

# 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.



**NATURE'S LAW OF SELECTION.**

TRUSTING to your desire that every man should have his own, I hope you will give place to the following communication.

In your Number of March 3d I observe a long quotation from the *Times*, stating that Mr. Darwin "professes to have discovered the existence and *modus operandi* of the natural law of selection," that is, "the power in nature which takes the place of man and performs a selection, *ad sponte*," in organic life. This discovery recently published as "the results of 20 years' investigation and reflection" by Mr. Darwin turns out to be what I published very fully and brought to apply practically to forestry in my work "*Naval Timber and Arboriculture*," published as far back as January 1, 1831, by Adam & Charles Black, Edinburgh, and Longman & Co., London, and reviewed in numerous periodicals, so as to have full publicity in the "*Metropolitan Magazine*," the "*Quarterly Review*," the "*Gardeners' Magazine*," by London, who spoke of it as *the* book, and repeatedly in the "*United Service Magazine*" for 1831, &c. The following is an extract from this volume, which clearly proves a prior claim. The same volume contains the first proposal of the steam ram (also claimed since by several others, English, French, and Americans,) and a navy of steam gun-boats as requisite in future maritime war, and which, like the organic selection law, are only as yet making way:—

"There is a law universal in Nature, tending to render every reproductive being the best possibly suited to its condition that its kind, or that organised matter, is susceptible of, which appears intended to model the physical and mental or instinctive powers, to their highest perfection, and to continue them so. This