

Combining genomics with experimental studies of adaptation



Katie Peichel
University of Bern

Disclaimer: I don't really know how to do anything with genomic data!



But, the talented people that I have had in my group over the years do!

You will hear more from the amazing Majda Bohutínská this afternoon!

Plan for this morning*

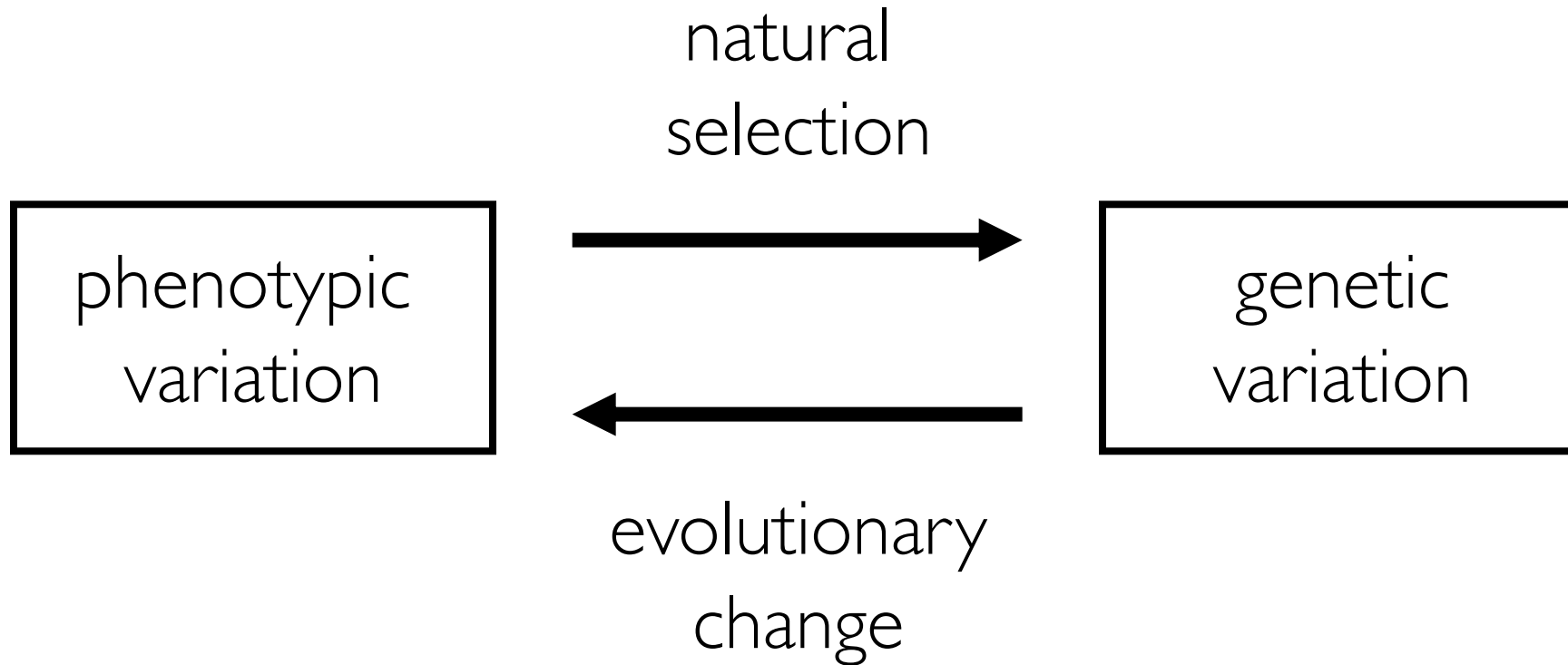
- Part 1: Introduction to forward and reverse genetic approaches and QTL mapping (~45 min including an exercise)
 - Short break
- Part 2: Combining genomics and experimental studies to understand the role of chromosomal rearrangements in adaptation to divergent environments (~45 min)
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- Part 3: Combining genomics and experimental studies to determine why evolution is repeatable (~45 min)

*Please always interrupt with questions as you have them!!!

How do organisms adapt to different environments?

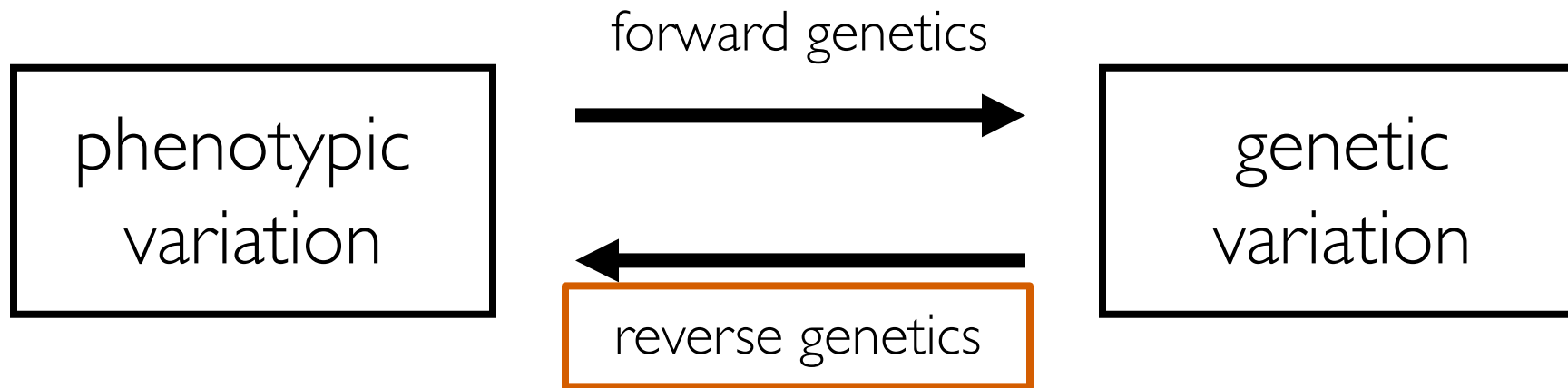


Genetics of adaptation



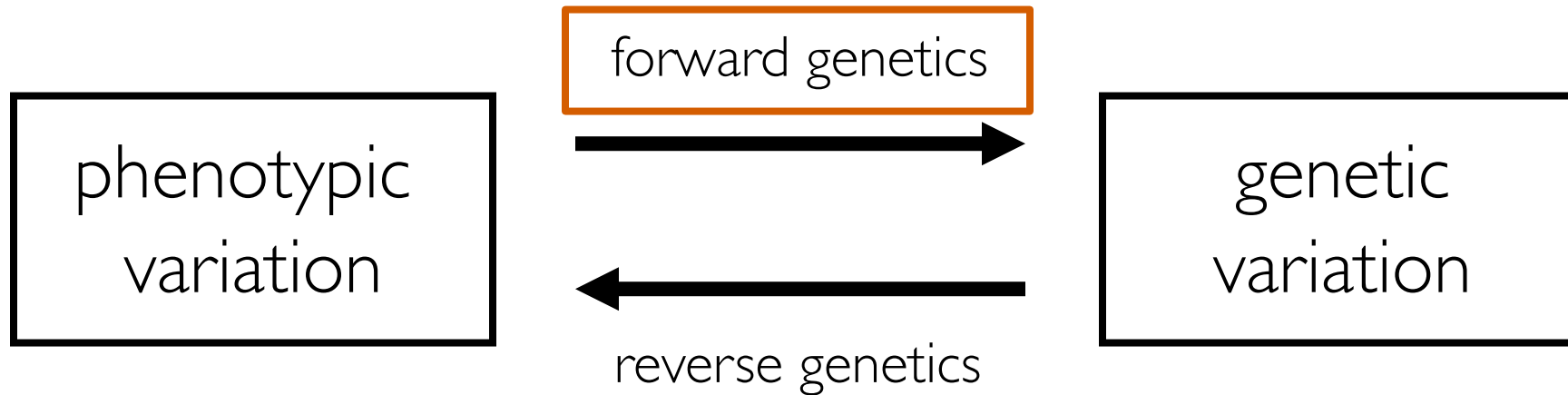
How do we make these connections?

Two complementary approaches



What phenotypes are affected by this genotype?

Two complementary approaches

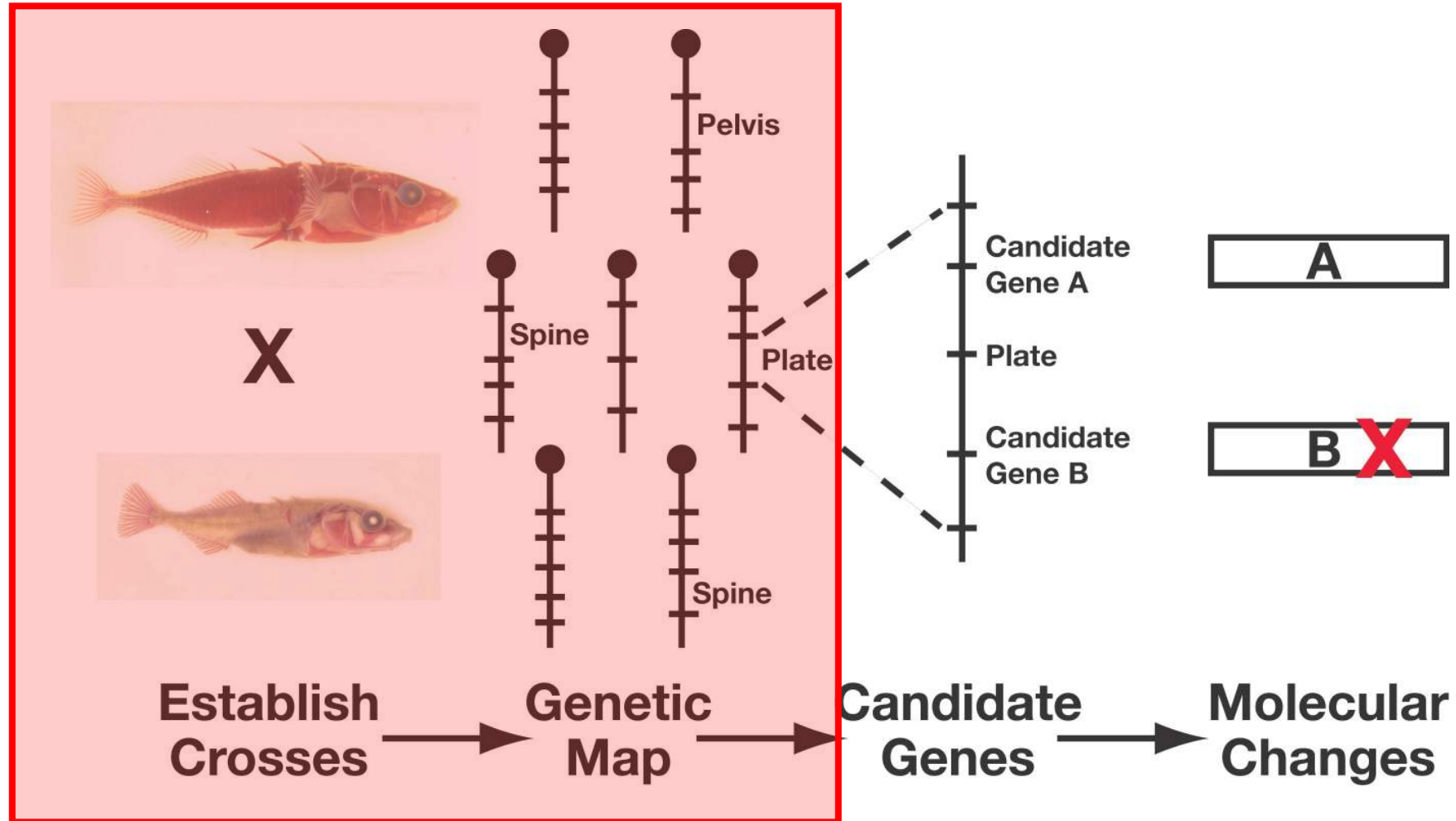


What genotypes underlie this phenotype?

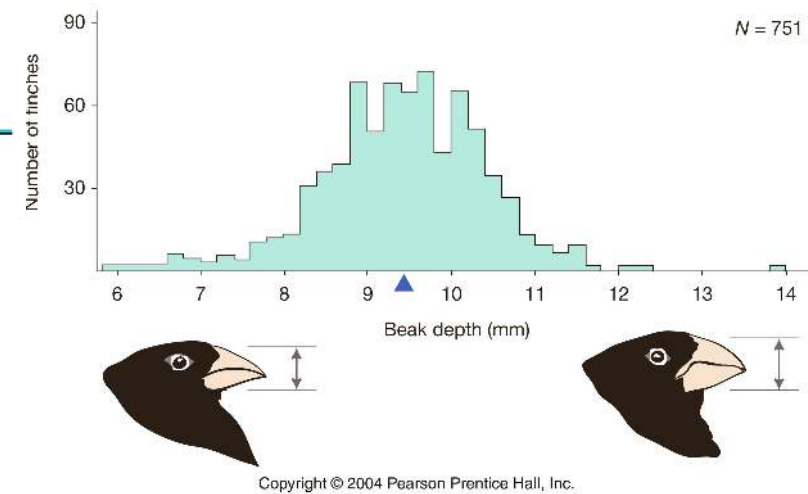
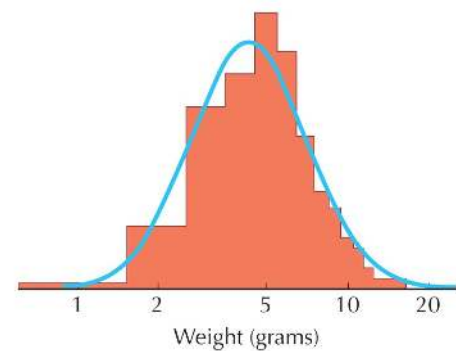
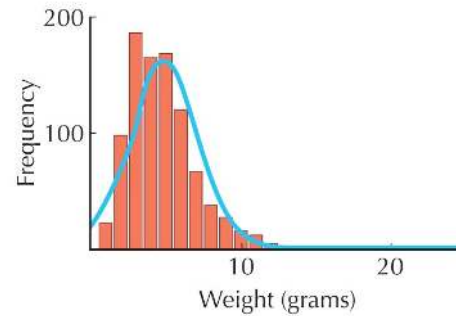
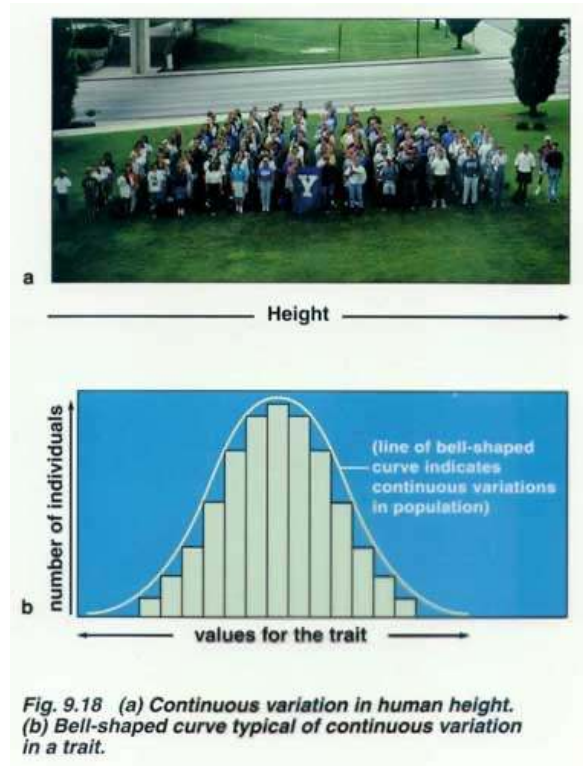
Two complementary approaches

- Reverse genetics
 - Genotype driven: what is the function of the genes or genomic variants identified as targets of selection?
 - This is what you will learn from Majda this afternoon
- Forward genetics
 - Phenotype driven: what genes or genomic variants contribute to this adaptive phenotype?
 - This is what I will focus on for the first part of the morning

Forward genetics: quantitative trait loci (QTL) mapping approach



Quantitative traits



Human disease, domesticated crops and animals,
and most traits in natural populations!

Quantitative traits

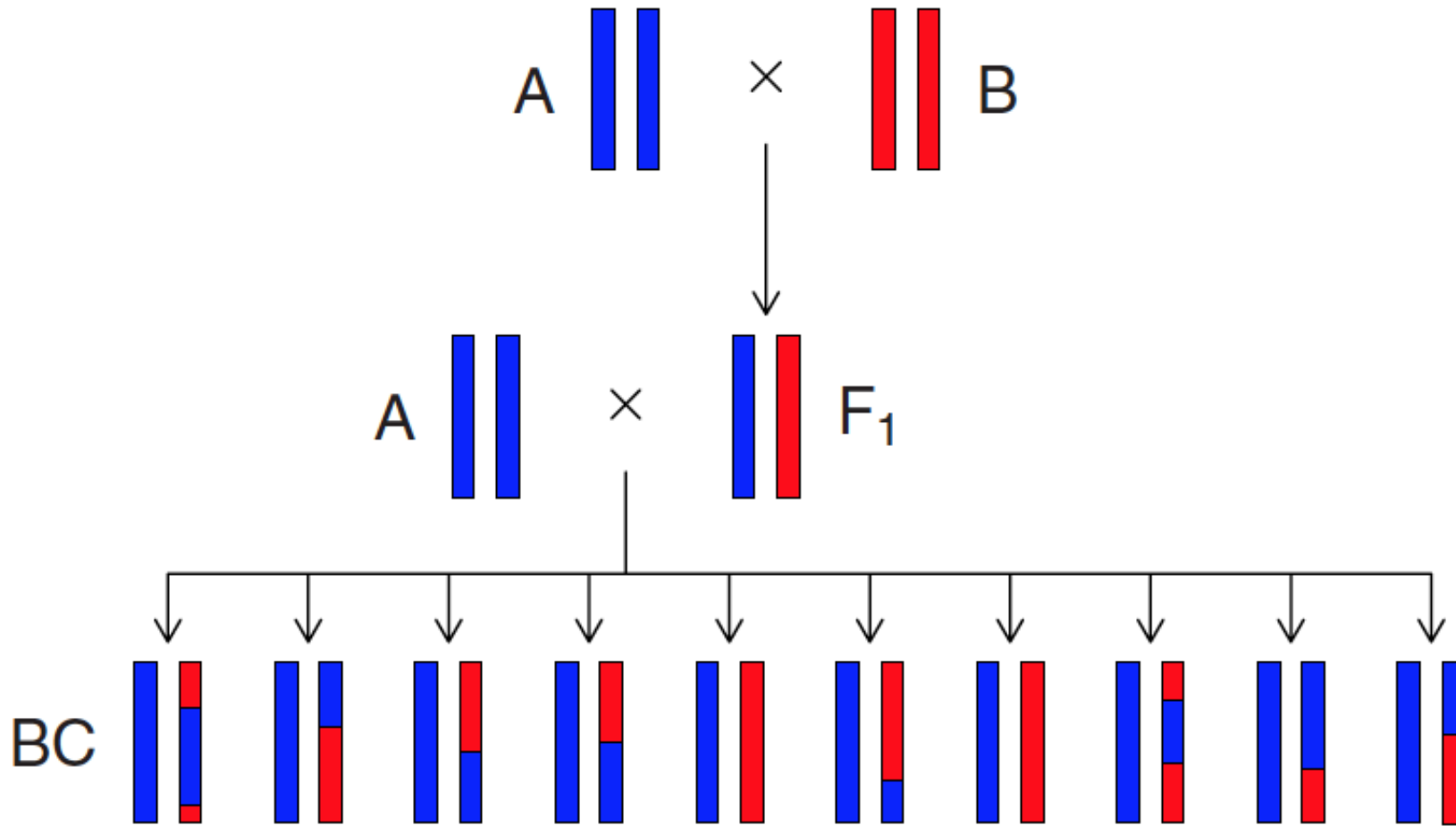
- Most phenotypic traits
- NOT a perfect correlation between phenotype and genotype
- Multiple genetic factors as well as environmental factors contribute
- Example:
 - Human height

Quantitative trait locus (QTL) mapping

What do you need for QTL mapping?

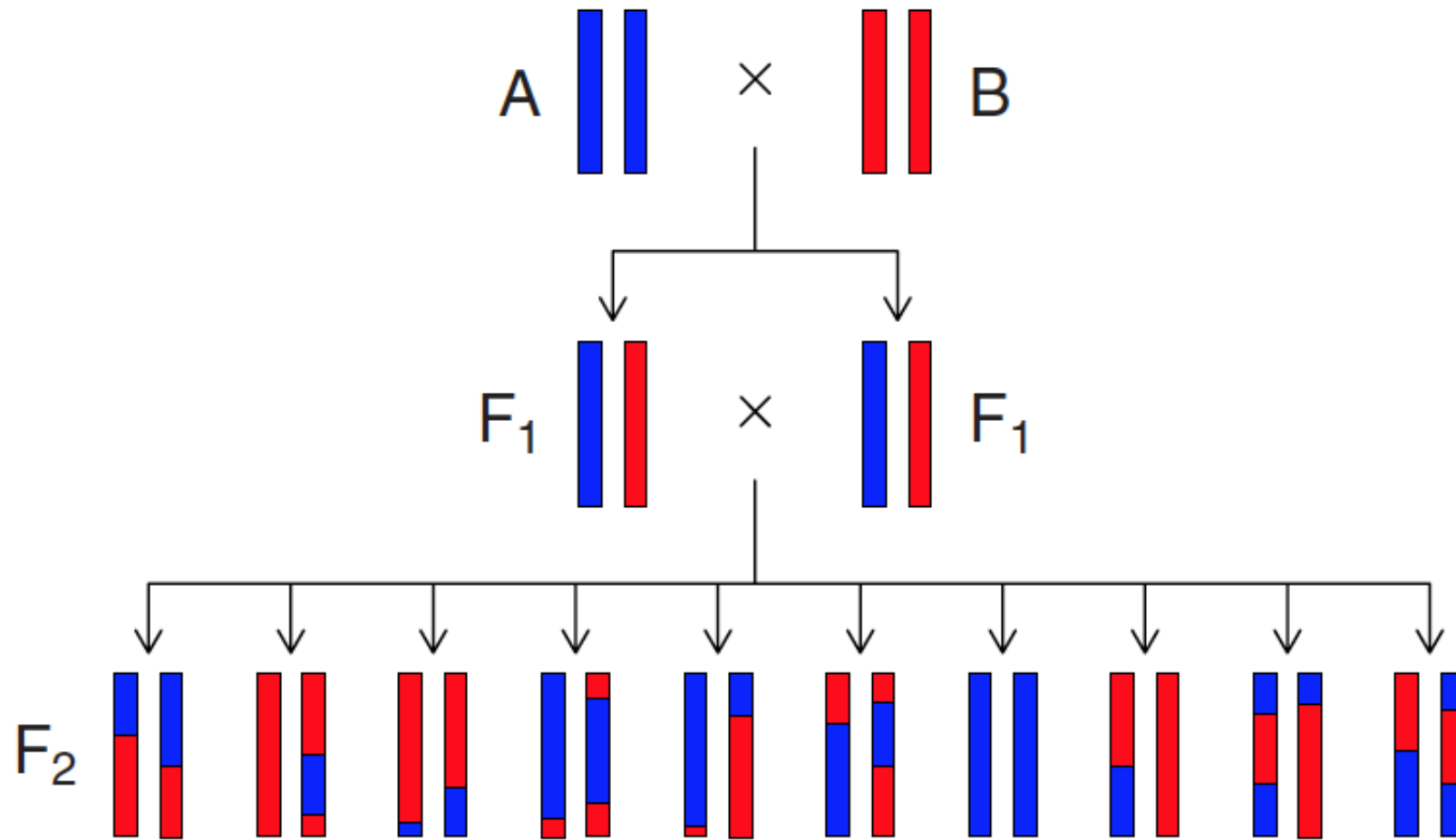
1. Genetic cross
2. Good phenotypic assays = phenotypes
3. Genetic markers = genotypes
4. Linkage map
5. Software for analyses

Genetic cross: backcross



Which genotype class is missing?

Genetic cross: intercross



Why might it not be possible to do an F₁ intercross?

Genetic crosses

- Backcross vs F2 intercross
- Number of individuals is crucial
 - More individuals provide more power to detect loci of relatively small effect on phenotype
 - At least 500 backcross or F2 individuals is ideal, though not always feasible
 - 100 individuals is enough to detect loci with a moderate effect and often a good start!

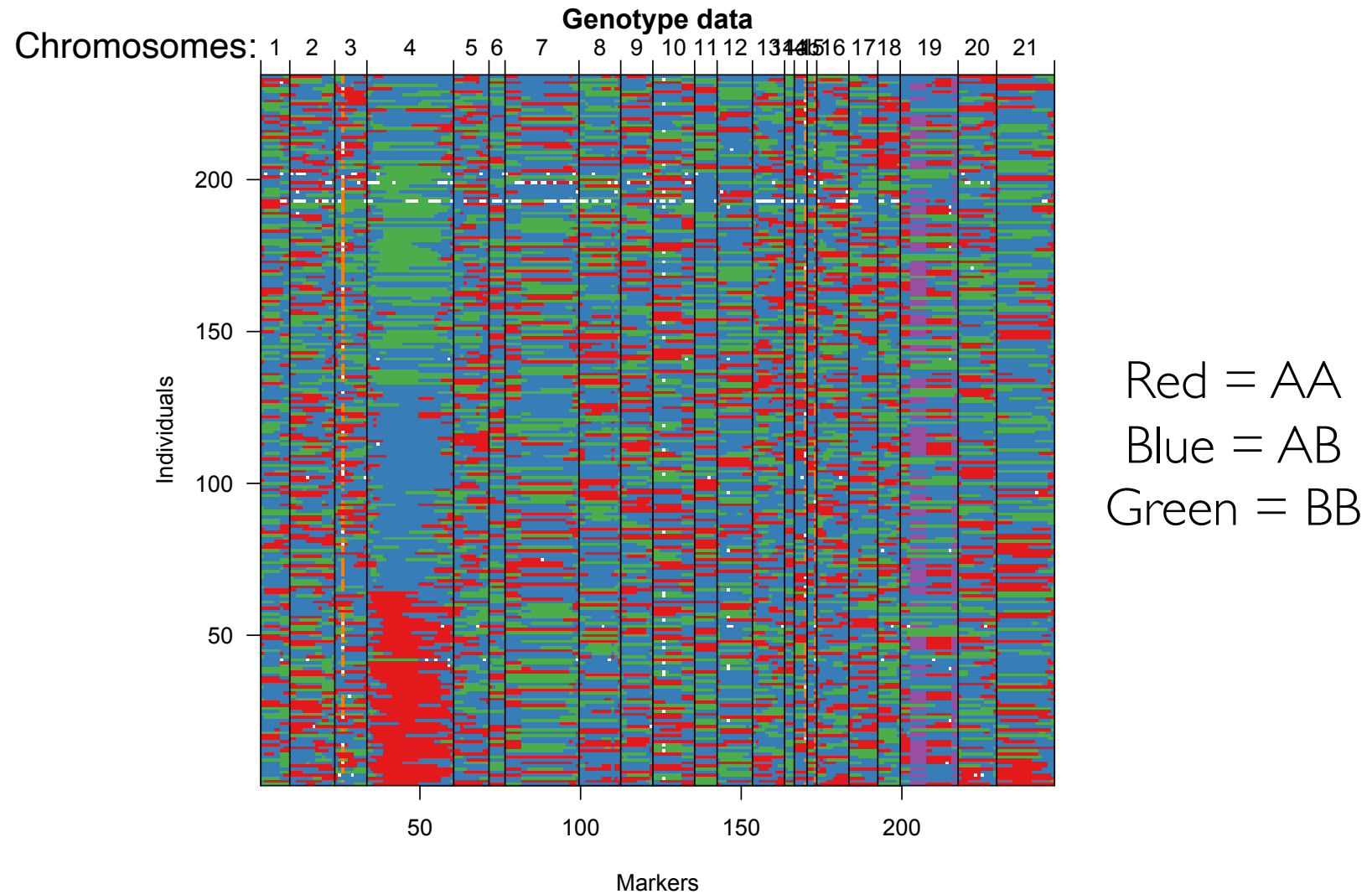
Phenotypes

- Careful phenotypic analyses is one of the most important and under-looked components of linkage mapping!
- Measure “component” traits of complex phenotypes
- Want to minimize sources of variation to isolate genetic component of variation
 - environmental effects
 - measurement error

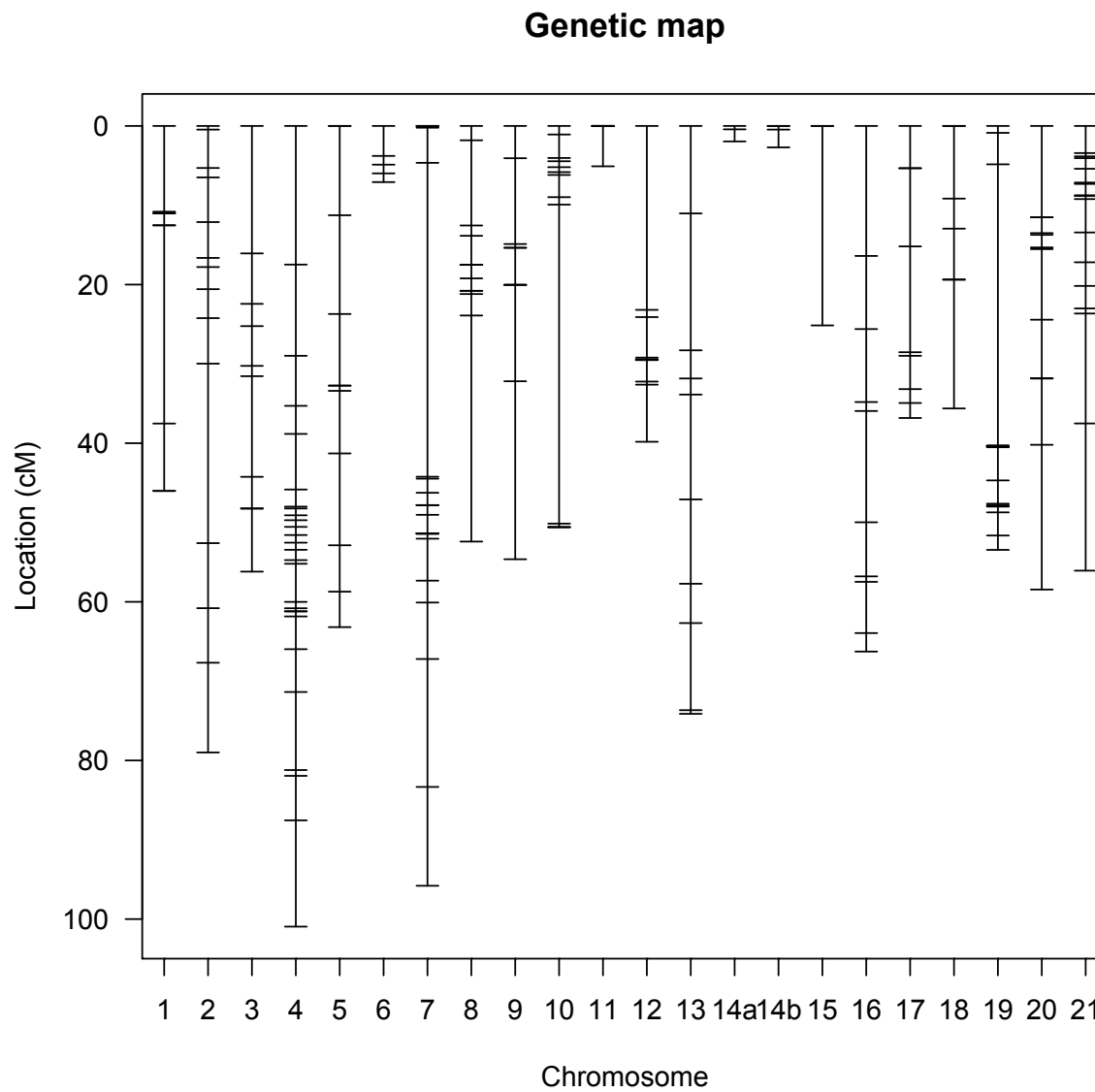
Genotypes

- Need genetic markers that allow you to determine whether an individual inherited two alleles from one grandparent (AA), two alleles from the other grandparent (BB), or is heterozygous (AB)
- Need many markers per chromosome
- Next-generation sequencing has provided a relatively easy way to identify these markers

Genotypes



Linkage map



Analyses software

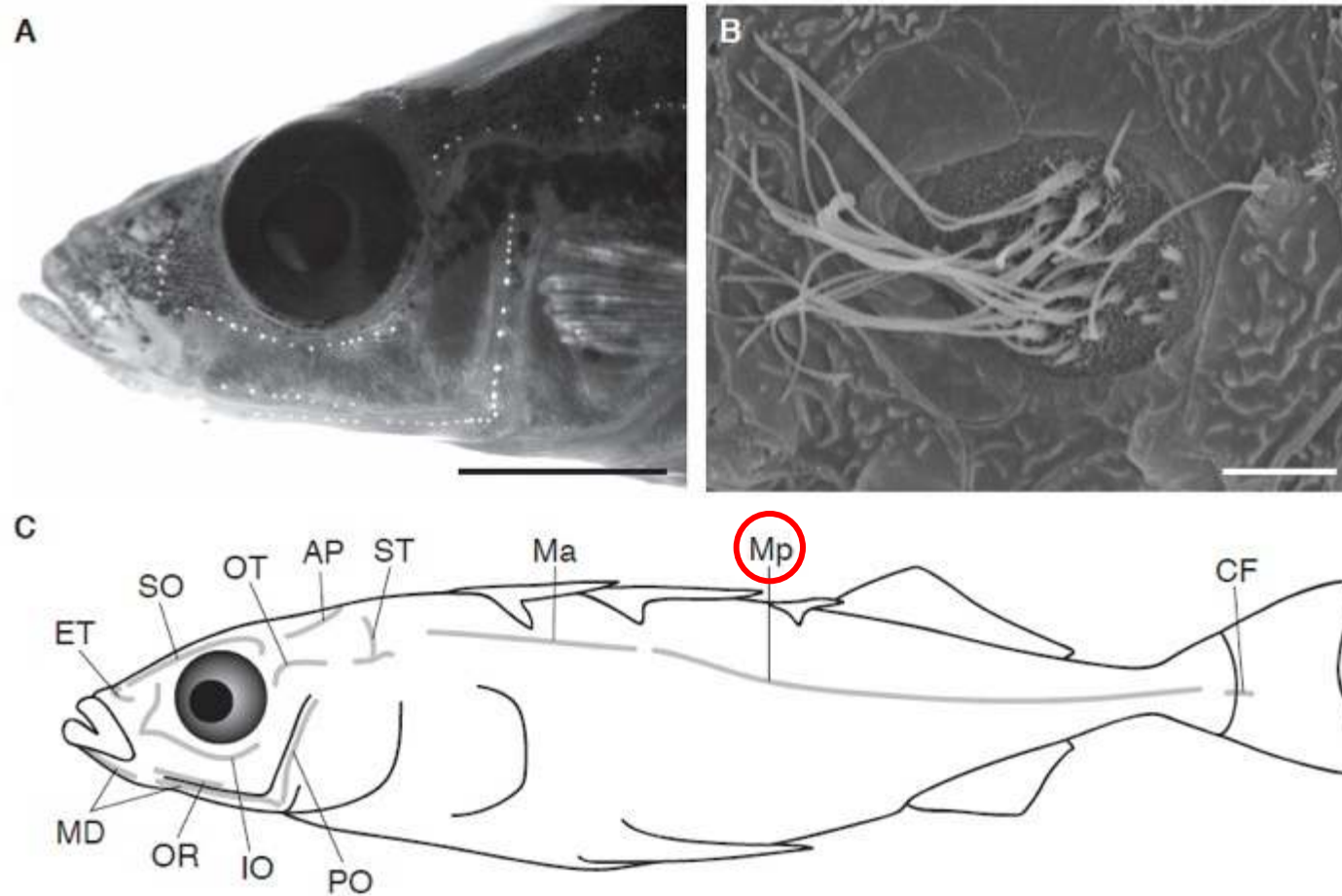
- R/qtl is the best!
- Broman and Sen (2009) A guide to QTL mapping with R/qtl
- Open source!
- <https://rqtl.org/>

