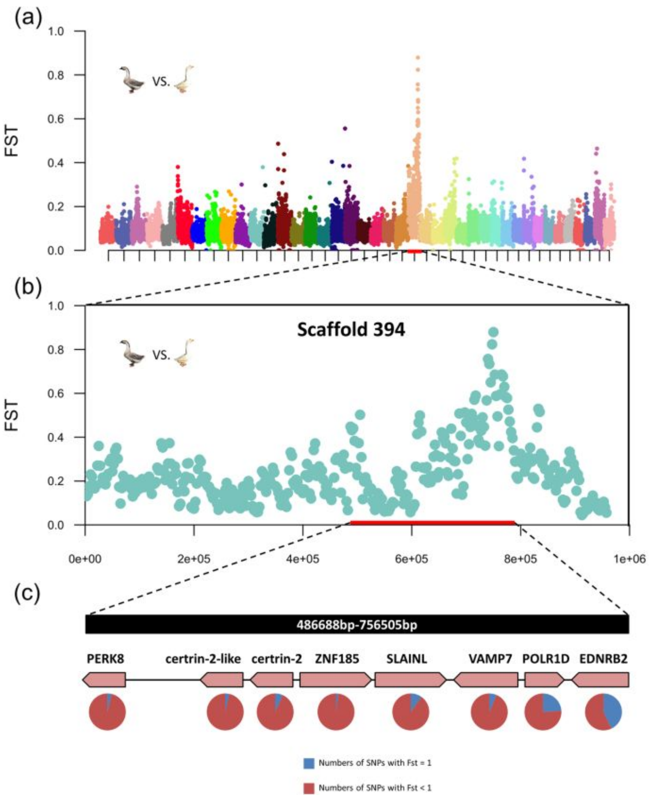
Detecting Selection Using Genomic Data: Methods and Characteristics

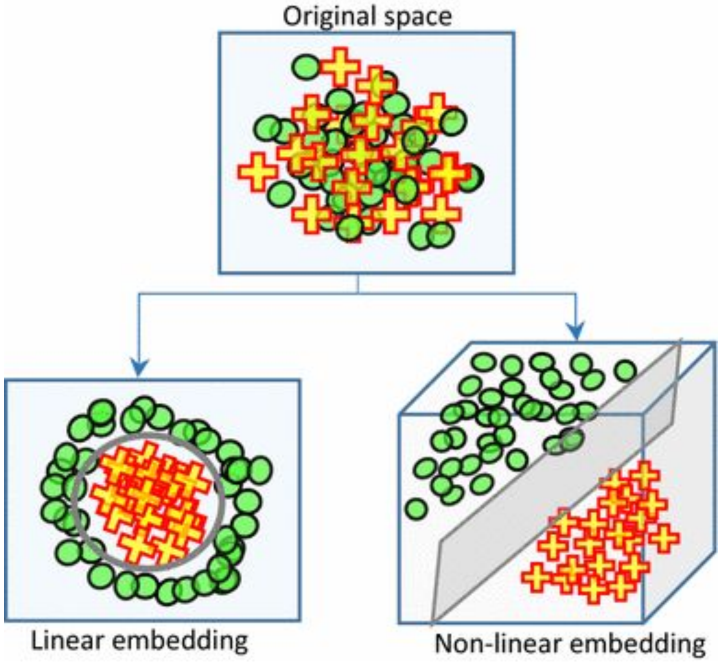
November 8, 2023

Fst statistics



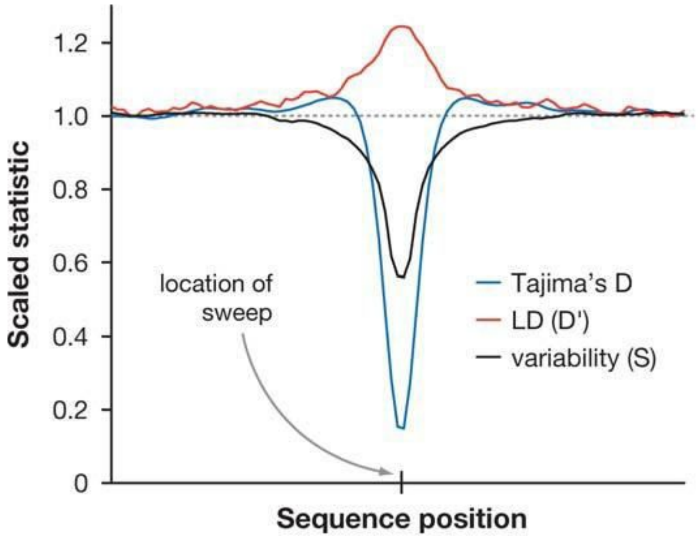
- **Ideal Situation:** Well-suited for studying populations with clear geographical or ecological boundaries.
- **Strengths:** Provides a straightforward measure of genetic differentiation between populations. Robust and widely applicable.
- **Weaknesses:** Sensitive to marker choice, may miss subtle population structure nuances.

Spatial FST (SFS)



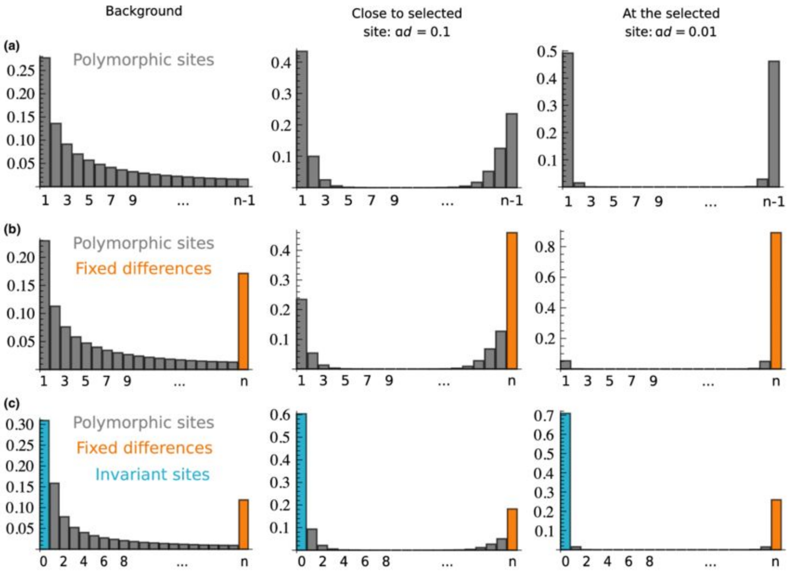
- **Ideal Situation:** Investigating the geographical patterns of genetic variation in a species with known migration corridors or barriers, such as a river or mountain range.
- **Strengths:** Incorporates geographical information, providing insights into spatial patterns of genetic differentiation.
- **Weaknesses:** Sensitivity to the choice of the kernel and potential bias introduced by uneven sampling across space.

