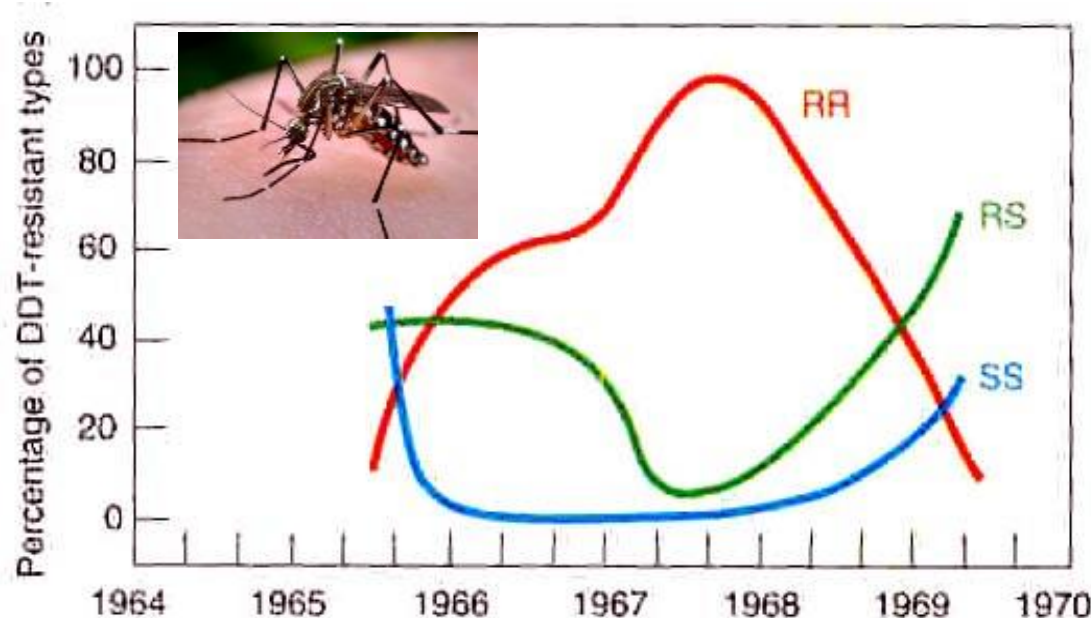


Selection and Adaptive Potential

Adam Stow

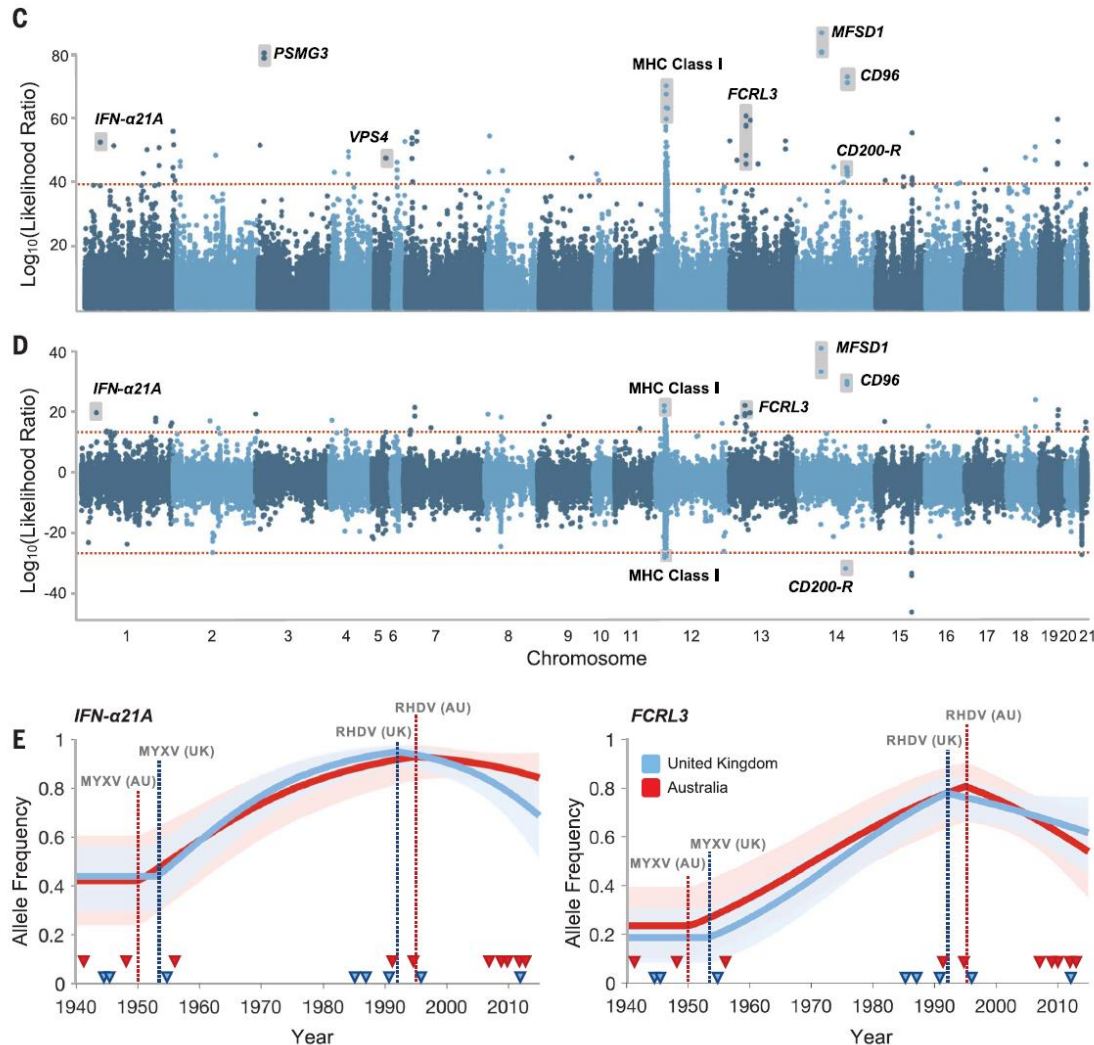
What is adaptive potential?

The ability of a population to respond adaptively to a new selective pressure



How genotype frequencies among populations of *A. aegypti* mosquito larvae change in response to Insecticide. (a) Mosquitoes and larvae. (b) Changing proportions of resistance genotypes of *A. aegypti* (larvae) under selection with DDT, and after selection was relaxed, in a suburb of Bangkok, Thailand.

Enough standing genetic variation for evolution



Alleles selected for
by myxoma virus

Decrease in
Myxoma virulence

Can we use genomics to estimate adaptive potential?

Using genomics to characterize evolutionary potential for conservation of wild populations

Katherine A. Harrisson, Alexandra Pavlova, Marina Telonis-Scott and Paul Sunnucks

Evolutionary Applications

doi:10.1111/eva.12149

We could try and get estimates from genes of known function....but,

Given the current levels of understanding of how genomes work in non-model organisms screening genome wide diversity will usually give a better estimate of evolutionary potential.

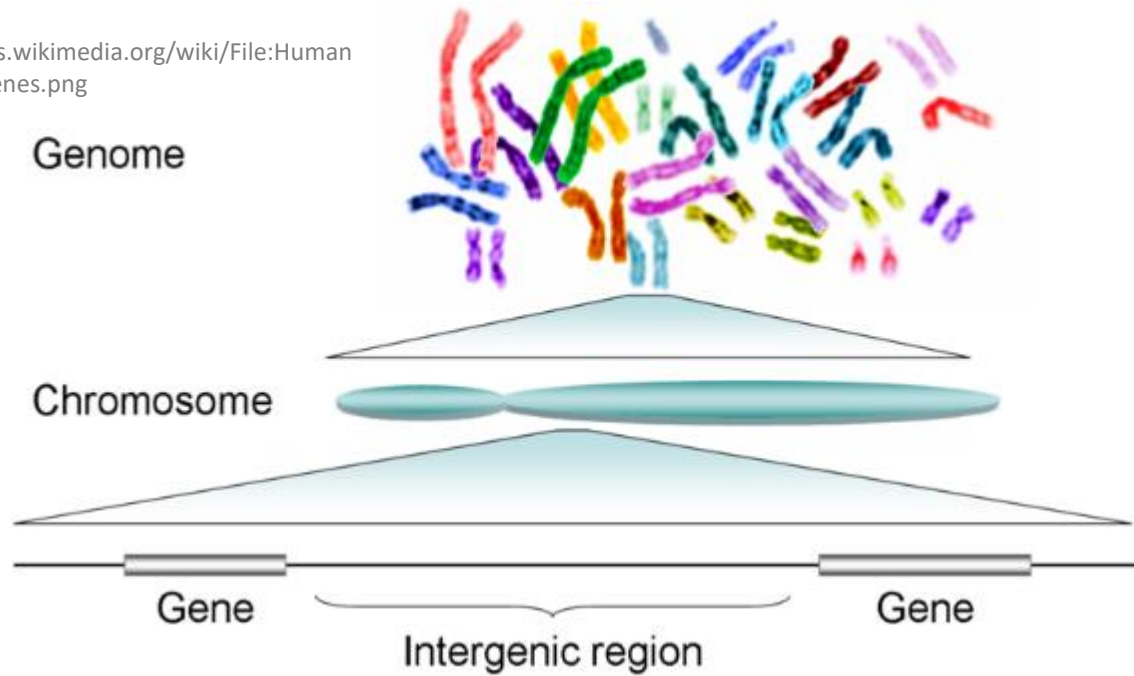
Two distinct components of evolutionary potential

- **Genetic** (DNA-sequence-based)
- **Epigenetic** (non-DNA-sequence-based)

Molecular basis of evolutionary potential		
Epigenetic	Genetic (sequence-based)	
<i>Histone modification, DNA methylation, small non-coding RNAs (microRNA, small interfering RNA)</i>	<i>Distal/long-range transcription factor binding sites (enhancers), splice junctions, splicing enhancers, synonymous mutations, silencers, tandem repeats, non-coding variation of unknown function</i>	<i>Non-synonymous coding changes, known transcription factor binding sites (enhancers/promoters)</i>
Unknown	small	LARGE
effect size on phenotype	effect size on phenotype	

Adaptive variation has been found in parts of the genome previously thought non-functional

Figure:
http://commons.wikimedia.org/wiki/File:Human_genome_to_genes.png



Comparing rat and mouse genomes, a great number of evolutionarily conserved sequences (i.e probably have a function) were intergenic, far from known genes

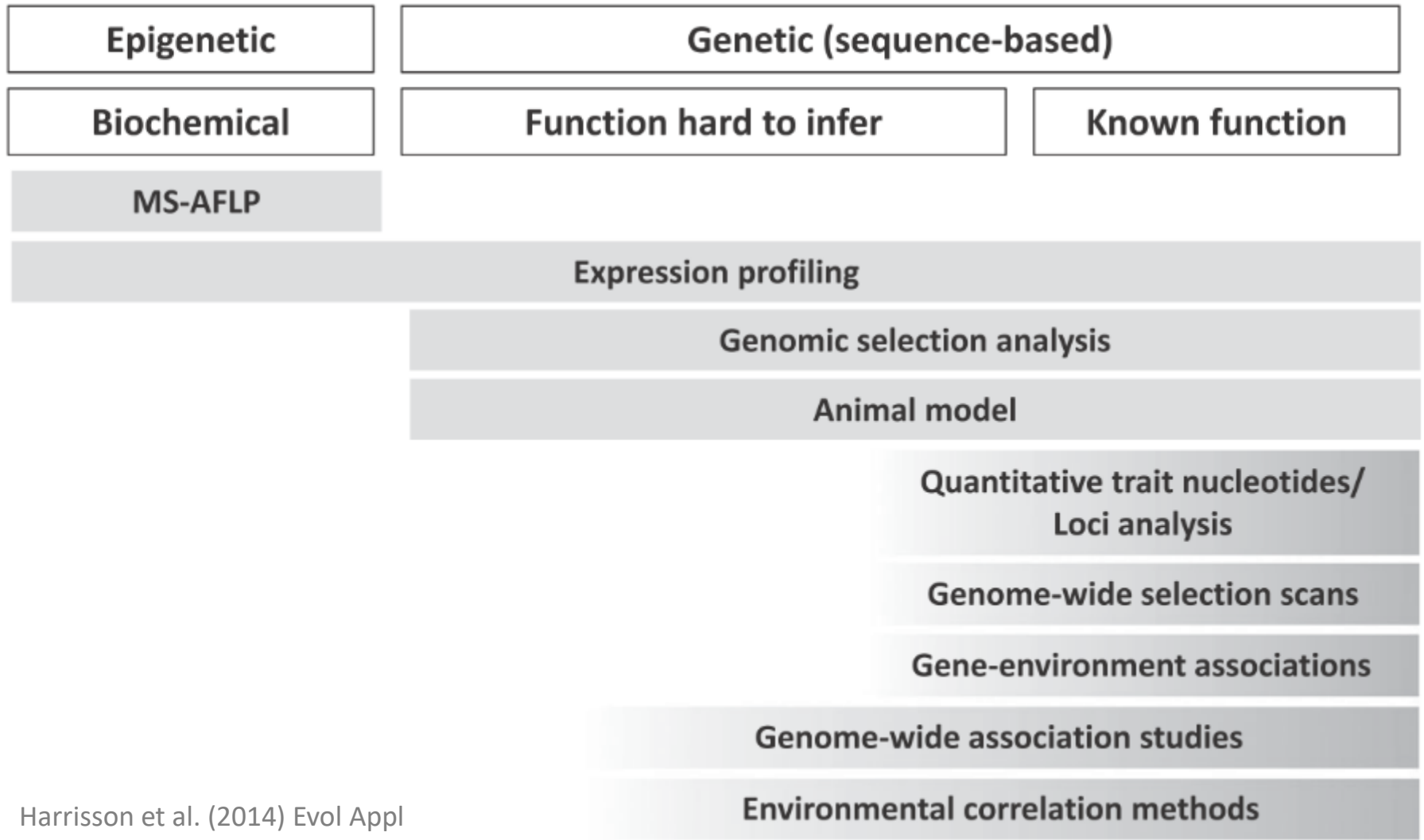
How much of the genome has a function?

