Violaine Llaurens
With Y LePoul, S Billiard, M Chouteau, F Prunier & M Joron

Evolution of dominance

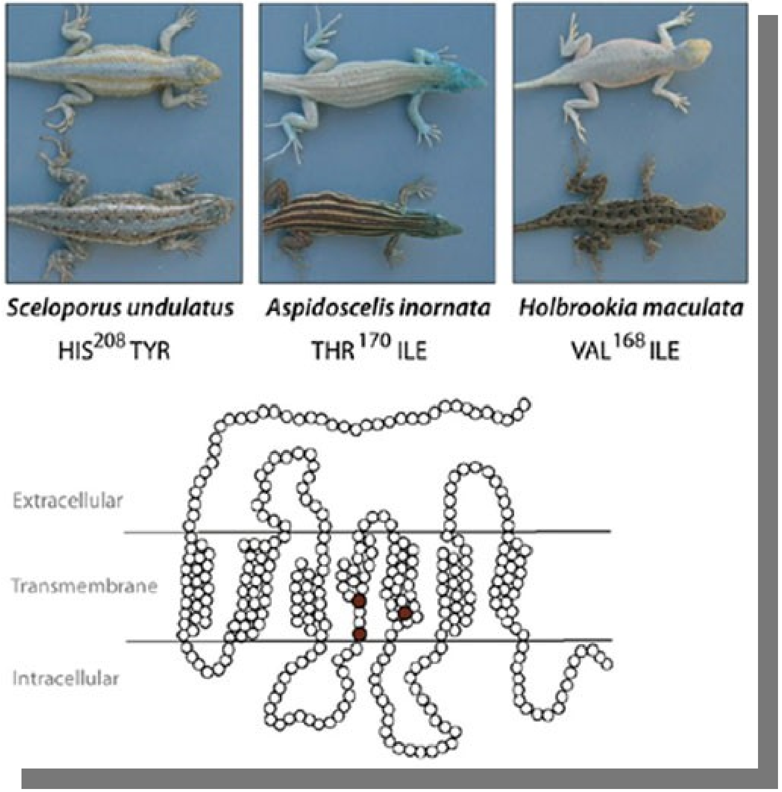
Aussois, May 15th 2018

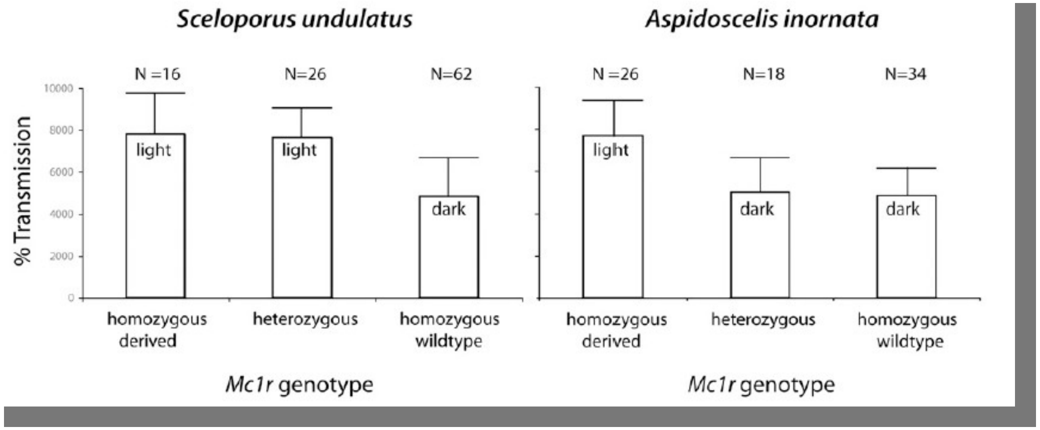
What is dominance ?

- For a behavioural biologist…

What is dominance ?

- For a molecular biologist…

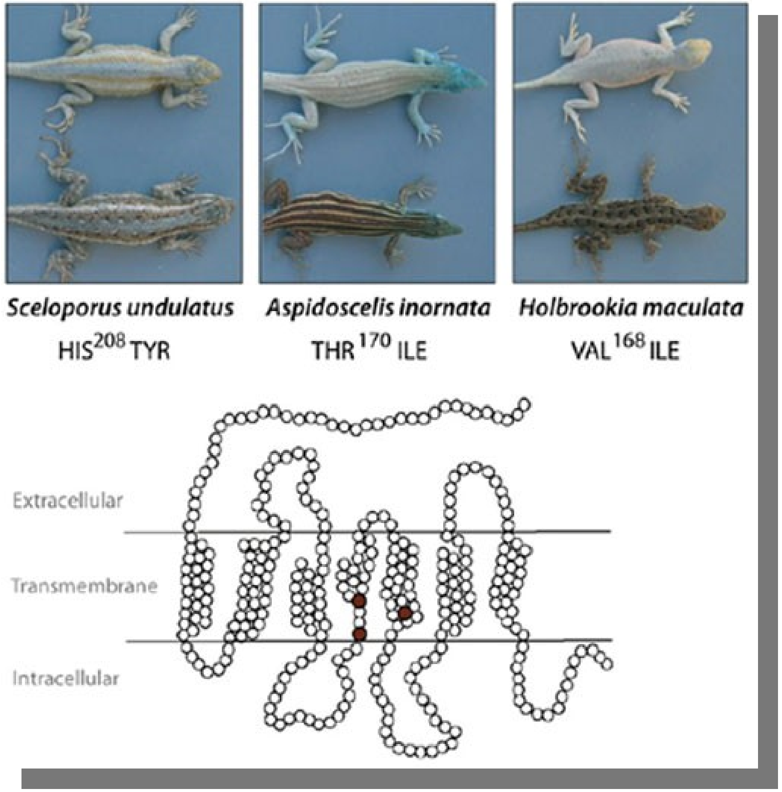




Rosenblum *et al.* PNAS 2010

What is dominance ?

- For a molecular biologist...



➔ Dominance is a by-product of the mutation.

➔ Dominance is a property of the allele.

Rosenblum *et al.* PNAS 2010

What is dominance ?

- For a quantitative genetics biologist

Herbicide resistance cost in *A. thaliana*

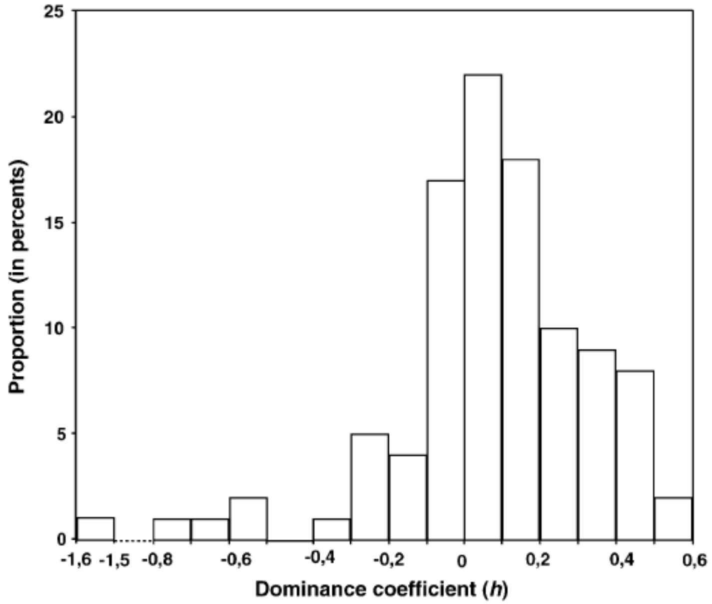


FIGURE 2.—Overall distribution of dominance coefficients. The resistant allele is dominant for the fitness cost when $h = 1$, semidominant when $h = 0.5$, recessive when h approaches 0, and overdominant and underdominant when $h > 1$ and <0, respectively.

Roux *et al.* 2005 Genetics

What is dominance ?

- For a quantitative genetics biologist

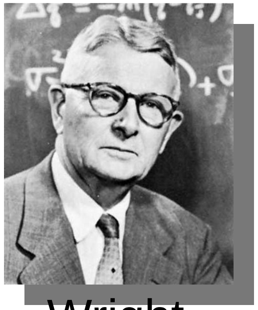
Herbicide resistance cost in *A. thaliana*

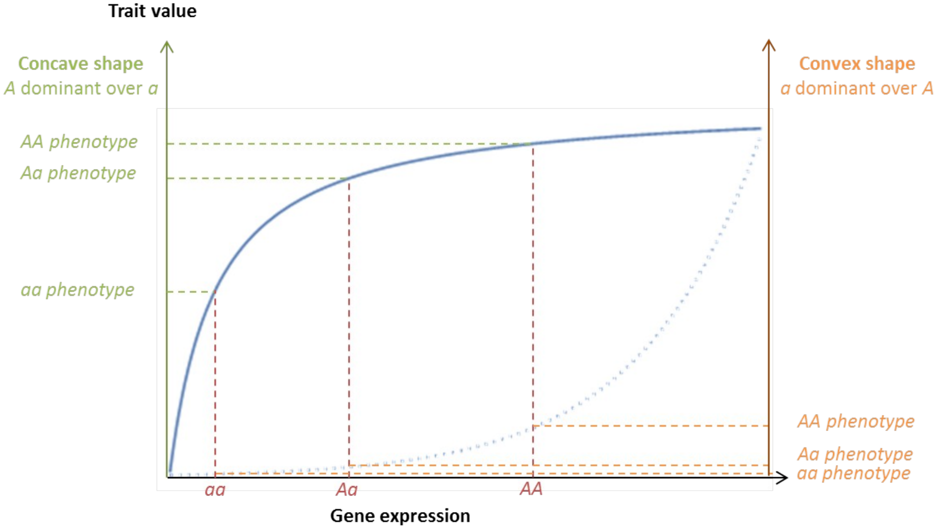
→ Dominance is quantitative

→ Dominance depend on the genetic background

What is dominance ?

- For population geneticists


Wright

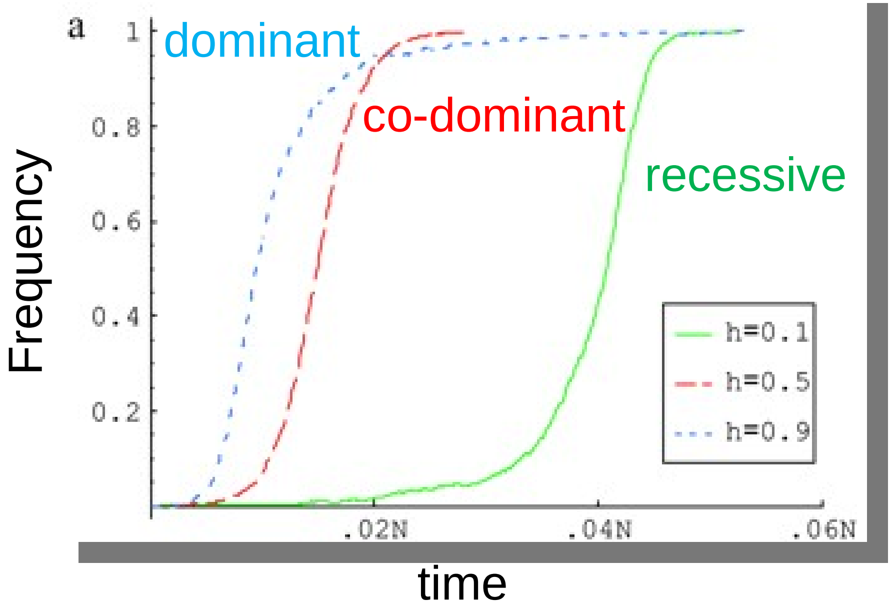


➔ Dominance depends on the link between genotype and phenotype

➔ Direct property of the allele

What is dominance ?

- For population geneticists

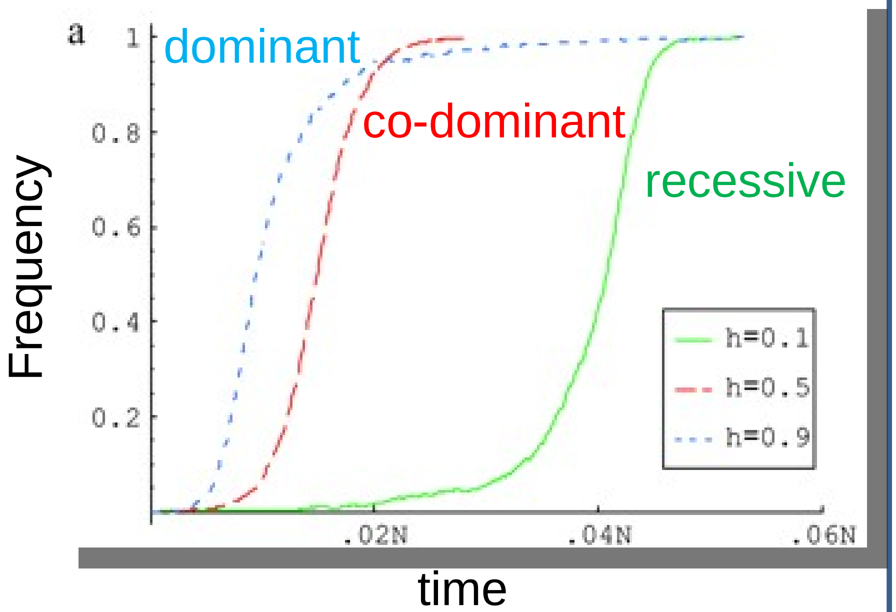


Teshima & Przeworki 2006 Genetics

➔ Dominance influences fixation of allele under positive selection

What is dominance ?

