

Compensatory coevolution

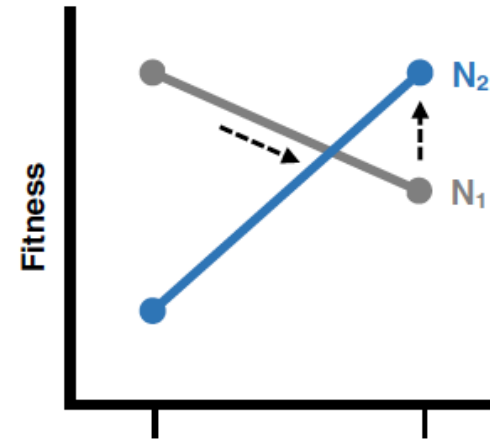
Some definitions

- Cytonuclear coevolution – a change in one genome causes selection for *complementary* changes in the other genome
- Compensatory coevolution – a type of coevolution where a *deleterious* change in one genome is offset by a *compensatory* change in the other genome
- Nuclear compensation – *deleterious* changes in the **mt genome** are offset by *compensatory* changes in the nuclear genome

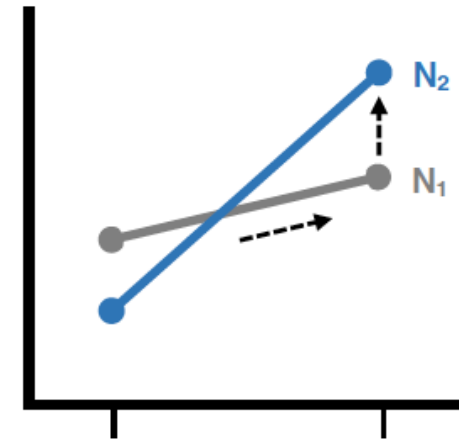
Many possible forms of cytonuclear coevolution

- Changes in one genome reshape the fitness landscape of possible changes in the other genome

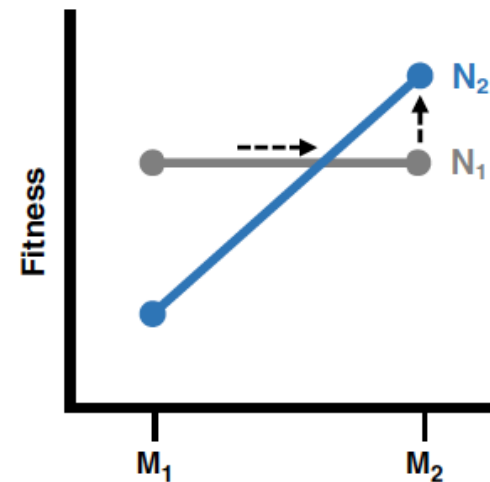
(C) Deleterious - Compensatory



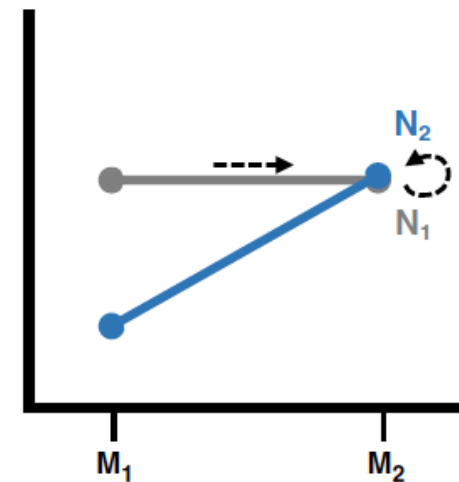
Beneficial - Synergistic



Neutral - Beneficial

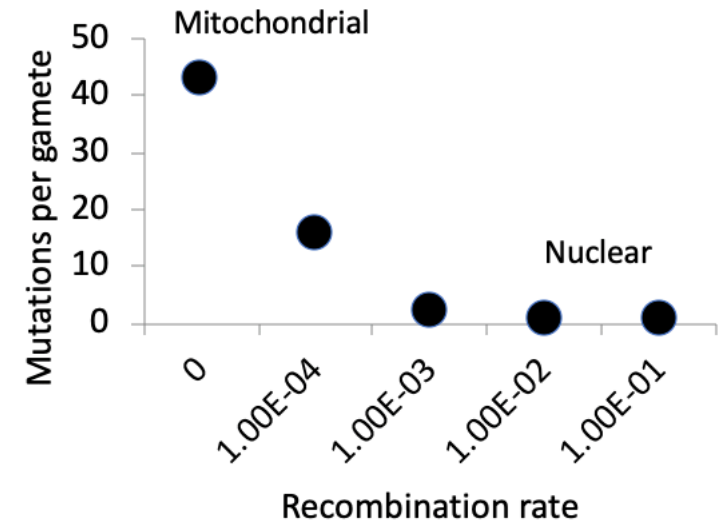
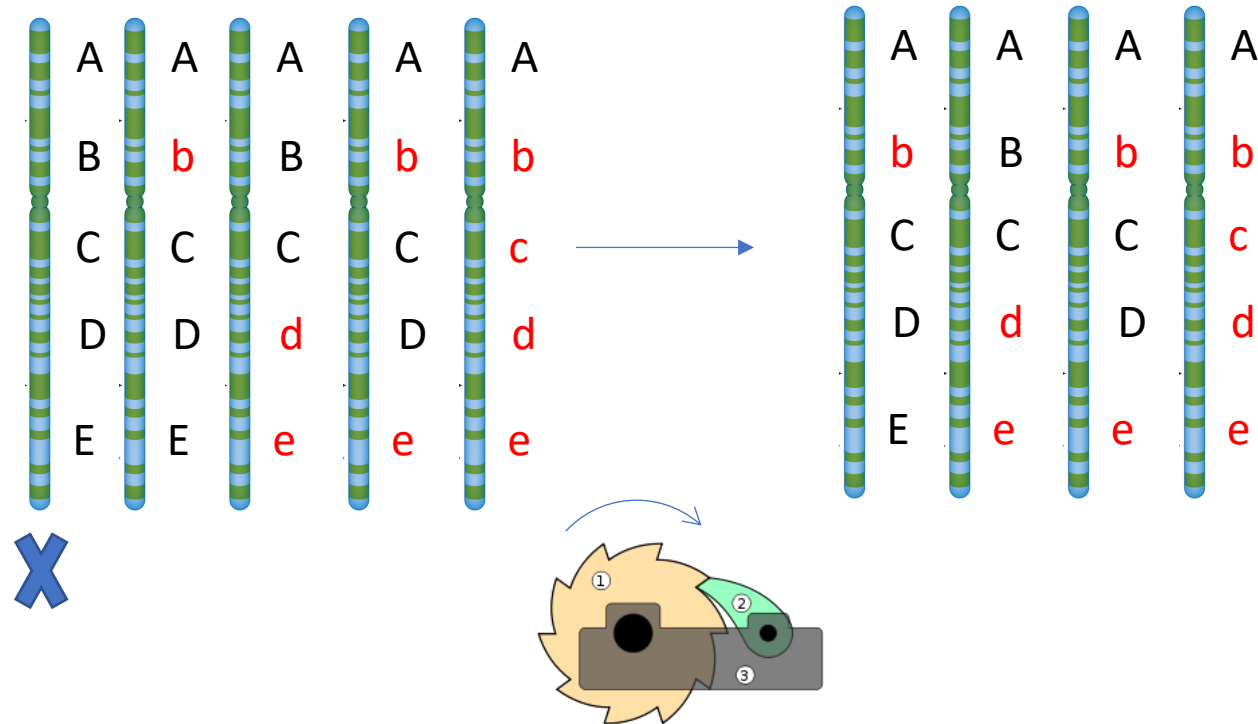


