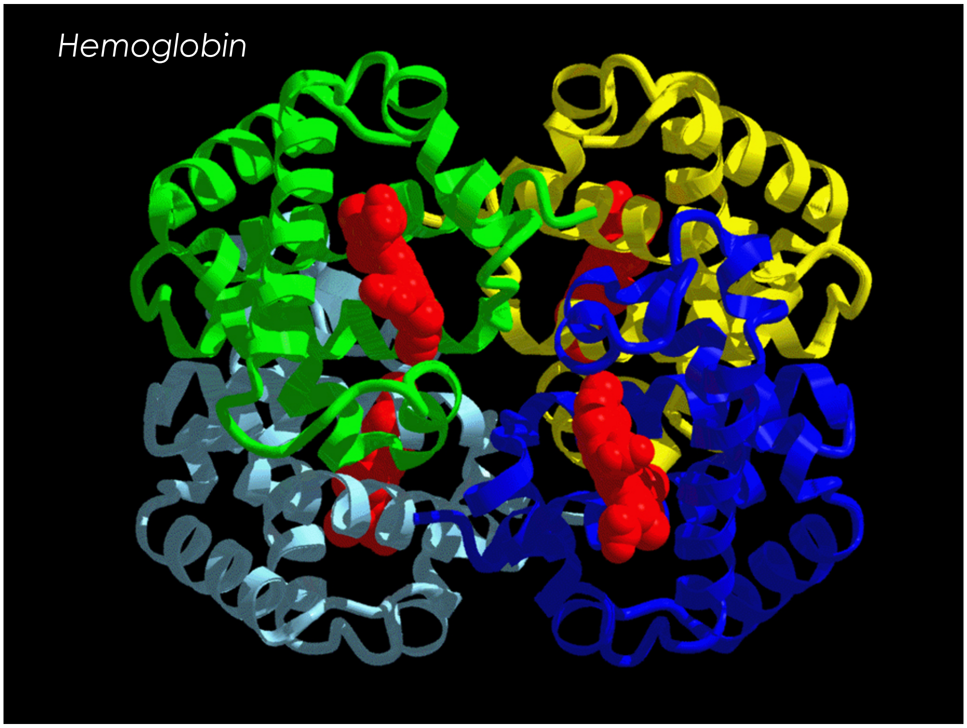
Migration/Selection Equilibrium

- what level of migration is sufficient to counter the effects of selection?
  - “divergence with gene flow”



Hemoglobin

Waterfowl Hemoglobin

- waterfowl adapted to high-altitude
  - Bar-headed goose: Pro-119-alpha --> Ala
  - Andean goose: Leu-55-beta --> Ser

Waterfowl Hemoglobin

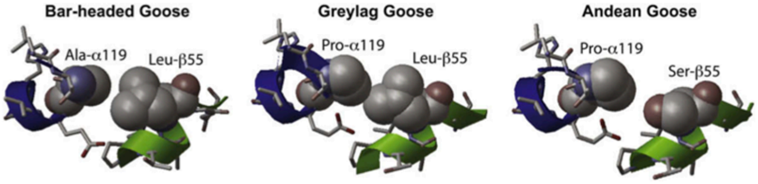
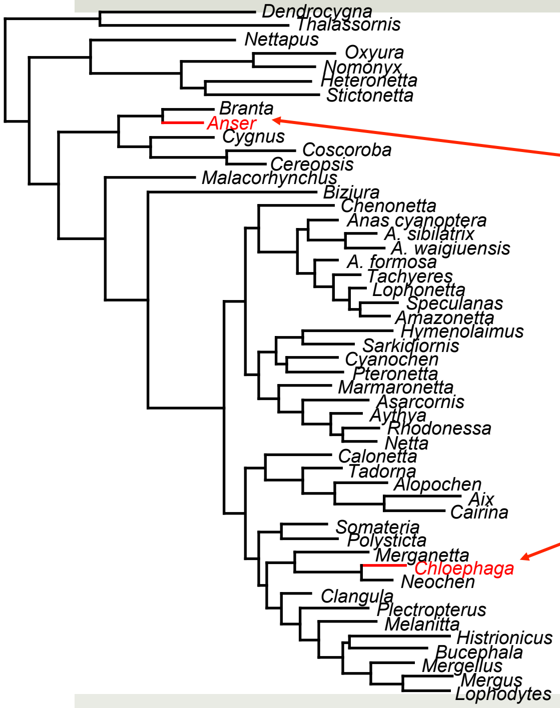


Fig. 1. Illustration of the $\alpha^{A}119/\beta^{A}55$ intersubunit contact in bar-headed goose, greylag goose, and Andean goose. Pro-$\alpha^{A}119$ and Leu-$\beta^{A}55$ lie adjacent to each other on different polypeptide subunits, and in the greylag goose make a van der Waals contact that stabilizes the deoxygenated (T-state) conformation of the HbA structure. van der Waals interactions between $\alpha^{A}119$ and $\beta^{A}55$ are eliminated by substitution of Ala-$\alpha^{A}119$ in bar-headed goose and Ser-$\beta^{A}55$ in Andean goose. Protein crystal structures for greylag goose and bar-headed goose were illustrated using Protein Data Bank 1FAW and 1A4F, respectively. The Andean goose structure was illustrated using 1FAW, with a Leu → Ser-$\beta^{A}55$ replacement modeled in Swiss-PdbViewer 3.7. The structures were illustrated with Python Molecular Viewer 1.5.2.

