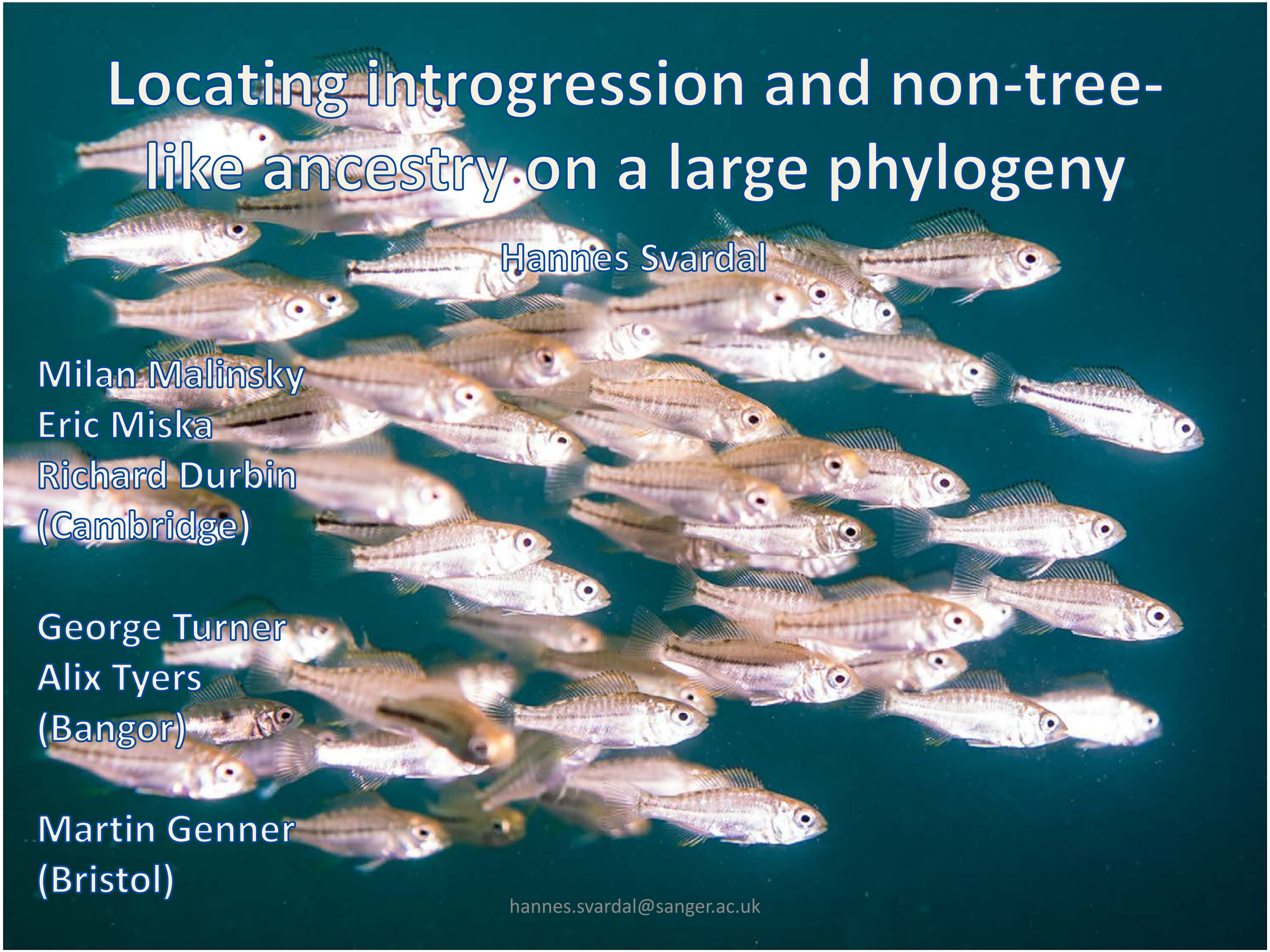

Locating introgression and non-tree-like ancestry on a large phylogeny

Hannes Svardal

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(Cambridge)

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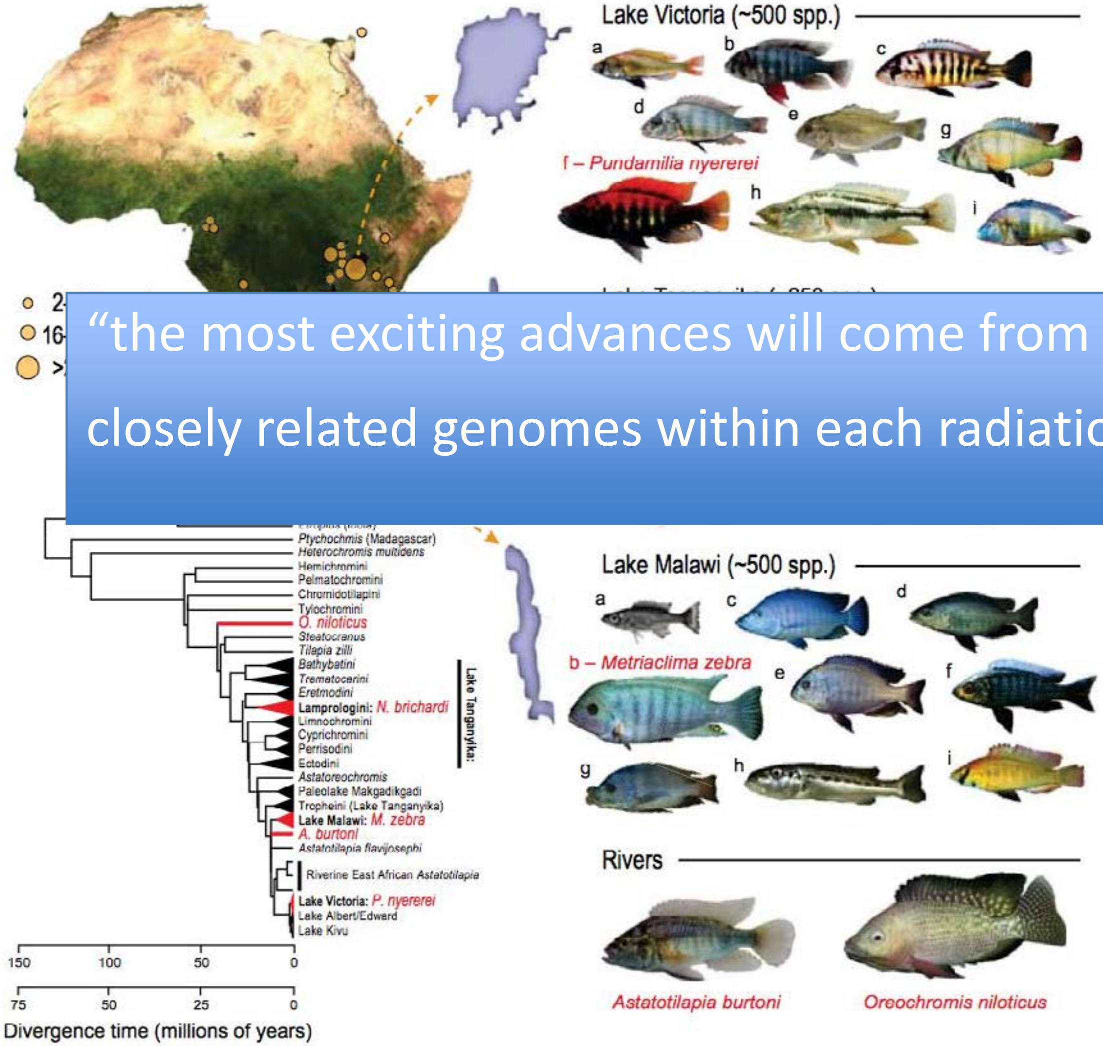
Cichlids like to radiate

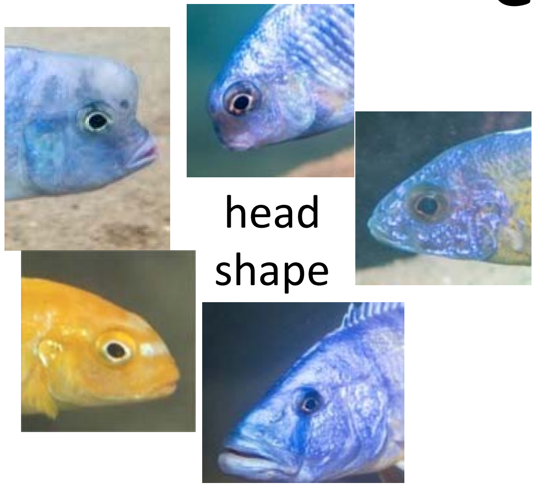


“the most exciting advances will come from analysis of more-closely related genomes within each radiation” (Jiggins 2014)

a – pelagic zooplanktivore;
b – rock-dwelling algae scraper;
c – paedophage;
d – scale eater;
e – snail crusher;
e;

Brawand et al. Nature 2014

Remarkable phenotypic adaptations allowed Lake Malawi cichlids to conquer ecological niches



