

## CRISPR-Cas9

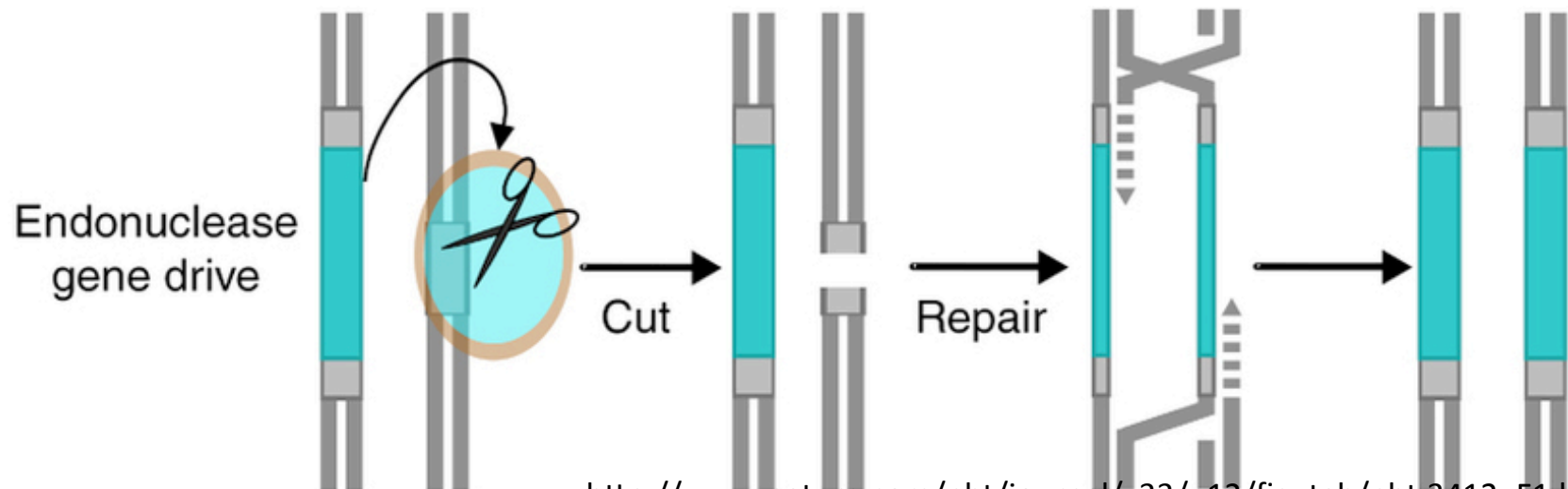
Very precise method for genome-editing

Emmanuelle Charpentier & Jennifer Doudna



Homozygote for insertion

**a**



[http://www.nature.com/nbt/journal/v33/n12/fig\\_tab/nbt.3412\\_F1.html](http://www.nature.com/nbt/journal/v33/n12/fig_tab/nbt.3412_F1.html)

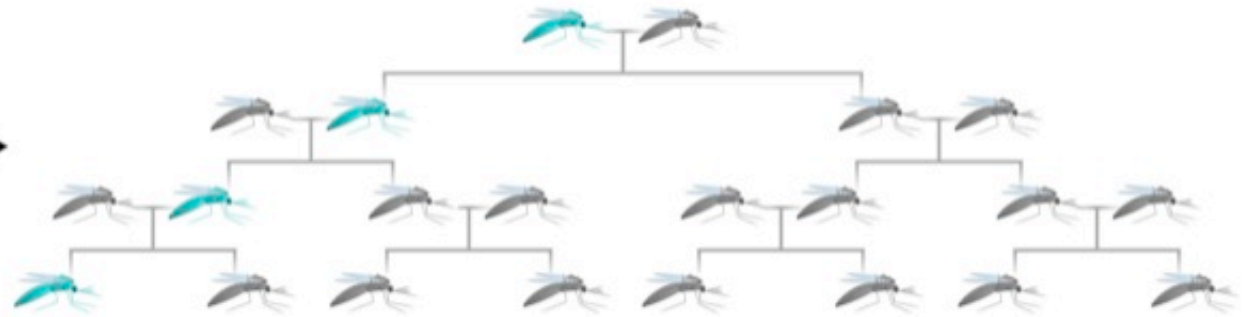
# CRISPR-based Gene drive

Altered Gene Wild-Type



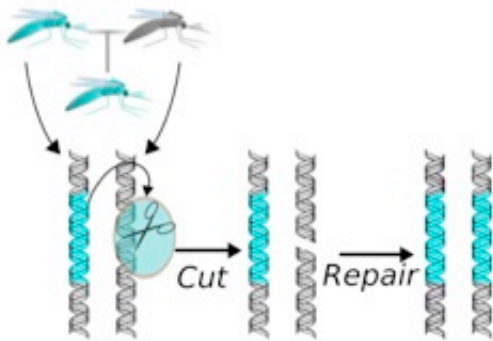
Altered Gene Only  
1 copy inherited from 1 parent  
50% chance of passing it on

**Normal Inheritance**



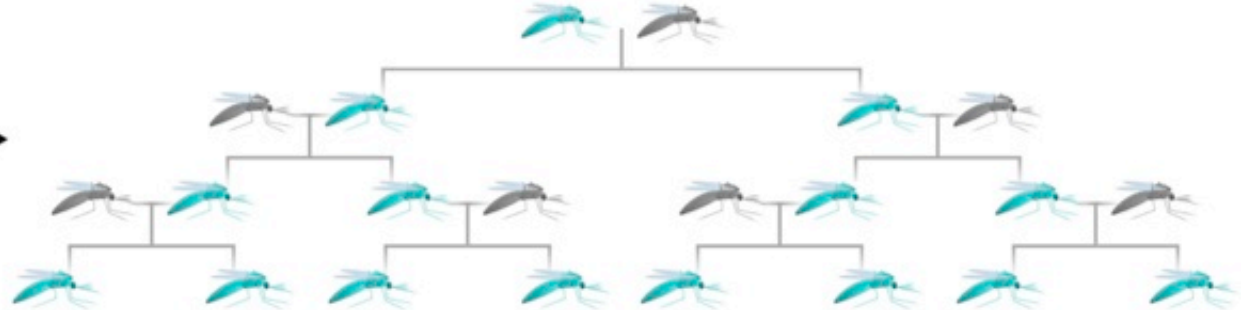
Altered gene does not increase

Gene Drive Wild-Type



Altered Gene + Gene Drive  
1 copy  $\rightarrow$  2 copies  
100% chance of passing it on

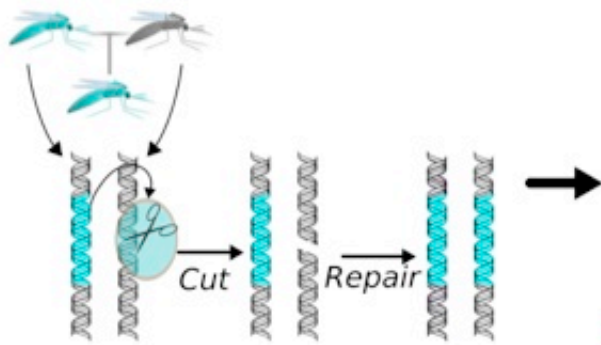
**Gene Drive Inheritance**



Altered gene is always inherited due to gene drive

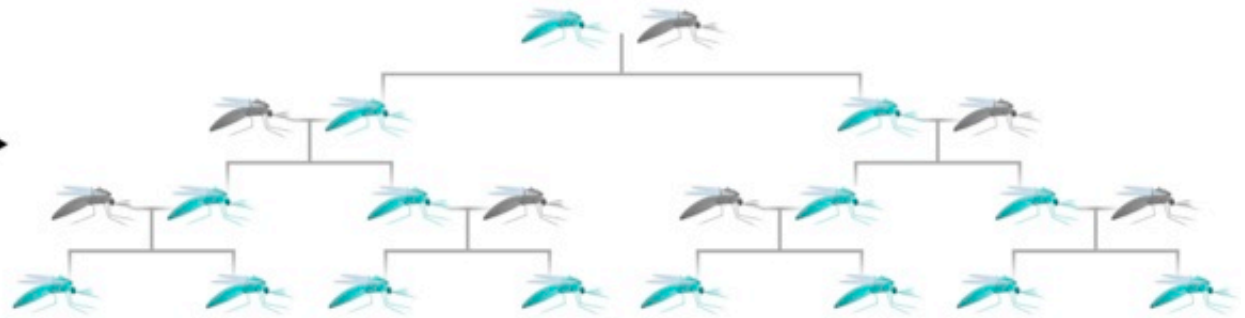
# CRISPR-based Gene drive

Gene Drive Wild-Type



Altered Gene + Gene Drive  
1 copy → 2 copies  
100% chance of passing it on

Gene Drive Inheritance



Altered gene is always inherited due to gene drive

***Panel Endorses 'Gene Drive' Technology  
That Can Alter Entire Species***

3y AMY HARMON JUNE 8, 2016



mosquitoes infecting native Hawaiian birds  
with malaria

weed called Palmer amaranth that has  
become resistant to herbicides and a scourge  
for some farmers.