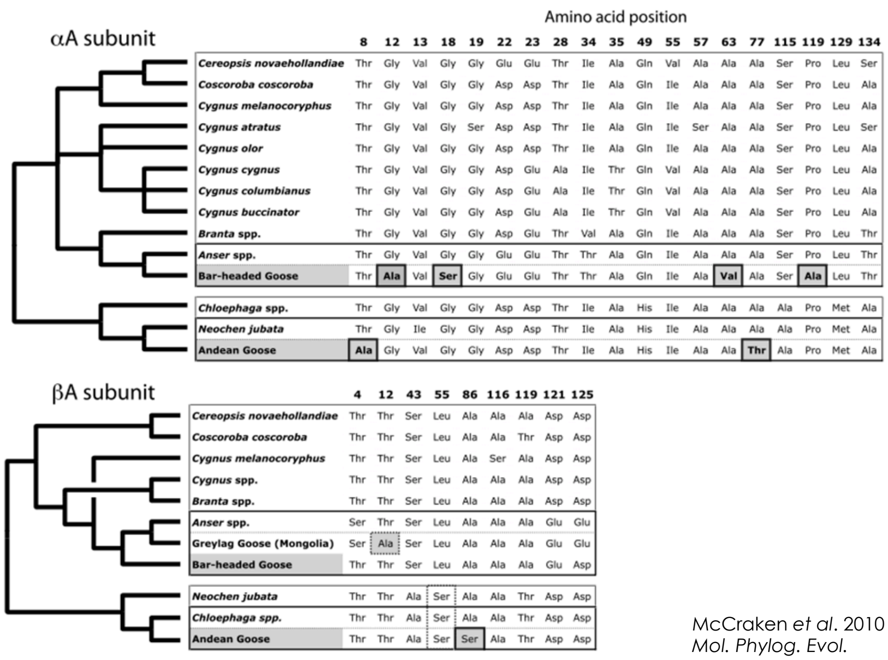


Bar-headed Goose: *Anser indicus*

Andean Goose: *Chloephaga melanoptera*

Jessen et al. 1991 Adaptation of bird hemoglobins to high altitudes - demonstration of molecular mechanism by protein engineering. *PNAS* 88 (15): 6519-6522.

- bar-headed goose: Pro-119-alpha --> Ala
- Andean goose: Leu-55-beta --> Ser
- both mutations destabilize the deoxygenated state of hemoglobin
- site-directed mutagenesis to engineer Ser-55-beta into human hemoglobin
- increases affinity of molecule for oxygen
- crystal structure of engineered molecule identical to human hemoglobin except for the 2-carbon gap left by the replacement of methionine with serine