Tajima's D



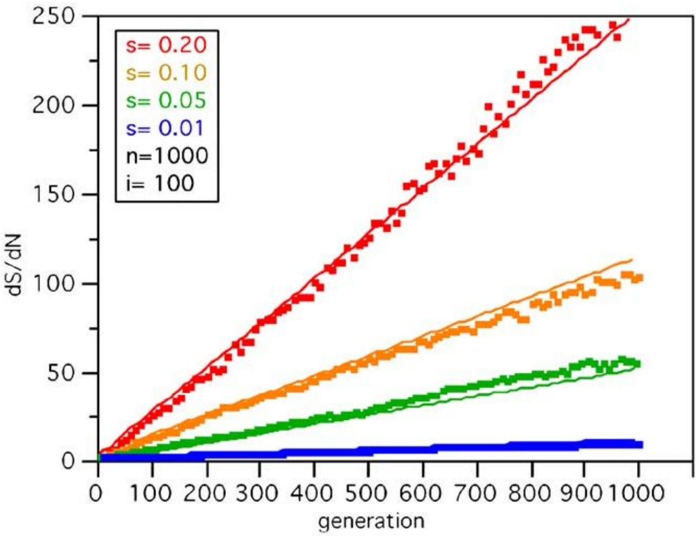
- **Ideal Situation:** Assessing signatures of natural selection in a population with a recent demographic change, like a population recovering from a bottleneck.
- **Strengths:** Sensitive to selection and demographic events, provides information about the frequency spectrum of mutations.
- **Weaknesses:** Susceptible to population structure and demographic history effects.

Site Frequency Spectrum (SFS)



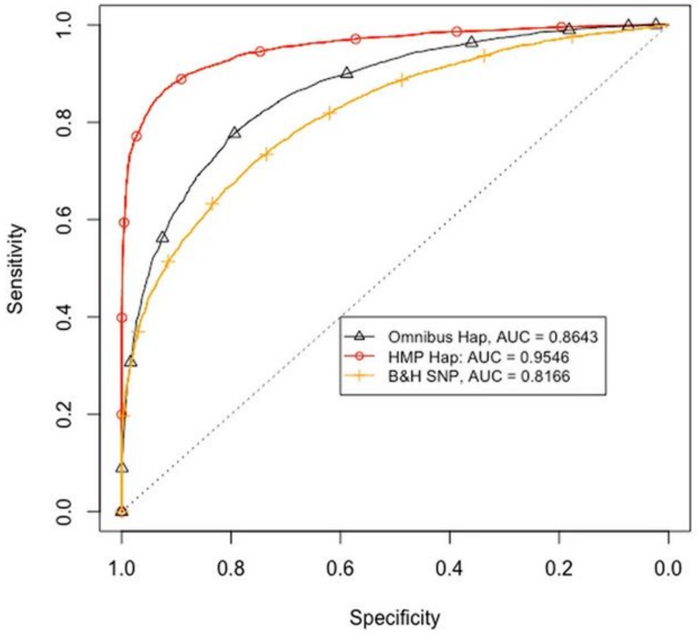
- **Ideal Situation:** Analyzing a population with a known demographic history, such as recent expansion or contraction, to understand the impact on allele frequencies.
- **Strengths:** Directly examines allele frequency distributions, useful for detecting demographic changes.
- **Weaknesses:** May not distinguish between different evolutionary processes affecting allele frequencies.

dN/dS Ratio



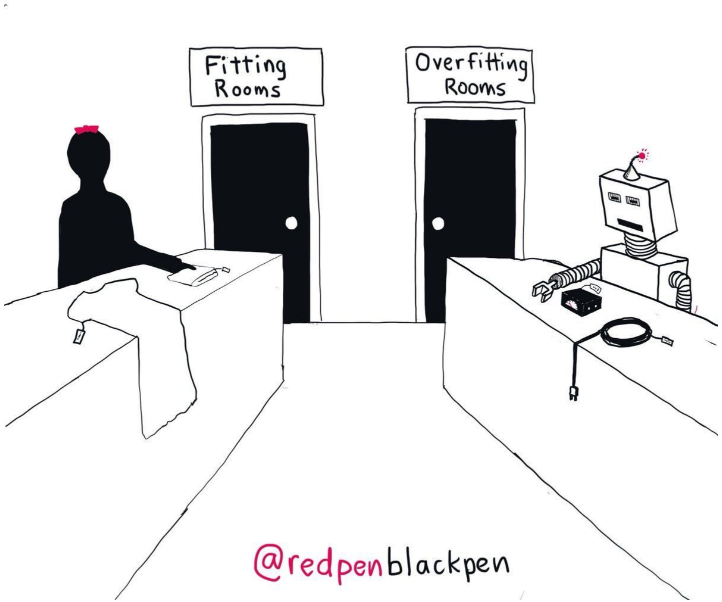
- **Ideal Situation:** Investigating positive selection on protein-coding genes in a population facing strong selective pressures, such as a pathogen-host arms race.
- **Strengths:** Focuses on protein-coding genes, highlighting signatures of positive selection.
- **Weaknesses:** Relies on accurate gene annotation and assumptions about synonymous mutations.

Haplotype-based Tests



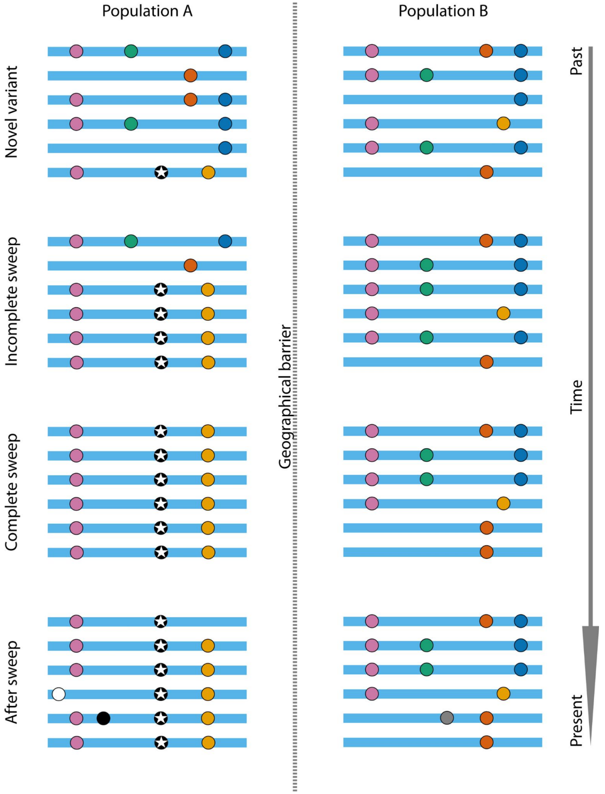
- **Ideal Situation:** Exploring patterns of selection in regions with complex haplotype structures, like genomic regions associated with disease resistance.
- **Strengths:** Captures information on linkage disequilibrium and haplotype structure.
- **Weaknesses:** Sensitive to recombination rates and complex demographic scenarios.

Machine learning based approaches



- **Ideal Situation:** Employing machine learning techniques like neural networks to recognize subtle patterns indicative of positive selection in genomic sequences, especially in non-coding regions.
- **Strengths:** Can capture intricate patterns and dependencies in data. Suitable for high-dimensional and non-linear relationships.
- **Weaknesses:** Requires substantial computational resources and large training datasets. Interpretability may be challenging.

Selective Sweep Analysis



- **Ideal Situation:** Detecting selective sweeps in a population exposed to a sudden environmental change, such as a change in climate or the introduction of a new predator.
- **Strengths:** Detects regions where selected alleles rapidly rise in frequency.
- **Weaknesses:** May miss soft sweeps and is sensitive to demographic history and recombination rates.