- For population geneticists



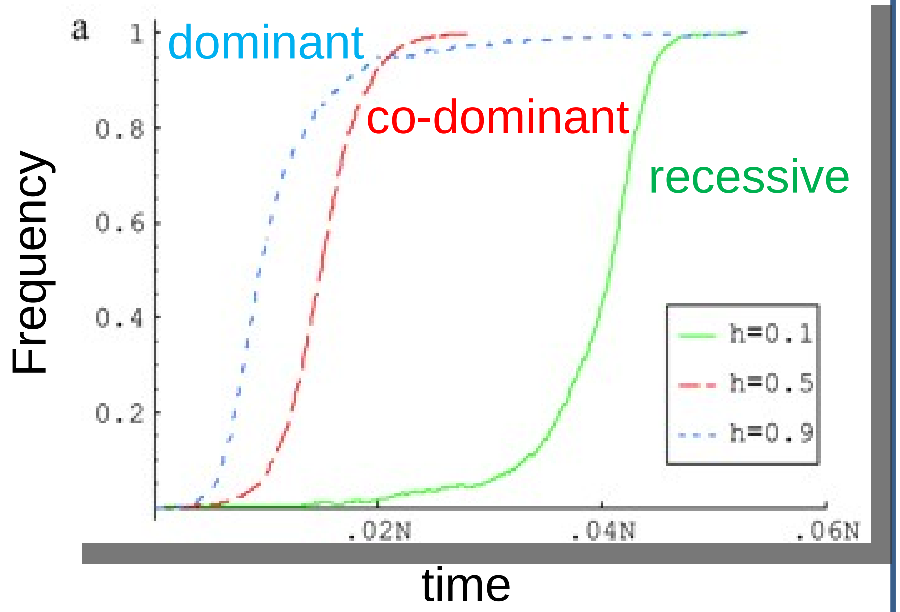
Teshima & Przeworki 2006 Genetics

Haldane

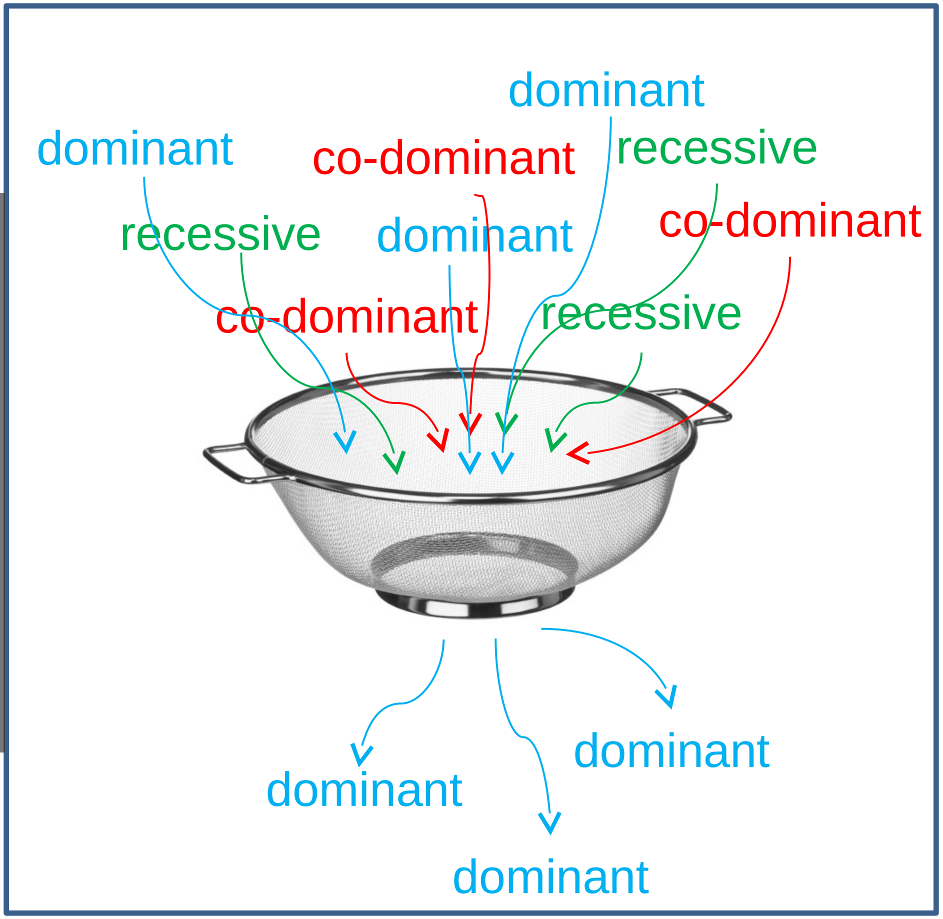
Haldane’s sieve

What is dominance ?

- For population geneticists



Teshima & Przeworki 2006 Genetics

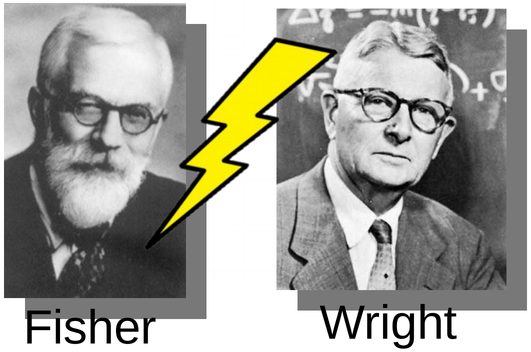


Haldane’s sieve

Evolution of dominance ?

➔ NATURAL SELECTION ACTING ON DOMINANCE

➔ DRIVING EVOLUTION OF DOMINANCE ?



Fisher (1928):

– Selection on dominance modifiers can trigger evolution of dominance

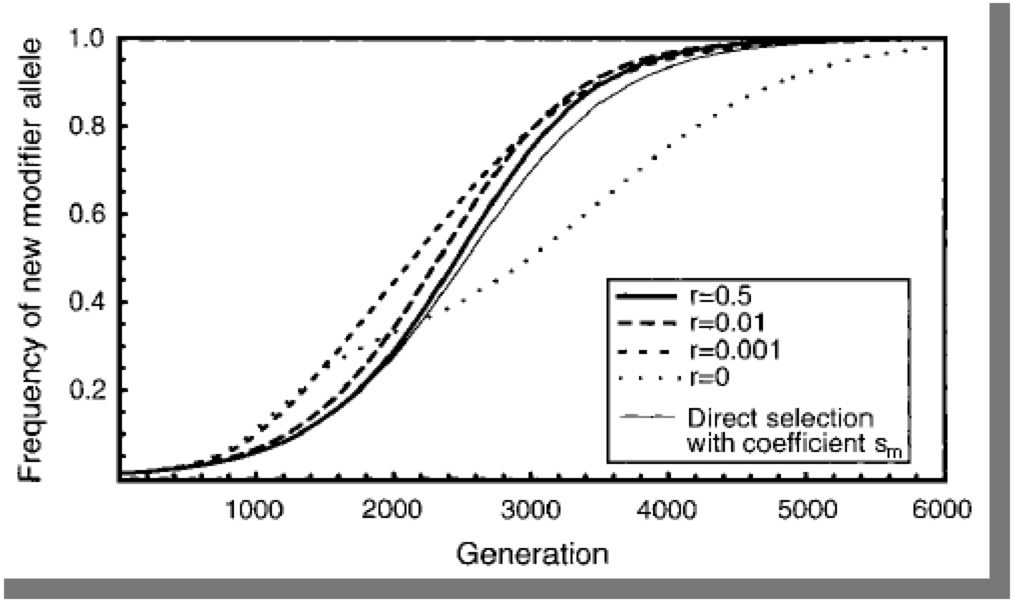
Wright (1929):

– Selection on modifier acts on heterozygotes only

– Unlikely to be efficient in natural populations where heterozygotes are rare

Evolution of dominance ?

➔ Evolution of dominance possible when heterozygotes are frequent: in locus under balancing selection

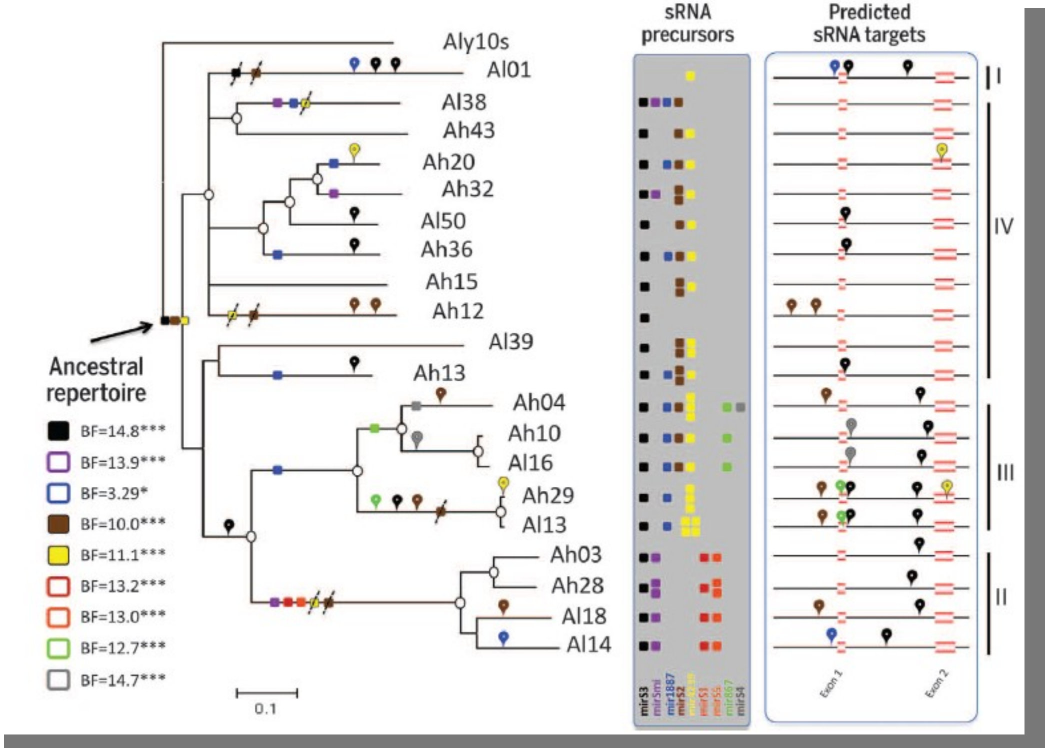


Otto & Bourguet 1999 Am. Nat.

 Fixation of unlinked dominance modifiers

Evolution of dominance ?

➔ Evolution of dominance possible when heterozygotes are frequent: in locus under balancing selection



Durand et al. 2014 Science

sRNA controlling dominance at the polymorphic *SCR* locus in *A. halleri*

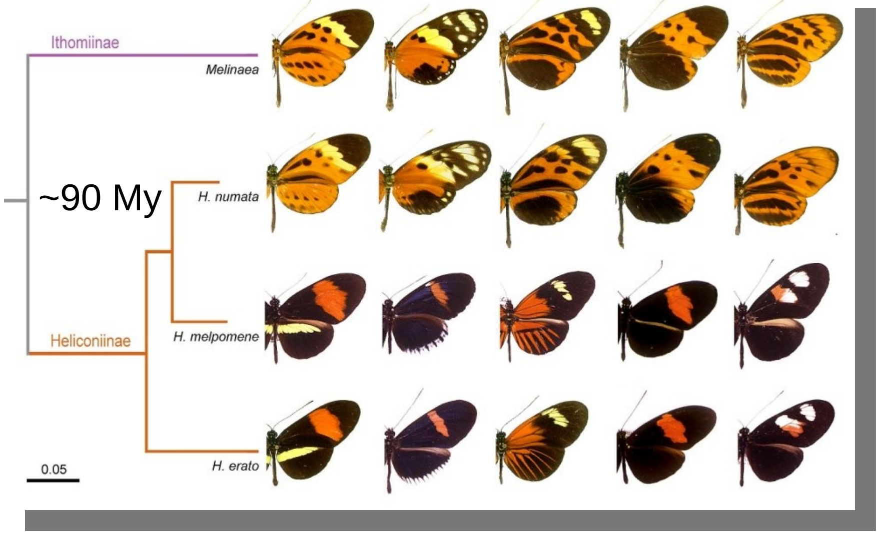
POLYMORPHIC MIMICRY AS A CASE-STUDY

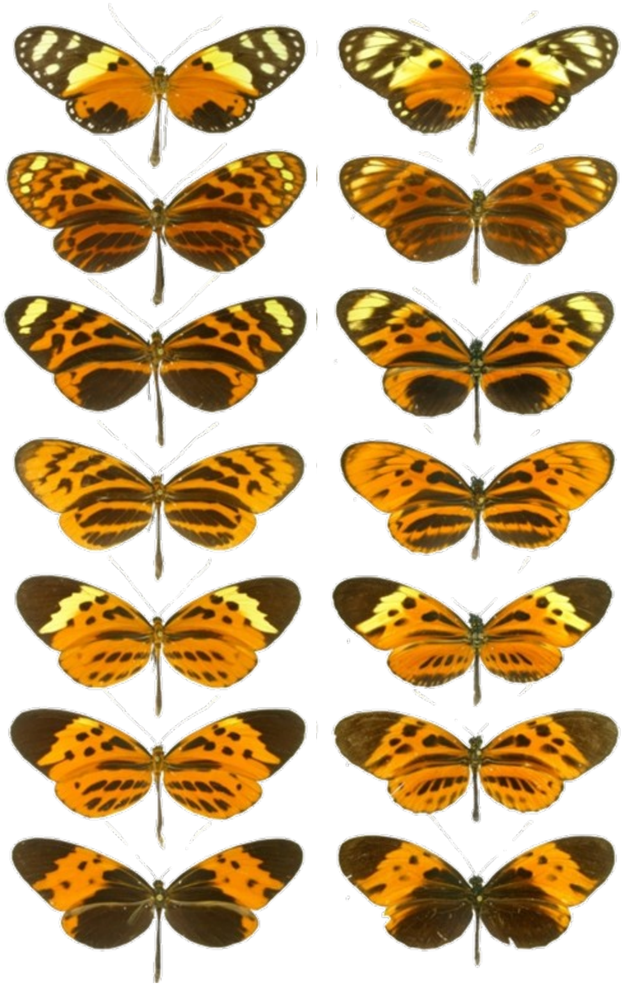
- Butterfly wing colour pattern:
- → Relevant example of complex phenotype under selection
  - Predators
  - Sexual selection

from: www.butterfliesofamerica.com

POLYMORPHIC MIMICRY AS A CASE-STUDY *HELICONIUS NUMATA*

- *H. numata* : striking resemblance with several species from the distantly related genus Melinaea (~90 My divergence)