- In humans only ~ 1.5% of sequence codes for amino acids
- at least ~ 10–15% of sequence is evolutionarily conserved in a way that suggests it is potentially under selection and has a function

To better understand evolutionary potential and what drives localised adaptation it's useful to find parts of the genome influenced by selection.

How is it done, and how effective is it?

Methods to infer selection are complex, numerous, emerging



Three main recent insights into evolutionary potential

summarized by Harrison et al. 2014:

- (1) Rapid adaptive evolution is driven predominantly by changes in gene expression
- (2) Most traits are polygenic (controlled by lots of genes of small effect)
- (3) Most recent adaptation is due to subtle shifts of allele frequencies

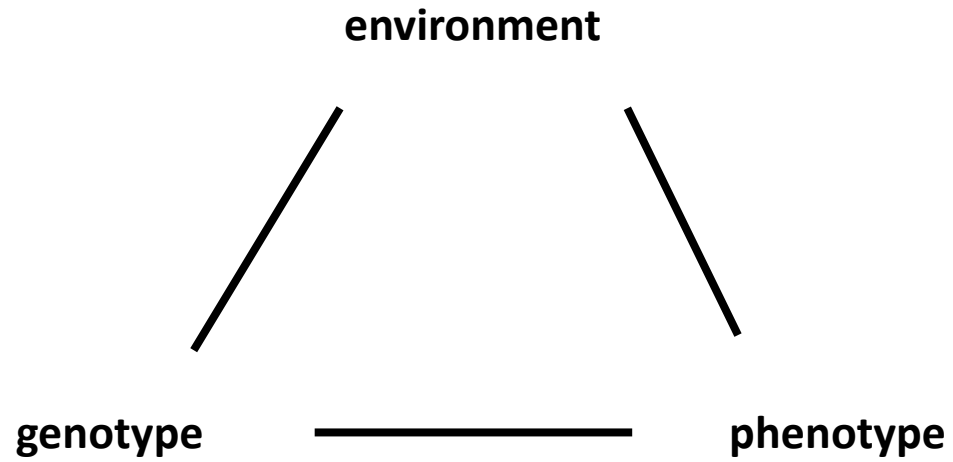
Detecting environmental selection using genomic data

Goals

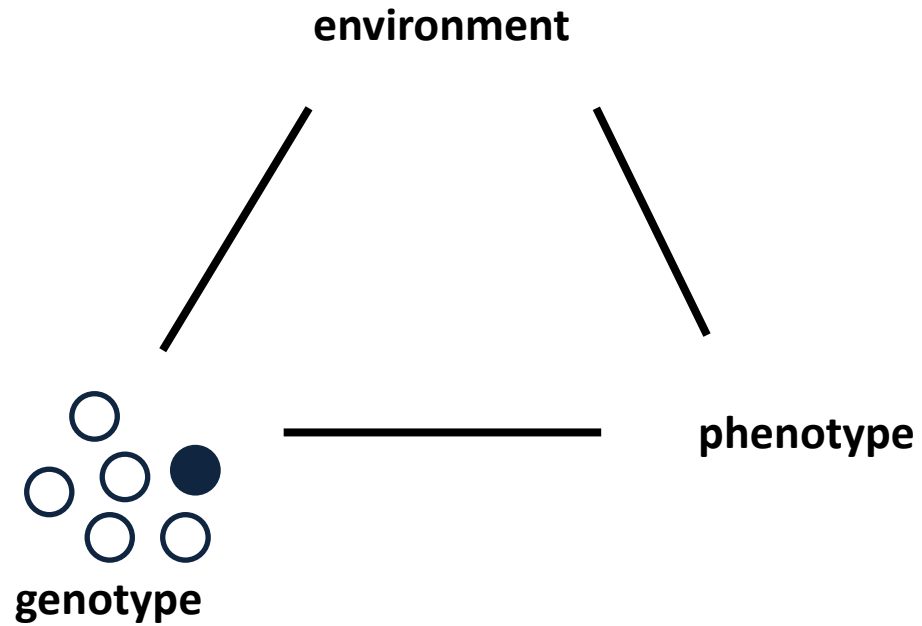
environmental variables that shape adaptive variation