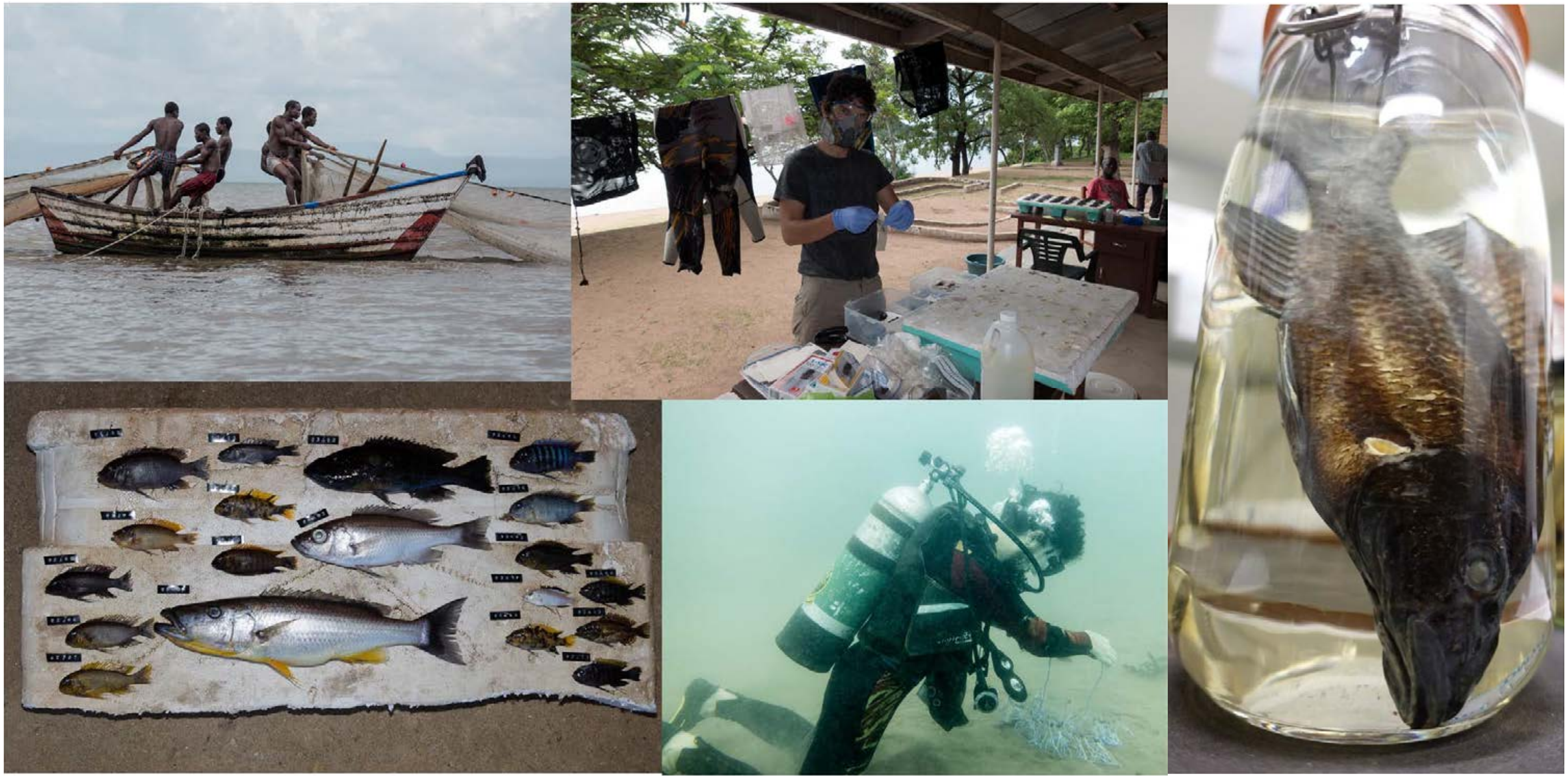
head shape

feeding apparatus

pigmentation

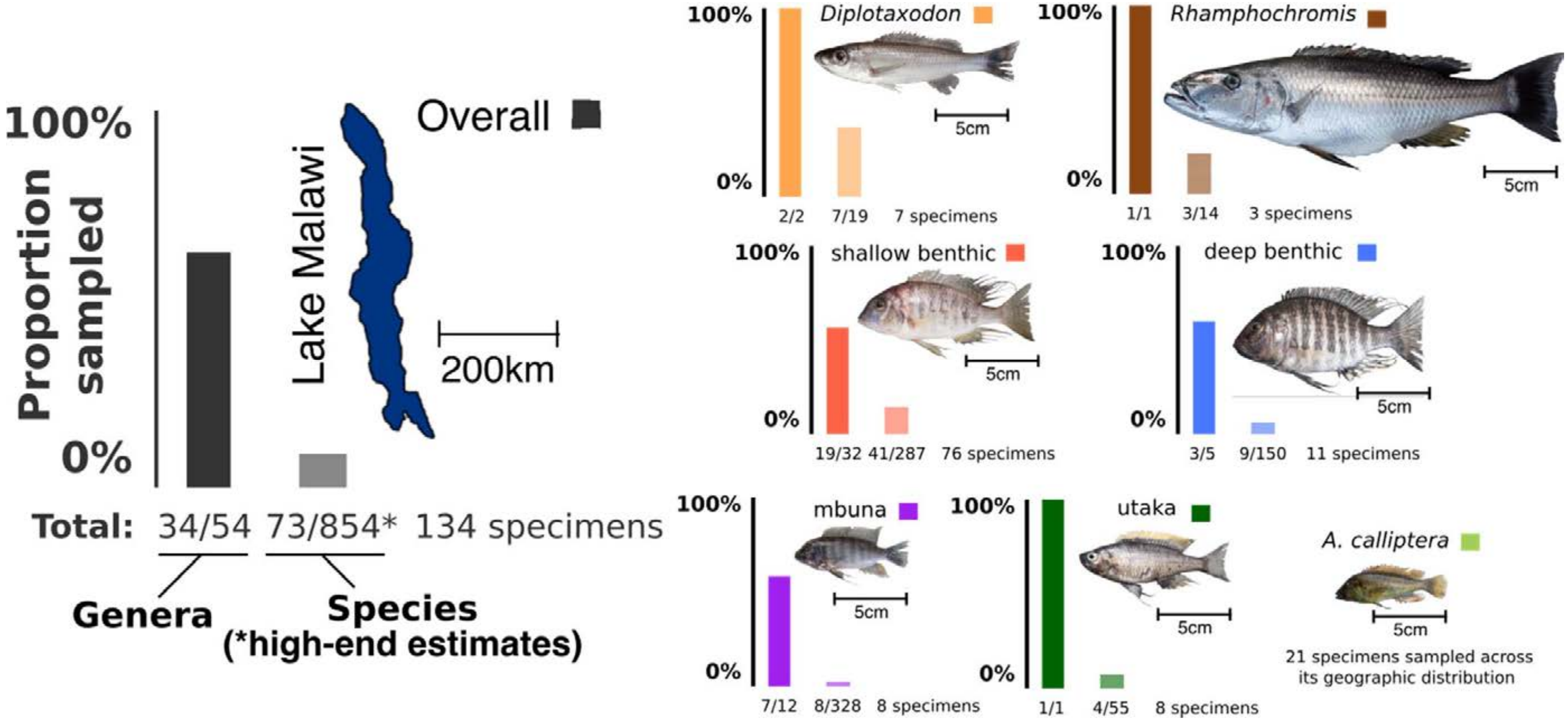
And size, body shape, behaviour…

Sampling: >2500 samples; >250 species; >1800 museum specimen



This talk: ~ 140 samples from 70 species
whole genome sequencing at 15X/5X

Samples from all major morpho-ecological groups



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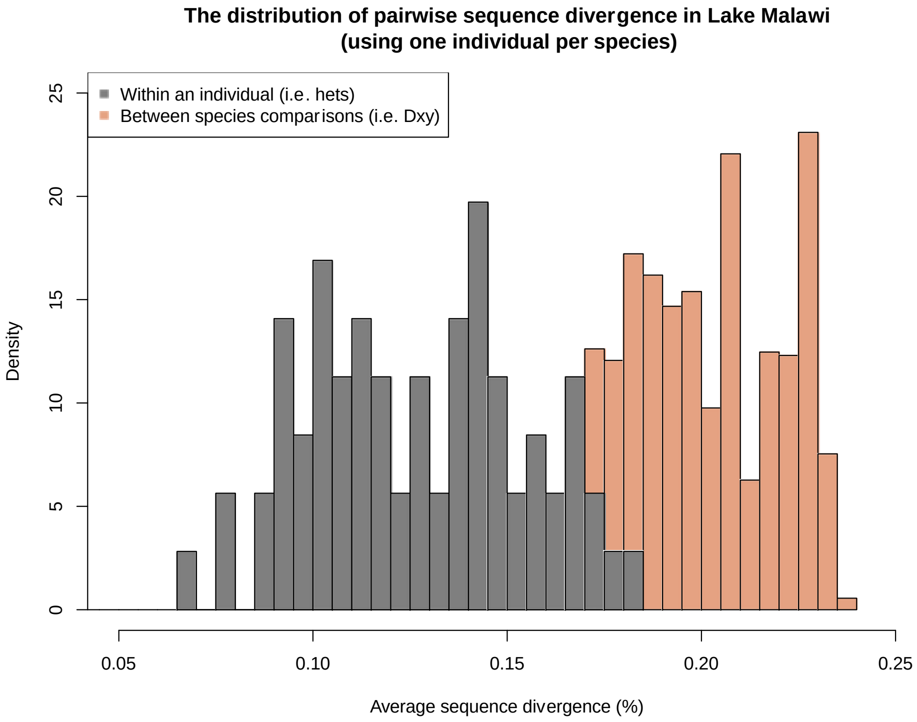
Questions

- Genetic relatedness
- Do species hybridise? Can we quantify gene flow?
- Which genes were under selection?
- Is there any evidence for adaptive introgression?

Genetic relatedness

- Lots of phenotypic diversity and hundreds of species with little genetic divergence
  - max. 0.25% sequence divergence, five times less than human-chimp (1.23%)



Genetic relatedness

- Lots of phenotypic diversity and hundreds of species with little genetic divergence
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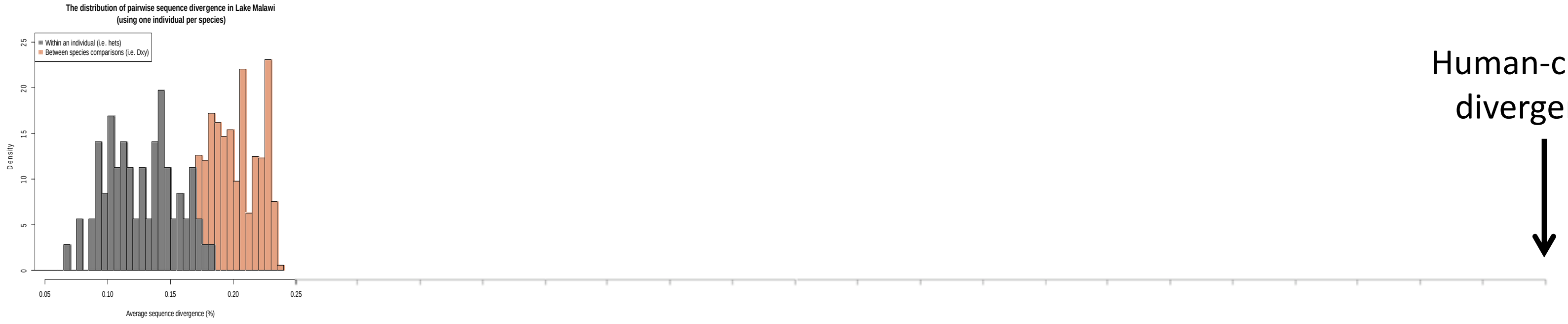
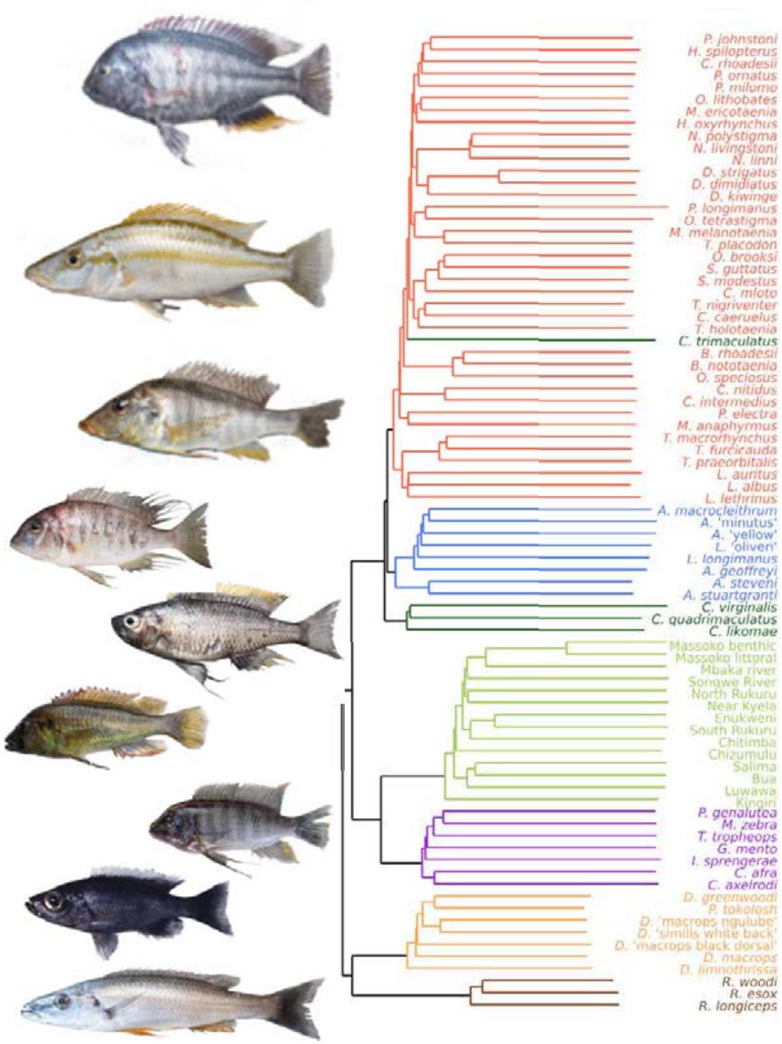


Human-chimp divergence

http://www.spacedaily.com/images-lg/human-child-chimpanzee-baby-lg.jpg

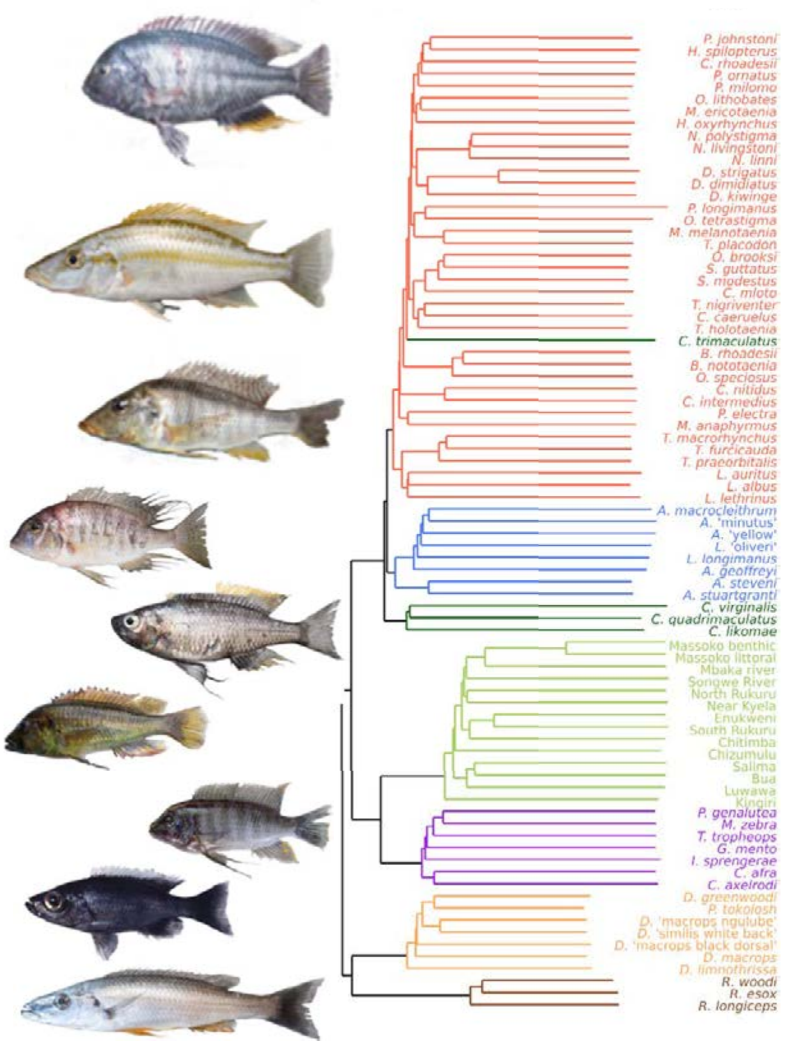
More or less well-defined major clades...