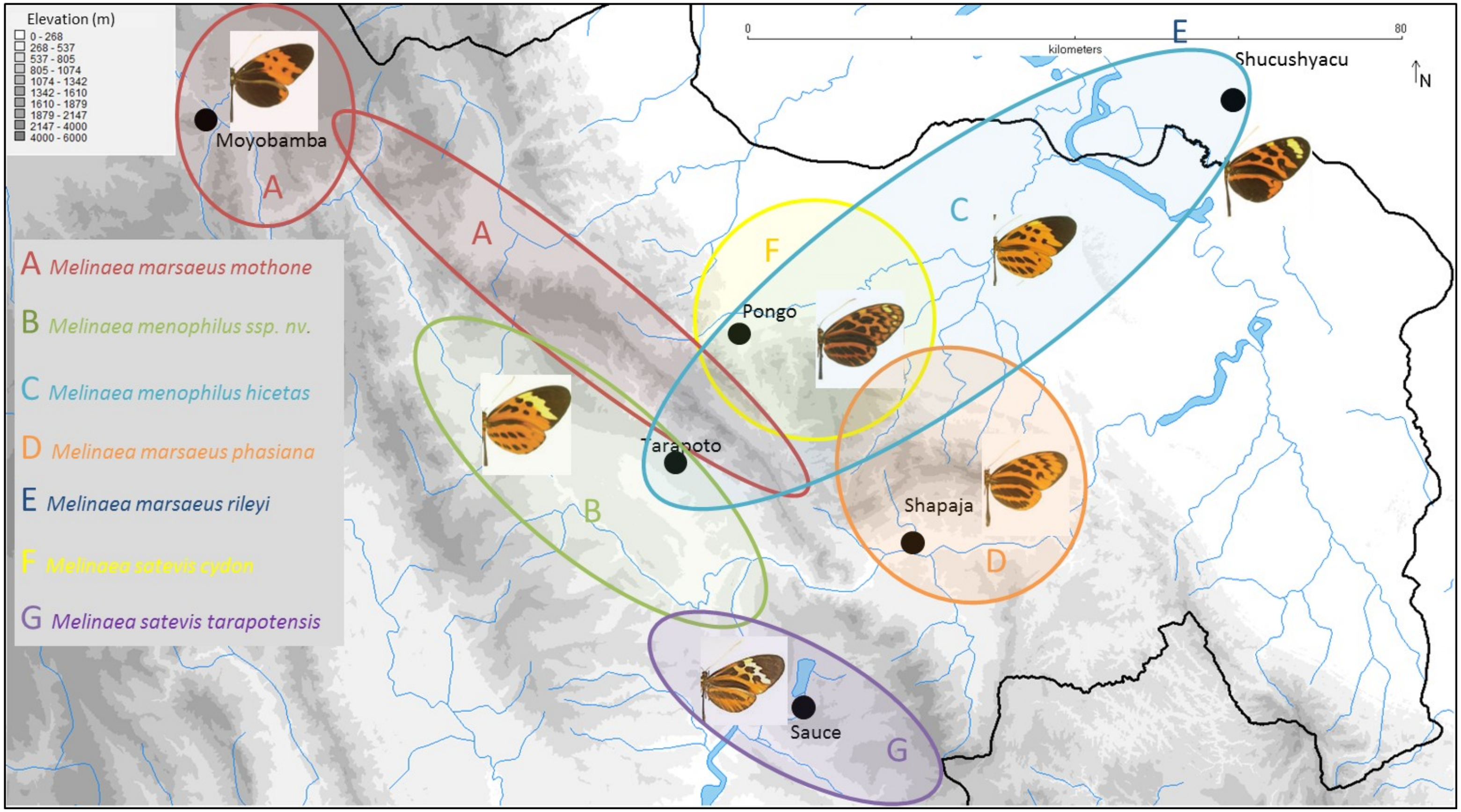




7 Melinaea sp.   H. numata

POLYMORPHIC MIMICRY AS A CASE-STUDY *HELICONIUS NUMATA*

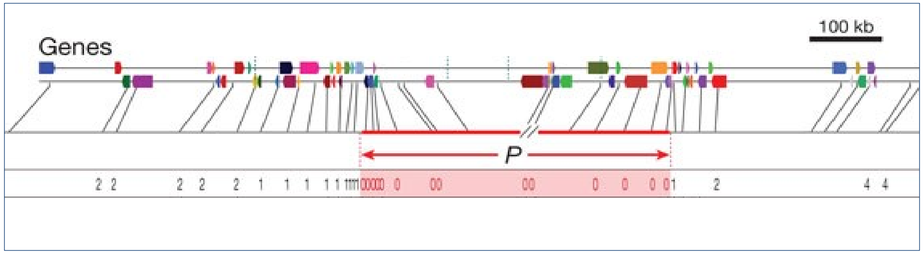
- Polymorphism driven by selection-migration equilibrium



Distribution of *Melinaea ssp* (San Martin Department – PERU) – from Mélanie McClure

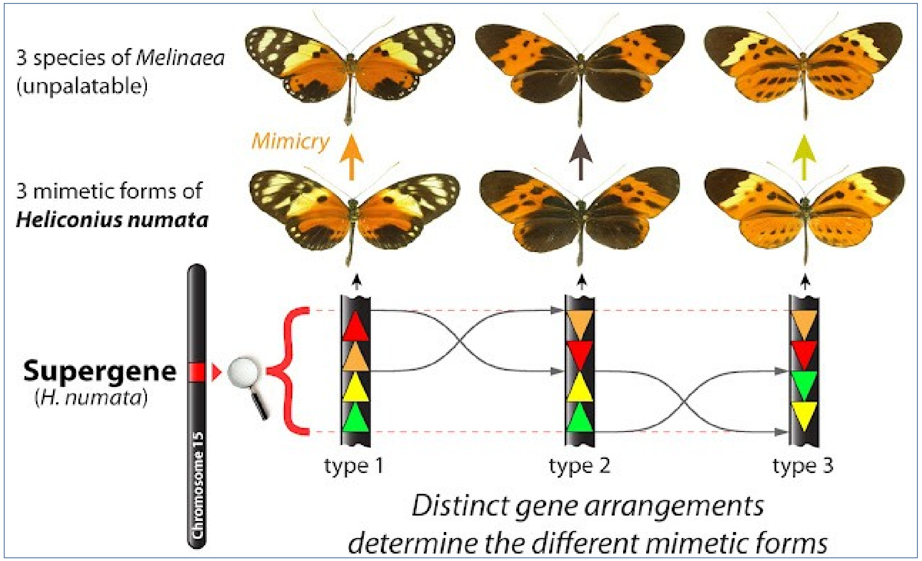
EVOLUTION OF DOMINANCE IN POLYMORPHIC MIMICRY

- Supergene encoding for color pattern variations



- Polymorphic gene order corresponding to different mimetic alleles
- Limited recombination

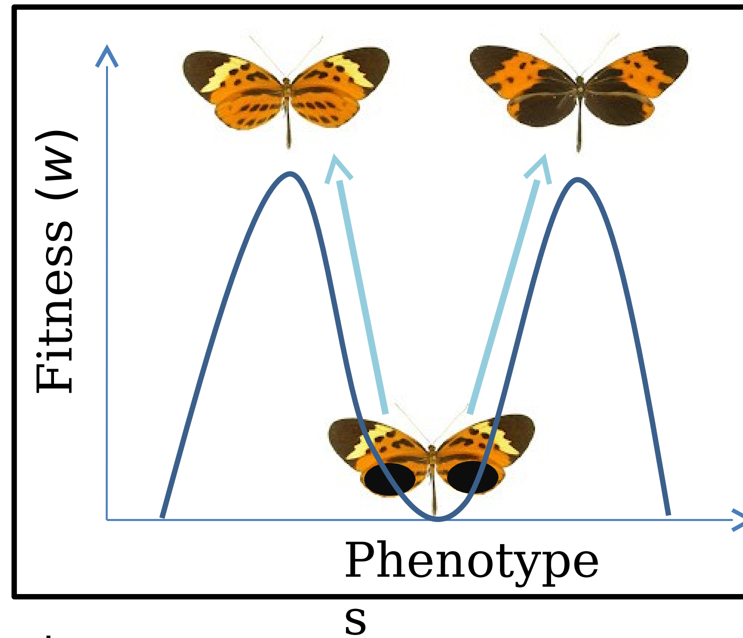
 GENETIC ARCHITECTURE FAVOURING POLYMORPHISM



Joron et al. 2011

POLYMORPHIC MIMICRY AS A CASE-STUDY *HELICONIUS NUMATA*

- Polymorphic species
  - High number of heterozygotes



- Negative selection on intermediate phenotype by predators

➔ Selection on dominance in natural populations ?

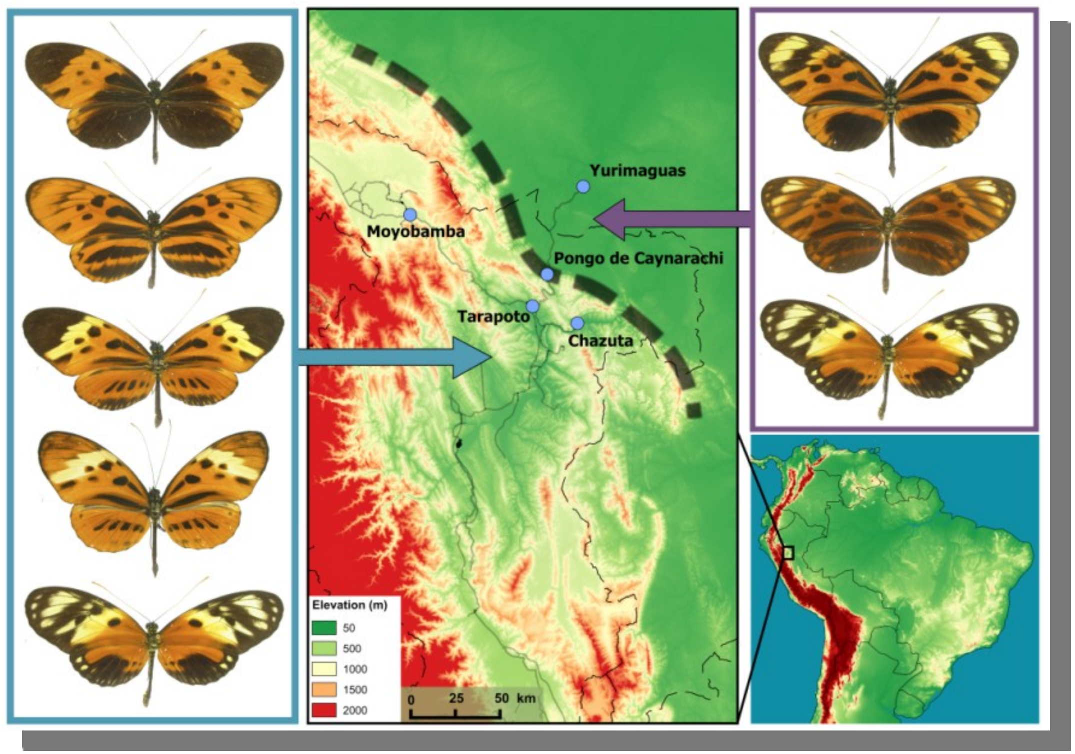
➔ Evolution of dominance ?

- Complex color pattern phenotype

➔ Mechanisms of dominance at the supergene *P* ?

DOMINANCE IN SYMPATRY *VS.* PARAPATRY

- Measuring dominance in 32 controlled brood
  - Genotyping: microsatellites within supergene.
  - Combination of 7 alleles → 21 genotypes.
  - N= 588 individuals in total.