QTL mapping exercise

Lateral plate and lateral line differences between marine and benthic sticklebacks



Mechanosensory lateral line



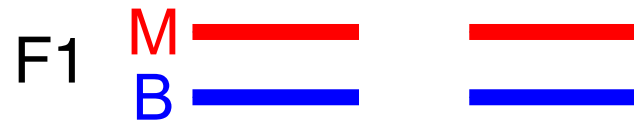
marine



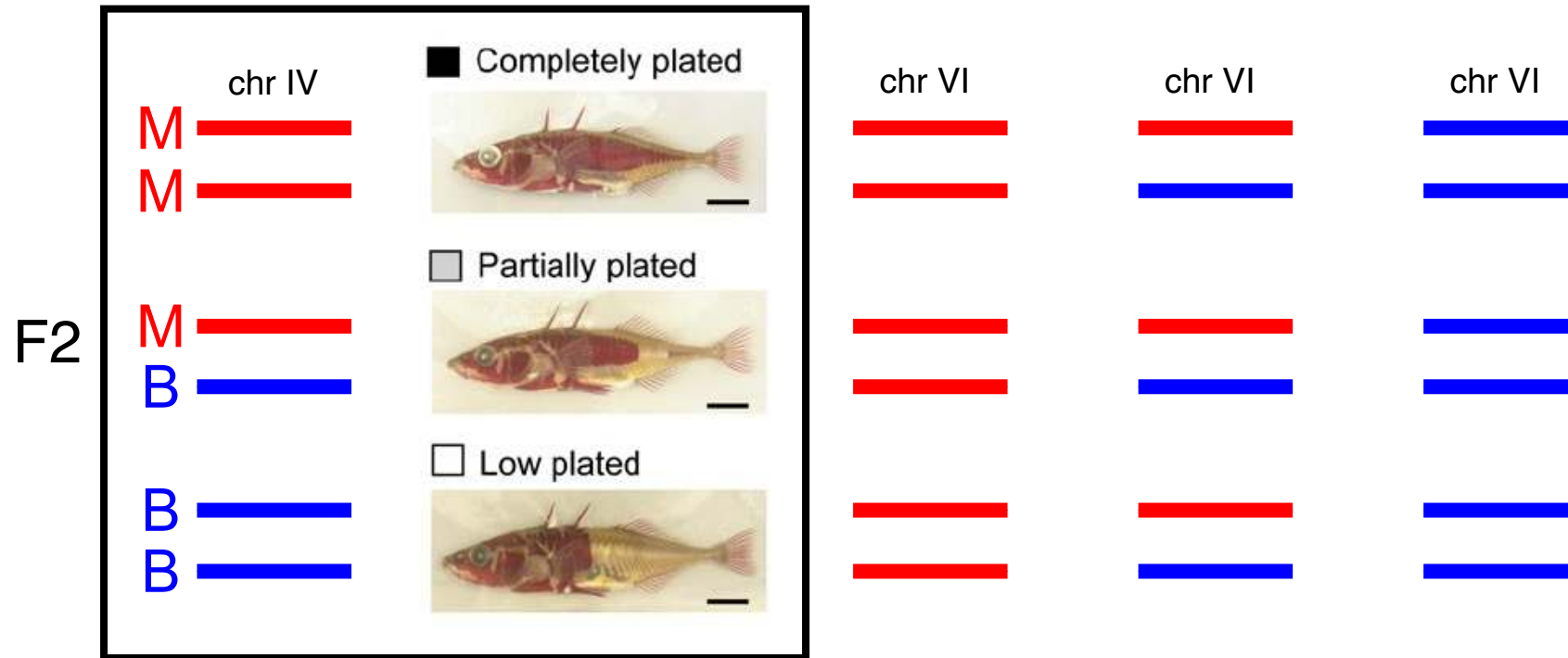
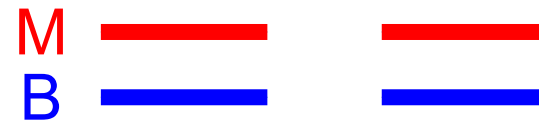
benthic



X



X

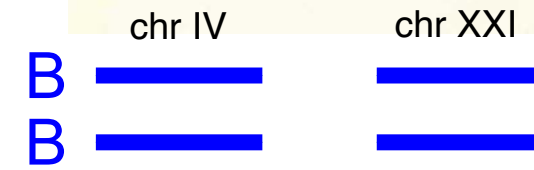
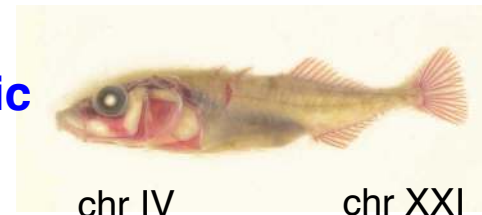


Gene for plates is on chr IV

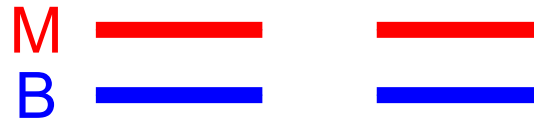
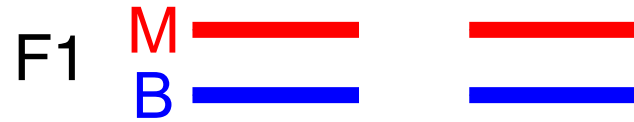
marine



benthic



X



X

F2

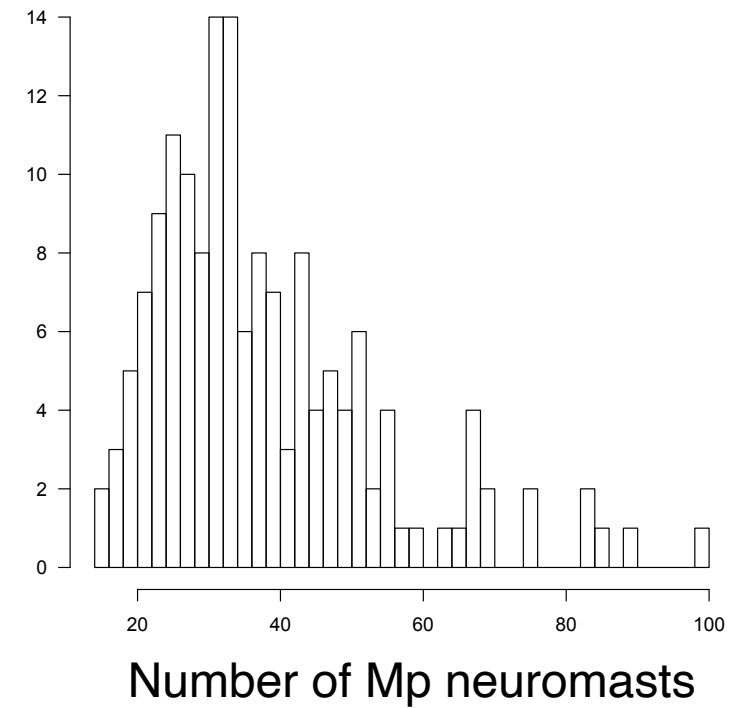
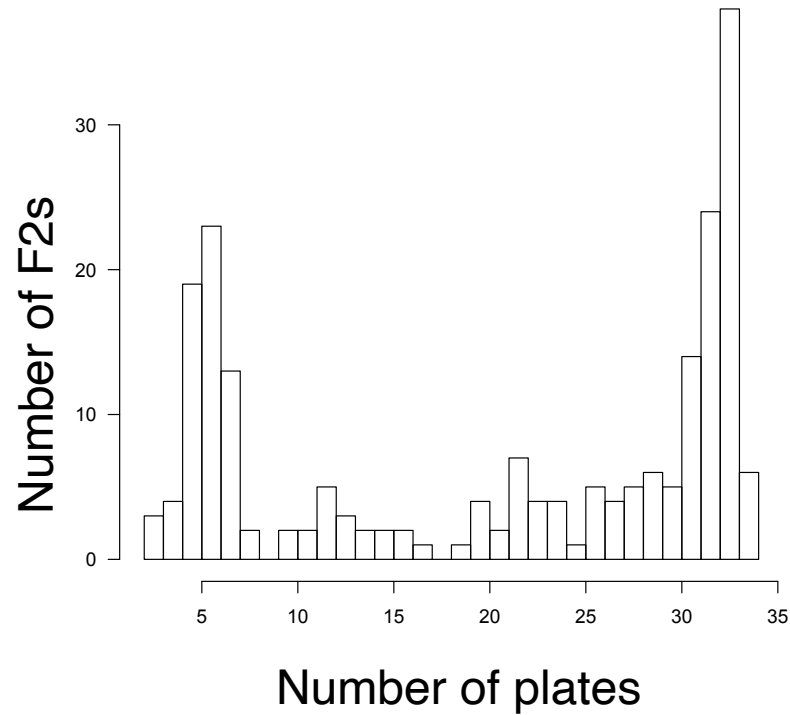


Plate number: no genotype-phenotype association at chrVI marker

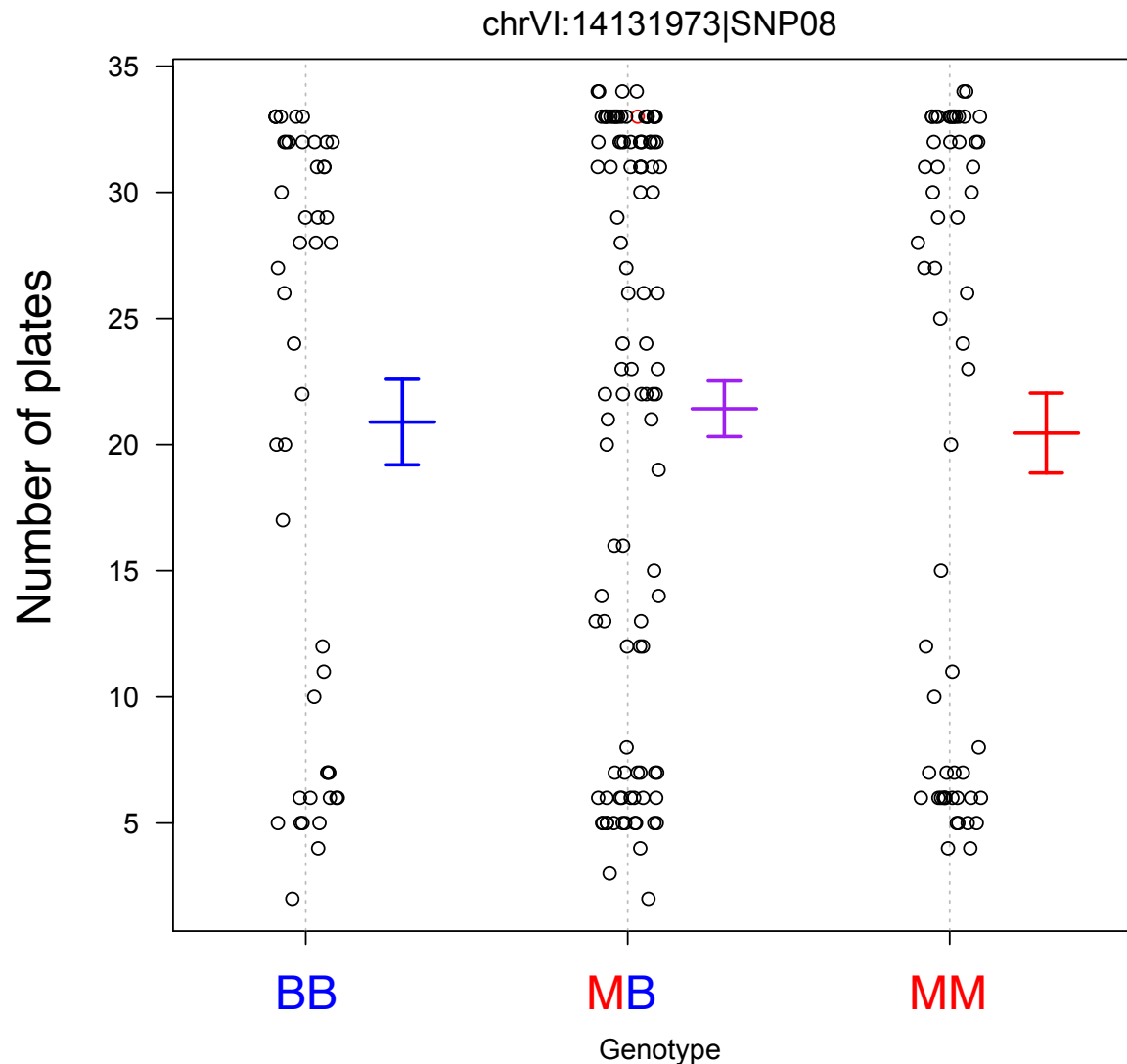


Plate number: genotype-phenotype association
at chr IV marker

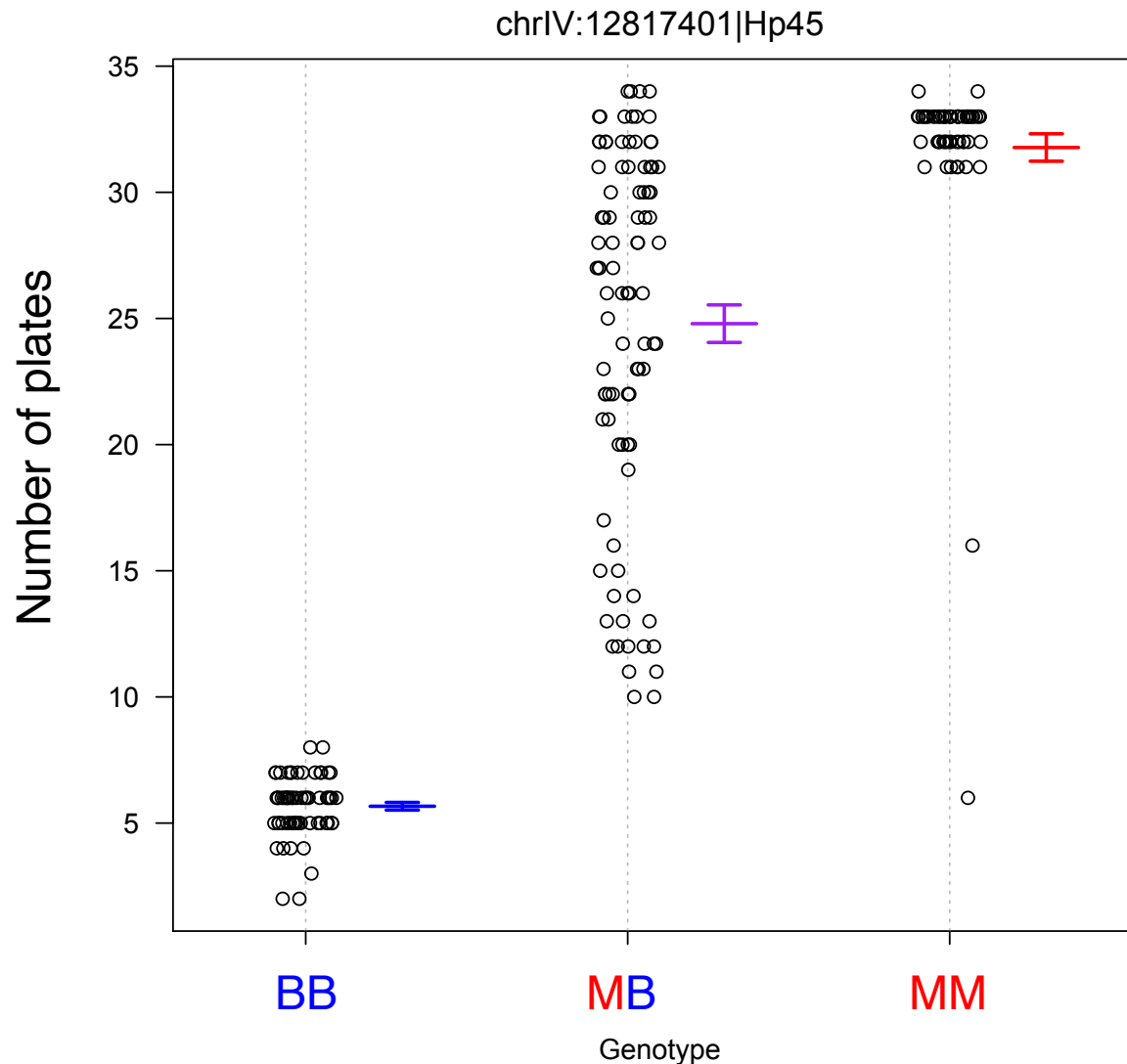


Plate number: genotype-phenotype association at chr XXI marker

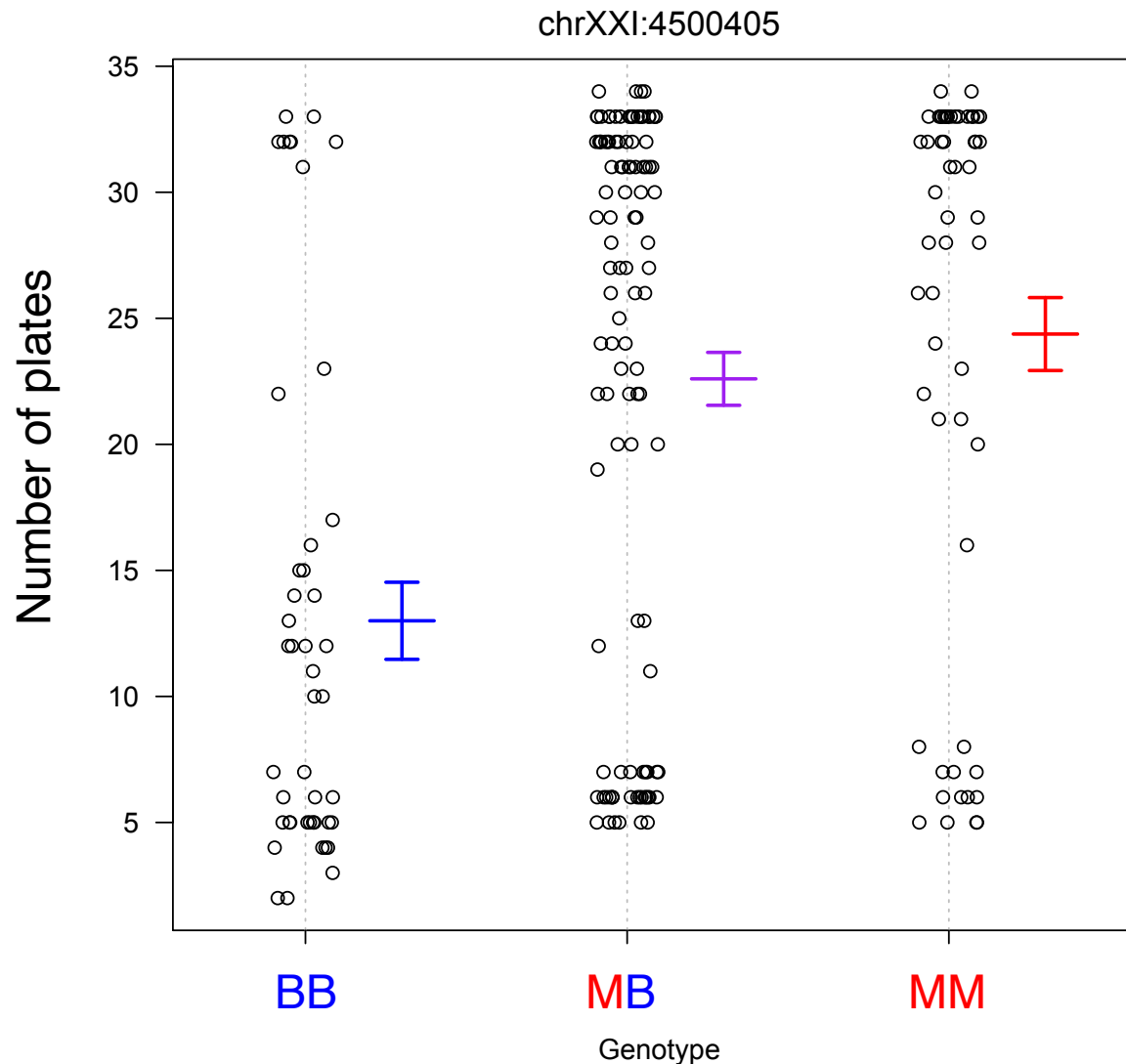
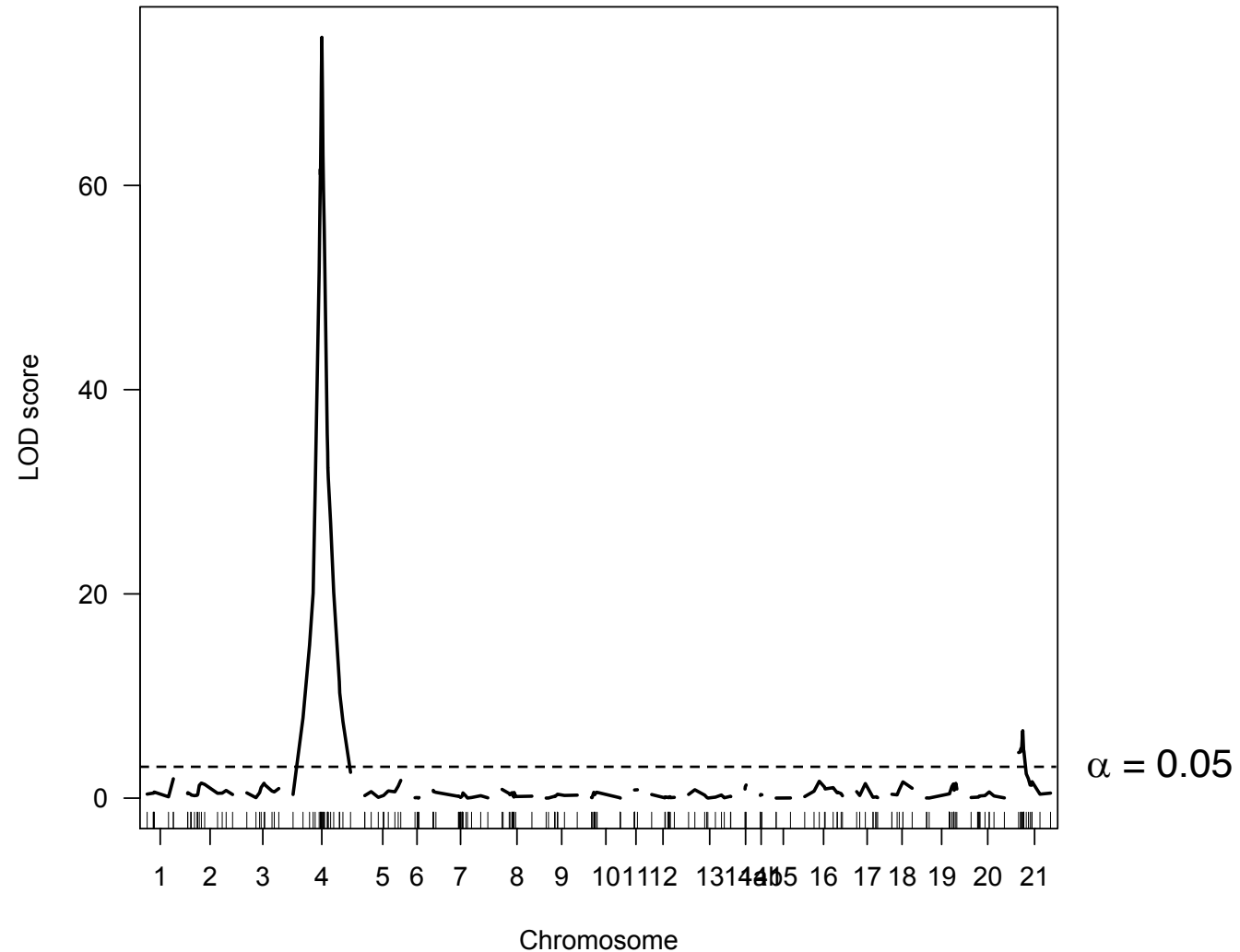


Plate number: QTL mapping



What is a LOD score?

- LOD score is the strength of evidence for the presence of a genotype-phenotype association at a particular locus
- $\text{LOD} = \log_{10}$ likelihood ratio comparing the hypothesis of an association at a locus versus the null hypothesis of no association
- LOD of 3 is generally considered significant
 - probability of only 1 in 1000 that there is no association at a single locus
- But, we test many loci so we use permutation tests to empirically determine the significance threshold
 - Usually $\alpha = 0.05$ (5% false positive rate)

marine



P

M
M

chr IV

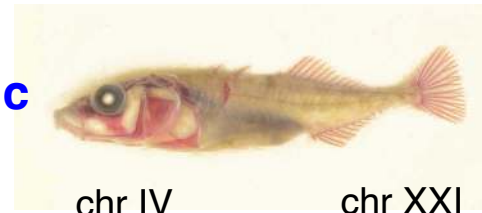


chr XXI



X

benthic



B
B

chr IV



chr XXI



F1

M
B

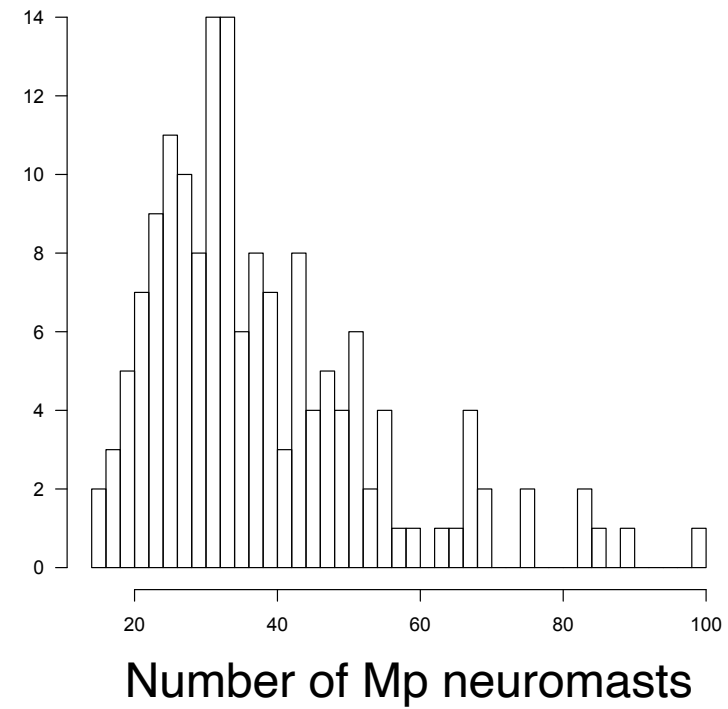
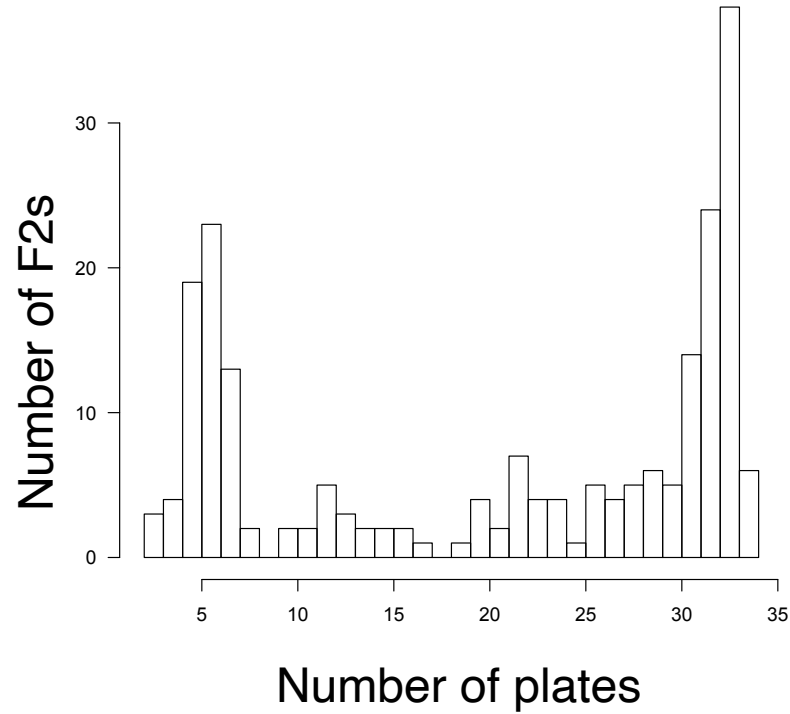


X

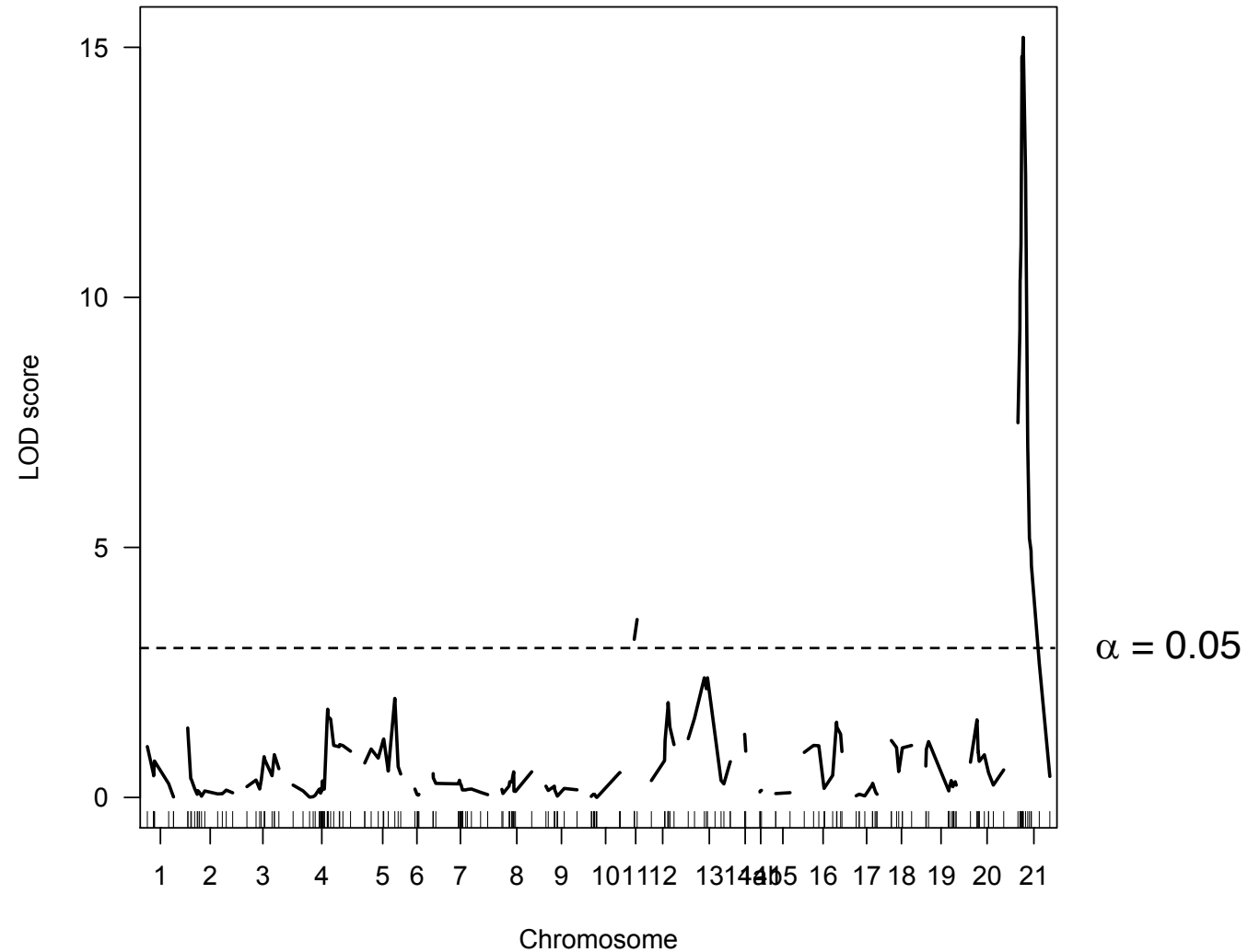
M
B



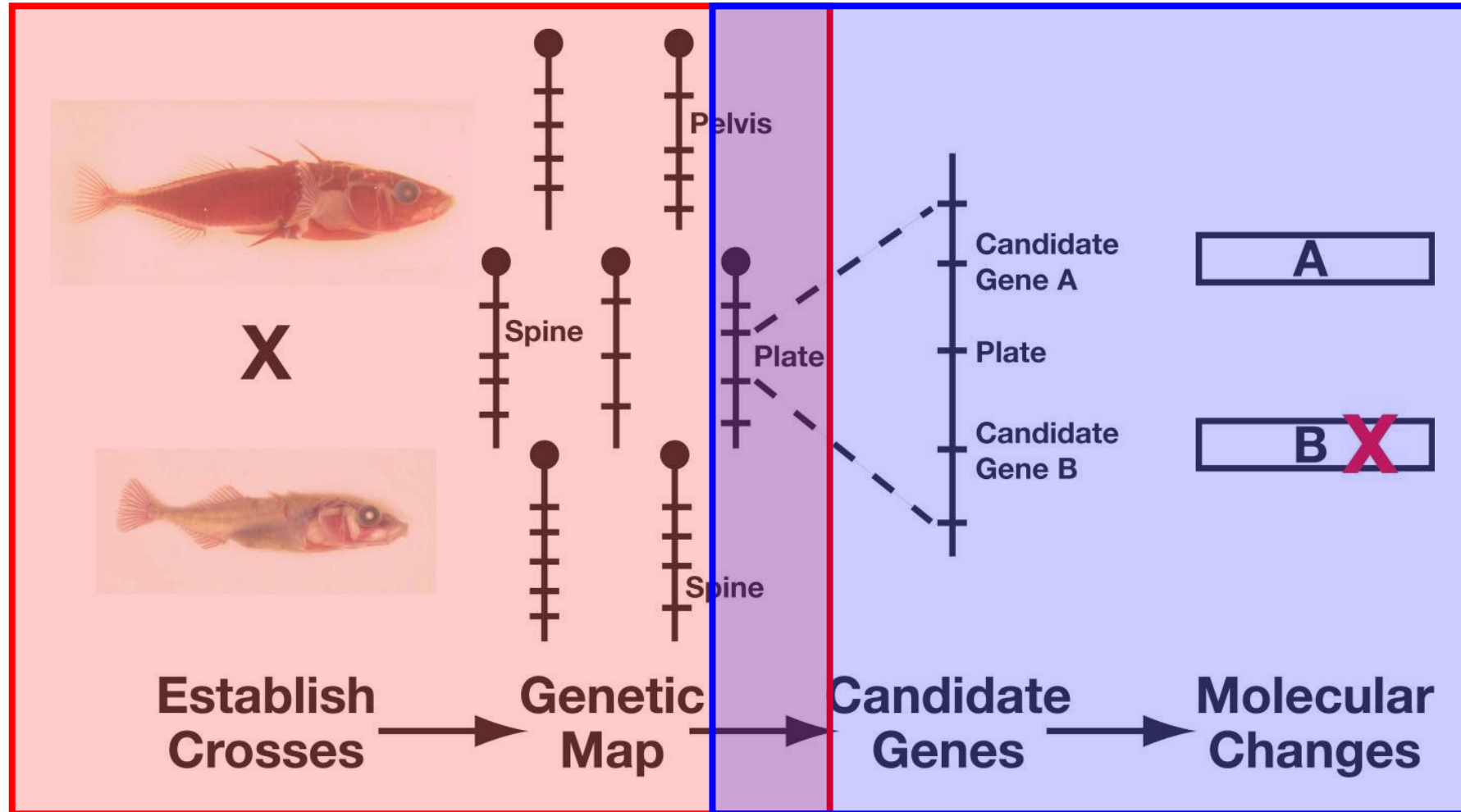
F2



Mp neuromast number: QTL mapping



Forward genetics: quantitative trait loci (QTL) mapping approach



We have a QTL: now what?