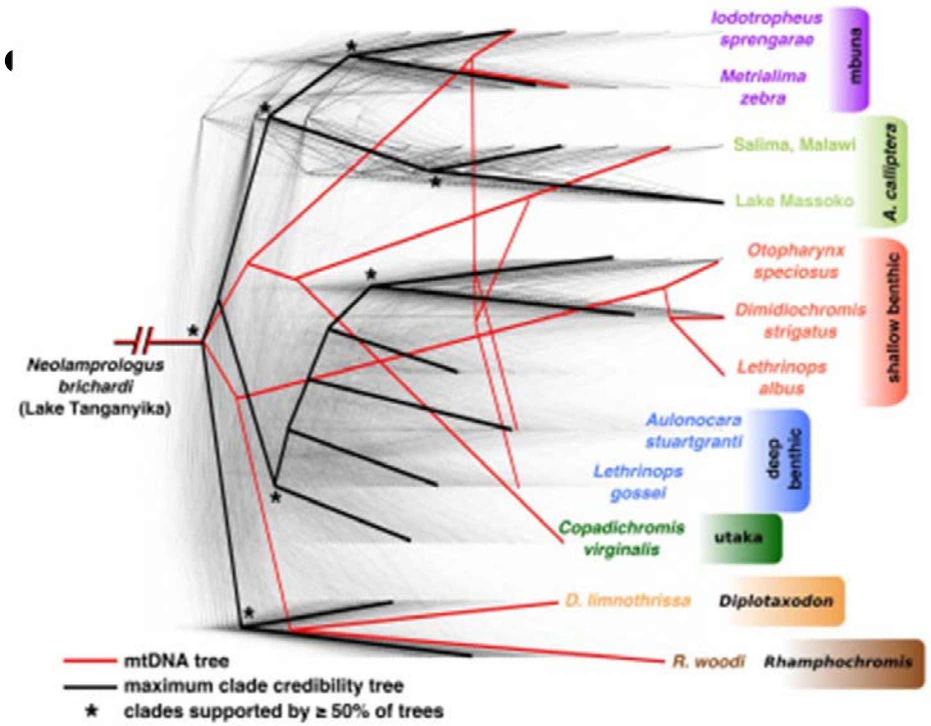
NJ tree



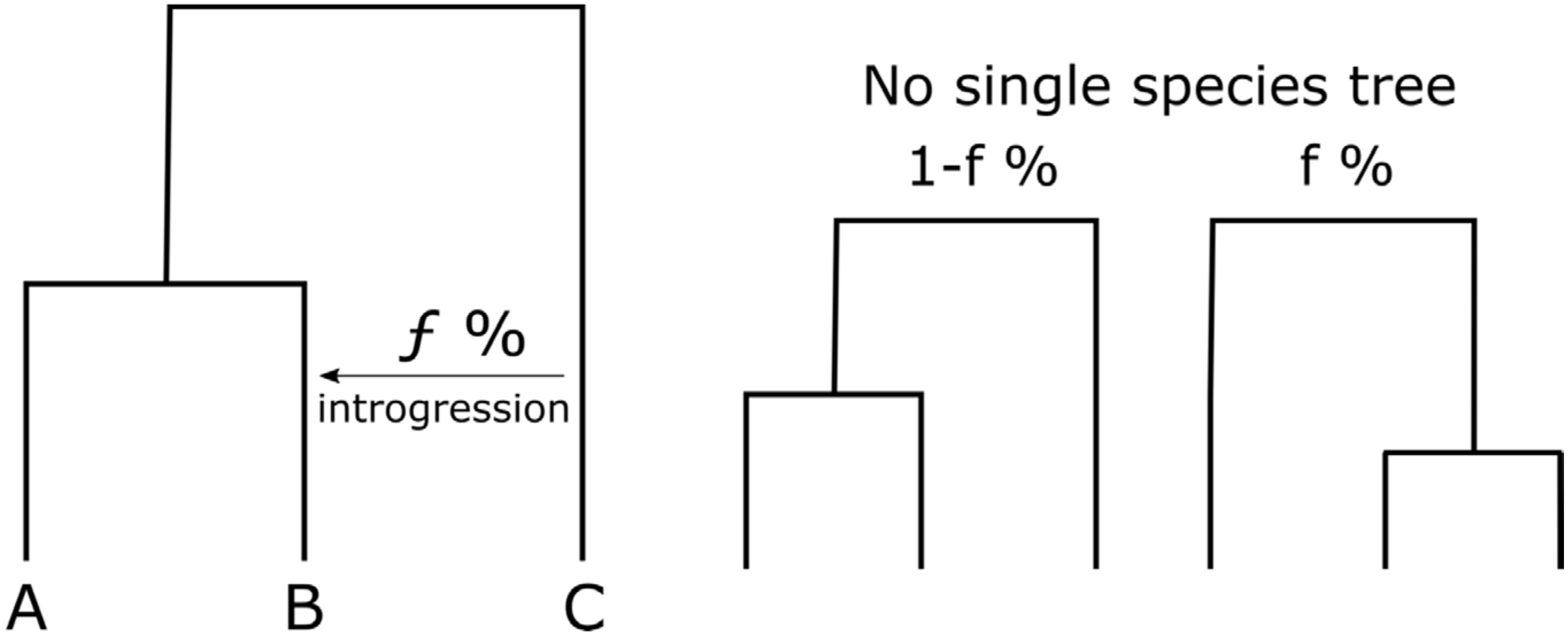
Interesting observations

- Tree topology sensitive to method used, samples and loci included

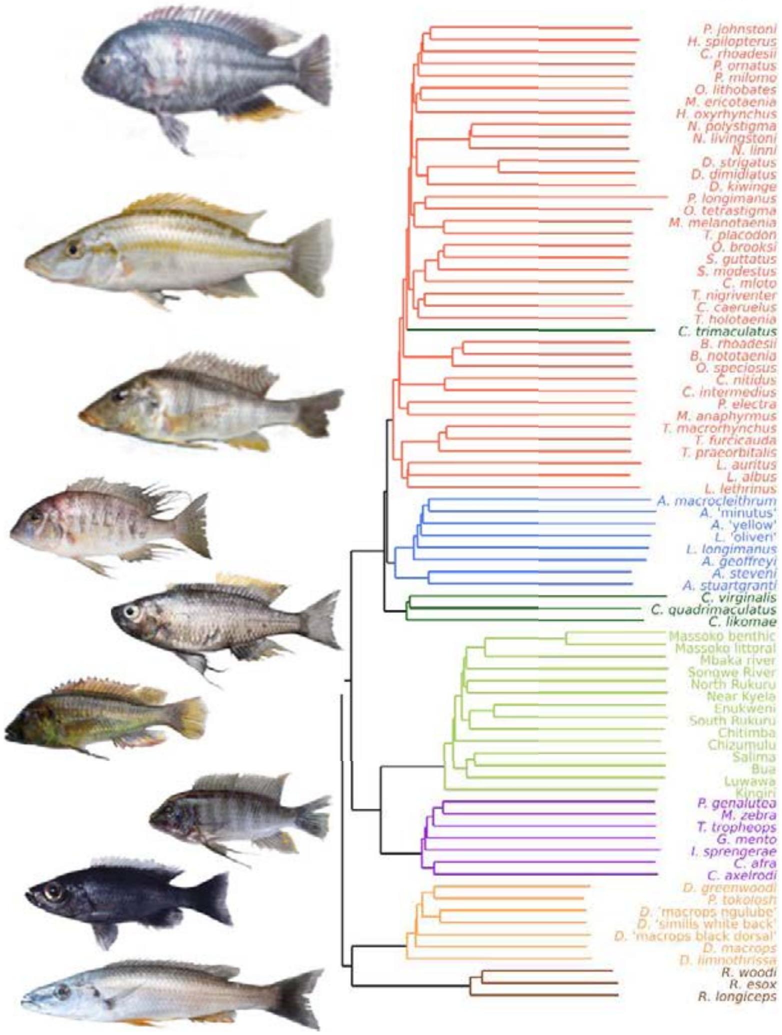




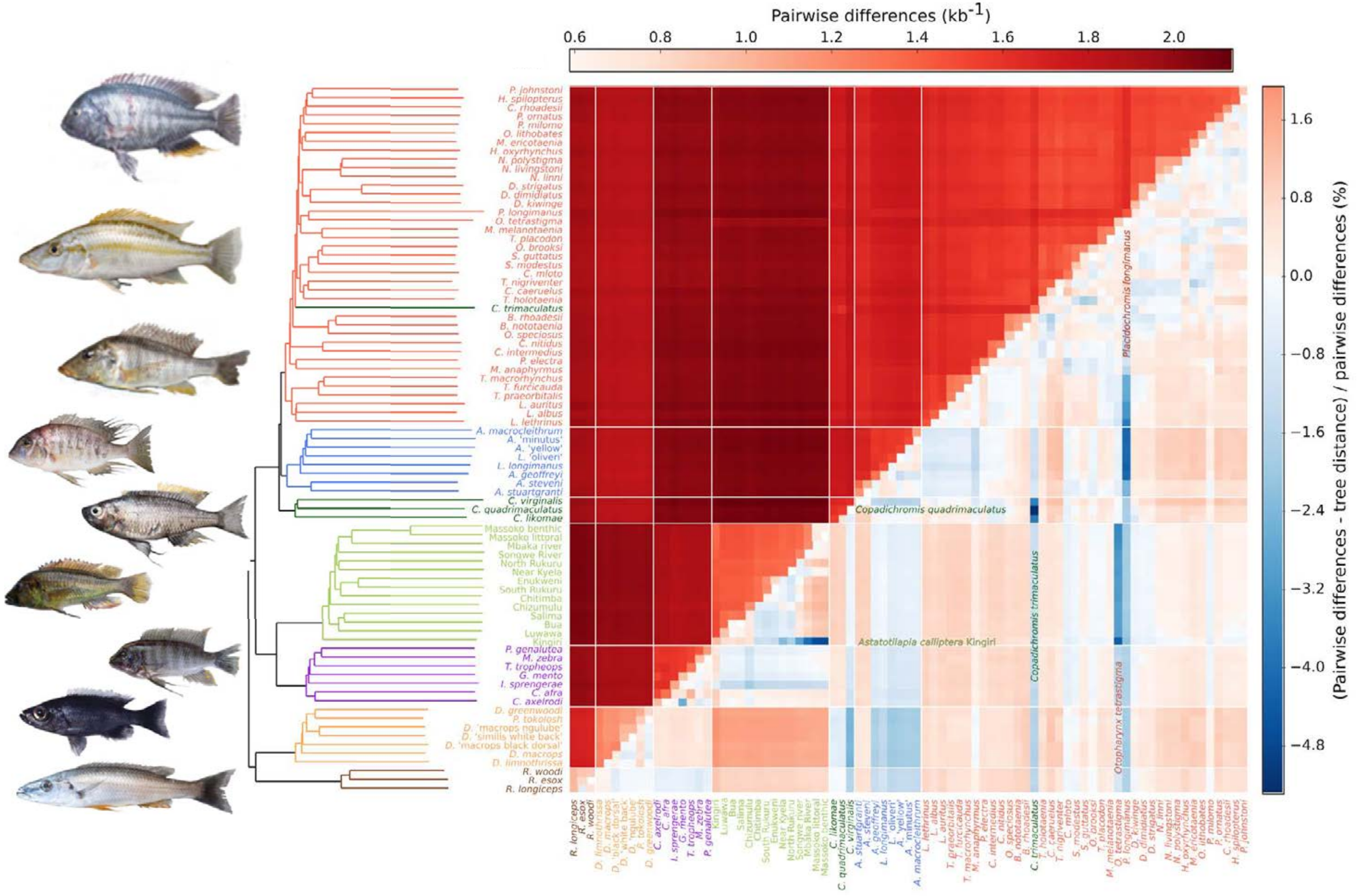
Under introgression, a phylogeny cannot capture the data.



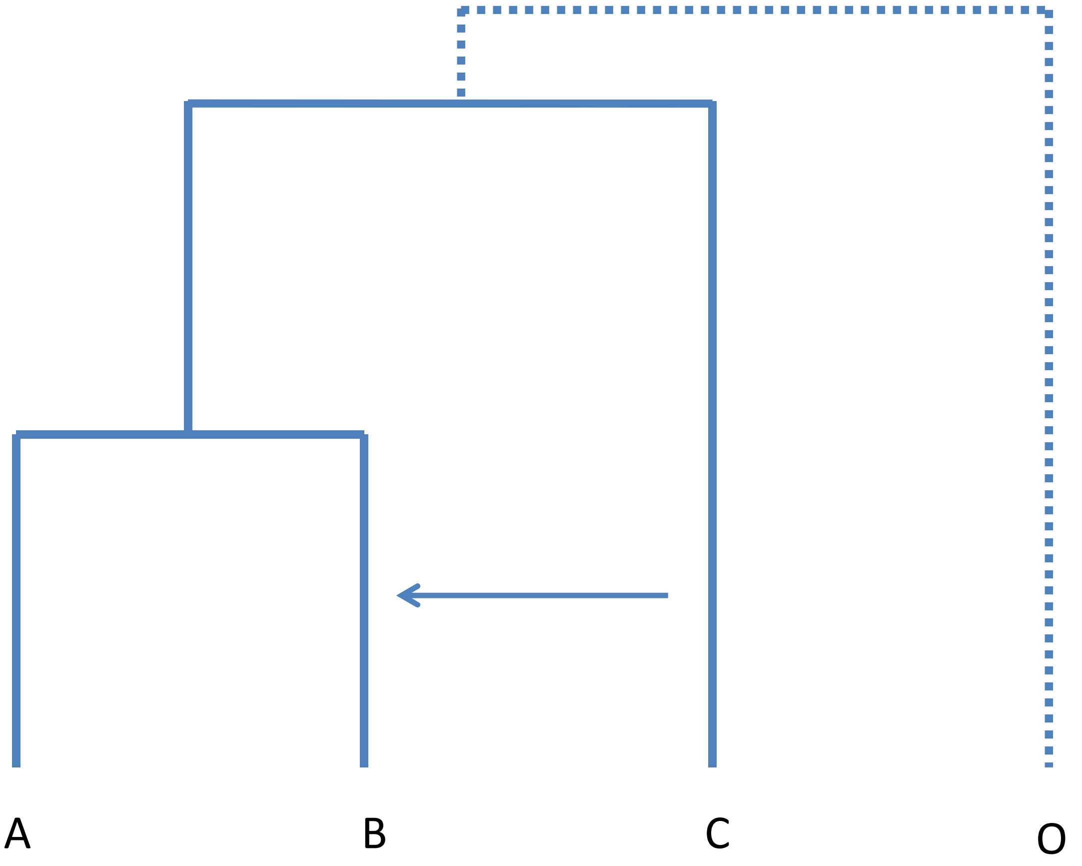
More or less well-defined major clades...



Relatedness not tree-like



Measuring gene-flow: D/F4-statistic

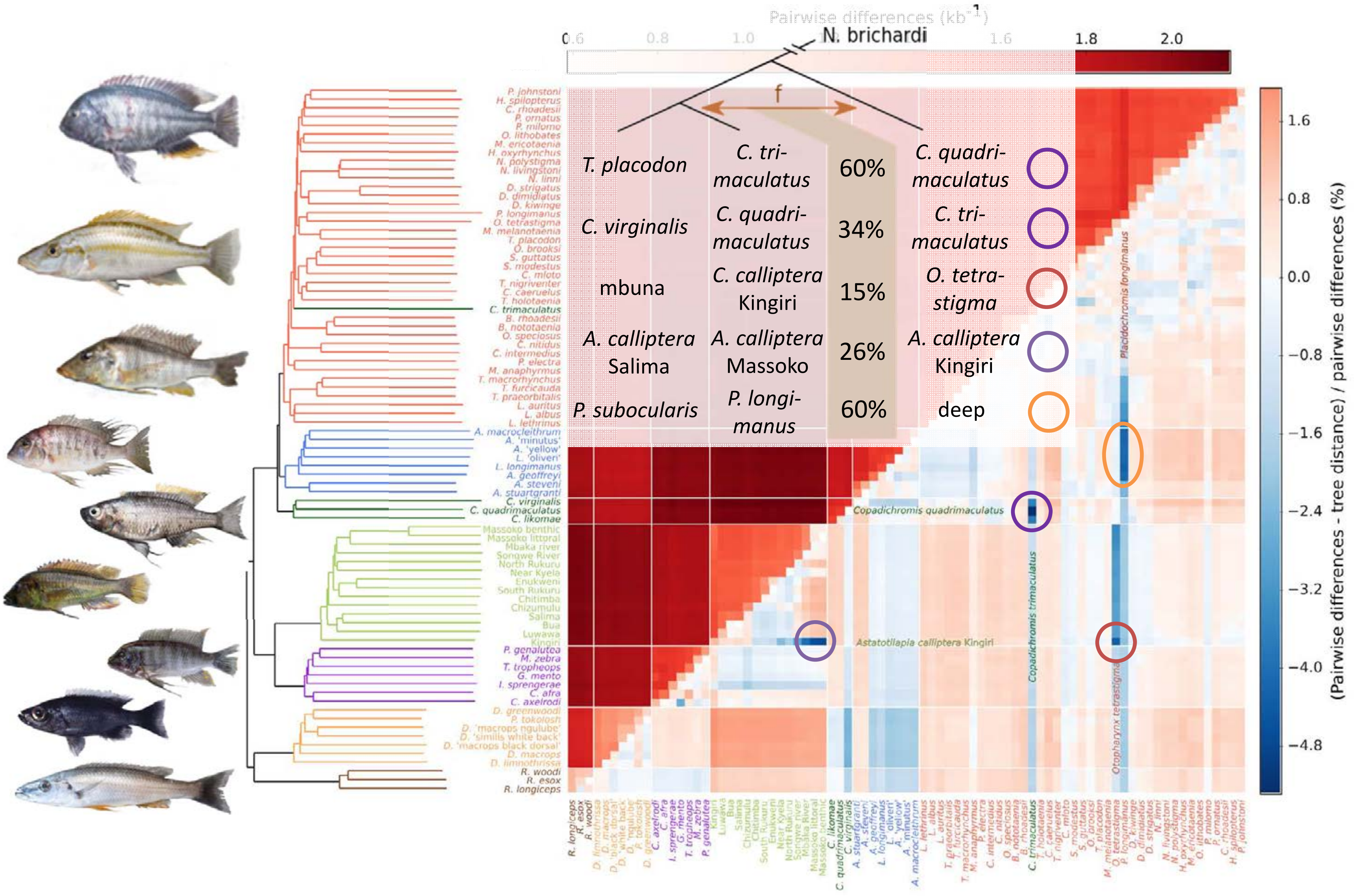


- A and B should be equally closely related to C
- However, if there was gene flow between B and C then B should be (a bit) more closely related to C than A is to C