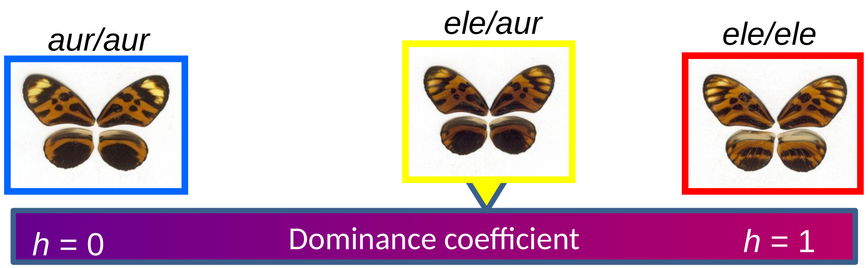
Le Poul *et al.* , Nature Com 2014

ESTIMATING DOMINANCE THROUGHOUT THE WING

- Measuring dominance throughout the wing:

$$h = \frac{T_{aur/ele} - T_{aur/aur}}{T_{ele/ele} - T_{aur/aur}}$$

Y. Le Poul



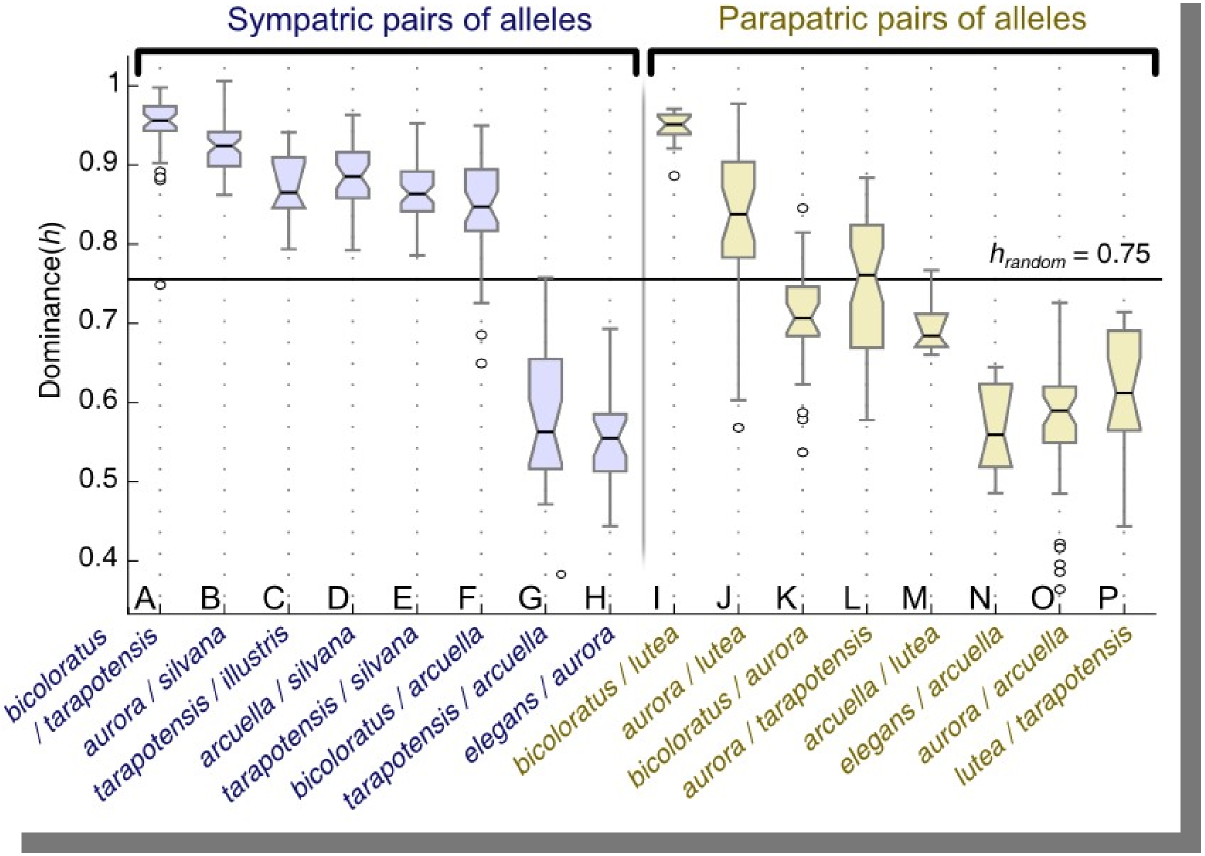
➔ Colour pattern modeling (CPM)

➔ Proportion of surface of the heterozygote shared with respective homozygotes

Le Poul *et al.* , Nature Com 2014

DOMINANCE IN SYMPATRY *VS.* PARAPATRY

- Variation of dominance in sympatry vs. parapatry



DOMINANCE THROUGHOUT THE WING

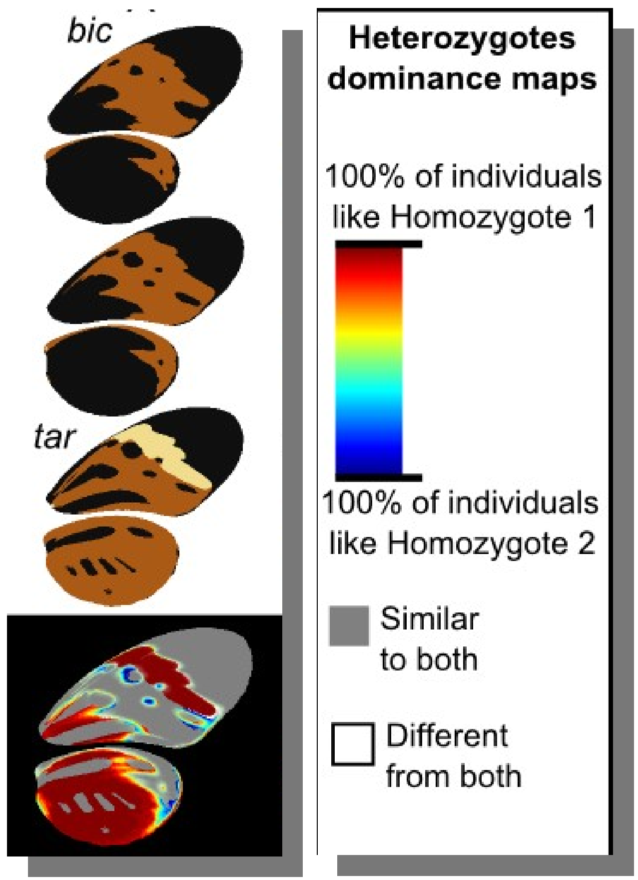
- Mosaic of dominance:

Homozygote 1

Heterozygote

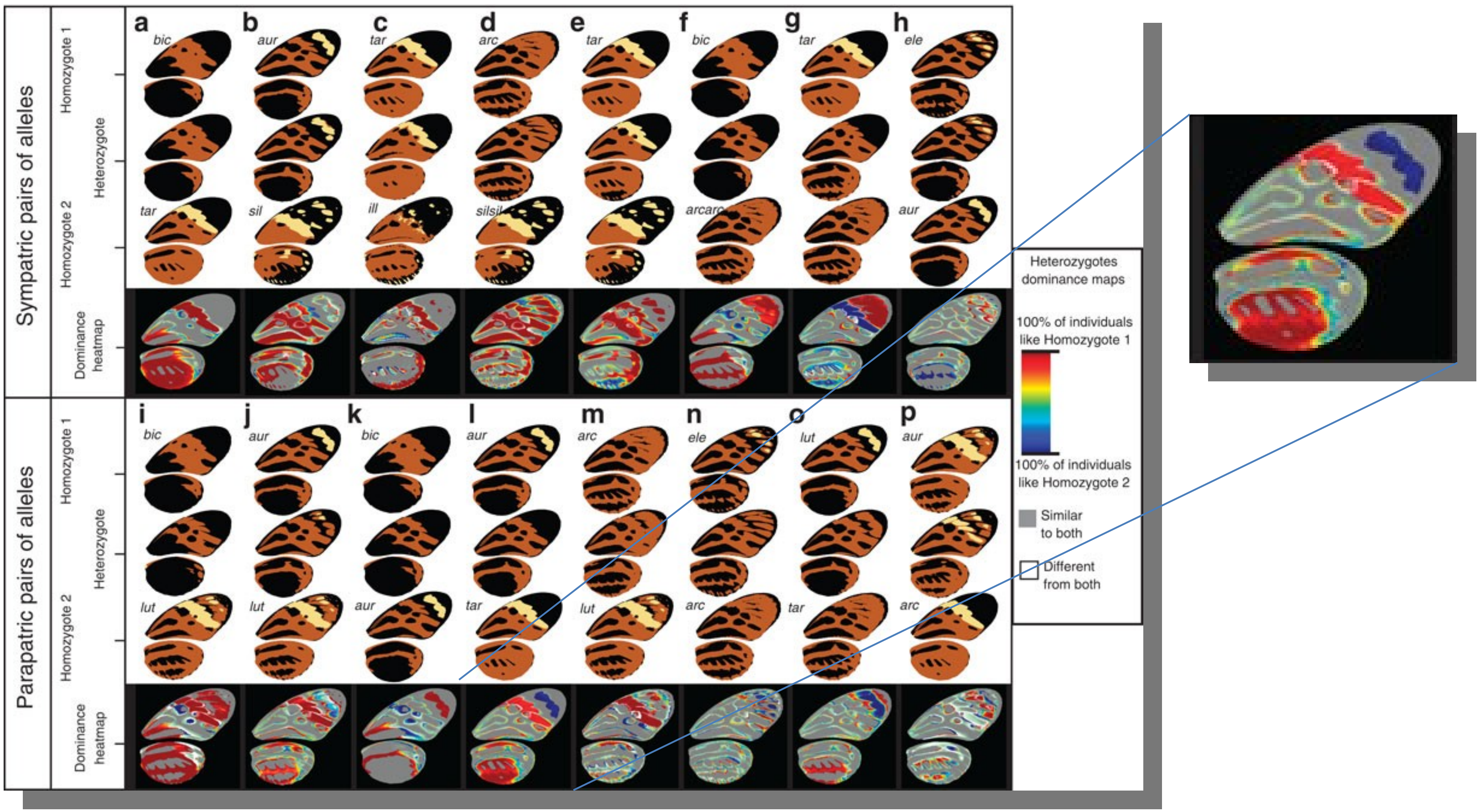
Homozygote 2

Dominance
heatmap



DOMINANCE THROUGHOUT THE WING

- Mosaic of dominance:

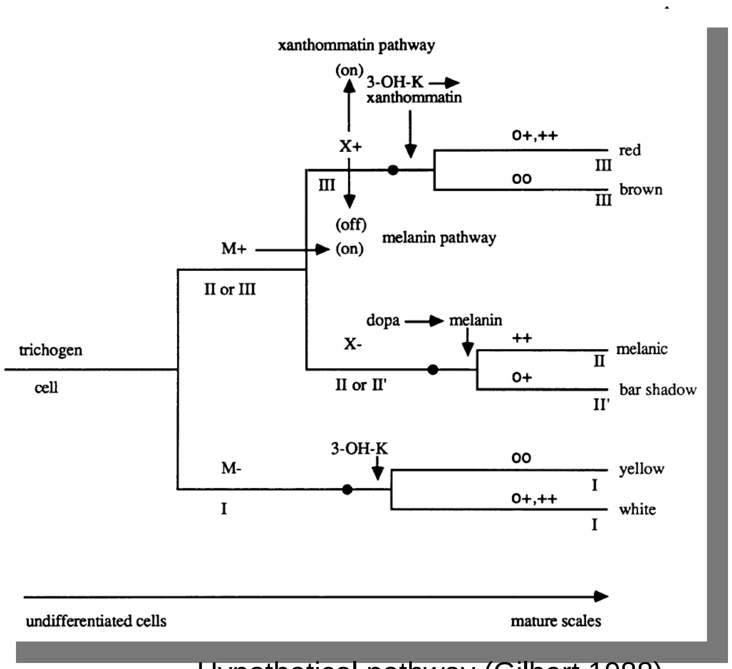


EVOLUTION OF DOMINANCE MECHANISMS

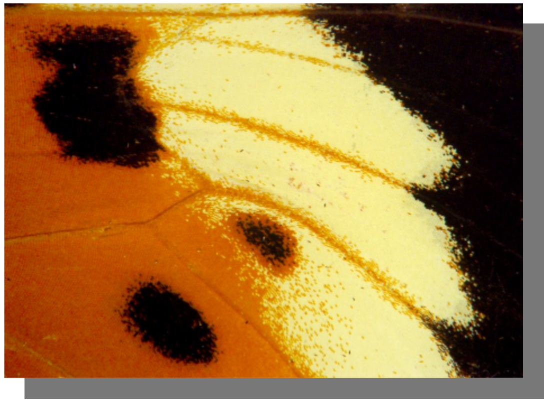
- Origin of the mosaic ?

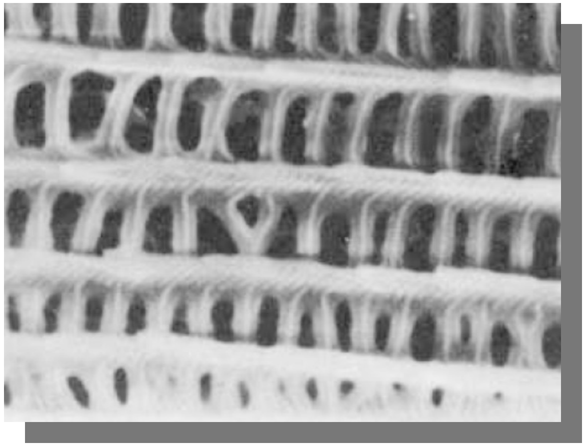
Color pattern: formed by mosaic of colored scales

- Hierarchy in color expression
- Dominance linked to developmental switch among scale types



Hypothetical pathway (Gilbert 1988)



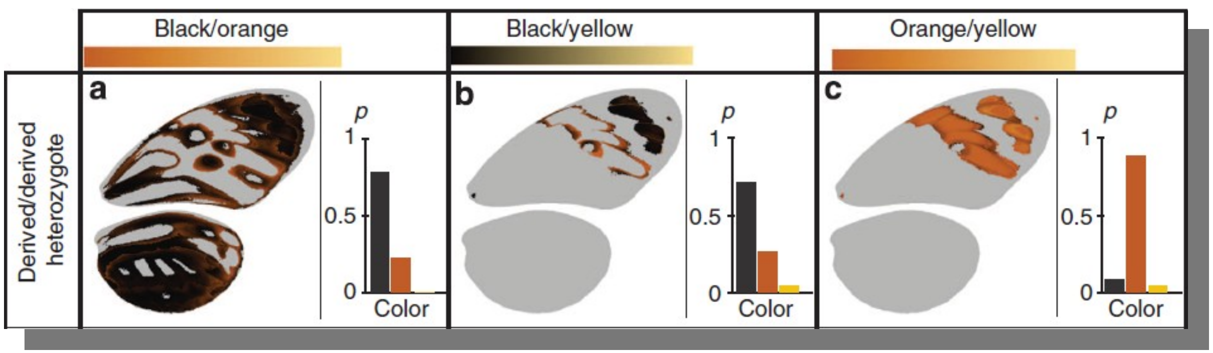


Wing scale microstructure
(Gilbert 1988)

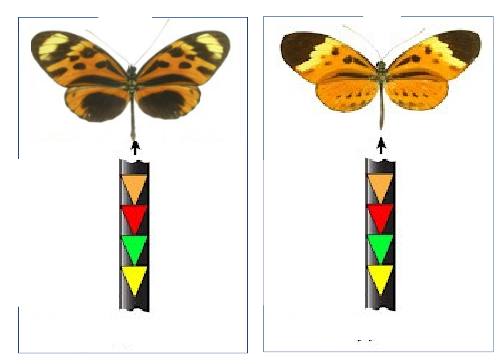
EVOLUTION OF DOMINANCE MECHANISMS

- Origin of the mosaic ? Hierarchy in colour expression in *H. numata* ?