Neutral - Neutral

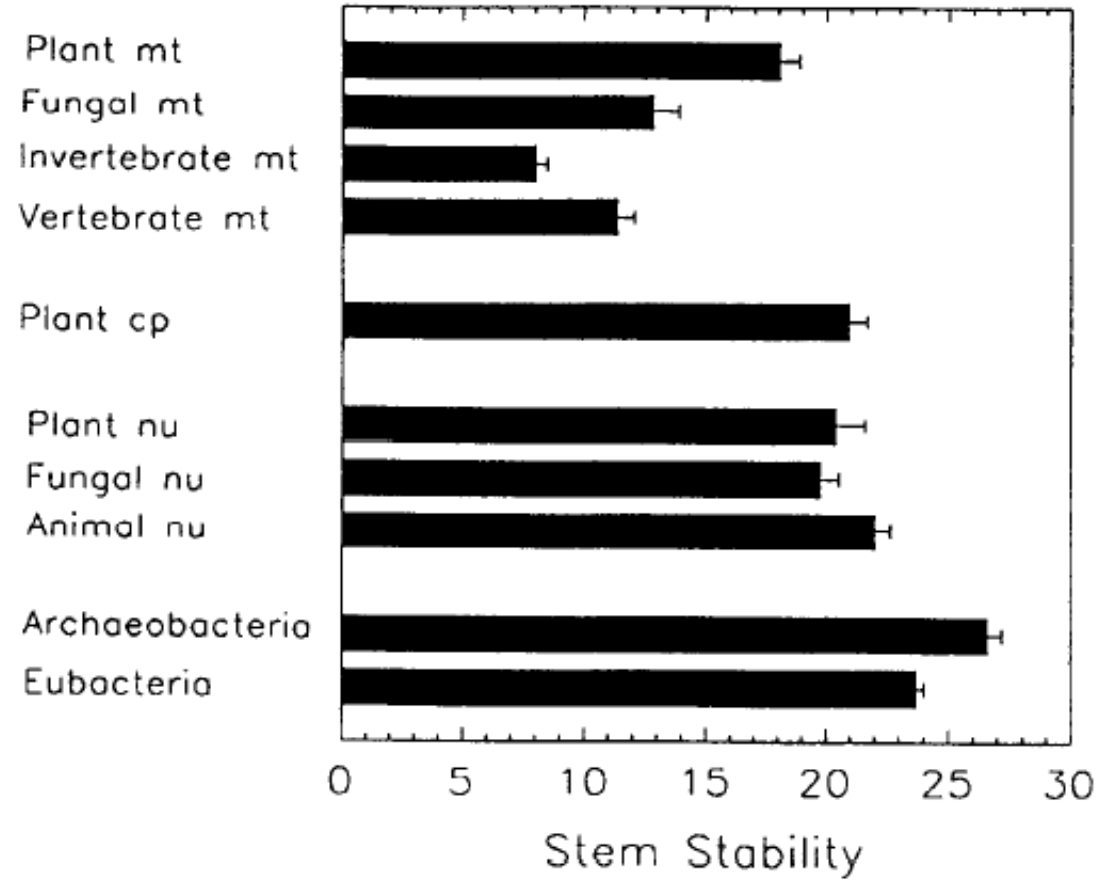


Mitochondrial haplotype

Why organelle genomes are expected to accumulate deleterious mutations

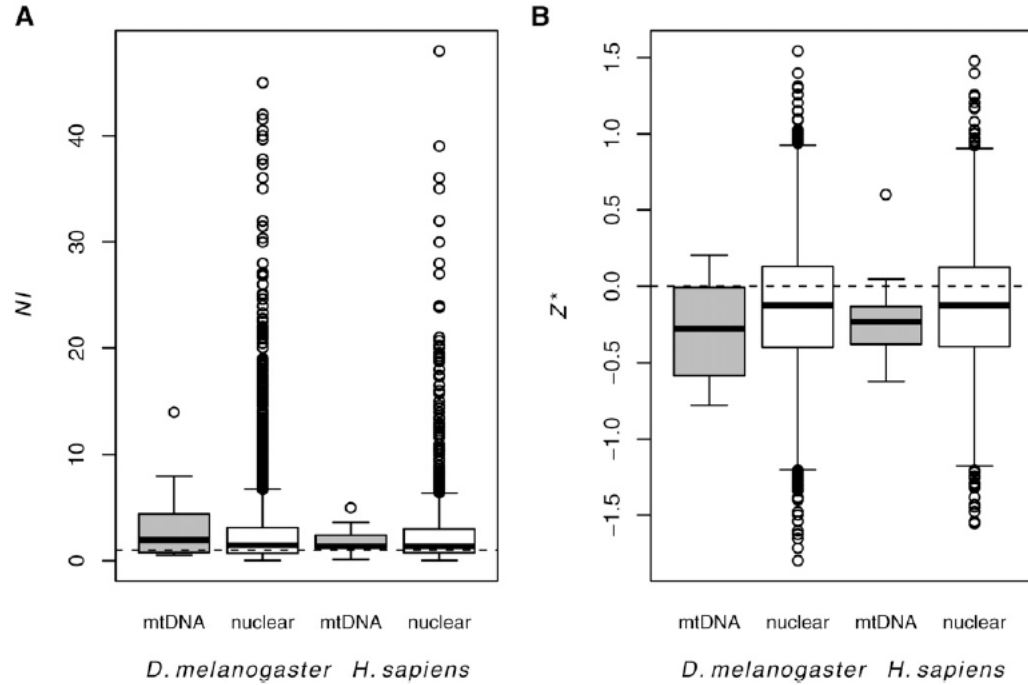


Some evidence

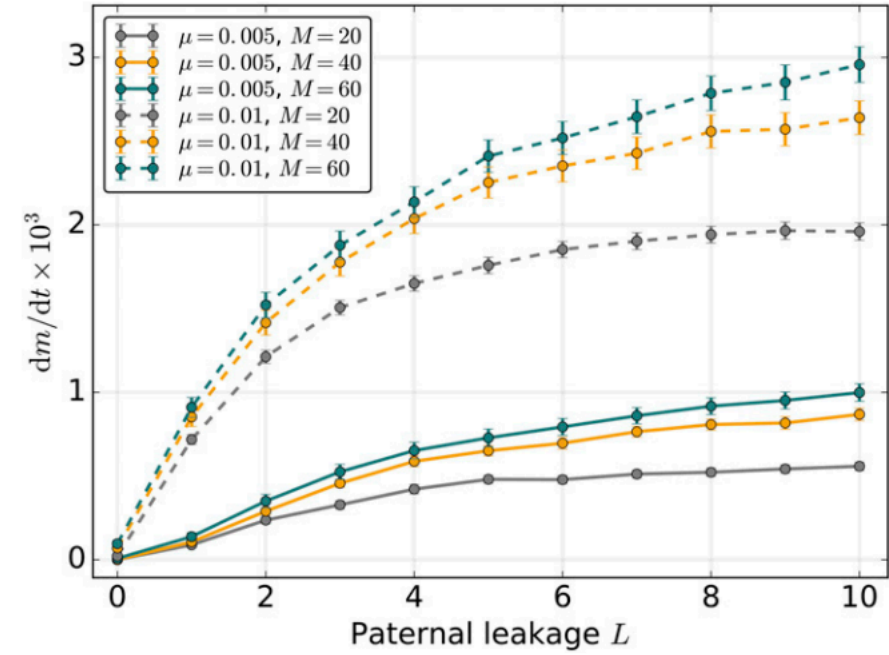


Lynch 1997