αA subunit

Amino acid position

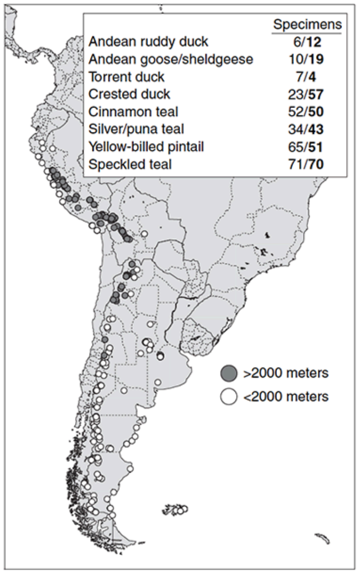
	8	12	13	18	19	22	23	28	34	35	49	55	57	63	77	115	119	129	134
Cereopsis novaehollandiae	Thr	Gly	Val	Gly	Gly	Glu	Glu	Thr	Ile	Ala	Gln	Val	Ala	Ala	Ala	Ser	Pro	Leu	Ser
Coscoroba coscoroba	Thr	Gly	Val	Gly	Gly	Asp	Asp	Thr	Ile	Ala	Gln	Ile	Ala	Ala	Ala	Ser	Pro	Leu	Ala
Cygnus melanocoryphus	Thr	Gly	Val	Gly	Gly	Asp	Asp	Thr	Ile	Ala	Gln	Ile	Ala	Ala	Ala	Ser	Pro	Leu	Ala
Cygnus atratus	Thr	Gly	Val	Gly	Ser	Asp	Asp	Thr	Ile	Ala	Gln	Ile	Ser	Ala	Ala	Ser	Pro	Leu	Ser
Cygnus olor	Thr	Gly	Val	Gly	Gly	Asp	Asp	Thr	Ile	Ala	Gln	Ile	Ala	Ala	Ala	Ser	Pro	Leu	Ala
Cygnus cygnus	Thr	Gly	Val	Gly	Gly	Asp	Glu	Ala	Ile	Thr	Gln	Val	Ala	Ala	Ala	Ser	Pro	Leu	Ala
Cygnus columbianus	Thr	Gly	Val	Gly	Gly	Asp	Glu	Ala	Ile	Thr	Gln	Val	Ala	Ala	Ala	Ser	Pro	Leu	Ala
Cygnus buccinator	Thr	Gly	Val	Gly	Gly	Asp	Glu	Ala	Ile	Thr	Gln	Val	Ala	Ala	Ala	Ser	Pro	Leu	Ala
***Branta* spp.**	Thr	Gly	Val	Gly	Gly	Asp	Glu	Thr	Val	Ala	Gln	Ile	Ala	Ala	Ala	Ser	Pro	Leu	Thr
***Anser* spp.**	Thr	Gly	Val	Gly	Gly	Glu	Glu	Thr	Thr	Ala	Gln	Ile	Ala	Ala	Ala	Ser	Pro	Leu	Thr
Bar-headed Goose	Thr	**Ala**	Val	**Ser**	Gly	Glu	Glu	Thr	Thr	Ala	Gln	Ile	Ala	**Val**	Ala	Ser	**Ala**	Leu	Thr
***Chloephaga* spp.**	Thr	Gly	Val	Gly	Gly	Asp	Asp	Thr	Ile	Ala	His	Ile	Ala	Ala	Ala	Ala	Pro	Met	Ala
Neochen jubata	Thr	Gly	Ile	Gly	Gly	Asp	Asp	Thr	Ile	Ala	His	Ile	Ala	Ala	Ala	Ala	Pro	Met	Ala
Andean Goose	**Ala**	Gly	Val	Gly	Gly	Asp	Asp	Thr	Ile	Ala	His	Ile	Ala	Ala	**Thr**	Ala	Pro	Met	Ala

βA subunit

	4	12	43	55	86	116	119	121	125
Cereopsis novaehollandiae	Thr	Thr	Ser	Leu	Ala	Ala	Ala	Asp	Asp
Coscoroba coscoroba	Thr	Thr	Ser	Leu	Ala	Ala	Thr	Asp	Asp
Cygnus melanocoryphus	Thr	Thr	Ser	Leu	Ala	Ser	Ala	Asp	Asp
***Cygnus* spp.**	Thr	Thr	Ser	Leu	Ala	Ala	Ala	Asp	Asp
***Branta* spp.**	Thr	Thr	Ser	Leu	Ala	Ala	Ala	Asp	Asp
***Anser* spp.**	Ser	Thr	Ser	Leu	Ala	Ala	Ala	Glu	Glu
Greylag Goose (Mongolia)	Ser	Ala	Ser	Leu	Ala	Ala	Ala	Glu	Glu
Bar-headed Goose	Thr	Thr	Ser	Leu	Ala	Ala	Ala	Glu	Asp
Neochen jubata	Thr	Thr	Ala	Ser	Ala	Ala	Thr	Asp	Asp
***Chloephaga* spp.**	Thr	Thr	Ala	Ser	Ala	Ala	Thr	Asp	Asp
Andean Goose	Thr	Thr	Ala	Ser	Ser	Ala	Thr	Asp	Asp

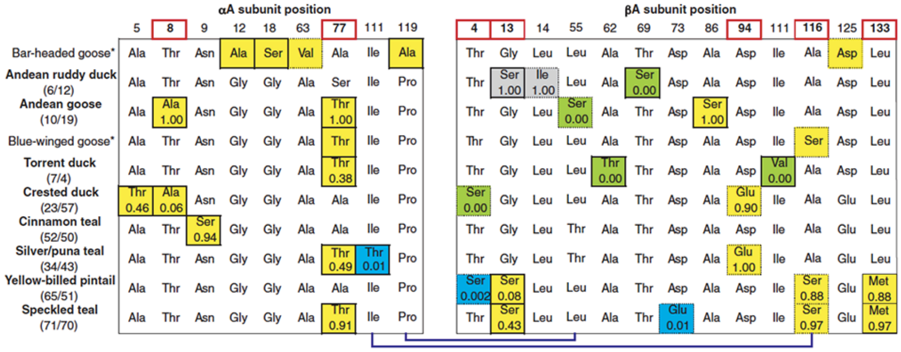
McCraken *et al*. 2010
Mol. Phylog. Evol.