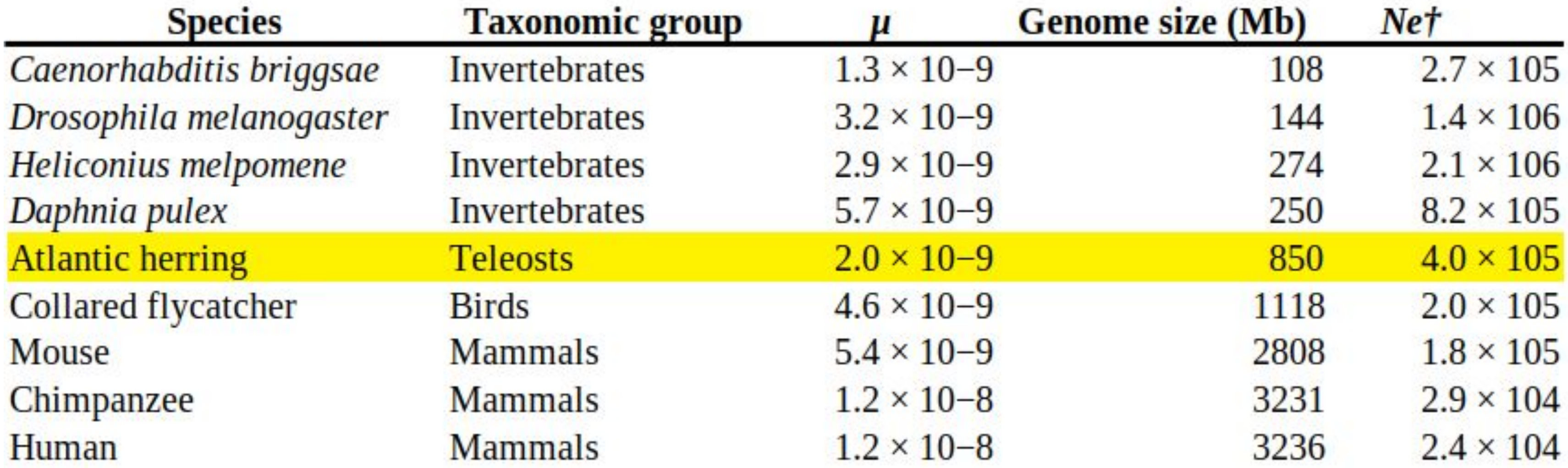
Detecting signatures of selection in Atlantic herring using whole genome sequencing

Photo Per Eide

http://sointularipple.ca

- A near ideal population structure
- huge population size (census population size about 10^{12})
- random mating
- high fecundity
- natural selection very effective
- genetic drift at selectively neutral loci is minute

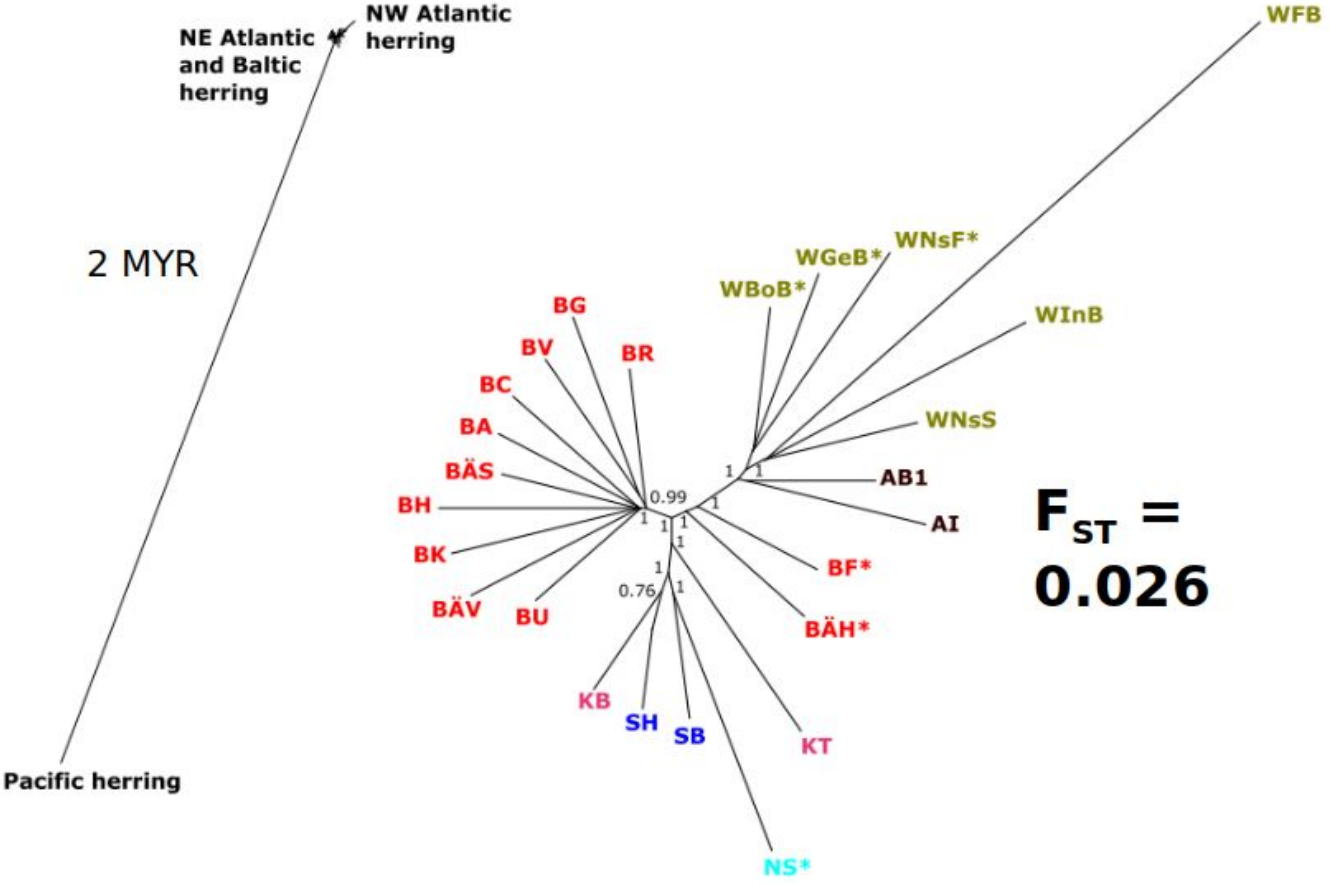
The herring has a very low mutation rate



Species	Taxonomic group	*μ*	Genome size (Mb)	*Ne†*
Caenorhabditis briggsae	Invertebrates	1.3 × 10−9	108	2.7 × 105
Drosophila melanogaster	Invertebrates	3.2 × 10−9	144	1.4 × 106
Heliconius melpomene	Invertebrates	2.9 × 10−9	274	2.1 × 106
Daphnia pulex	Invertebrates	5.7 × 10−9	250	8.2 × 105
Atlantic herring	Teleosts	2.0 × 10−9	850	4.0 × 105
Collared flycatcher	Birds	4.6 × 10−9	1118	2.0 × 105
Mouse	Mammals	5.4 × 10−9	2808	1.8 × 105
Chimpanzee	Mammals	1.2 × 10−8	3231	2.9 × 104
Human	Mammals	1.2 × 10−8	3236	2.4 × 104