New studies

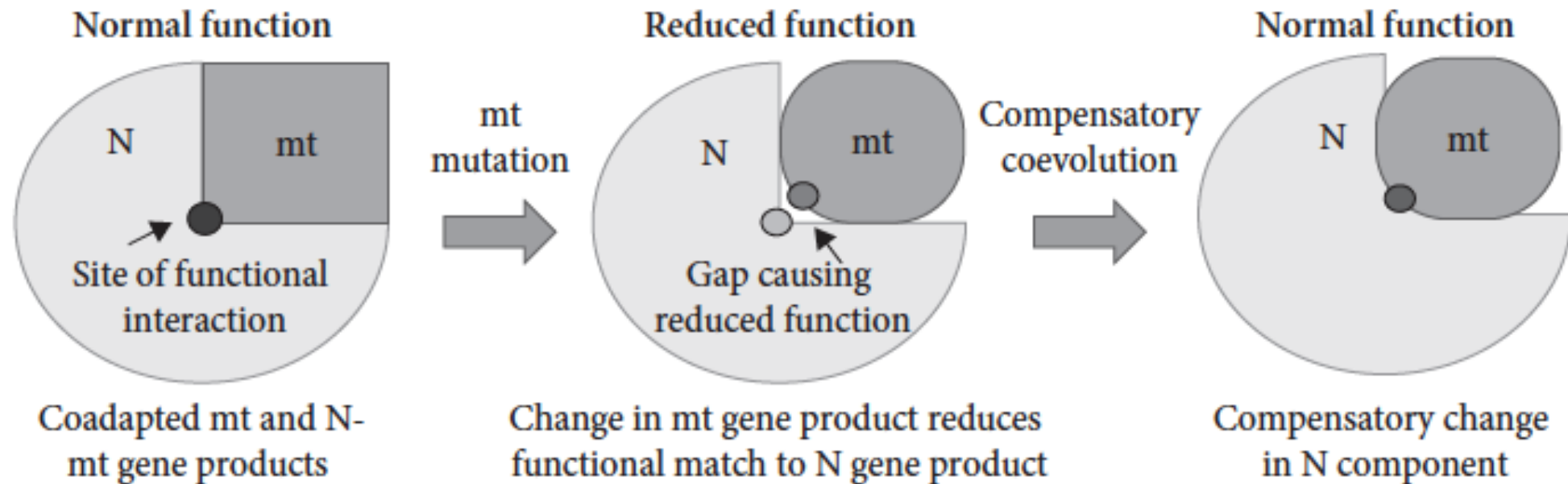


Cooper et al. 2015

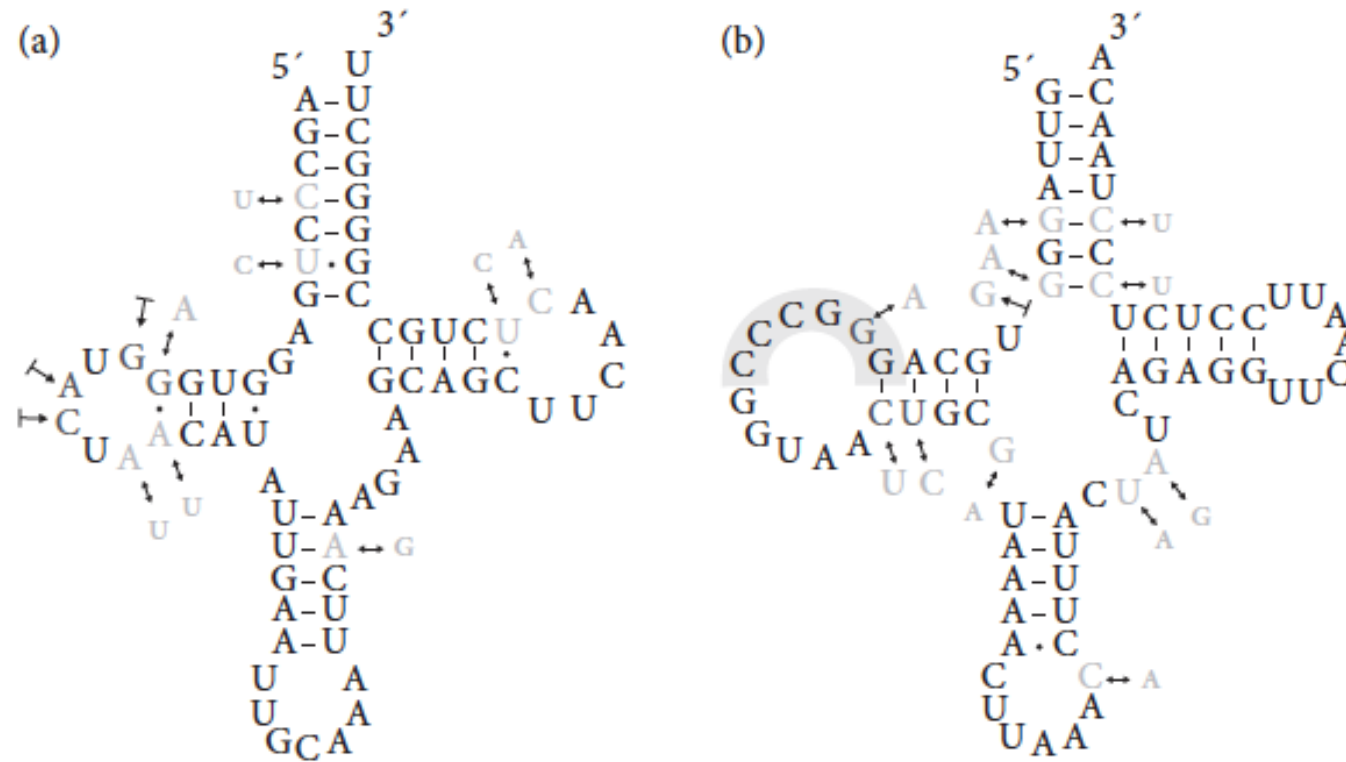


Christie et al. 2017

Nuclear compensation – the “evidence”

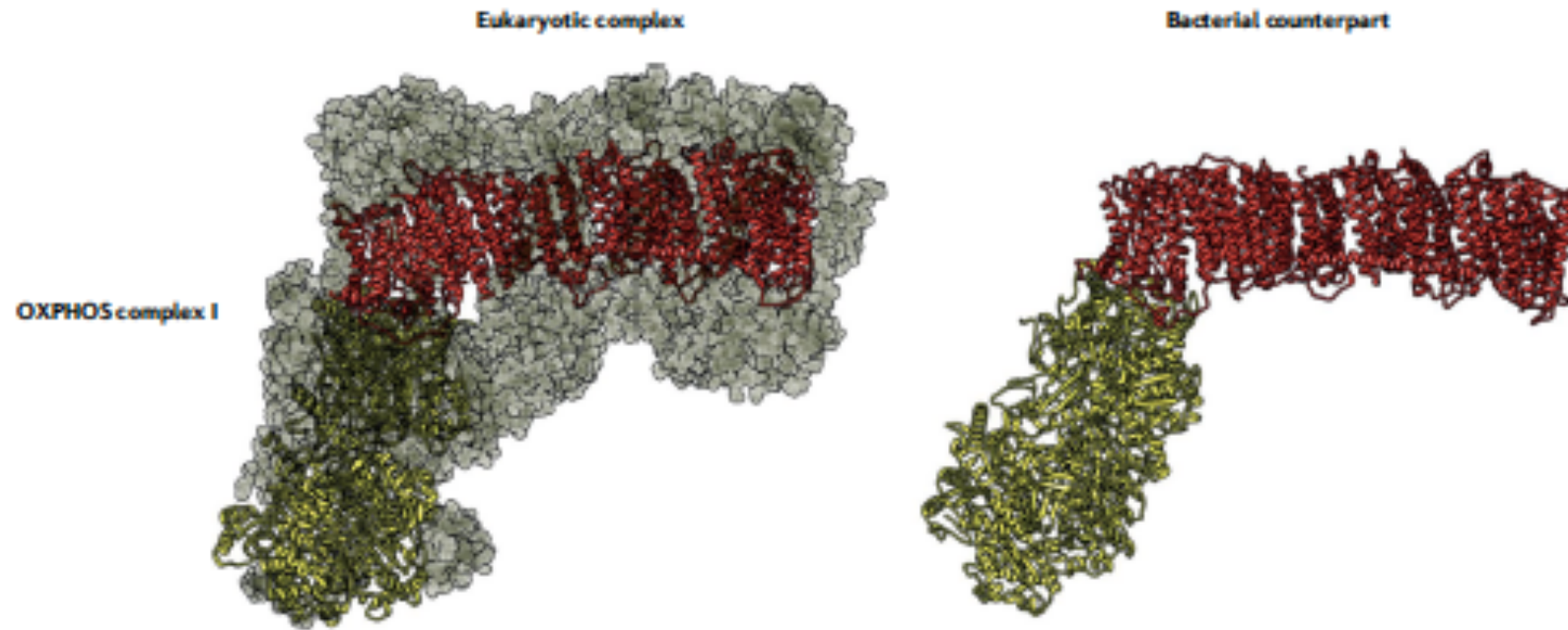


Nuclear compensation – the “evidence”



