Outline

- Brief background and examples of natural selection
- dN/dS as a tool to measure the action of natural selection, explained using the first counting method for estimating dN/dS (Nei-Gojobori, 1986) and its extensions.
- Codon substitution models the basis of modern (1998-) dN/dS estimation approaches
- Confounding processes (synonymous rate variation, recombination, multiple nucleotide substitutions)
- On the suitability of dN/dS for within-species inference

- Different types of selection analyses enabled by dN/dS, told by examples from West Nile virus and HIV and analogies from image analysis
 - Gene-wide selection (BUSTED)
 - Lineage-specific selection (aBSREL)
 - Site-level episodic selection (MEME)
 - Site-level **pervasive** selection (SLAC, FEL, FUBAR)
 - Relaxed or intensified selection (RELAX)
 - Detecting differences in selective pressure (Contrast-FEL)

A bit of trivia

- The theory of natural selection was first proposed by ...Patrick Matthew
- Matthew seemed to regard the idea as more or less self-evident and not in need of further development.
- In a stunning example of how **not** to communicate science, he published his ideas in appendices B and F of his book "On Naval Timber and Arboriculture" (1831).
- Unsurprisingly, his peers failed to discover his ideas in such an obscure source, and

his work had no impact on the subsequent, more developed, work of Darwin and Wallace (1859).

Do not emulate Patrick Matthew.