$$S(A,B,C,O) = \sum_{loci} (\hat{p}_A - \hat{p}_B)(\hat{p}_C - \hat{p}_O)$$

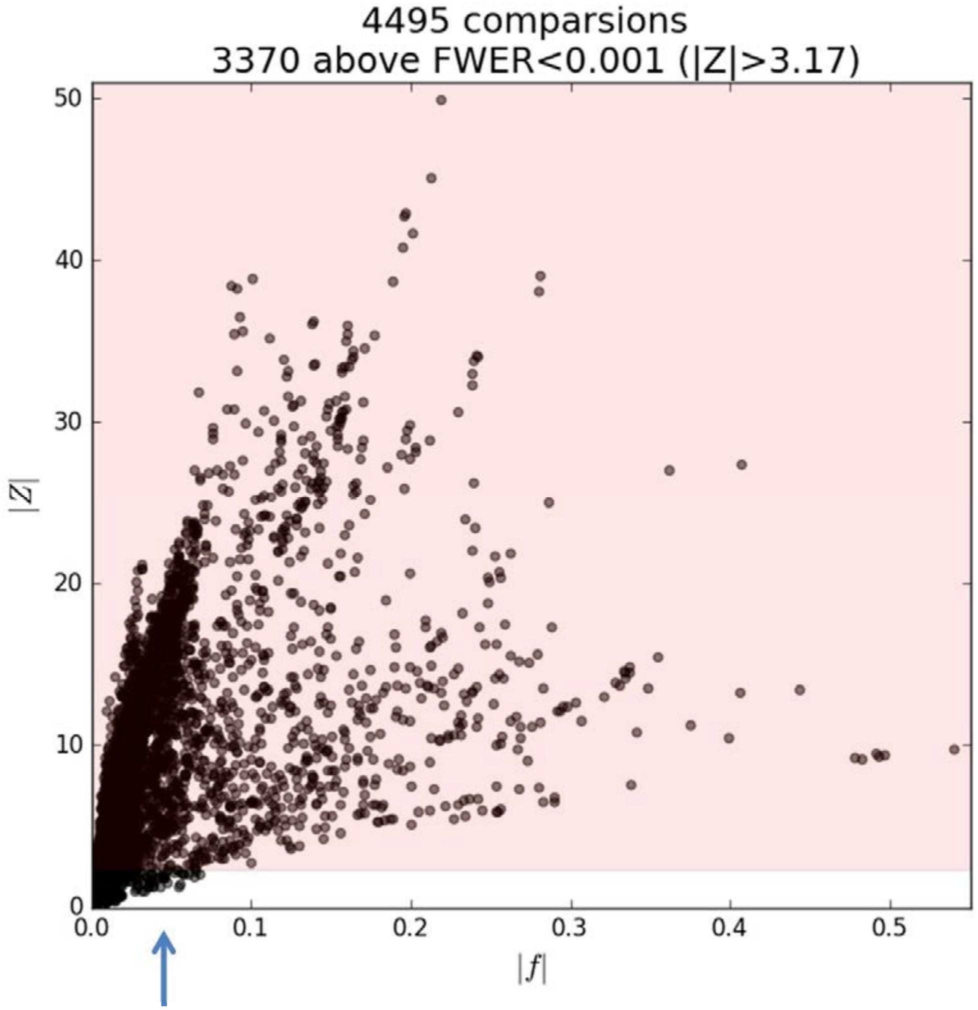
$$f = \frac{S(A,B,C,O)}{S(A,C_1,C_2,O)}$$

Relatedness not tree-like



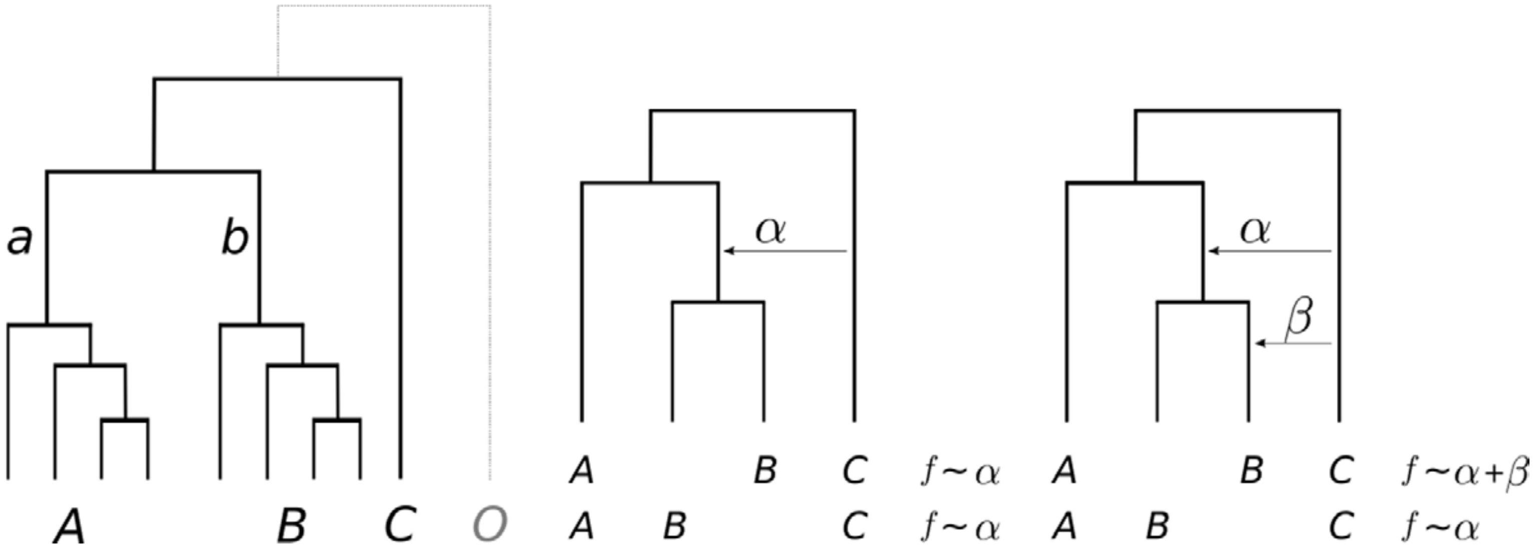
T. placodon	*C. trimaculatus*	60%	*C. quadrimaculatus*
C. virginalis	*C. quadrimaculatus*	34%	*C. trimaculatus*
mbuna	*C. calliptera* Kingiri	15%	*O. tetrastigma*
A. calliptera Salima	*A. calliptera* Massoko	26%	*A. calliptera* Kingiri
P. subocularis	*P. longimanus*	60%	deep

Many ABBA BABA tests are highly significant



human -- Neanderthal

ABBA-BABA tests not independent



Branch specific f-score f_b:

$$f_b(C) = median_A[min_B[f(A,B,C)]]$$

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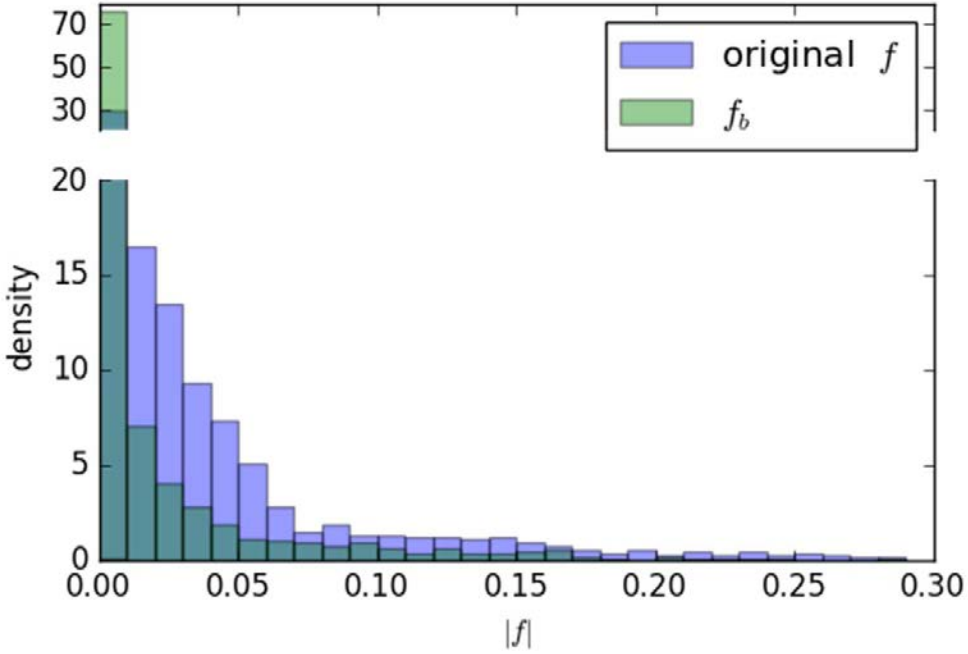
Branch specific f-score f_b



- Reduces the amount of tests
- Removes some of the correlation
- Allows to infer non-tree like relationships at internal and terminal branches.

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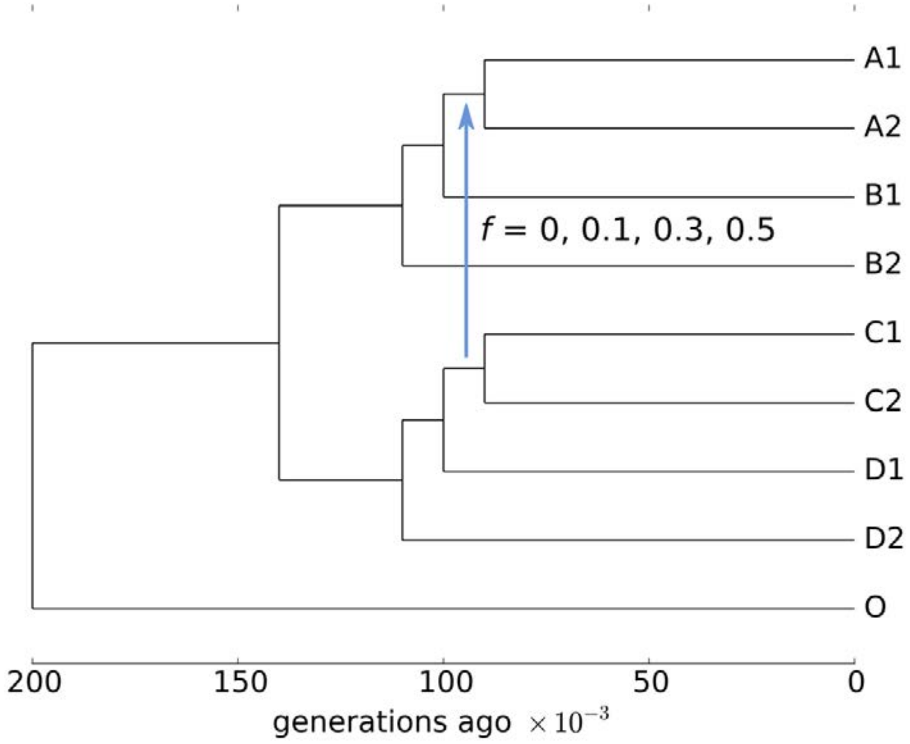
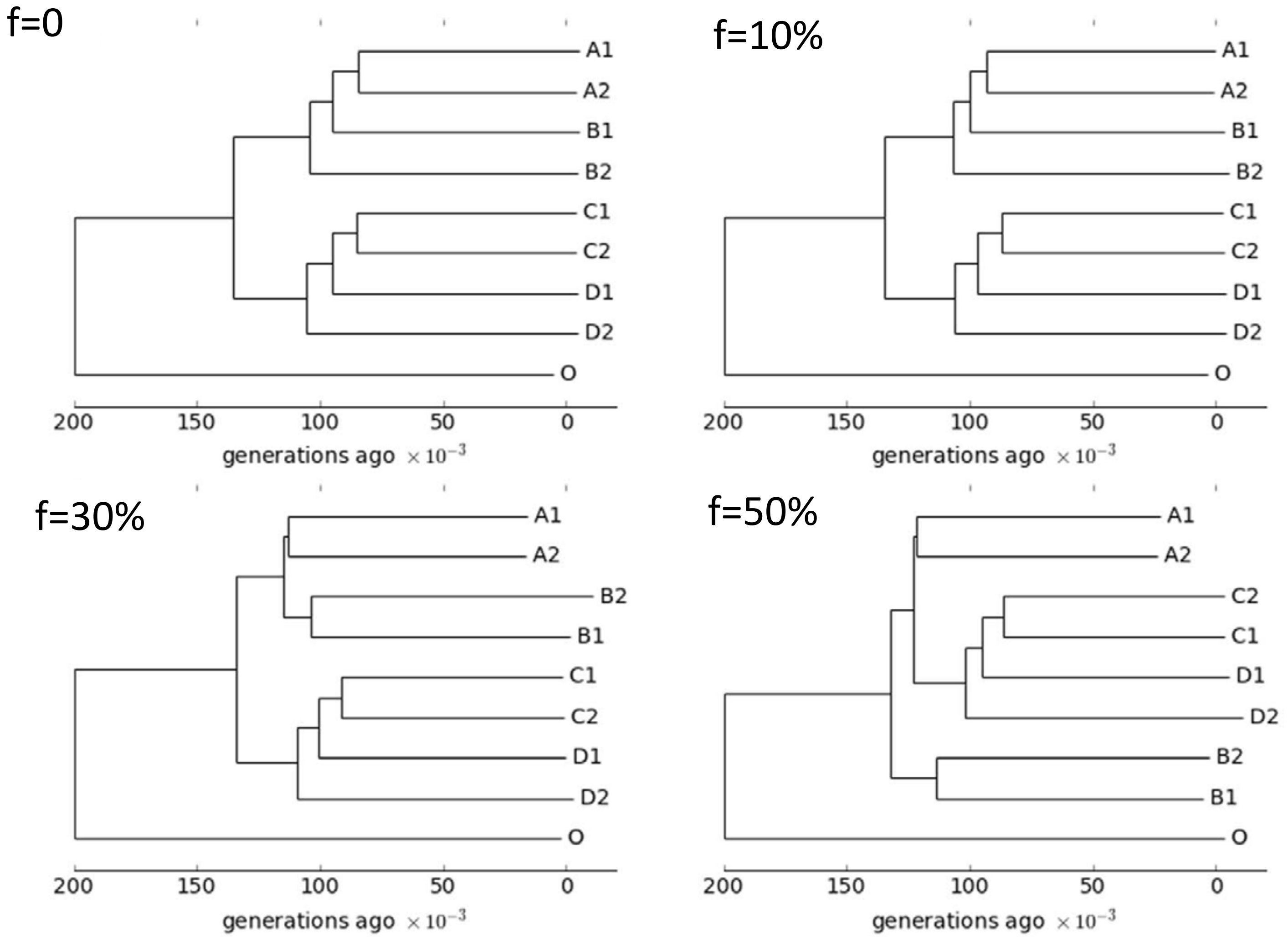
Test f_b with Simulations