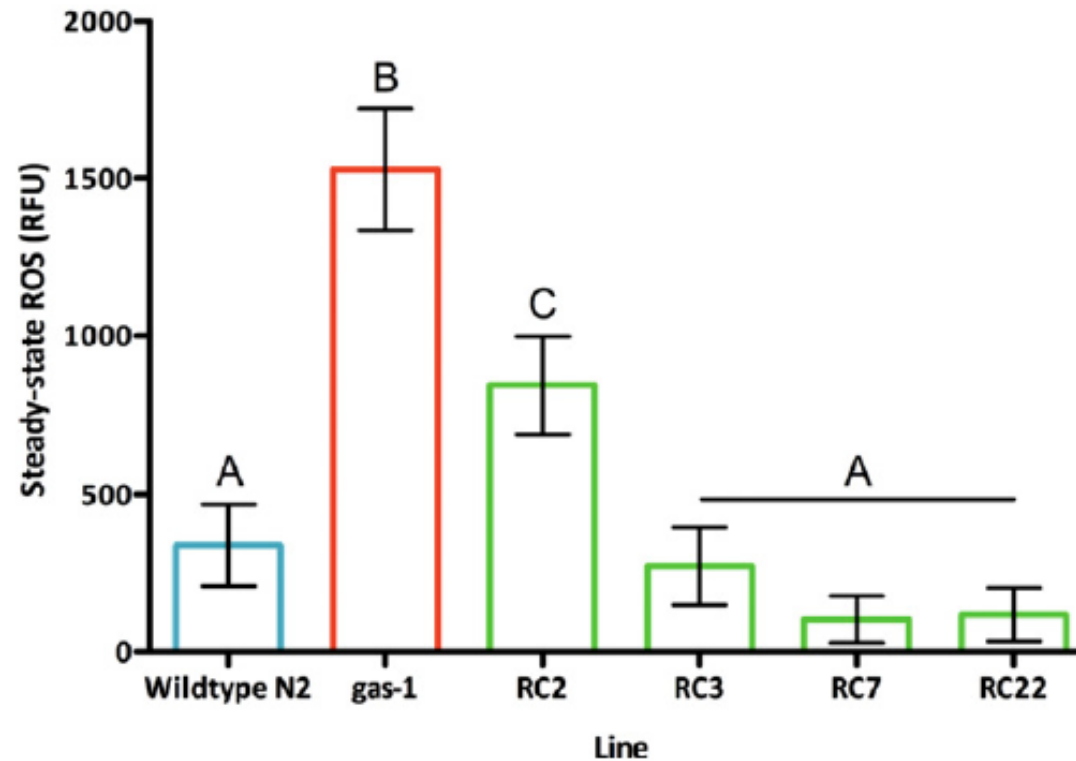
- Disease alleles in humans are common in animals

Nuclear compensation – the “evidence”



- Stability and supernumerary proteins

Nuclear compensation – the “evidence”



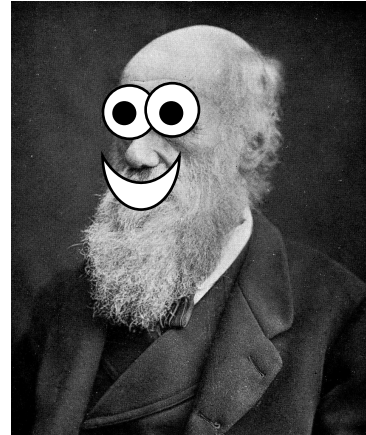
Wernick et al. 2019

- Gas-1 and restored fitness

Nuclear compensation – the “evidence”

- Disease mutations in humans
 - Supernumerary proteins and stability
 - Gas-1 and restored fitness
-
- Osada and Akashi 2012

d_N/d_S as a metric for molecular evolution

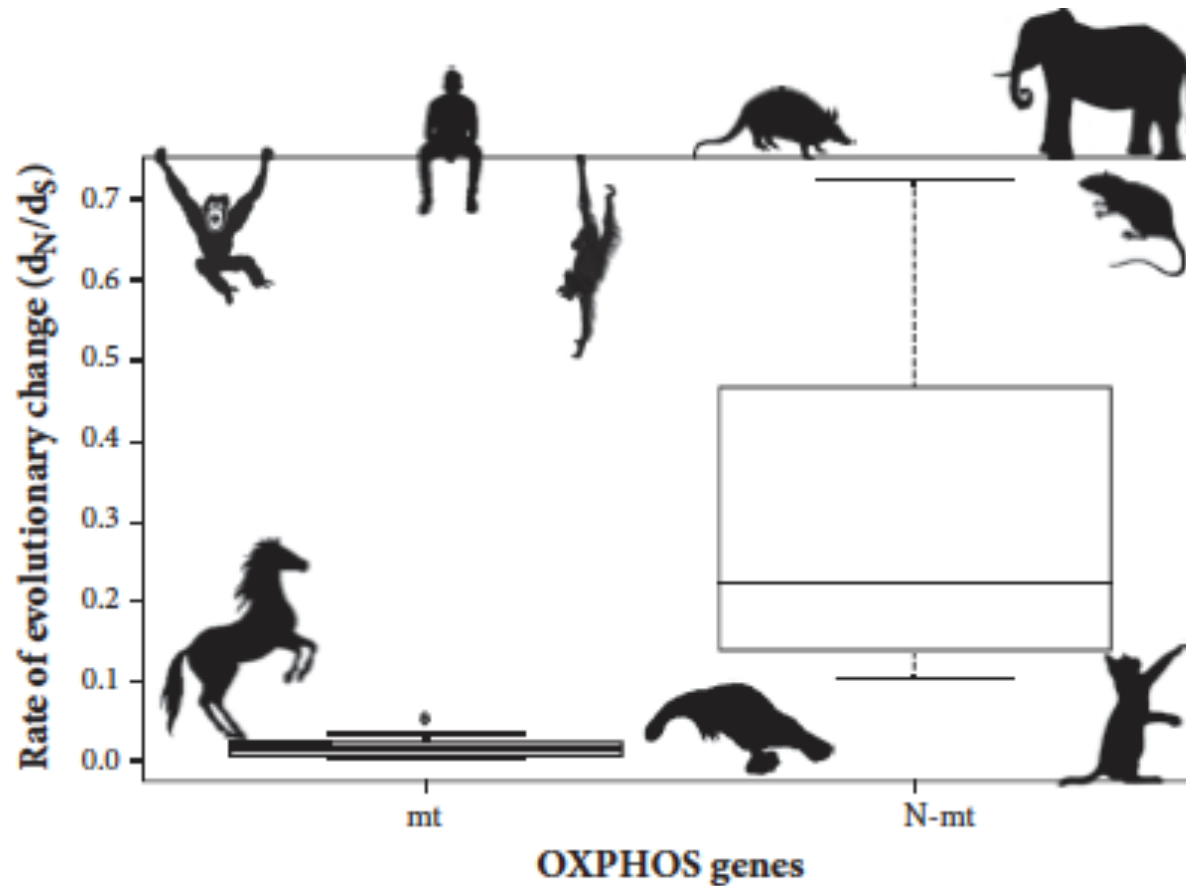


- $d_N/d_S < 1$
 - Most mutations are deleterious
 - Negative selection dominates
 - Most functional genes
- $d_N/d_S = 1$
 - Mutations are neutral
 - Drift dominates
 - Pseudogenes
- $d_N/d_S > 1$
 - Mutations are beneficial
 - Positive selection dominates
 - Immune genes

