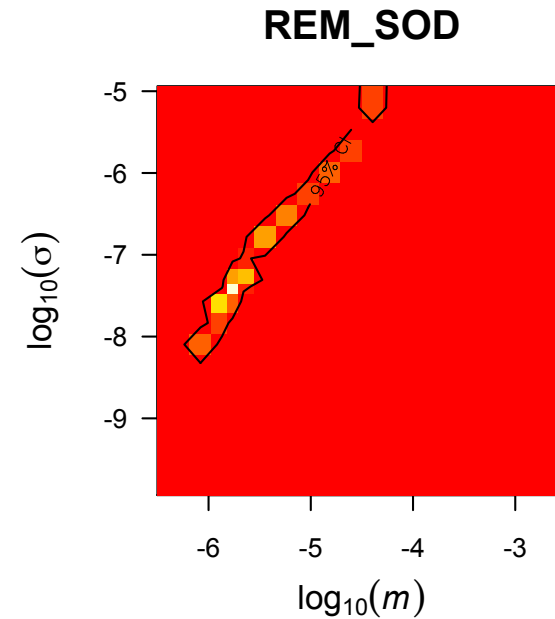
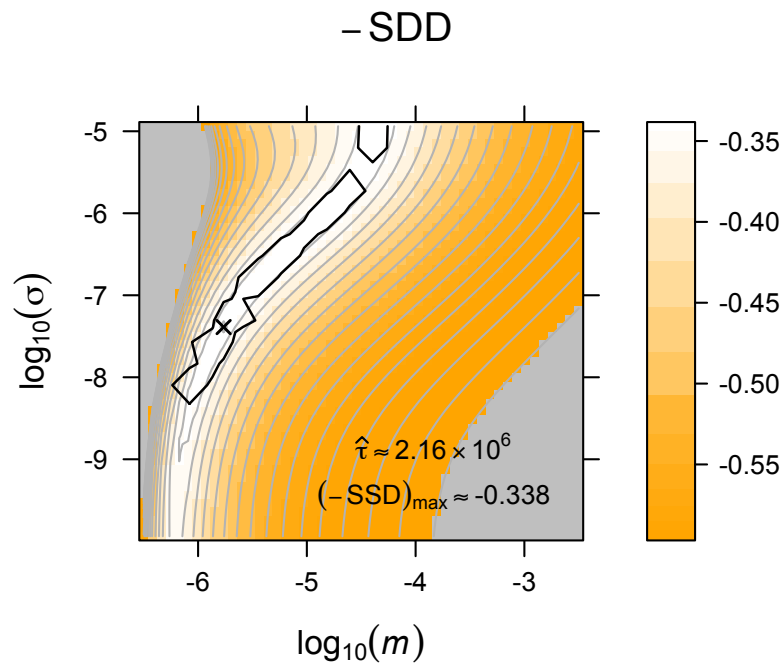
Support for a compound parameter “selection density” $\sigma = s\nu$

For the Coast Range population pair:



Selection density and migration are separable

For the Coast Range population pair:



Conclusion

- **Genome-wide aggregate approach** to quantify selection against maladaptive gene flow

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- **Genome-wide aggregate approach** to quantify selection against maladaptive gene flow
- Compound parameter $\sigma = s\nu$: the **density of selection against gene flow per base pair**
- Application to *Mimulus guttatus*:
 - ▶ **Strong selection against deleterious introgression** from selfing sister species *M. nasutus*
 - ▶ **Adaptation to serpentine despite strong gene flow** from off-serpentine population(s)

Acknowledgements

- Graham Coop
- Coop lab, Chenling Xu
- Yaniv Brandvain, Lex Flagel, Uffe Hellsten
- Jessica P. Selby, Kevin Wright, John Willis



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