BLACK > ORANGE> YELLOW



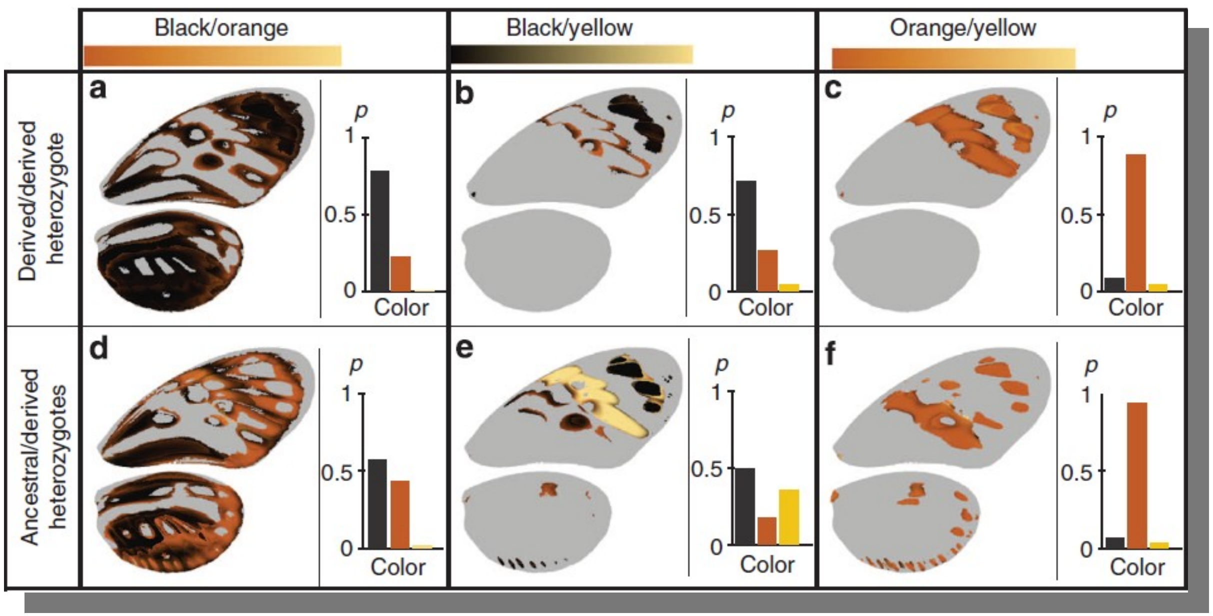
Controlling dominance between derived alleles



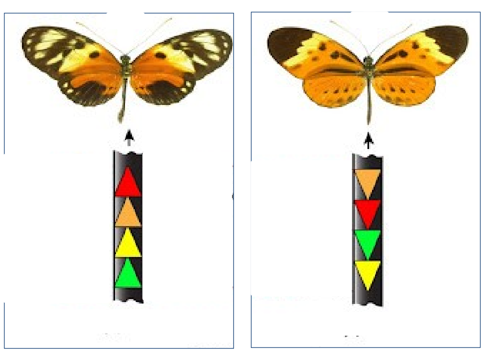
EVOLUTION OF DOMINANCE MECHANISMS

- Hierarchy in colour expression in *H. numata*

BLACK > ORANGE> YELLOW



Does not control dominance between derived and ancestral alleles



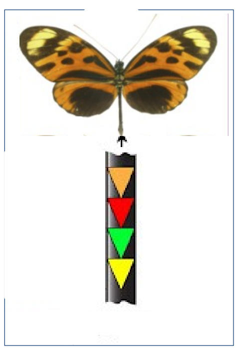
EVOLUTION OF DOMINANCE ?

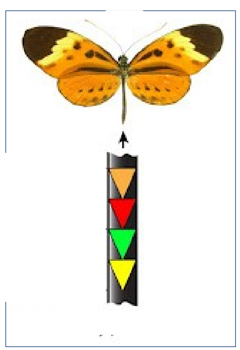
- Two distinct dominance mechanisms, associated with inversions.

Hierarchy in colour expression

BLACK > ORANGE> YELLOW

Controlling dominance among derived alleles

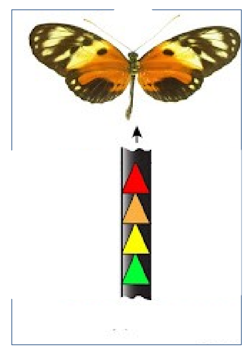




Strict dominance, independent from colours

DERIVED > ANCESTRALS

Controlling dominance between derived and ancestral alleles

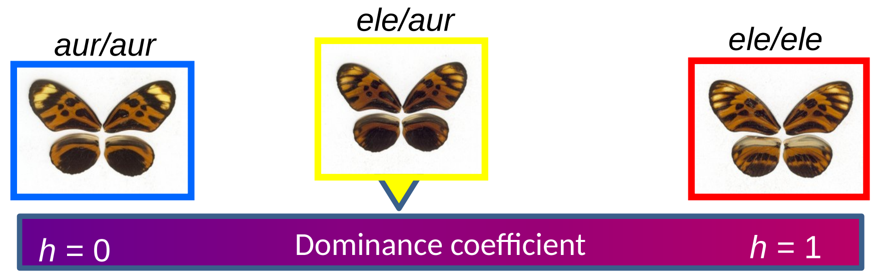


Evolution of dominance mechanisms during allelic diversification at the supergene *P* ?

MODELING THE EVOLUTION OF DOMINANCE

- Modelling dominance

$$h = \frac{T_{aur/ele} - T_{aur/aur}}{T_{ele/ele} - T_{aur/aur}}$$



Llaurens *et al.* J Theor. Biol. 2013

MODELING EVOLUTION OF DOMINANCE

- Modelling dominance

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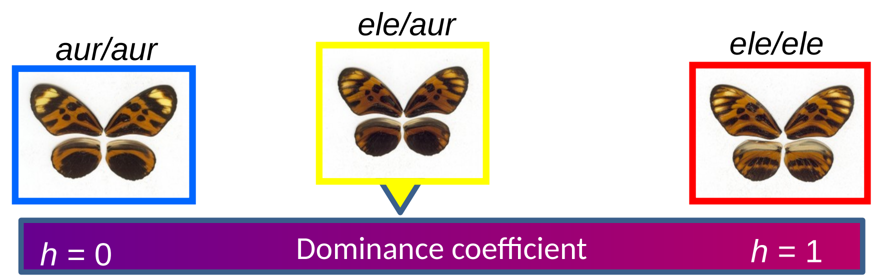
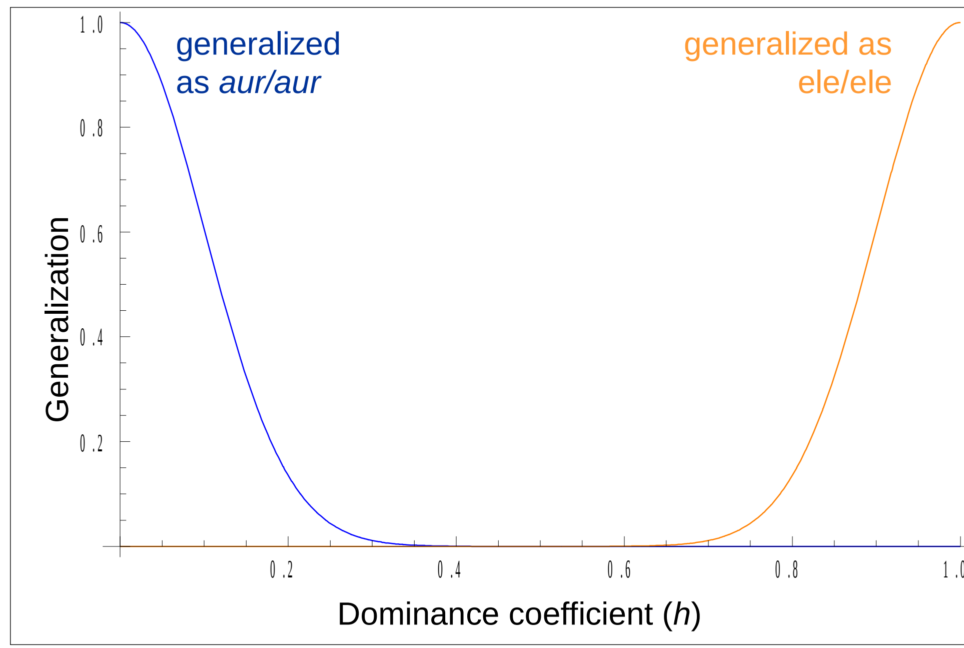


- Modelling predator behavior

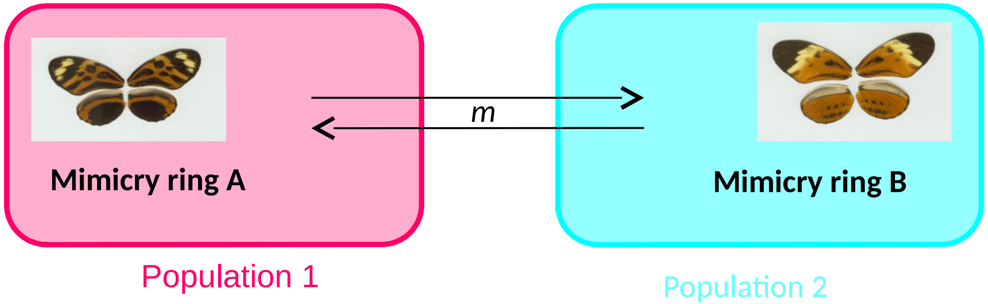
Modelling predator behavior



Llaurens *et al.* J Theor. Biol. 2013

MODELING THE EVOLUTION OF DOMINANCE

- Two mimicry rings:
  - Local rings (no migration)
  - Same abundance in each locality
- One mimetic species:
  - Two populations
  - Migration *m*



Llaurens *et al.* J Theor. Biol. 2013

MODELING THE EVOLUTION OF DOMINANCE

- Two mimicry rings:
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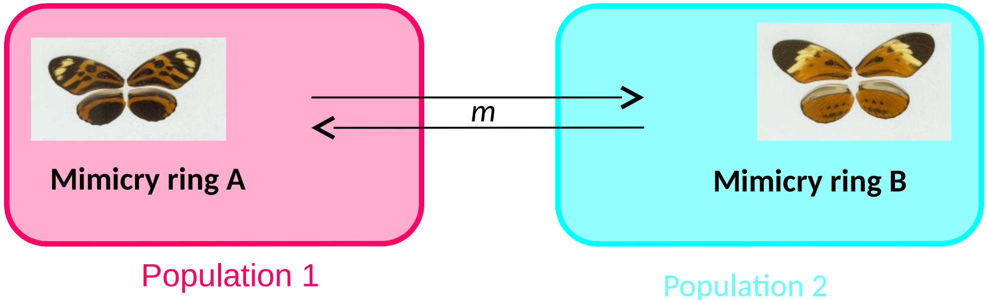
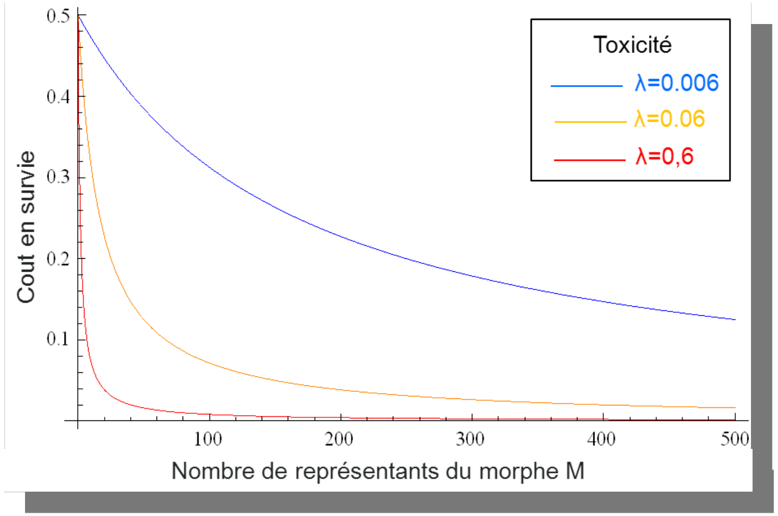
- One mimetic species:
  - Two populations
  - Migration *m*

  - Number dependent selection

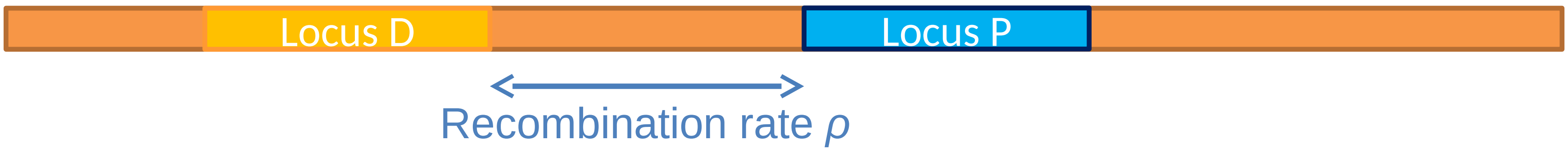




Llaurens *et al.* J Theor. Biol. 2013

EVOLUTION OF DOMINANCE THROUGH MODIFIERS ?