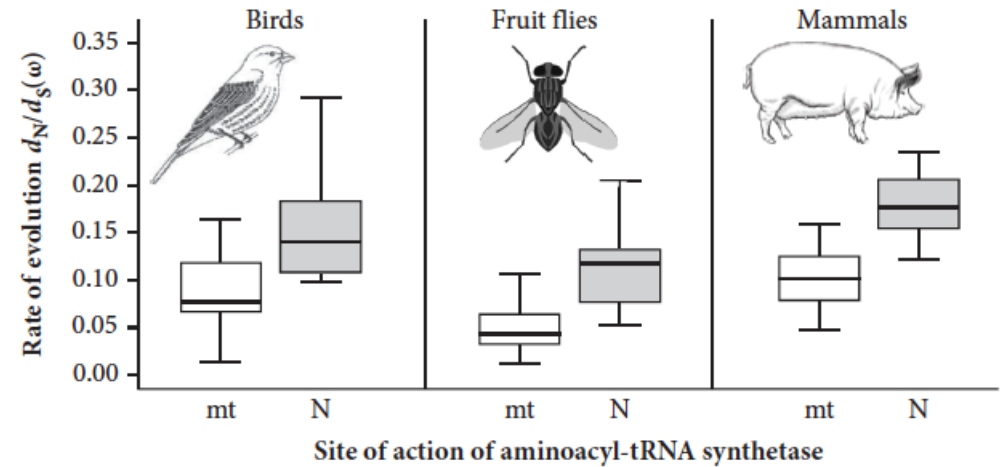
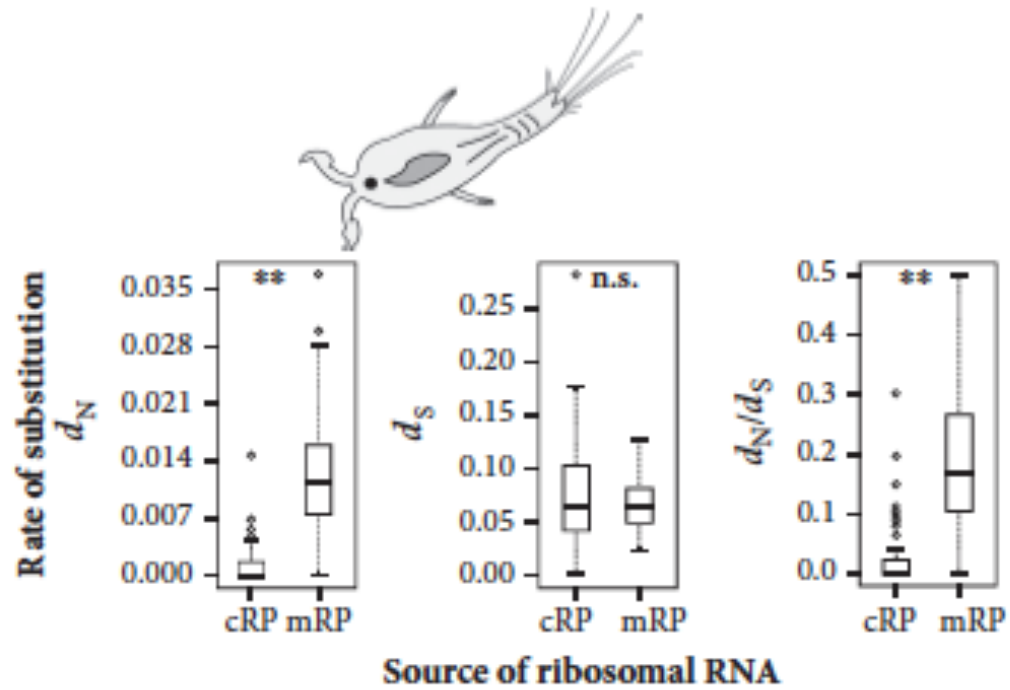
Human locus (No. comparisons)	Antigen recognition site (ARS) ($N = 57$)		Remaining codons in exons 2 and 3 ($N = 124$)	
	d_S	d_N	d_S	d_N
A (45)	32.8 ± 8.8	39.3 ± 5.0	30.4 ± 6.0	$12.9 \pm 2.9^{**}$
B (36)	29.4 ± 8.0	36.6 ± 4.4	32.0 ± 6.0	$14.4 \pm 2.0^{**}$
C (27)	27.7 ± 7.8	35.4 ± 4.8	36.5 ± 7.8	$14.8 \pm 2.0^{**}$
Mean (108)	30.4 ± 8.0	37.4 ± 4.2	32.5 ± 5.8	$13.9 \pm 1.8^{**}$
$d_S > d_N : d_N > d_S$		22 : 86		108 : 0