gene variants that drive local adaptation

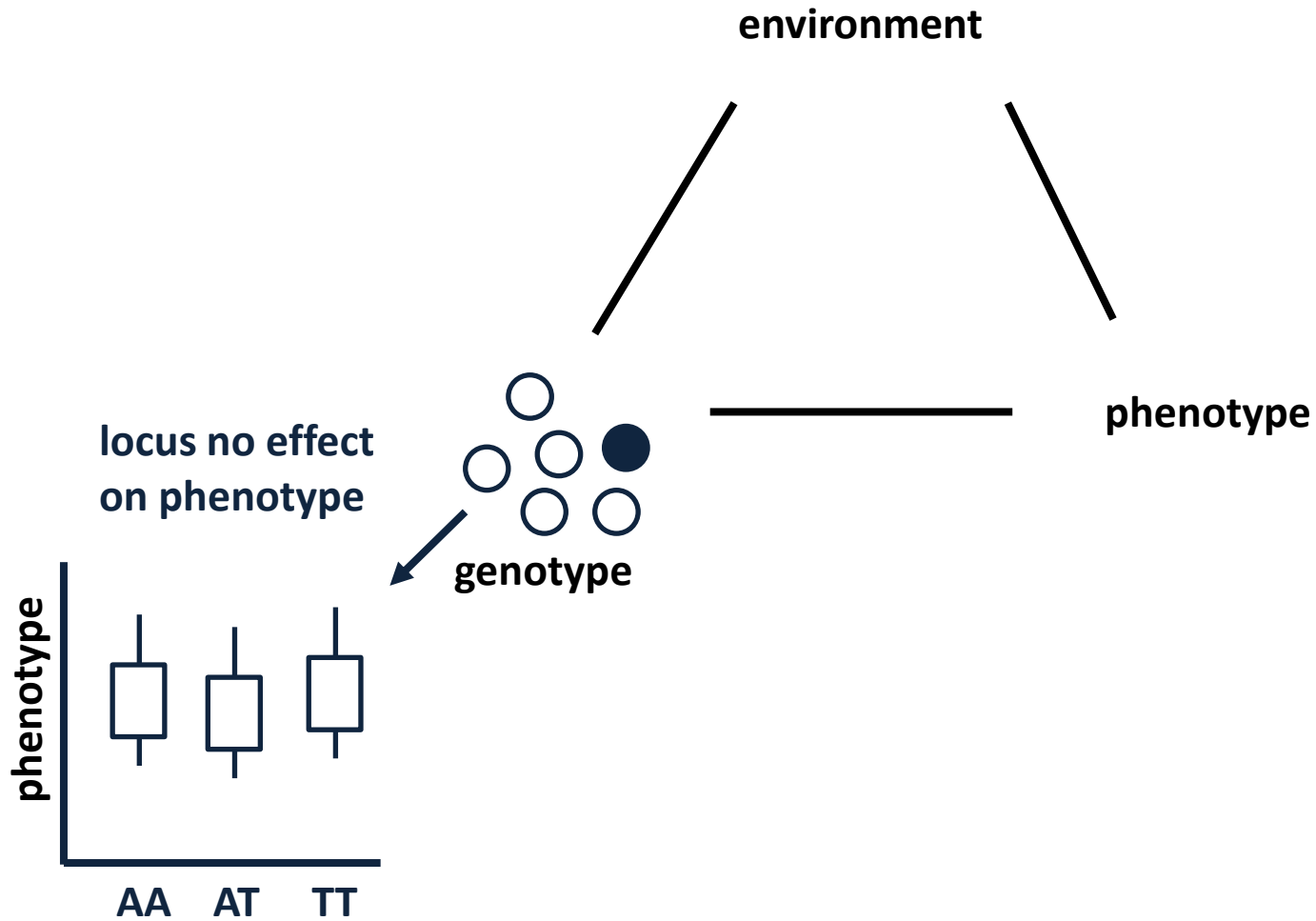
Adaptation: process and patterns



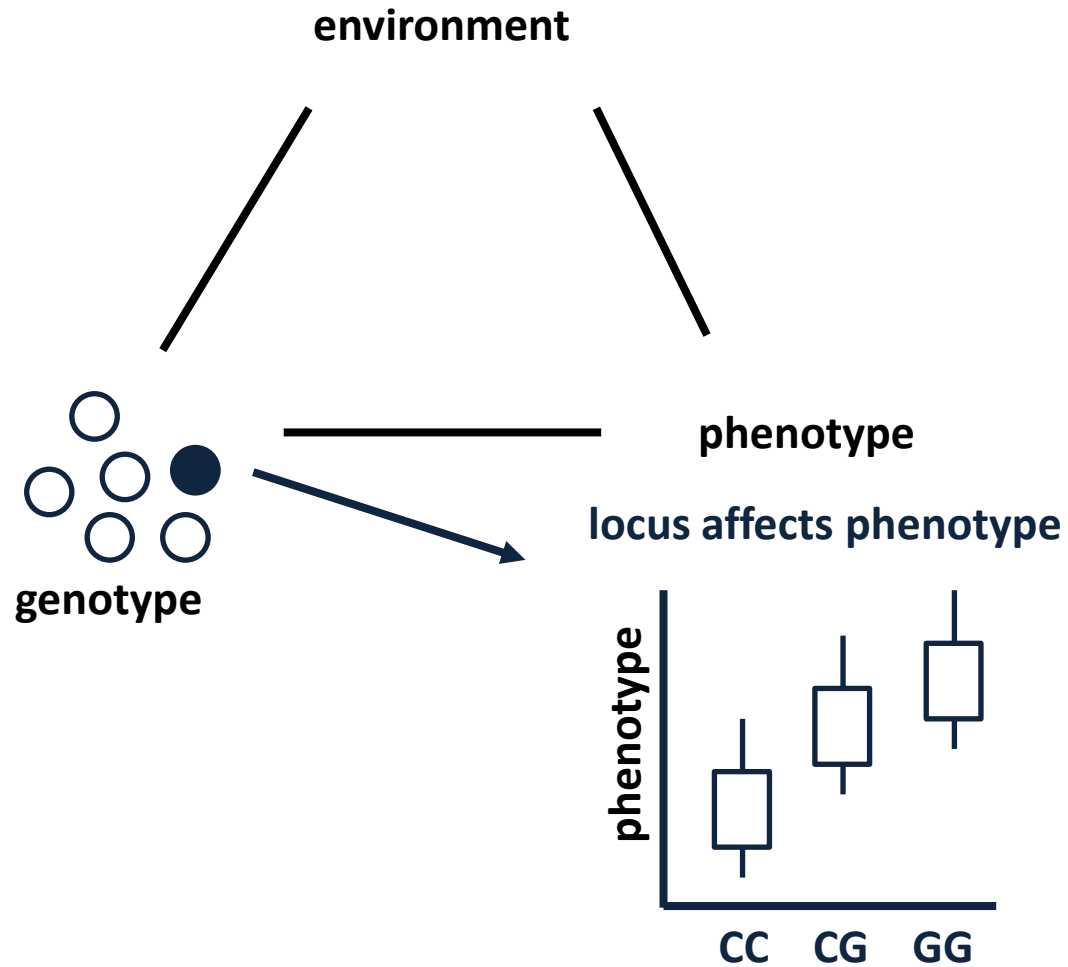
Adaptation: process and patterns



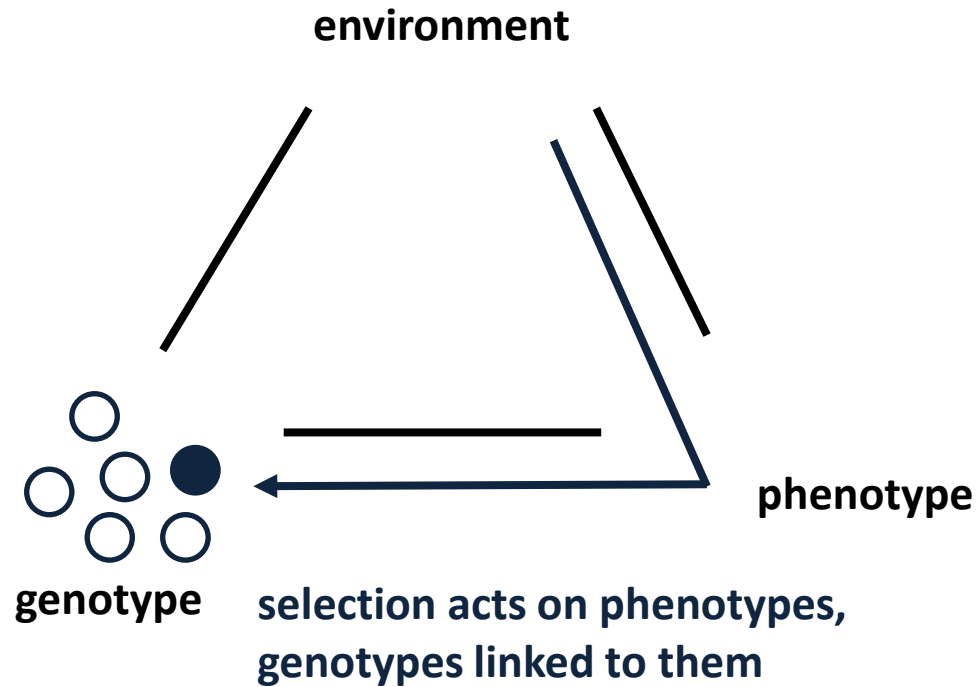
Adaptation: process and patterns



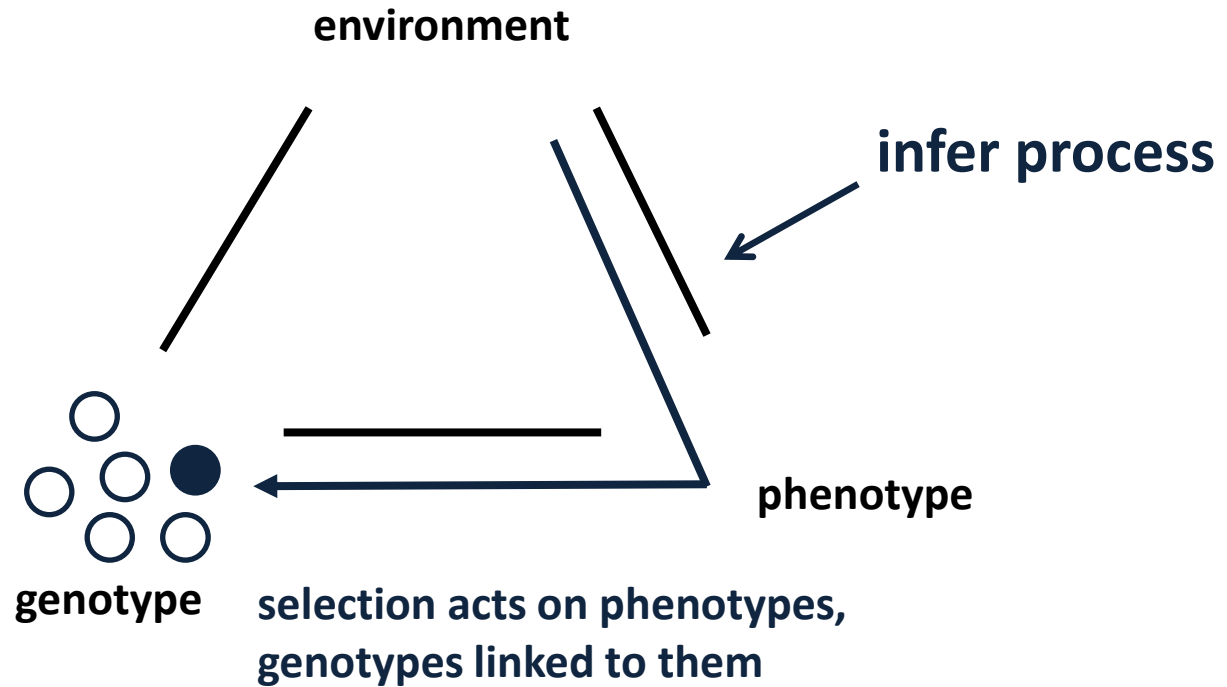
Adaptation: process and patterns



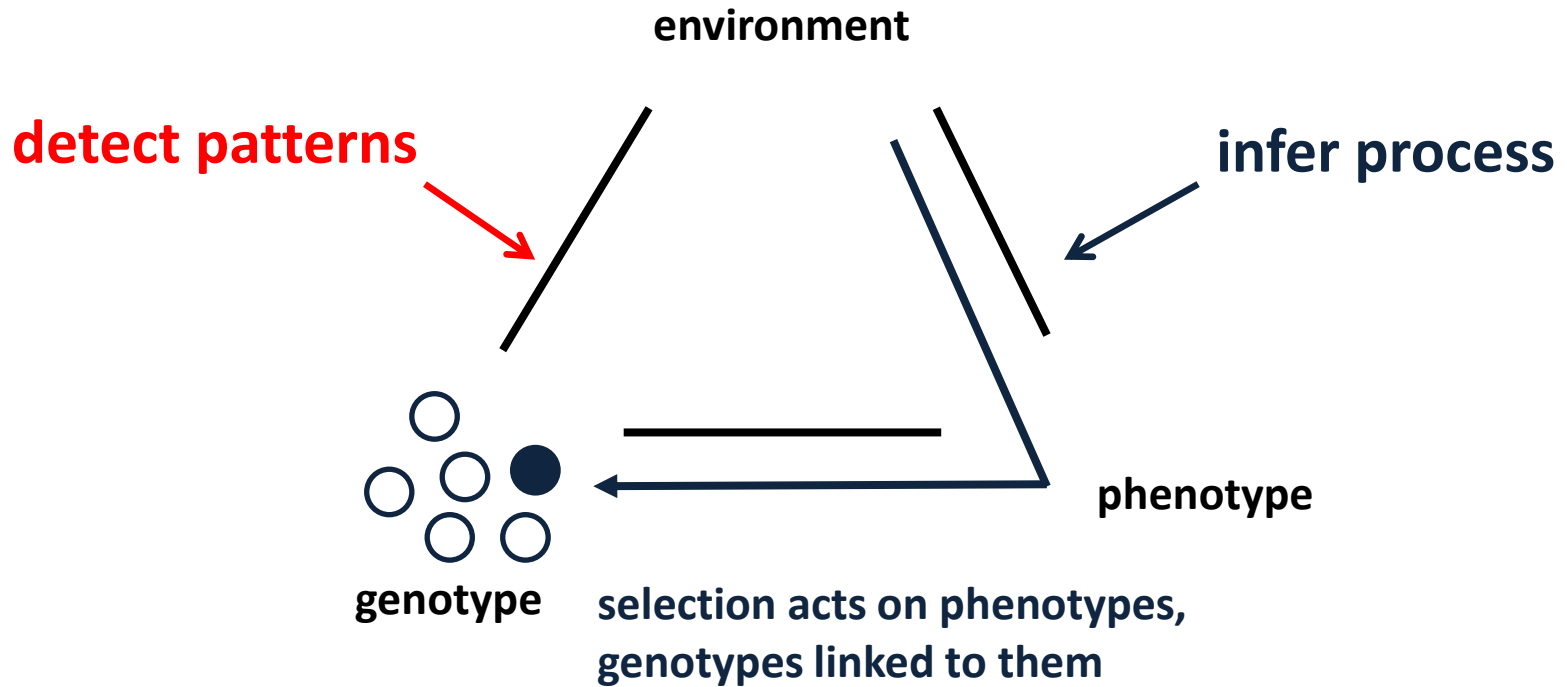
Adaptation: process and patterns



Adaptation: process and patterns

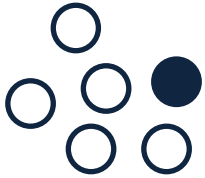


Adaptation: process and patterns



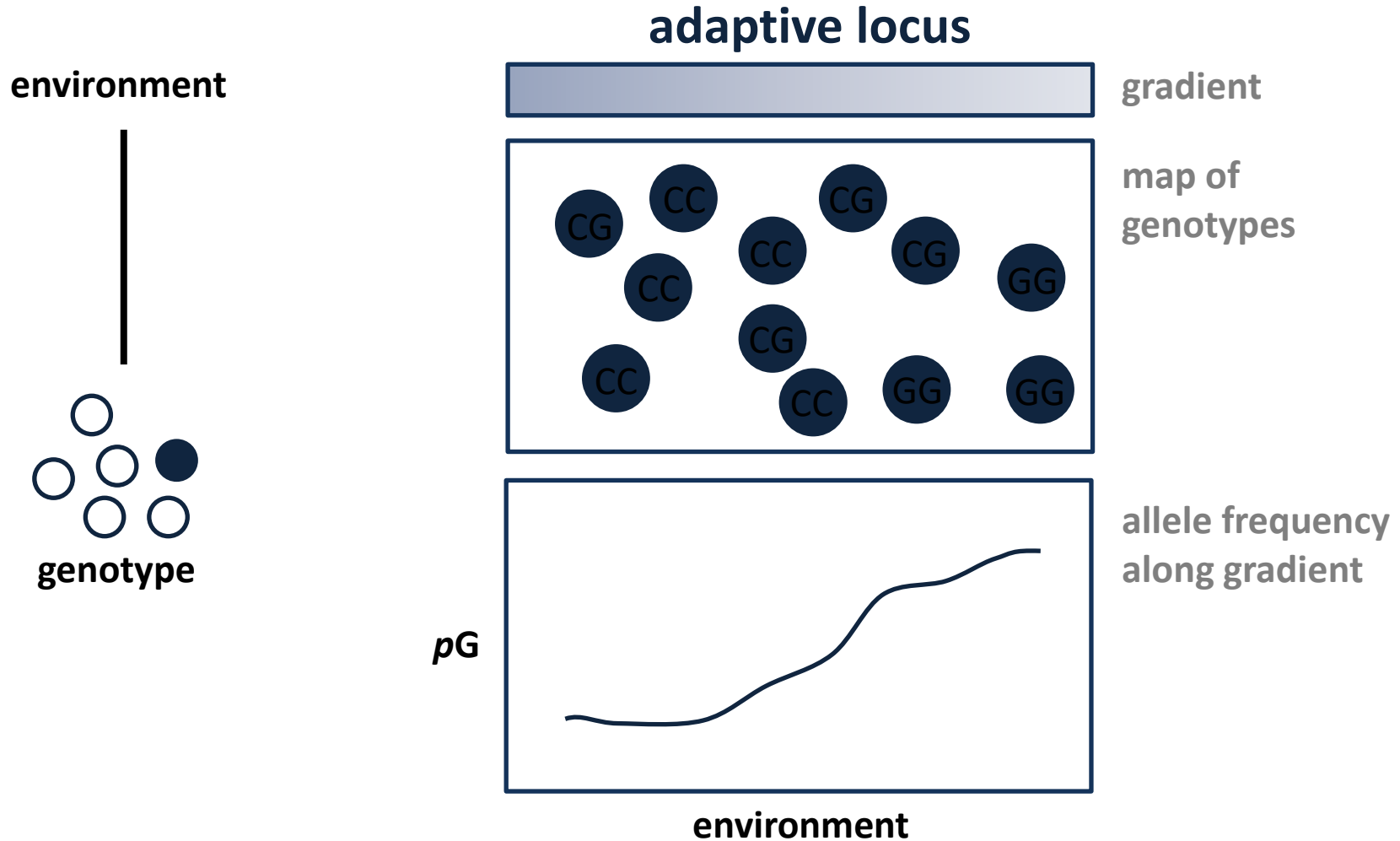
Adaptation: process and patterns

environment



genotype

Adaptation: process and patterns

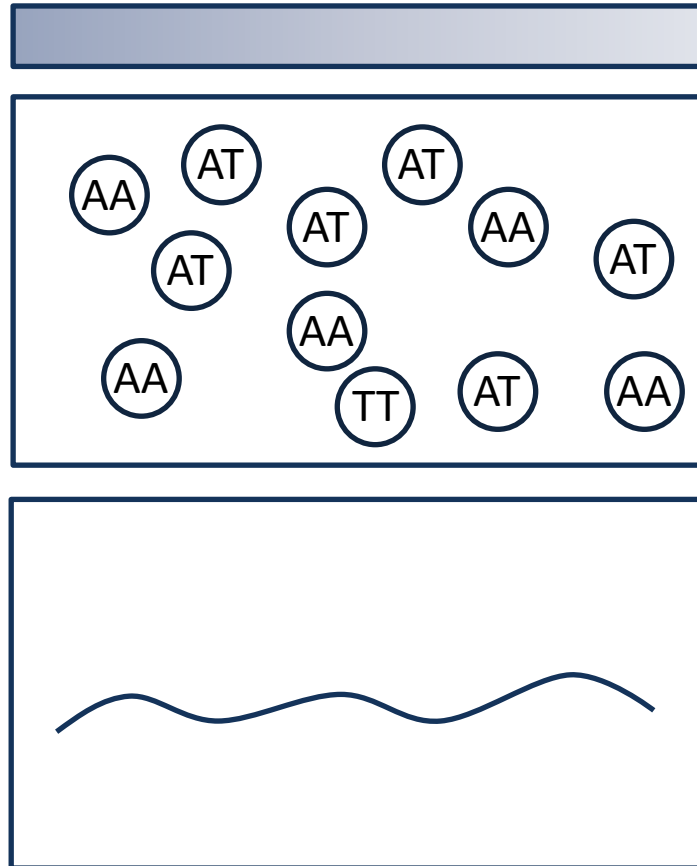


Adaptation: process and patterns

environment



neutral locus



gradient

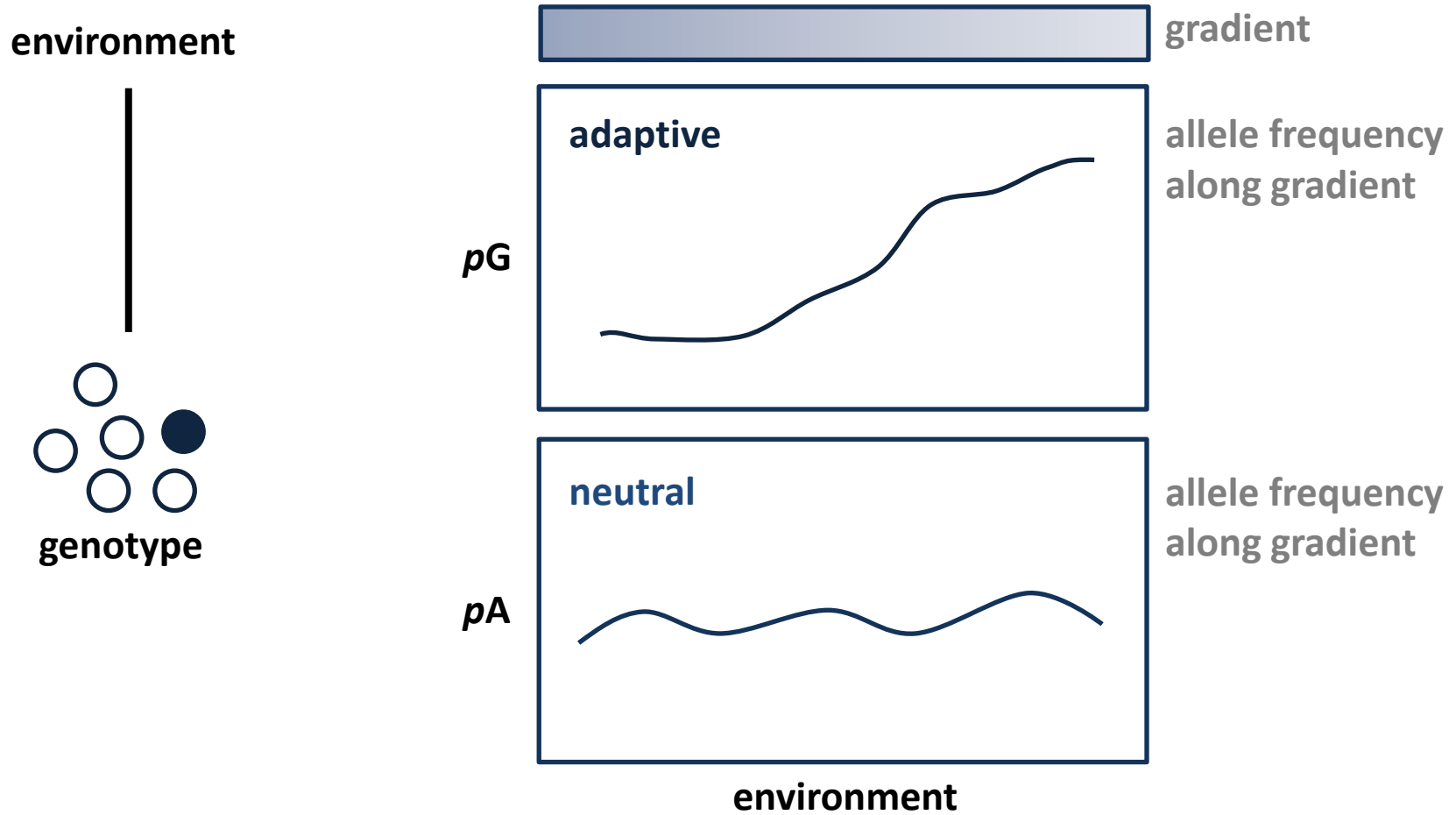
map of
genotypes

allele frequency
along gradient

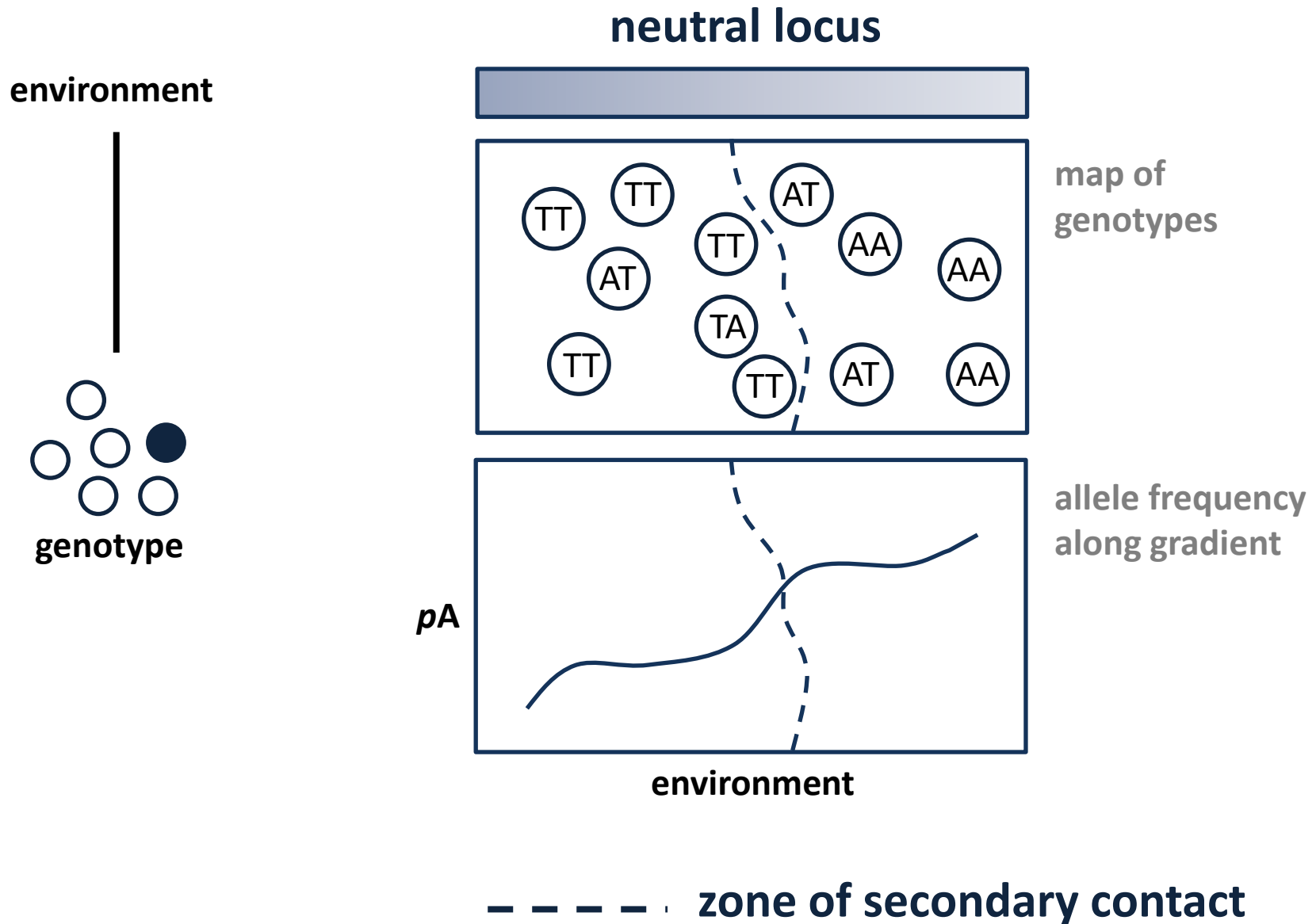
p_A

environment

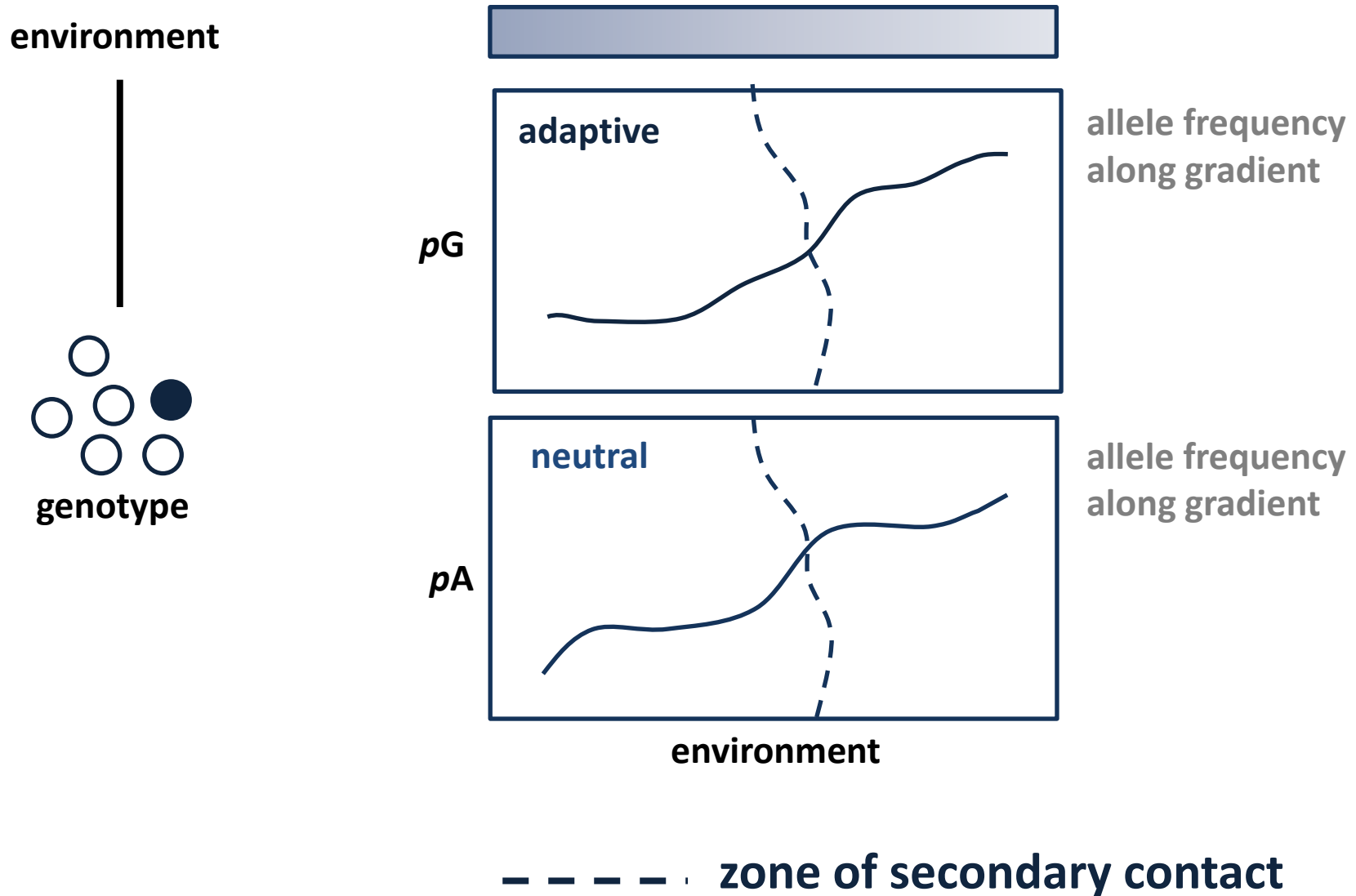
Adaptation: process and patterns