1. Use additional recombination mapping to further narrow QTL interval
2. Identify candidate genes in QTL interval
3. Look for molecular differences in candidate genes between populations with different phenotypes
4. Use genetic manipulation to show that a molecular difference is necessary and sufficient for phenotypic difference

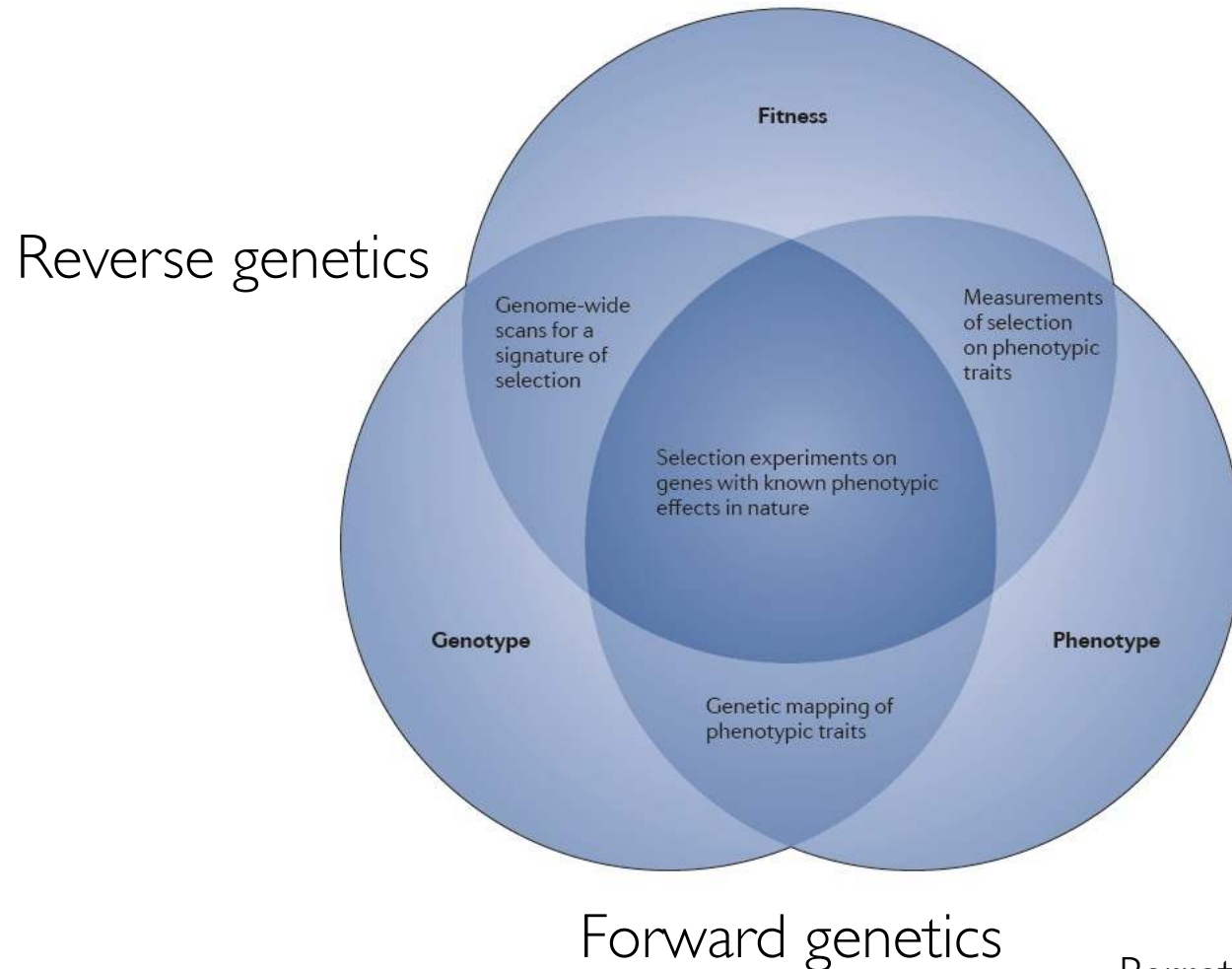
Forward genetic approach

- Strengths?
 - Identifies the specific genes and mutations that underlie phenotypic traits
- Limitations?
 - Path from phenotype to genotype is long
 - Ability to cross the populations of interest
 - Limited by recombination events in crosses
 - Best to focus on traits that you know are adaptive

Reverse genetic approach

- Strengths?
 - Next generation sequencing makes this approach feasible in any natural population
 - Can survey entire genome
 - Identifies genes that are targets of selection
- Limitations?
 - Can be difficult to link genetic variation to phenotypic variation

Integrated conceptual framework to understand the genetics of adaptation

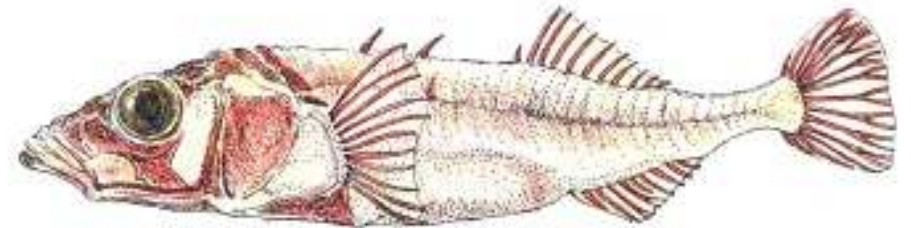
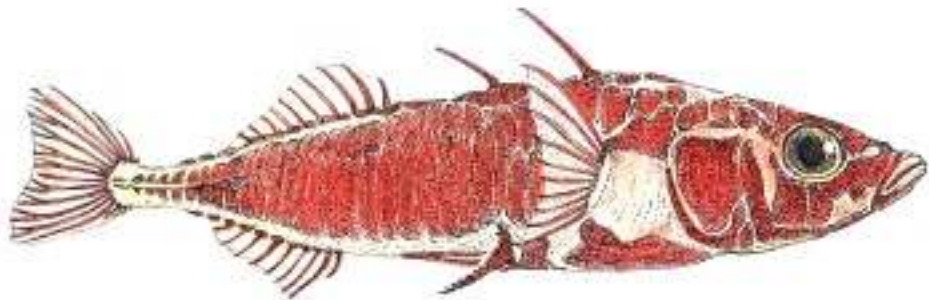


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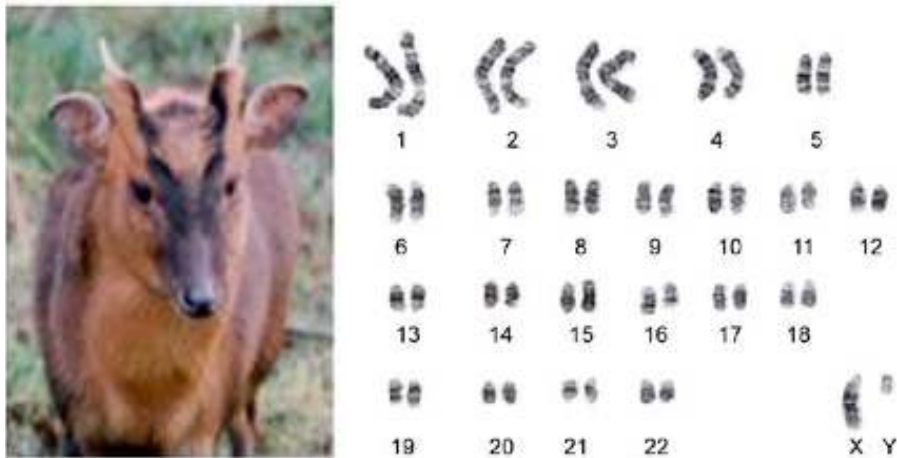
Combining genomics and experimental studies to understand the role of chromosomal rearrangements in adaptation to divergent environments



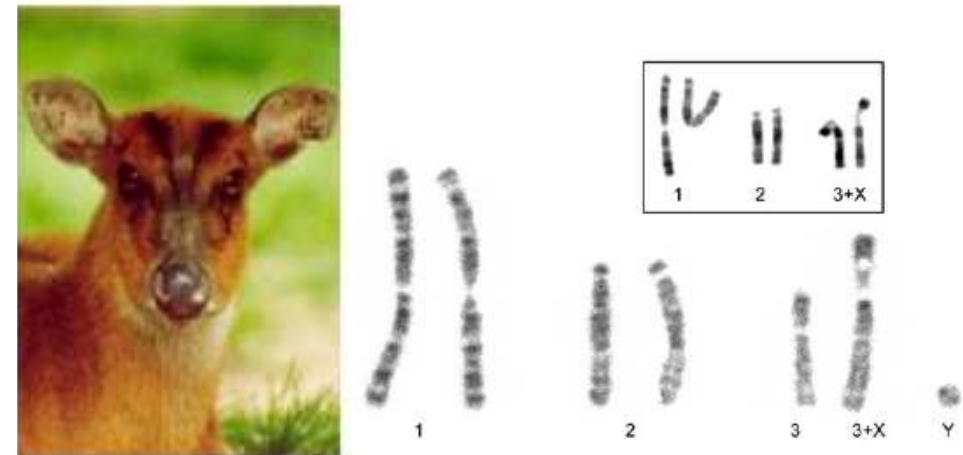
Katie Peichel
University of Bern

Chromosome number and structure can vary dramatically between species

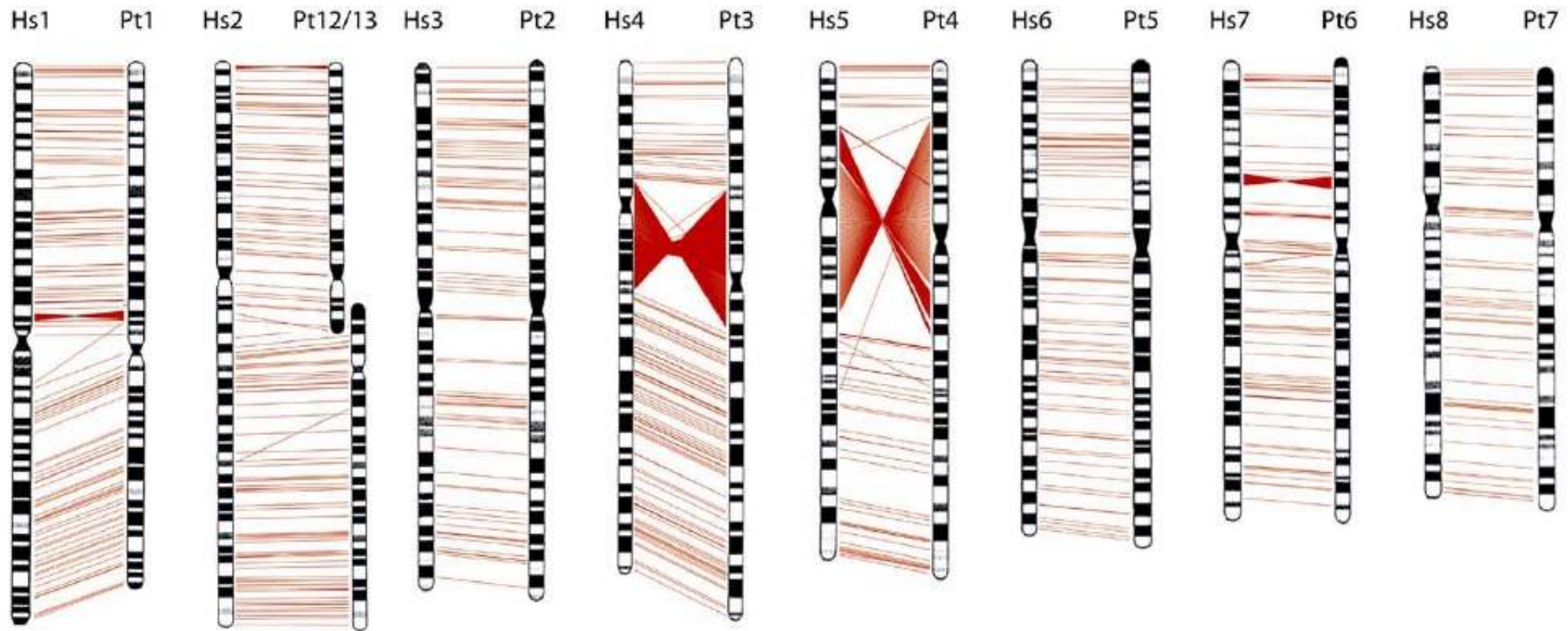
Chinese muntjac
 $2n = 46$



Indian muntiac
 $2n = 6,7$

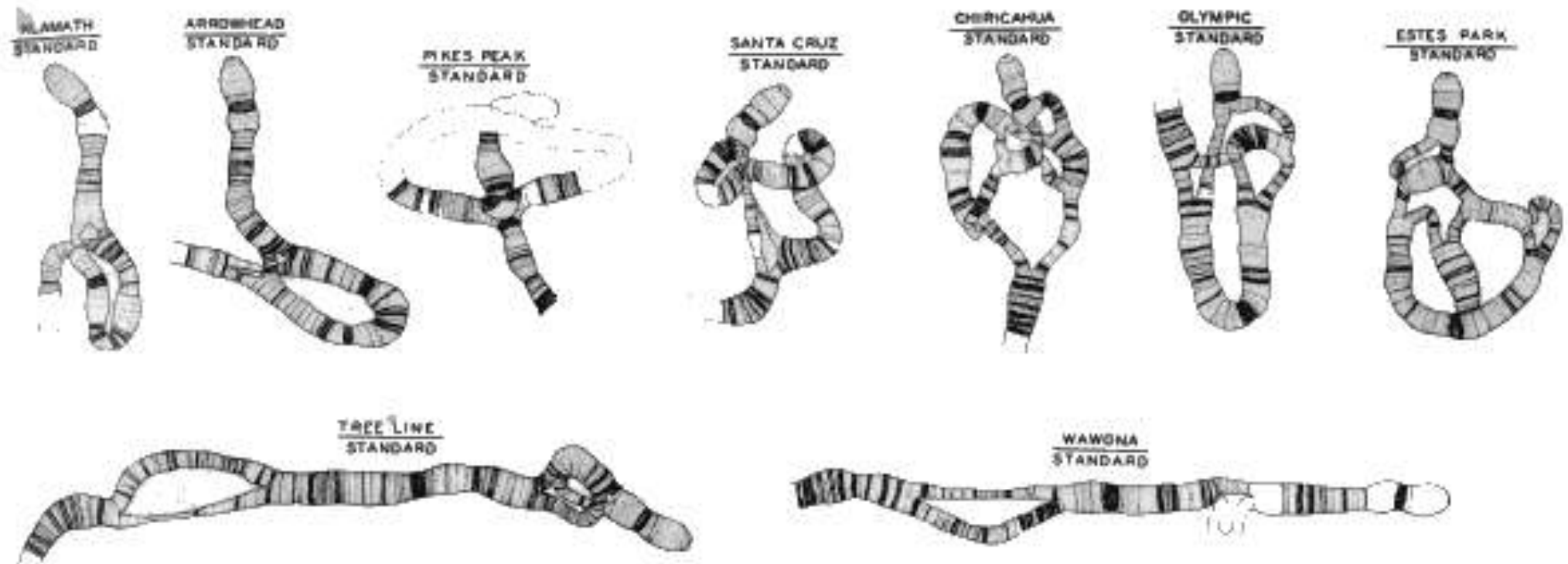


Chromosome number and structure can vary dramatically between species



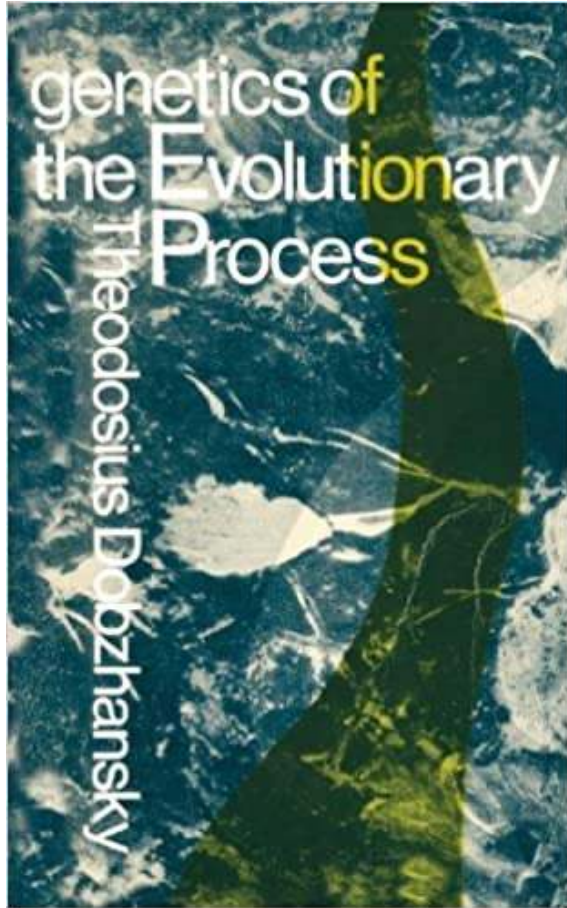
Human vs chimpanzee: fusion and inversions

Chromosome number and structure can even vary dramatically within species

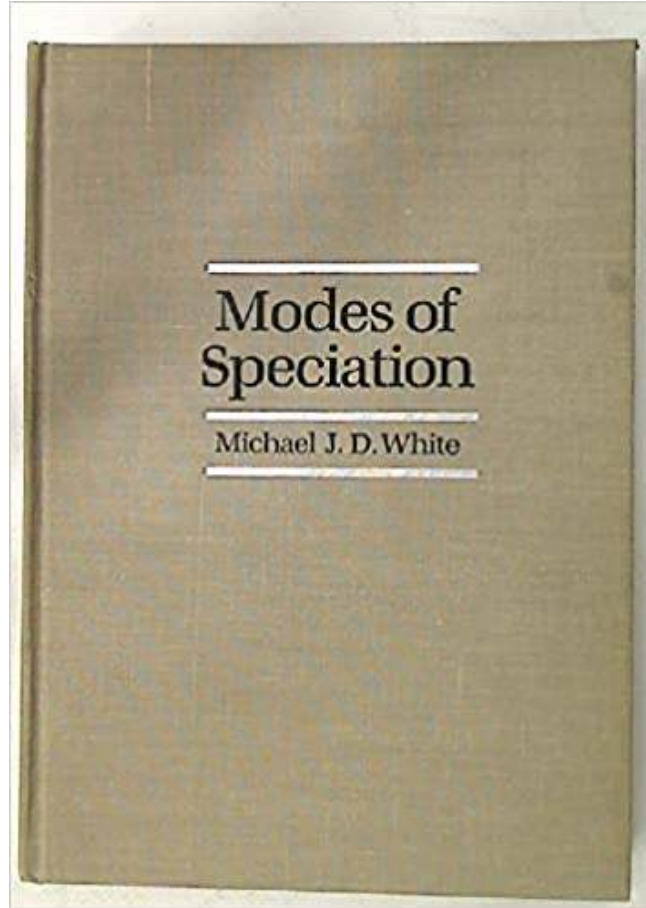


Drosophila pseudoobscura inversion polymorphisms

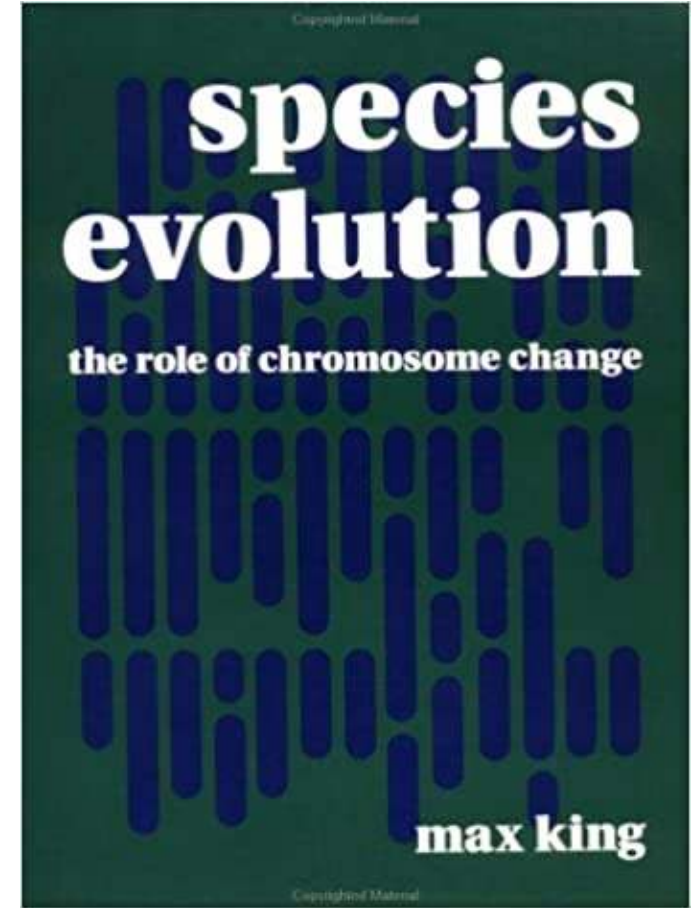
Chromosomal changes as drivers of adaptation and speciation?



Dobzhansky 1970



White 1978



King 1993

Chromosomal changes as drivers of adaptation and speciation?

Chromosomal rearrangements and speciation

Loren H. Rieseberg

Chromosomal inversions and the reproductive isolation of species

Mohamed A. F. Noor*, Katherine L. Grams, Lisa A. Bertucci, and Jane Relland

Genomic rearrangements and the evolution of clusters of locally adaptive loci

Sam Yeaman^{a,b,1}

Chromosomal speciation revisited: rearranging theory with pieces of evidence

Rui Faria^{1,2} and Arcadi Navarro^{1,3}

Chromosome Inversions, Local Adaptation and Speciation

Mark Kirkpatrick^{*,1} and Nick Barton[†]

Revisiting the Impact of Inversions in Evolution: From Population Genetic Markers to Drivers of Adaptive Shifts and Speciation?

Ary A. Hoffmann¹ and Loren H. Rieseberg²

Eco-Evolutionary Genomics of Chromosomal Inversions

Maren Wellenreuther^{1,3,*} and Louis Bernatchez²

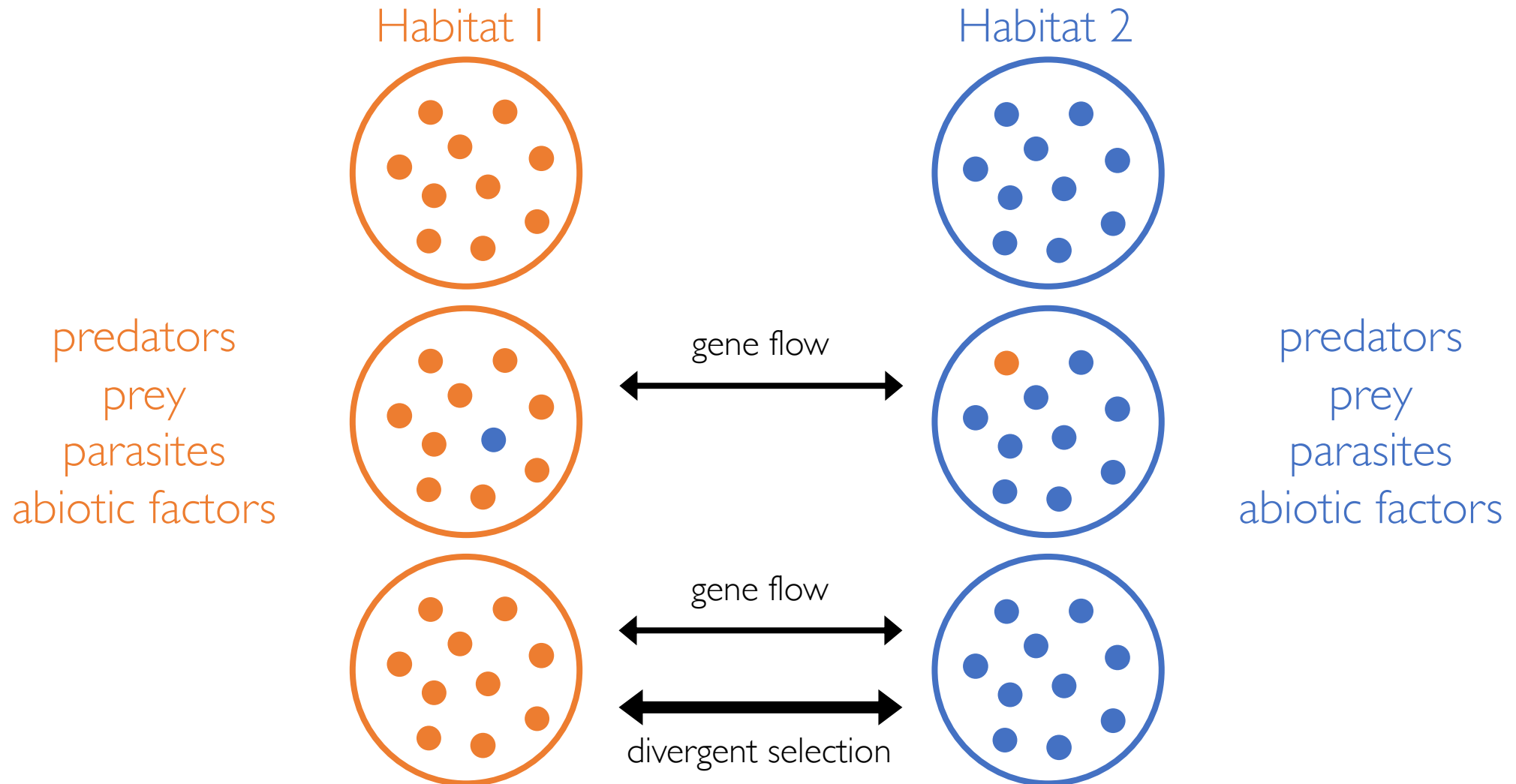
LOCAL ADAPTATION AND THE EVOLUTION OF CHROMOSOME FUSIONS

Rafael F. Guerrero^{1,2} and Mark Kirkpatrick¹

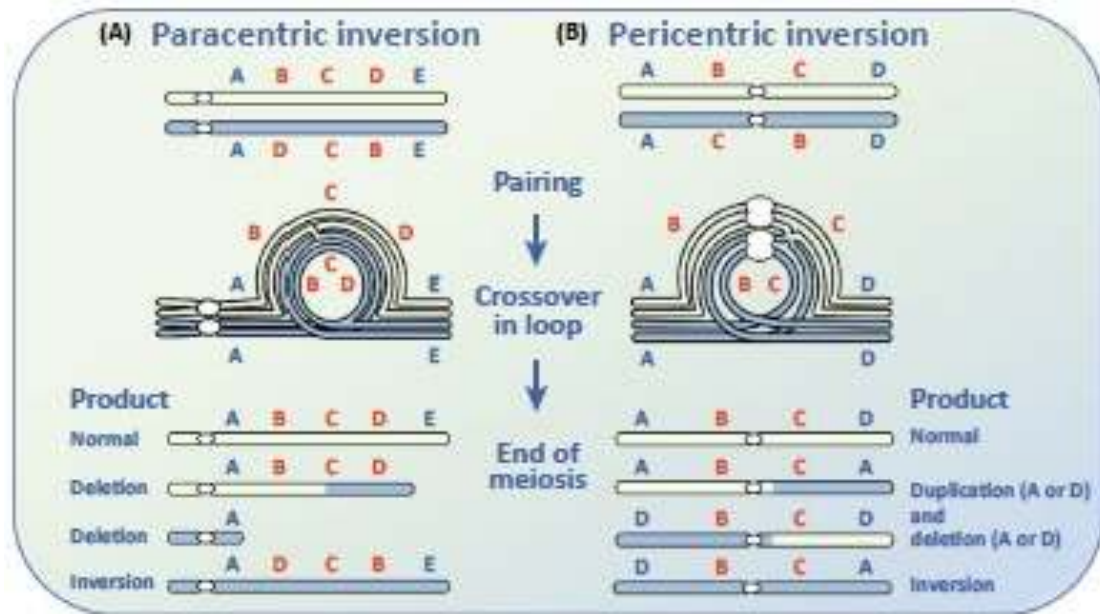
Chromosomal changes as drivers of adaptation and speciation?

- Many current sequencing studies are revealing evidence for changes in chromosome number and structure within and between species
- But, there is relatively little data directly linking these chromosomal changes to **adaptation** and speciation
 - Kitano *et al* 2009 *Nature*: chromosomal fusions and speciation
 - Peichel *et al* 2020 *Genome Biology*: inversions and sex chromosome evolution

Local adaptation to divergent environments



Chromosomal changes could facilitate local adaptation by linking together adaptive alleles



Wellenreuther and Bernatchez 2018 *TREE*

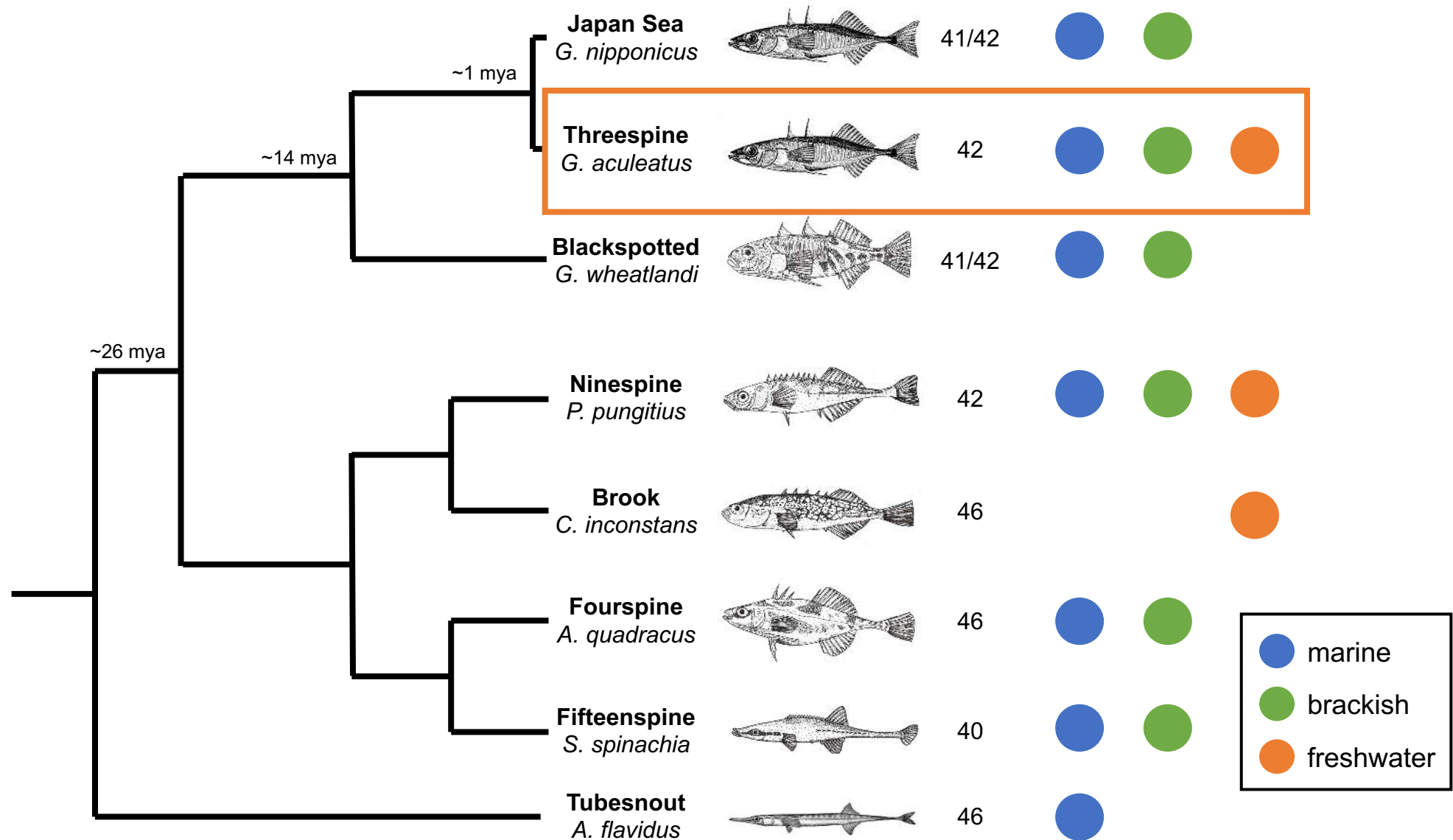
- If recombination happens within an inversion heterozygote, recombinant gametes are inviable
- Thus, recombination is effectively suppressed within inversions
- Inversions might be particularly important to link multiple adaptive alleles in cases of local adaptation with gene flow, where heterozygotes can be formed
- This theory predicts that we will find linkage of multiple adaptive traits to chromosomal inversions (or fusions*)

*Chromosomal fusions also lead to a local reduction of recombination but through a different mechanism

Do chromosomal changes facilitate local adaptation?