Hughes and Nei 1998

dN/dS ratios are elevated in N-mt compared to mt genes



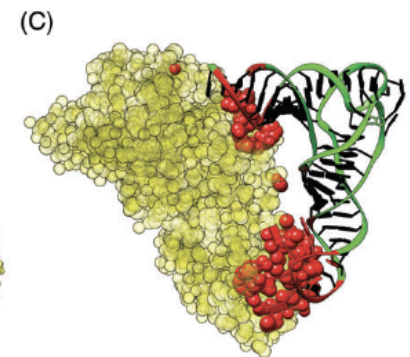
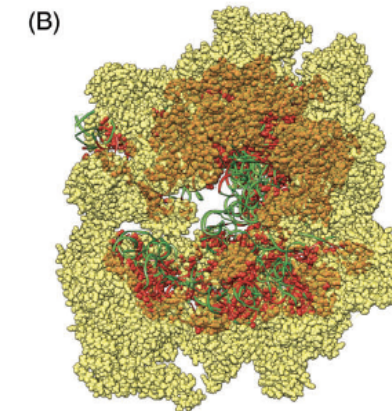
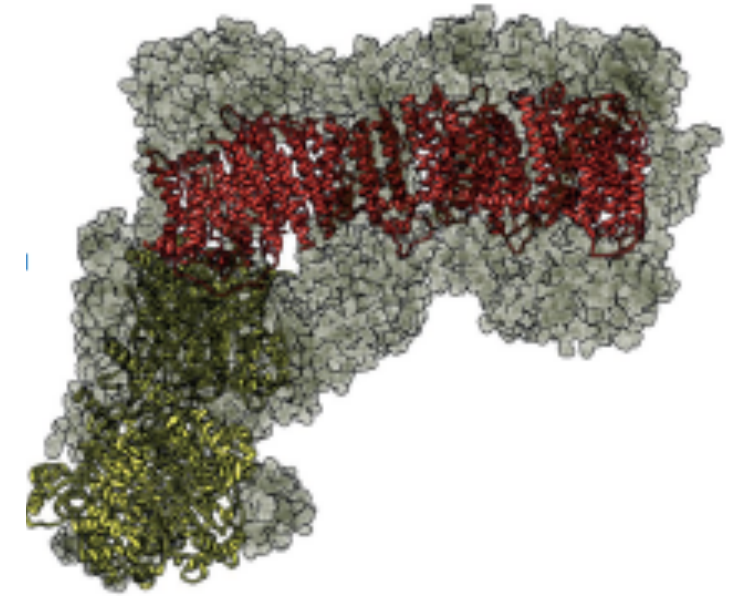
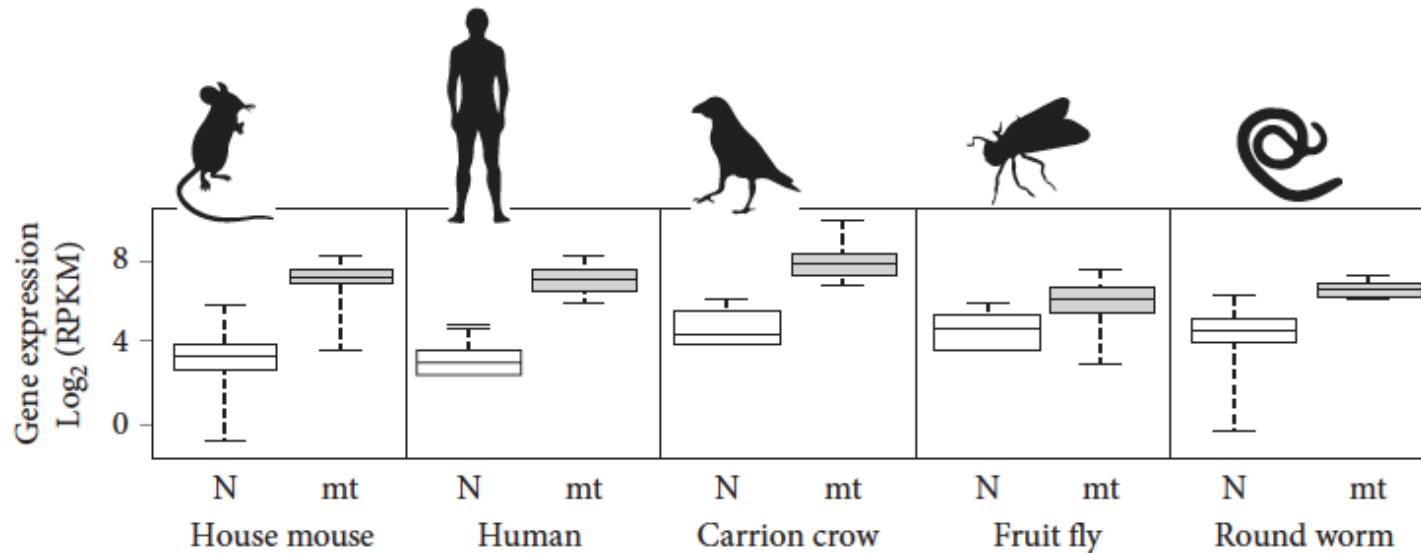
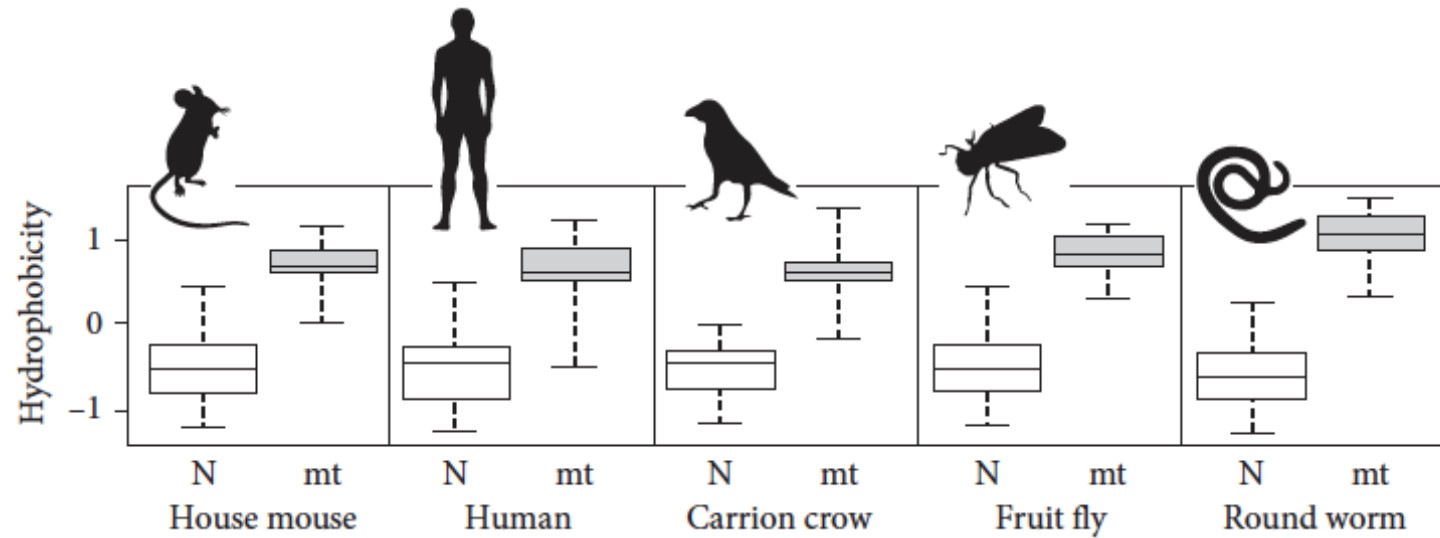
dN/dS ratios are elevated in N-mt compared to control N genes



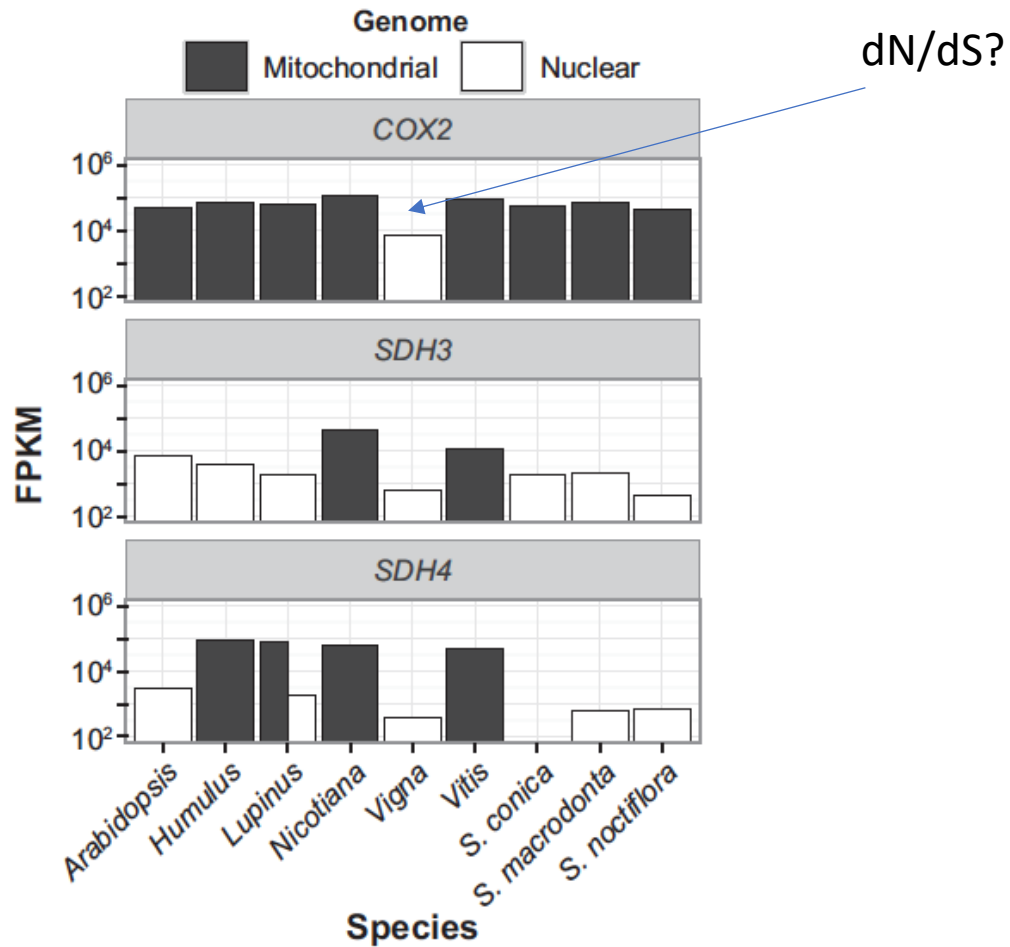
Why elevated dN/dS ratios?