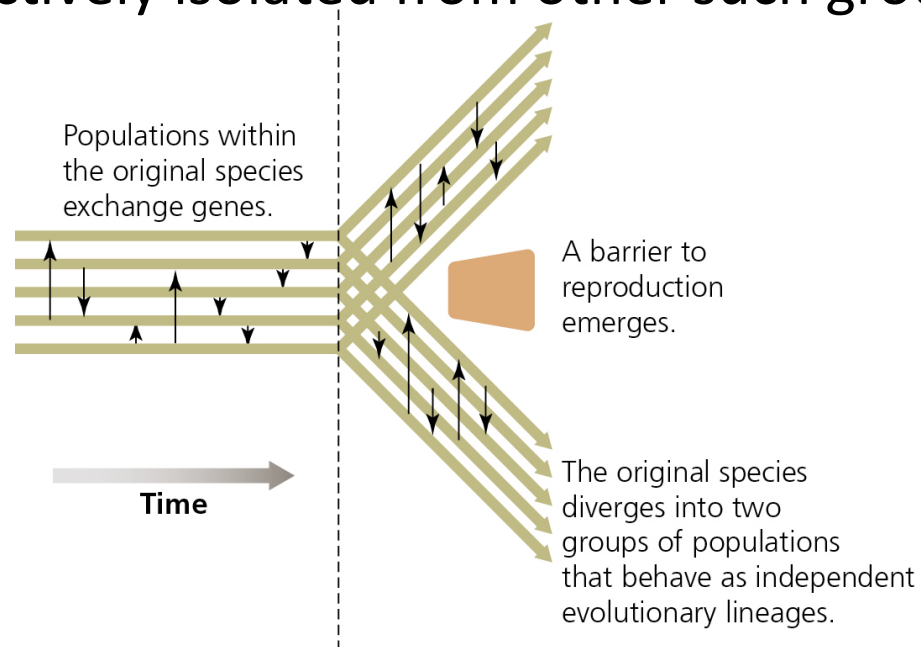
Mosquitoes (*Aedes aegypti*) to control zika/  
malaria

# Geographic population structure & Speciation

# Speciation

## Biological Species Concept:

species are groups of actually or potentially interbreeding populations *in nature*, reproductively isolated from other such groups.



- Speciation is the evolution of biological barriers to gene flow. Speciation forms a bridge between popgen & macroevol
- **Species are set of alleles/traits held in linkage disequilibrium through evolution of biological barriers to gene flow**

# Speciation consists of the evolution of biological barriers to gene flow

## **Pre-mating isolation** (Organisms occur in the same area but don't mate)

Potential mates don't meet:

- Different habitats

- Different mating seasons/times

Potential mates meet but don't mate:

- Different mating behavior in animals

- Different pollinators in plants

## **Postmating, prezygotic** (Potential mates try to mate but can't form a zygote)

- Incompatible genitalia

- Incompatible gametes

## **Postzygotic isolation** (Hybrids are formed but have low fitness)

- "Intrinsic" mechanisms

  - Hybrid lethality

  - Hybrid sterility (physiological)

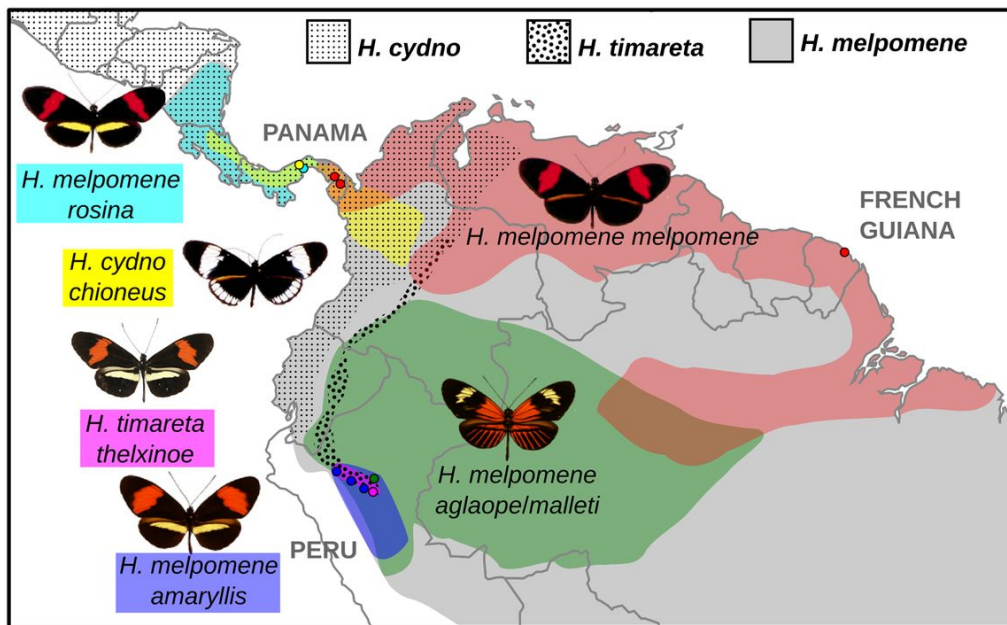
- "Extrinsic" mechanisms

  - Ecological: hybrids don't fit into either ecological niche

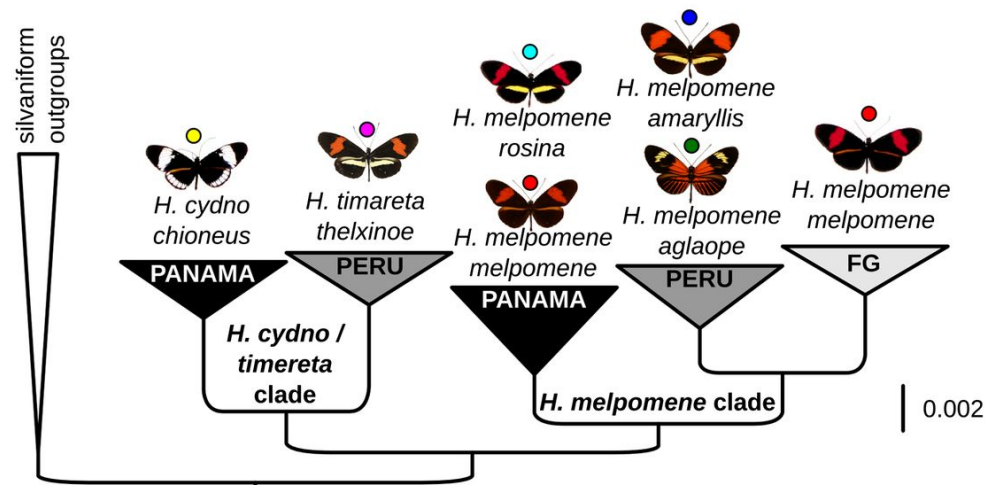
  - Mate recognition: mating behavior not appropriate for either species

