

# NG86 limitations: averaging across all sites in a gene

- **Different sites in a gene will be subject to different selective forces.**
  - *A gene-wide* measure of selection is going to average these effects.
- **Most** sites in **most** genes will be maintained by purifying selection.
  - **Positively selected sites** are of great biological interest, because they point to how a particular gene can respond to selective pressures.
  - **Negatively selected sites** are also of interest, because they point to functional constraint, and could be used to guide drug or vaccine design.
- **We must develop methods** that are able to disentangle the contributions of individual sites.

# Any questions on the previous material?



- **We have covered:**
  - 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)
  - **Next section:** Codon substitution models — the basis of modern (1998-) dN/dS estimation approaches