- Almost always $\ll 1$
- Increase due to positive selection for coevolutionary nuclear changes
- Increase due to relaxed purifying selection

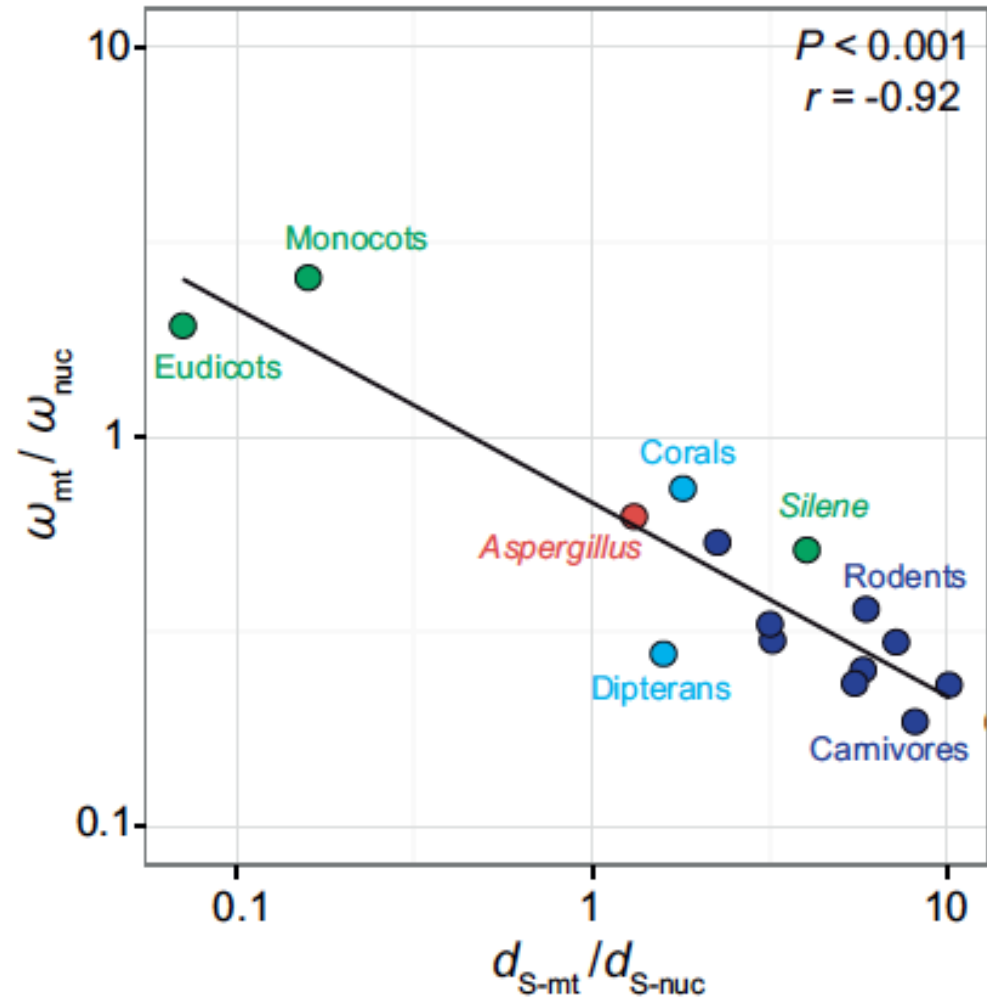
Reasons to expect relaxed relaxed selection