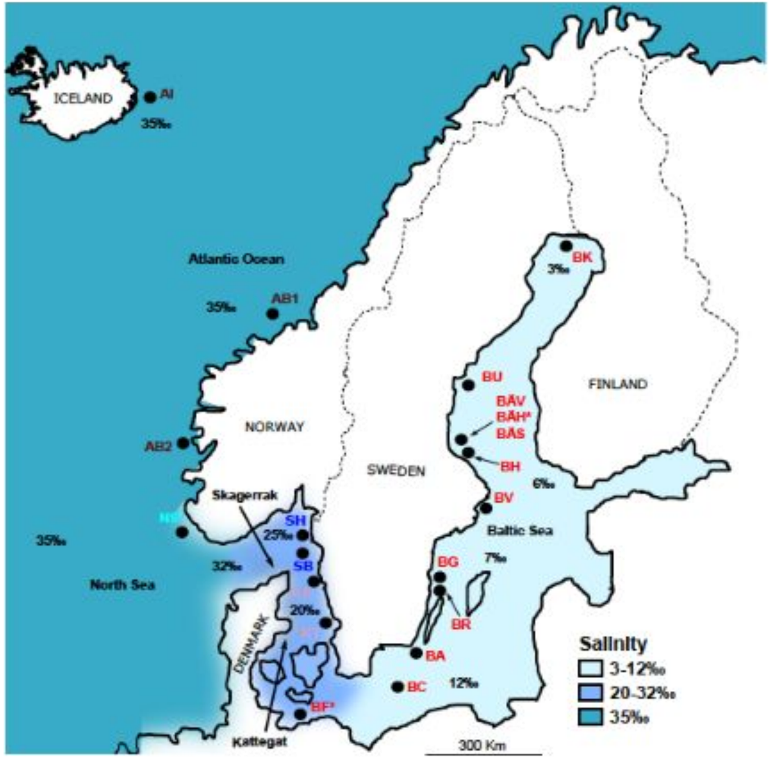
….but in each generation **each** nucleotide site mutates thousands of times!

Phylogenetic analysis



F_{ST} = 0.026

A genetic screen for loci underlying adaptation to the Baltic Sea vs. Atlantic Ocean



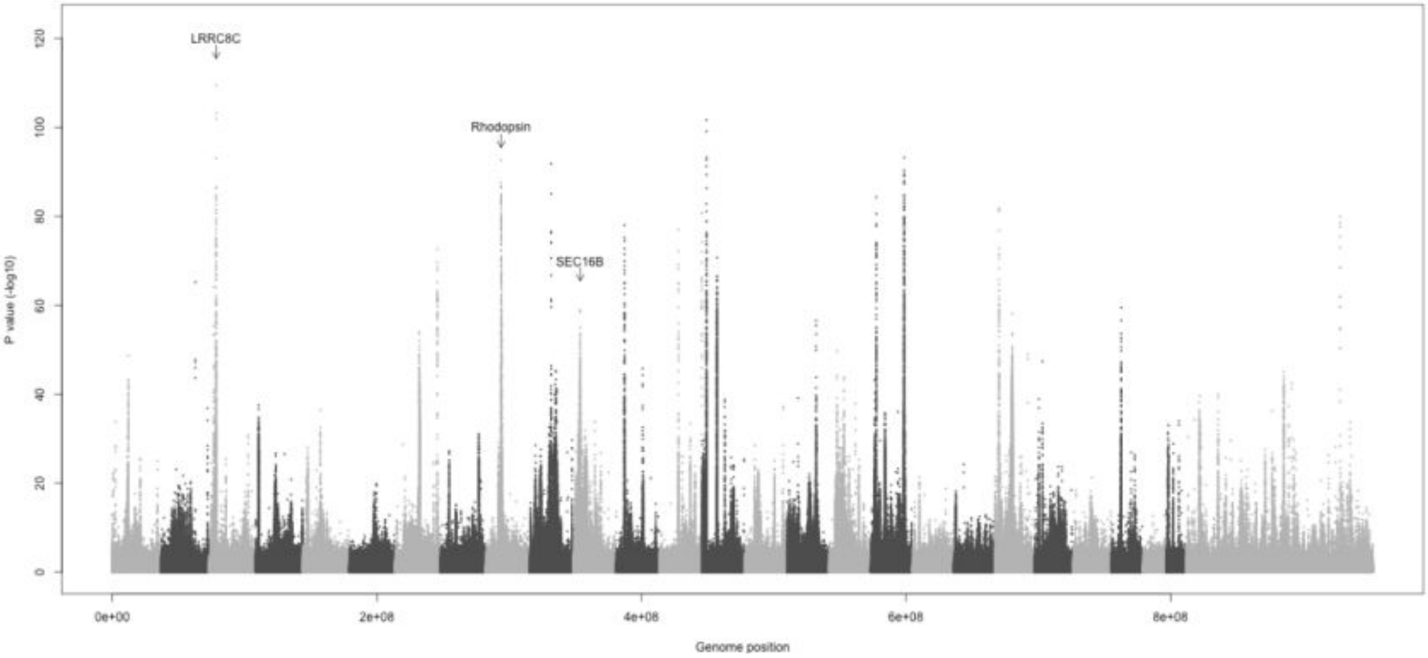
<u>Pool Atlantic</u>: All samples from Skagerrak, Kattegat, North Sea and Atlantic Ocean