# Geographic population structure

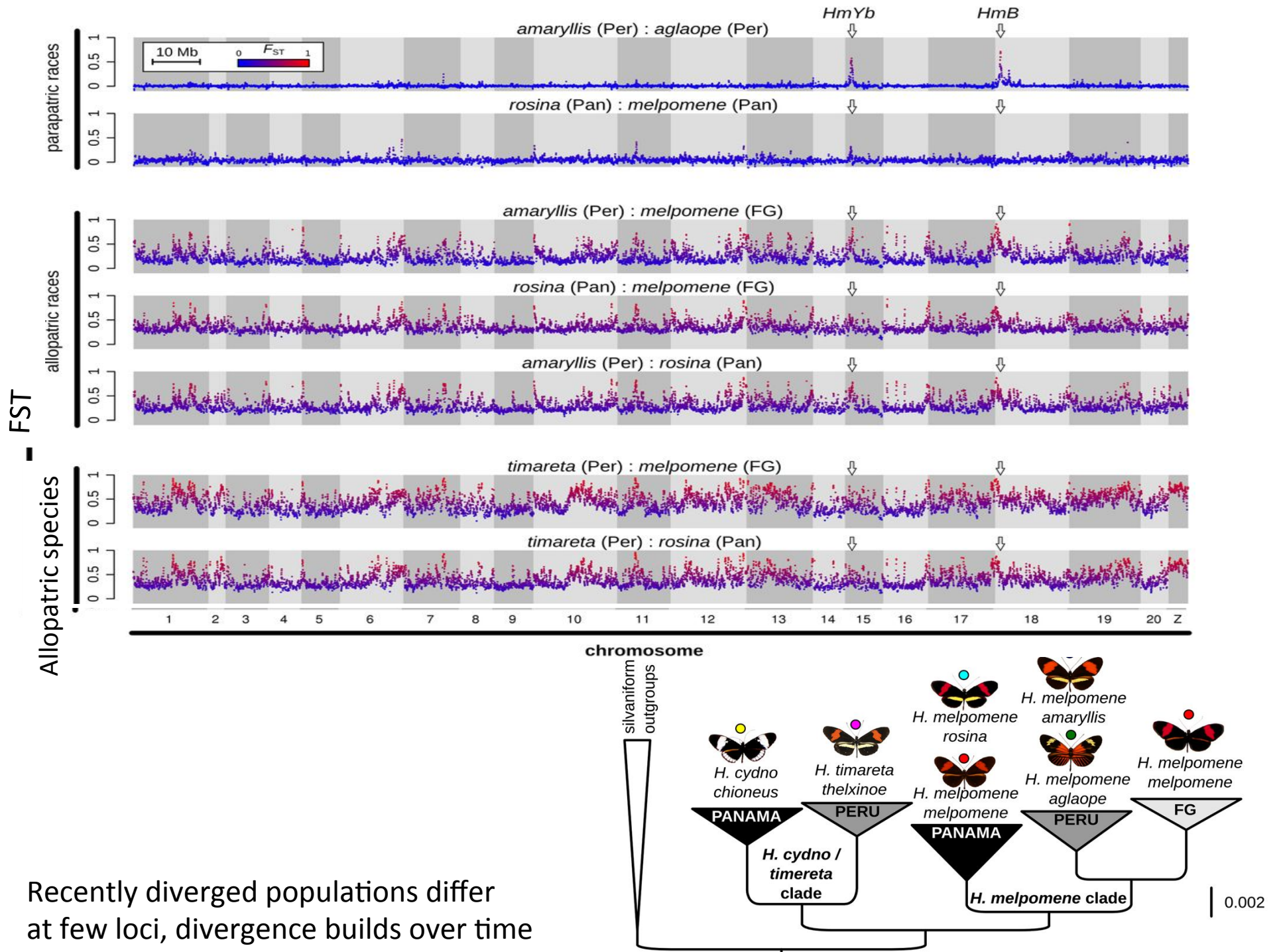
- Low levels of migration between populations allow LD to be maintained even between non-epistatic (or non-assortative mating) combinations.
  - Allows build up of locally adaptive alleles, forming locally adapted forms (ecotypes/races).
  - Neutral differentiation
- Local adaptation, through selection against migrants, can further lower effective migration rate



Melpomene aglaope



"Heliconius Melpomene Rosina" by Wikifan75 - Own work. [http://commons.wikimedia.org/wiki/File:Heliconius\\_Melpomene\\_Rosina.jpg](http://commons.wikimedia.org/wiki/File:Heliconius_Melpomene_Rosina.jpg)