Hemoglobin in Andean Waterfowl



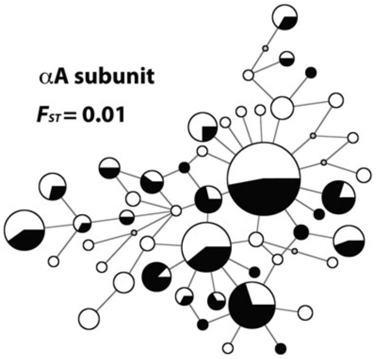
	Specimens
Andean ruddy duck	6/**12**
Andean goose/sheldgeese	10/**19**
Torrent duck	7/**4**
Crested duck	23/**57**
Cinnamon teal	52/**50**
Silver/puna teal	34/**43**
Yellow-billed pintail	65/**51**
Speckled teal	71/**70**

Hemoglobin in Andean Waterfowl



	αA subunit position									βA subunit position												
	5	8	9	12	18	63	77	111	119	4	13	14	55	62	69	73	86	94	111	116	125	133
Bar-headed goose*	Ala	Thr	Asn	Ala	Ser	Val	Ala	Ile	Ala	Thr	Gly	Leu	Leu	Ala	Thr	Asp	Ala	Asp	Ile	Ala	Asp	Leu
Andean ruddy duck (6/12)	Ala	Thr	Asn	Gly	Gly	Ala	Ser	Ile	Pro	Thr	Ser 1.00	Ile 1.00	Leu	Ala	Ser 0.00	Asp	Ala	Asp	Ile	Ala	Asp	Leu
Andean goose (10/19)	Ala	Ala 1.00	Asn	Gly	Gly	Ala	Thr 1.00	Ile	Pro	Thr	Gly	Leu	Ser 0.00	Ala	Thr	Asp	Ser 1.00	Asp	Ile	Ala	Asp	Leu
Blue-winged goose*	Ala	Thr	Asn	Gly	Gly	Ala	Thr	Ile	Pro	Thr	Gly	Leu	Leu	Ala	Thr	Asp	Ala	Asp	Ile	Ser	Asp	Leu
Torrent duck (7/4)	Ala	Thr	Asn	Gly	Gly	Ala	Thr 0.38	Ile	Pro	Thr	Gly	Leu	Leu	Thr 0.00	Thr	Asp	Ala	Asp	Val 0.00	Ala	Asp	Leu
Crested duck (23/57)	Thr 0.46	Ala 0.06	Asn	Gly	Gly	Ala	Ala	Ile	Pro	Ser 0.00	Gly	Leu	Leu	Ala	Thr	Asp	Ala	Glu 0.90	Ile	Ala	Glu	Leu
Cinnamon teal (52/50)	Ala	Thr	Ser 0.94	Gly	Gly	Ala	Ala	Ile	Pro	Thr	Gly	Leu	Thr	Ala	Thr	Asp	Ala	Asp	Ile	Ala	Glu	Leu
Silver/puna teal (34/43)	Ala	Thr	Asn	Gly	Gly	Ala	Thr 0.49	Thr 0.01	Pro	Thr	Gly	Leu	Thr	Ala	Thr	Asp	Ala	Glu 1.00	Ile	Ala	Glu	Leu
Yellow-billed pintail (65/51)	Ala	Thr	Asn	Gly	Gly	Ala	Ala	Ile	Pro	Ser 0.002	Ser 0.08	Leu	Leu	Ala	Thr	Asp	Ala	Asp	Ile	Ser 0.88	Glu	Met 0.88
Speckled teal (71/70)	Ala	Thr	Asn	Gly	Gly	Ala	Thr 0.91	Ile	Pro	Thr	Ser 0.43	Leu	Leu	Ala	Thr	Glu 0.01	Ala	Asp	Ile	Ser 0.97	Glu	Met 0.97

Yellow-billed pintail (*Anas georgica*)



McCracken *et al.* 2009 *Mol. Biol. Evol.*

MIGRATE (LAMARC)

assumptions:
- system at mutation/drift equilibrium
- constant population sizes and migration rates through time
- no selection

