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.