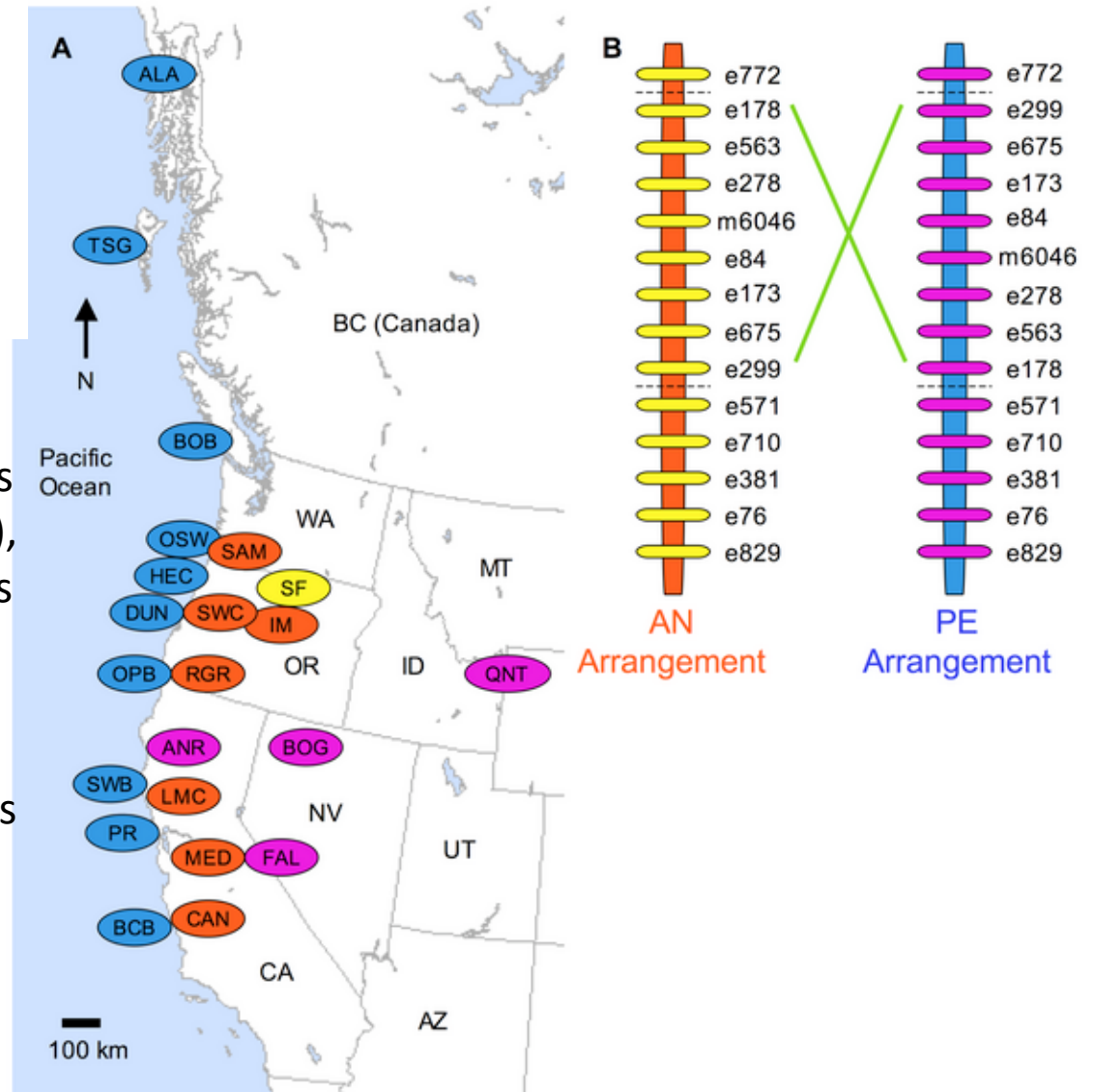


coastal perennial and inland annual

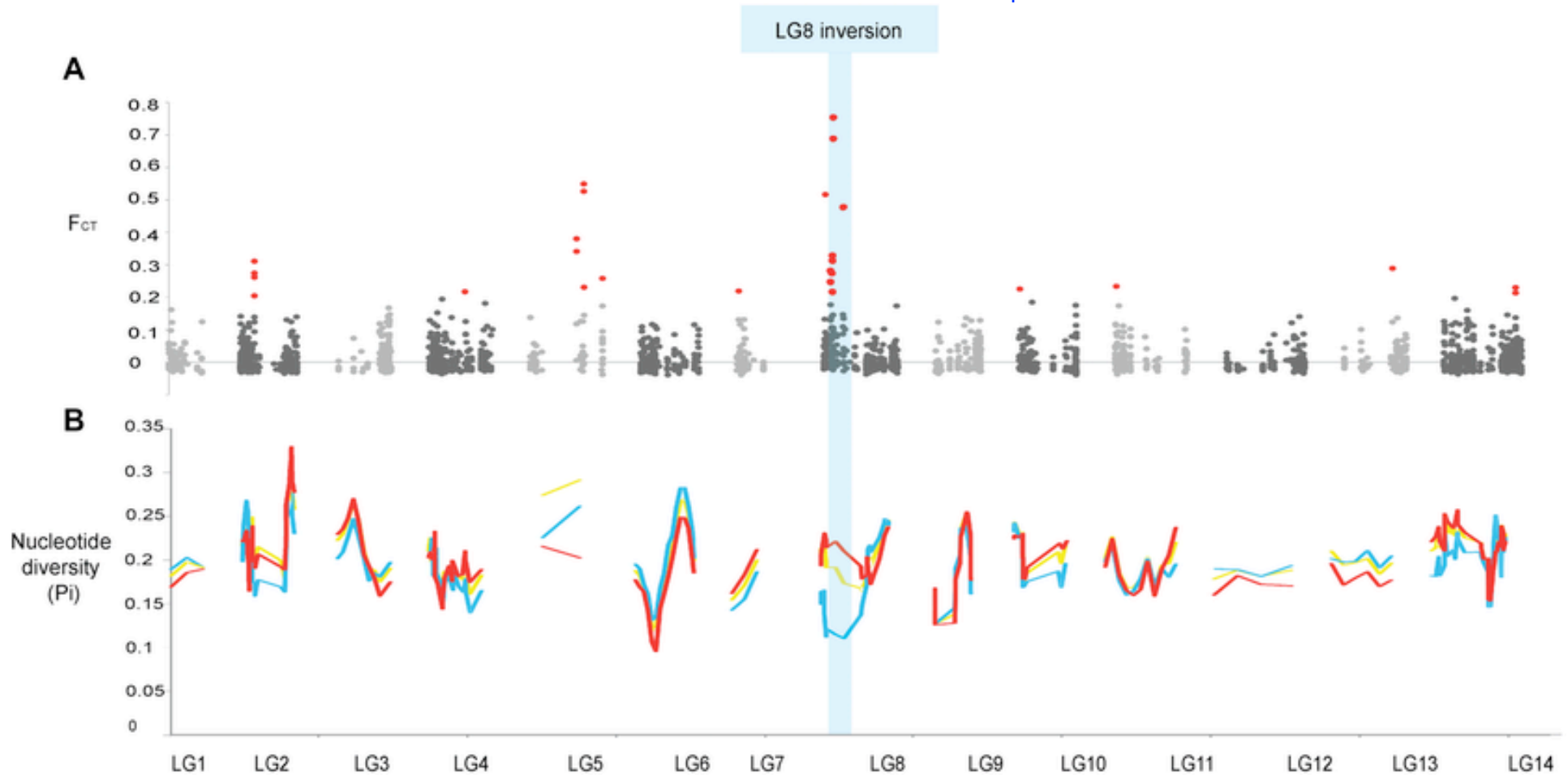
coastal perennials (blue), inland annuals (orange), and inland perennials (purple), as well as obligate self-fertilizing species *M. nasutus* (yellow)

Local adaptation mediated by inversions  
Also seen in *Drosophila* & Mosquitos  
And likely many other species

## A Widespread Chromosomal Inversion Polymorphism Contributes to a Major Life-History Transition, Local Adaptation, and Reproductive Isolation. 2010 Lowry & Willis

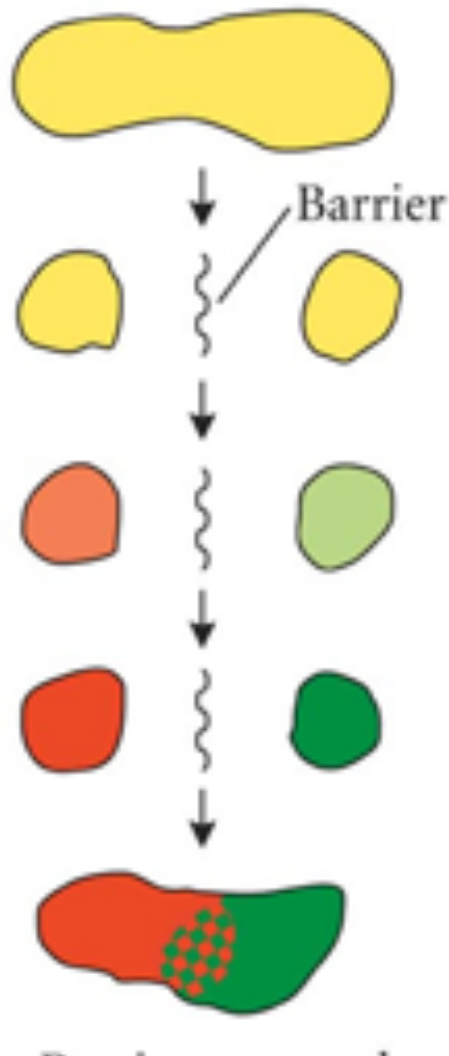


Pairwise nucleotide divergence between ecotypes ( $D_{XY}$ ) is shown in yellow, nucleotide diversity in annuals ( $\pi_A$ ), perennials ( $\pi_P$ ) in blue.



Twyford & Friedman. **Adaptive divergence in the monkey flower *Mimulus guttatus* is maintained by a chromosomal inversion**

# Allopatric speciation is potentially easy



No (low) interbreeding due to geographic barriers

Anagenesis proceeds independently

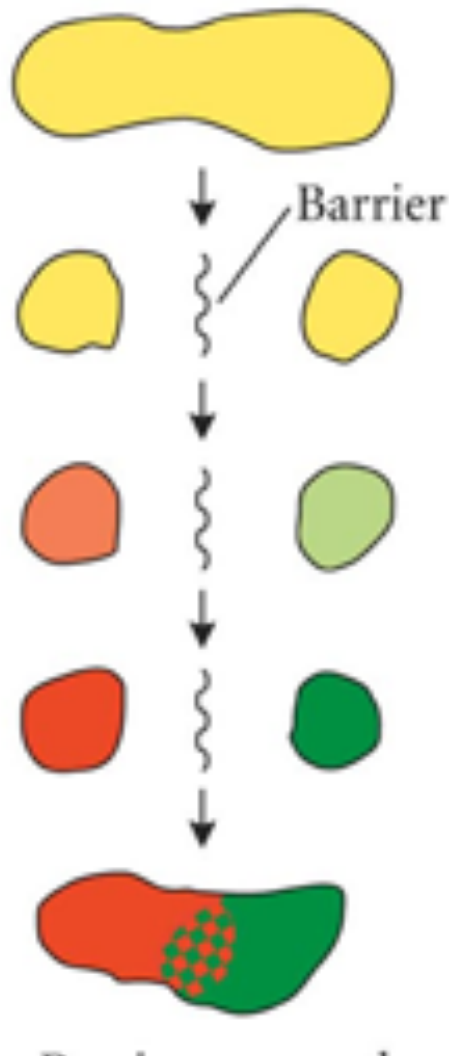
Barriers to reproduction evolve as a passive side effect of anagenesis

This may happen rapidly if ecology of the populations differs

# The difficulty with sympatric speciation

- Disruptive selection on phenotype has to be very strong
  - i.e. selection against intermediates has to be strong
- And:
- Individuals must mate assortatively with others of similar phenotype.
- The process is helped if alleles have a pleiotropic effect on both phenotype and choice
- Or if they are closely genetically linked.
- ...But if they are genetically closely linked then gene flow can occur in rest of genome

# Allopatric speciation is potentially easy



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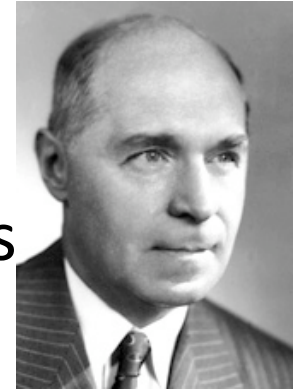
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Barriers to reproduction evolve as a passive side effect of anagenesis