- Dominance modifier locus:



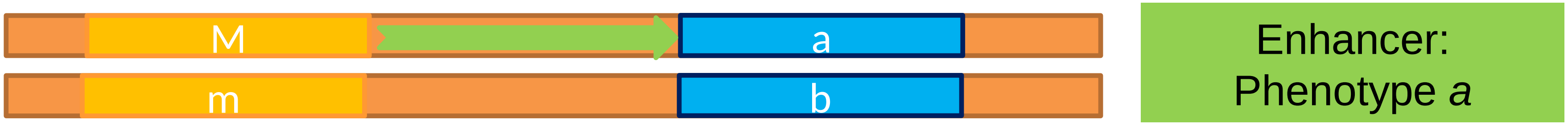
- Wild-type allele *m* with no effect
- Mutant allele *M* acting on the phenotype of heterozygotes *ab*

Mimetic alleles:
a and *b*

- The mutant *M* has an effect *e* on the dominance coefficient $h \rightarrow h+e$

MECHANIMS OF DOMINANCE MODIFICATION

- Mechanisms of dominance involving regulation of expression
  - Action : ENHANCER or REPRESSOR of expression



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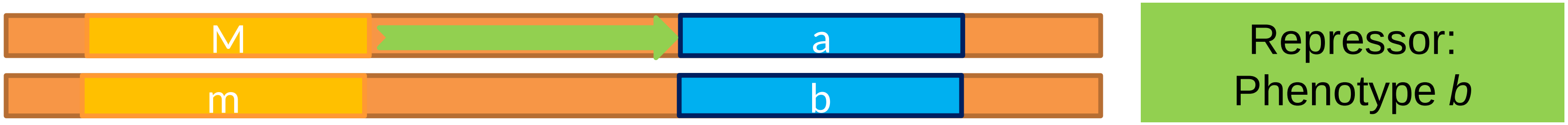
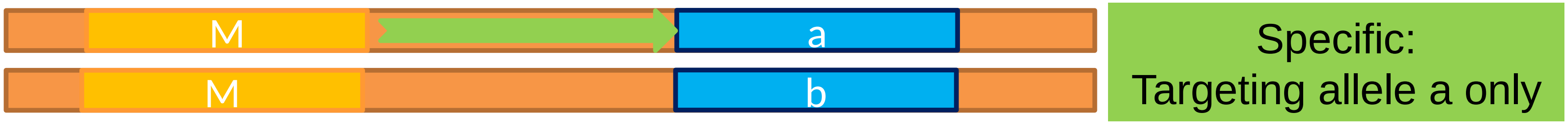


MECHANIMS OF DOMINANCE MODIFICATION

- Mechanisms of dominance involving regulation of expression
  - Action : ENHANCER or REPRESSOR of expression
  - Target specificity



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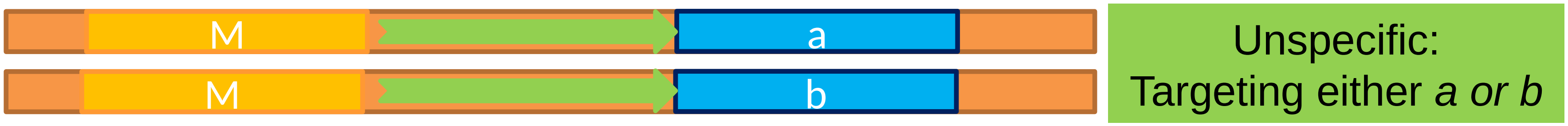


MECHANIMS OF DOMINANCE MODIFICATION

- Mechanisms of dominance involving regulation of expression
  - Action : ENHANCER or REPRESSOR of expression
  - Target specificity
  - Association

Cis-acting: Targeting the associated allele

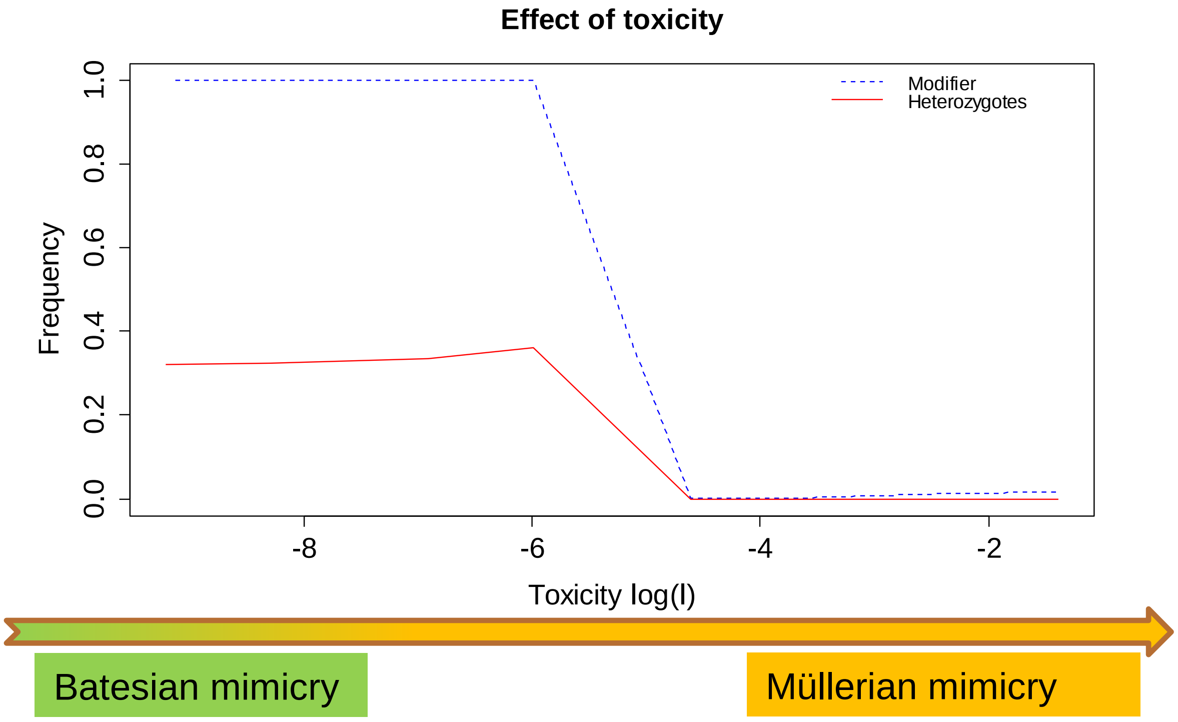
MECHANIMS OF DOMINANCE MODIFICATION

- Mechanisms of dominance involving regulation of expression
  - Action : ENHANCER or REPRESSOR of expression
  - Target specificity
  - Association

Trans-acting: Targeting the non-associated allele

INVASION CONDITIONS

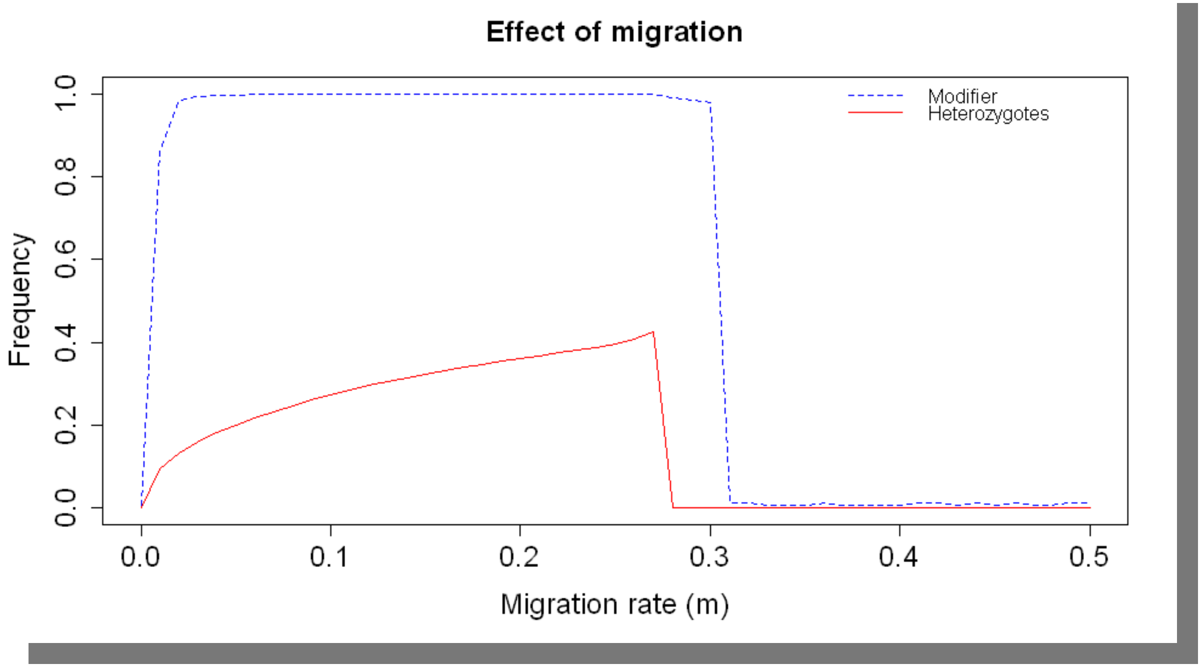
- Balancing selection as a condition of invasion for the modifier



Assuming a specific *cis* and *trans* acting enhancer
m = 0.2, h = 0.5, e = 0.5, ρ = 0.5

INVASION CONDITIONS

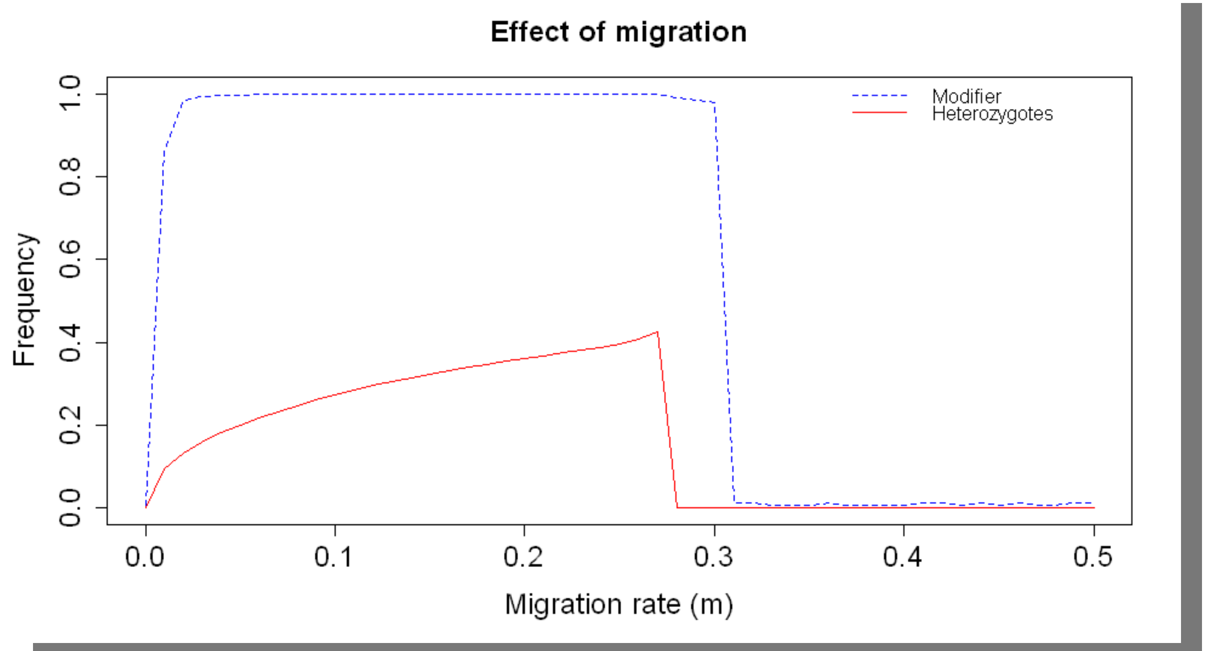
- Balancing selection as a condition of invasion for the modifier



Assuming a specific *cis* and *trans* acting enhancer
$l = 0.0025$, $h = 0.5$, $e = 0.5$, $\rho = 0.5$

INVASION CONDITIONS

- Balancing selection as a condition of invasion for the modifier



➔ DOMINANCE MODIFIERS POSITIVELY SELECTED WHEN THE COLOUR PATTERN LOCUS IS POLYMORPHIC

Assuming a specific *cis* and *trans* acting enhancer
$l = 0.0025$, $h = 0.5$, $e = 0.5$, $\rho = 0.5$

EVOLUTION OF DOMINANCE THROUGH SPECIFIC MODIFIERS ?

- Fixation of the modifier

Target specificity	Action	Association	Mutant frequency
Specific	Enhancer	cis and trans	**1.00**
Specific	Repressor	cis and trans	0.35
Unspecific	Enhancer	cis	0.50
Unspecific	Enhancer	trans	0.50
Unspecific	Repressor	cis	0.00
Unspecific	Repressor	trans	0.00
Specific	Enhancer	cis	**1.00**
Specific	Enhancer	trans	**1.00**
Specific	Repressor	cis	0.00
Specific	Repressor	trans	0.35

Assuming l = 0.0025, h = 0.5, e = 0.5, m = 0.2, ρ = 0.5

EVOLUTION OF DOMINANCE THROUGH SPECIFIC MODIFIERS ?

- Mechanisms of dominance involving regulation of expression
  - Action : ENHANCER or REPRESSOR of expression

Enhancer:
Phenotype *a*

  - Target specificity

Specific:
Targeting allele a only

  - Association

Cis-acting:
Targeting the associated allele

EVOLUTION OF DOMINANCE THROUGH SPECIFIC MODIFIERS ?