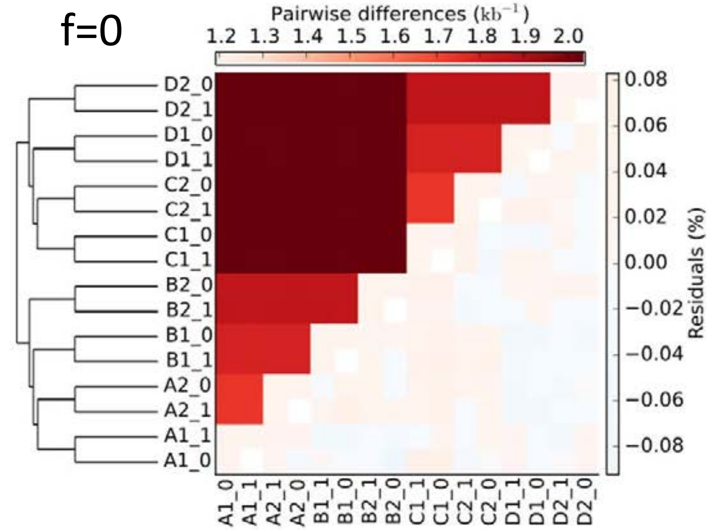
A1, A2, …, D2 ... 2 diploid individuals
outgroup O ... single diploid individual
Effective population size constant at 10^5.
Recombination rate $2*10^{-8}$, mutation rate $3*10^{-9}$.
120 independent stretches of $5*10^6$ bp (600 10^9 bp in total)