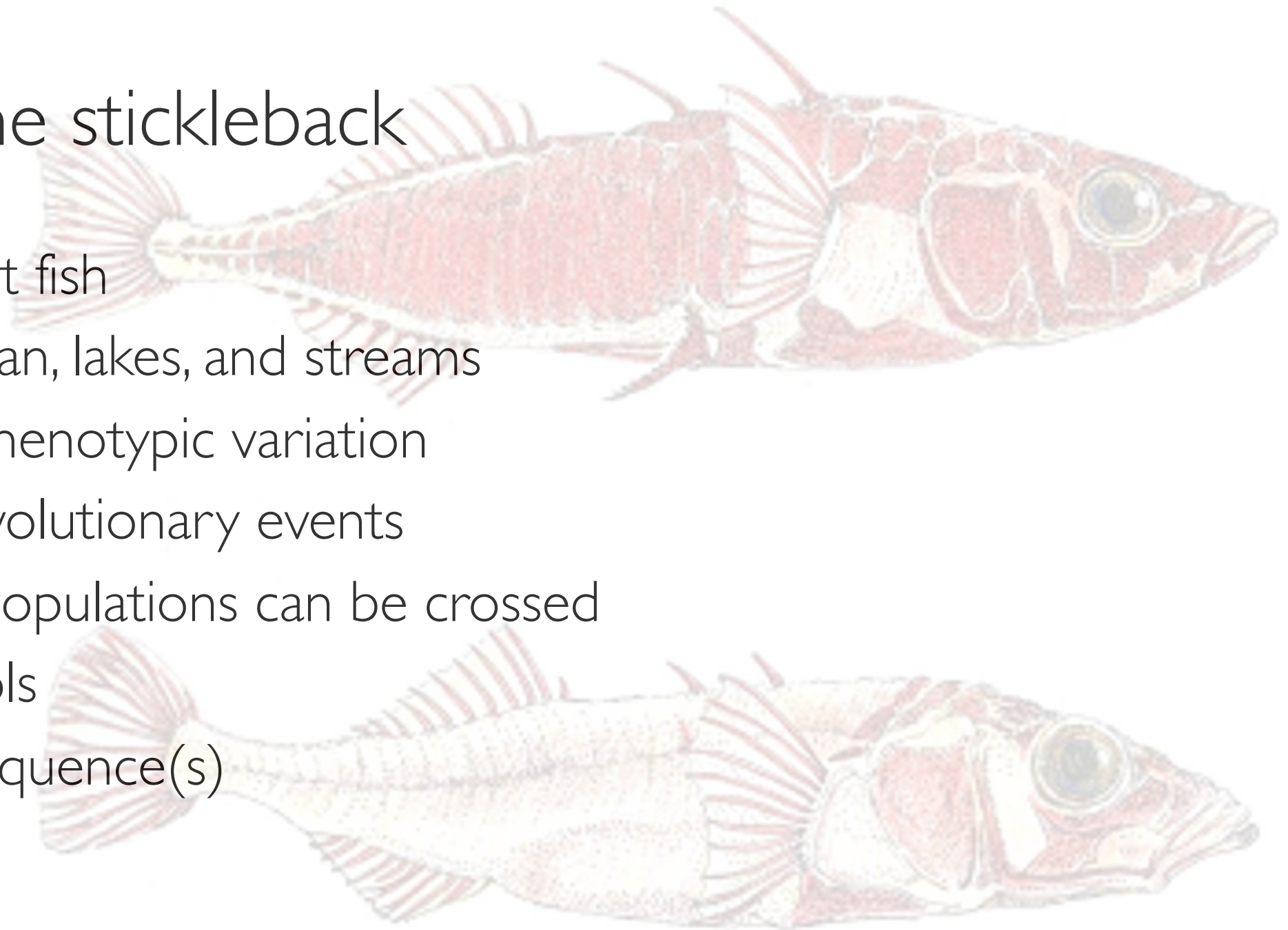
- Are chromosomal changes, such as inversions or fusions, under divergent selection in nature?
- Are multiple adaptive traits linked to chromosomal inversions or fusions?
- Do chromosomal inversions or fusions harbor multiple adaptive alleles?

Stickleback family of fish (Gasterosteidae)



Threespine stickleback

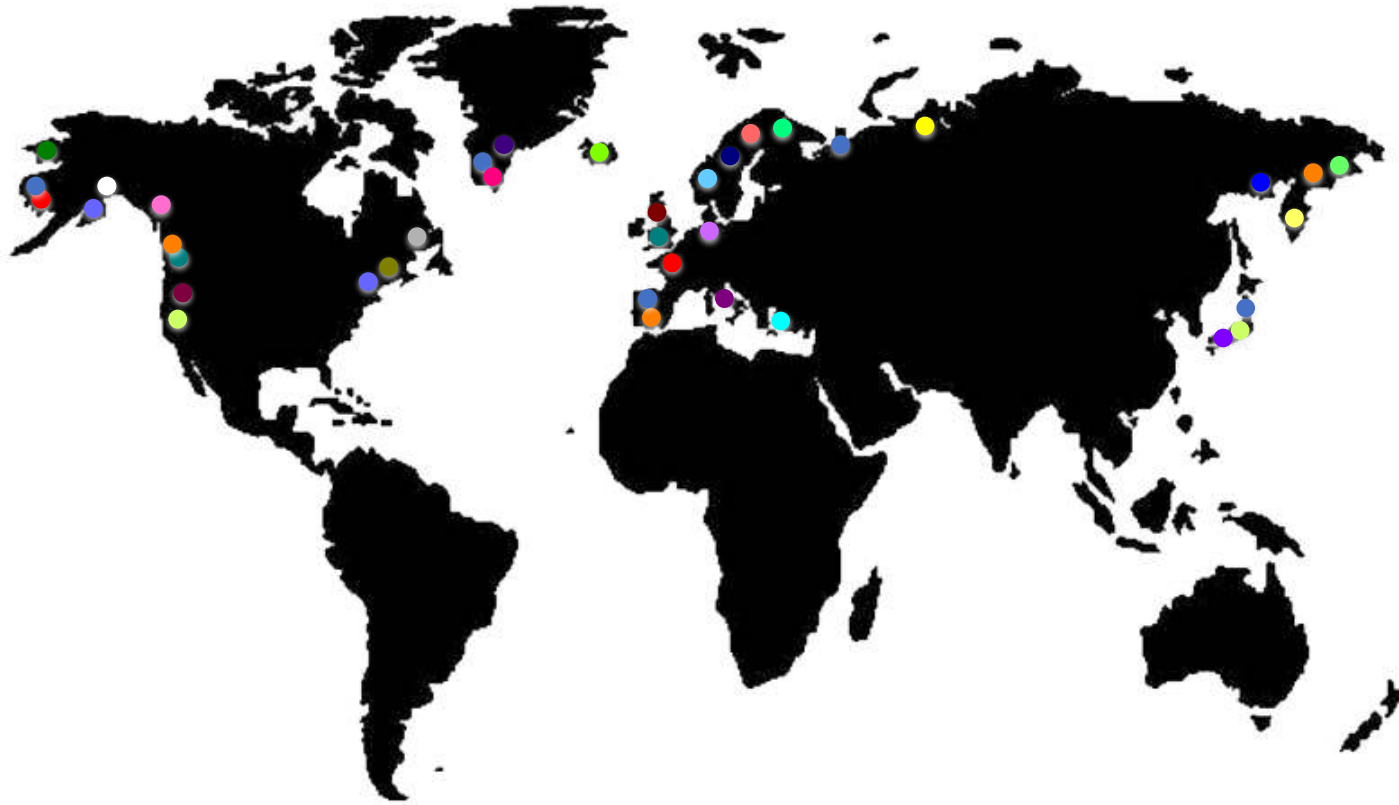
- Small teleost fish
- Lives in ocean, lakes, and streams
- Extensive phenotypic variation
- Replicate evolutionary events
- Divergent populations can be crossed
- Genetic tools
- Genome sequence(s)



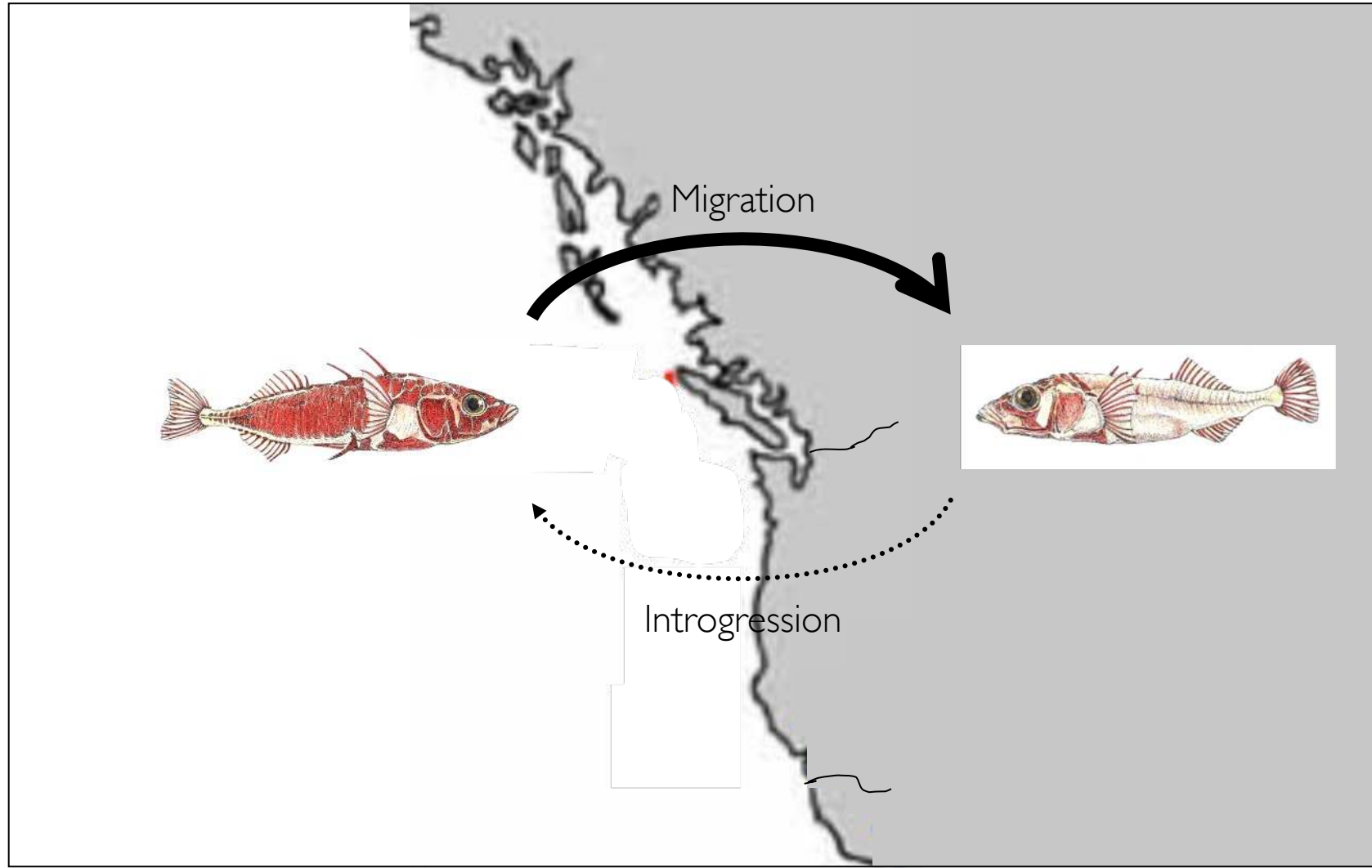
Ancestral marine populations



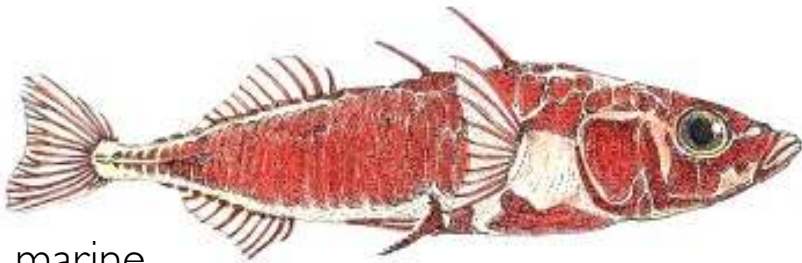
Derived freshwater populations



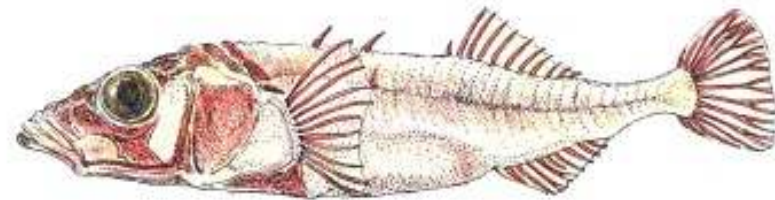
Gene flow between marine and freshwater populations



Marine vs freshwater sticklebacks



marine



freshwater

Drawings by Kirsten Bomblies
Photos by Seiichi Mori and Jun Kitano

Marine vs freshwater sticklebacks



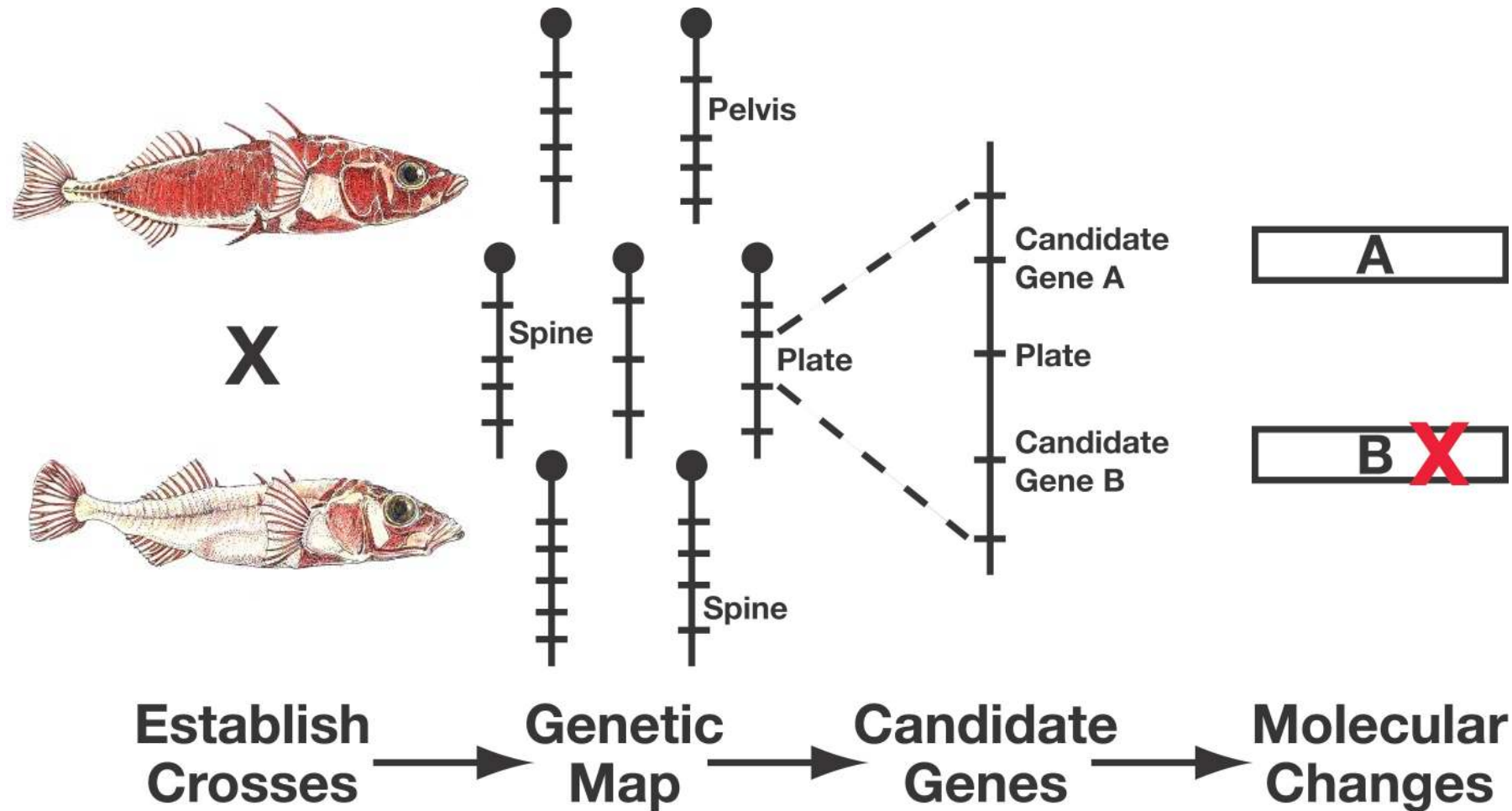
Large, silvery, plated
Migratory, schooling
Saltwater & freshwater tolerant
Lives 2 years



Small, striped, unplated
Resident, non-schooling
Saltwater intolerant
Lives 1 year

Is there genetic linkage of these multiple adaptive traits?

Quantitative trait locus (QTL) mapping



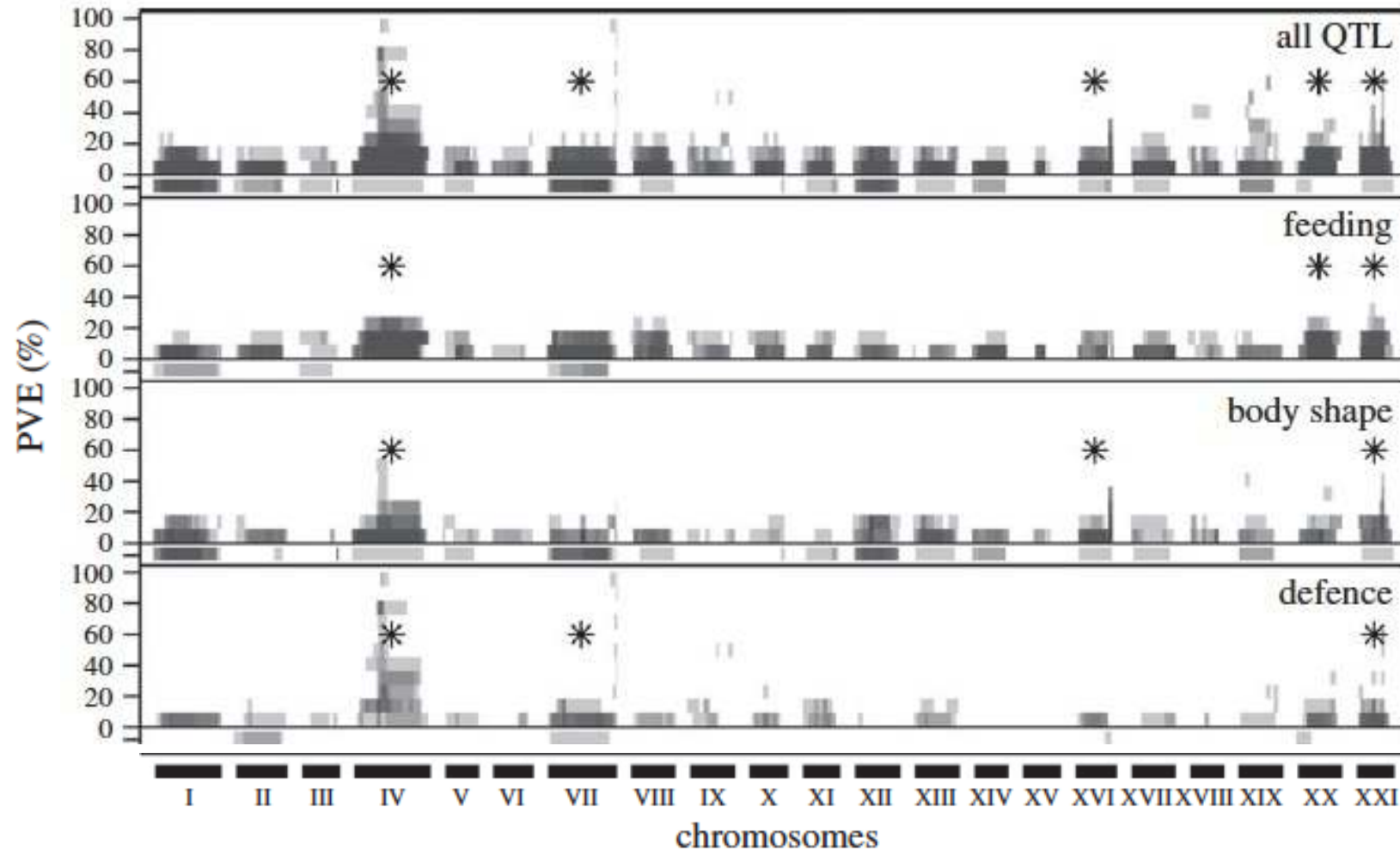
Are QTL clustered in the genome?

- 28 quantitative trait locus (QTL) mapping studies
- 1034 QTL identified in 9 trait categories
 - Morphology
 - Feeding, defense, body shape
 - Swimming, pigment, body size, respiration
 - Reproduction
 - Behaviour

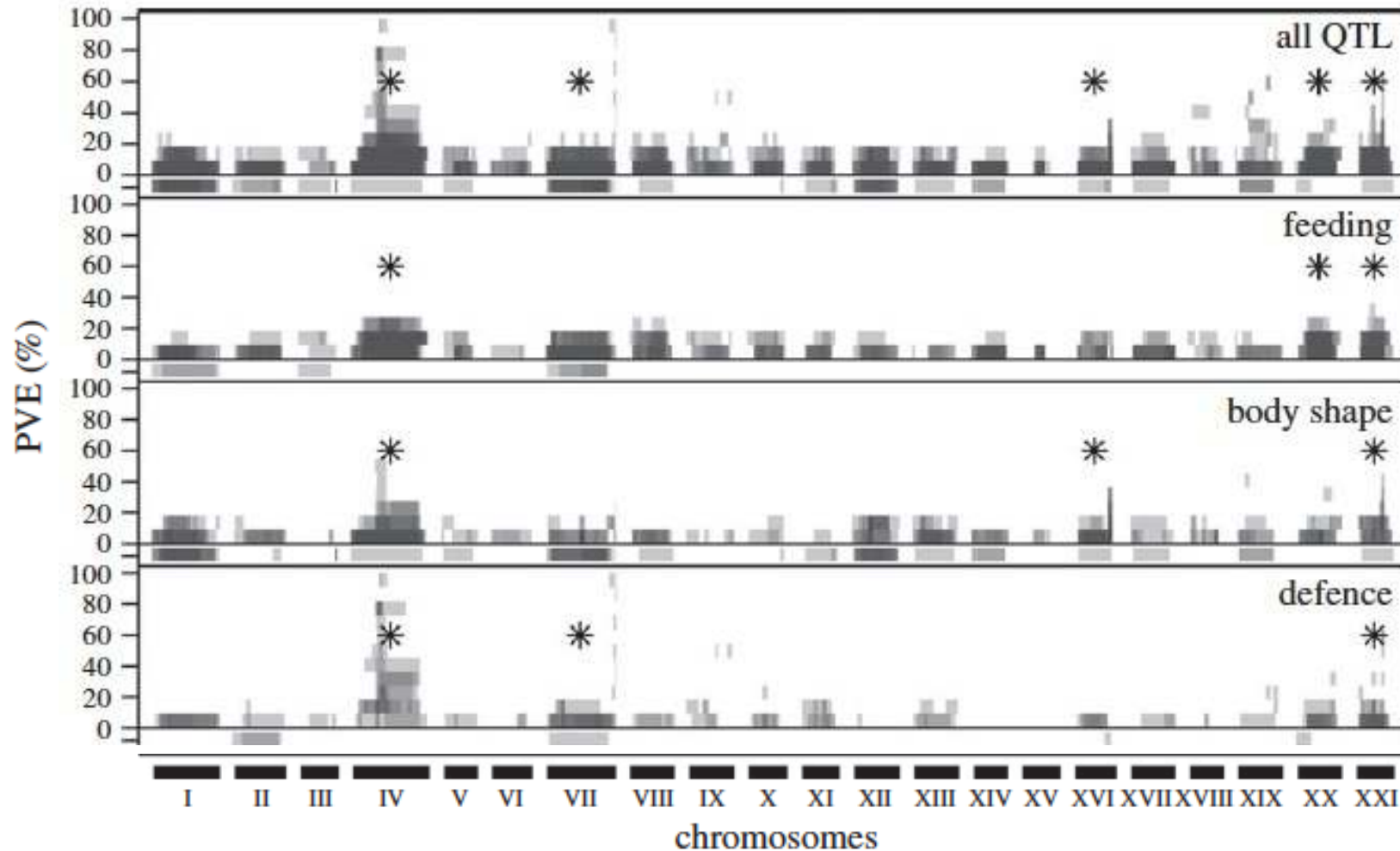


David Marques

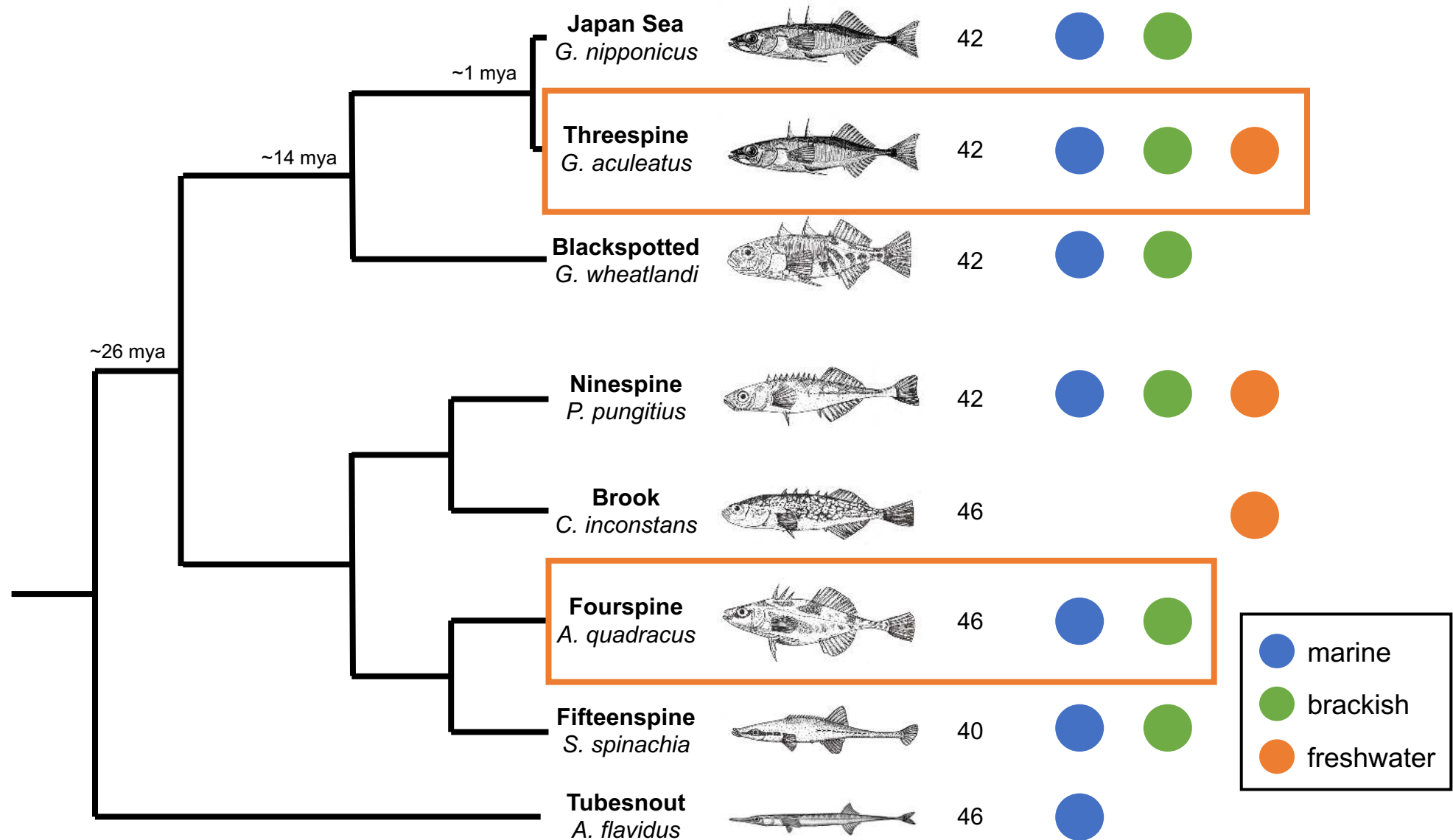
QTL are clustered in the genome!



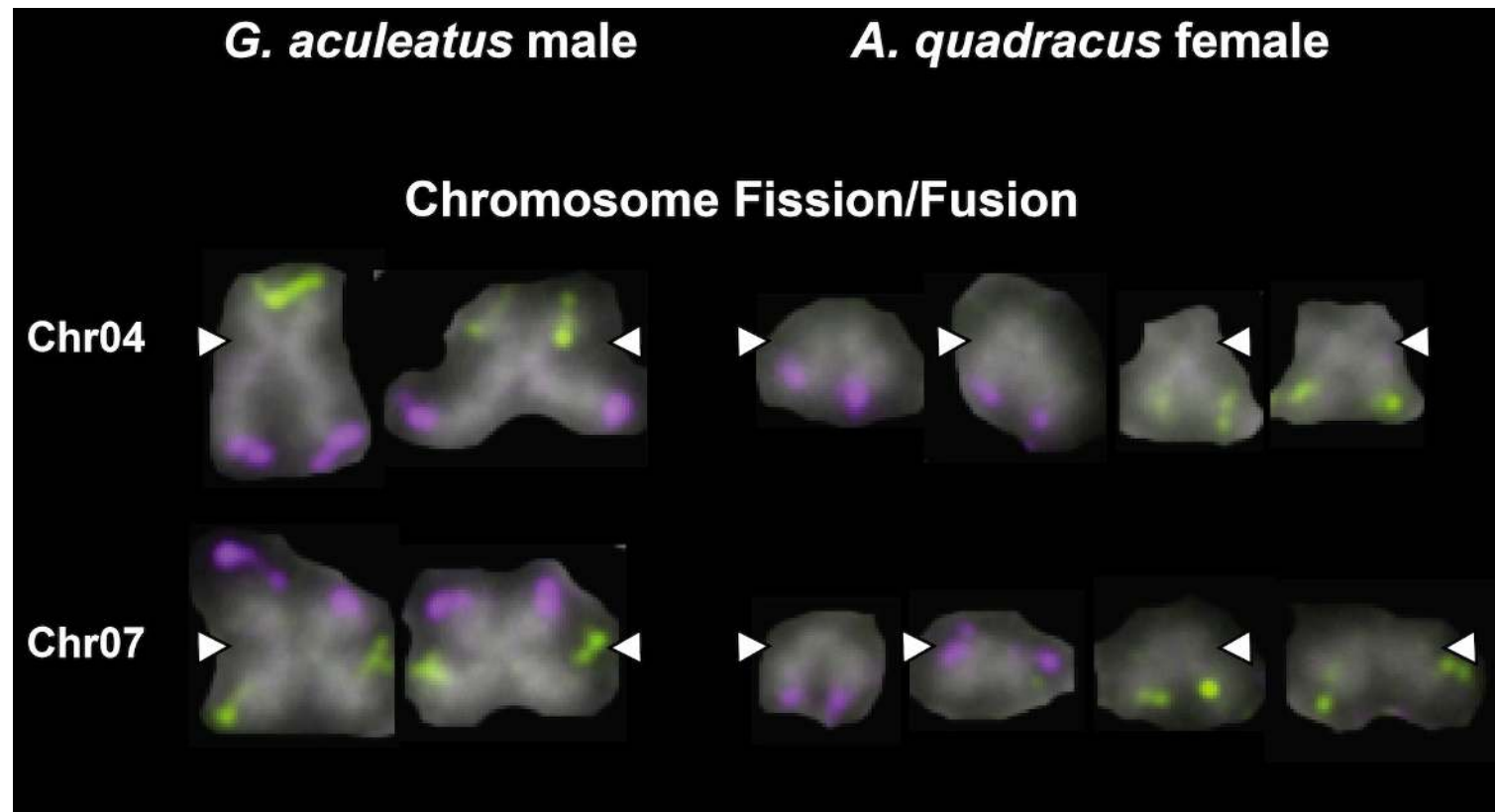
Are these QTL clusters associated with chromosomal rearrangements?



Stickleback family of fish (Gasterosteidae)



Chromosomes 4 and 7 are rearranged



Did chromosomal fusions facilitate local adaptation in threespine stickleback?