This may happen rapidly if ecology of the populations differs



# Isolation allows the evolution of Dobzhansky-Muller (intrinsic hybrid sterility/inviability) Incompatibilities

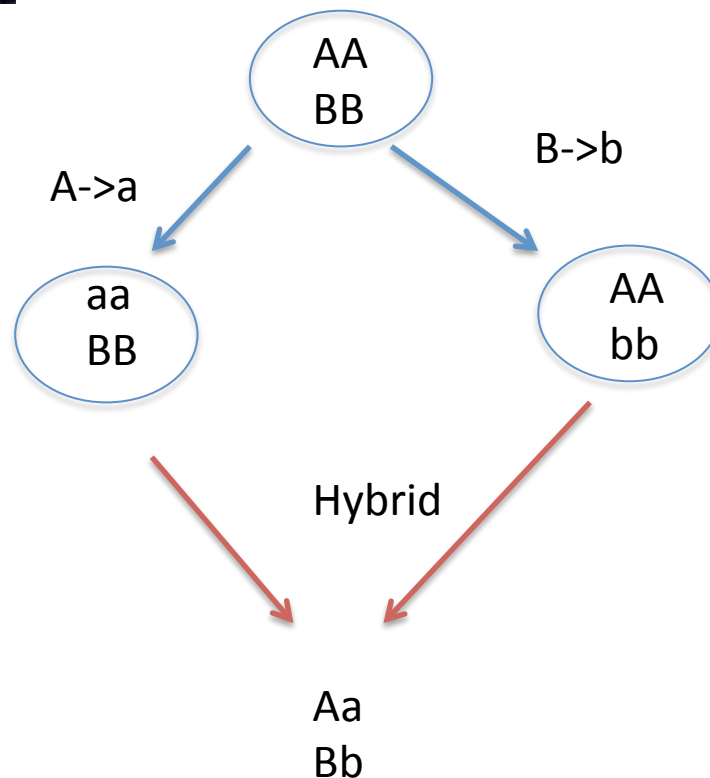


One locus model does not work.

Substitutions at two or more loci  
can generate incompatible  
genotypes

These have never been tested in  
the background of the other

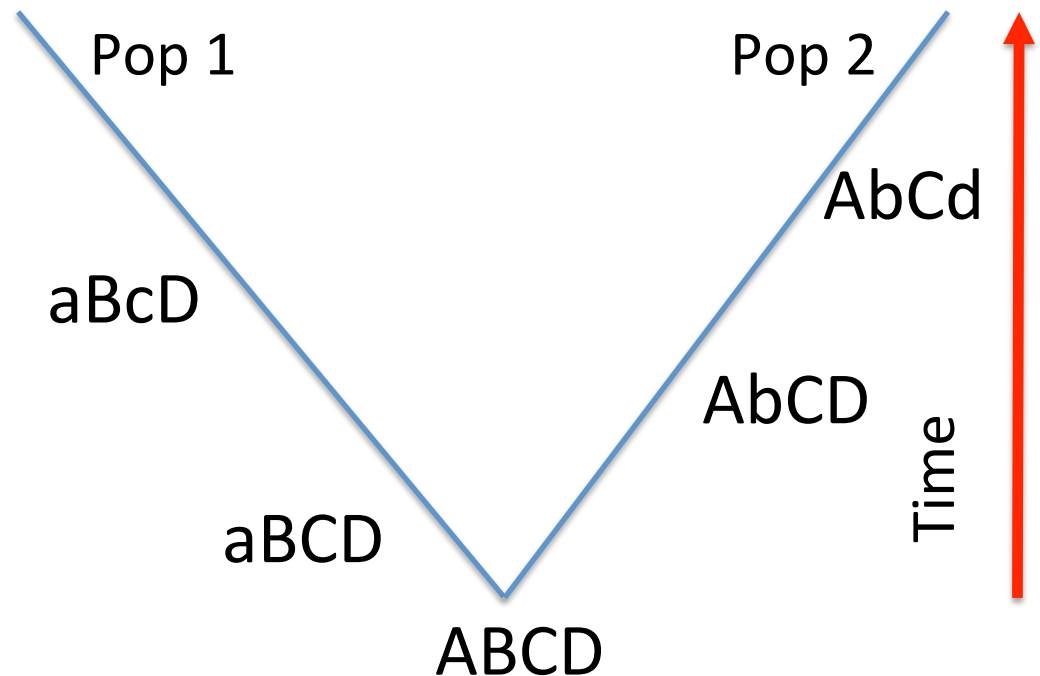
Such incompatibilities are termed  
Dobzhansky-Muller  
Incompatibilities (DMIs)  
(This is an example of epistasis )

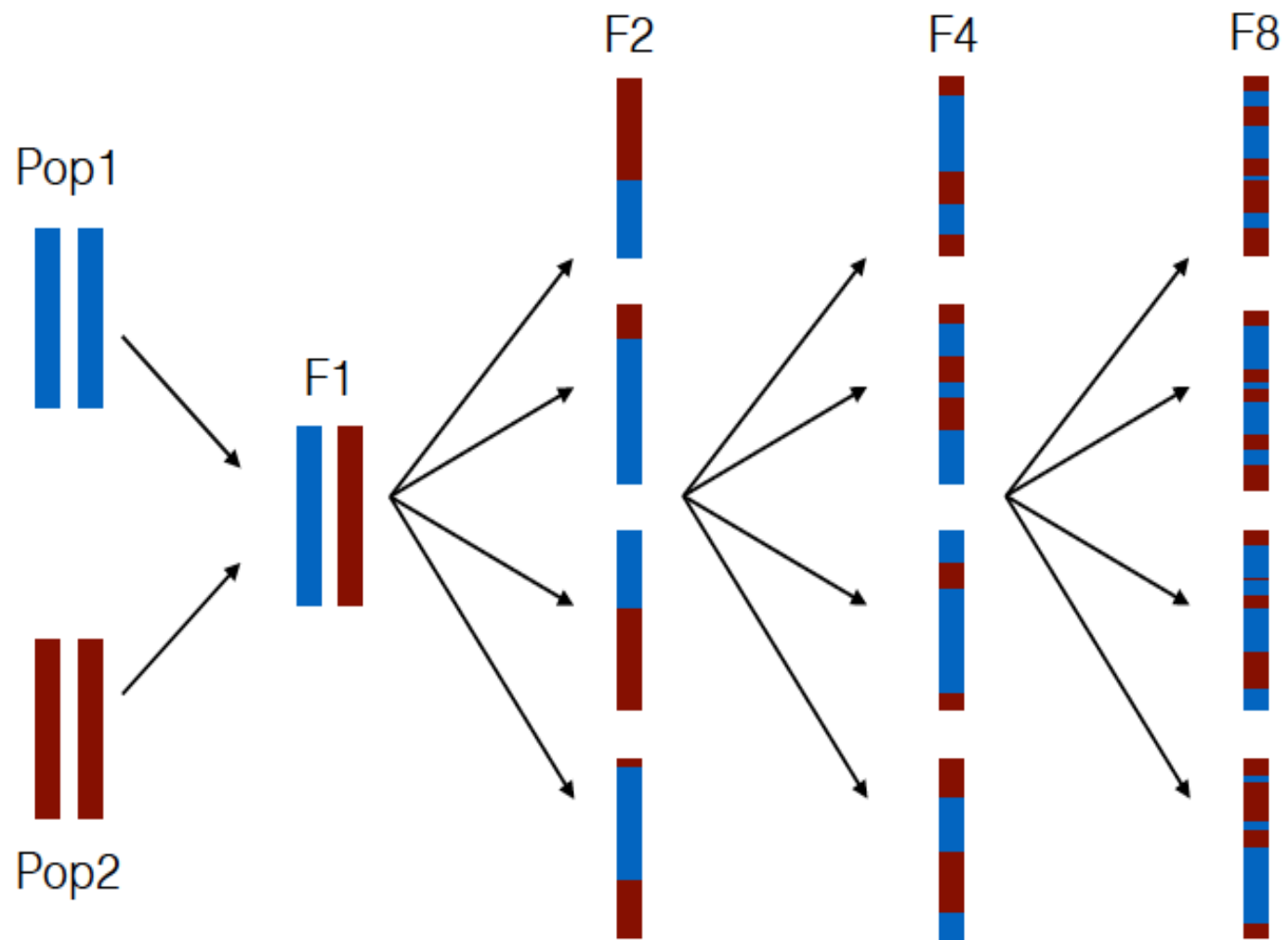


Substitutions accumulate linearly,  
but DMI pairs accumulate faster than  
that

Substitutions	DMIs
0	0
1	0
2	1
3	3
4	6

d fixes in pop 2,  
Potential DMIs = 6 ...  
(c & b, c & A, b & a,  
d & c, d & a, d & B)





Adapted from Buerkle and Lexer 2008

Slide from Alisa Sedghifar

# House mouse

## Hybrid zone



A map of Europe showing the distribution of *M. musculus* and *M. domesticus*. A black line separates the two species, with *M. musculus* to the north and *M. domesticus* to the south. Two rectangular boxes on the line indicate the locations of the studied populations in Central Europe.