<u>Pool Baltic</u>: All samples from the Baltic Sea

Compare allele frequencies between the two pools SNP by SNP

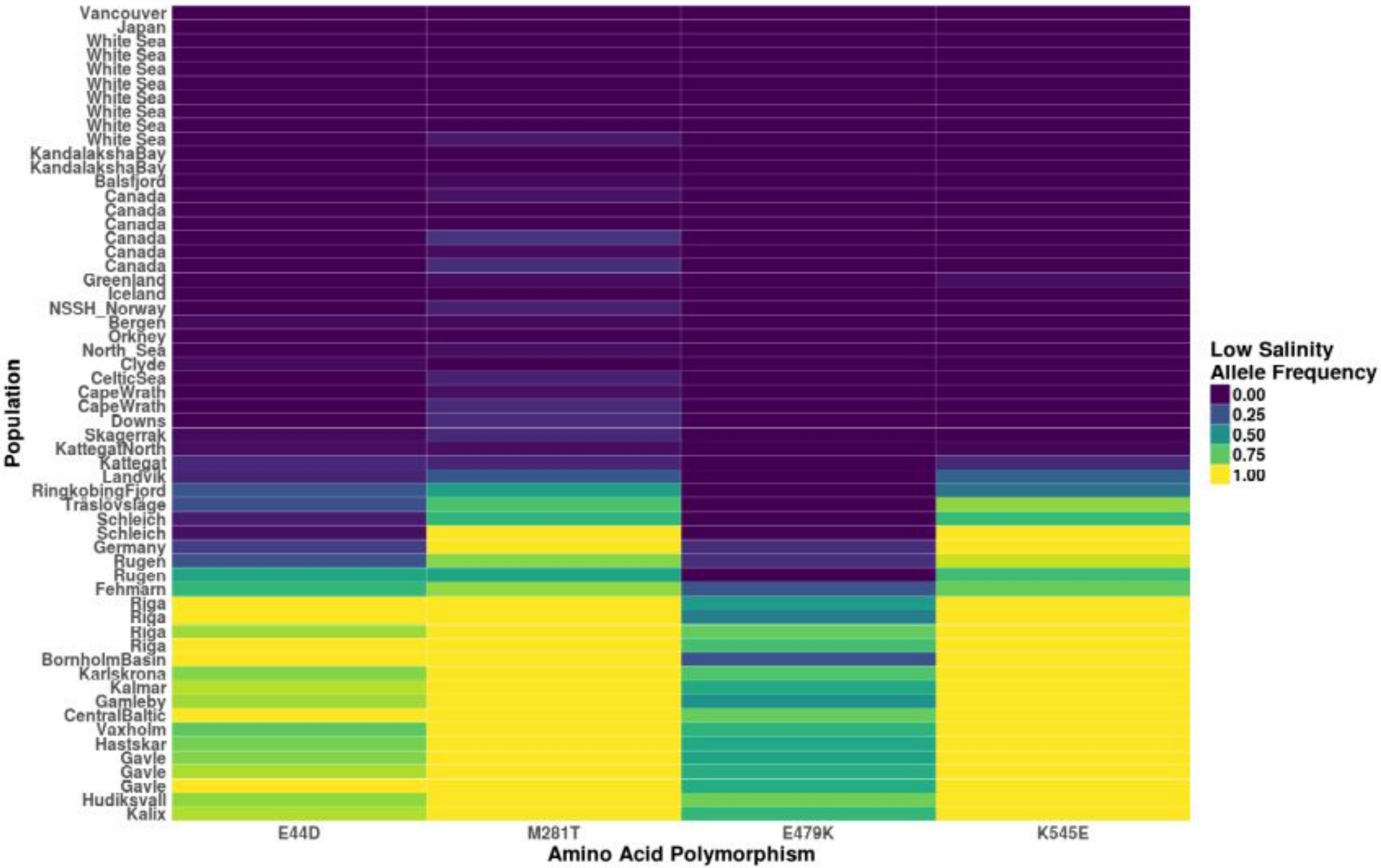
How polygenic is ecological adaptation in a species with a huge breeding population?