LOCAL ADAPTATION AND THE EVOLUTION OF CHROMOSOME FUSIONS

Rafael F. Guerrero^{1,2} and Mark Kirkpatrick¹

- Fusions are proposed to facilitate adaptation by:
1. Bringing together previously unlinked adaptive alleles
 2. Creating a region of reduced recombination where adaptive alleles can accumulate

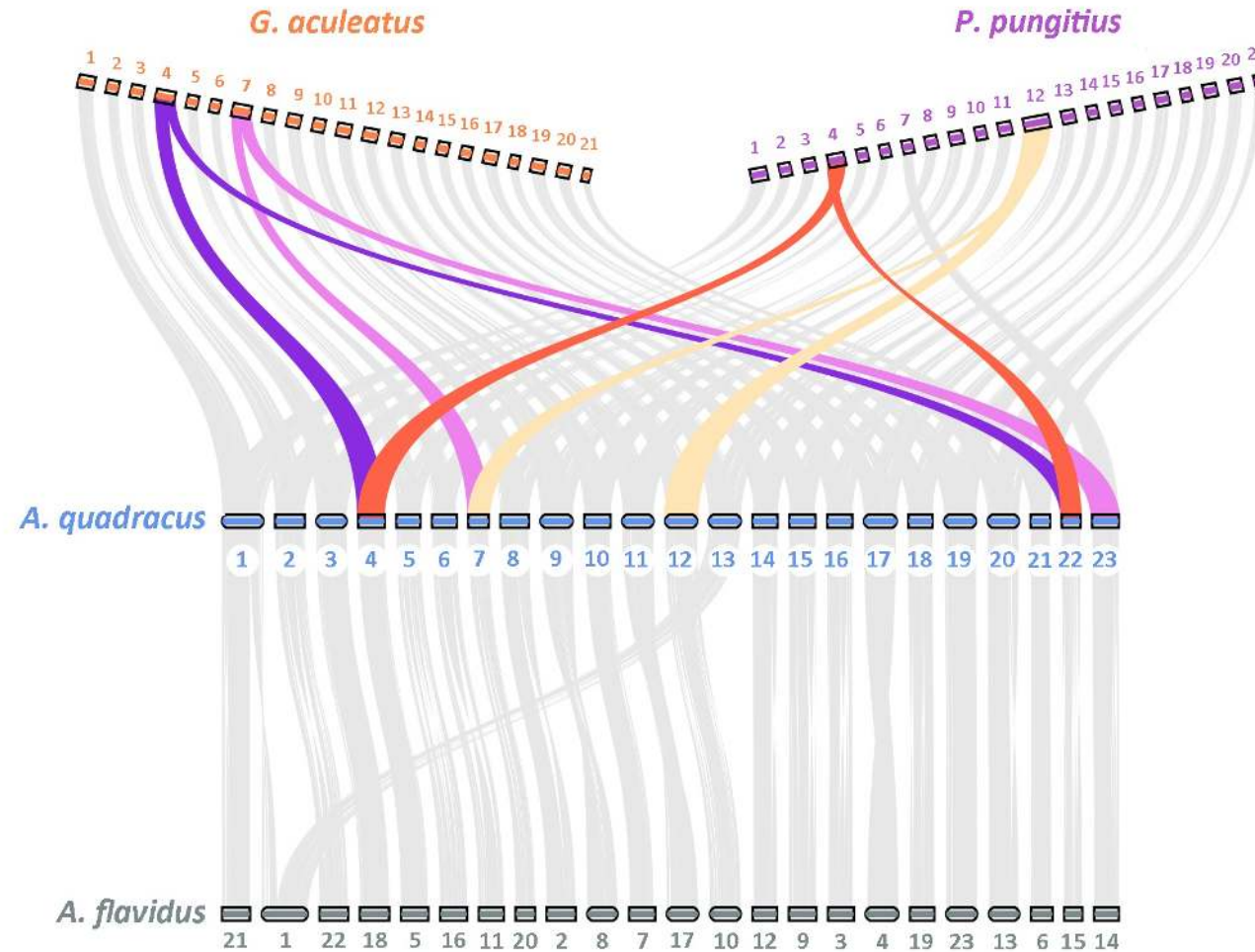


Zuyao Liu

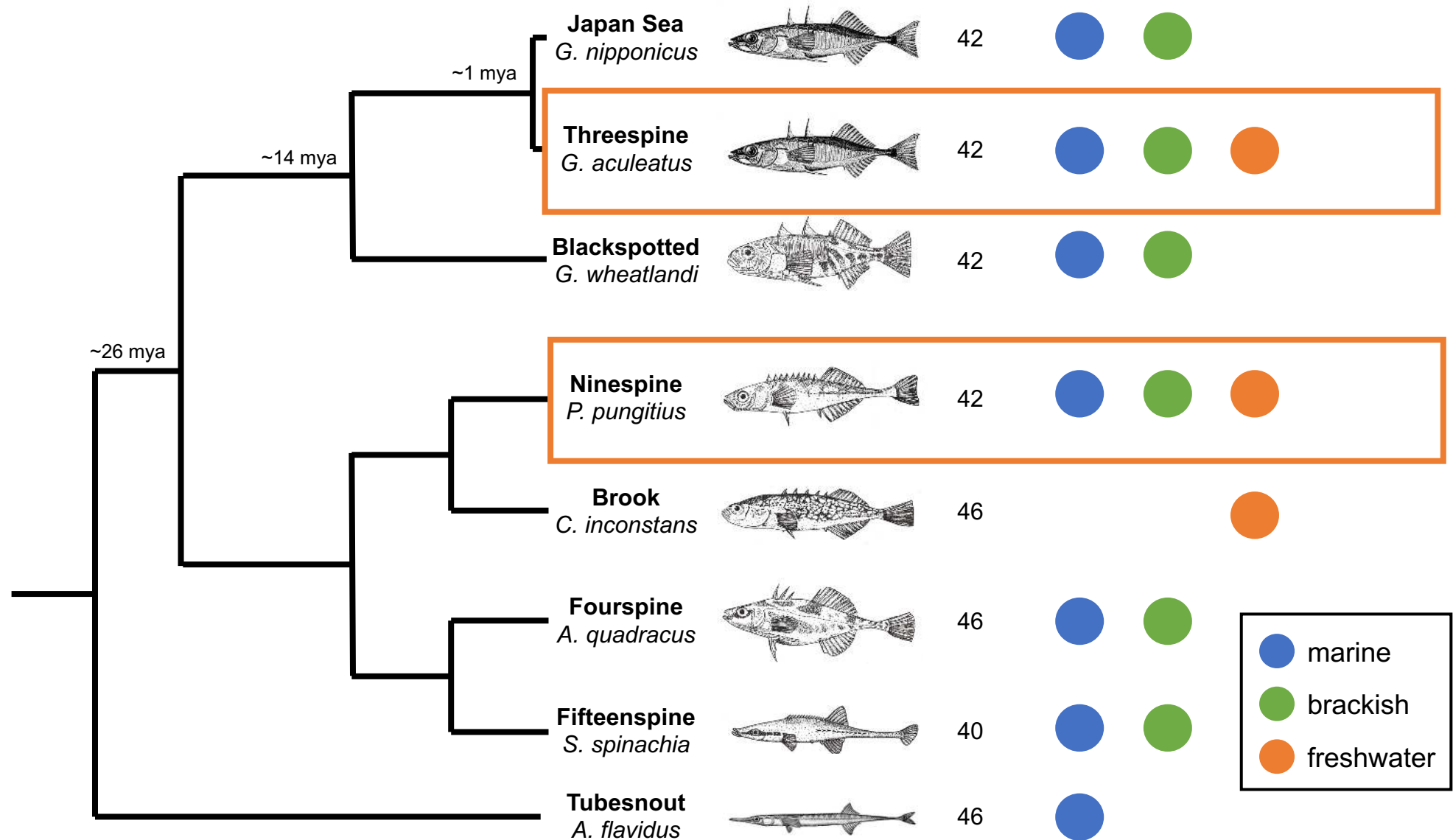
Did chromosomal fusions facilitate local adaptation in threespine stickleback?

- I) Is the difference in chromosome number between threespine stickleback and fourspine stickleback due to chromosomal fusion in threespine or chromosomal fission in fourspine?
 - Built a high-quality genome assembly of fourspine stickleback based on PacBio and Hi-C data

Independent fusions of the same chromosomes in threespine and ninespine stickleback



Stickleback family of fish (Gasterosteidae)



Did chromosomal fusions facilitate local adaptation in threespine stickleback?

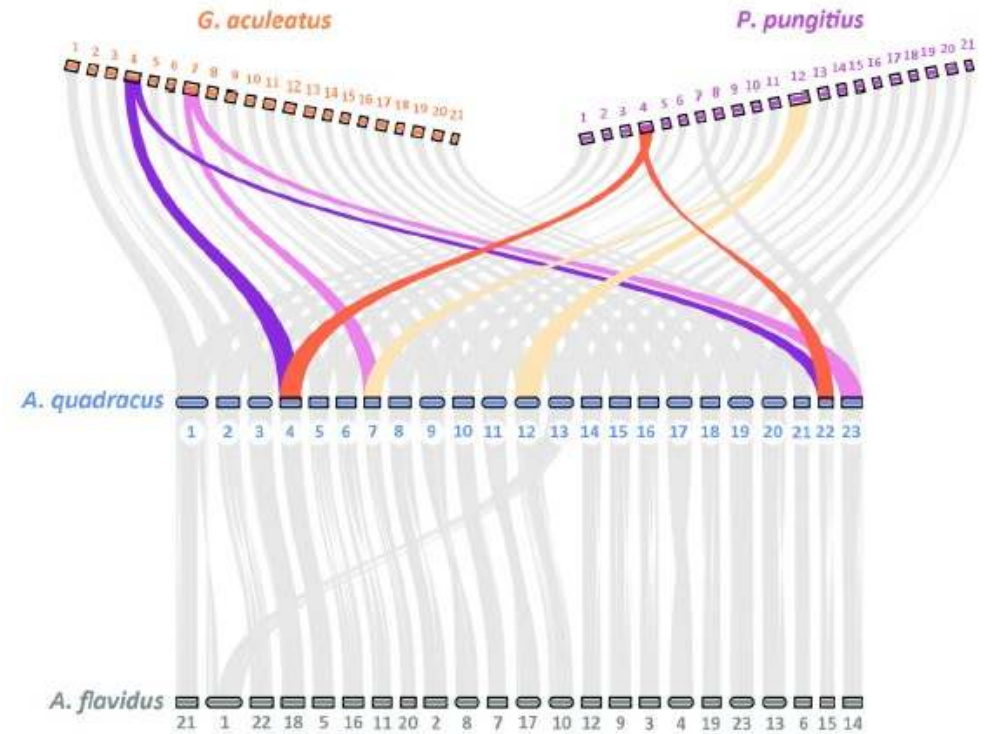
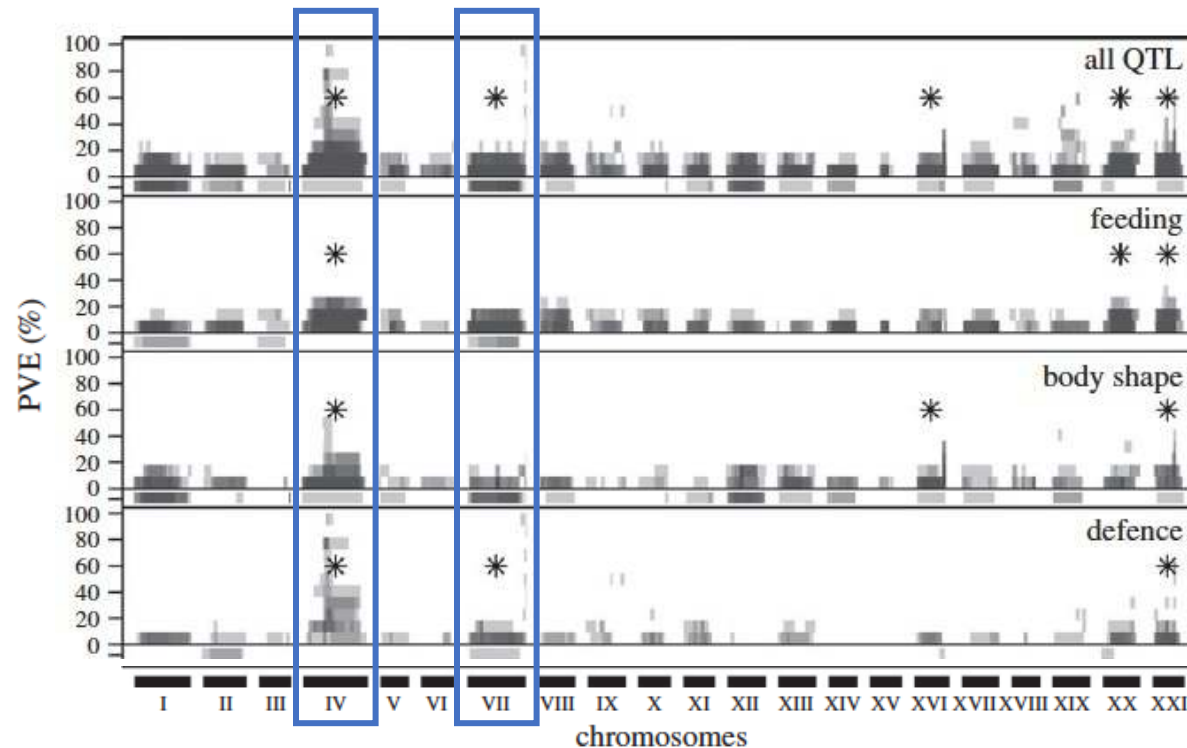
- 1) Is the difference in chromosome number between threespine stickleback and fourspine stickleback due to chromosomal fusion in threespine or chromosomal fission in fourspine?
 - Fusion!
- 2) Is there an enrichment of QTL contributing to adaptive divergence in traits on chromosomes 4 and 7 in threespine stickleback?
 - YES!
- 3) Is there an enrichment of molecular signatures of divergent adaptation on chromosomes 4 and 7 in threespine stickleback?
 - YES!
- 4) How did chromosomal fusions facilitate adaptation to divergent habitats in threespine stickleback?

How did chromosomal fusions facilitate local adaptation in threespine stickleback?

1. Bringing together previously unlinked adaptive alleles?
 - Probably not but difficult to test because the fusions are fixed in *Gasterosteus* genus, but only threespine stickleback can inhabit freshwater
2. Creating a region of reduced recombination where adaptive alleles can accumulate?
 - Probably!

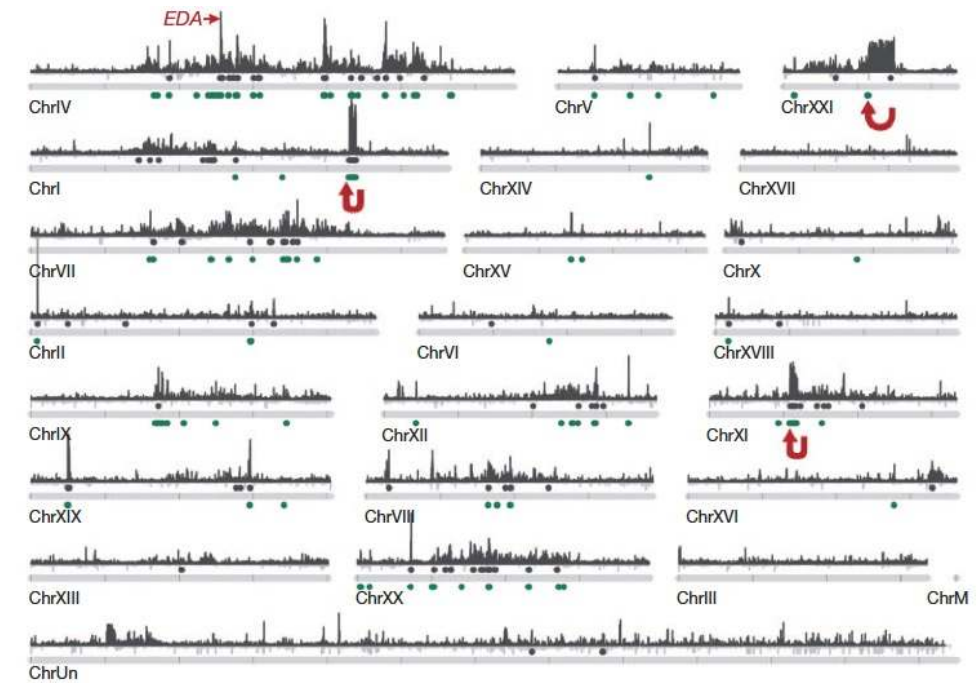
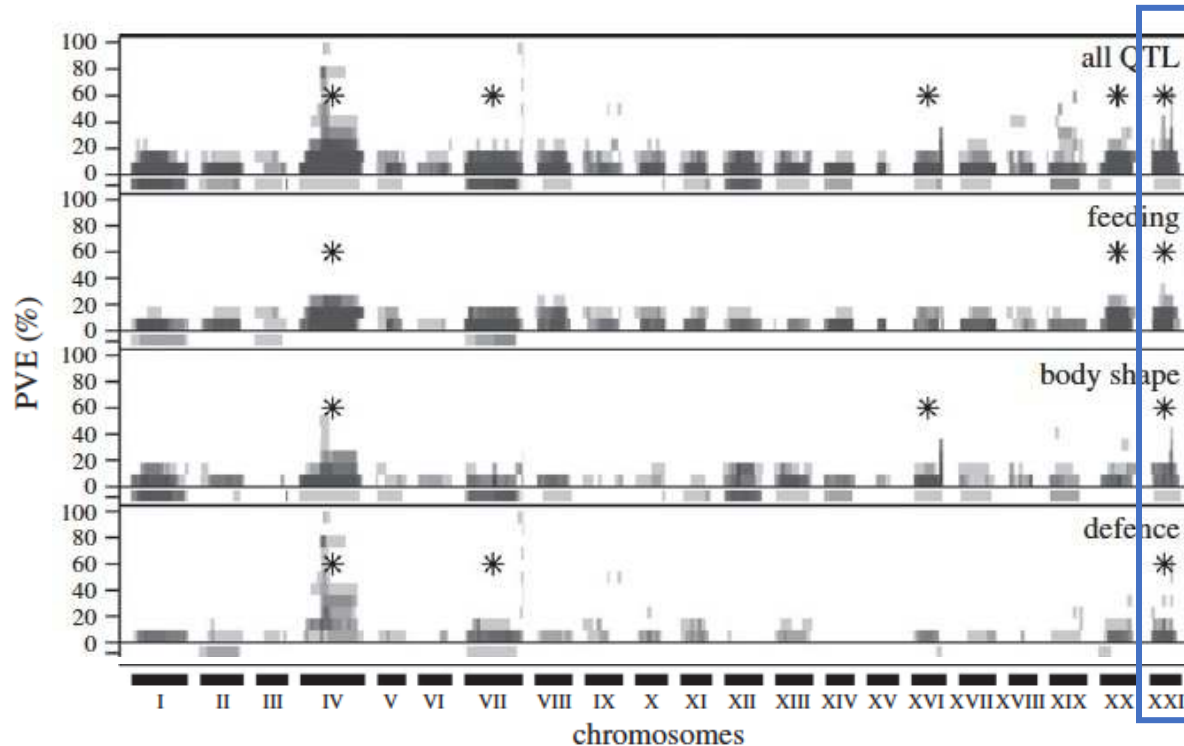
Linked QTL clusters are associated with chromosomal **fusions** and inversions

Fusions on chromosomes 4 and 7

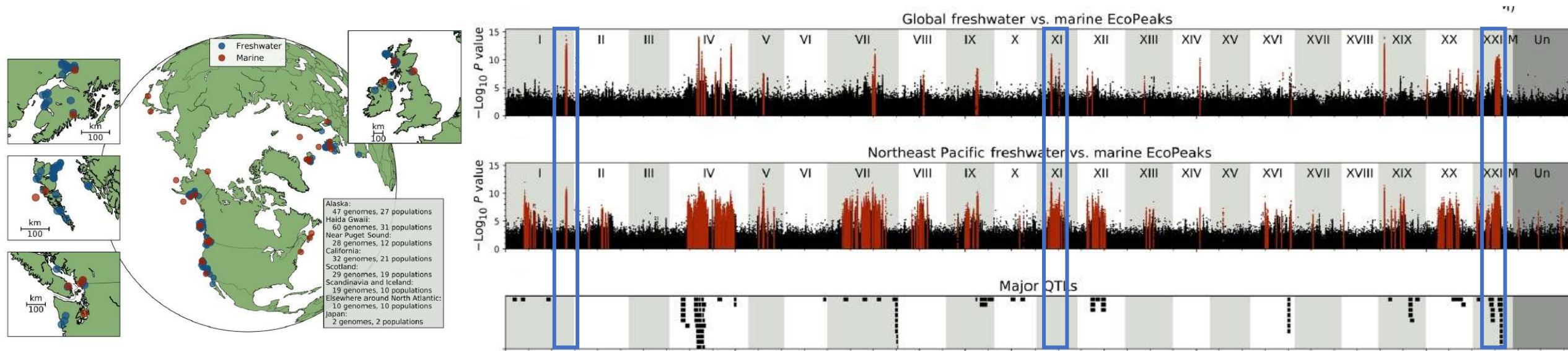


Linked QTL clusters are associated with chromosomal fusions and **inversions**

Inversions on chromosomes I, II & 2I



Three inversions distinguish global marine and freshwater threespine stickleback populations



How do these inversions contribute to local adaptation?

Chr	Size in Mbp	Number of genes	Gene at breakpoint	QTL hotspot	TMRCA	Ancestral orientation
1	0.5	24	no	no	7 mya	marine
11	0.46	25	yes	no	6 mya	freshwater
21	2.2	109	no	yes	8 mya	freshwater



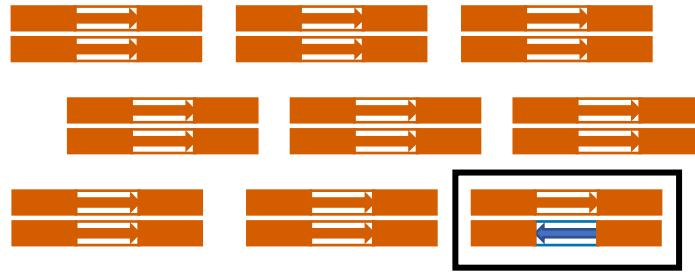
- What are the phenotypic effects of these inversions?
- Are these inversions under selection in freshwater?
- Can we identify the targets of selection within these inversions?

What are the phenotypic effects of inversions?

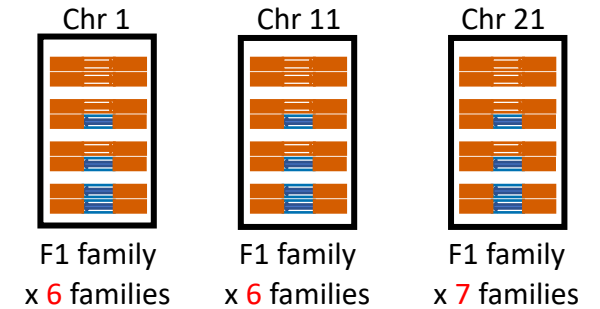
- Association mapping in wild populations that are polymorphic for the inversions
 - Freshwater sticklebacks from Lake Constance, Switzerland
 - Extensive phenotyping of morphology, physiology, and behavior
- Genetic mapping in crosses between marine inversion heterozygotes
 - Marine sticklebacks from British Columbia, Canada
 - Extensive phenotyping of morphology, physiology, and behavior

Genetic mapping in crosses between marine inversion heterozygotes

Screen marine fish to find heterozygous carriers of 3 freshwater inversions (2022)



Cross heterozygous carriers to generate F1s



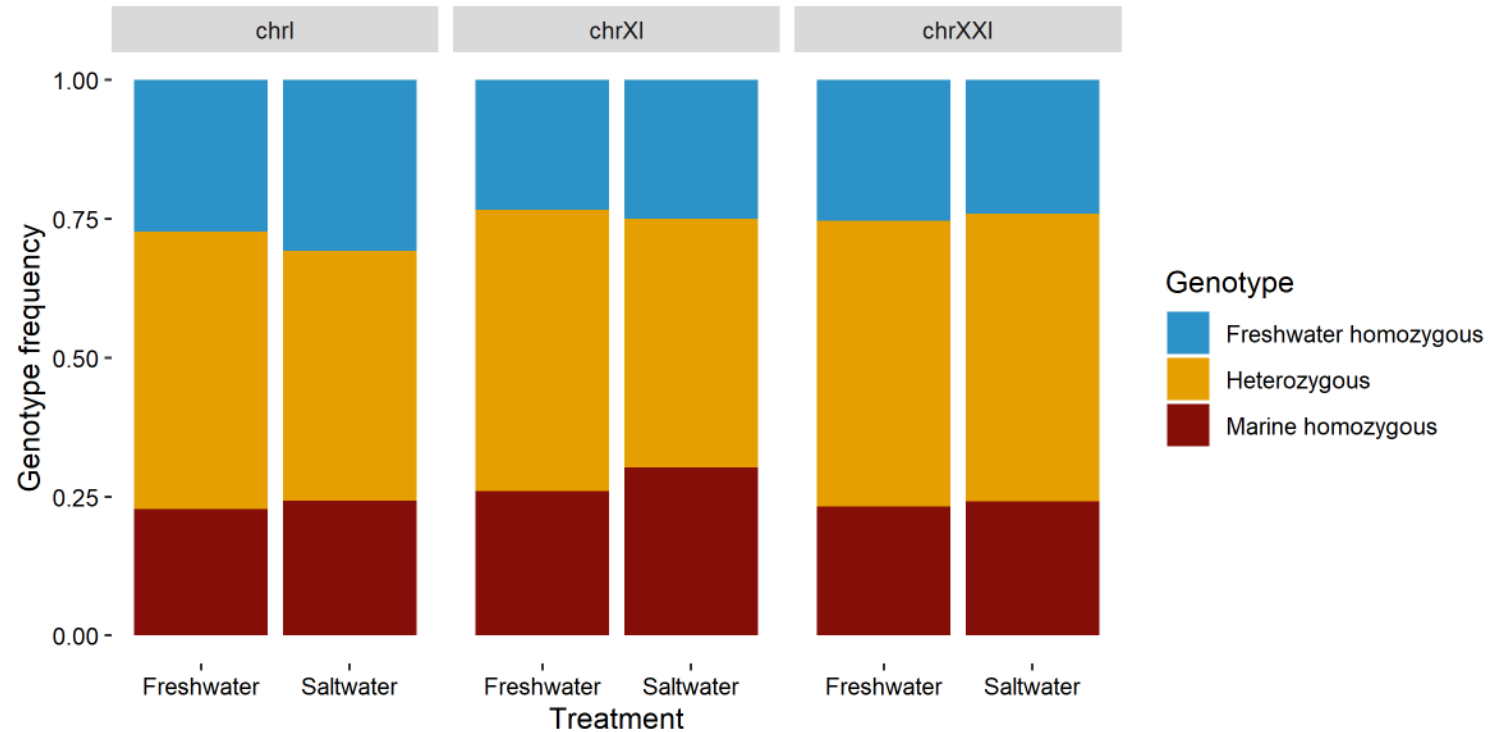
Ship **21** F1 families to Bern

Grow half the family in saltwater and half in freshwater

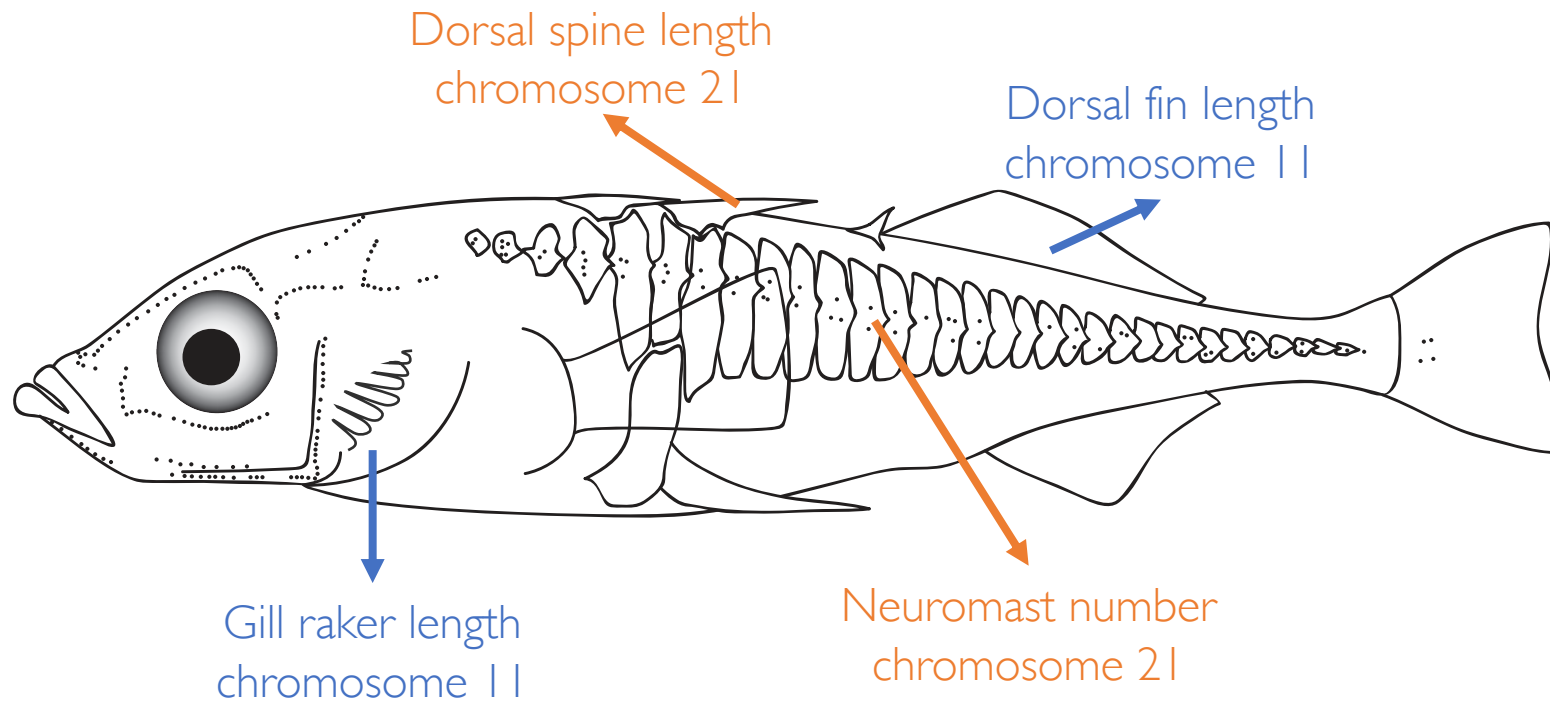
Genotype and phenotype



No intrinsic lethality associated with inversion genotype in saltwater or freshwater



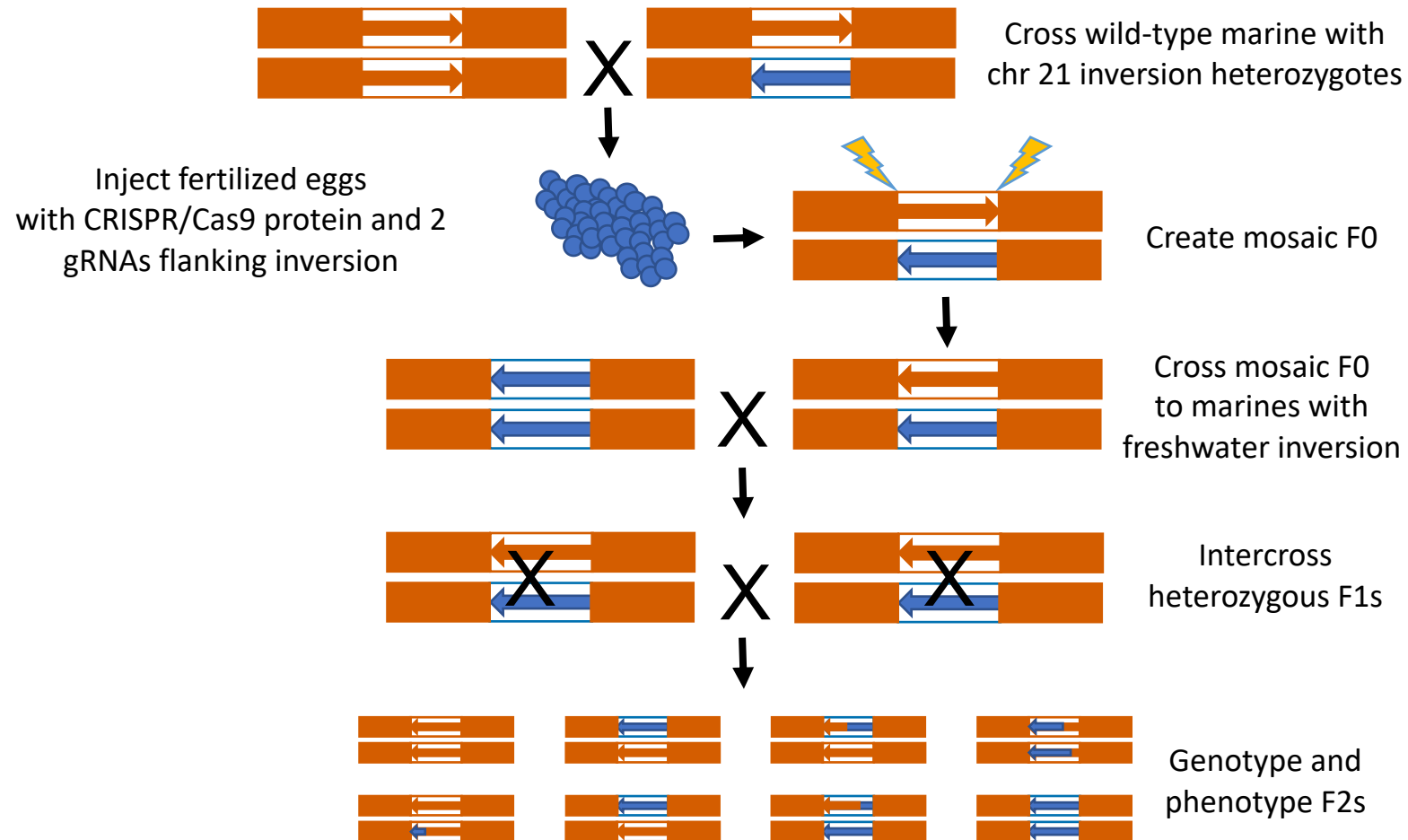
Preliminary results: multiple morphological traits map to chromosome 11 and 21 inversions



Do multiple traits map to the inversions because there are linked adaptive alleles?

- Problem: we cannot do fine mapping within inversions because there is no recombination between the marine and freshwater inversions in heterozygotes!
- Solution: “flip” the freshwater inversion to (hopefully) restore recombination in marine-freshwater heterozygotes!

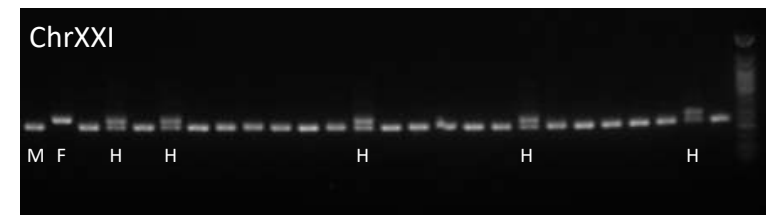
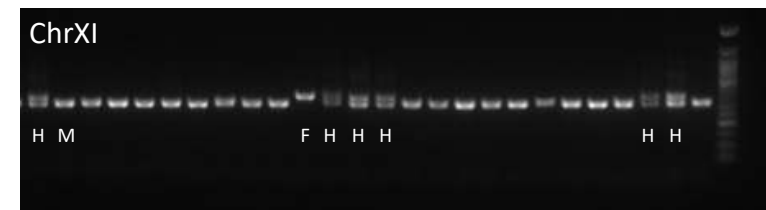
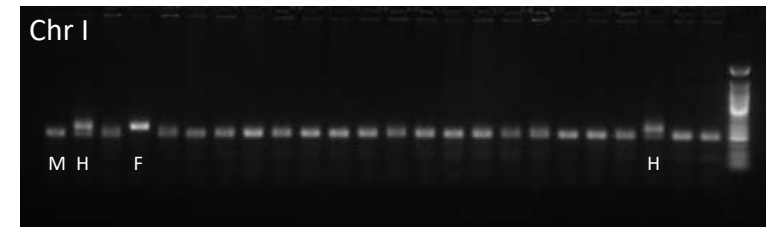
We flipped the inversion on chromosome 21!



We are here!

What are the phenotypic effects of inversions?