- Mechanisms of dominance involving regulation of expression
  - Action : ENHANCER or REPRESSOR of expression

Enhancer:
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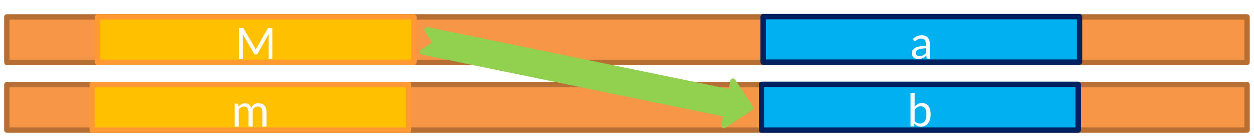
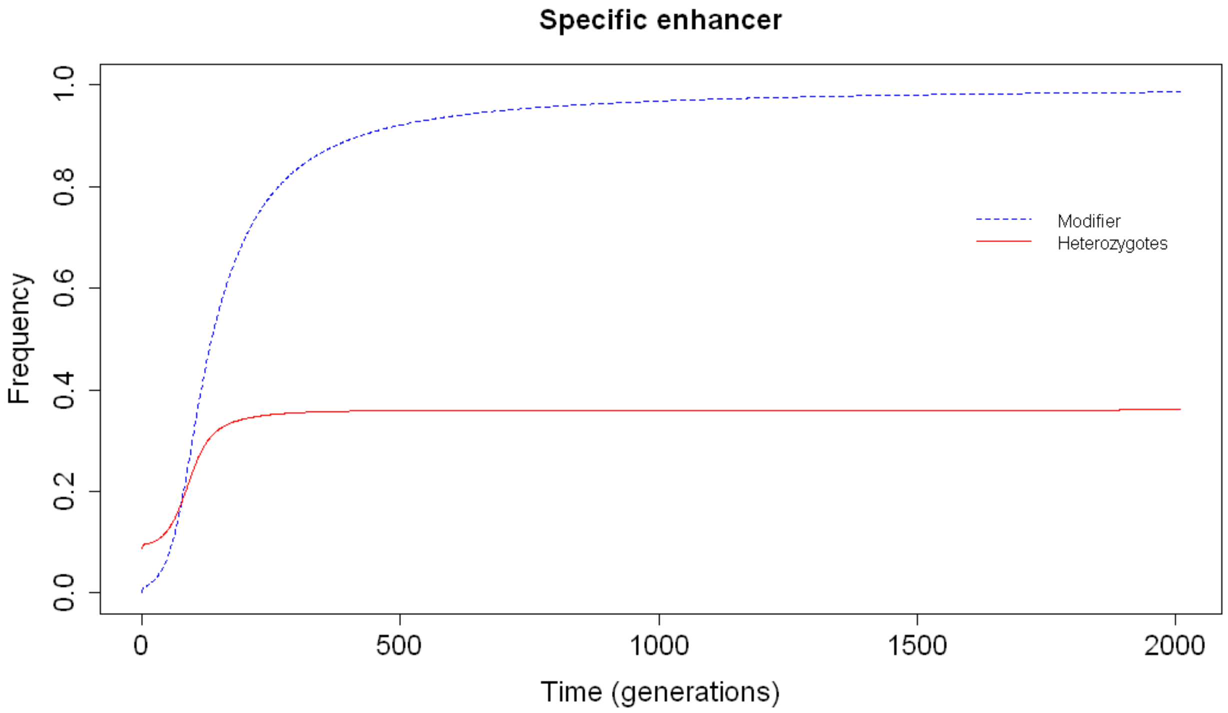


Trans-acting:
Targeting the non-associated allele

EVOLUTION OF DOMINANCE THROUGH SPECIFIC MODIFIERS ?

- Fixation of the modifier for specific enhancers



Assuming l = 0.0025, h = 0.5, e = 0.5, m = 0.2, ρ = 0.5

EVOLUTION OF DOMINANCE THROUGH **UN**SPECIFIC MODIFIERS ?

- Fixation of the modifier

Target specificity	Action	Association	Mutant frequency
Specific	Enhancer	cis and trans	1.00
Specific	Repressor	cis and trans	0.35
Unspecific	Enhancer	cis	**0.50**
Unspecific	Enhancer	trans	**0.50**
Unspecific	Repressor	cis	0.00
Unspecific	Repressor	trans	0.00
Specific	Enhancer	cis	1.00
Specific	Enhancer	trans	1.00
Specific	Repressor	cis	0.00
Specific	Repressor	trans	0.35

Assuming $l = 0.0025$, $h = 0.5$, $e = 0.5$, $m = 0.2$, $\rho = 0.5$

EVOLUTION OF DOMINANCE THROUGH SPECIFIC MODIFIERS ?

- Mechanisms of dominance involving regulation of expression
  - Action : ENHANCER or REPRESSOR of expression

Enhancer:
Phenotype *a*

  - Target specificity

Unspecific:
Targeting the associated allele

  - Association

Cis-acting:
Targeting the allele on the same chromosome

EVOLUTION OF DOMINANCE THROUGH **UN**SPECIFIC MODIFIERS ?

- Mechanisms of dominance involving regulation of expression
  - Action : ENHANCER or REPRESSOR of expression

Enhancer:
Phenotype *a*

  - Target specificity

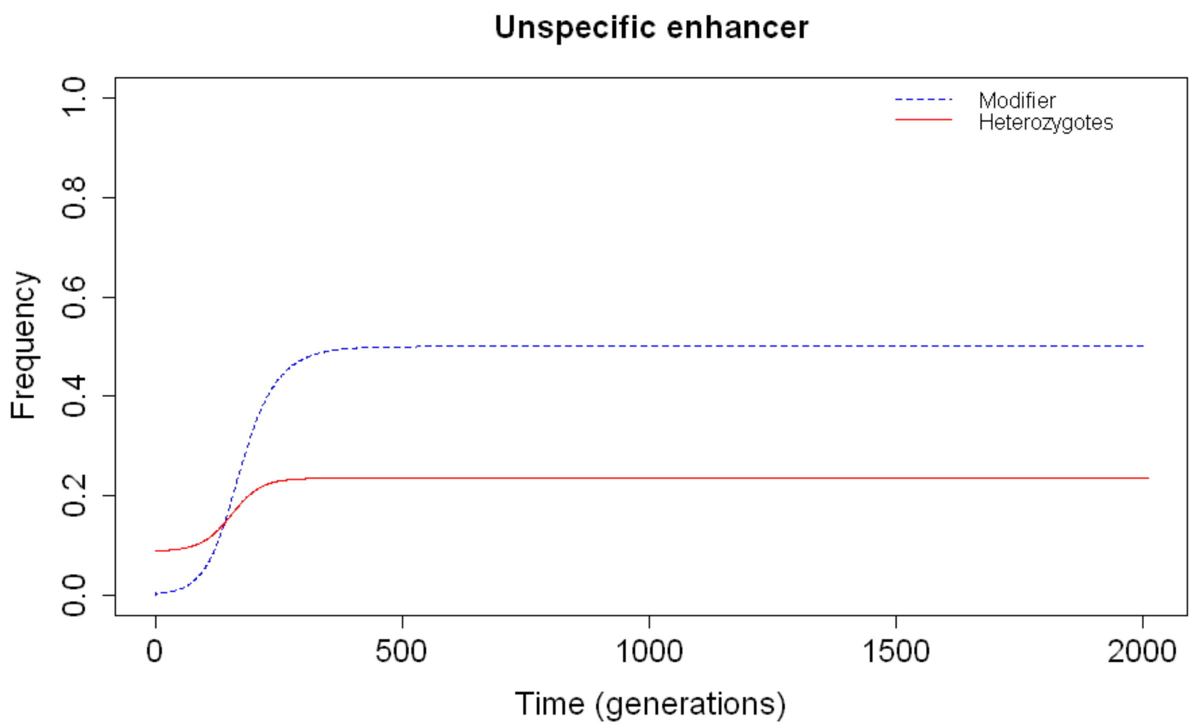
Unspecific:
Targeting allele the associated allele

  - Association

Trans-acting:
Targeting the non-associated allele

EVOLUTION OF DOMINANCE THROUGH **UN**SPECIFIC MODIFIERS ?

- Persistence of the modifier at medium frequency: balancing selection on **unspecific enhancers**



Assuming l = 0.0025, h = 0.5, e = 0.5, m = 0.2, ρ = 0.5

EVOLUTION OF DOMINANCE THROUGH SPECIFIC *TRANS*-ACTING **REPRESSORS** ?

- Fixation of the modifier

Target specificity	Action	Association	Mutant frequency
Specific	Enhancer	cis and trans	1.00
Specific	Repressor	cis and trans	**0.35**
Unspecific	Enhancer	cis	0.50
Unspecific	Enhancer	trans	0.50
Unspecific	Repressor	cis	0.00
Unspecific	Repressor	trans	0.00
Specific	Enhancer	cis	1.00
Specific	Enhancer	trans	1.00
Specific	Repressor	cis	0.00
Specific	Repressor	trans	**0.35**

Assuming l = 0.0025, h = 0.5, e = 0.5, m = 0.2, ρ = 0.5

EVOLUTION OF DOMINANCE THROUGH SPECIFIC *TRANS*-ACTING **REPRESSORS** ?

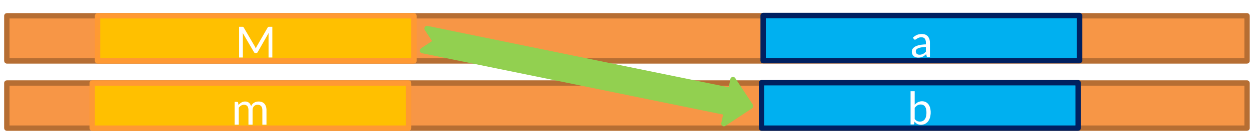
- Mechanisms of dominance involving regulation of expression
  - Action : ENHANCER or REPRESSOR of expression

Repressor
Phenotype *b*

  - Target specificity

Specific:
Targeting allele a only

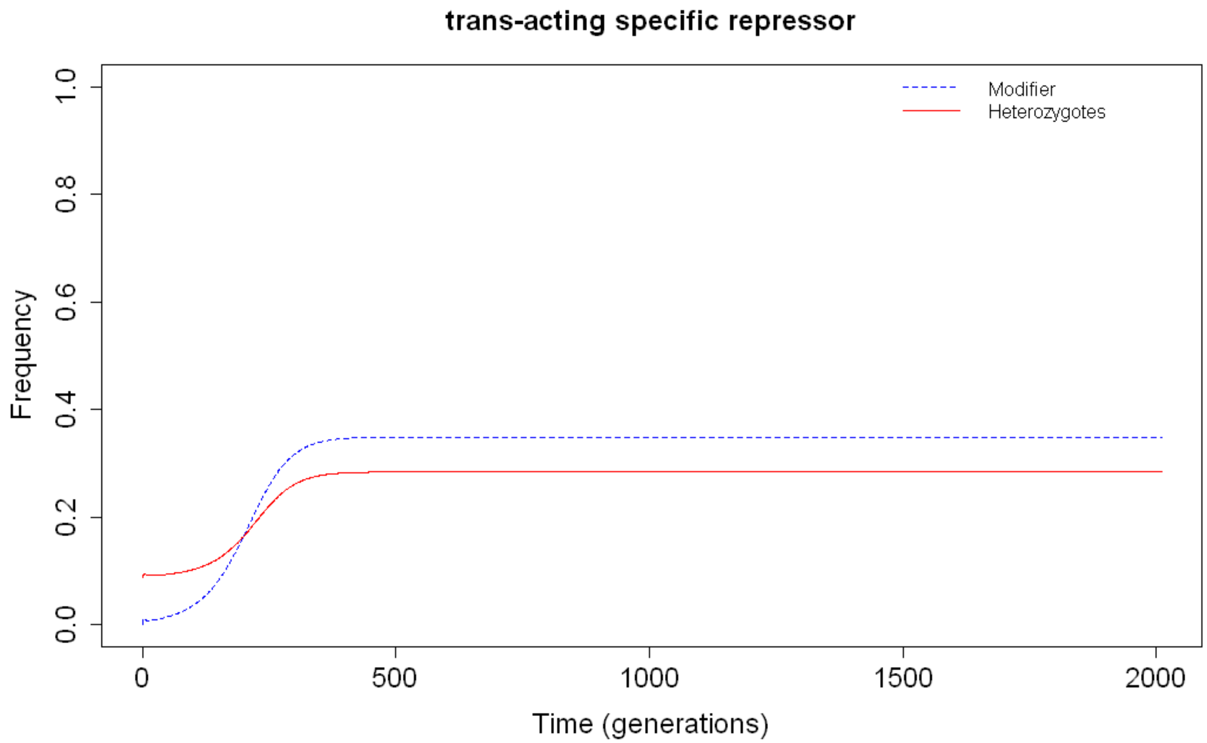
  - Association



Trans-acting:
Targeting the non-associated allele

EVOLUTION OF DOMINANCE THROUGH SPECIFIC *TRANS*-ACTING REPRESSORS ?

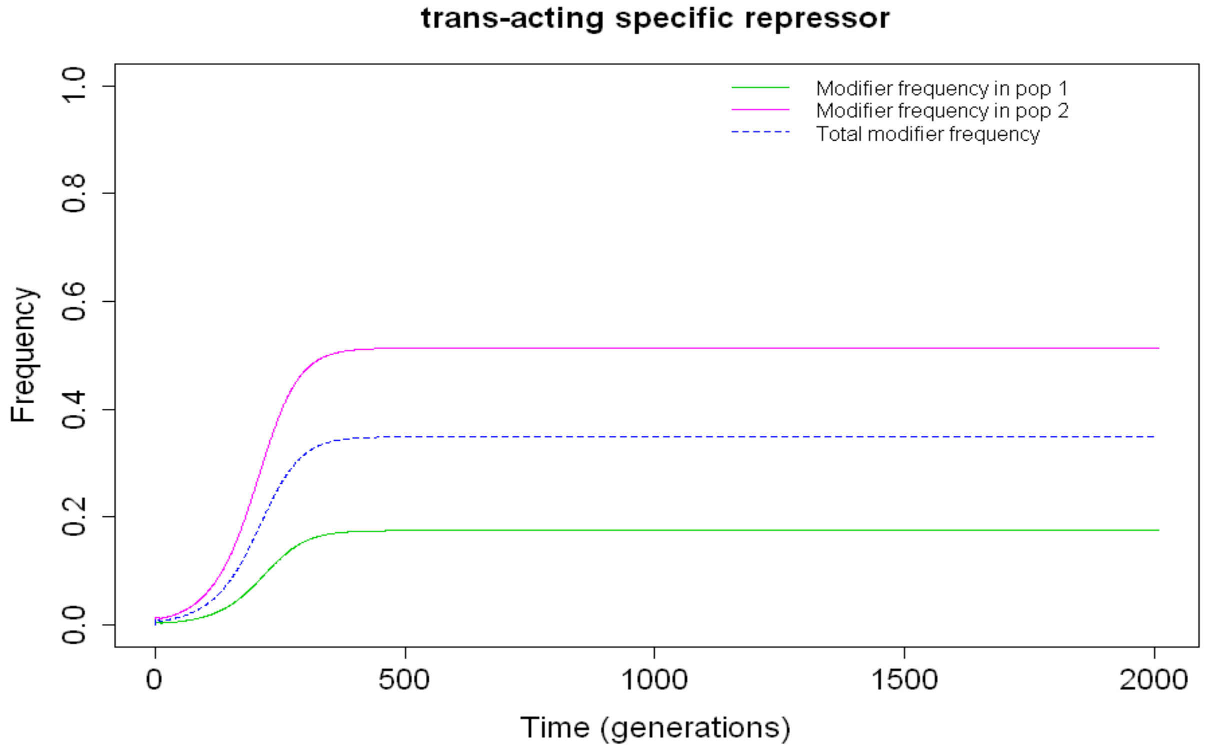
- Persistence of the modifier at medium frequency: balancing selection on unspecific enhancers and **specific trans-acting repressors**



Assuming *l* = 0.0025, *h* = 0.5, *e* = 0.5, *m* = 0.2, *ρ* = 0.5

EVOLUTION OF DOMINANCE THROUGH SPECIFIC *TRANS*-ACTING REPRESSORS ?