Inferred split trees

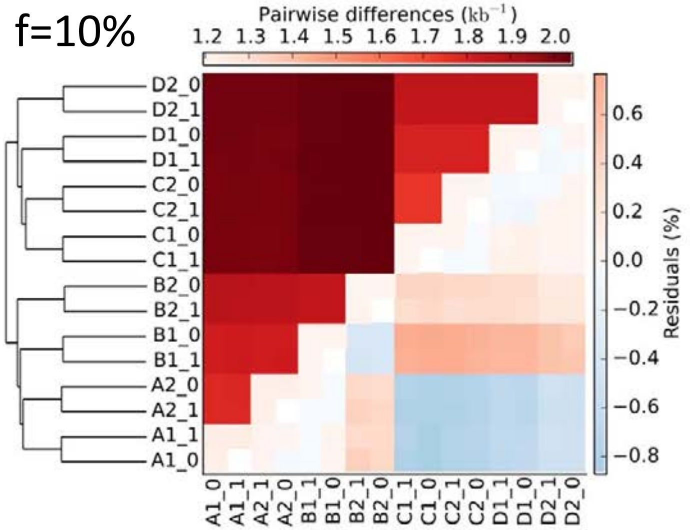


Pairwise differences and residuals

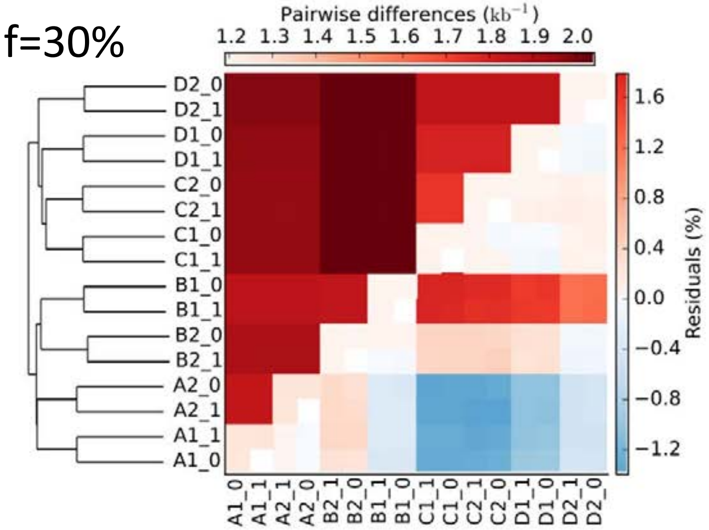
f=0



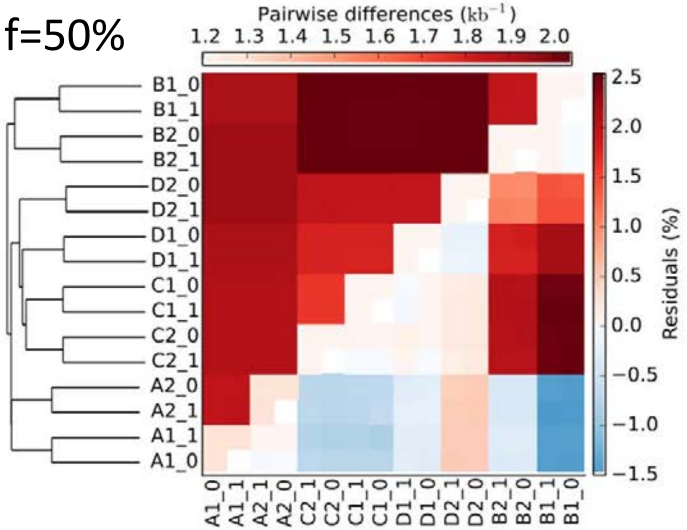
f=10%



f=30%

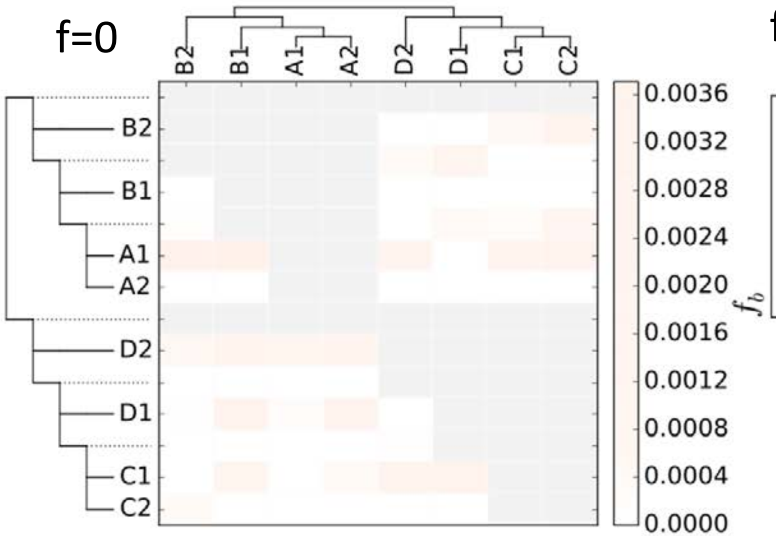


f=50%

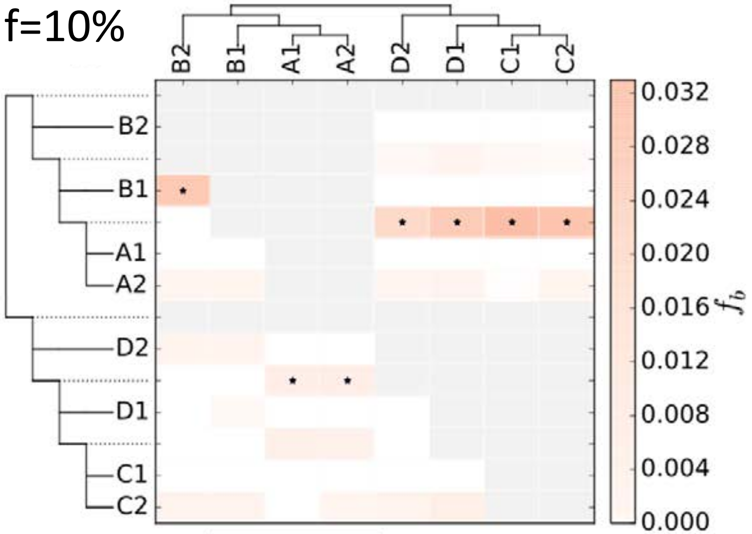


f-branch

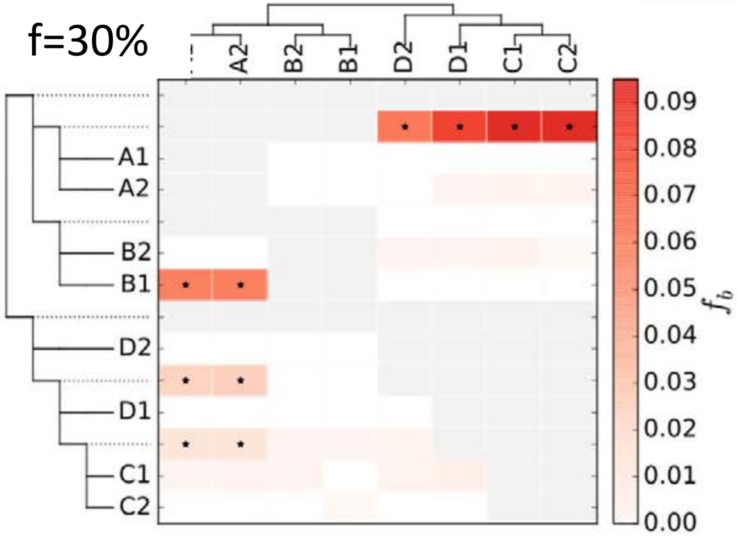
f=0



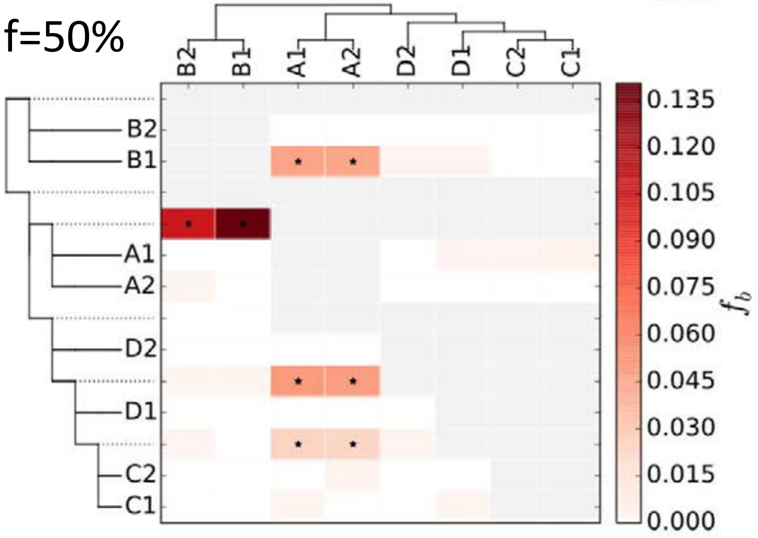
f=10%



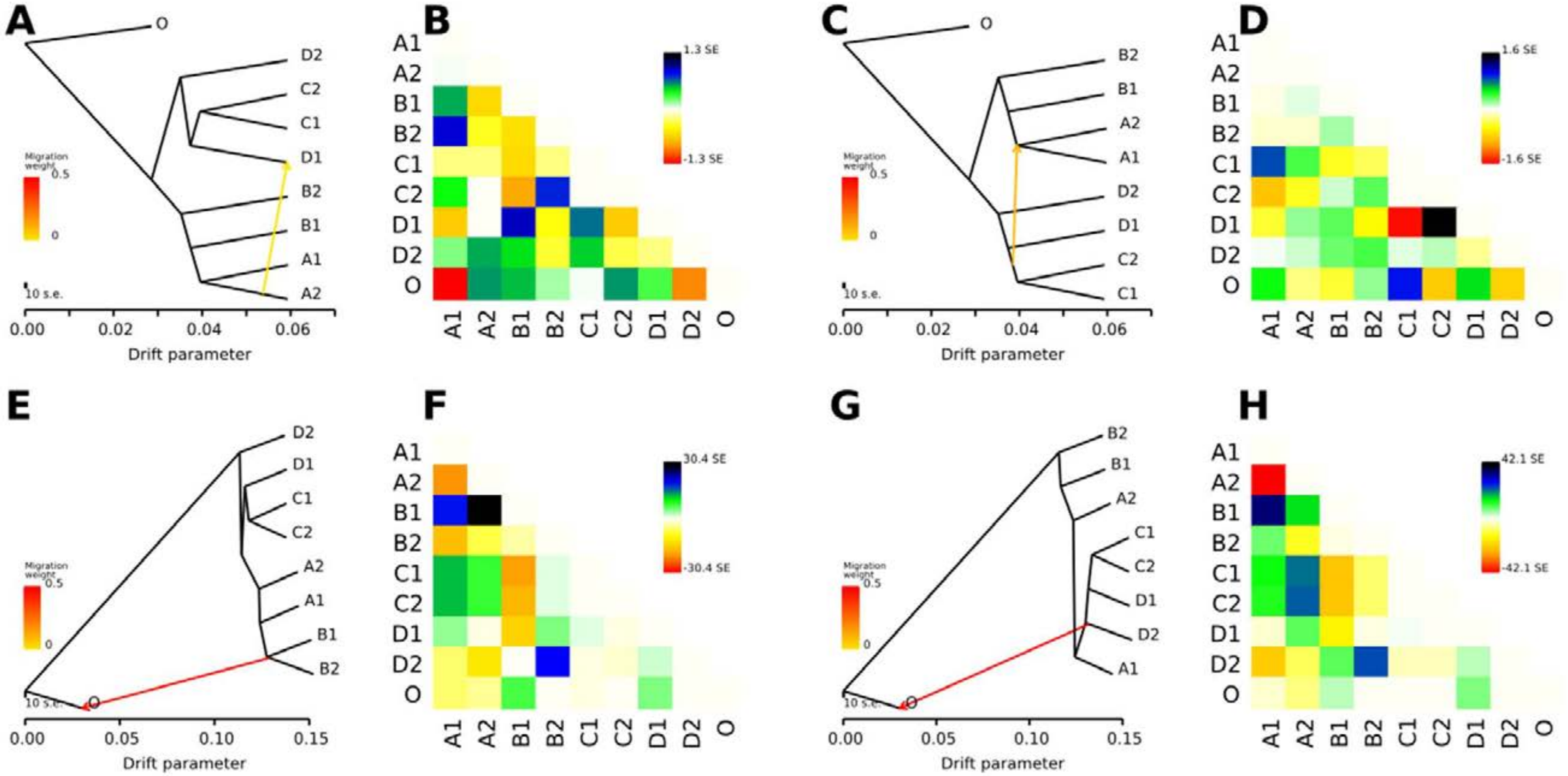
f=30%



f=50%

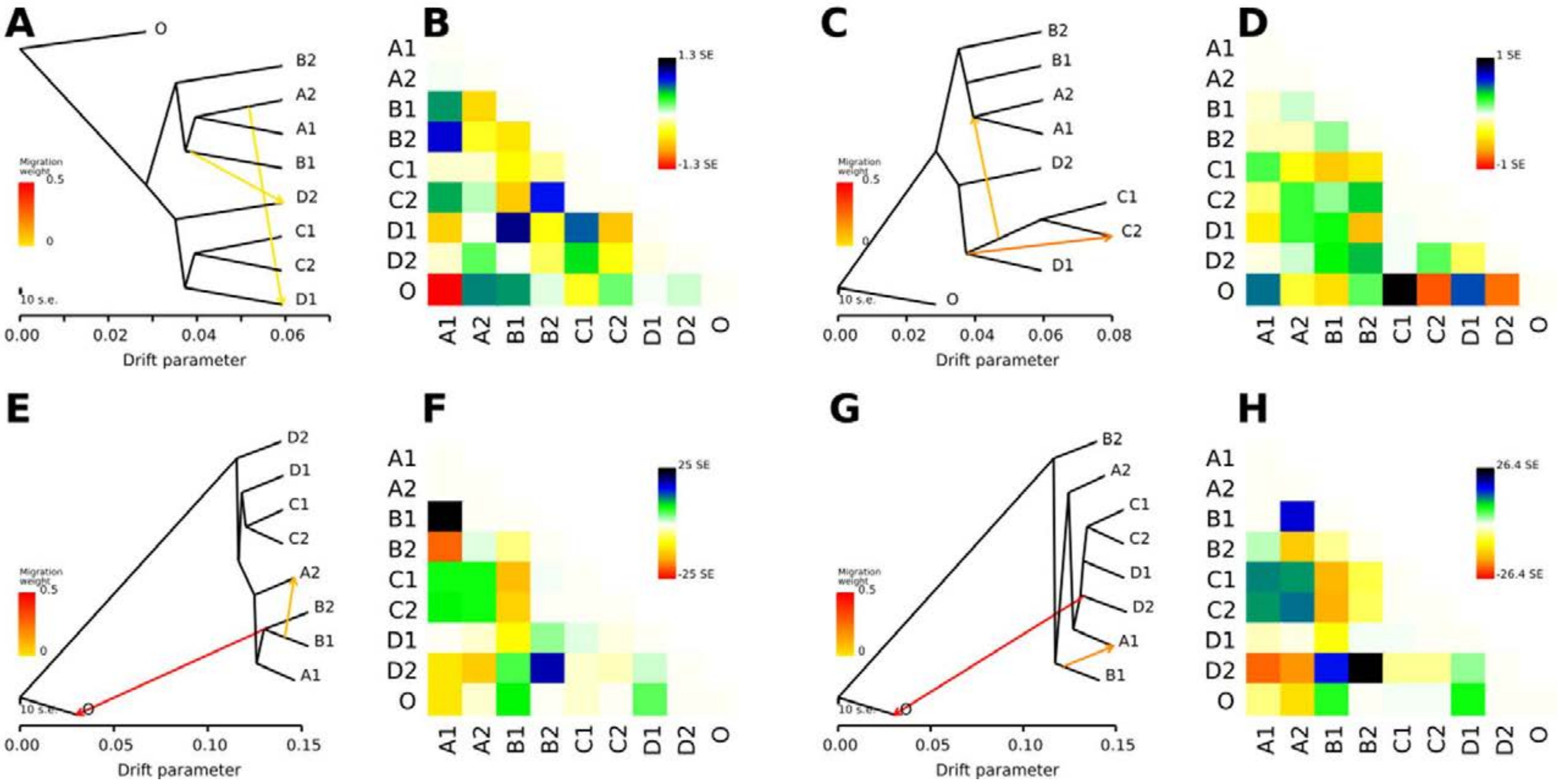


Comparison to treemix: m=1

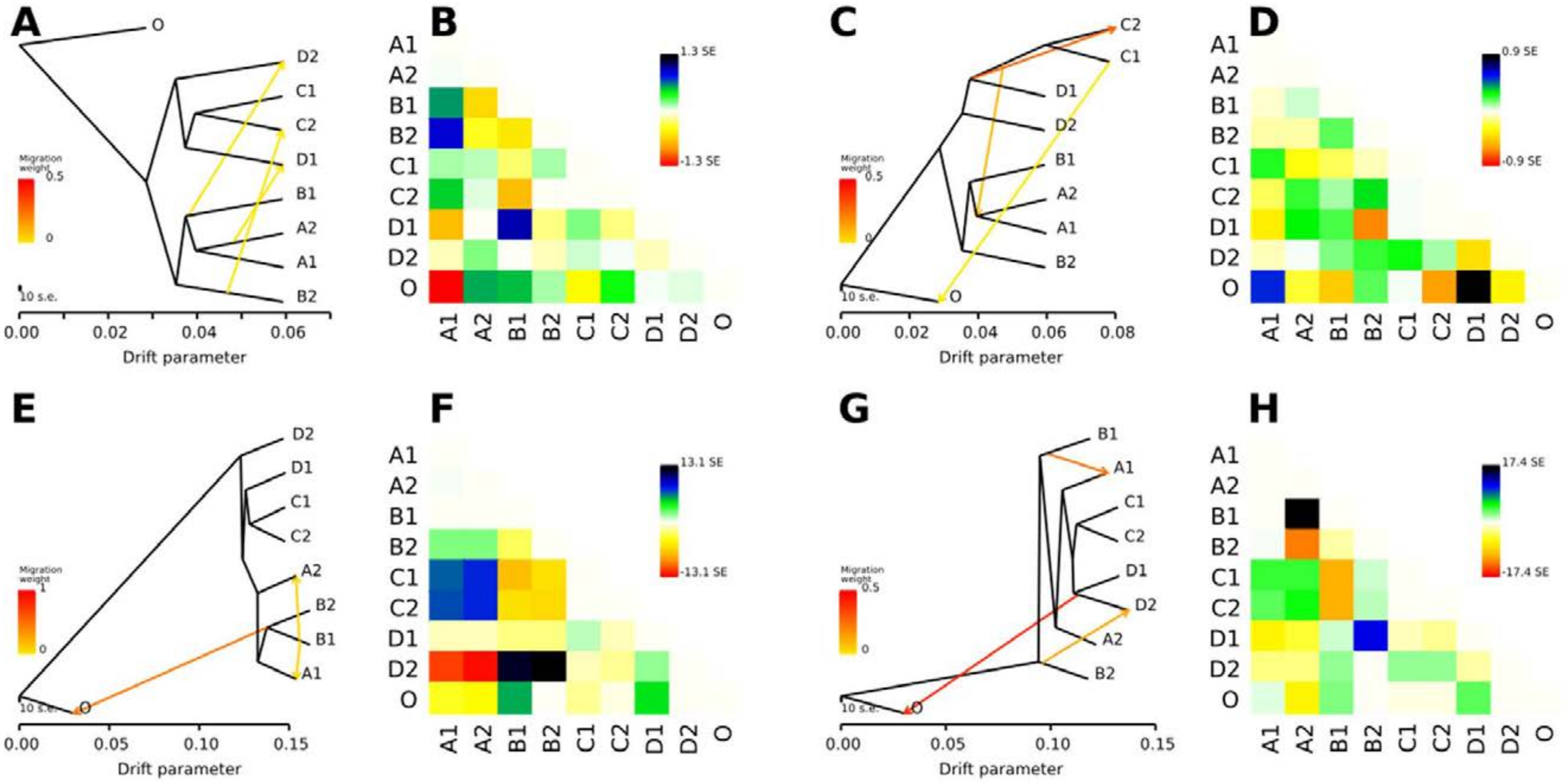


Pickrell and Pritchard 2012, PLOS Genetics

treemix m=2


A
O
B2
A2
A1
B1
D2
C1
C2
D1
Migration weight
0.5
0
10 s.e.
0.00
0.02
0.04
0.06
Drift parameter
B
A1
A2
B1
B2
C1
C2
D1
D2
O
1.3 SE
-1.3 SE
C
B2
B1
A2
A1
D2
C1
C2
D1
O
Migration weight
0.5
0
10 s.e.
0.00
0.02
0.04
0.06
0.08
Drift parameter
D
1 SE
-1 SE
E
D2
D1
C1
C2
A2
B2
B1
A1
O
Migration weight
0.5
0
10 s.e.
0.00
0.05
0.10
0.15
Drift parameter
F
25 SE
-25 SE
G
B2
A2
C1
C2
D1
D2
A1
B1
O
Migration weight
0.5
0
10 s.e.
0.00
0.05
0.10
0.15
Drift parameter
H
26.4 SE
-26.4 SE

treemix m=3


A
B
C
D
E
F
G
H
O
D2
C1
C2
D1
B1
A2
A1
B2
Migration weight
0.5
0
1
10 s.e.
Drift parameter
0.00
0.02
0.04
0.06
0.08
0.05
0.10
0.15
1.3 SE
-1.3 SE
0.9 SE
-0.9 SE
13.1 SE
-13.1 SE
17.4 SE
-17.4 SE

Conclusion simulations

- A single gene-flow event generally leads to multiple significant f_b
- f_b can identify problematic branches that are not consistent with tree like ancestry
- f_b scores have a biologically sensible interpretation even if the inferred tree is wrong
- treemix is sensitive to correct inference of the tree --> results not sensible in scenarios with strong gene flow