Adaptation: process and patterns

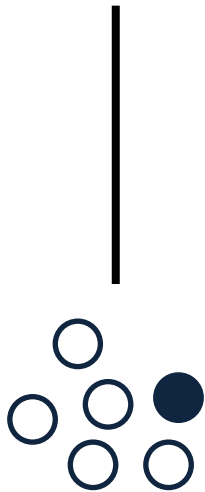


Key challenge: distinguishing from neutral variation



Data

environment



genotype

Sample	Pop	Lat	Lon	RF	Temp
S1	P1	-15.1	132.3	328.4	23.6
S2	P1	-15.1	132.3	328.4	23.6
S3	P1	-15.1	132.3	328.4	23.6
S4	P1	-15.1	132.3	328.4	23.6
S5	P2	-15.7	135.4	312.8	21.2
S6	P2	-15.7	135.4	312.8	21.2
S7	P2	-15.7	135.4	312.8	21.2

Data

environment

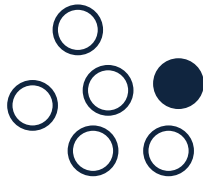


Sample	Pop	Lat	Lon	RF	Temp
S1	P1	-15.1	132.3	328.4	23.6
S2	P1	-15.1	132.3	328.4	23.6
S3	P1	-15.1	132.3	328.4	23.6
S4	P1	-15.1	132.3	328.4	23.6
S5	P2	-15.7	135.4	312.8	21.2
S6	P2	-15.7	135.4	312.8	21.2
S7	P2	-15.7	135.4	312.8	21.2

sampling

Data

environment



genotype

Sample

S1
S2
S3
S4
S5
S6
S7

Lat

-15.1
-15.2
-15.4
-15.4
-15.5
-15.7
-15.7

Lon

132.3
132.5
132.1
132.7
133.6
134.2
135.4

RF

328.4
329.2
326.3
324.4
318.6
314.8
312.8

Temp

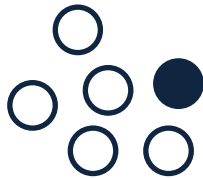
23.6
23.3
24.0
22.4
22.6
21.8
21.2

measure these
(map datum)

how to get
these?