A map of Germany showing the distribution of 100 sampling sites. The sites are marked with black triangles. Major cities are labeled: Berlin, Hamburg, Frankfurt, Köln, Stuttgart, München (Munich), and Saarbrücken. A scale bar indicates distances of 0, 25, 50, and 100 kilometers. The map shows a high density of sampling sites in the northern and central regions, particularly around Berlin and Hamburg, and a lower density in the southern regions.

homozygotes *M. domesticus* alleles, homozygotes for *M. musculus*  
heterozygotes

A heatmap showing the presence (green) and absence (white) of 35 genetic markers across 400 individuals from the Bavaria transect. The markers are listed on the y-axis, and individuals are numbered on the x-axis. The markers are: 1.014, 1.046, 1.159, 2.032, 2.078, 2.165, 3.007, 3.14, 4.057, 4.129, 5.007, 5.097, 6.088, 6.115, 7.083, 7.126, 8.078, 8.101, 9.052, 9.075, 10.045, 11.053, 11.089, 12.031, 12.099, 13.029, 13.056, 14.031, 14.074, 15.065, 15.099, 16.064, 17.046, 17.091, 18.028, 18.064, 19.044, and 19.052.

# THE VARIABLE GENOMIC ARCHITECTURE OF ISOLATION BETWEEN HYBRIDIZING SPECIES OF HOUSE MICE

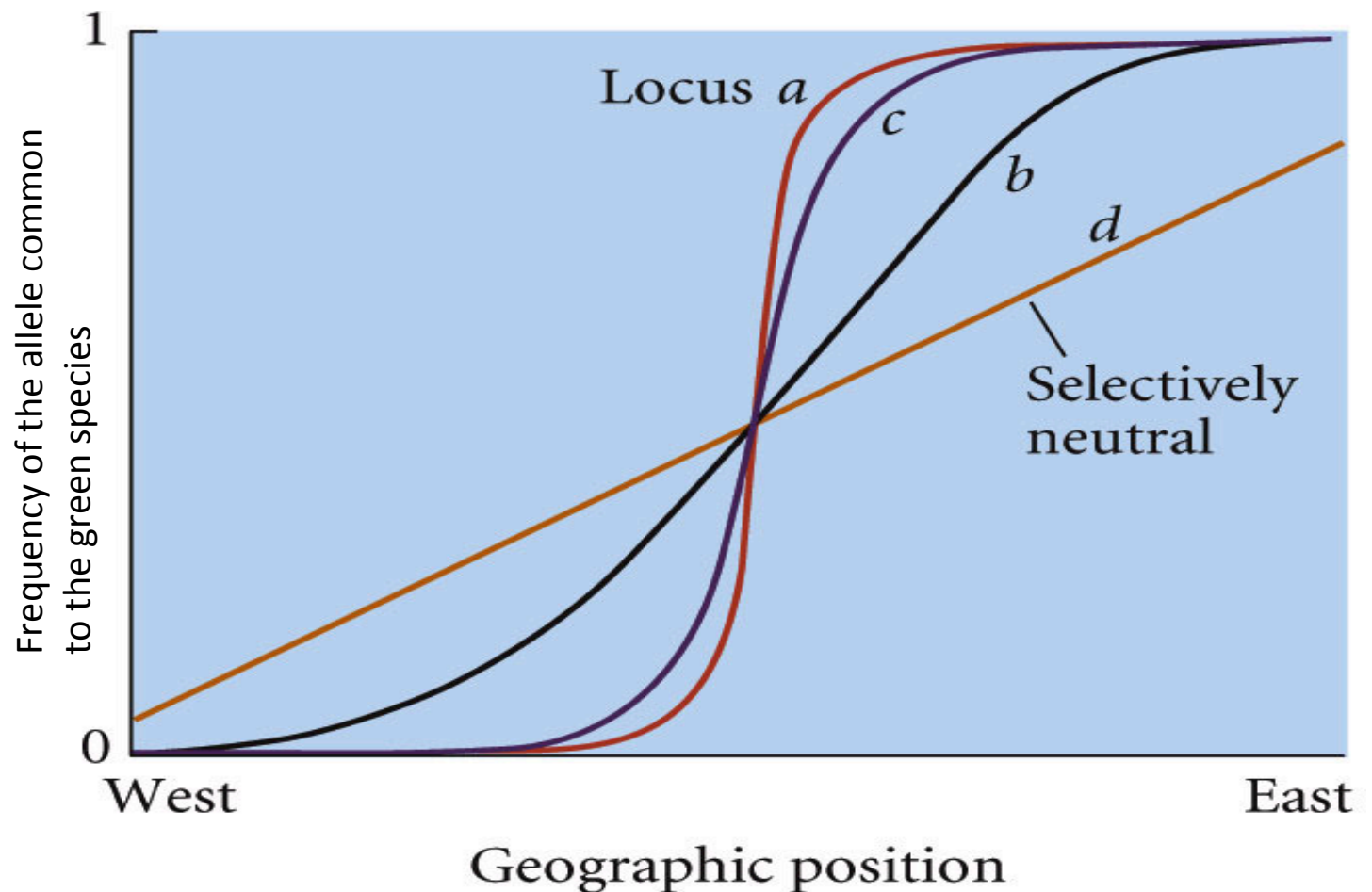
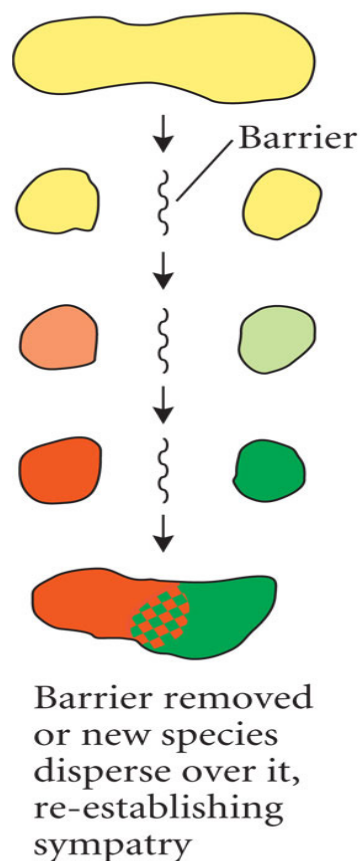
Katherine C. Teeter , Lisa M. Thibodeau, Zachariah Gompert, C. Alex Buerkle,  
Michael W. Nachman, Priscilla K. Tucker

Hybrid zones can form when once isolated populations spread back into secondary contact.