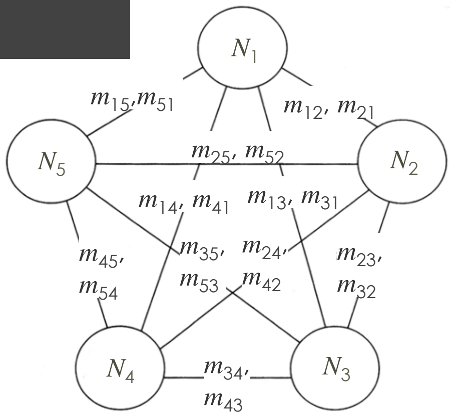
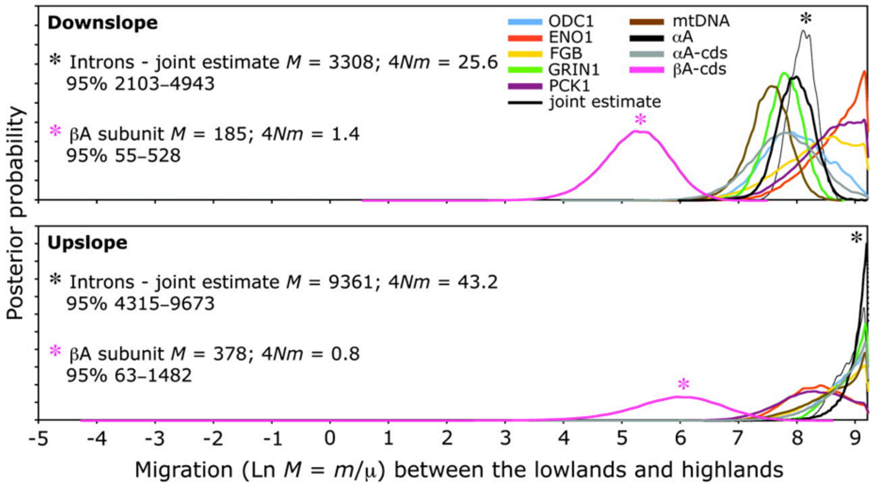


FIGURE 6.18 The island model of migration with five subpopulations. Migration is completely symmetrical. Each subpopulation contributes individuals or gametes to a pool of migrants, which then distribute themselves randomly among the subpopulations. In this model, a migrant can re-enter the same subpopulation it came from, indicated by the loops.

Migrate Results



McCracken *et al*. 2009 *Mol. Biol. Evol.*

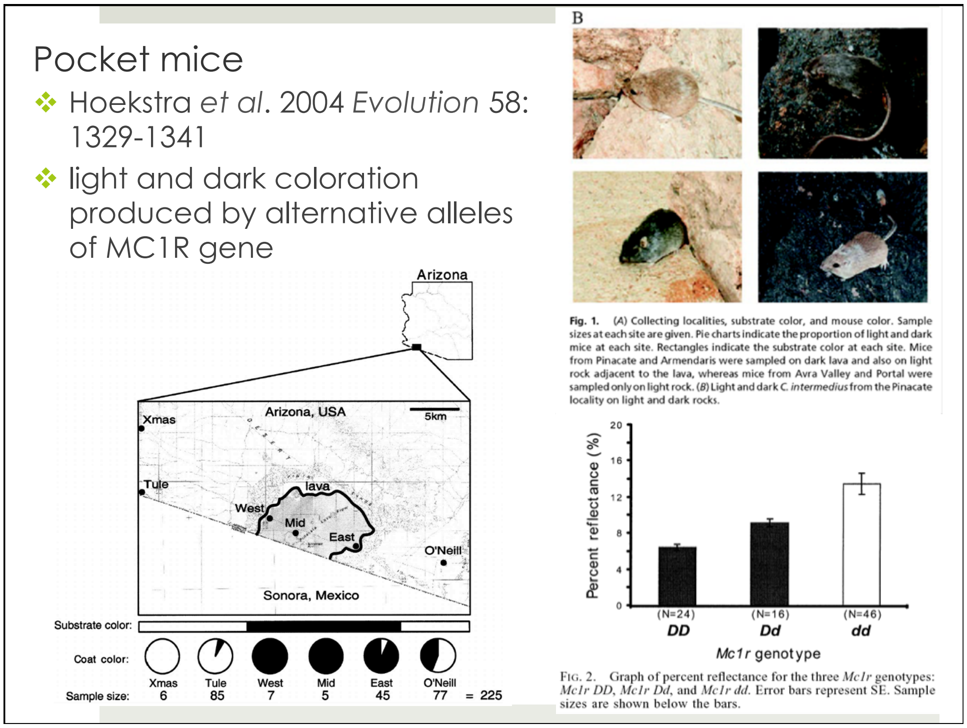
Migration/Selection Equilibrium

- what level of migration is sufficient to counter the effects of selection? $m > s$
  - "divergence with gene flow"

Migration/Selection Equilibrium

- suppose an allele (a) is disadvantageous in one population but not another
- fitness of genotypes
  - AA: 1, Aa: 1-hs, aa: 1-s
- q^*: frequency of a in incoming migrants
- m_i, m_o: incoming and outgoing migration rates

$$\Delta q = \frac{-spq\left[q + h\left(p - q\right)\right]}{1 - sq\left(2hp + q\right)} + m_i q^* - m_o q$$



Pocket mice

- Hoekstra *et al*. 2004 *Evolution* 58: 1329-1341
- light and dark coloration produced by alternative alleles of MC1R gene

Fig. 1. (*A*) Collecting localities, substrate color, and mouse color. Sample sizes at each site are given. Pie charts indicate the proportion of light and dark mice at each site. Rectangles indicate the substrate color at each site. Mice from Pinacate and Armendaris were sampled on dark lava and also on light rock adjacent to the lava, whereas mice from Avra Valley and Portal were sampled only on light rock. (*B*) Light and dark *C. intermedius* from the Pinacate locality on light and dark rocks.