Data

environment



genotype

Sample

S1
S2
S3
S4
S5
S6
S7

Lat

-15.1
-15.2
-15.4
-15.4
-15.5
-15.7
-15.7

Lon

132.3
132.5
132.1
132.7
133.6
134.2
135.4

RF

328.4
329.2
326.3
324.4
318.6
314.8
312.8

Temp

23.6
23.3
24.0
22.4
22.6
21.8
21.2

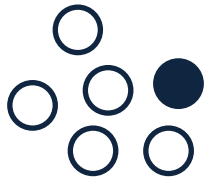
measure these
(map datum)

how to get
these?

WorldClim
(consider local
measurements...)

Data

environment

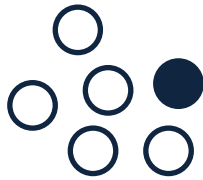


genotype

Sample	Lat	Lon	RF	Temp
S1	-15.1	132.3	328.4	23.6
S2	-15.2	132.5	329.2	23.3
S3	-15.4	132.1	326.3	24.0
S4	-15.4	132.7	324.4	22.4
S5	-15.5	133.6	318.6	22.6
S6	-15.7	134.2	314.8	21.8
S7	-15.7	135.4	312.8	21.2

Data

environment



genotype

Sample	Lat	Lon	RF	Temp
S1	-15.1	132.3	328.4	23.6
S2	-15.2	132.5	329.2	23.3
S3	-15.4	132.1	326.3	24.0
S4	-15.4	132.7	324.4	22.4
S5	-15.5	133.6	318.6	22.6
S6	-15.7	134.2	314.8	21.8
S7	-15.7	135.4	312.8	21.2

many choices

what matters to
your species?

Data

environment



Sample	Lat	Lon	RF	Temp
S1	-15.1	132.3	328.4	23.6
S2	-15.2	132.5	329.2	23.3
S3	-15.4	132.1	326.3	24.0
S4	-15.4	132.7	324.4	22.4
S5	-15.5	133.6	318.6	22.6
S6	-15.7	134.2	314.8	21.8
S7	-15.7	135.4	312.8	21.2

many choices

all available vs.
hypothesis-driven

what matters to
your species?

kinds of variables
(e.g. aquatic life-stages)

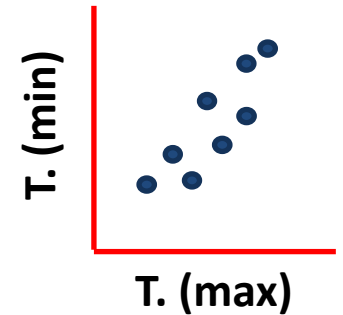
thresholds
(e.g. frost intolerance)

Data

environment

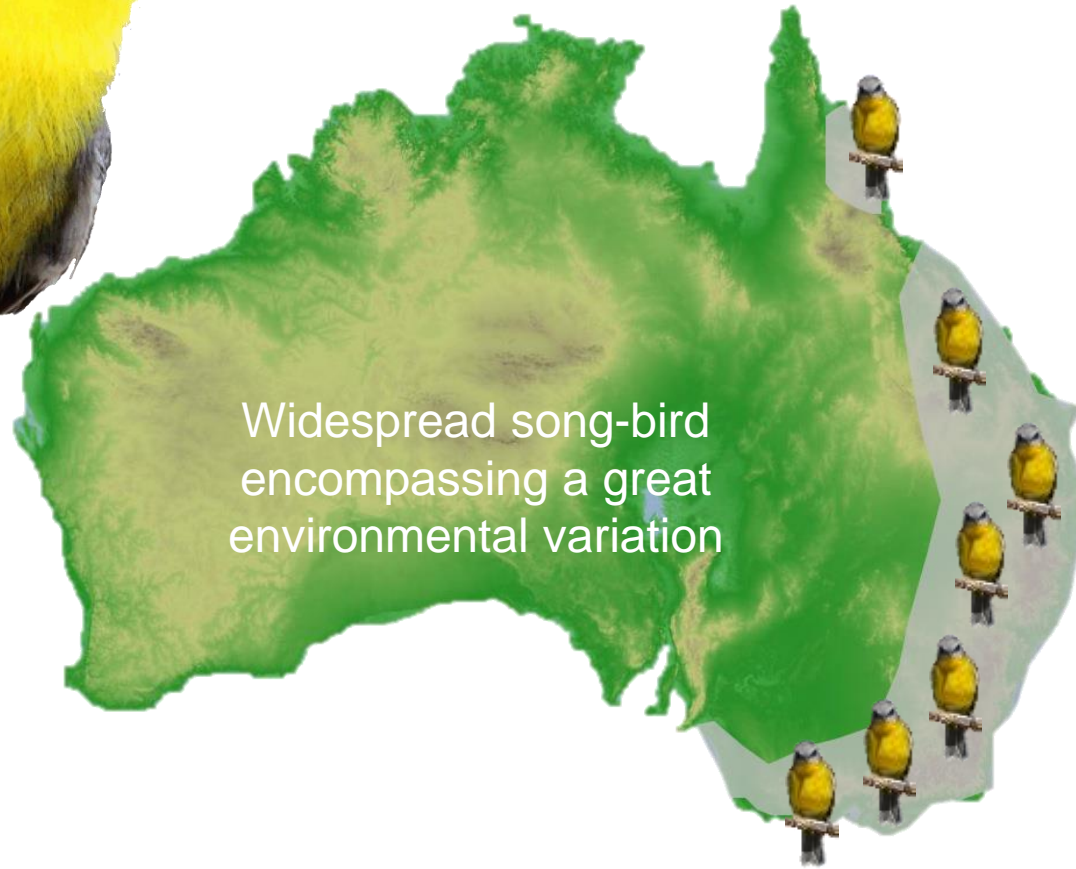


Sample	Lat	Lon	RF	T. (max)	T. (min)
S1	-15.1	132.3	328.4	29.6	23.6
S2	-15.2	132.5	329.2	29.3	23.4
S3	-15.4	132.1	326.3	30.0	25.5
S4	-15.4	132.7	324.4	28.4	22.4
S5	-15.5	133.6	318.6	28.6	24.1
S6	-15.7	134.2	314.8	27.8	20.6
S7	-15.7	135.4	312.8	27.2	22.1



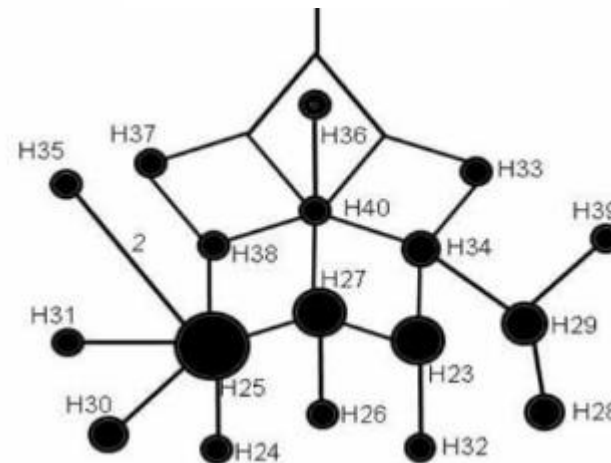
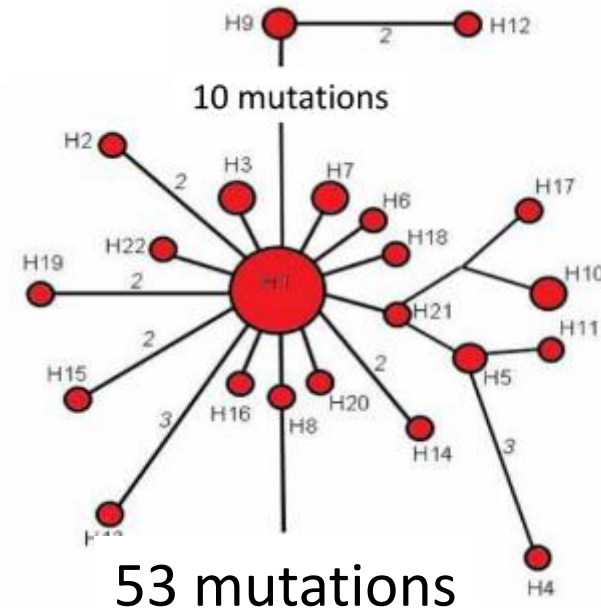
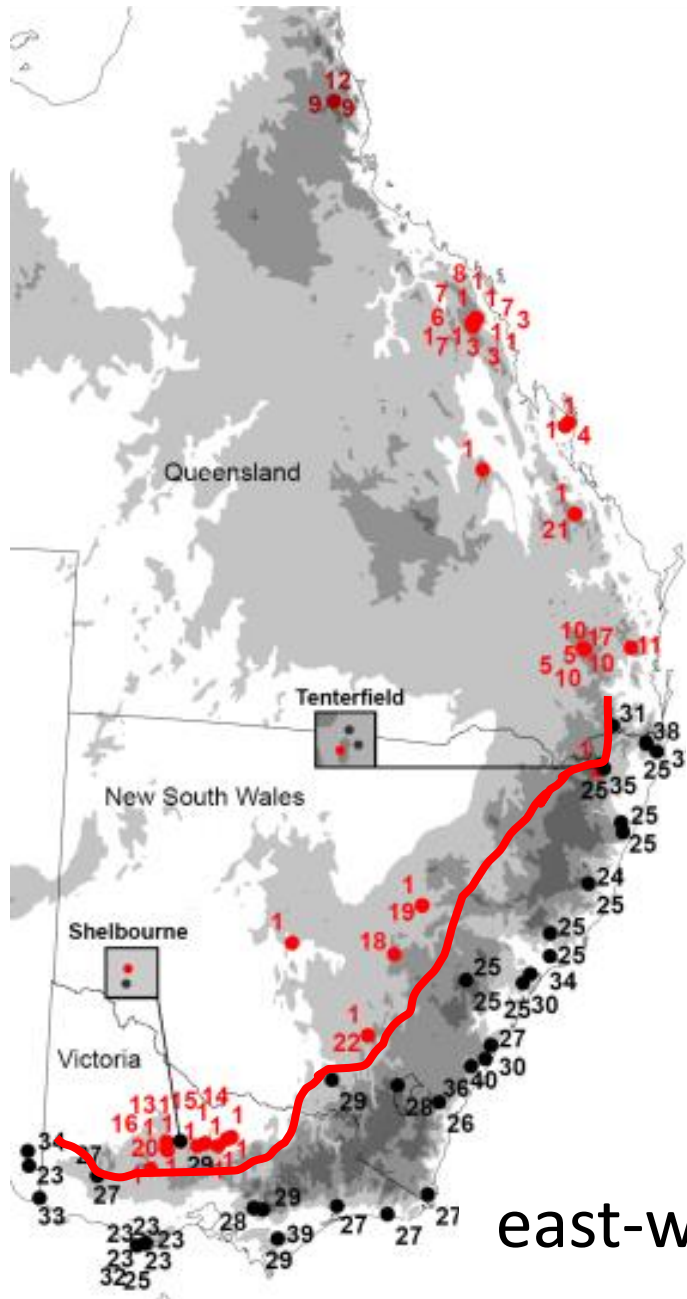


Eastern Yellow Robin



Widespread song-bird
encompassing a great
environmental variation

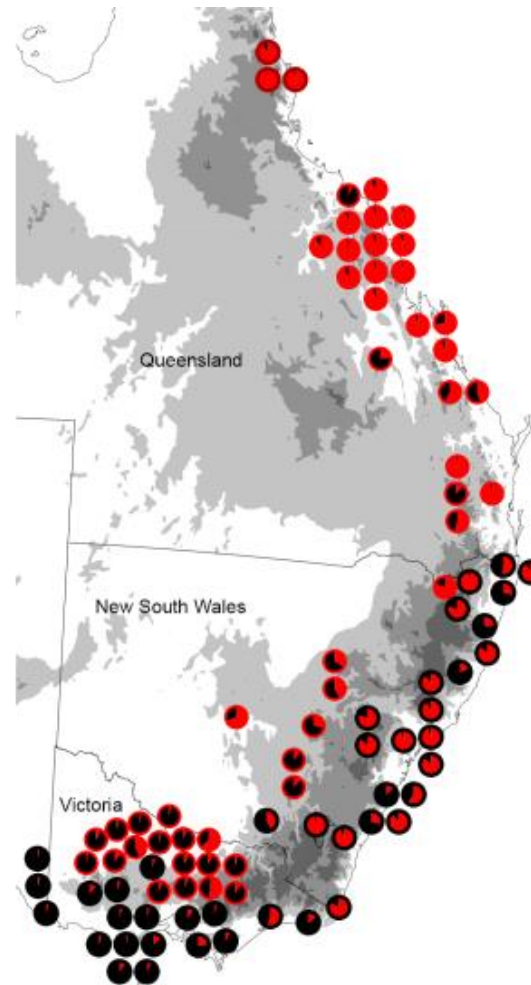
Pattern: Mitochondrial DNA sequences



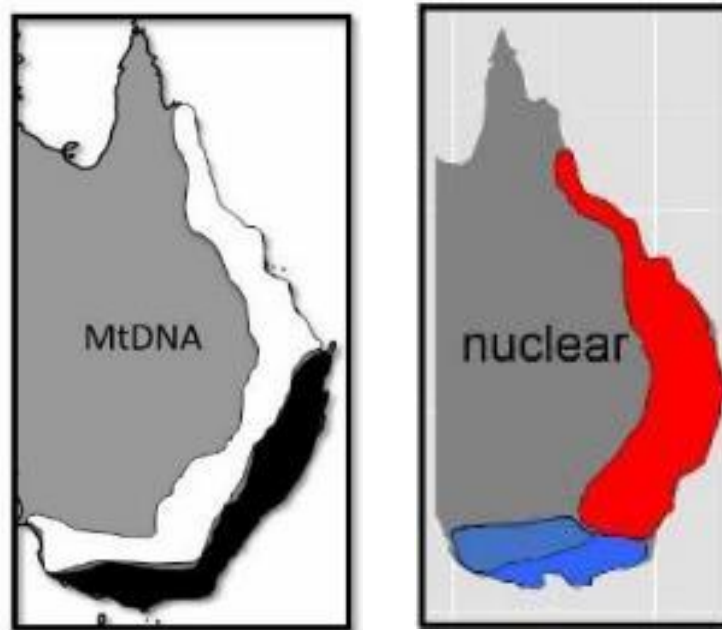
east-west split across Gt. Dividing Range