Genome-wide association analysis
Atlantic versus Baltic

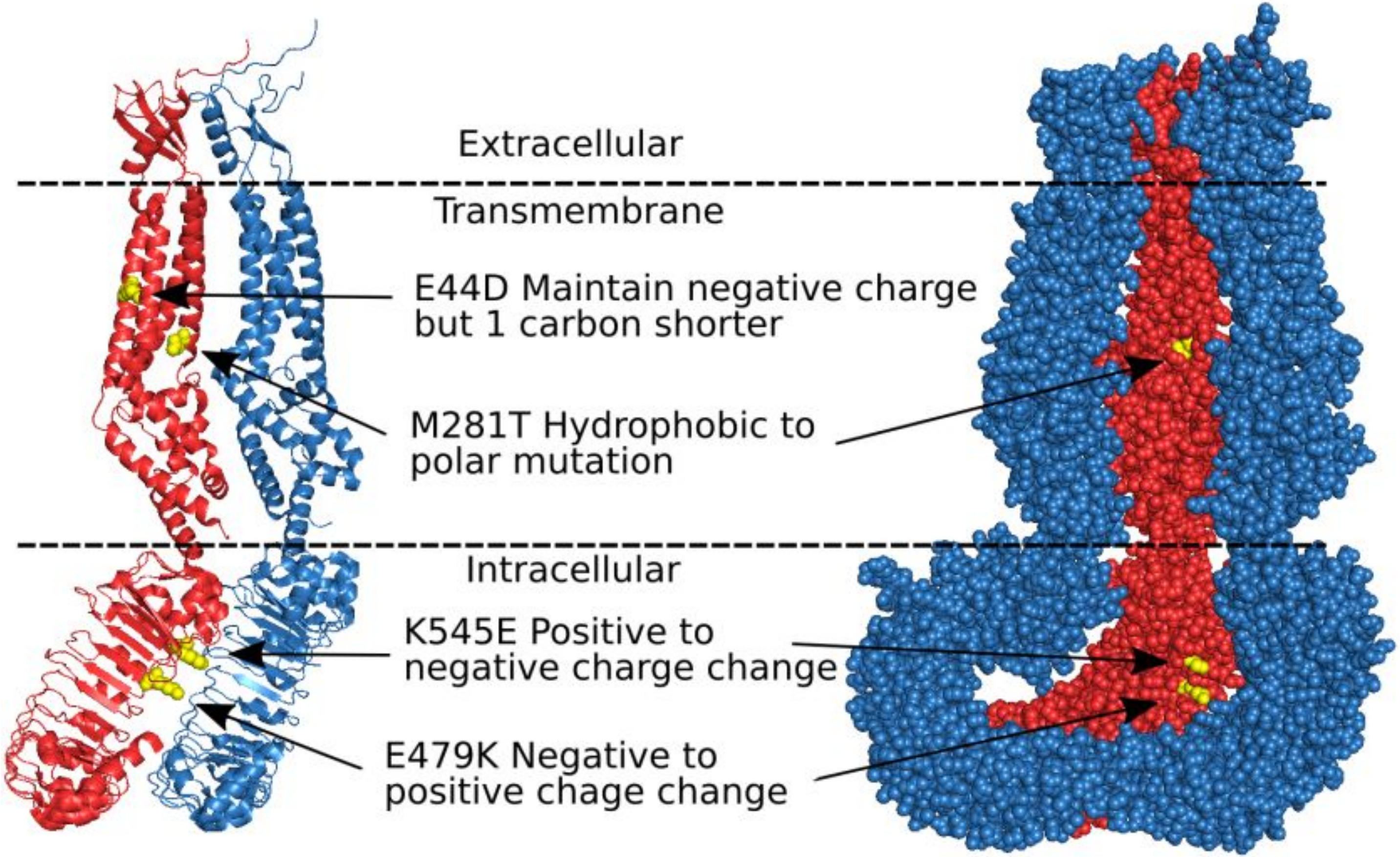


About 500 regions in the genome with highly differentiated SNPs $P<10^{-20}$

Frequency of Low-Salinity allele in LRRC8C



LRRC8C – AA sites > .65 ΔAF baltic/atlantic



Extracellular

Transmembrane

E44D Maintain negative charge
but 1 carbon shorter

M281T Hydrophobic to
polar mutation

Intracellular

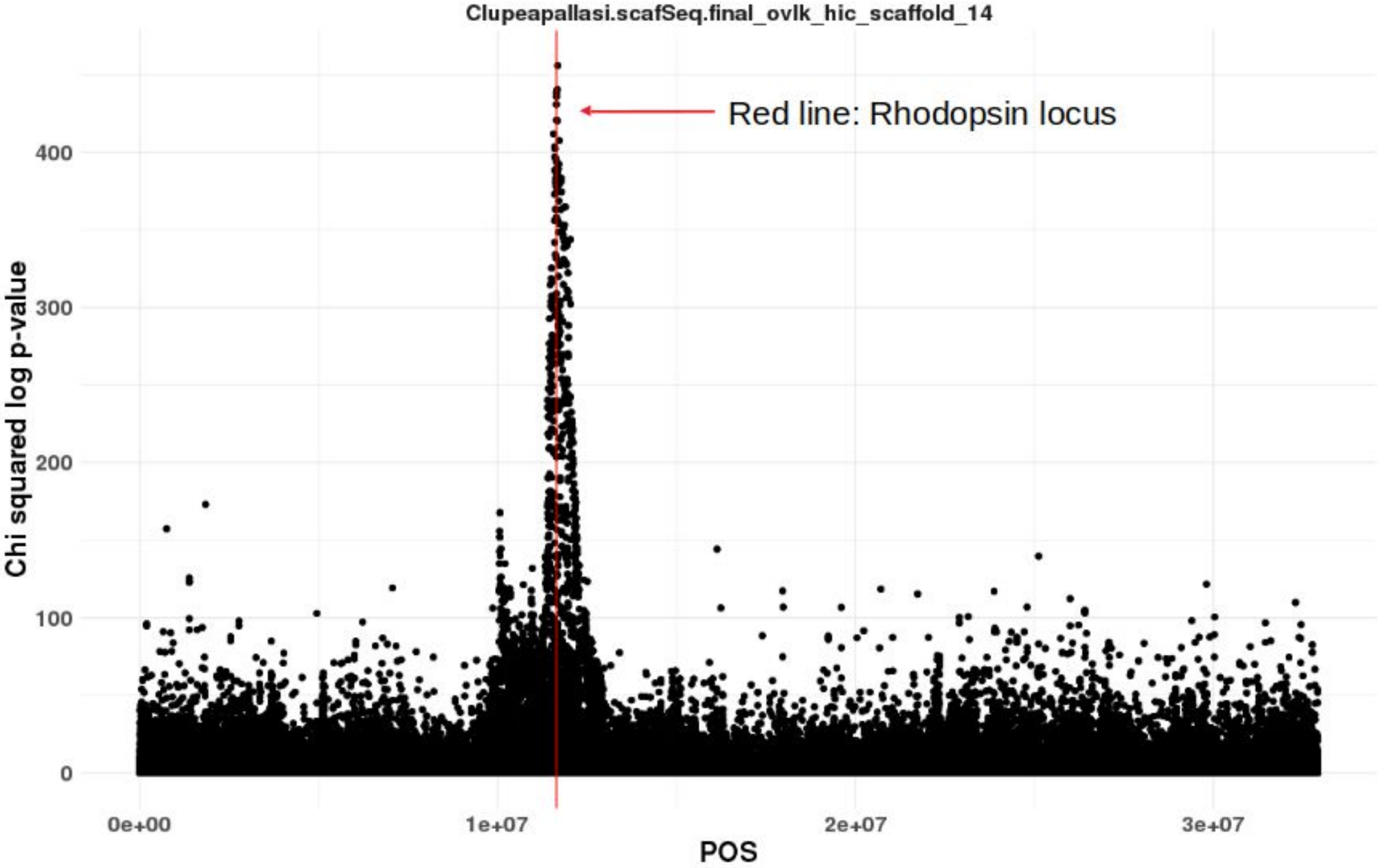
K545E Positive to
negative charge change

E479K Negative to
positive chage change

Exercise

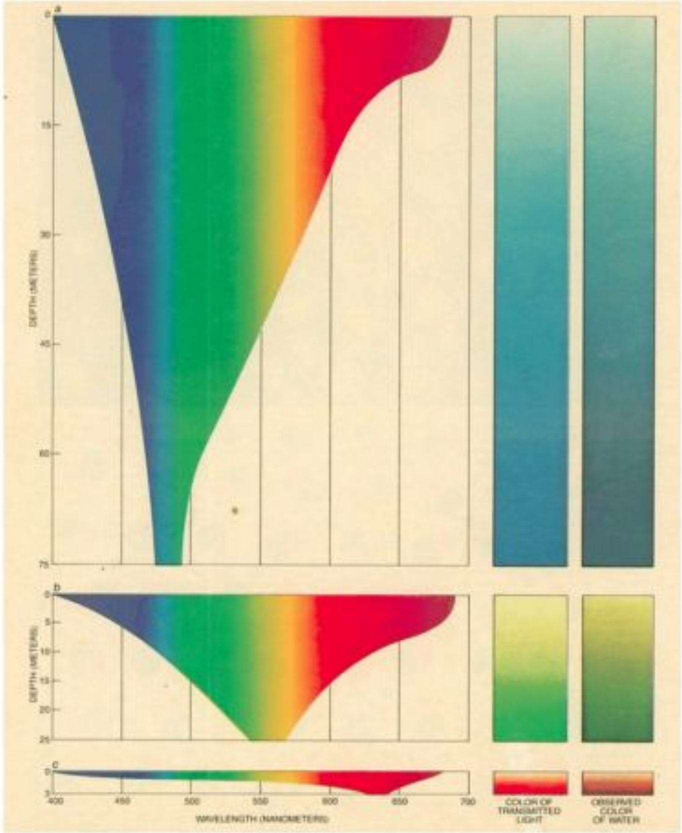
1) Inside your working directory: $ git clone https://github.com/JasonAnthonyHill/pgip
2) $ module load R/4.2.1 R_packages/4.2.1 RStudio
3) $ rstudio
4) Within rstudio load the file: herring_selection_scan.Rmd