FIG. 2. Graph of percent reflectance for the three *Mc1r* genotypes: *Mc1r DD*, *Mc1r Dd*, and *Mc1r dd*. Error bars represent SE. Sample sizes are shown below the bars.

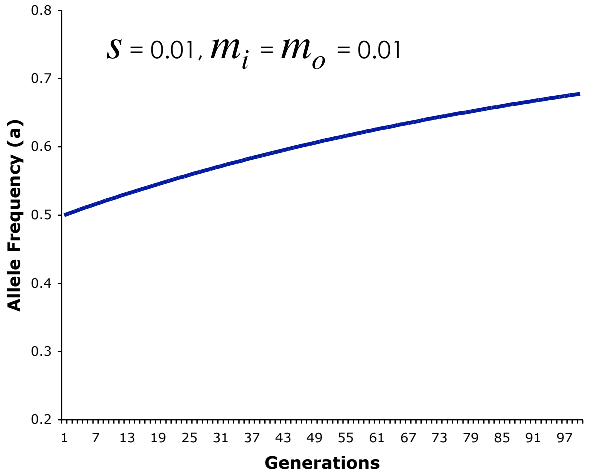
Estimating Selection in Pocket Mice

- m_i, m_o from MIGRATE analysis of mtDNA
- p, q, $q*$ from DNA sequencing
- h from phenotype/genotype comparison
- selection against the *Mc1r d* allele on dark substrate was 0.013 to 0.126
  - depending on estimate of N_e
- stronger than selection against dark mice on light substrate

$$\Delta q = \frac{-spq\left[q + h\left(p - q\right)\right]}{1 - sq\left(2hp + q\right)} + m_i q^* - m_o q$$

Hoekstra et al. 2004
Evolution 58: 1329-1341

h = 0.5, q^* = 0.9



Migration rate vs. Number of migrants

- migration rates yielding Nm = 1
  - N_e = 100, m = 0.01
  - N_e = 1,000, m = 0.001
  - N_e = 10,000, m = 0.0001
  - N_e = 100,000, m = 0.00001

Migration rate vs. Number of migrants

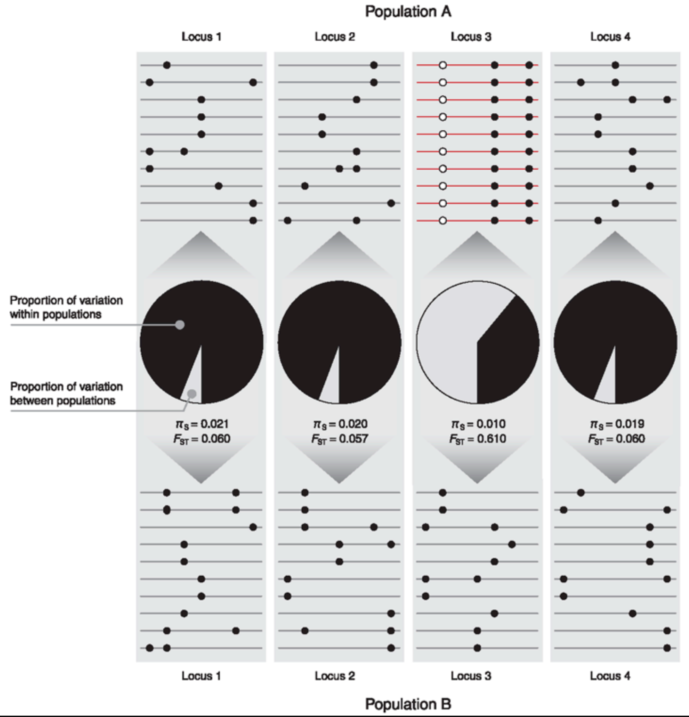
- number of migrants equivalent to $m > s$ for $s = 0.01$
  - N_e = 100, $Nm > 1$
  - N_e = 1,000, $Nm > 10$
  - N_e = 10,000, $Nm > 100$
  - N_e = 100,000, $Nm > 1{,}000$

Migration rate vs. Number of migrants

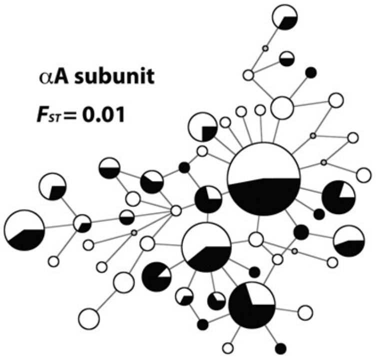
- migration rate yielding $Nm = 1$
  - N_e = 10,000, m = 0.0001 = 0.01%
- number of migrants equivalent to $m > s$
  - N_e = 10,000, s = 0.01, $Nm > 100$
- the level of migration needed to prevent adaptive divergence is generally much greater than the level needed to prevent neutral divergence
- **populations can diverge due to selection despite ongoing gene flow!**