Pattern: Nuclear microsatellites

north-south pattern



Summary 2 genomes, completely different patterns



Having ruled out the boring alternatives, we inferred interesting female-associated selection:

Reasons in Pavlova *et al.* 2013 Perched at the mito-nuclear crossroads: divergent mitochondrial lineages correlate with environment in the face of ongoing nuclear gene flow in an Australian bird. *Evolution* 67, 3412–3428

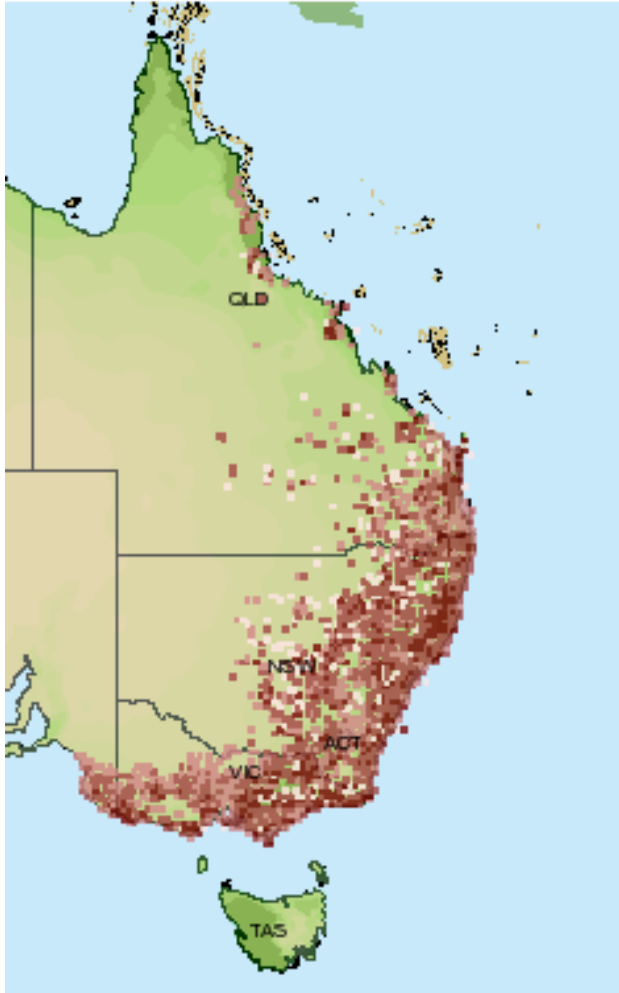


Sasha Pavlova

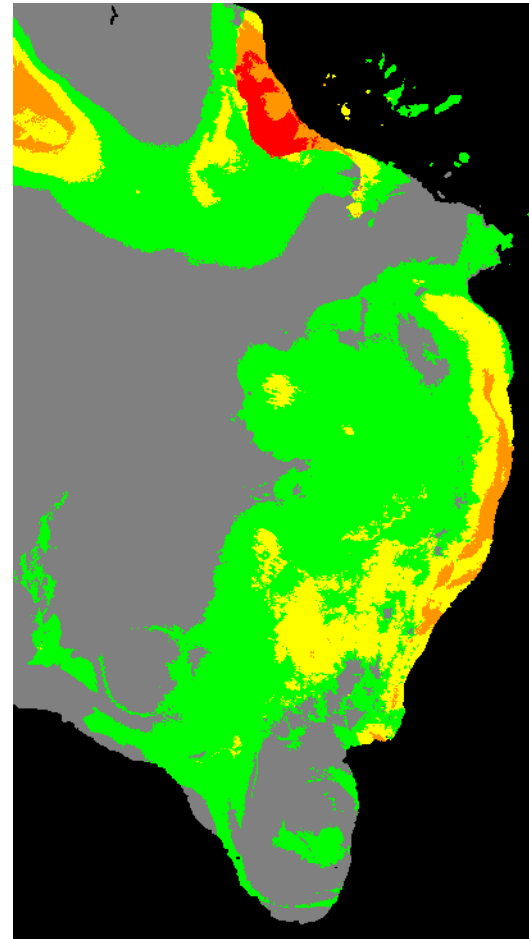
1. Vicariance: Is/was the Great Dividing Range a barrier?

No

Current distribution is continuous

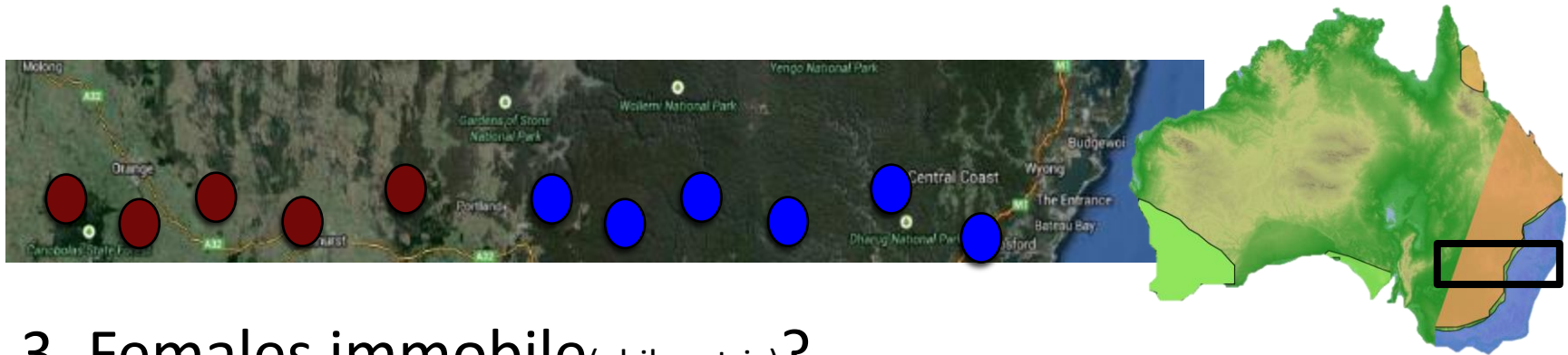


Last glacial maximum –
no split over the GDR



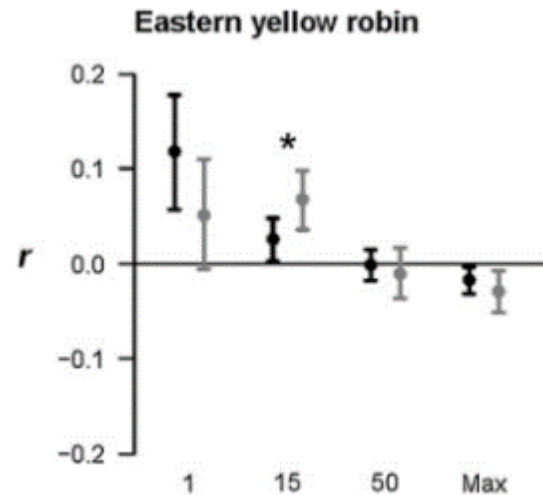
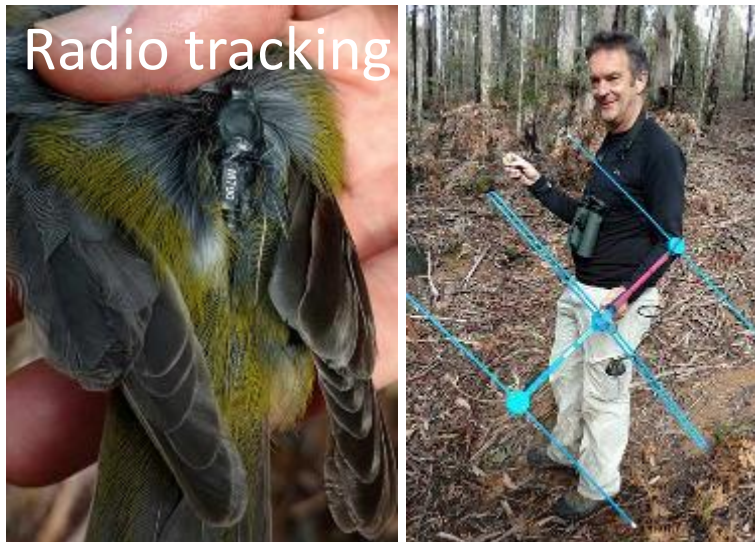
2. Chance mtDNA split? **No**

mtDNA lineages remain geographically distinct for >1500 km, even though they are well within the dispersal distance of a robin



3. Females immobile_(philopatric)?

No Dispersal is **female-biased**

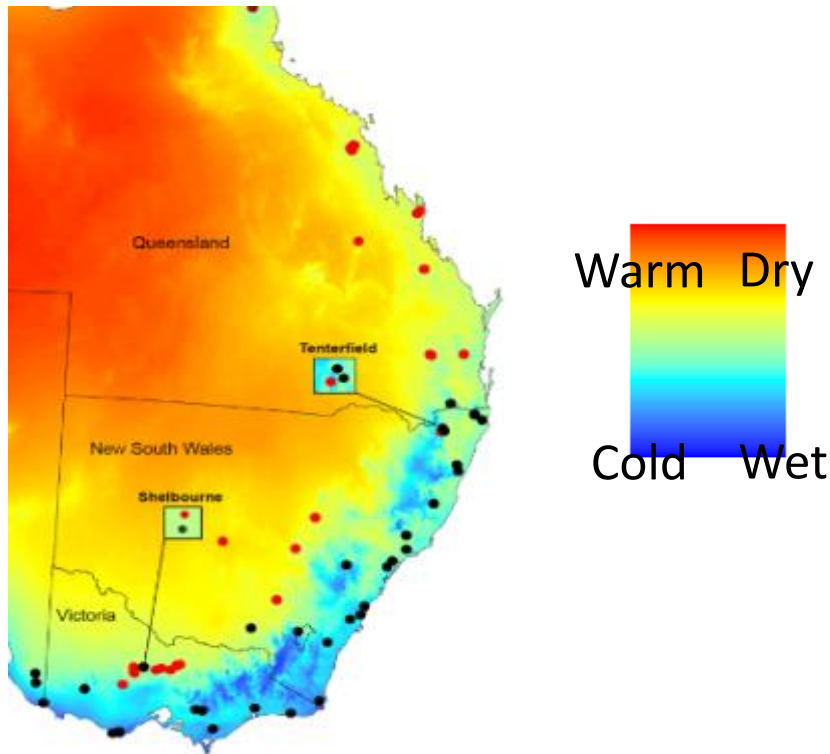


Harrison et al. (2012) spatial autocorrelation
Female in grey, male in black

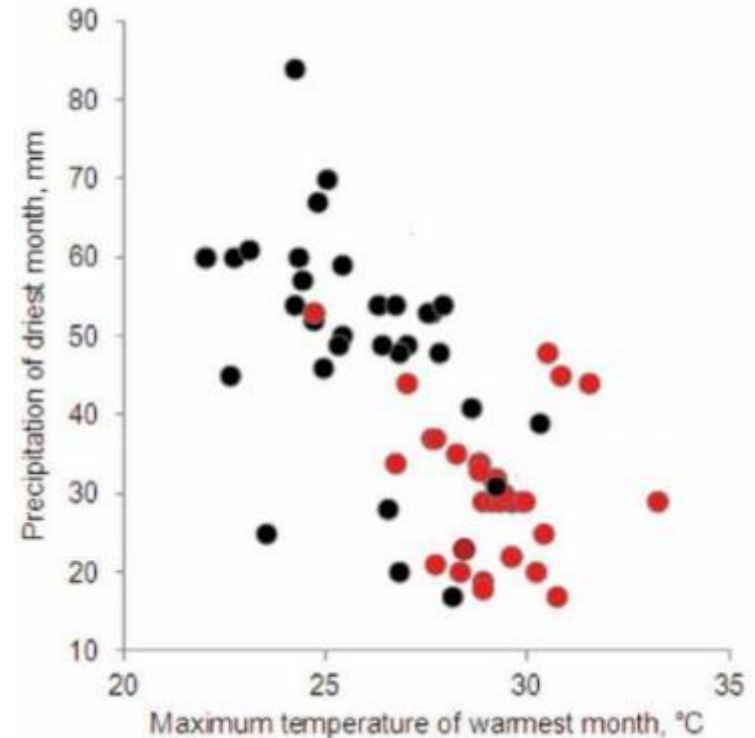
4. Female-associated selection – looks like it

Significant correlation of mtDNA with climate variables

Max. temp of the warmest month



Environmental Association Analysis (EAA)
(also called Genetic–environment associations (GEA): alleles correlate with environments