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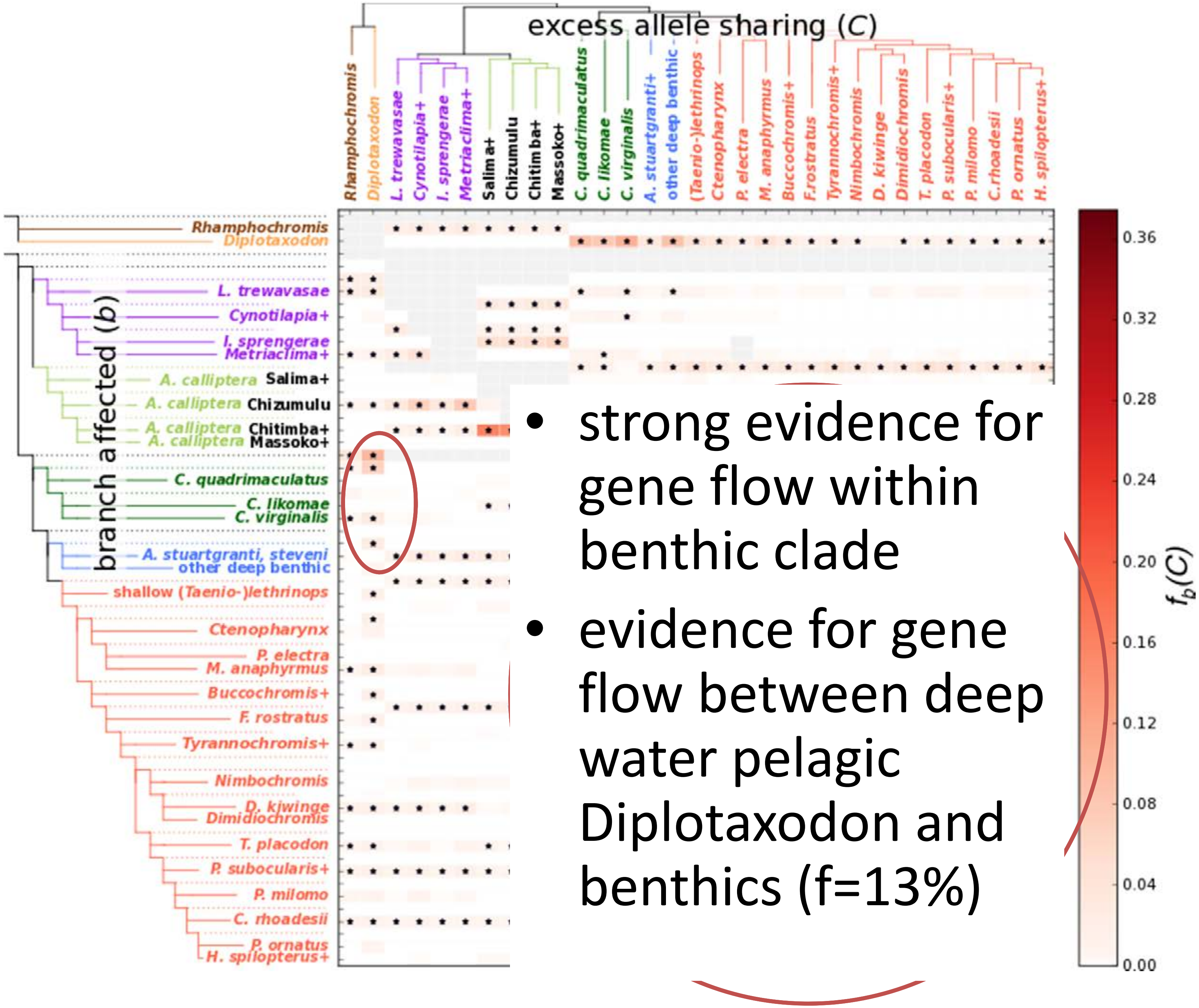
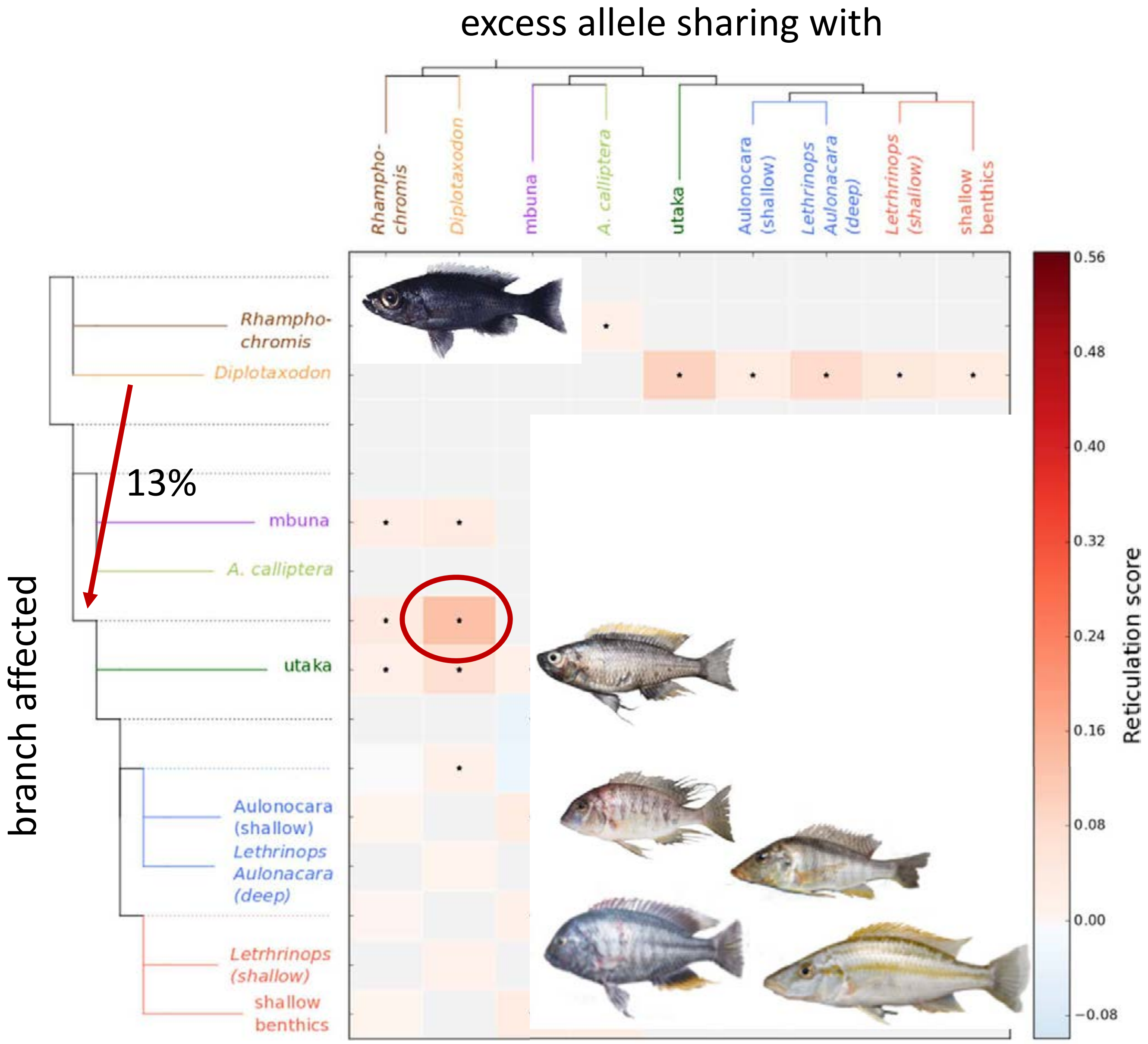
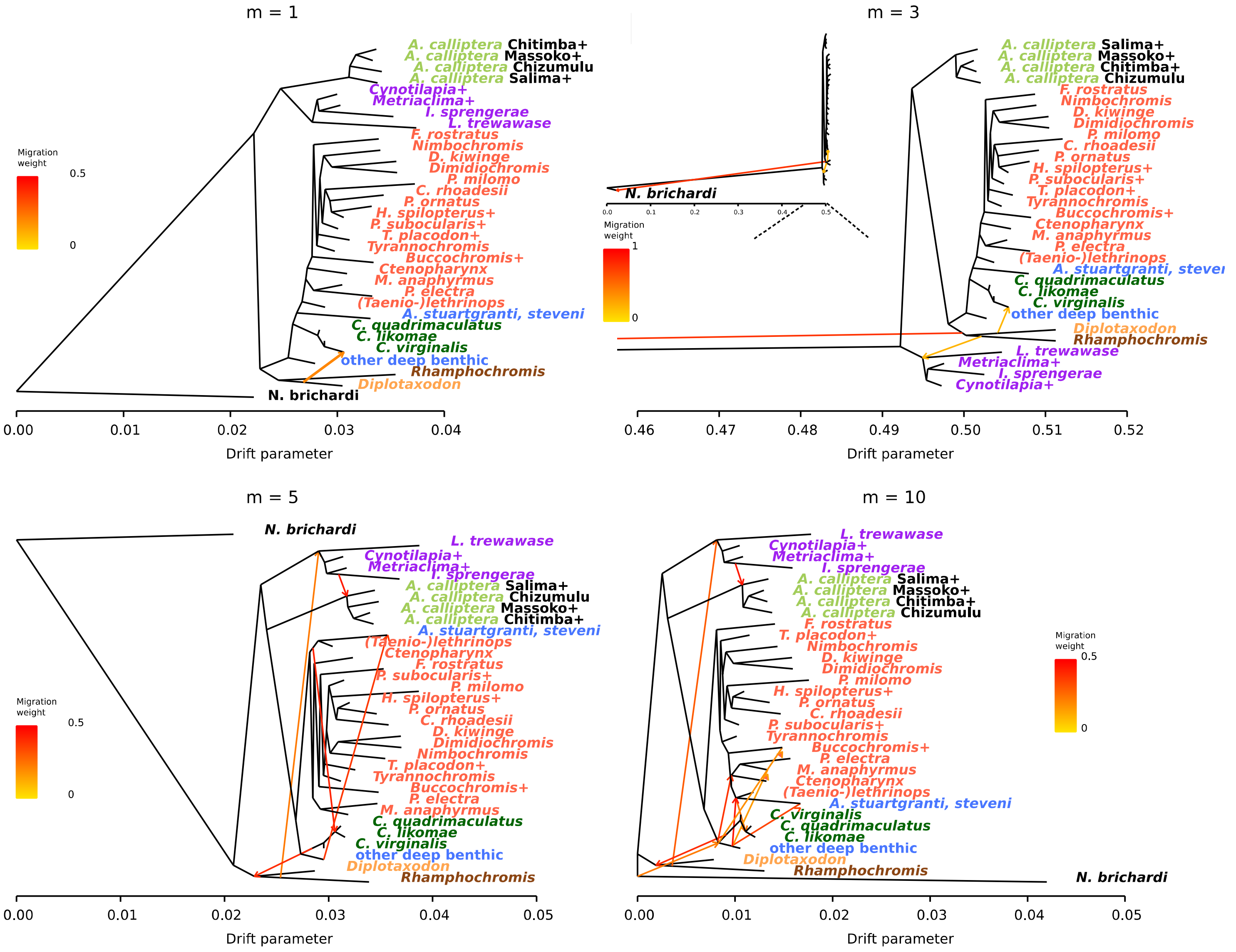


- strong evidence for gene flow within benthic clade
- evidence for gene flow between deep water pelagic Diplotaxodon and benthics (f=13%)

Diplotaxodon—benthics introgression



treemix on cichlid data



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SELECTION

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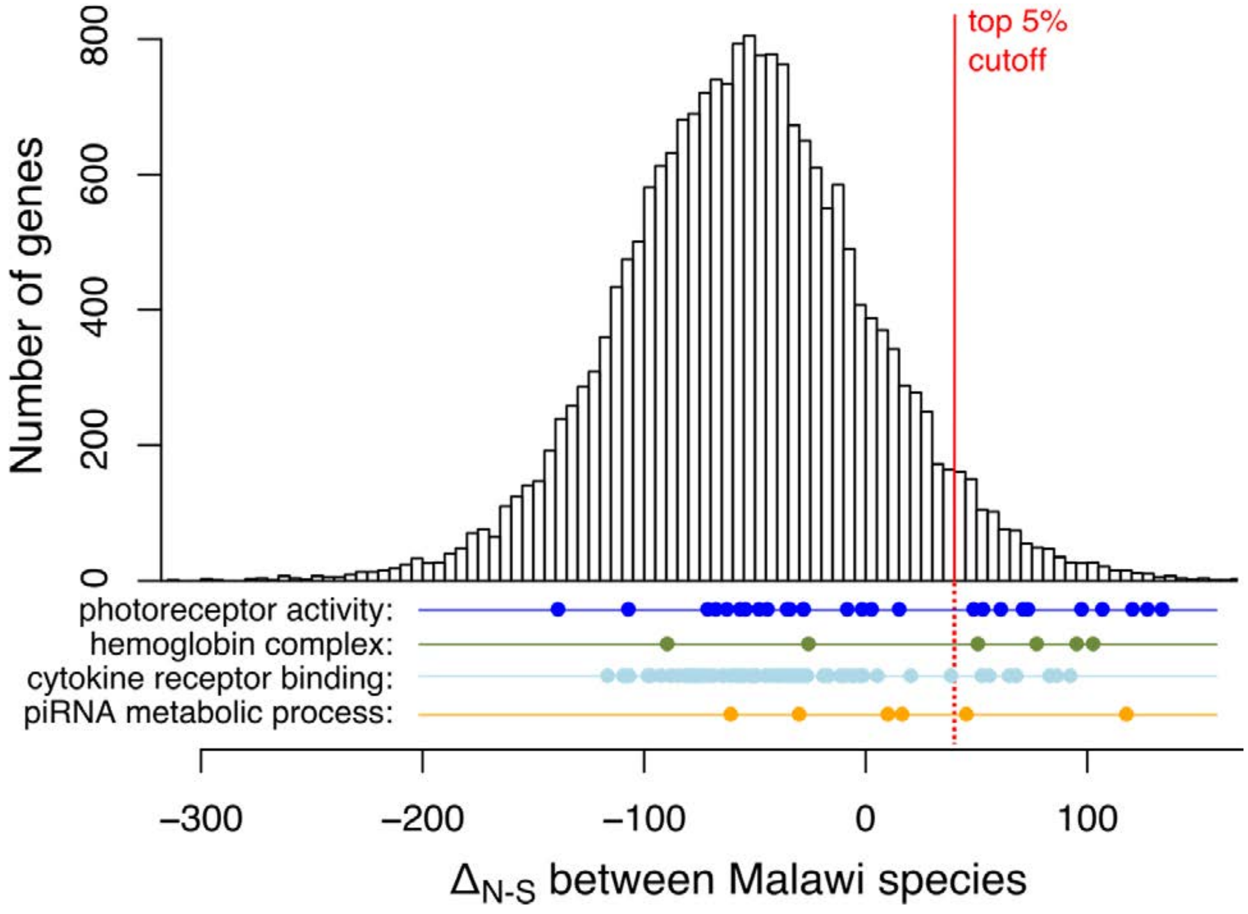
Nonsynonymous vs synonymous diversity



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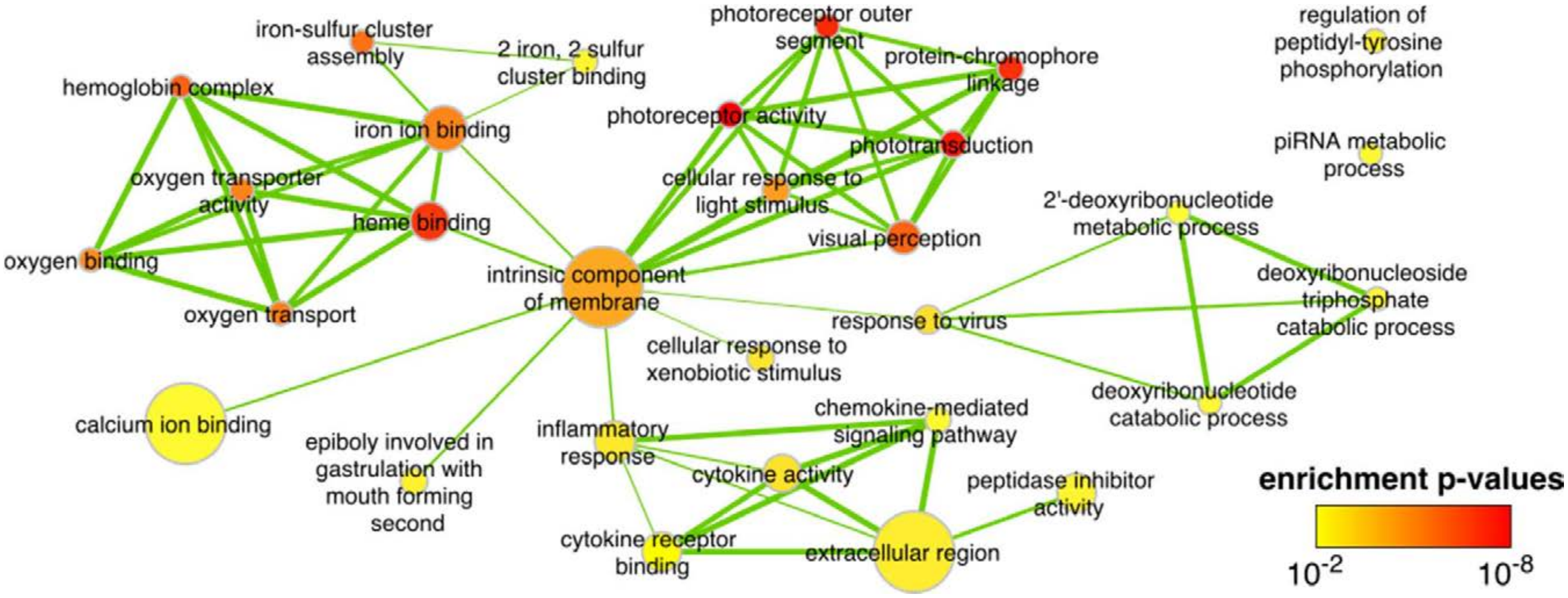
Visual system and oxygen transport pathways enriched for high selection scores