Genome scan

- compare F_{ST} at multiple loci to look for outliers that may be under selection



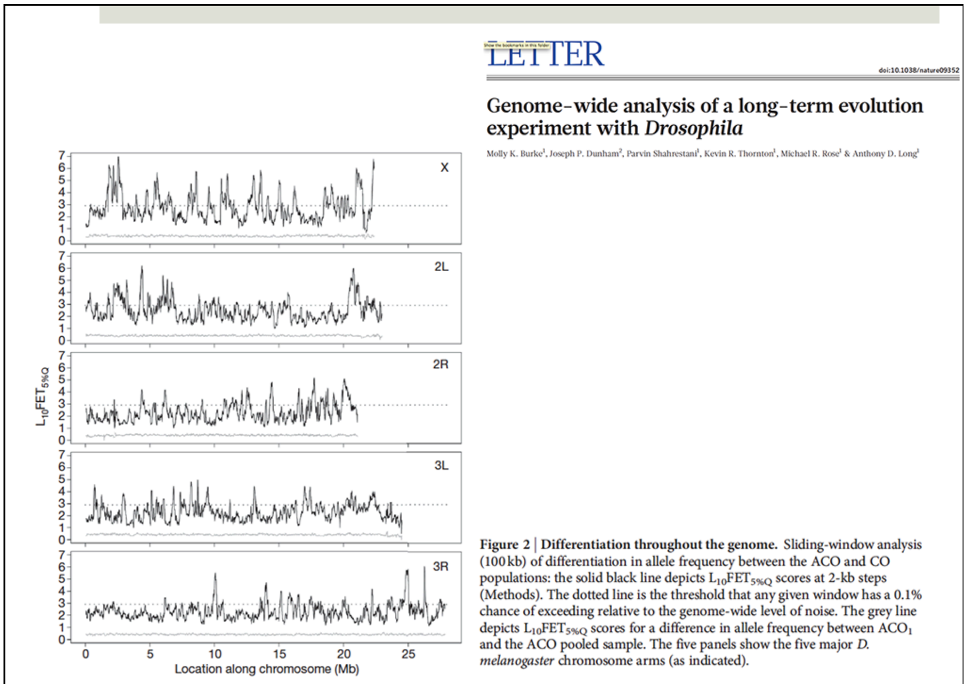
Yellow-billed pintail (*Anas georgica*)



αA subunit

F_{ST} = 0.01

McCracken *et al.* 2009 *Mol. Biol. Evol.*



LETTER

doi:10.1038/nature09352

Genome-wide analysis of a long-term evolution experiment with *Drosophila*

Molly K. Burke[1], Joseph P. Dunham[2], Parvin Shahrestani[1], Kevin R. Thornton[1], Michael R. Rose[1] & Anthony D. Long[1]

Figure 2 | Differentiation throughout the genome. Sliding-window analysis (100 kb) of differentiation in allele frequency between the ACO and CO populations: the solid black line depicts $L_{10}FET_{5\%Q}$ scores at 2-kb steps (Methods). The dotted line is the threshold that any given window has a 0.1% chance of exceeding relative to the genome-wide level of noise. The grey line depicts $L_{10}FET_{5\%Q}$ scores for a difference in allele frequency between ACO$_1$ and the ACO pooled sample. The five panels show the five major *D. melanogaster* chromosome arms (as indicated).