Baltic vs. Atlantic SNPS

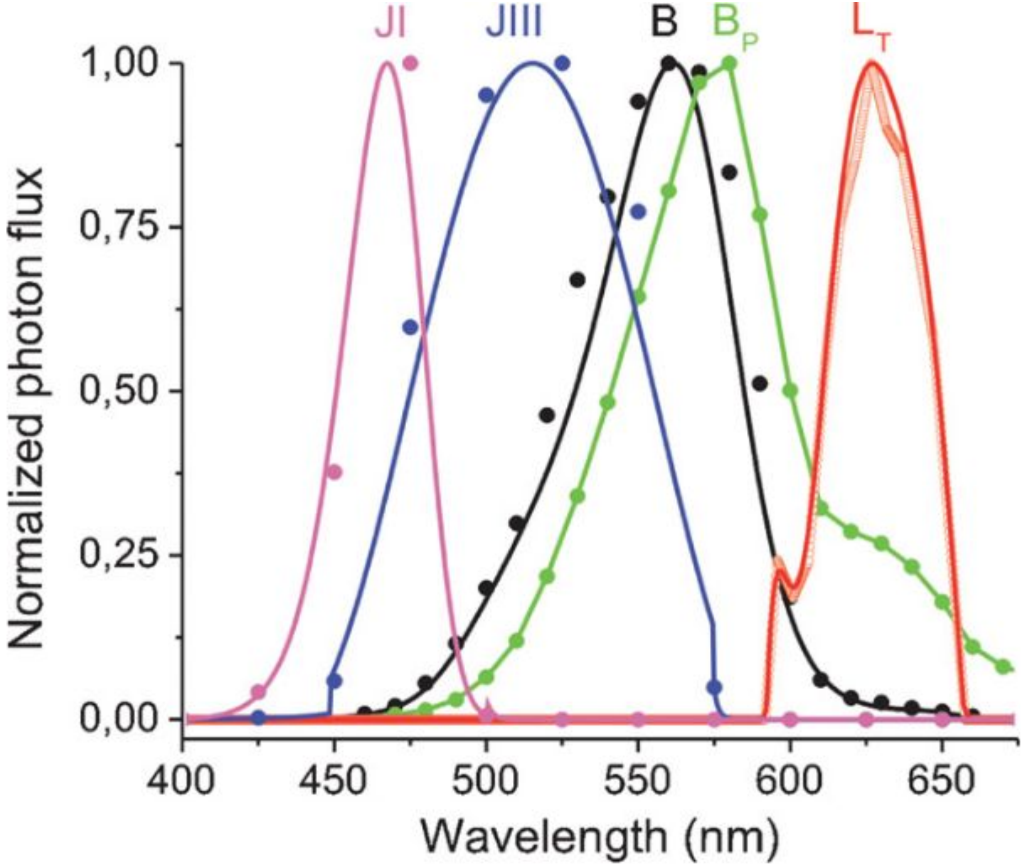


Clupeapallasi.scafSeq.final_ovlk_hic_scaffold_14

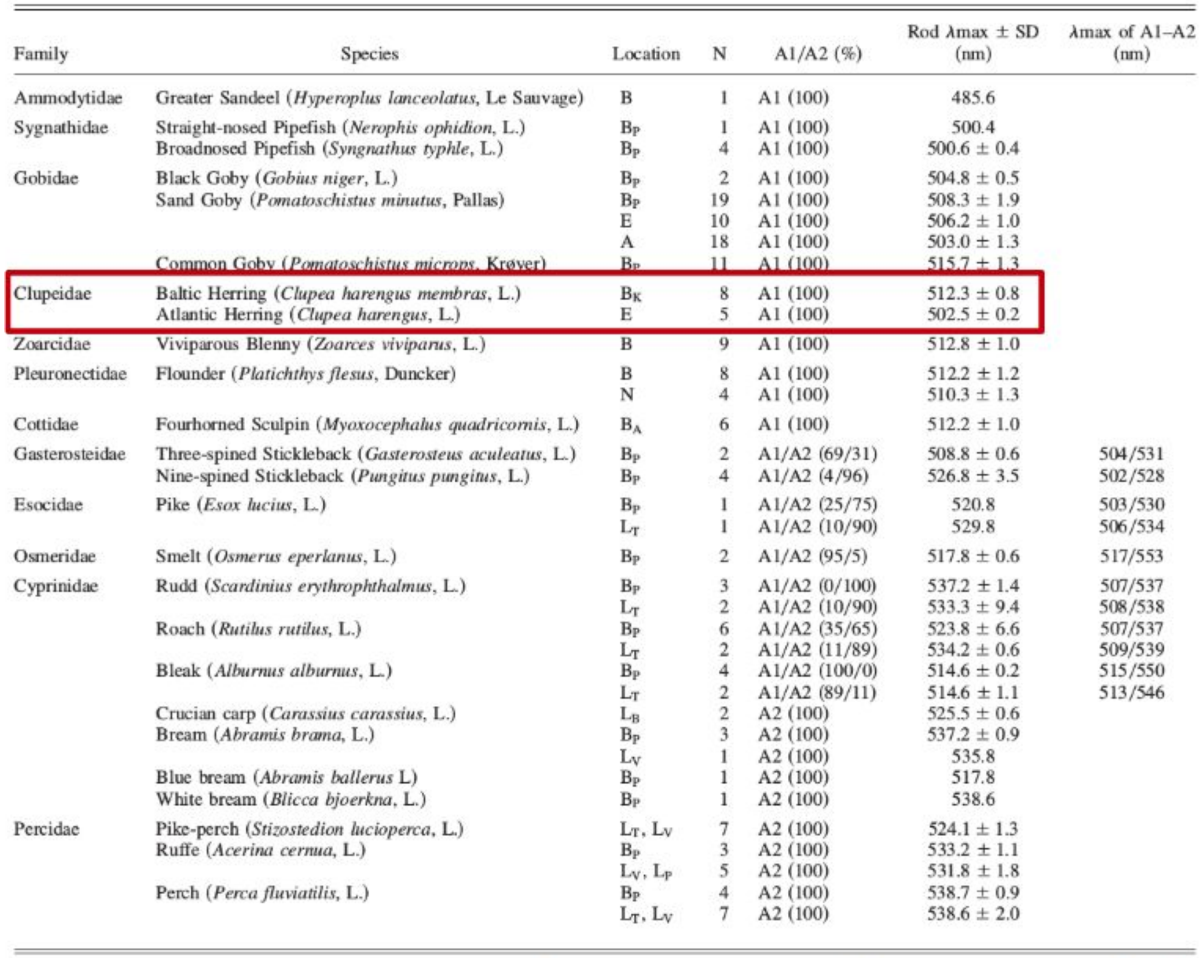
Red line: Rhodopsin locus



J. Pahlberg (2007)



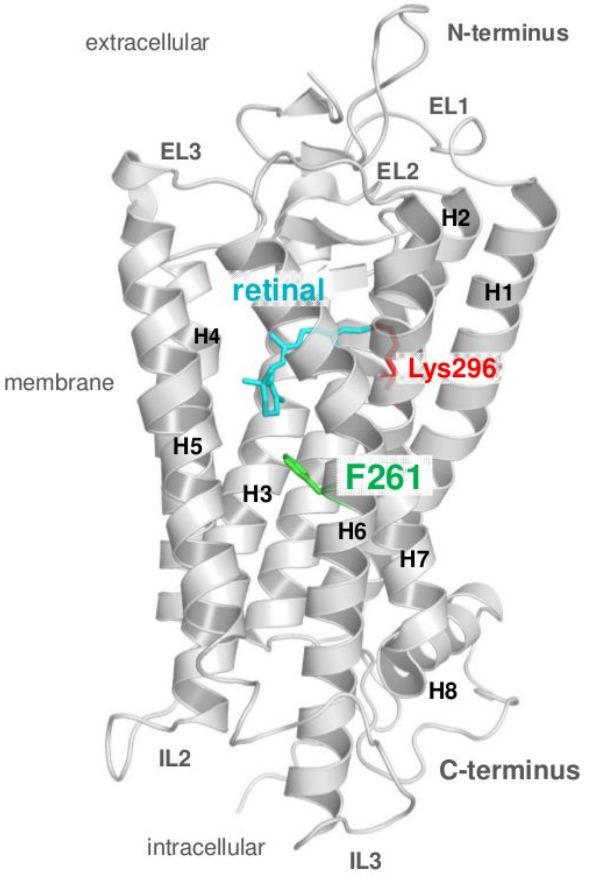
M. Jokela-Määttä *et al.* Visual Neuroscience (2007)