- Persistence of the modifier at medium frequency: balancing selection on unspecific enhancers and **specific trans-acting repressors**



Assuming l = 0.0025, h = 0.5, e = 0.5, m = 0.2, ρ = 0.5

EVOLUTION OF DOMINANCE THROUGH REPRESSORS ?

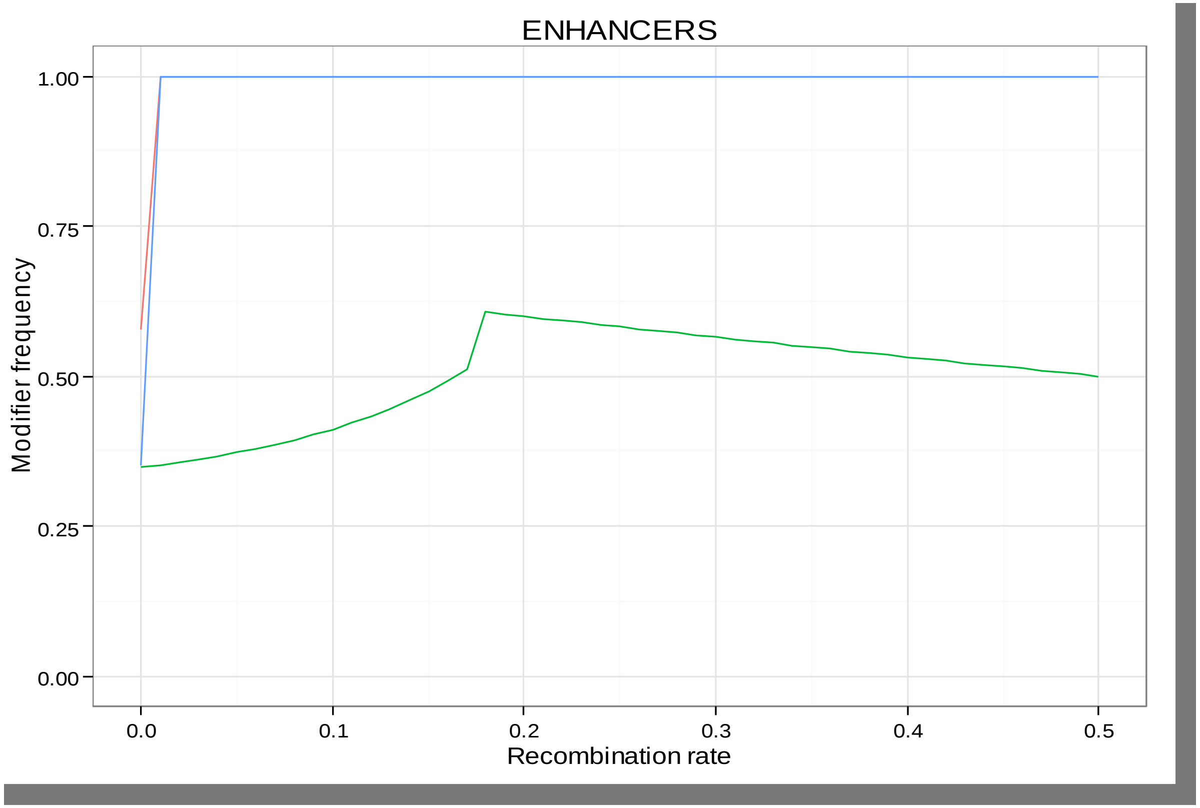
- Eliminated modifiers: negative impact of the modifier on the phenotype of homozygotes *aa*

Target specificity	Action	Association	Mutant frequency
Specific	Enhancer	cis and trans	1.00
Specific	Repressor	cis and trans	0.35
Unspecific	Enhancer	cis	0.50
Unspecific	Enhancer	trans	0.50
Unspecific	Repressor	cis	**0.00**
Unspecific	Repressor	trans	**0.00**
Specific	Enhancer	cis	1.00
Specific	Enhancer	trans	1.00
Specific	Repressor	cis	**0.00**
Specific	Repressor	trans	0.35

Assuming l = 0.0025, h = 0.5, e = 0.5, m = 0.2, ρ = 0.5

IMPACT OF RECOMBINATION

- On **cis- acting enhancer** frequency



Specific

Unspecific

Assuming *l* = 0.0025, *h* = 0.5, *e* = 0.5, *m* = 0.2

EVOLUTION OF DOMINANCE THROUGH MODIFIERS

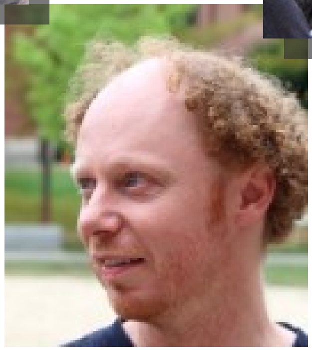
- Positive selection on dominance BUT invasion of modifier depend on the molecular mechanisms involved
- Specific modifiers are likely to get fixed in populations
- Unspecific modifiers could be maintained in populations
  - Modifier under balancing selection themselves
  - Spatial heterogeneity of modifiers
- Fixation of modifiers decrease the overall predation risk

Llaurens *et al.* 2015 Evolution.

Thank you for your attention

- Thanks to collaborators
- Fundings: ATM “Formes, Labex BcDiv, UMR7205, ANR Domevol, Projet ‘Emergence’ – ville de Paris



EVOLUTION OF DOMINANCE THROUGH **UN**SPECIFIC MODIFIERS ?

- Persistence of the modifier at medium frequency: balancing selection on **unspecific enhancers**

					Frequency of a at locus P			Frequency of M at locus D			
Model Family	Model number	Target specificity	Action	Association	Pop. 1	Pop. 2	Overall	Pop. 1	Pop. 2	Overall	Δ Population size
I	1	Specific	Enhancer	cis and trans	0.53	0.17	0.35	1.00	1.00	1.00	89.34
	3	Specific	Repressor	cis and trans	0.79	0.38	0.58	0.18	0.51	0.35	25.34
II	4	**Unspecific**	Enhancer	cis	0.73	0.27	0.50	0.50	0.50	0.50	29.35
	5	**Unspecific**	Enhancer	trans	0.73	0.27	0.50	0.50	0.50	0.50	29.35
	6	Unspecific	Repressor	cis	0.78	0.22	0.50	0.00	0.00	0.00	0.00
	7	Unspecific	Repressor	trans	0.78	0.22	0.50	0.00	0.00	0.00	0.00
III	8	Specific	Enhancer	cis	0.53	0.17	0.35	1.00	1.00	1.00	89.34
	9	Specific	Enhancer	trans	0.53	0.17	0.35	1.00	1.00	1.00	89.34
	11	Specific	Repressor	cis	0.78	0.22	0.50	0.00	0.00	0.00	0.00
	13	Specific	Repressor	trans	0.78	0.35	0.56	0.18	0.51	0.35	15.32

Assuming $l = 0.0025$, $h = 0.5$, $e = 0.5$, $m = 0.2$, $\rho = 0.5$

INFLUENCE OF MODIFIER'S INVASION ON POPULATION SIZE

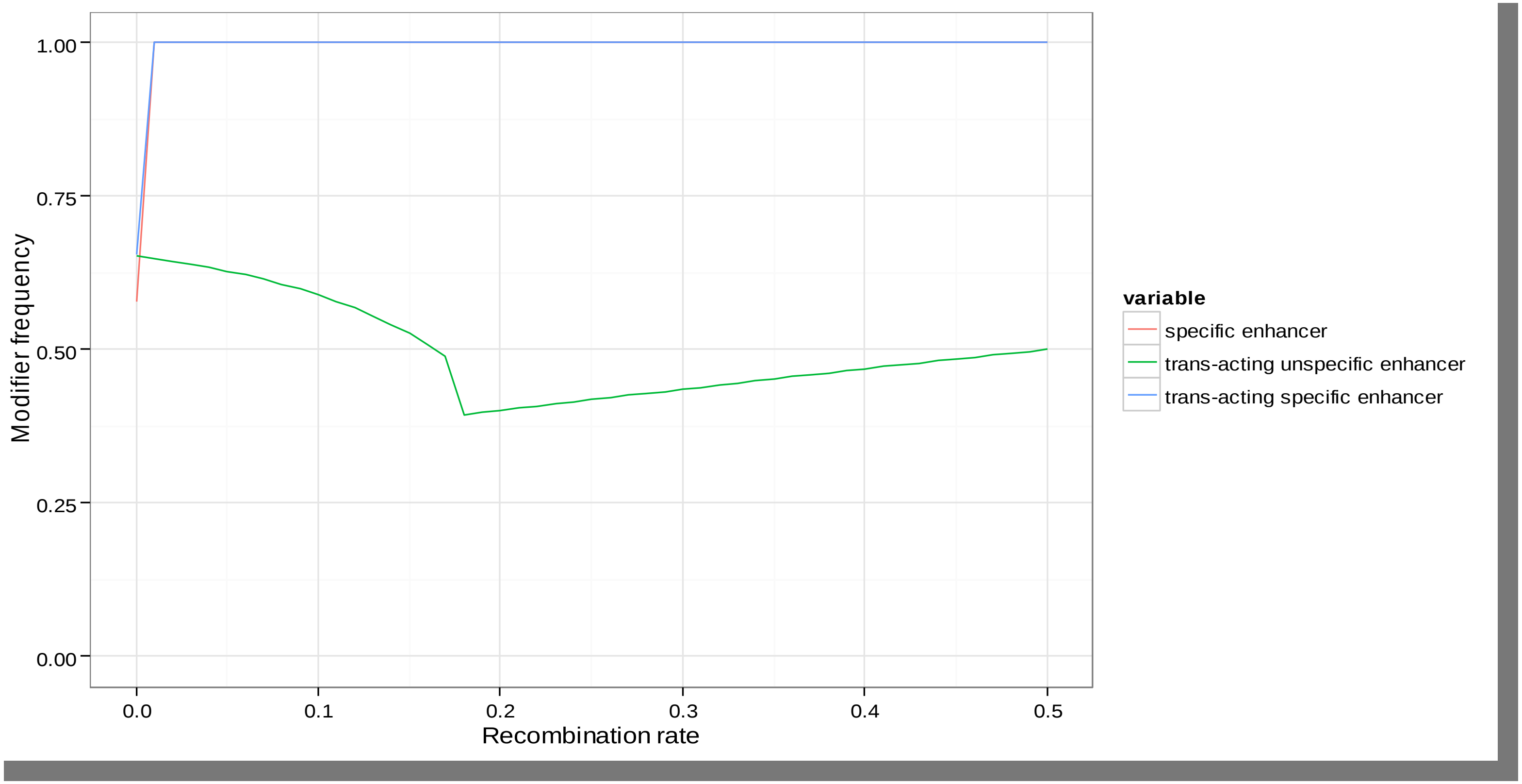
- Fixation of modifier increases population size of 5.84%

					Frequency of a at locus P			Frequency of M at locus D			
Model Family	Model number	Target specificity	Action	Association	Pop. 1	Pop. 2	Overall	Pop. 1	Pop. 2	Overall	Δ Population size
I	1	Specific	Enhancer	cis and trans	0.53	0.17	0.35	1.00	1.00	1.00	89.34
	3	Specific	Repressor	cis and trans	0.79	0.38	0.58	0.18	0.51	0.35	25.34
II	4	Unspecific	Enhancer	cis	0.73	0.27	0.50	0.50	0.50	0.50	29.35
	5	Unspecific	Enhancer	trans	0.73	0.27	0.50	0.50	0.50	0.50	29.35
	6	Unspecific	Repressor	cis	0.78	0.22	0.50	0.00	0.00	0.00	0.00
	7	Unspecific	Repressor	trans	0.78	0.22	0.50	0.00	0.00	0.00	0.00
III	8	Specific	Enhancer	cis	0.53	0.17	0.35	1.00	1.00	1.00	89.34
	9	Specific	Enhancer	trans	0.53	0.17	0.35	1.00	1.00	1.00	89.34
	11	Specific	Repressor	cis	0.78	0.22	0.50	0.00	0.00	0.00	0.00
	13	Specific	Repressor	trans	0.78	0.35	0.56	0.18	0.51	0.35	15.32

Assuming $l = 0.0025$, $h = 0.5$, $e = 0.5$, $m = 0.2$, $\rho = 0.5$

EVOLUTION OF DOMINANCE THROUGH UNLINKED MODIFIERS ?

- Impact of recombination on enhancer frequency



Assuming *l* = 0.0025, *h* = 0.5, *e* = 0.5, *m* = 0.2