- Worldwide association mapping project
 - Inversion frequencies: PCR genotyping of inversions in ~600 populations from across the entire stickleback distribution (~20,000 samples)
 - Phenotype data (population averages)
 - Ecological data (biotic/abiotic variables)



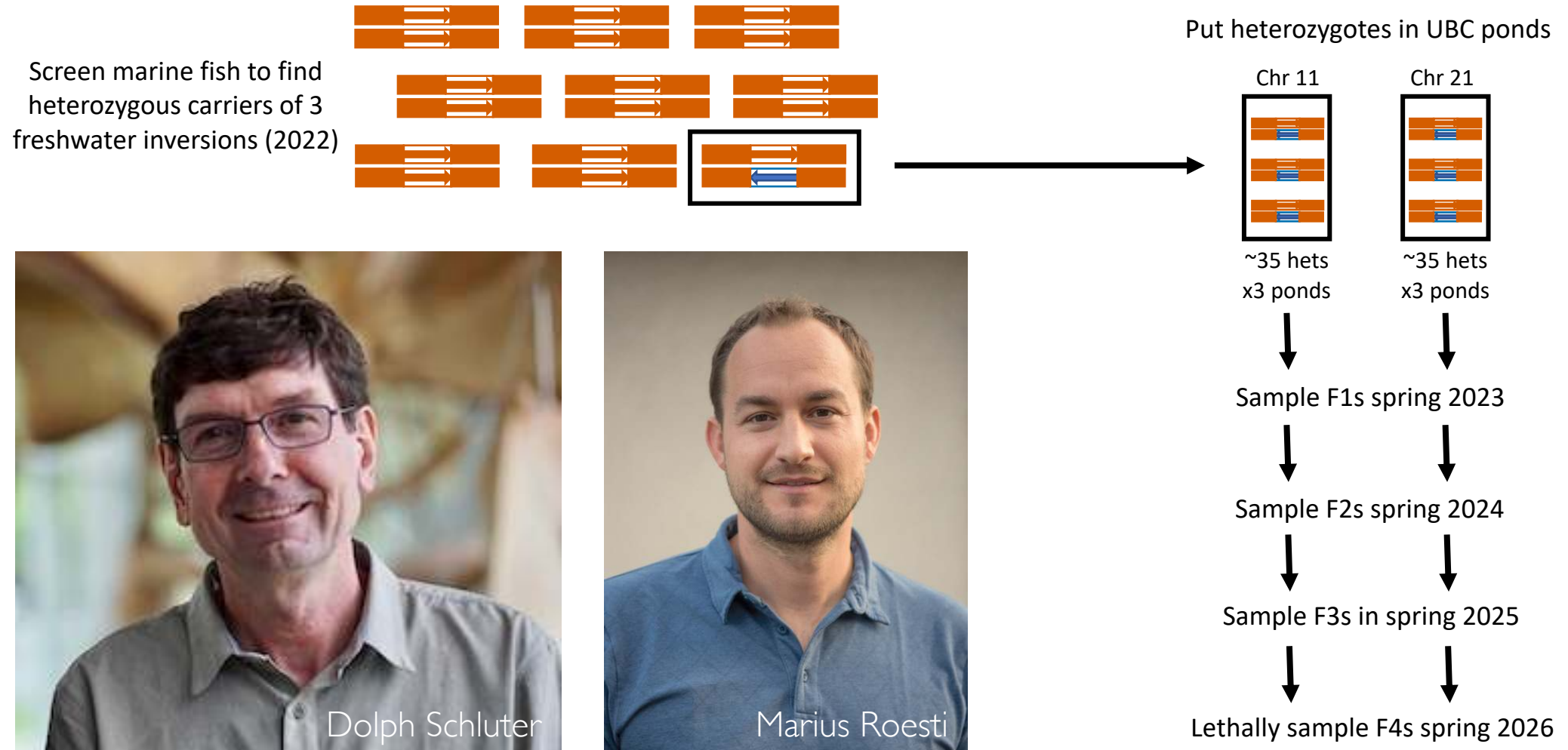
How do these inversions contribute to local adaptation?

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- What are the phenotypic effects of these inversions?
- Are these inversions under selection in freshwater?
- Can we identify the targets of selection within these inversions?

Are the inversions under selection in freshwater?



Preliminary results: increase in frequency of freshwater allele at chromosome 11 inversion!

chr	pond	year	M	HET	FW	Total fish	P-value
11	2	2023	28	57	21	106	NS
11	2	2024	23	78	58	159	0.0004
11	7	2023	0	0	0	0	ND
11	7	2024	1	2	4	7	ND
11	14	2023	26	65	32	123	NS
11	14	2024	2	27	23	52	0.0002

How do these inversions contribute to local adaptation?

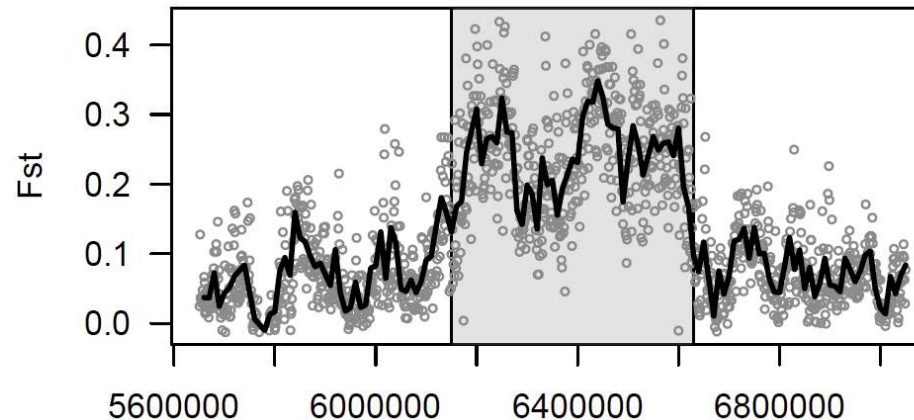
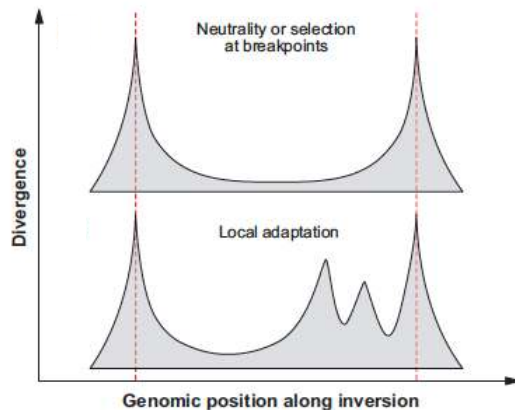
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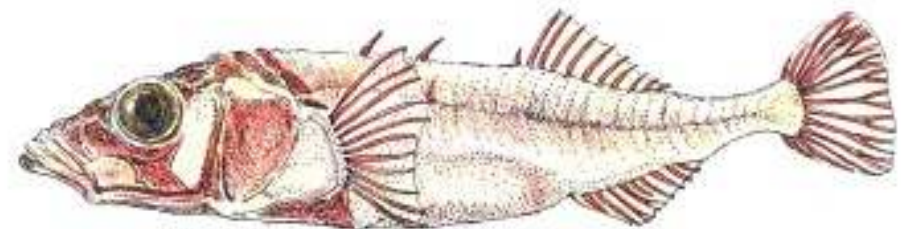
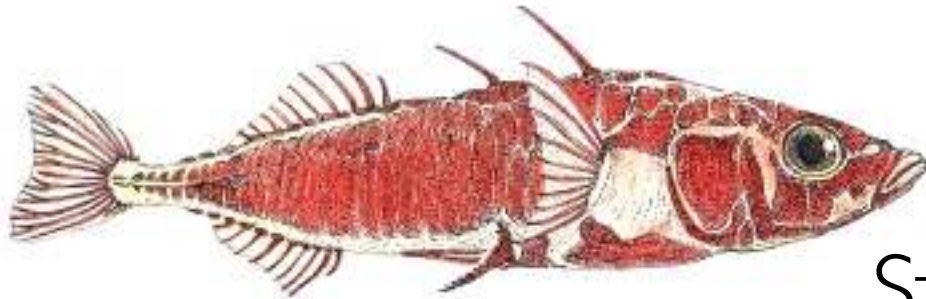
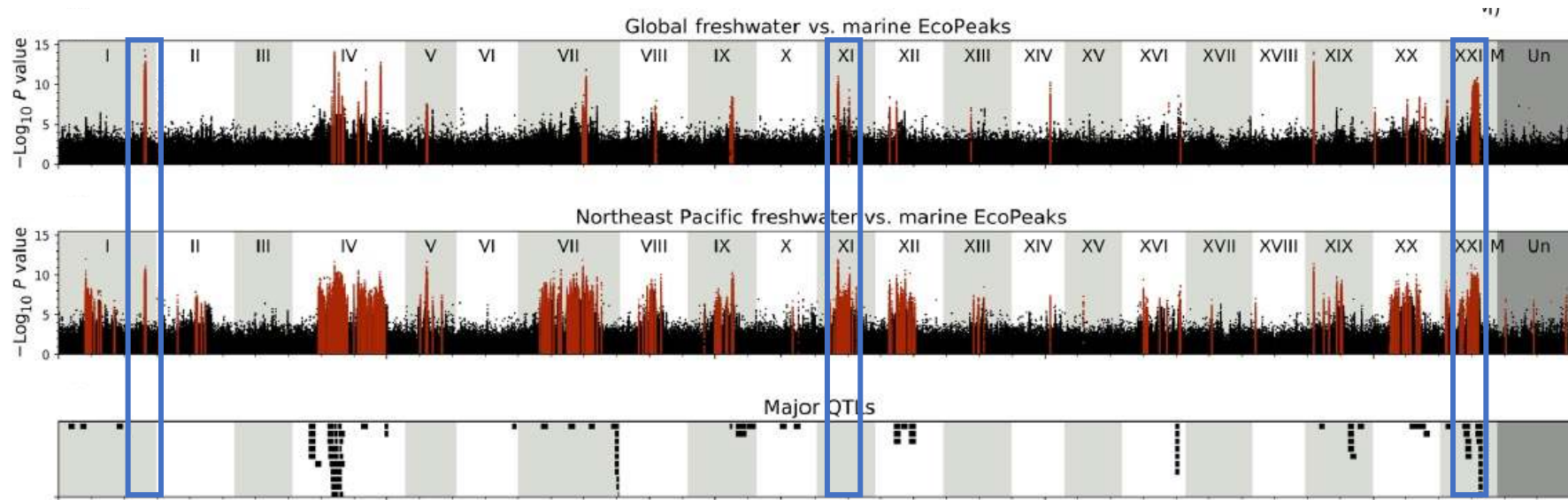
- What are the phenotypic effects of these inversions?
- Are these inversions under selection in freshwater?
- Can we identify the targets of selection within these inversions?

What are the molecular signatures of selection within inversions?

- Generate phased sequencing data (Swiss and Canadian populations)
 - Question 1. What form(s) of selection are acting on the inversions?
 - Question 2. Is there evidence for selection on multiple loci within the inversion or only on the inversion itself?
 - Question 3. Did selection for linkage of adaptive alleles contribute to the establishment of the inversion, or did adaptive alleles accumulate after the establishment of the inversions? (i.e. capture vs gain?)



How do these inversions contribute to local adaptation?



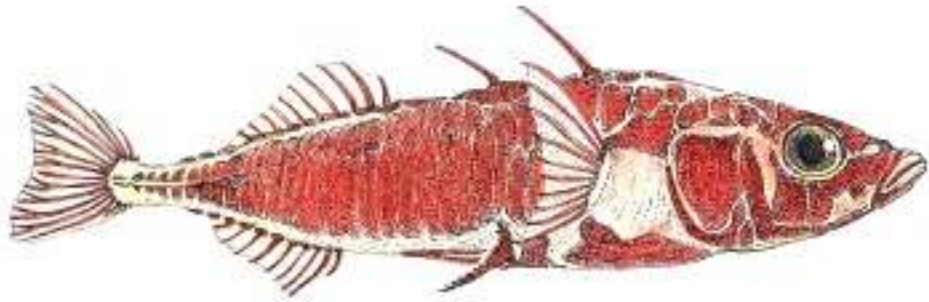
Stay tuned!

Do chromosomal changes facilitate local adaptation?

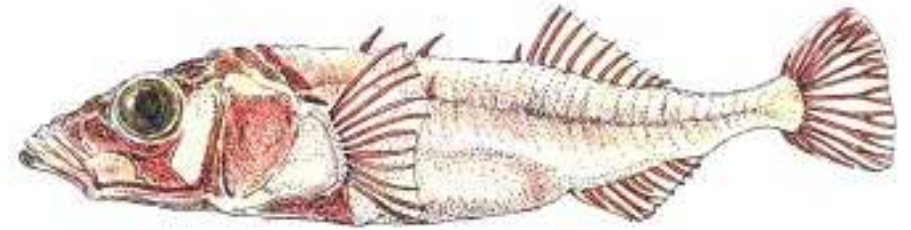
- Are chromosomal changes, such as inversions or fusions, under divergent selection in nature?
 - Preliminary results say yes (for chromosome 11)
- Are multiple adaptive traits linked to chromosomal inversions or fusions?
 - Preliminary results say yes (for chromosomes 11 and 21)
- Do chromosomal inversions or fusions harbor multiple adaptive alleles?
 - Flipped inversions will help us find out!

Chromosomal changes as drivers of adaptation and speciation?

- I think so!
- But, an integration of lab and field studies are really needed to directly link these chromosomal changes to adaptation and speciation!

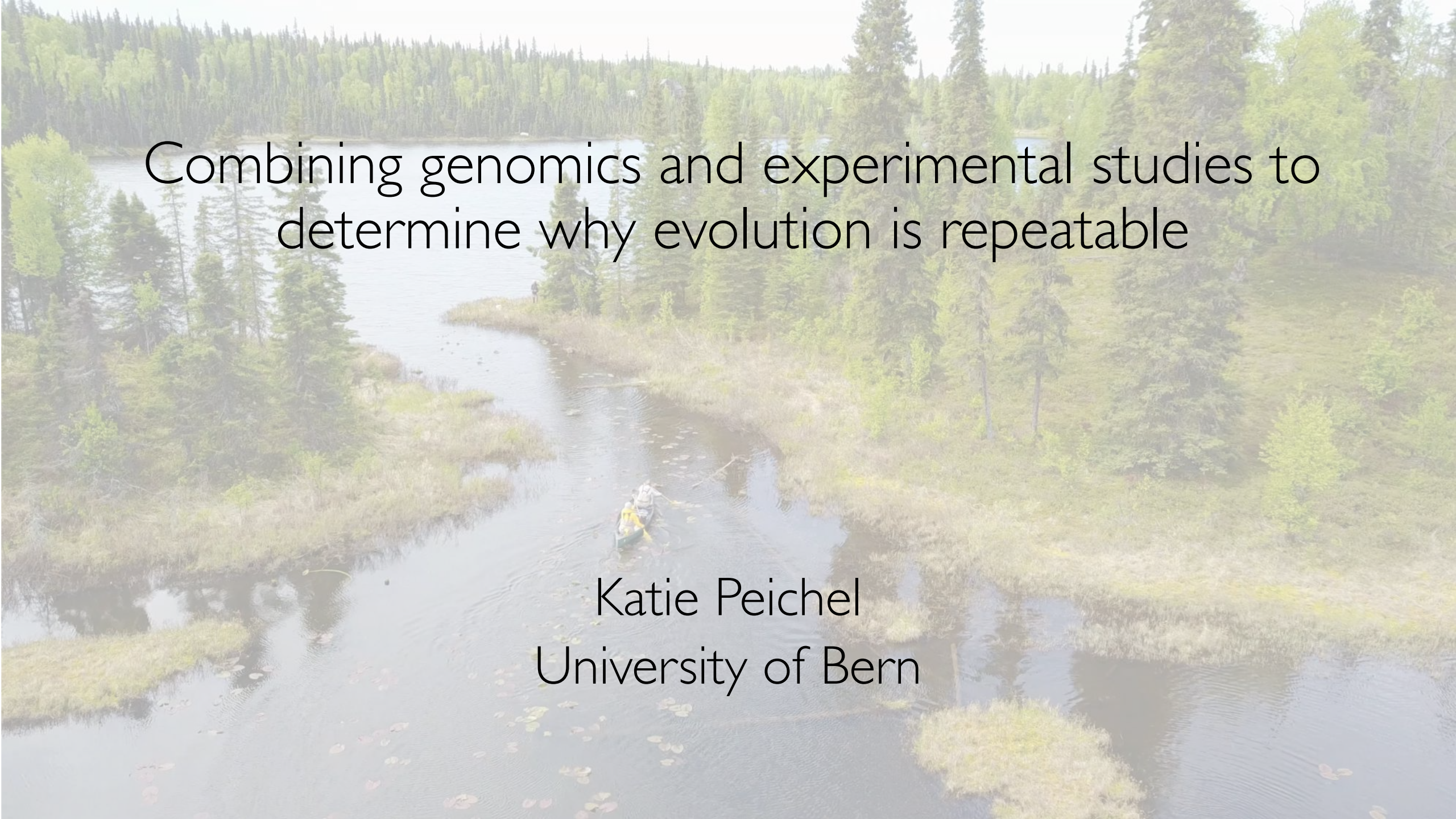


Thanks!



Zuyao Liu
Nicole Nesvadba
Marius Roesti
Juliana Rodriguez Fuentes
Delia Sclabas

David Marques
Stephan Peischl
Dolph Schluter
Stickleback community
Uni Bern sequencing center

An aerial photograph of a calm lake surrounded by a dense forest of tall evergreen trees. In the center of the lake, a person is kayaking, leaving a small wake. The water is dark and reflects the surrounding greenery. The text is overlaid on the upper half of the image.

Combining genomics and experimental studies to
determine why evolution is repeatable

Katie Peichel
University of Bern

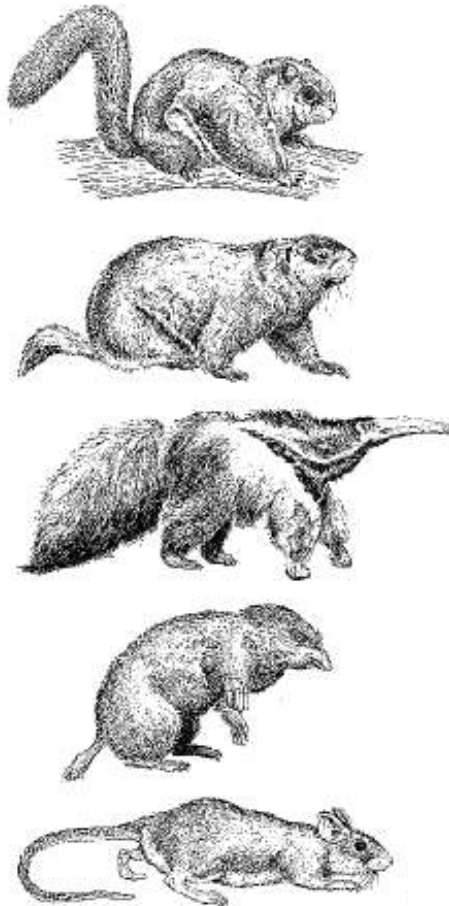
Is evolution repeatable?



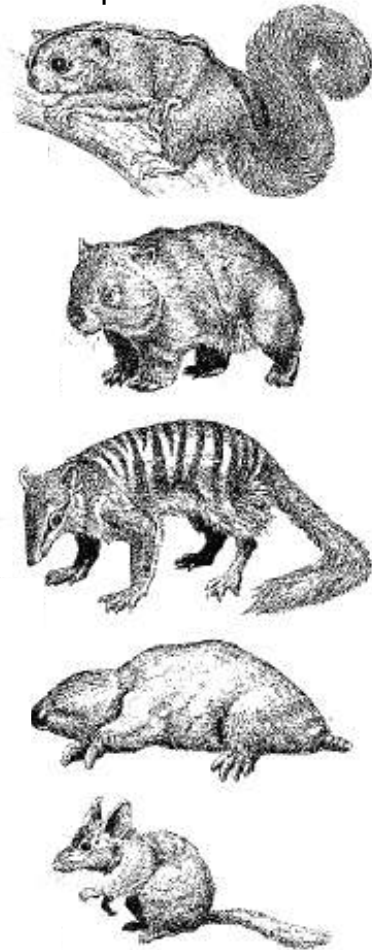
If we replayed the tape of life,
would evolution repeat itself?

Evolution repeats itself!

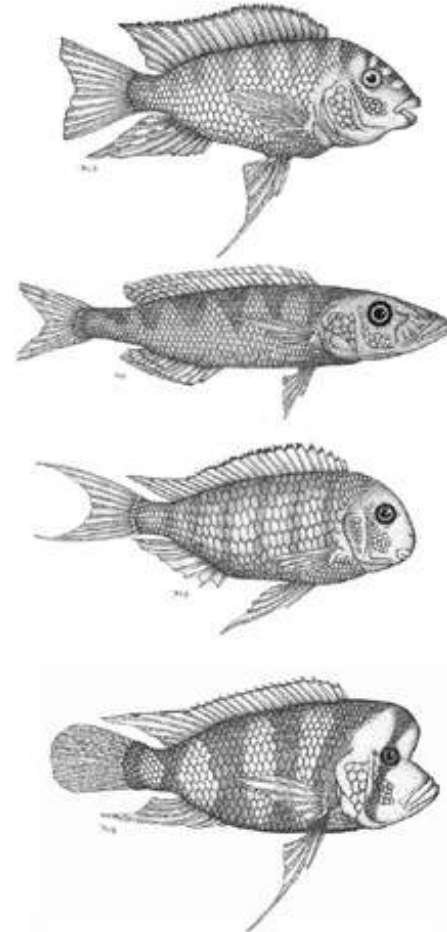
Placentals



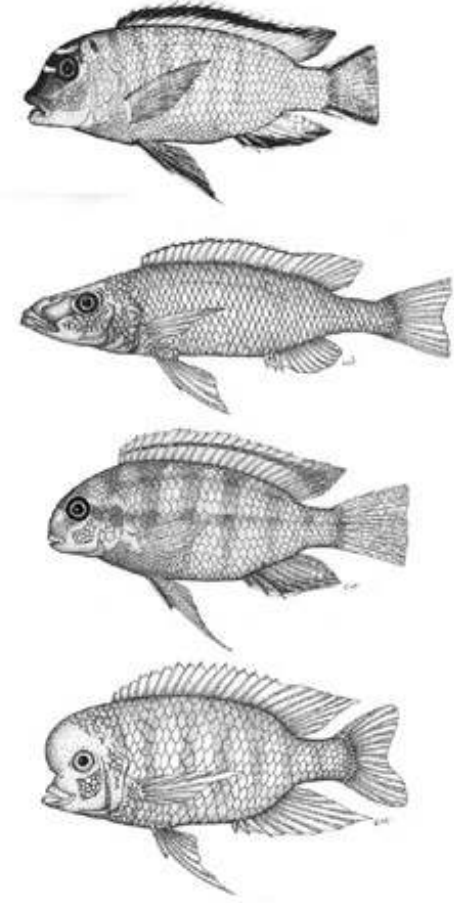
Marsupials



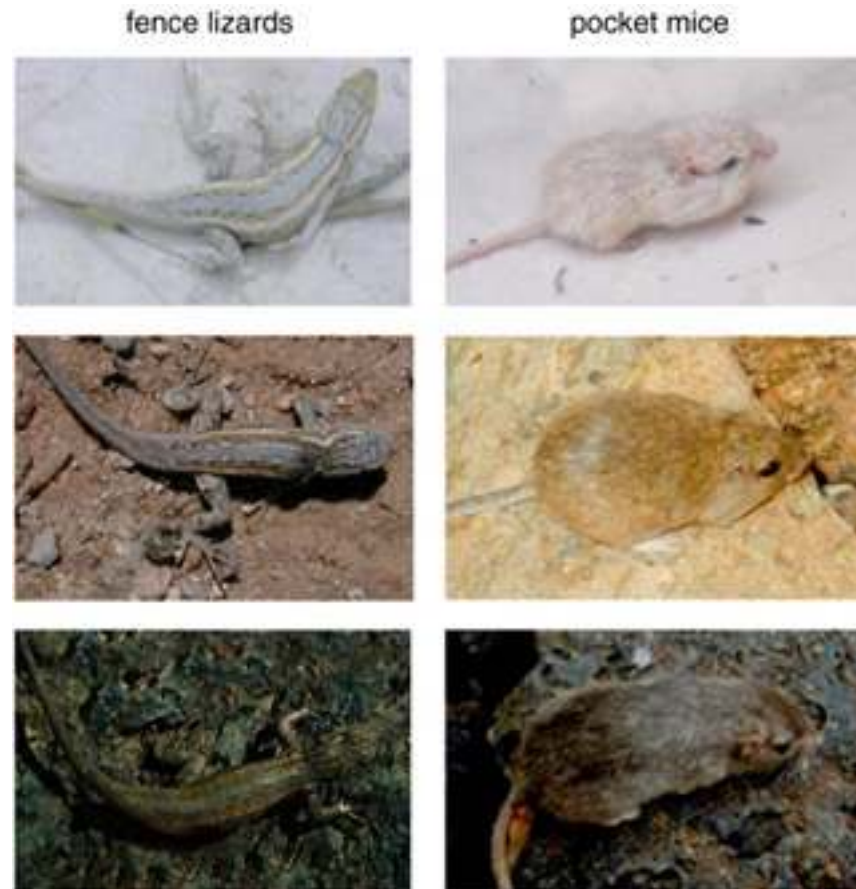
Lake Tanganyika



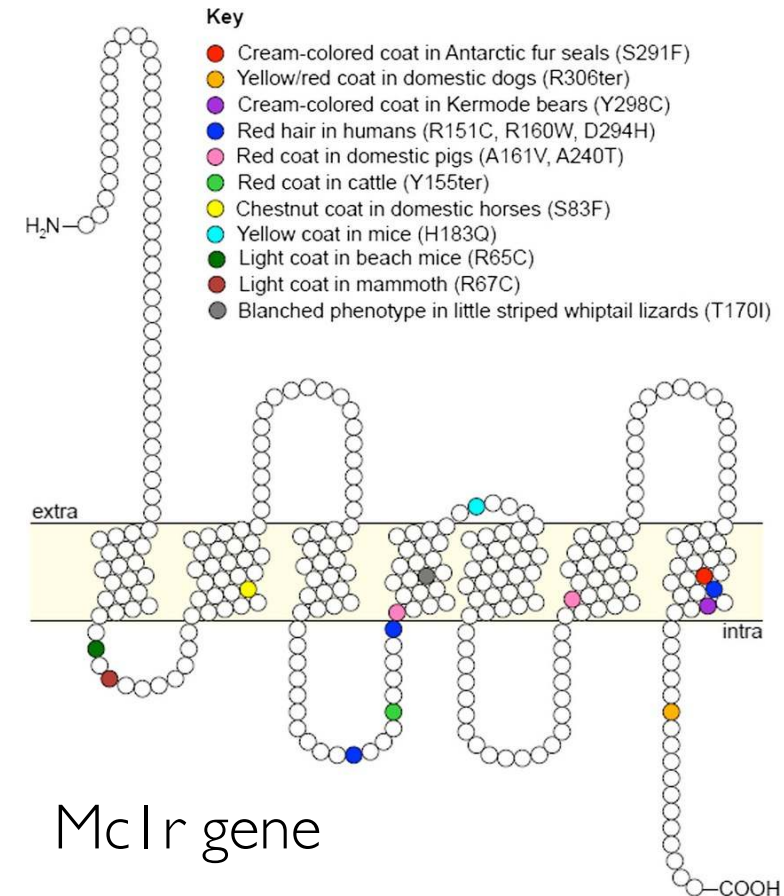
Lake Malawi



Evolution also repeats itself at the genetic level!



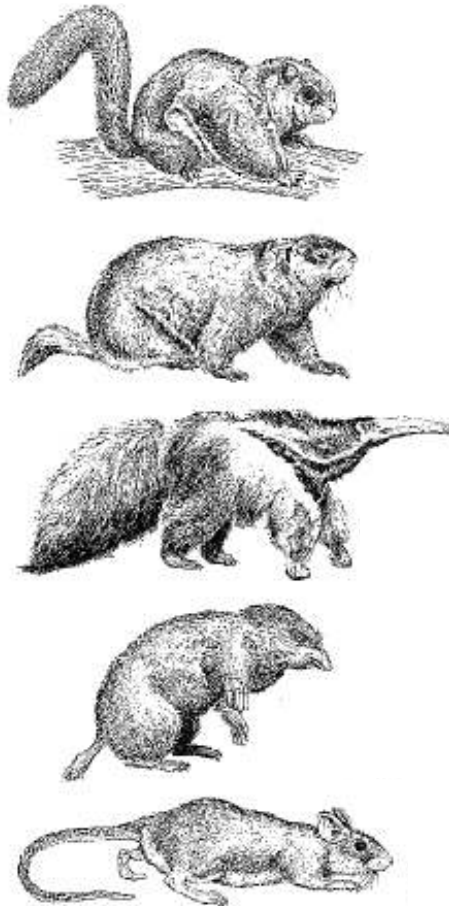
Hoekstra (2006) *Heredity*



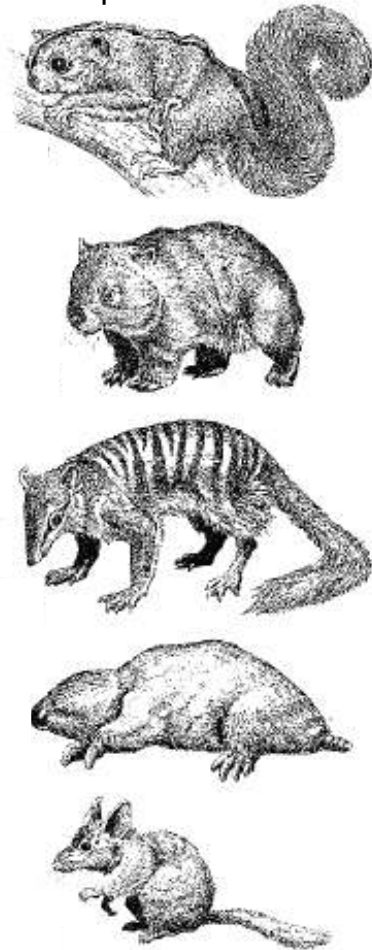
Peters et al (2016) *Ecology & Evolution*

Why is evolution repeatable?

Placentals



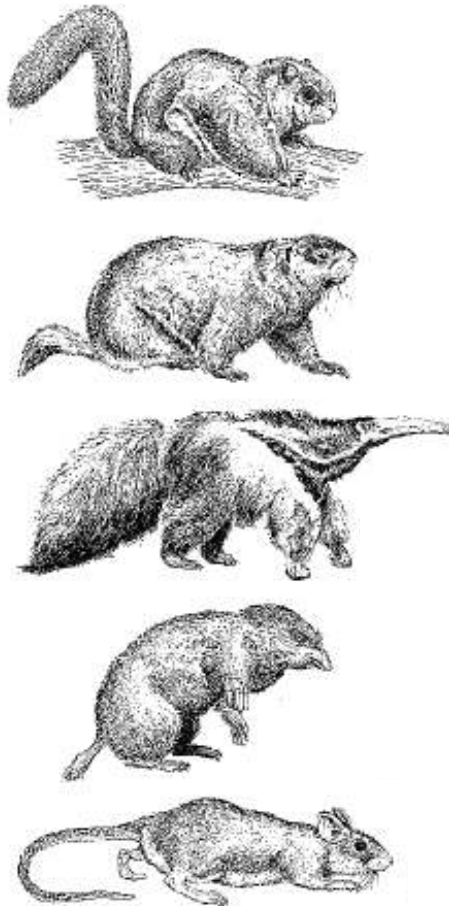
Marsupials



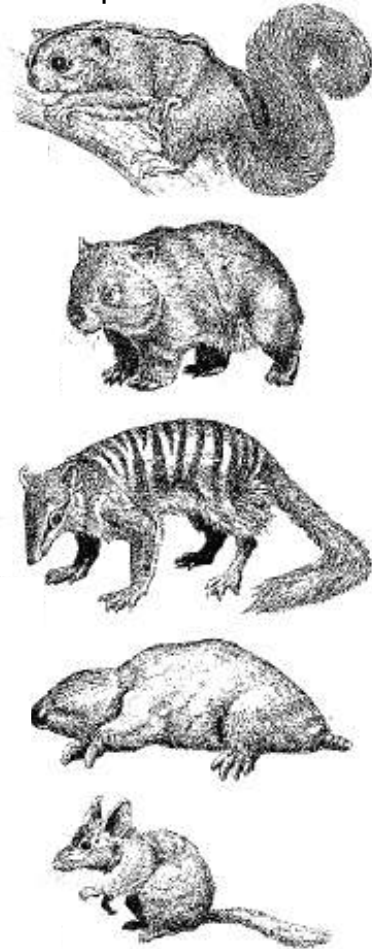
If we can understand why evolution repeats itself (or why it doesn't), maybe we can predict evolutionary responses in the future

Is evolution predictable?

Placentals



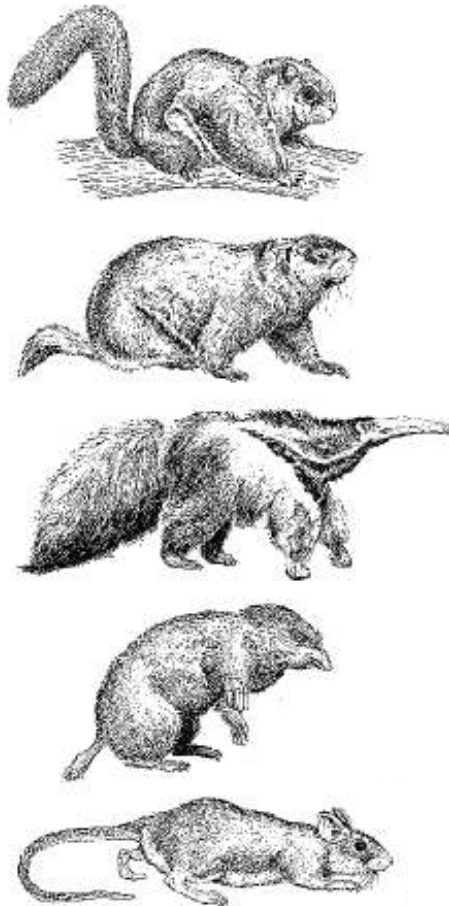
Marsupials



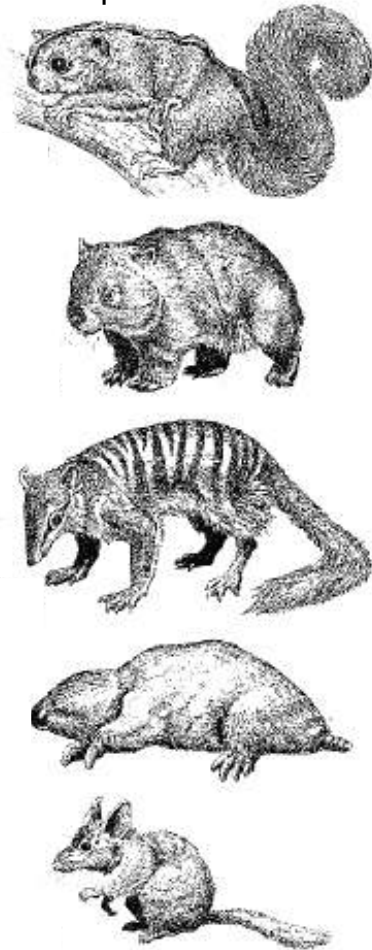
- Medicine
 - When and how will a virus evolve to escape a vaccine?
- Agriculture
 - When and how will a pest evolve to resist a pesticide?
- Conservation
 - Will a species survive as a result of climate change?