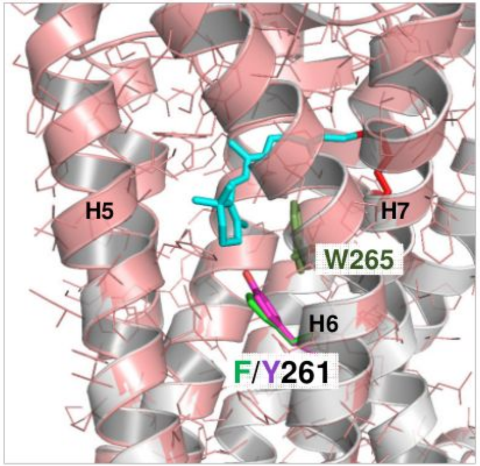
Family	Species	Location	N	A1/A2 (%)	Rod λmax ± SD (nm)	λmax of A1–A2 (nm)
Ammodytidae	Greater Sandeel (*Hyperoplus lanceolatus*, Le Sauvage)	B	1	A1 (100)	485.6	
Sygnathidae	Straight-nosed Pipefish (*Nerophis ophidion*, L.)	B_P	1	A1 (100)	500.4	
	Broadnosed Pipefish (*Syngnathus typhle*, L.)	B_P	4	A1 (100)	500.6 ± 0.4	
Gobidae	Black Goby (*Gobius niger*, L.)	B_P	2	A1 (100)	504.8 ± 0.5	
	Sand Goby (*Pomatoschistus minutus*, Pallas)	B_P	19	A1 (100)	508.3 ± 1.9	
		E	10	A1 (100)	506.2 ± 1.0	
		A	18	A1 (100)	503.0 ± 1.3	
	Common Goby (*Pomatoschistus microps*, Krøyer)	B_P	11	A1 (100)	515.7 ± 1.3	
Clupeidae	Baltic Herring (*Clupea harengus membras*, L.)	B_K	8	A1 (100)	512.3 ± 0.8	
	Atlantic Herring (*Clupea harengus*, L.)	E	5	A1 (100)	502.5 ± 0.2	
Zoarcidae	Viviparous Blenny (*Zoarces viviparus*, L.)	B	9	A1 (100)	512.8 ± 1.0	
Pleuronectidae	Flounder (*Platichthys flesus*, Duncker)	B	8	A1 (100)	512.2 ± 1.2	
		N	4	A1 (100)	510.3 ± 1.3	
Cottidae	Fourhorned Sculpin (*Myoxocephalus quadricornis*, L.)	B_A	6	A1 (100)	512.2 ± 1.0	
Gasterosteidae	Three-spined Stickleback (*Gasterosteus aculeatus*, L.)	B_P	2	A1/A2 (69/31)	508.8 ± 0.6	504/531
	Nine-spined Stickleback (*Pungitus pungitus*, L.)	B_P	4	A1/A2 (4/96)	526.8 ± 3.5	502/528
Esocidae	Pike (*Esox lucius*, L.)	B_P	1	A1/A2 (25/75)	520.8	503/530
		L_T	1	A1/A2 (10/90)	529.8	506/534
Osmeridae	Smelt (*Osmerus eperlanus*, L.)	B_P	2	A1/A2 (95/5)	517.8 ± 0.6	517/553
Cyprinidae	Rudd (*Scardinius erythrophthalmus*, L.)	B_P	3	A1/A2 (0/100)	537.2 ± 1.4	507/537
		L_T	2	A1/A2 (10/90)	533.3 ± 9.4	508/538
	Roach (*Rutilus rutilus*, L.)	B_P	6	A1/A2 (35/65)	523.8 ± 6.6	507/537
		L_T	2	A1/A2 (11/89)	534.2 ± 0.6	509/539
	Bleak (*Alburnus alburnus*, L.)	B_P	4	A1/A2 (100/0)	514.6 ± 0.2	515/550
		L_T	2	A1/A2 (89/11)	514.6 ± 1.1	513/546
	Crucian carp (*Carassius carassius*, L.)	L_B	2	A2 (100)	525.5 ± 0.6	
	Bream (*Abramis brama*, L.)	B_P	3	A2 (100)	537.2 ± 0.9	
		L_V	1	A2 (100)	535.8	
	Blue bream (*Abramis ballerus* L)	B_P	1	A2 (100)	517.8	
	White bream (*Blicca bjoerkna*, L.)	B_P	1	A2 (100)	538.6	
Percidae	Pike-perch (*Stizostedion lucioperca*, L.)	L_T, L_V	7	A2 (100)	524.1 ± 1.3	
	Ruffe (*Acerina cernua*, L.)	B_P	3	A2 (100)	533.2 ± 1.1	
		L_V, L_P	5	A2 (100)	531.8 ± 1.8	
	Perch (*Perca fluviatilis*, L.)	B_P	4	A2 (100)	538.7 ± 0.9	
		L_T, L_V	7	A2 (100)	538.6 ± 2.0	

M. Jokela-Määttä *et al.* Visual Neuroscience (2007)

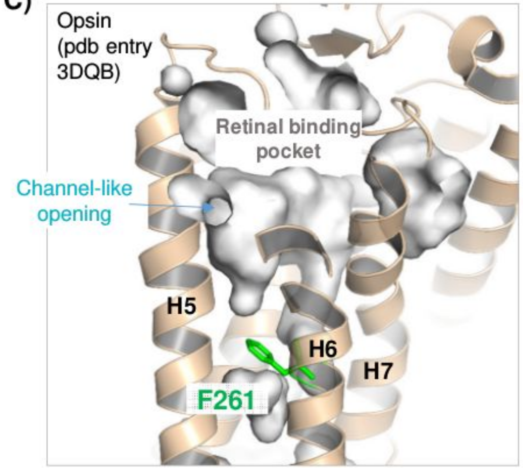
A) **Autumn spawning herring rhodopsin model, Meta-II state**



B) **Spring spawning rhodopsin model, Meta-II state**



C)



Insights from herring Rhodopsin models:

F261 is located in TMH6, close to the retinal binding site (**A**).

In consequence variant Y261 will be different to F261 in:

1. The electrostatics at this retinal binding region (additional OH group) (**B**)

2. The contact and interplay with Trp265 that is essentially involved in the retinal β-ionone ring/rhodopsin interplay and thereby activation of the receptor (**B**)

3. The variant could have impact on the channel-like opening for retinal release/entry as observed in the opsin structure (**C**)

- Park JH§, Scheerer P§, et al., Crystal structure of the ligand-free G-protein-coupled receptor opsin. *Nature* 2008, 454(7201):183-7.
- Piechnick R, Ritter E, Hildebrand PW, Ernst OP, Scheerer P, Hofmann KP, Heck M. Effect of channel mutations on the uptake and release of the retinal ligand in opsin. *PNAS* 2012;109(14):5247-52

Kleinau, Scheerer, Charité, Berlin, 03. Oct. 2018

Multiple observations of Tyr 261 involved in fish vision adaptation

Spectral Tuning and Molecular Evolution of Rod Visual Pigments in the Species Flock of Cottoid Fish in Lake Baikal

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Received 28 March 1995; in revised form 19 June 1995; in final form 14 August 1995

Rhodopsin From the Fish, *Astyanax:* Role of Tyrosine 261 in the Red Shift

Ruth Yokoyama, Barry E. Knox,† and Shozo Yokoyama**

The Journal of Experimental Biology 212, 3415-3421
Published by The Company of Biologists 2009
doi:10.1242/jeb.031344

Individual variation in rod absorbance spectra correlated with opsin gene polymorphism in sand goby (*Pomatoschistus minutus*)

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Accepted 28 July 2009

Summary

- Many methods exist for detecting selection using genomic data
- Selecting the right method for the right species can yield powerful results
- Carry through to structure and function