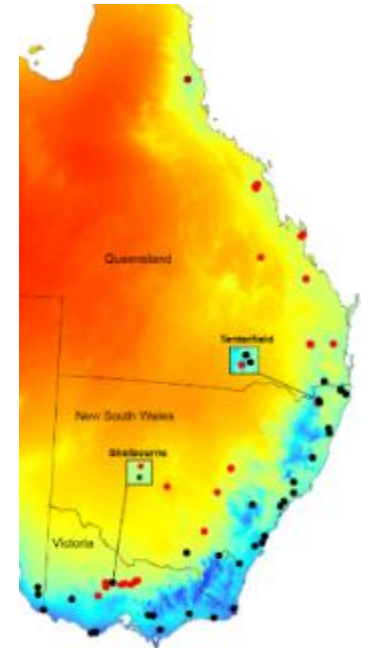
...remains significant after accounting for geography (by dbRDA)

EMPHASIS ...the fact that a potential driver remains significant after accounting for geography (by dbRDA)

Australia's climate is highly correlated with geography:

eg it's warmer in the north and cooler in the south

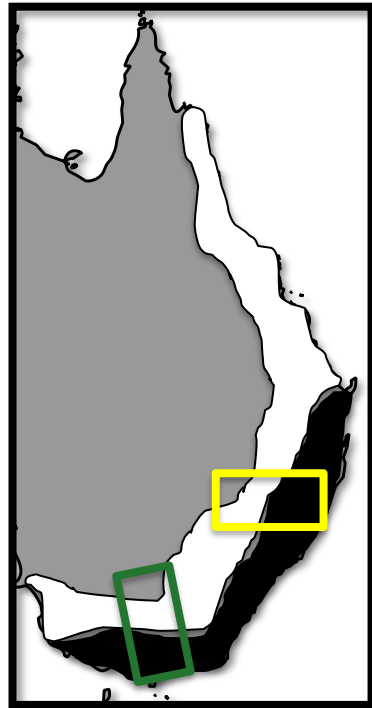
so any N-S pattern will look like it could be driven by climate



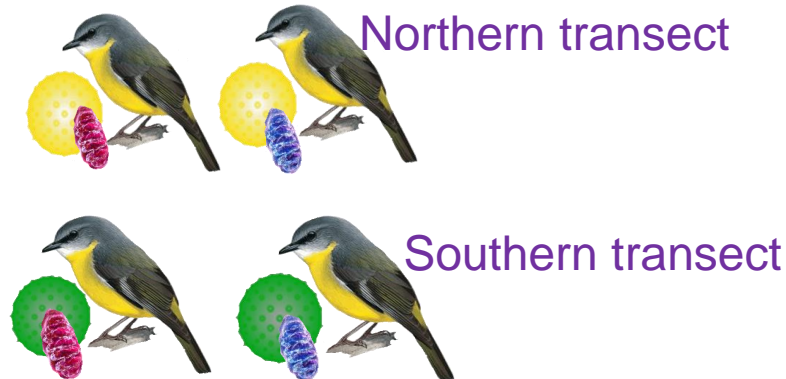
Need to test whether association of mtDNA with climate remains significant after accounting for ('partialling-out') the automatic correlation of climate with geography

eg using distance-based redundancy analysis (dbRDA)

Testing for nuclear genes with mitochondrial functioning being 'dragged along' with mtDNA during introgression



- Two transects across mtDNA split
- True replicates (different nuclear backgrounds)



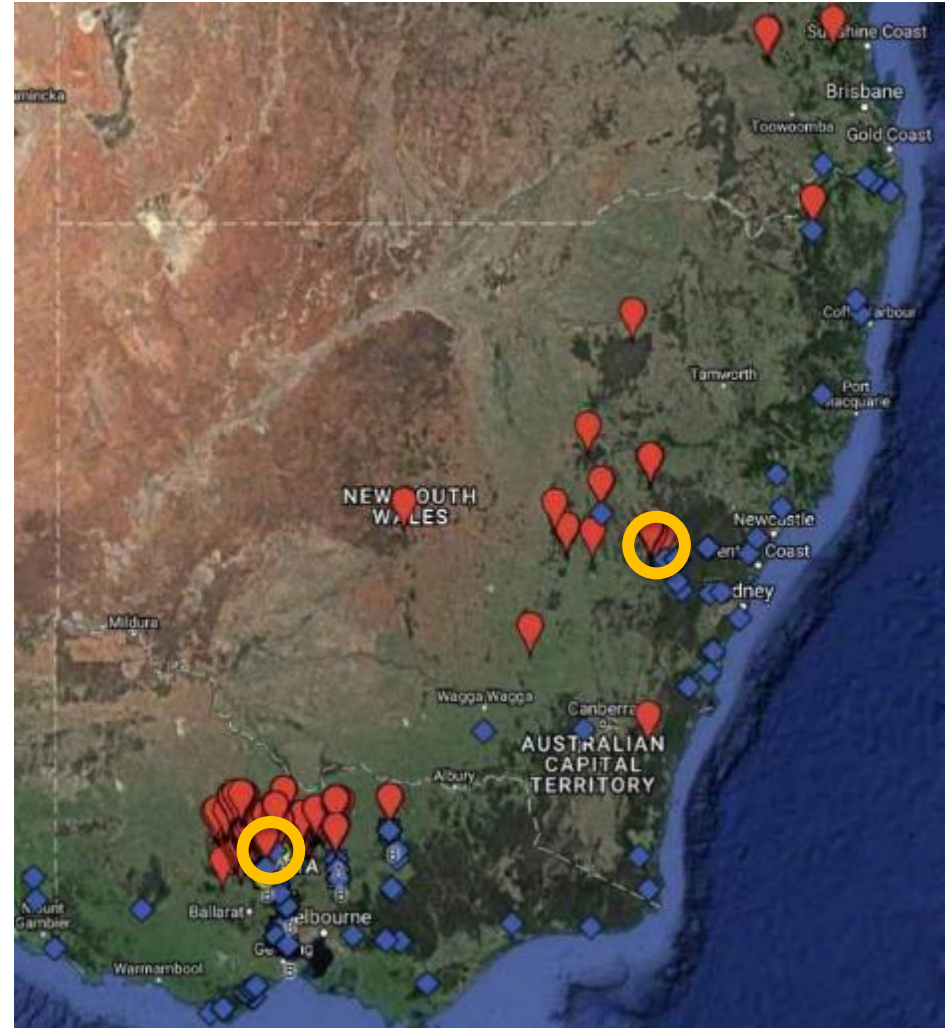
Nuclear genomewide marker scan >64,000 SNPs from short DNA sequences

Finding nuclear genes that differ between mitolineages

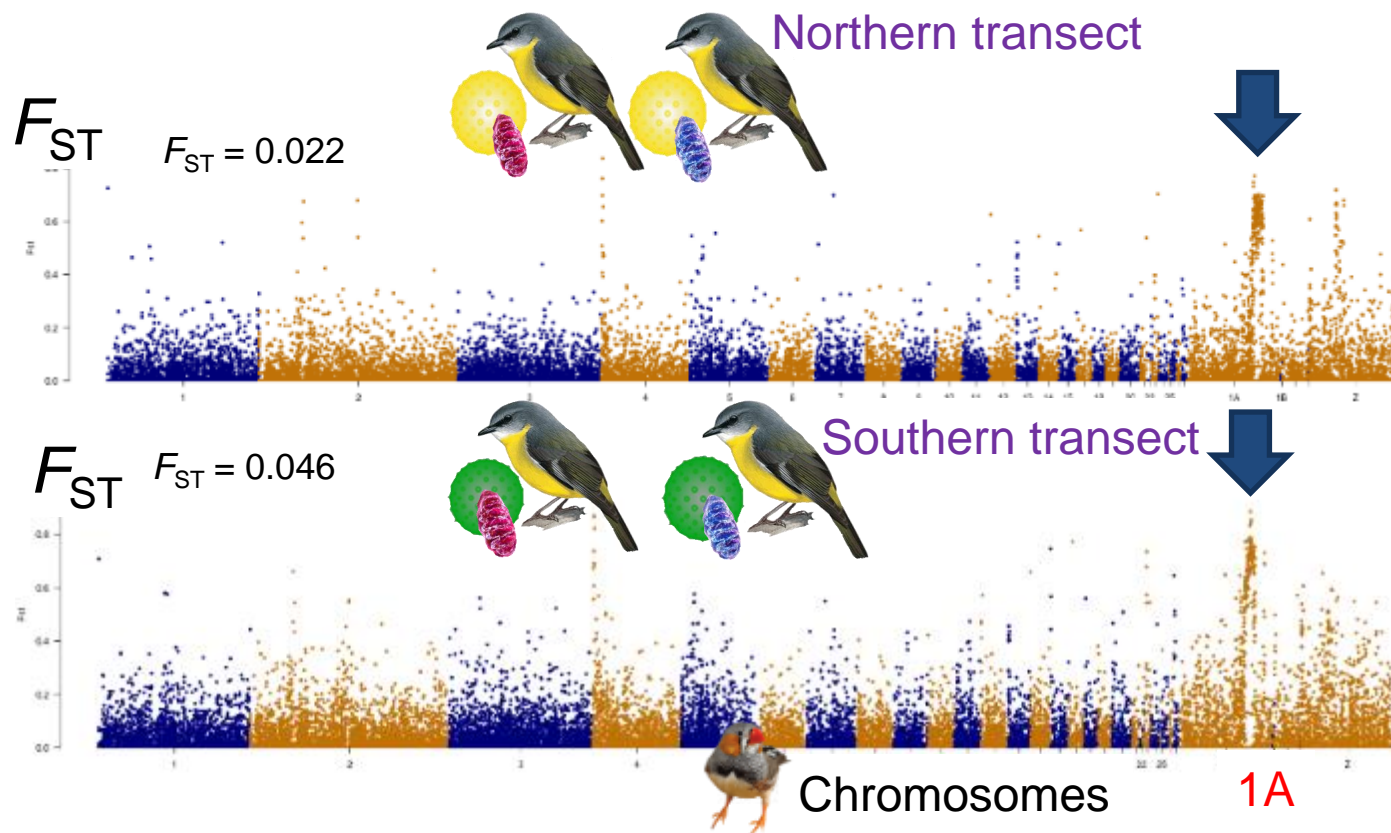
i.e. seeking high F_{ST}
between adjacent inland
and coastal robins

(This is a GWAS -
genome wide
association study)

Morales HE, Pavlova A, Amos JN, Major R, Kilian A, Greening C and Sunnucks P (2018)
Concordant divergence of mitogenomes and a
mitonuclear gene cluster in bird lineages
inhabiting different climates. *Nature Ecology &
Evolution* 2, 1258–1267

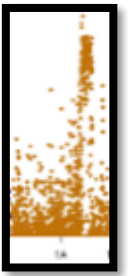


Genomewide differentiation between inland and coastal mitolineages



Outliers have average $F_{ST} > 0.48$

This chromosome 1A 'island of divergence' is special

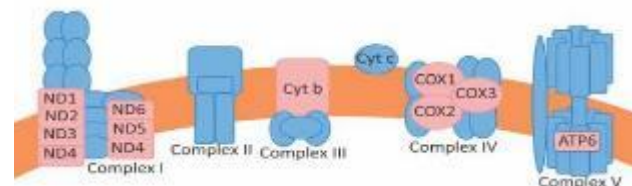


- (1) ~15 million nucleotides long containing ~340 genes
- (2) inherited as if one giant gene with two alleles
- (3) inherited along with mitochondrial DNA, even though the rest of the nuclear genome is not



- (4) Contains 32 genes that have functions in the mitochondrion (a significant excess)

including 4 OXPHOS genes



Three of these OXPHOS genes are partners of the mtDNA ones also showing signals of positive selection