Why is evolution repeatable?

Placentals



Marsupials



Why is evolution repeatable
at the phenotypic level?

Why is evolution repeatable
at the genotypic level?

Questions

- How often do the same genetic changes underlie repeated phenotypic evolution and adaptation?
- Why might some genetic changes be used more frequently during repeated phenotypic evolution and adaptation?

Stickleback fish are a model system to study phenotypic and genotypic repeatability

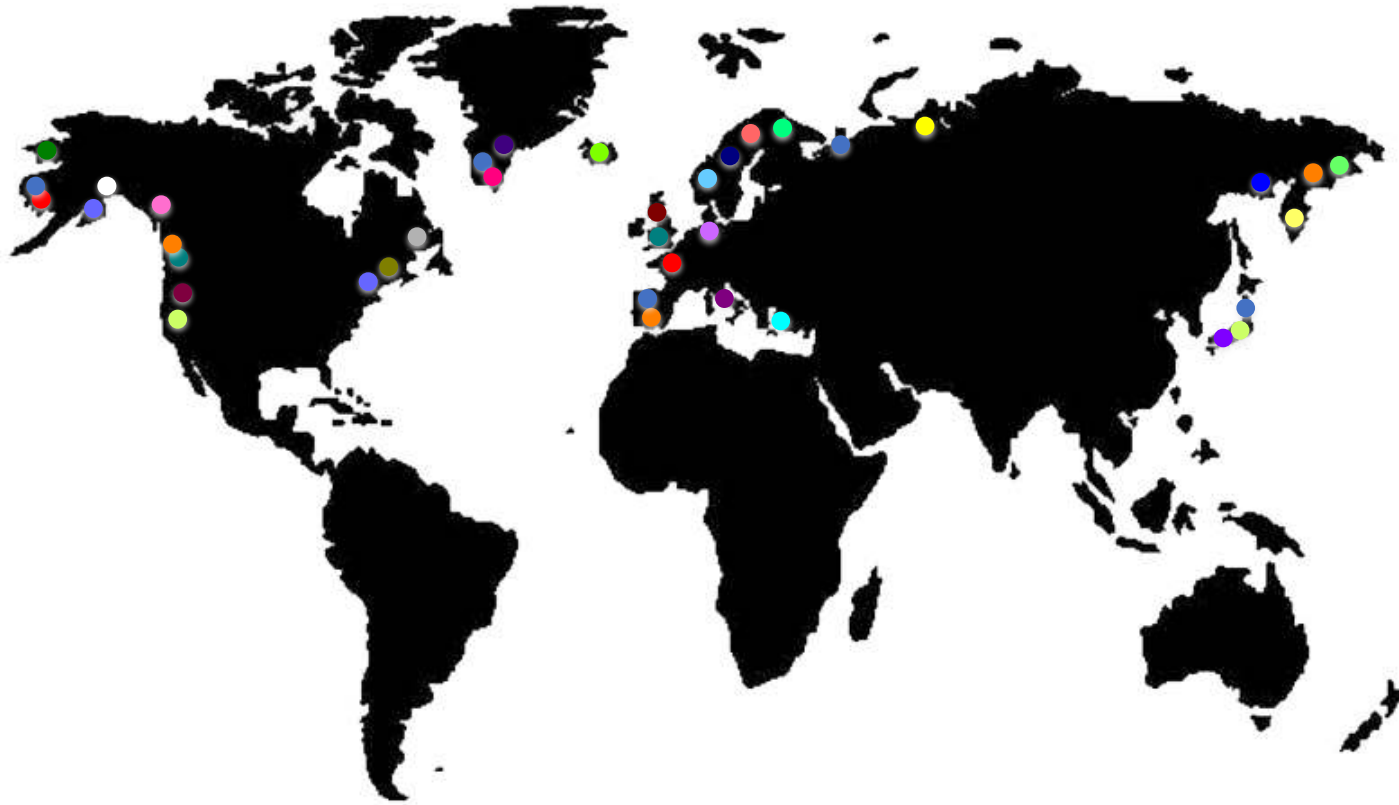


- Lives in ocean, lakes, and streams
- Well-studied biology in wild and in lab
- Extensive phenotypic variation
- Genetic resources
 - Peichel et al (2001) *Nature*
- High quality genome assembly
 - Jones et al (2012) *Nature*
 - Peichel et al (2020) *Genome Biology*
- Evolutionary “supermodel”
- Repeated phenotypic evolution

Repeated evolution of freshwater sticklebacks from the marine ancestor

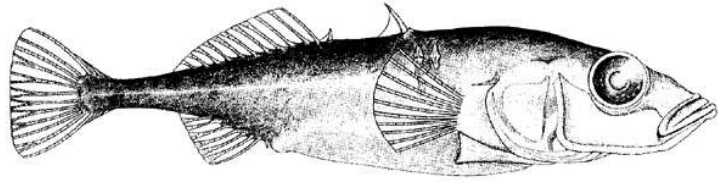


Repeated evolution of freshwater sticklebacks from the marine ancestor

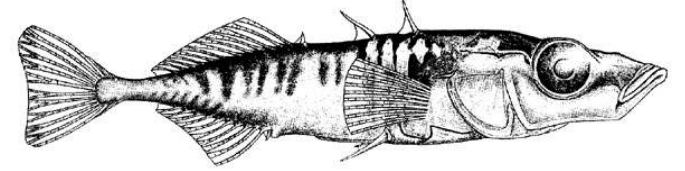


Repeated evolution of benthic and limnetic forms

benthic



limnetic



Repeated evolution of stream and lake forms



stream

lake



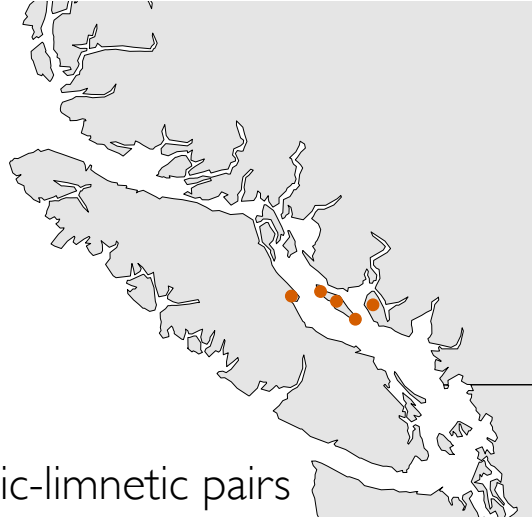
Questions

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Questions

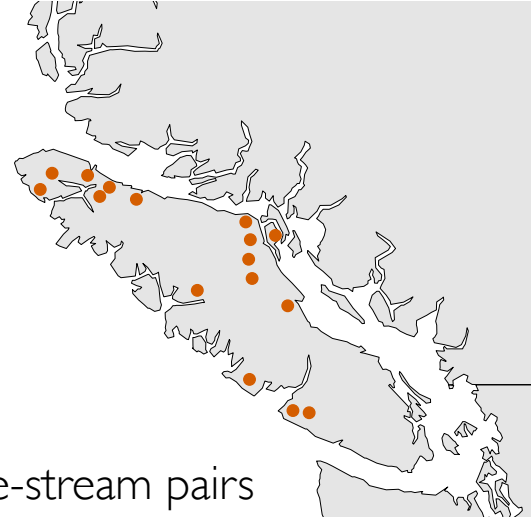
- How often do the same genetic changes underlie repeated phenotypic evolution and adaptation?
 - Forward genetics: QTL mapping
 - Reverse genetics: Population genomics
- Why might some genetic changes be used more frequently during repeated phenotypic evolution and adaptation?

Freshwater stickleback species pairs



Benthic-limnetic pairs

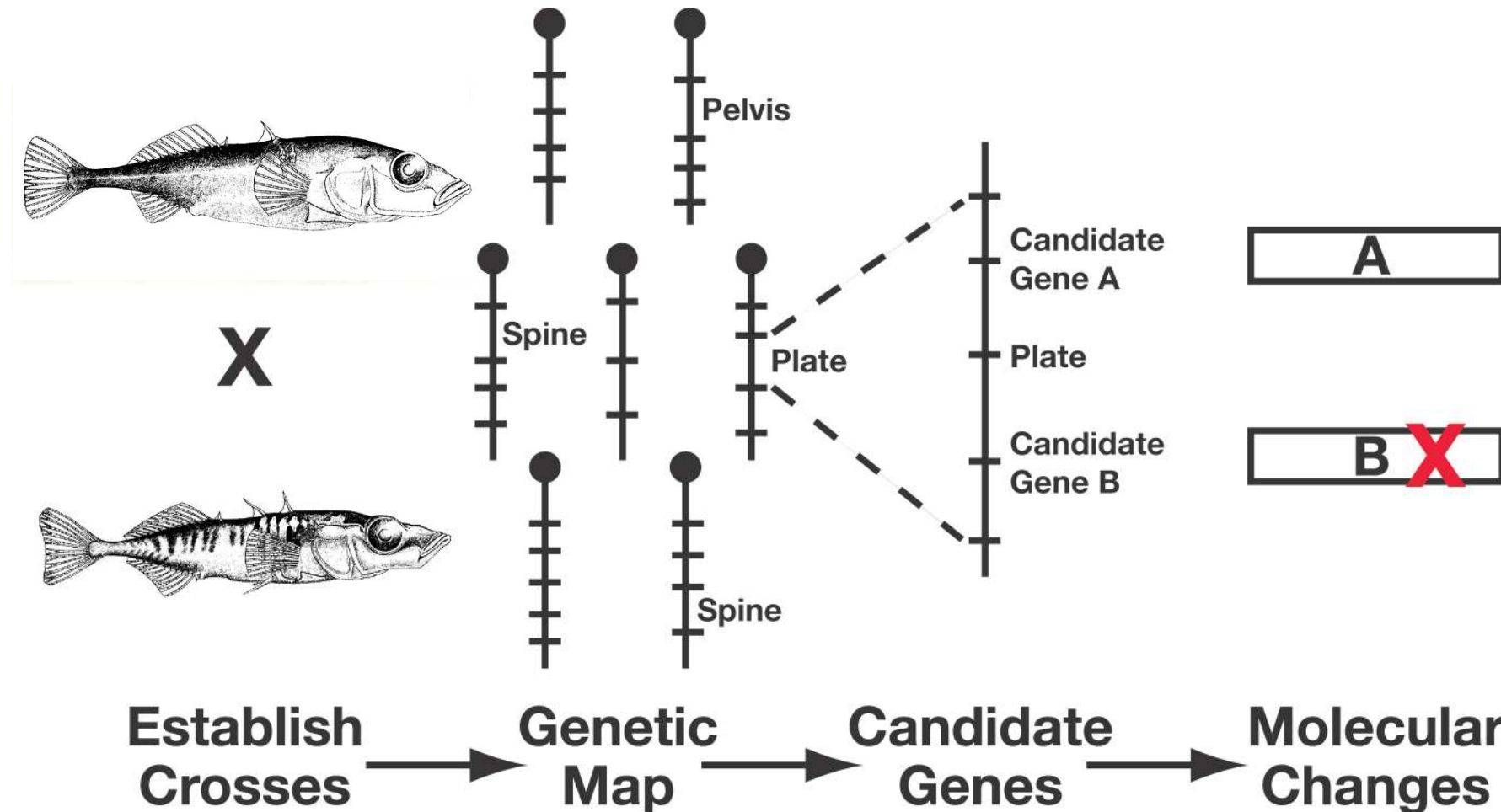
Collaboration with Dolph Schluter



Lake-stream pairs

Collaboration with Yoel Stuart,
Dan Bolnick, Andrew Hendry

Quantitative trait locus (QTL) mapping: which genotypes underlie repeated phenotypes?

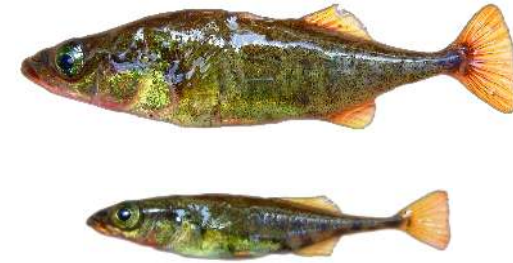


Repeated phenotypic evolution is not always repeated at the genetic level



Benthic-limnetic pairs

50% of QTL are shared between benthic-limnetic pairs
Conte et al (2015) *Genetics*



Lake-stream pairs

15% of QTL are shared between lake-stream pairs
Poore et al (2022) *Evolution*

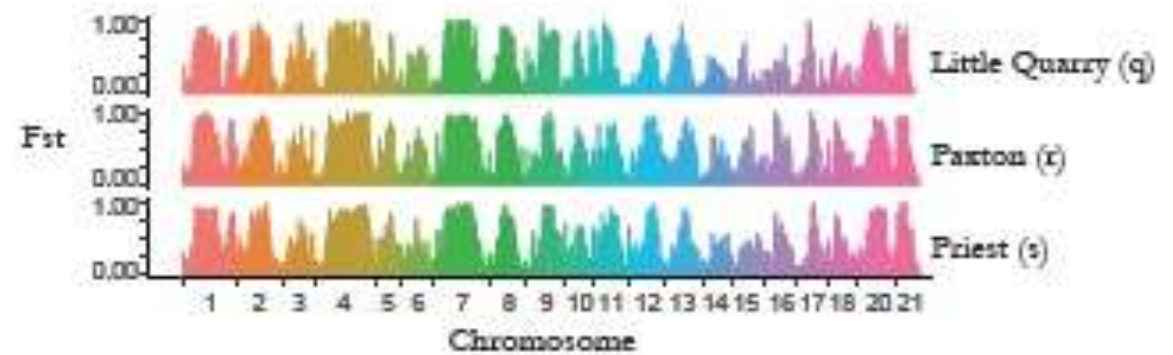
Population genomics: which genotypes are associated with repeated adaptation?



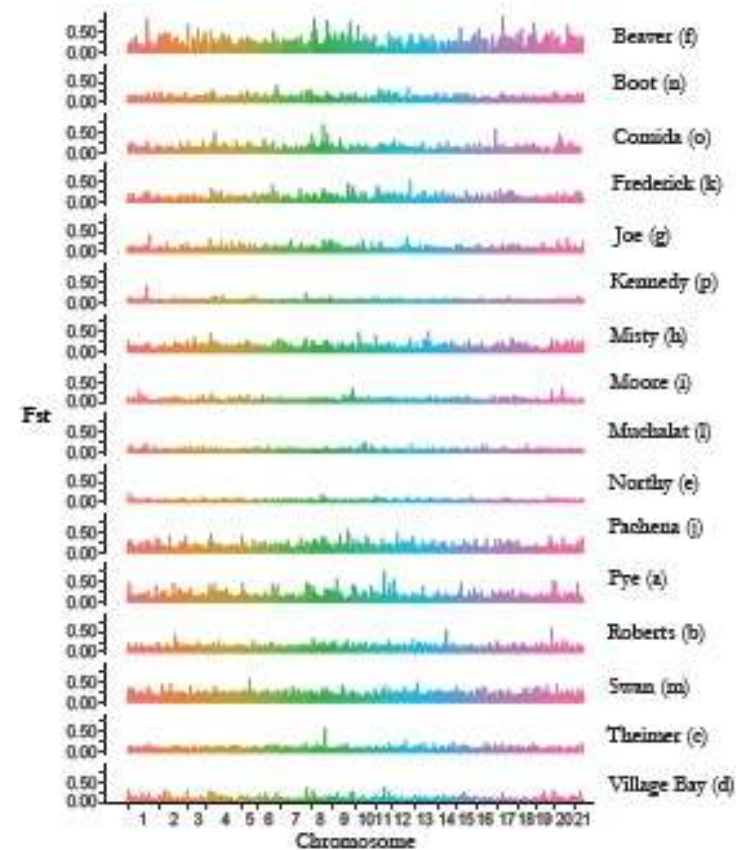
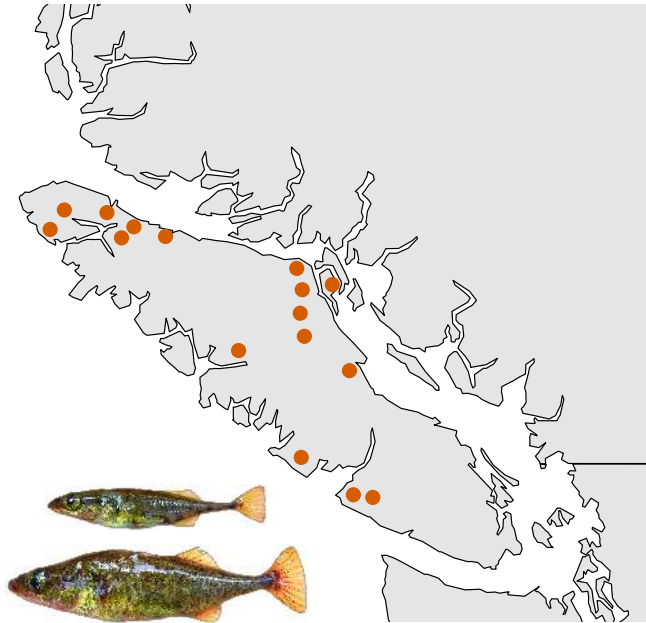
Diana Rennison
UC San Diego

- Lake-stream data
 - 16 lake-stream pairs (32 populations)
 - Sequencing for 24 individuals/population
- Benthic-limnetic data
 - 3 benthic-limnetic pairs (6 populations)
 - Sequencing for 20 individuals/population
- F_{st} between each lake-stream or benthic-limnetic pair was calculated in 50 kbp windows
 - 2513 windows in 16 lake-stream pairs
 - 5733 windows in 3 benthic-limnetic pairs

Highly repeatable genomic differentiation in benthic-limnetic pairs



Lower repeatability of genomic differentiation in lake-stream pairs



Questions

- How often do the same genetic changes underlie repeated phenotypic evolution and adaptation?
 - Sometimes, but not always, and differs between systems!
- Why might some genetic changes be used more frequently during repeated phenotypic evolution and adaptation?

Questions

- How often do the same genetic changes underlie repeated phenotypic evolution and adaptation?
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- Why might some genetic changes be used more frequently during repeated phenotypic evolution and adaptation?

Why is evolution repeatable at the genetic level?

- 1) Only one gene or mutation can produce the phenotype favoured by selection
- 2) Many genes or mutations can produce the phenotype but some:
 - a) are less pleiotropic and have fewer fitness constraints
 - b) have higher mutation rates
 - c) are in regions of low recombination

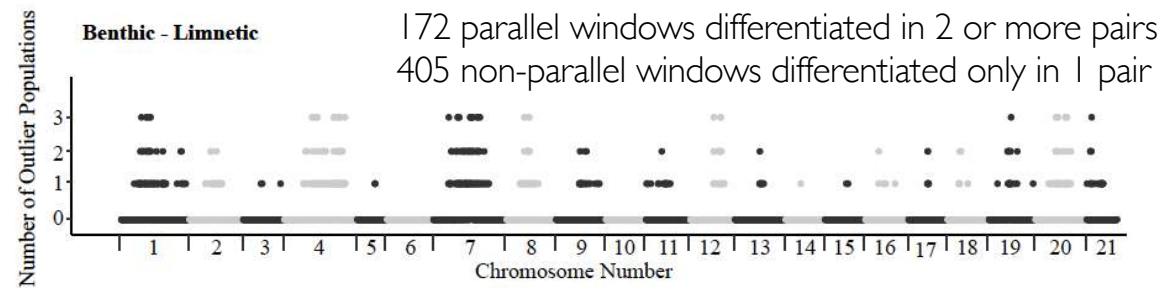
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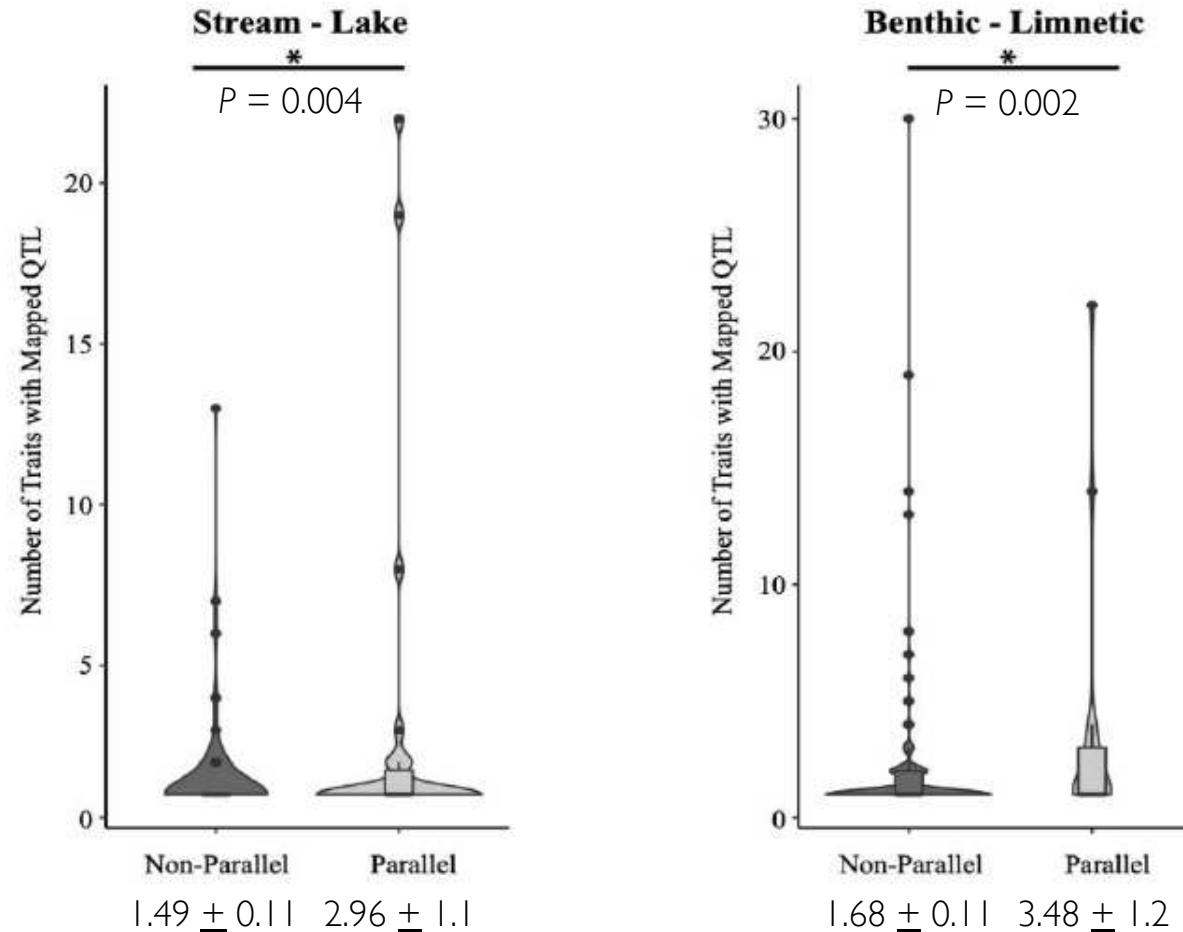
Parallel vs non-parallel 50 kb windows



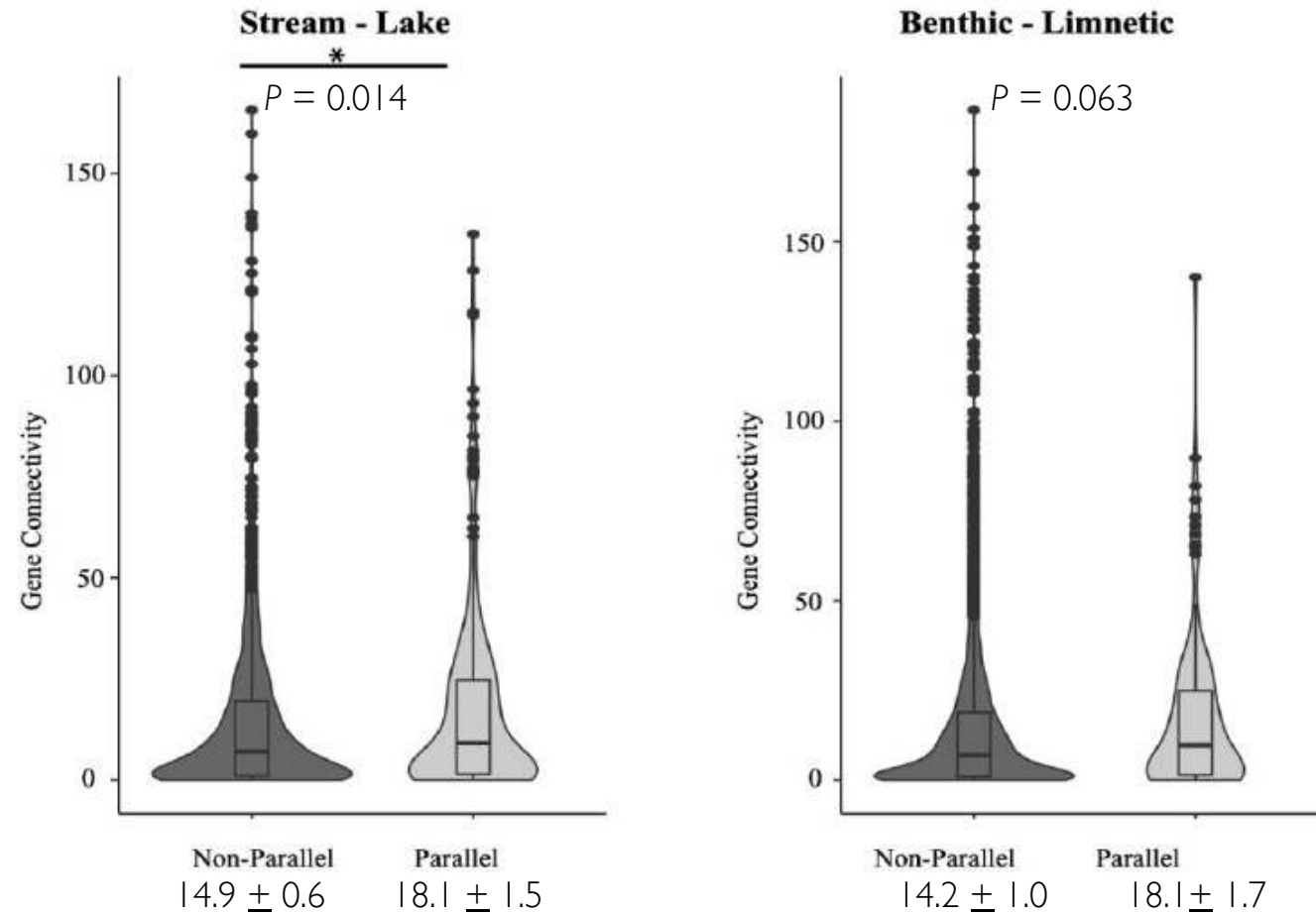
Do parallel and non-parallel windows differ?

- Level of pleiotropy?
 - Number of QTL (Marques & Peichel 2017)
 - Gene connectivity (RNAseq co-expression network)
- Gene number?
- Recombination rate?
- Mutation rate?

Parallel windows contain more QTL



Parallel windows contain genes with higher connectivity



Do parallel and non-parallel windows differ?

- Level of pleiotropy?
 - Parallel windows have more QTL and higher connectivity
 - But, non-parallel windows are the most pleiotropic
- Gene number?
 - No difference
- Recombination rate?
 - Parallel windows have a lower recombination rate, but only in benthic-limnetic pairs where there is high gene flow
 - If we only consider outlier windows, there is no difference between parallel and non-parallel windows
- Mutation rate?
 - No difference if account for difference in recombination rate

Conclusions

- Pleiotropy does not always seem to be a constraint
- Rather, intermediate (and synergistic) levels of pleiotropy might be adaptive
- Old alleles with synergistic pleiotropic effects might be maintained as standing variation in systems like stickleback in which repeated adaptation has occurred many times

Questions and answers from sticklebacks

- How often do the same genetic changes underlie repeated phenotypic evolution and adaptation?
 - Sometimes, but not always, and differs between systems!
- Why might some genetic changes be used more frequently during repeated phenotypic evolution and adaptation?
 - Pleiotropy and selection on standing variation?

Maybe sticklebacks are special?

Do we see similar patterns in other systems?

Questions

- How often do the same genetic changes underlie repeated phenotypic evolution and adaptation?
- Why might some genetic changes be used more frequently during repeated phenotypic evolution and adaptation?

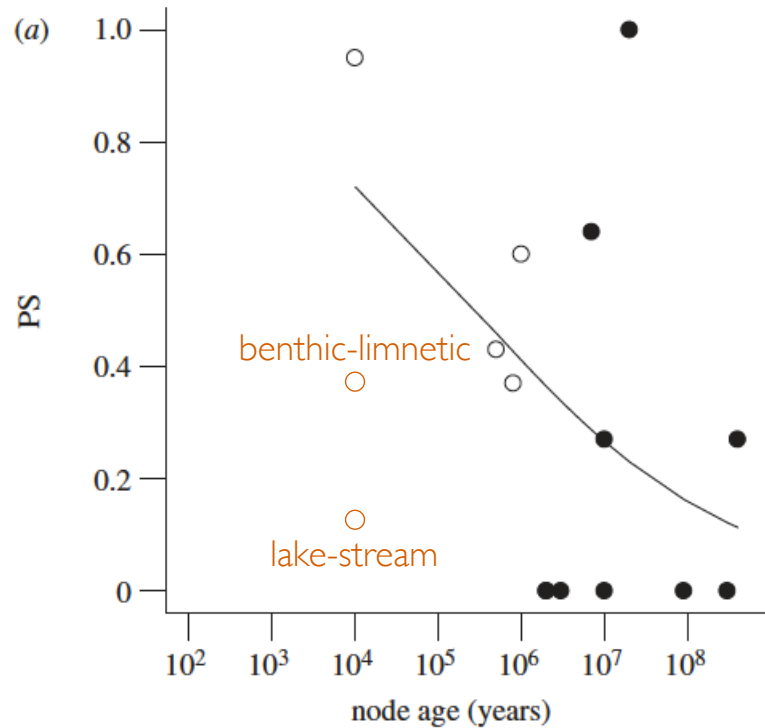
How often do the same genes underlie repeated phenotypic evolution?



How often do the same genes underlie repeated phenotypic evolution?

- Objective literature search revealed 25 case studies of two types:
 - genetic mapping studies
 - candidate gene studies
- Diverse taxa
 - fungi, plants, invertebrates, vertebrates
- Diverse traits
 - morphology, life history, toxins and toxin resistance, ability to utilize specific food sources

Probability of gene reuse is high!

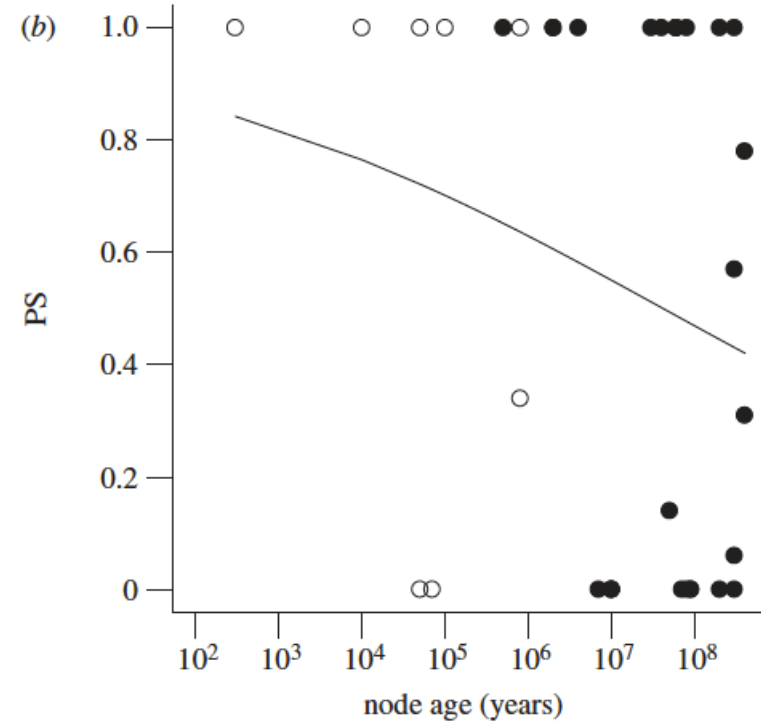


Genetic mapping

PS = 0.32 ± 0.10 s.e.

○ PS = 0.47 ± 0.15 s.e.

● PS = 0.24 ± 0.12 s.e.



Candidate gene

PS = 0.55 ± 0.08 s.e.

○ PS = 0.67 ± 0.17 s.e.

● PS = 0.51 ± 0.09 s.e.

Caveats

- Publication bias
- Small number of traits
- Detecting genes of small effect
- Different studies were done at different times in different ways
- Currently revisiting this meta-analyses
 - Stay tuned!

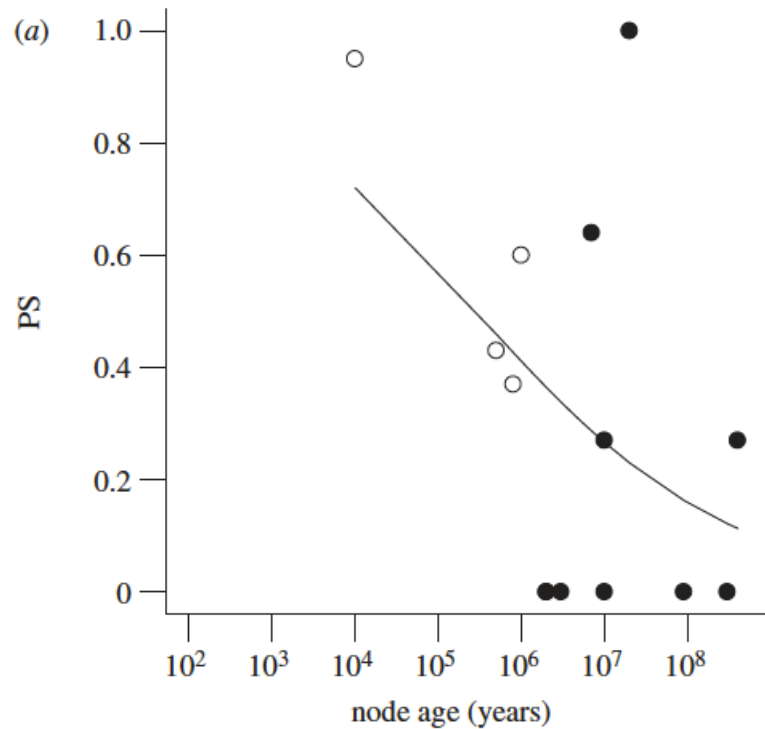


Magdalena Bohutínská

Questions

- How often do the same genetic changes underlie repeated phenotypic evolution and adaptation?
- Why might some genetic changes be used more frequently during repeated phenotypic evolution and adaptation?