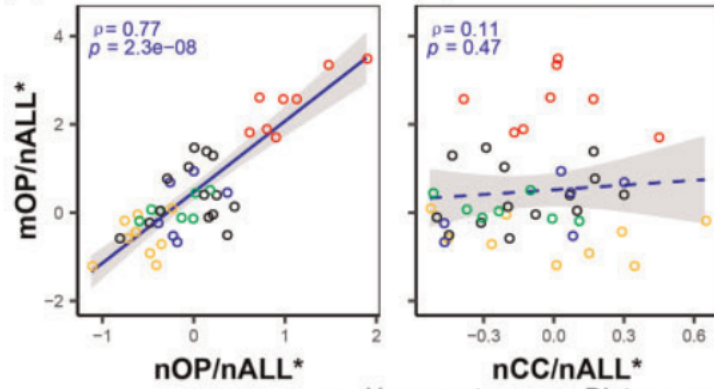
Using plants to disentangle these ideas



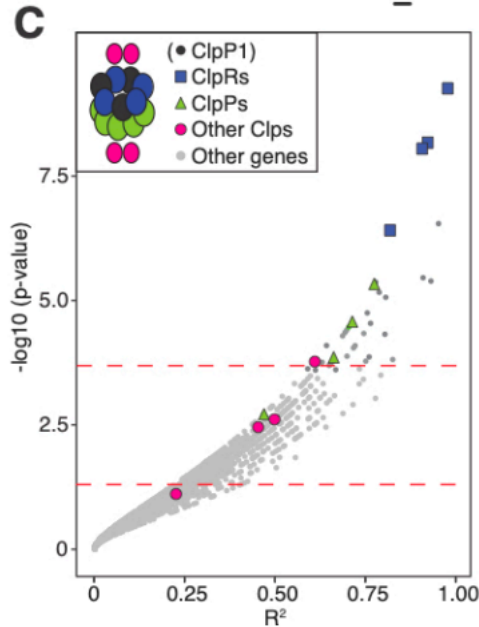
Havird and Sloan 2016



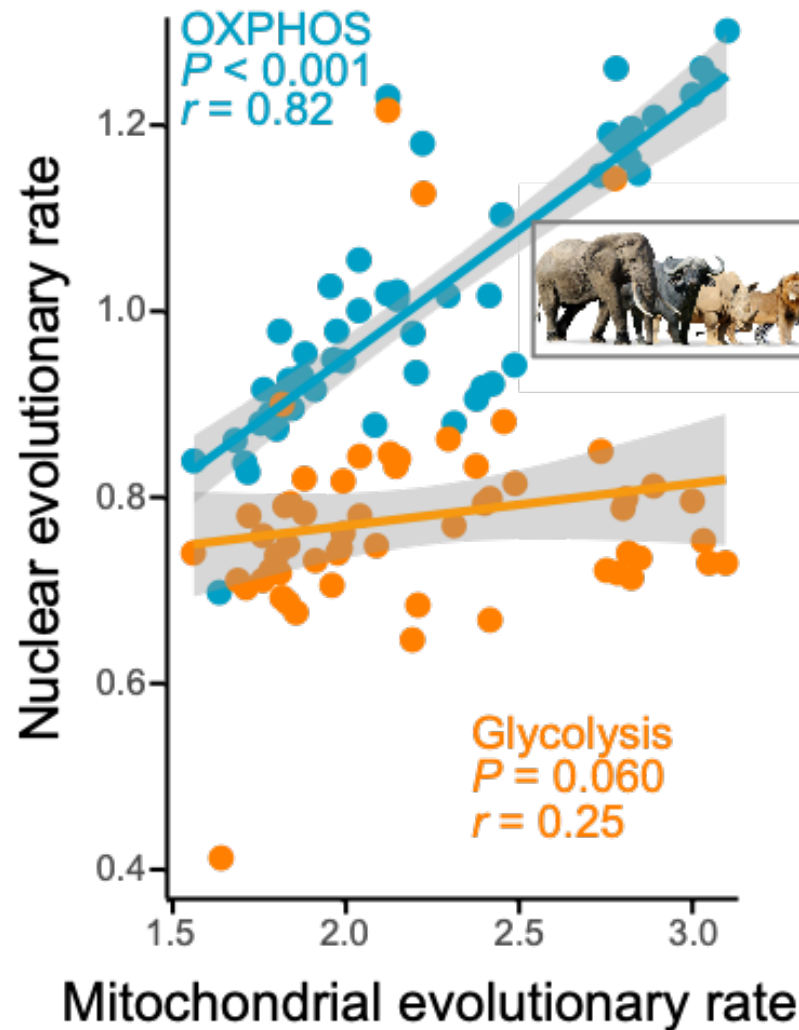
Evolutionary rate correlations



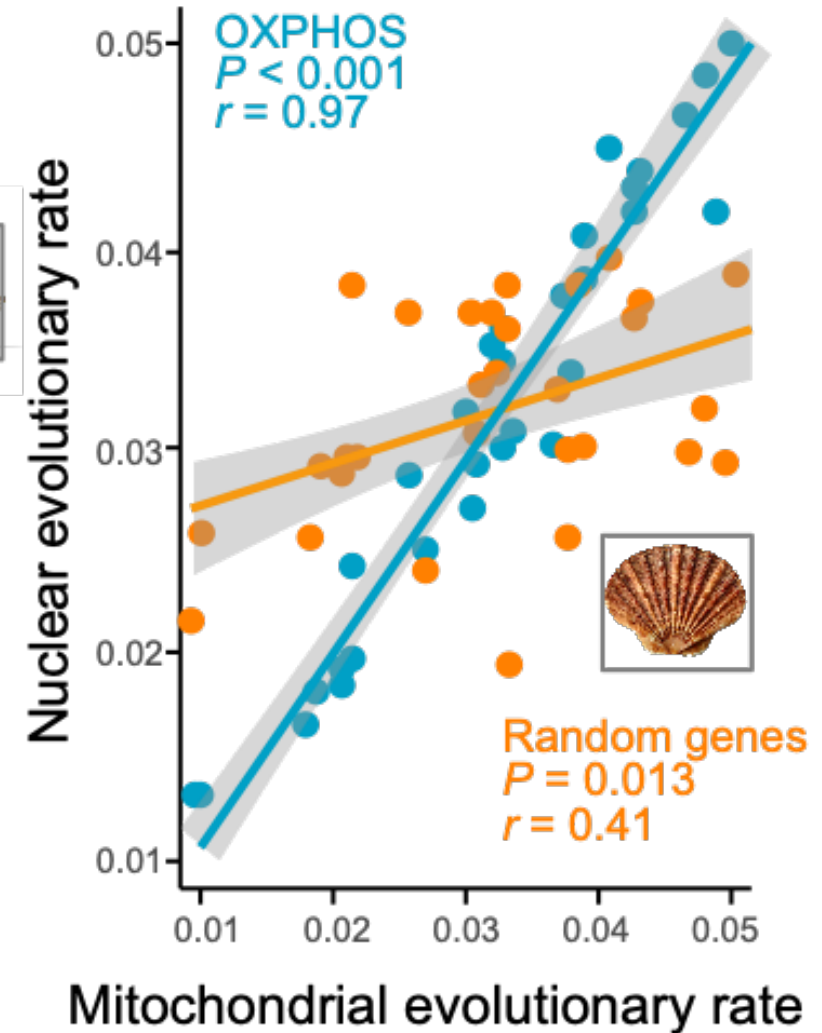
Yan et al. 2019 – Insects



Forsythe et al. 2021 – Plants and clp



Weaver et al.



Piccinini et al. in review

Supernumerary subunits and constructive neutral evolution

- Adaptation precedes deleterious mutation
- Likely happening in lots of PPR editing
- Not compensatory coevolution

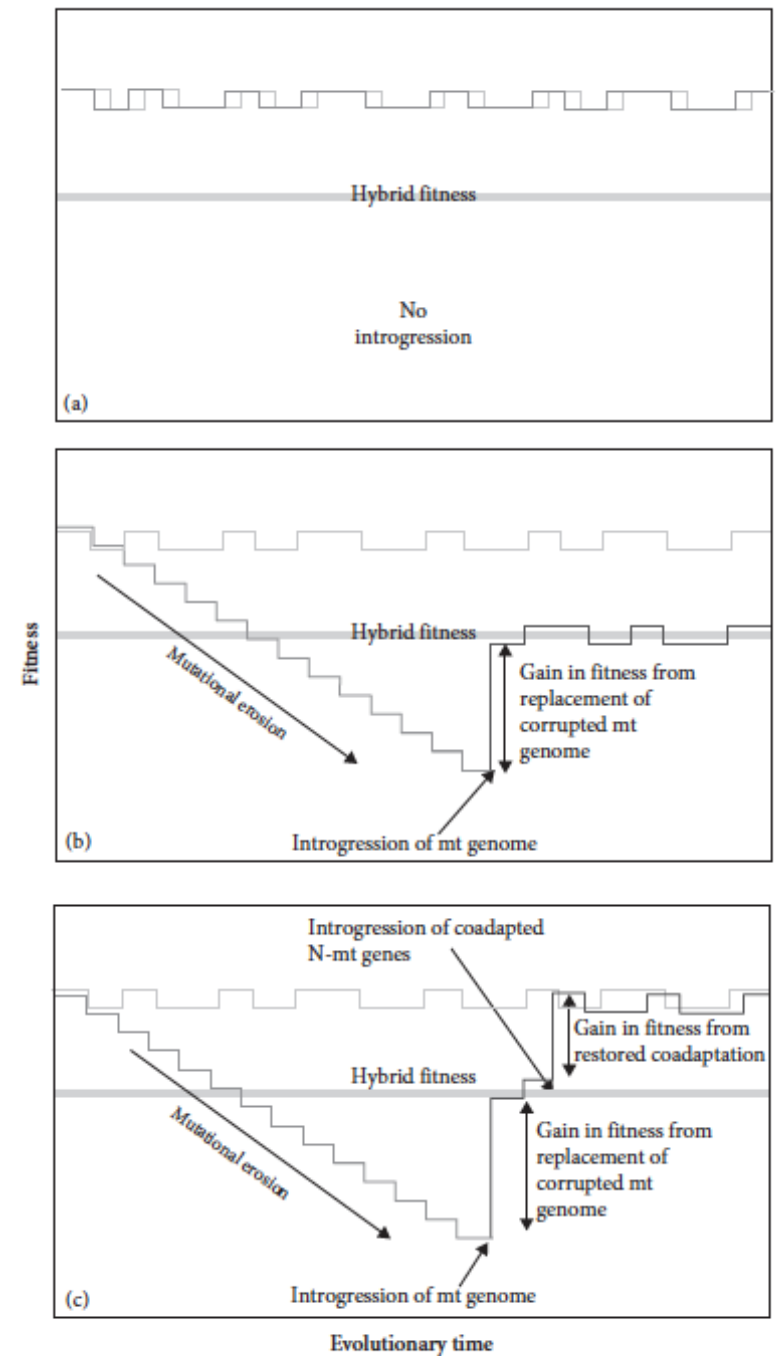
- “Gap filling” hypothesis

- Interesting CII stuff

Mt rescue introgression

- Co-introgression
- Fitness tradeoffs
- Little data

- Not nuclear compensation



Mt rescue introgression

- Complete vs. ongoing replacement