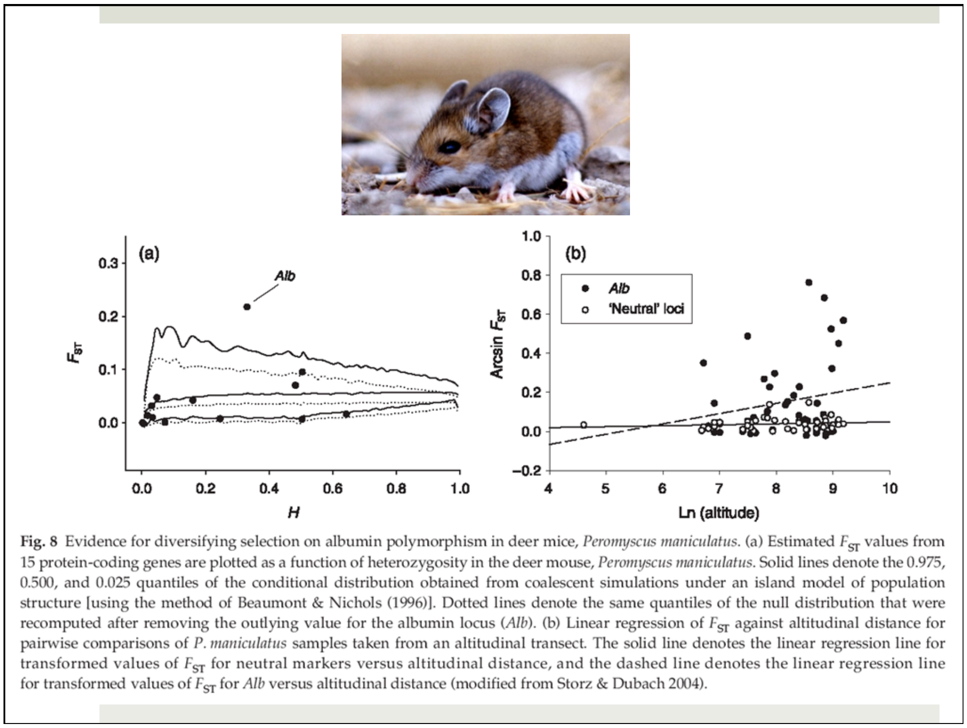


Fig. 8 Evidence for diversifying selection on albumin polymorphism in deer mice, *Peromyscus maniculatus*. (a) Estimated F_{ST} values from 15 protein-coding genes are plotted as a function of heterozygosity in the deer mouse, *Peromyscus maniculatus*. Solid lines denote the 0.975, 0.500, and 0.025 quantiles of the conditional distribution obtained from coalescent simulations under an island model of population structure [using the method of Beaumont & Nichols (1996)]. Dotted lines denote the same quantiles of the null distribution that were recomputed after removing the outlying value for the albumin locus (*Alb*). (b) Linear regression of F_{ST} against altitudinal distance for pairwise comparisons of *P. maniculatus* samples taken from an altitudinal transect. The solid line denotes the linear regression line for transformed values of F_{ST} for neutral markers versus altitudinal distance, and the dashed line denotes the linear regression line for transformed values of F_{ST} for *Alb* versus altitudinal distance (modified from Storz & Dubach 2004).

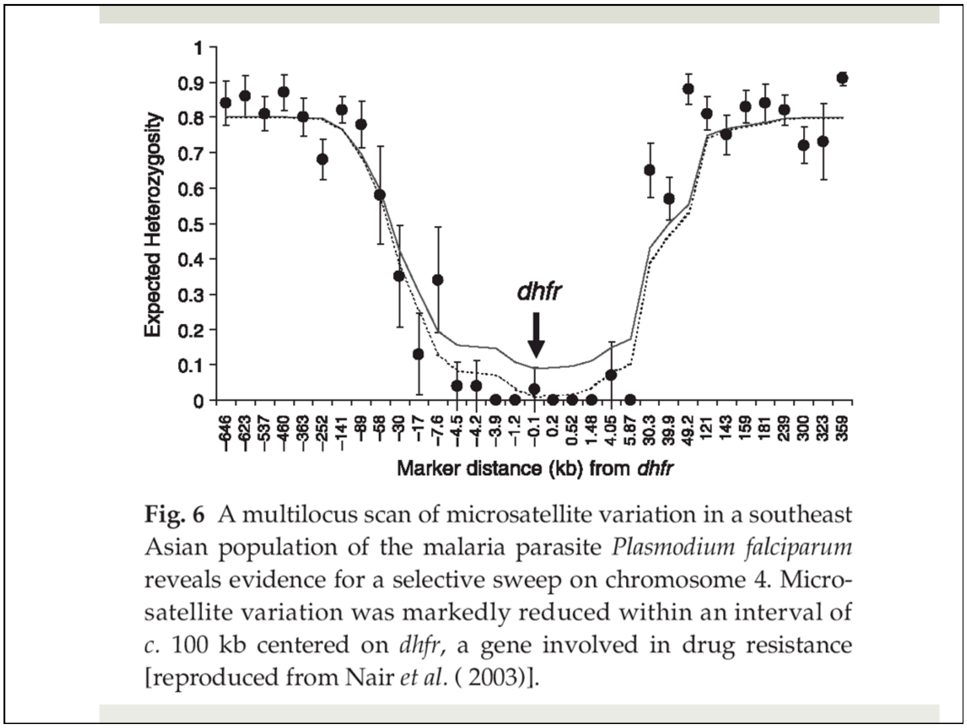


Fig. 6 A multilocus scan of microsatellite variation in a southeast Asian population of the malaria parasite *Plasmodium falciparum* reveals evidence for a selective sweep on chromosome 4. Microsatellite variation was markedly reduced within an interval of *c.* 100 kb centered on *dhfr*, a gene involved in drug resistance [reproduced from Nair *et al.* (2003)].