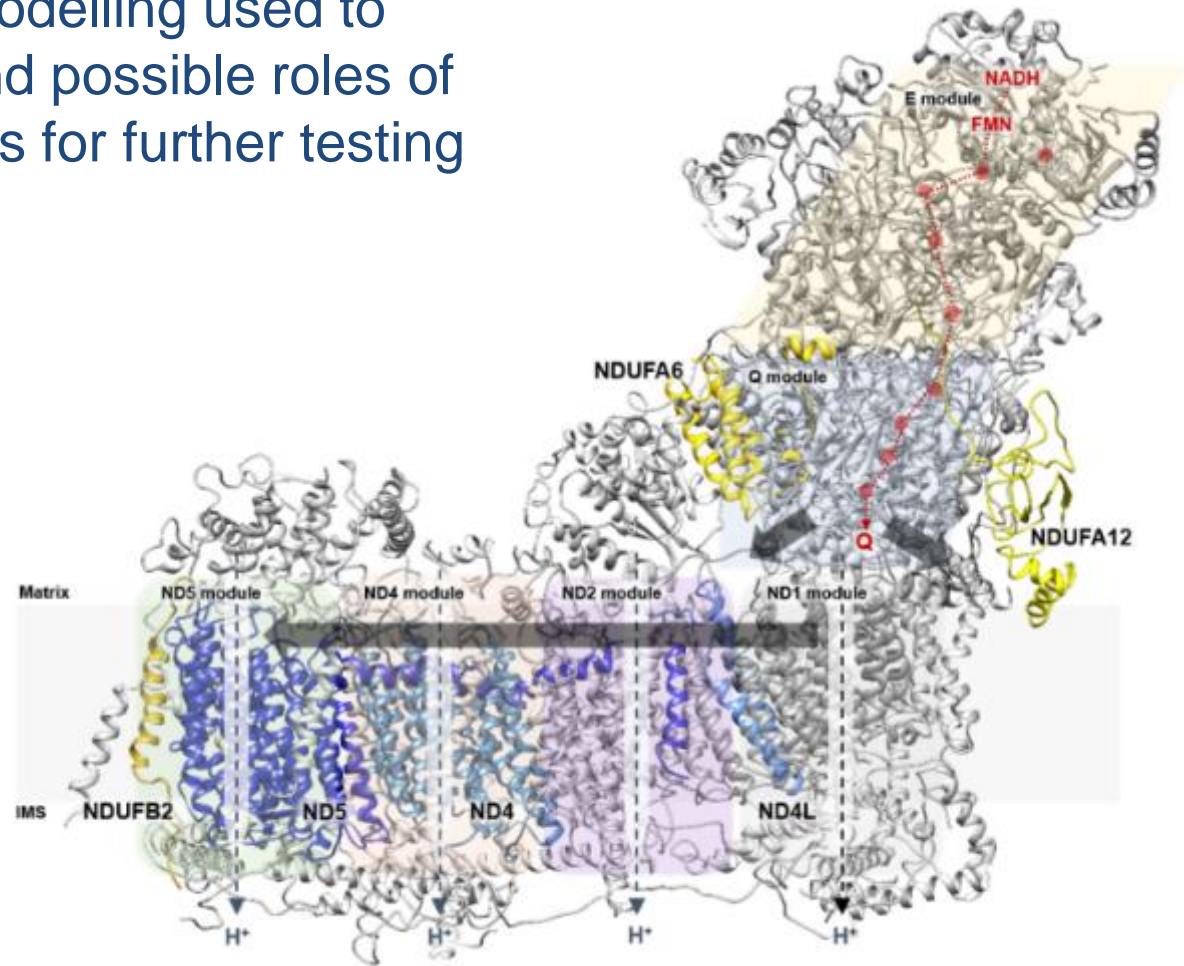


Chris Greening

Protein modelling used to understand possible roles of candidates for further testing

Nuclear mitochondrial gene products from in the 1A island in **YELLOW**

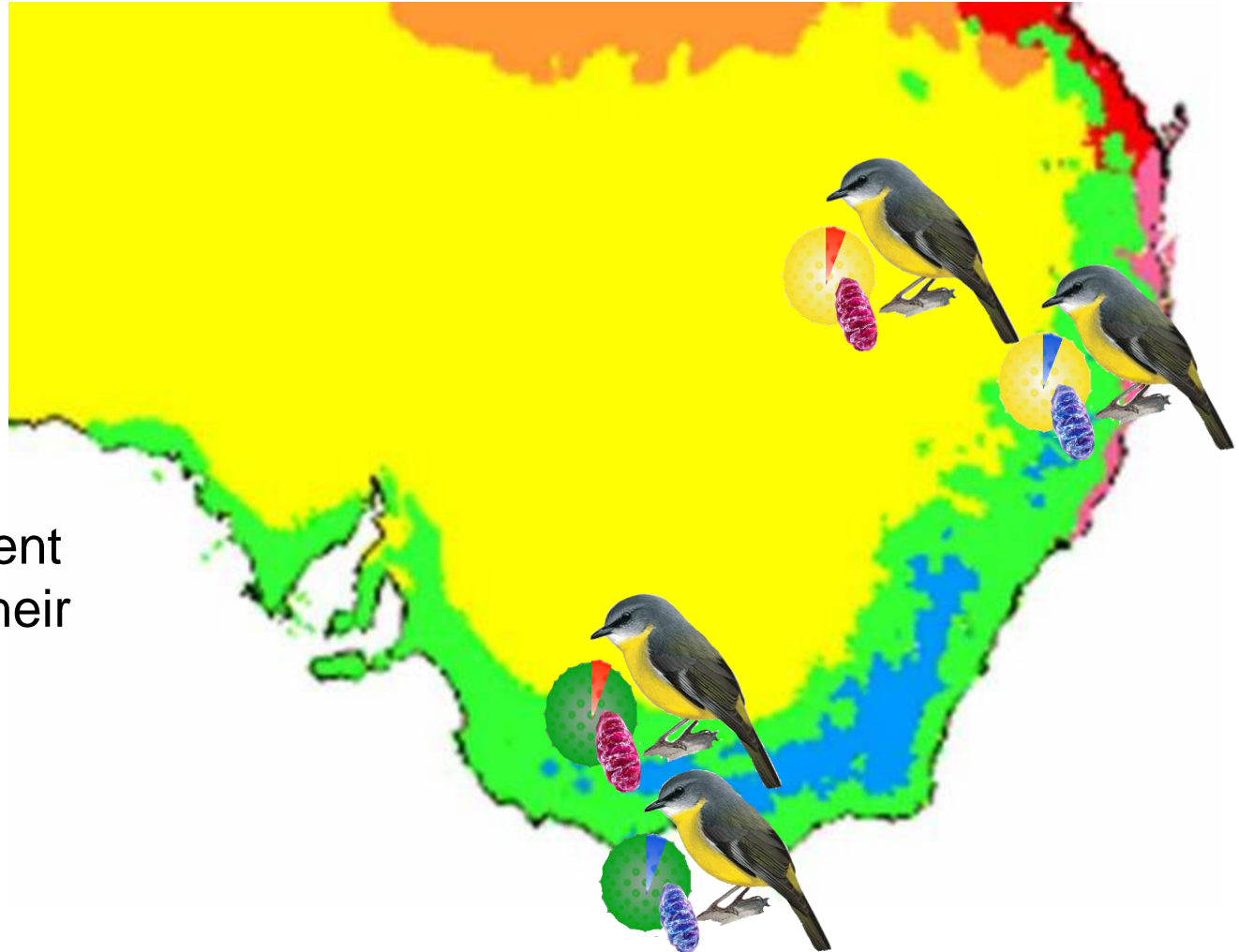
Mitochondrial gene products evidence for positive selection (ND4, ND4L and ND5) in **PURPLE**



Summary

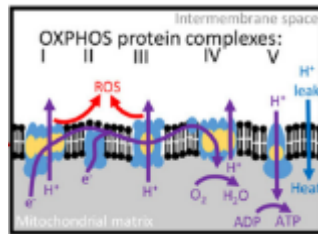
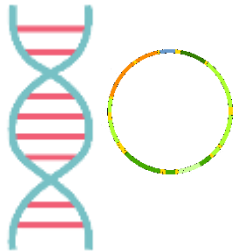
Two distinct mtDNA groups that also have set of putatively co-adapted nuclear genes

If adaptive, they should have different biology suited to their environments

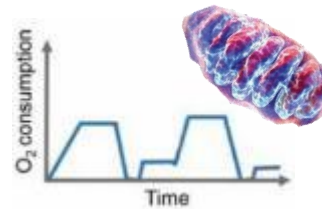


Local adaptation What to look for?

Genomes → OXPHOS → mitochondrial → metabolism



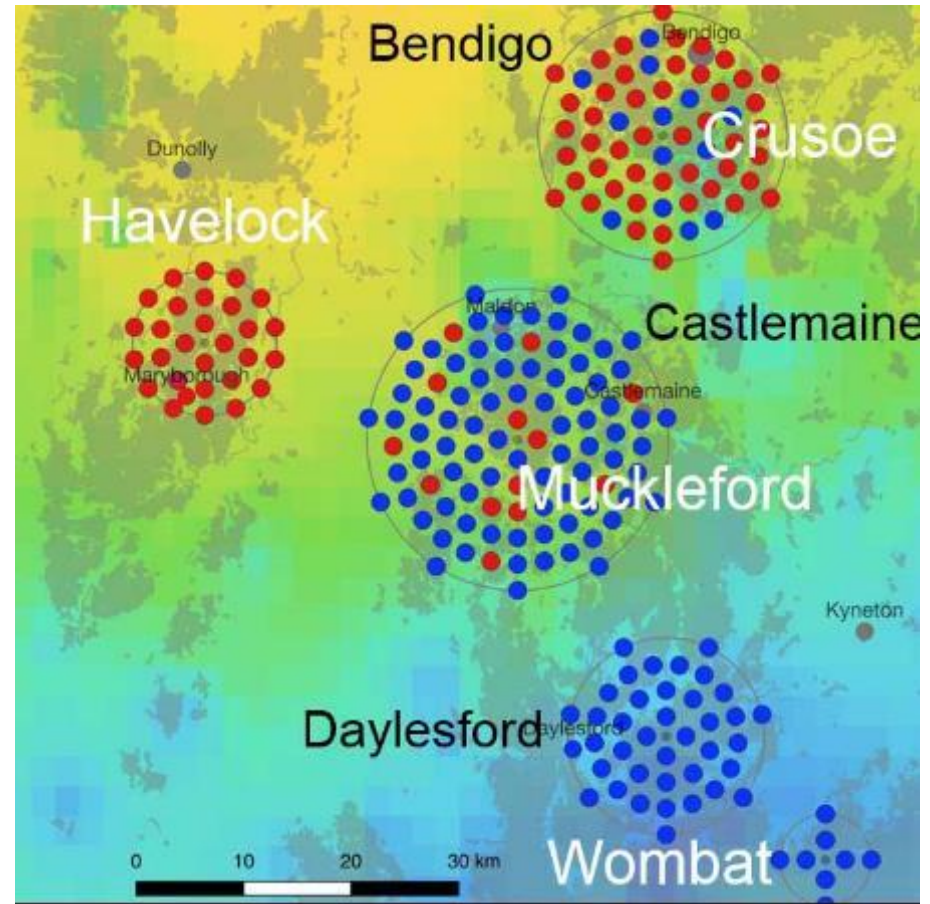
mitochondrial function



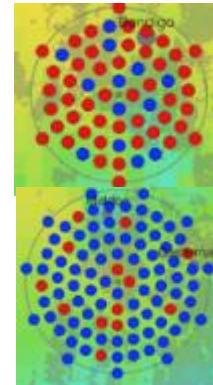
Some main items to measure that yield predictions

In a feasible design across an environmental gradient, with lineages side-by-side:

- (1) Mitochondrial function
- (2) Metabolism
- (3) Environments
- (4) Gene flow between the lineages
- (5) Fitness x environment indicators



(The lineages should evolve to recognize and not breed with each other)
Do females choose a mate of the same mitolineage?



Hons: Jessica Walters

Parentage analysis to find out:

- How often do mitolineages interbreed?
- Are there sex-specific consequences for their offspring?



Apparently no preference for mating with own lineage, but...

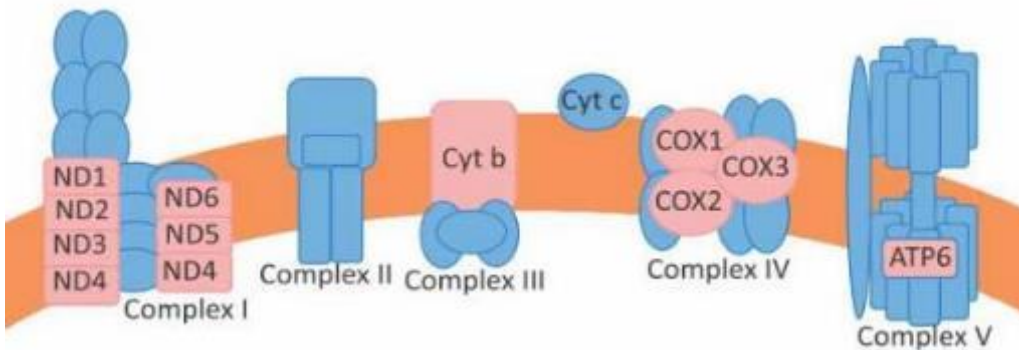
...admixed parents ♀♂ or ♂♀
have almost no daughters

That is, strong selection against hybrid females

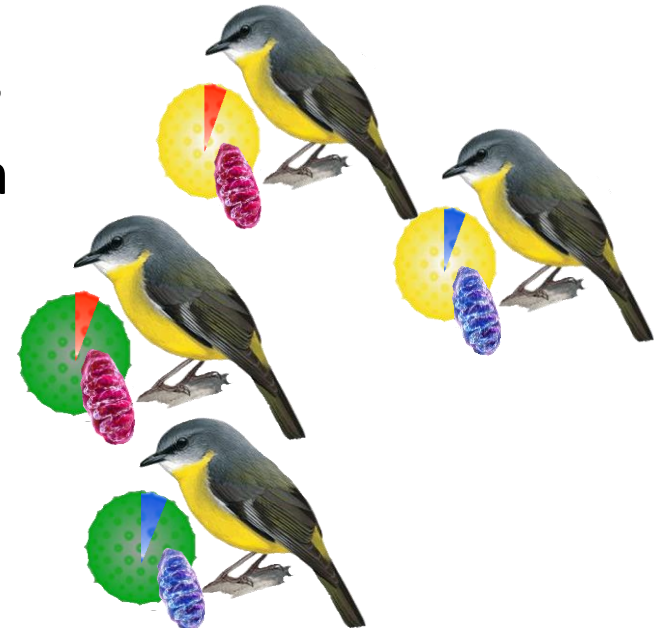
Implications

Inland and **coastal** Eastern yellow robins may be speciating by climate adaptation

through mitonuclear interactions



Hill (2015) Mol. Biol. Evol. 32(8):1917–1927



Next lecture – more on
selection/adaptation