Gene flow (migration) moves alleles between populations

Selection acts against this flow at loci tightly linked to genes

Involved in reproductive isolation



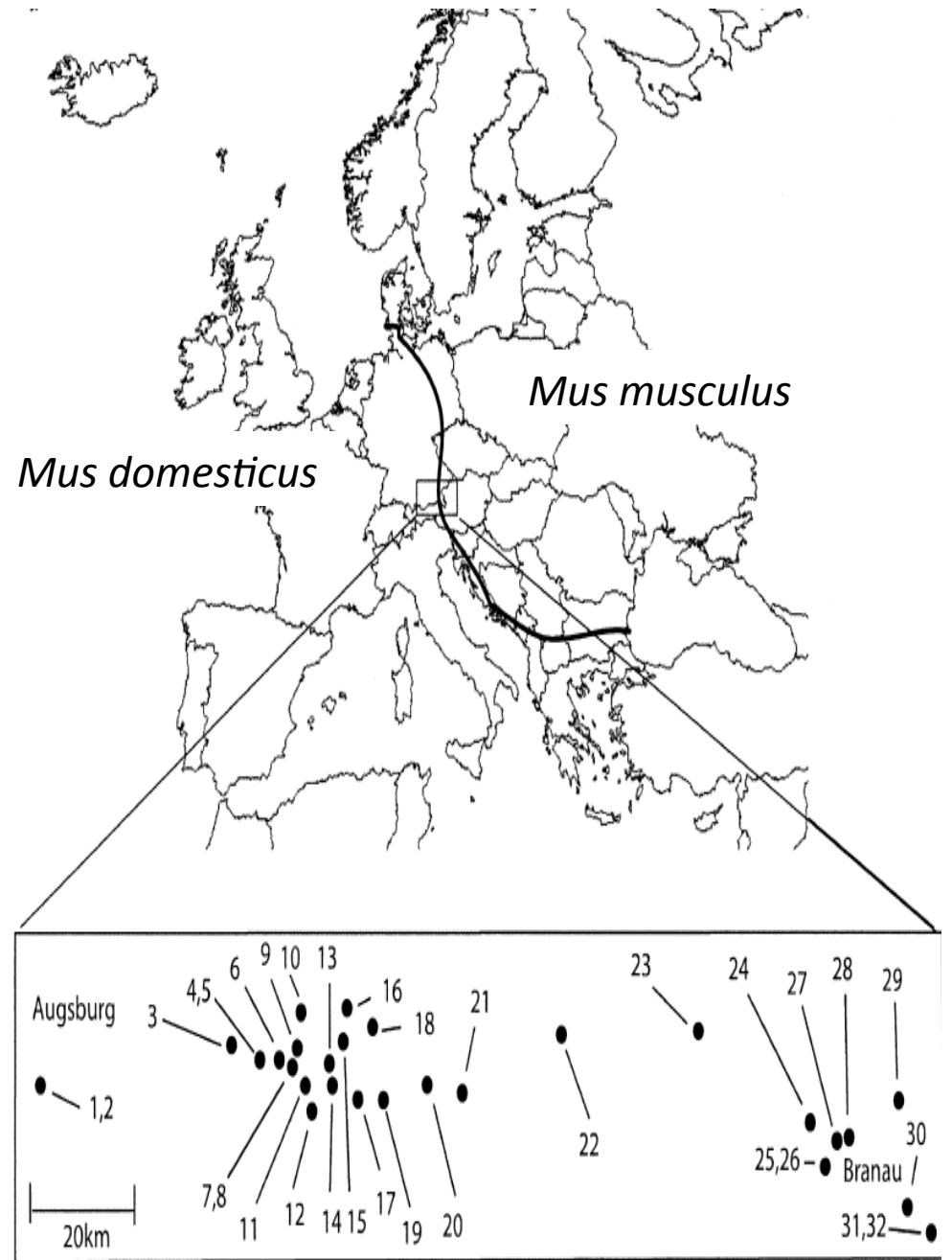
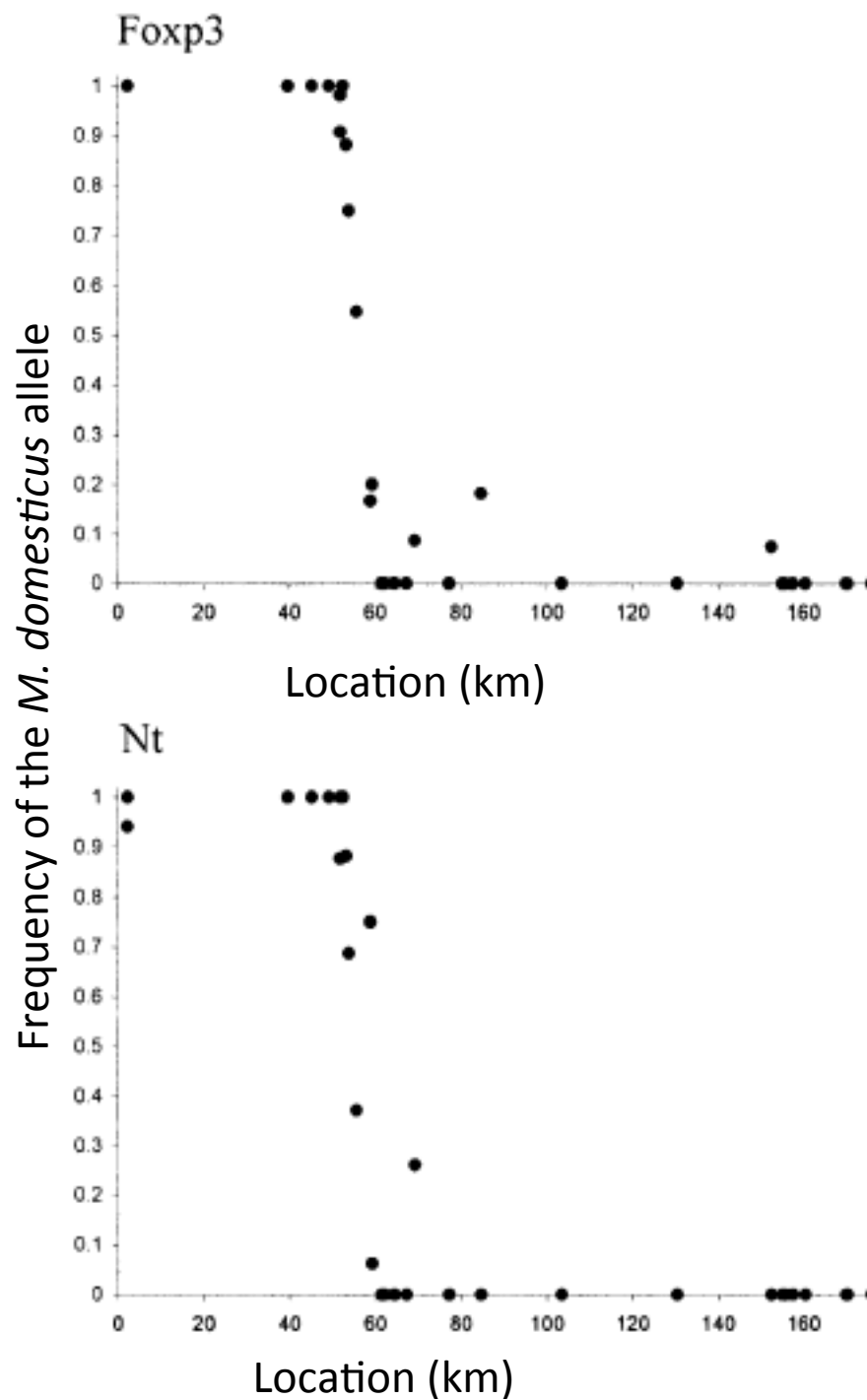
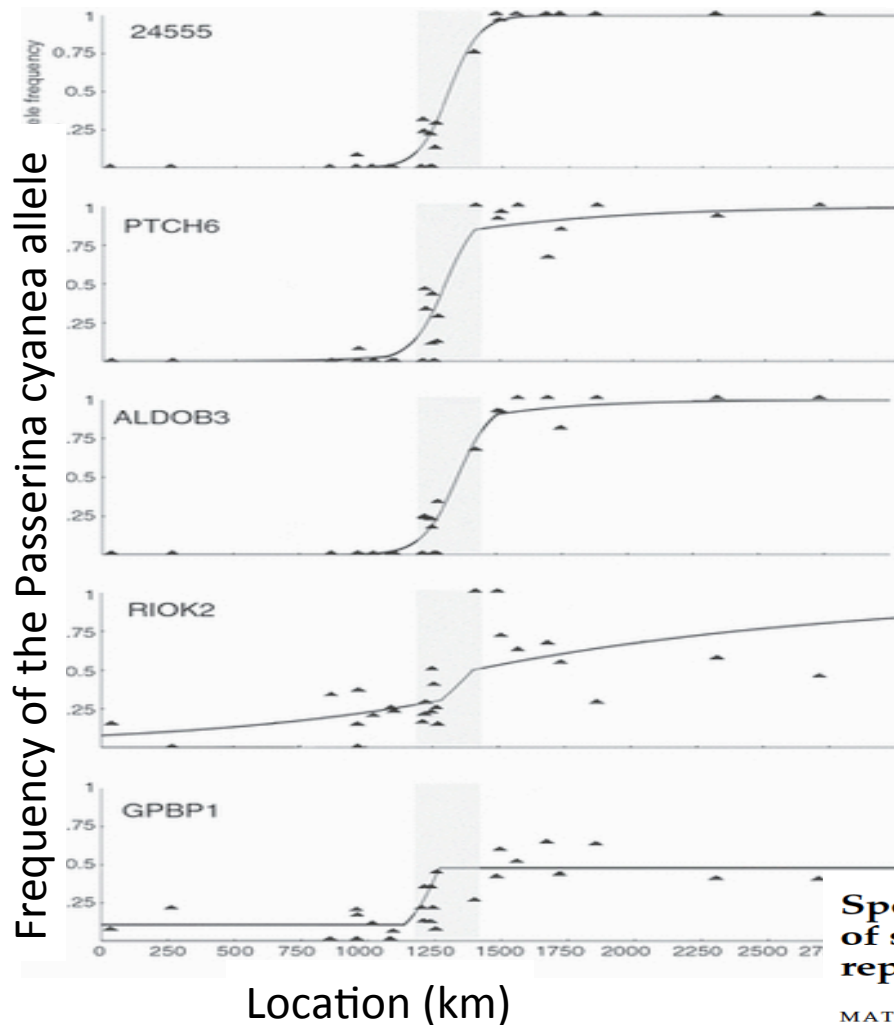
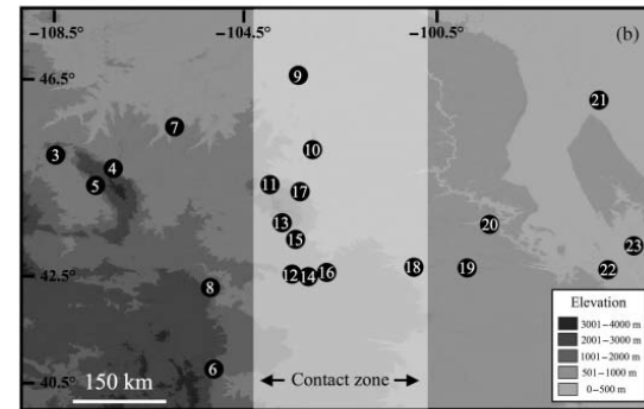
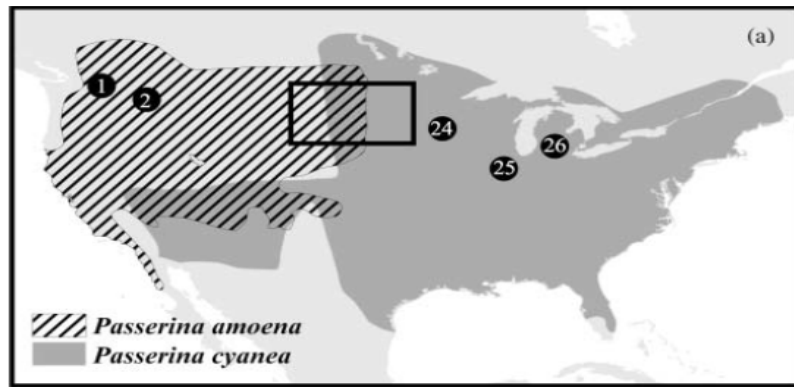
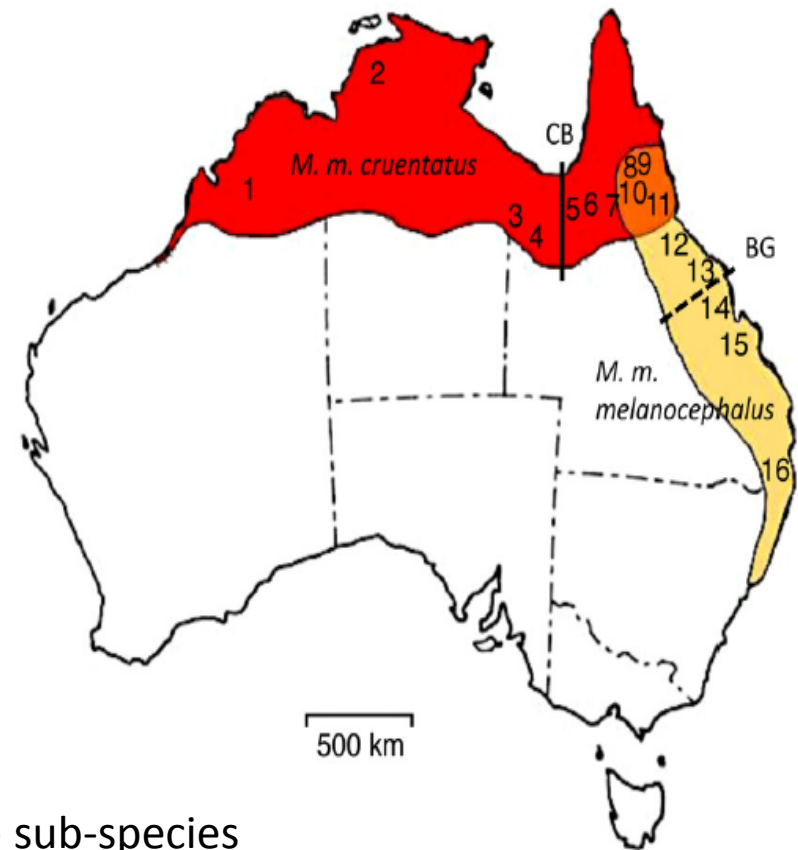
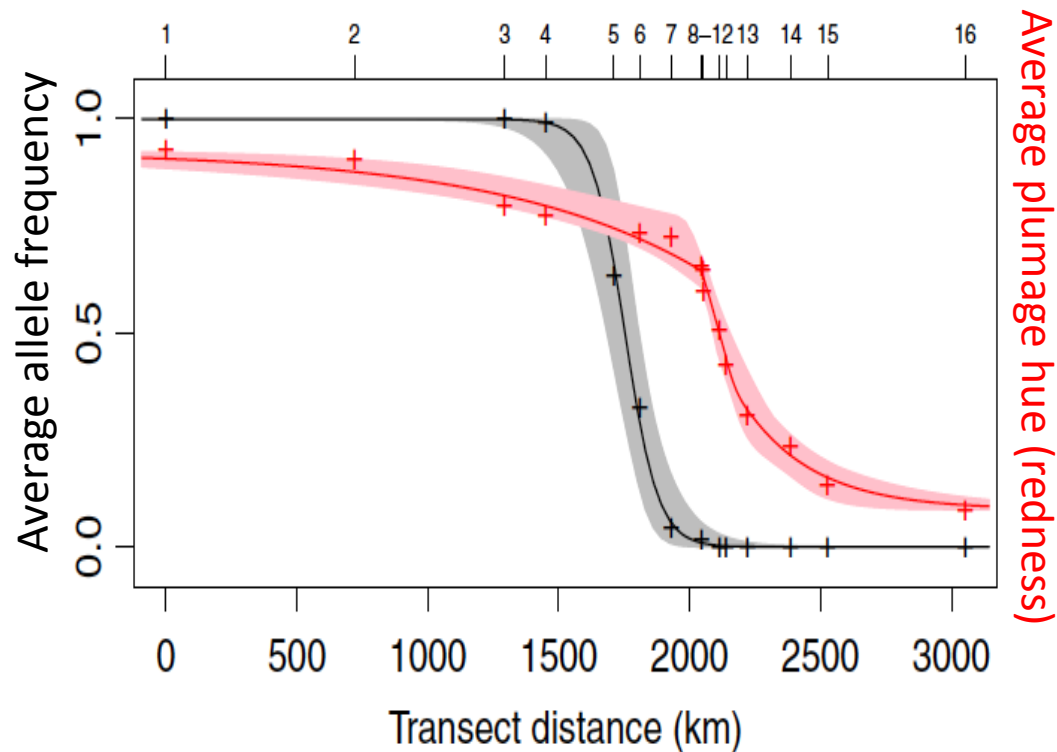


Fig. 1. Map of collecting localities along a transect through the hybrid zone between *Mus domesticus* and *M. musculus* in so Germany and western Austria. Locality numbers correspond to those in Table 1. The dark line shows the approximate position hybrid zone throughout Europe (modified from Sage et al. 1993).



**Speciation in *Passerina* buntings: introgression patterns of sex-linked loci identify a candidate gene region for reproductive isolation**

MATTHEW D. CARLING\* and ROBB T. BRUMFIELD



Two red-backed fairy-wren (*Malurus melanocephalus*) sub-species

## GENOMIC AND MORPHOLOGICAL ANALYSIS OF A SEMIPERMEABLE AVIAN HYBRID ZONE SUGGESTS ASYMMETRICAL INTROGRESSION OF A SEXUAL SIGNAL

Daniel T. Baldassarre,<sup>1,2,3</sup> Thomas A. White,<sup>4</sup> Jordan Karubian,<sup>5</sup> and Michael S. Webster<sup>1,2</sup>

Selection can sometimes favour the Introgression of particular alleles across Hybrid zones