Gene reuse decreases with divergence time

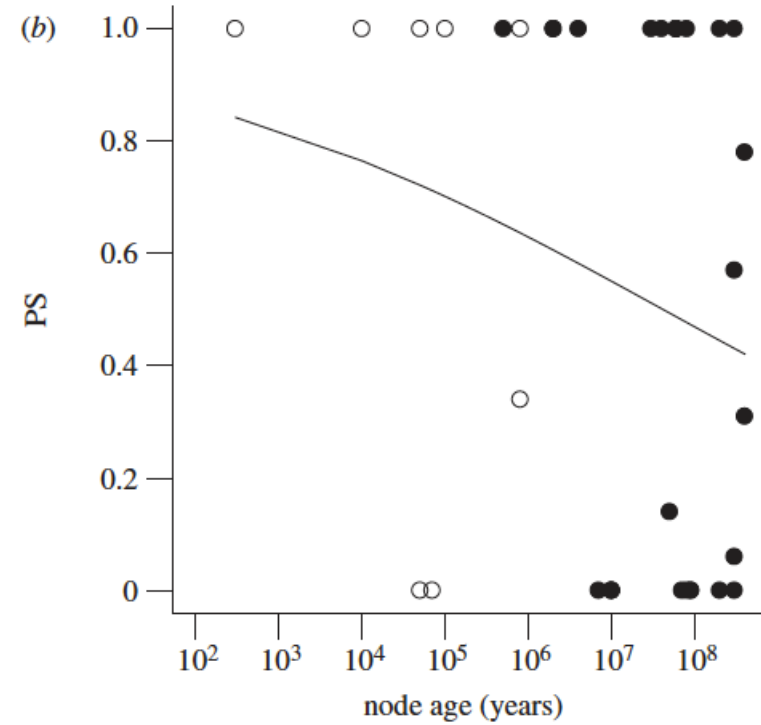


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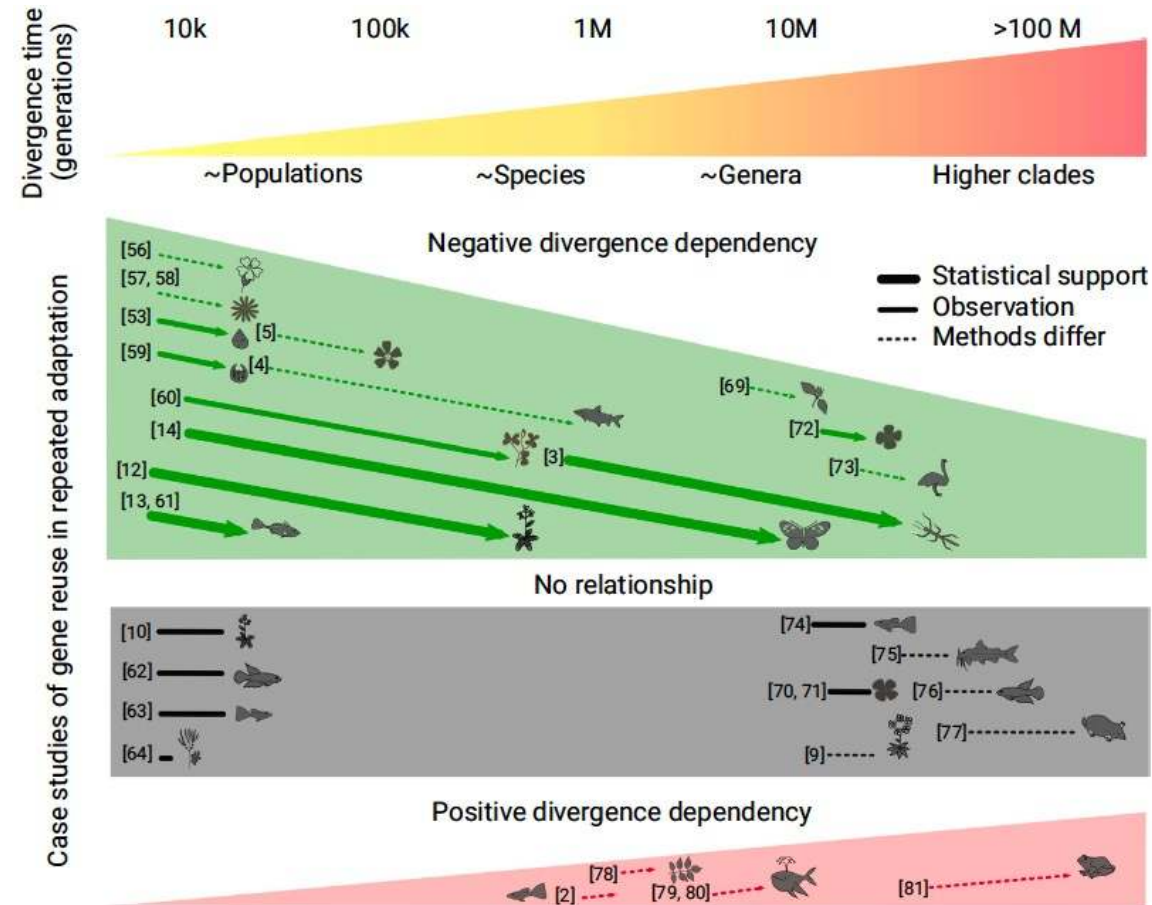
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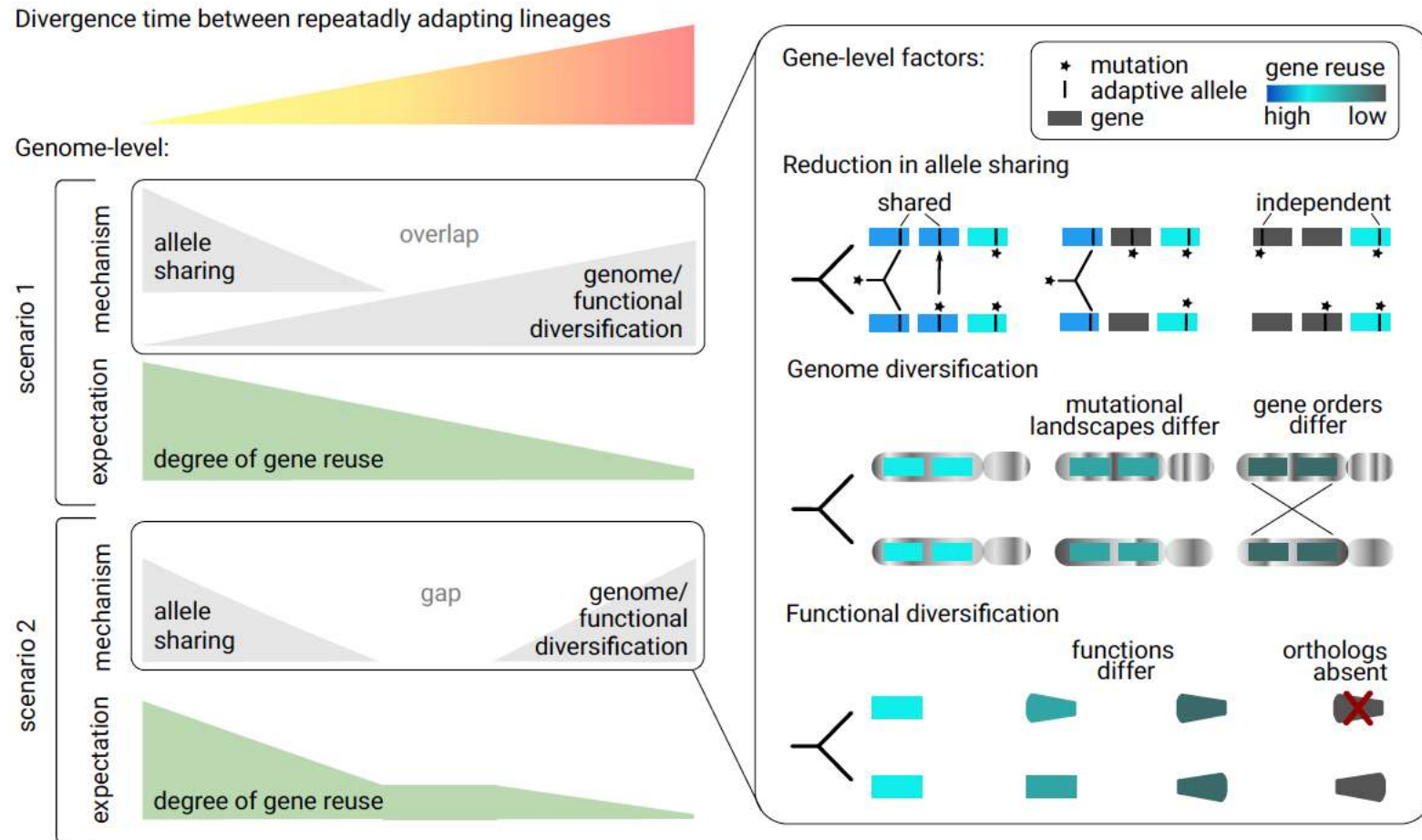
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Gene reuse decreases with divergence time



Possible genetic mechanisms



Questions and some answers

- How often do the same genetic changes underlie repeated phenotypic evolution and adaptation?
 - Sometimes, but not always!
- Why might some genetic changes be used more frequently during repeated phenotypic evolution and adaptation?
 - Synergistic pleiotropy (Rennison and Peichel 2022)
 - Gene flow (Bohutínská and Peichel 2024)
 - Other mechanisms?

Back to sticklebacks...

They are special😊

Why do the benthic-limnetic and lake-stream pairs differ?



Benthic-limnetic pairs

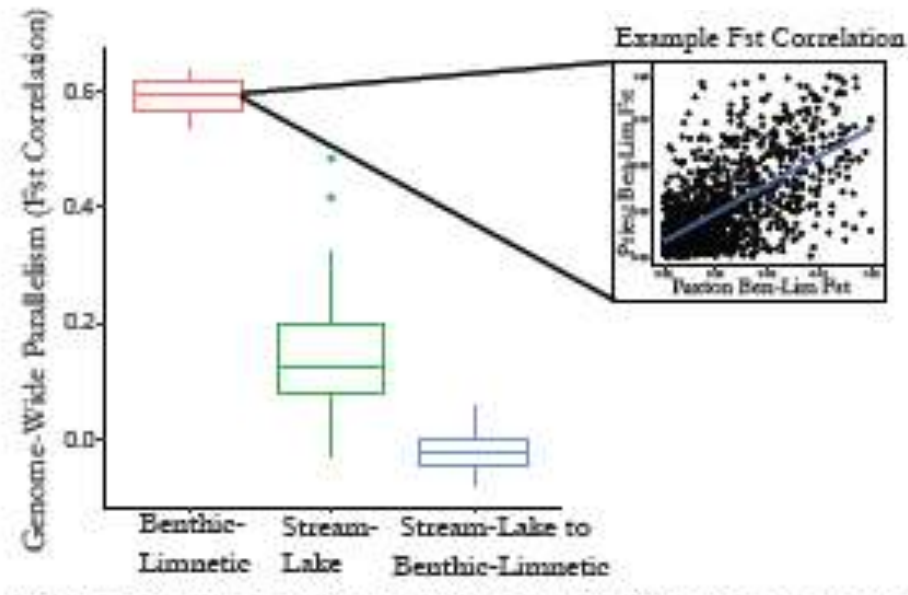
High genetic repeatability



Lake-stream pairs

Low genetic repeatability

Why do the benthic-limnetic and lake-stream pairs differ?



- Source of standing genetic variation?
- Evolutionary history?
- Extent of gene flow?
- Strength of repeated selection?

Problem!

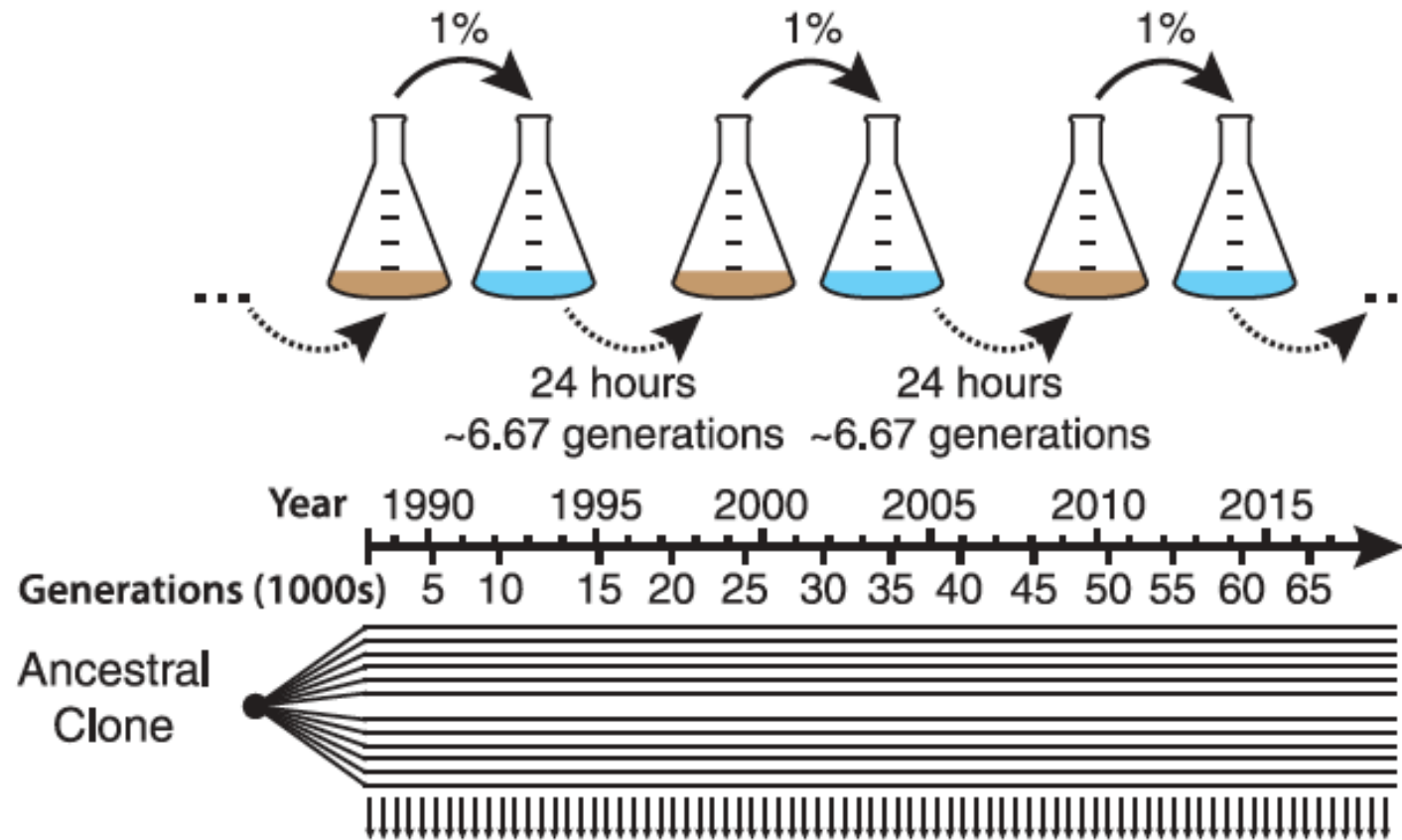
We are only examining extant populations and lack information on the founding ancestral populations and ecosystem changes over time

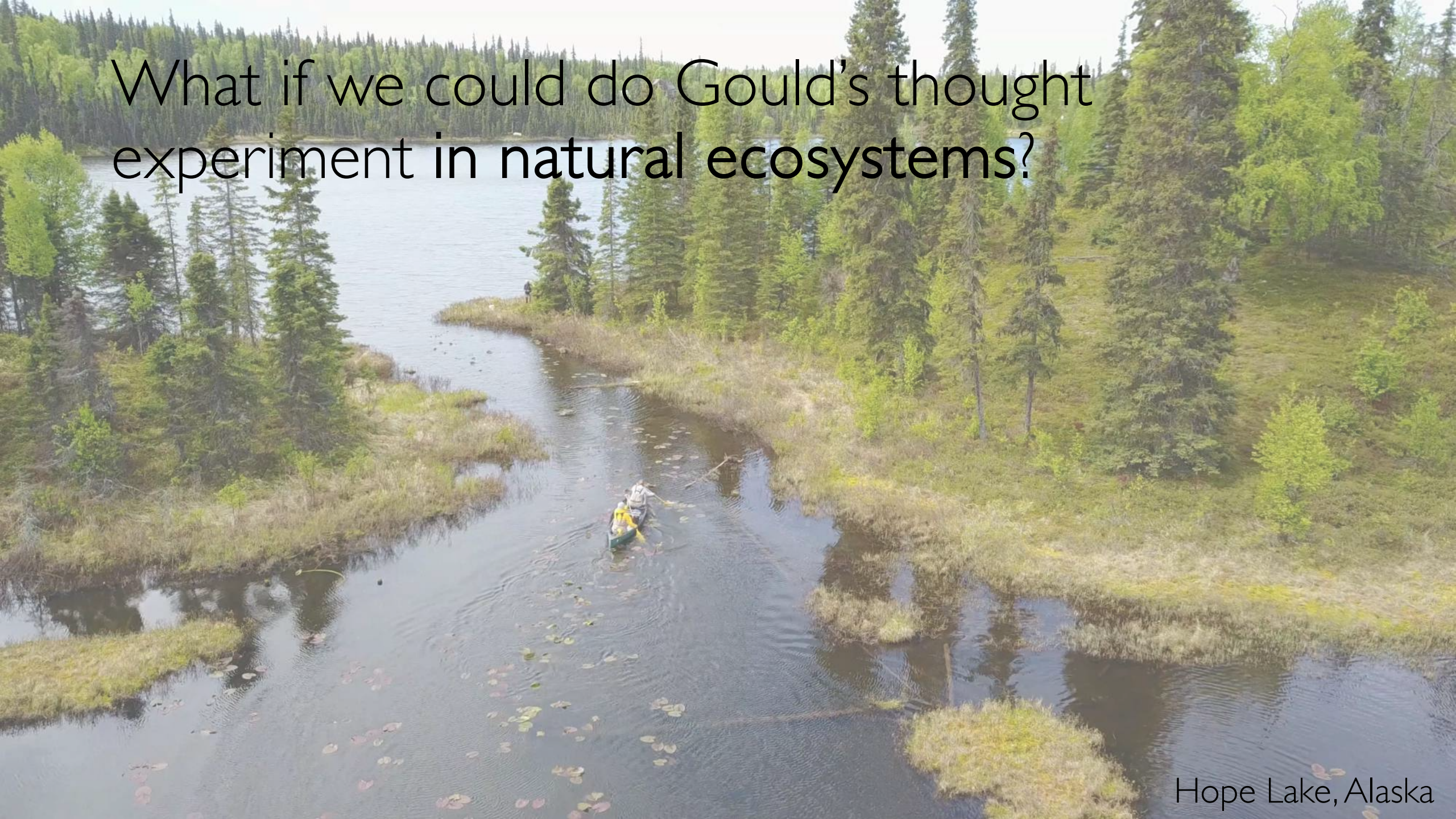
What if we could do Gould's thought experiment?



If we replayed the tape of life, would evolution repeat itself?

What if we could do Gould's thought experiment?

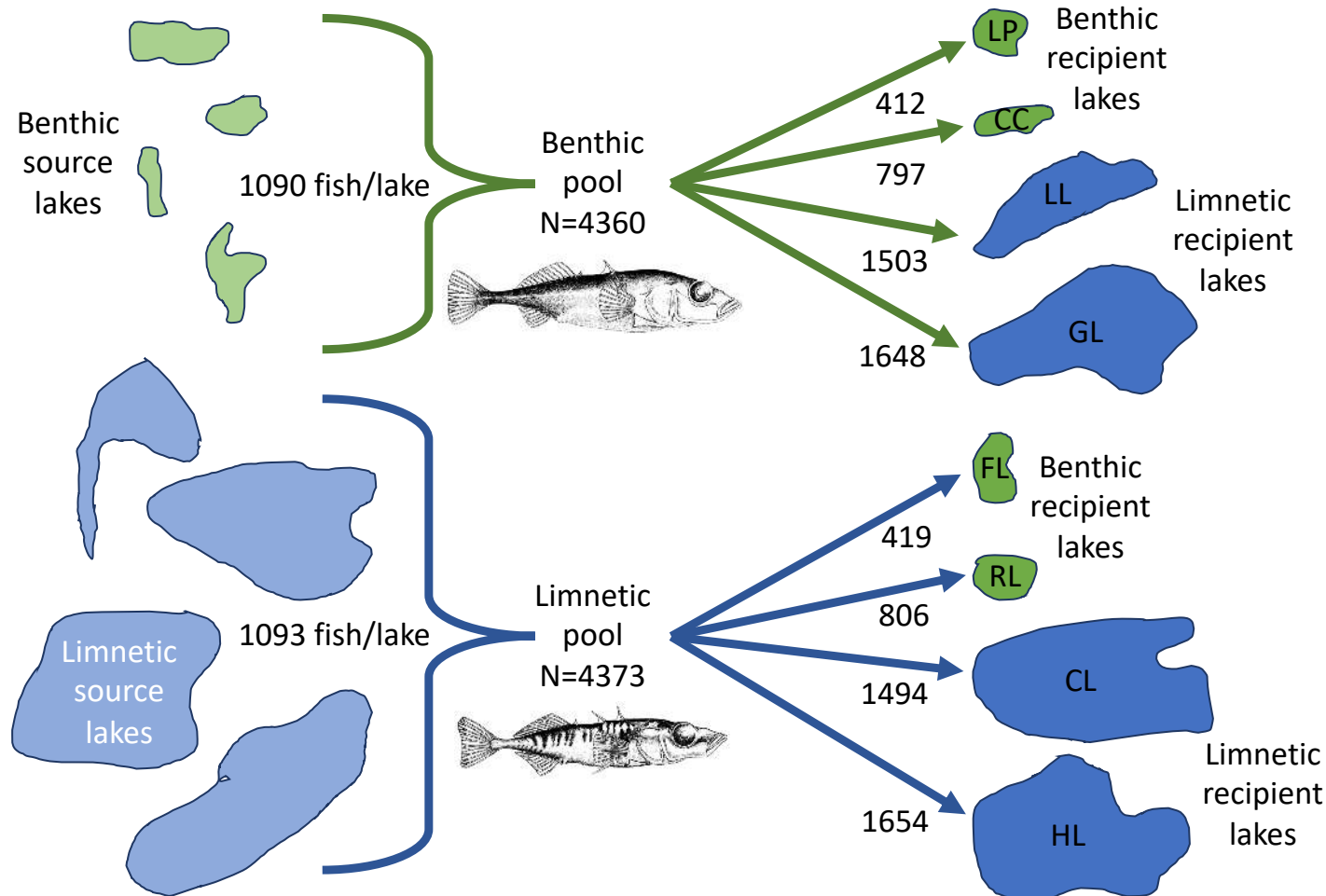


An aerial photograph of a lake in Hope Lake, Alaska. The lake is surrounded by a dense forest of evergreen trees. In the center of the lake, a person is paddling a small green canoe. To the left of the canoe, there is a small, grassy island where another person is standing. The water is dark and reflects the surrounding trees. The sky is overcast.

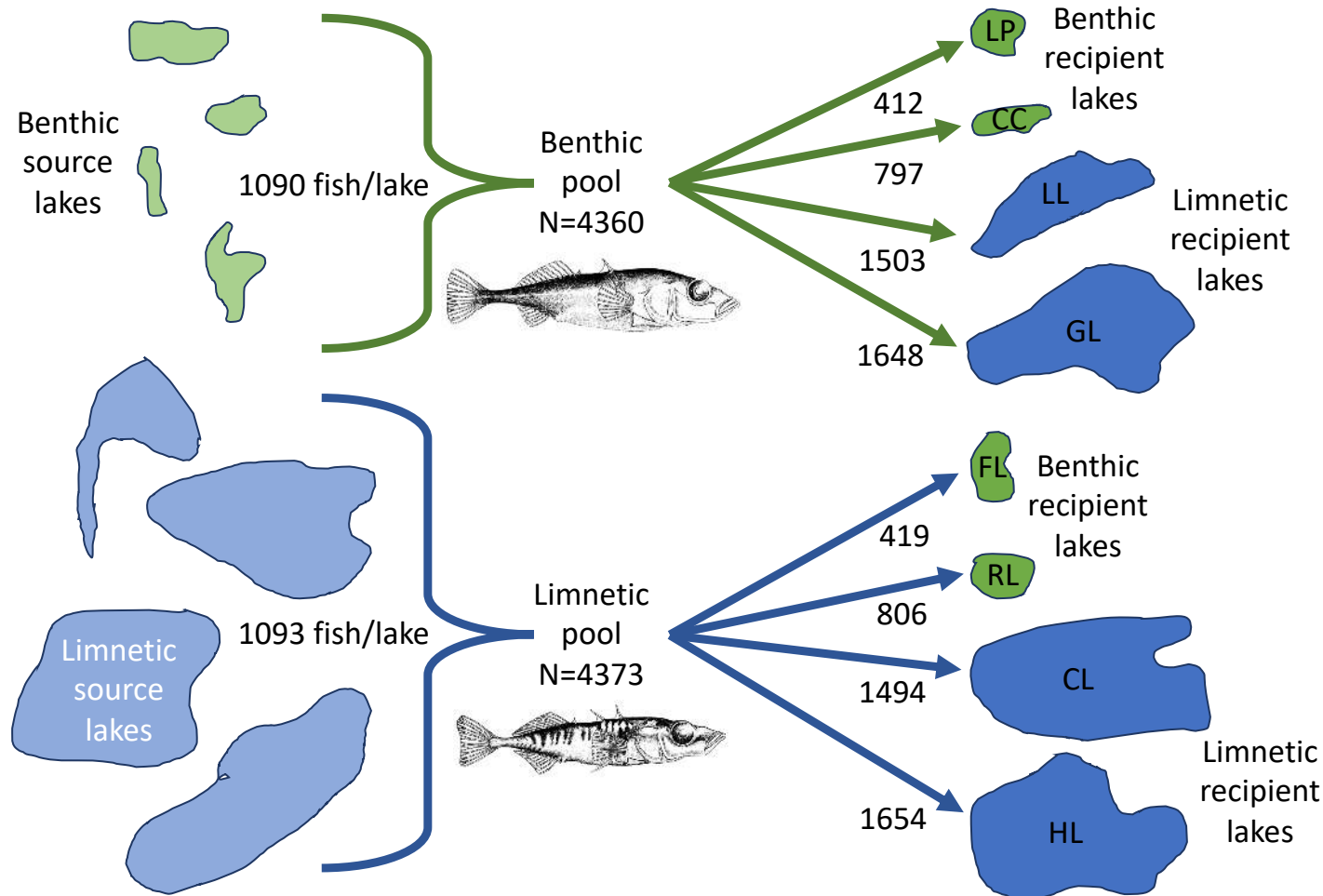
What if we could do Gould's thought
experiment in natural ecosystems?

Hope Lake, Alaska

FITNESS: Forward-In-Time Natural Experimental Study of Selection

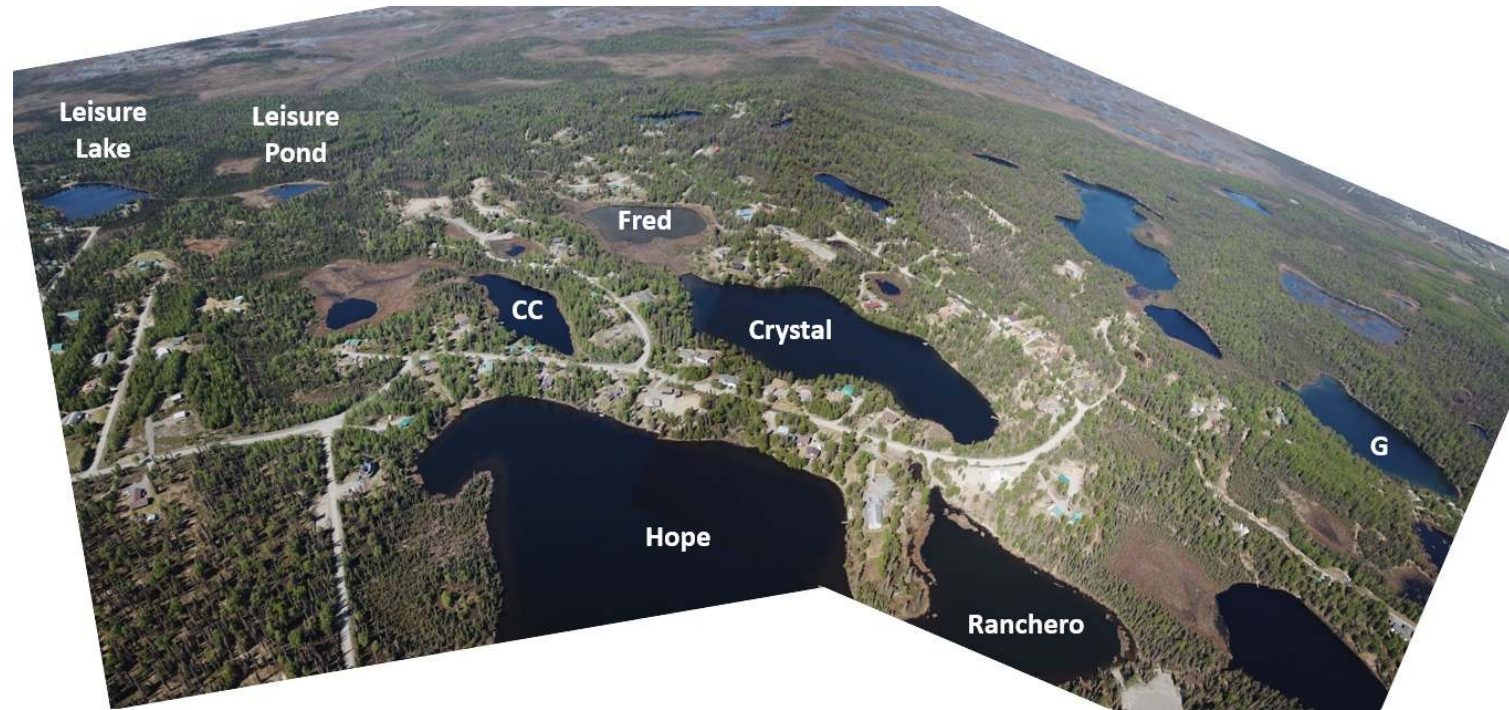


FITNESS: Experimental overview



- Whole genome sequences and phenotypes from 8733 founding fish
- Follow evolutionary trajectories of genotypes and phenotypes in recipient lakes for 8 generations (9216 fish)

FITNESS: Forward-In-Time Natural Experimental Study of Selection



How repeatable are genotypic and phenotypic trajectories?
Can we predict the evolutionary trajectories we see?

Today's workshop: detecting positive selection

- Majda will use sequencing data generated by Milan from some of the founding individuals used for the FITNESS experiment!

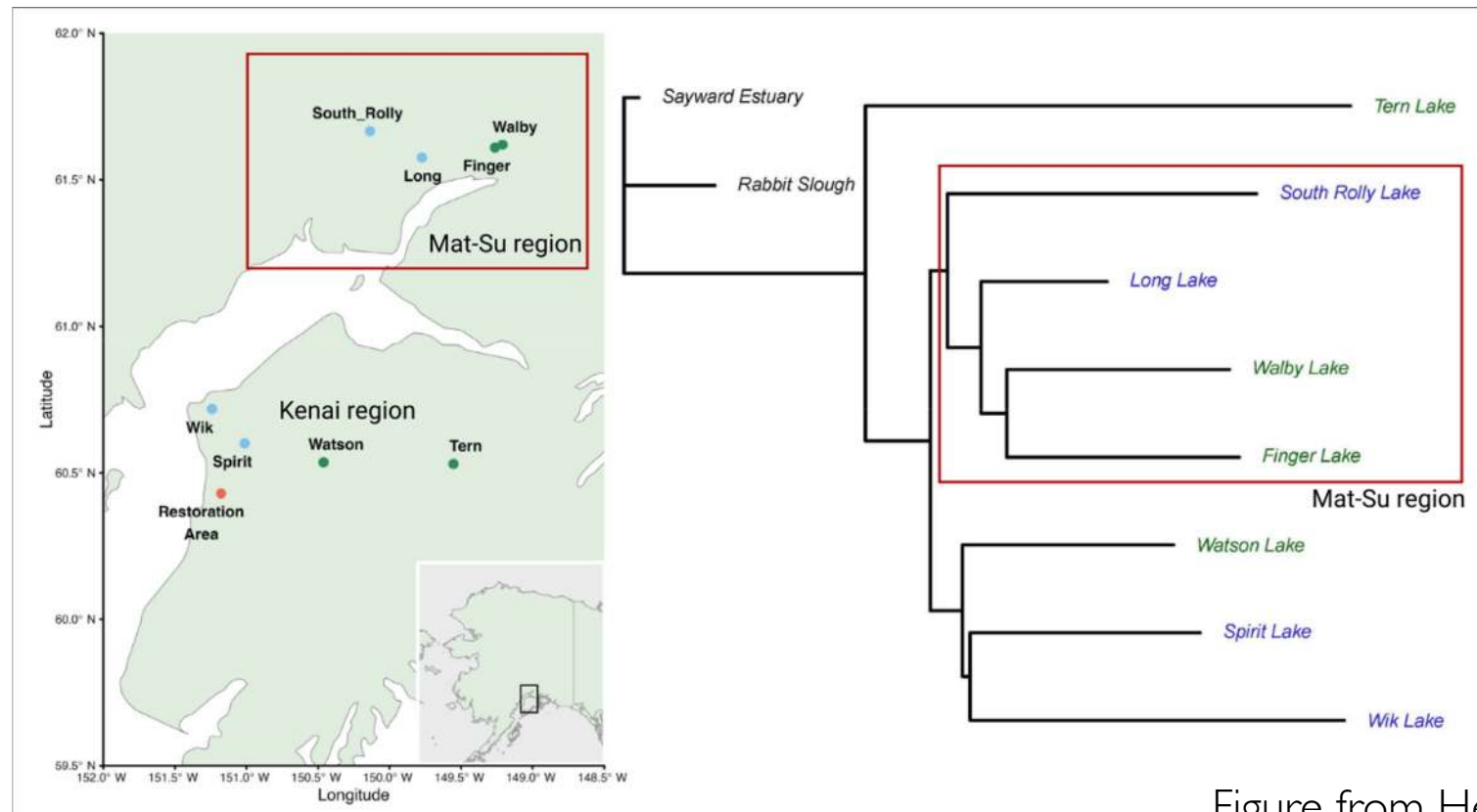


Figure from Hendry et al (2024) *Ecol Evol*

Benthic-limnetic pairs
Dolph Schluter (U British Columbia)
Gina Conte (U British Columbia)
Matt Arnegard (Fred Hutch)
Diana Rennison (UC San Diego)

Lake-stream pairs
Dan Bolnick (U Connecticut)
Andrew Hendry (McGill)
Rowan Barrett (McGill)
Yoel Stuart (Loyola University)
Diana Rennison (UC San Diego)
Hilary Poore (U Bern)

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