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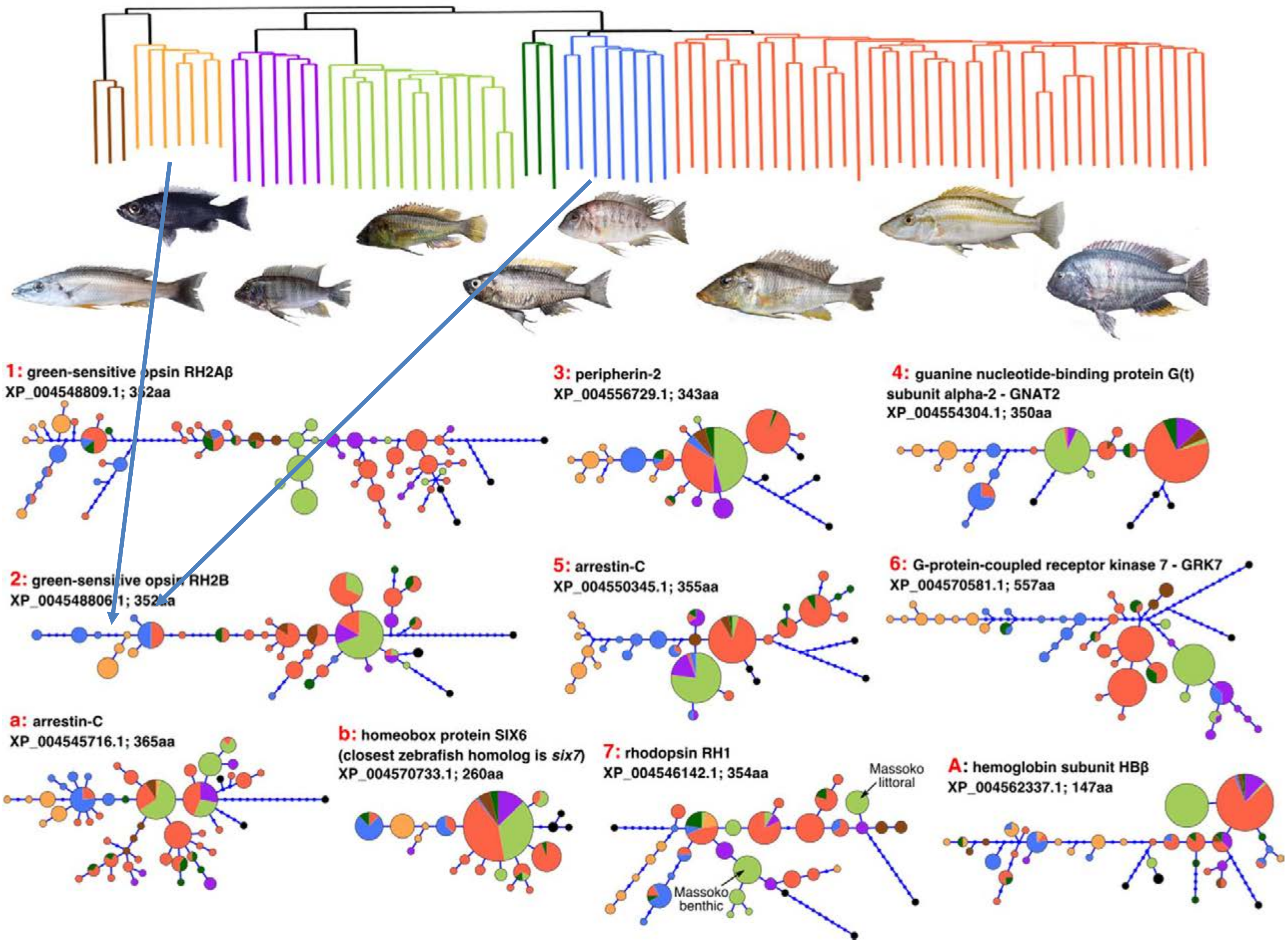
Haplotype networks of these genes show deep benthic – Diolotaxodon allele sharing



What is the mechanism behind deep benthic – Diolotaxodon allele sharing at these loci?

- Independent de-novo mutations?
- Selection on ancestral polymorphism?
- Adaptive introgression

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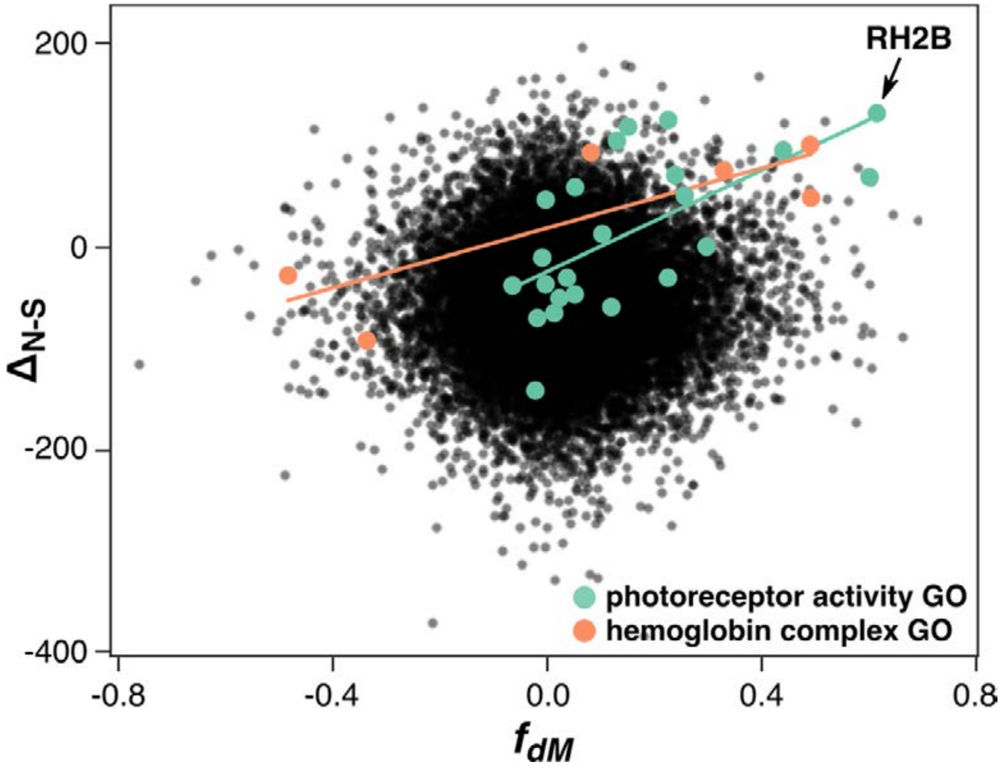
Elevated f-statistic for photoreceptor genes



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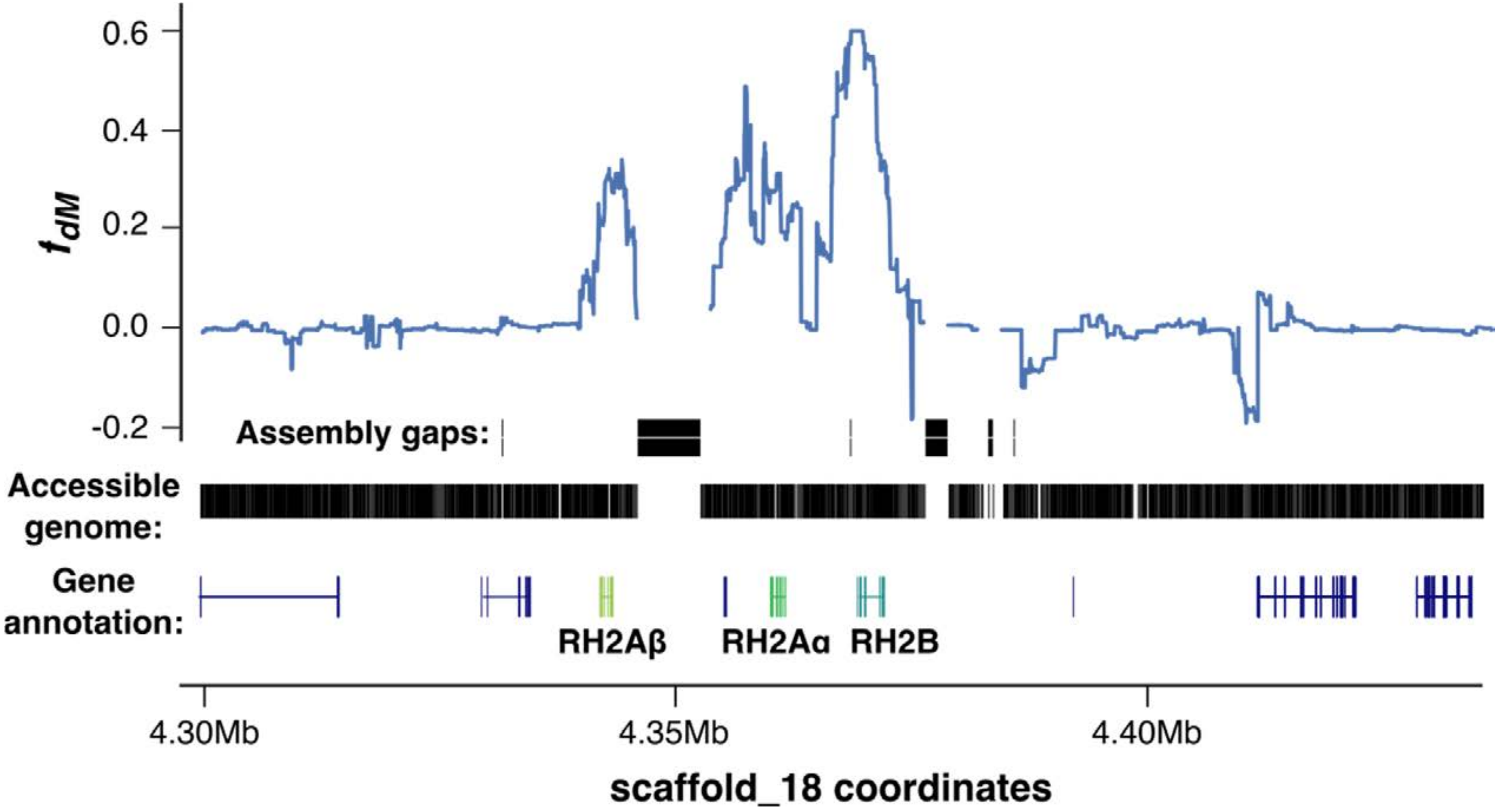
Some genes show long introgression haplotypes



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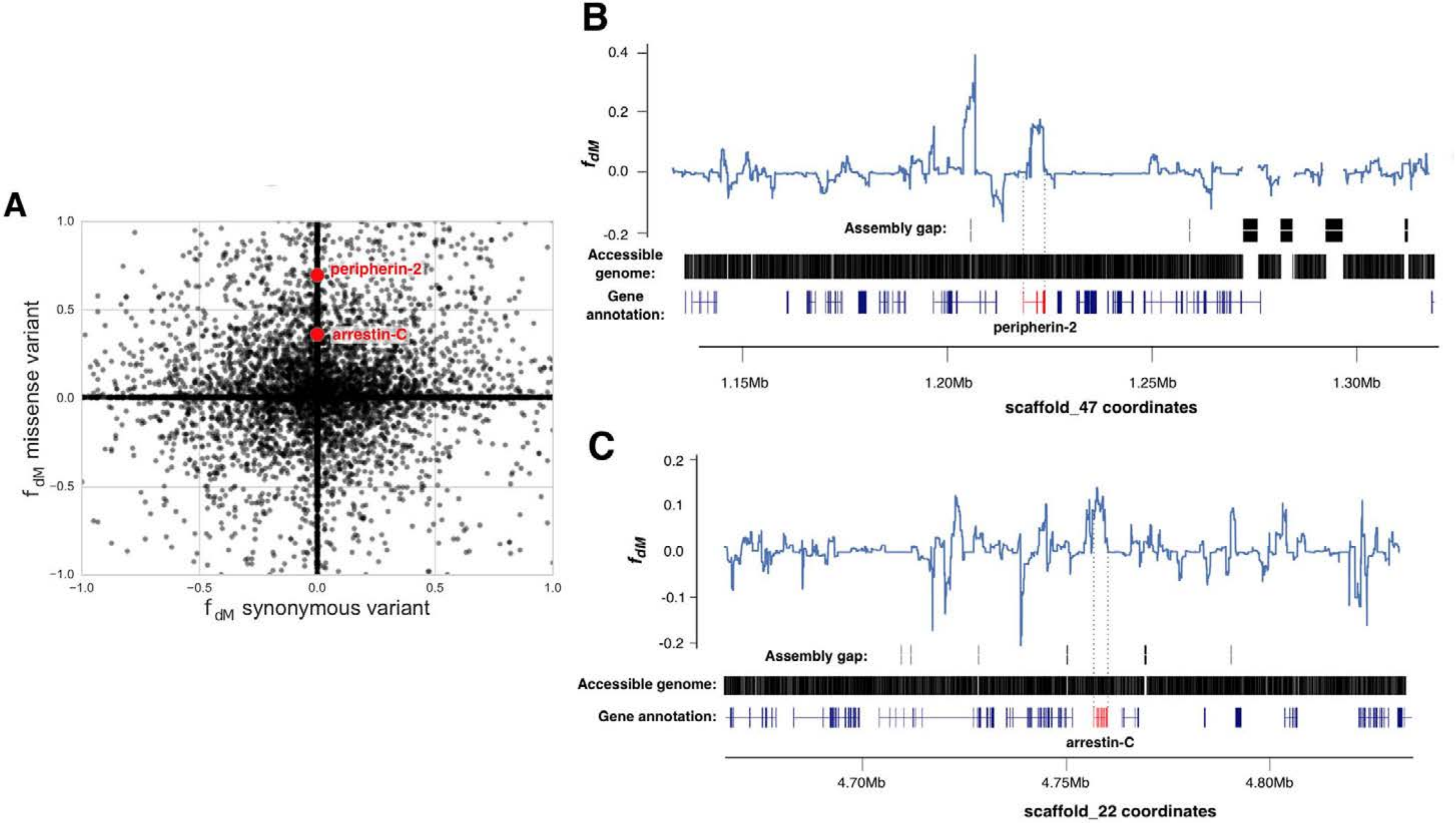
For others f is only elevated for non-synonymous variants



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Conclusion

- Developed branch specific f-statistic f_b
- Gene flow within and between major clades
- Evidence for selection on specific gene categories
- Excess allele sharing in ecologically relevant genes between two genetically distant groups sharing the same habitat (the deep)
- For some genes, the pattern is most consistent with adaptive introgression, for others with de-novo mutations or ancestral variation

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George Turner (Bangor)
Alexandra Tyers
Martin Genner (Bristol)

Data available at
cambridgecichlids.org

Preprint available soon.

Wellcome Trust Sanger Institute
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