

Purpose-built models

- It is tempting to “hack” existing tools to answer questions that they are not designed to answer
- A recent example we tackled is a rigorous test for relaxation of selection (or more generally a difference in selective regimes) in a part of the tree, relative to the rest of the tree
- Typical approaches have been to estimate dN/dS ratios from two sets of branches, and interpret an *elevation* in dN/dS as evidence of selective constraint relaxation
- Two problems with this approach:
 - An increase in mean dN/dS could also be caused by an **intensification** of selective forces.
 - *Post-hoc* analyses (e.g., estimate branch-level dN/dS and then compare [t-test, etc] them as if they were observed quantities) discard a lot of information (e.g., variance of individual estimates), and make obviously wrong assumptions (e.g., estimates are uncorrelated).

Reference Branches

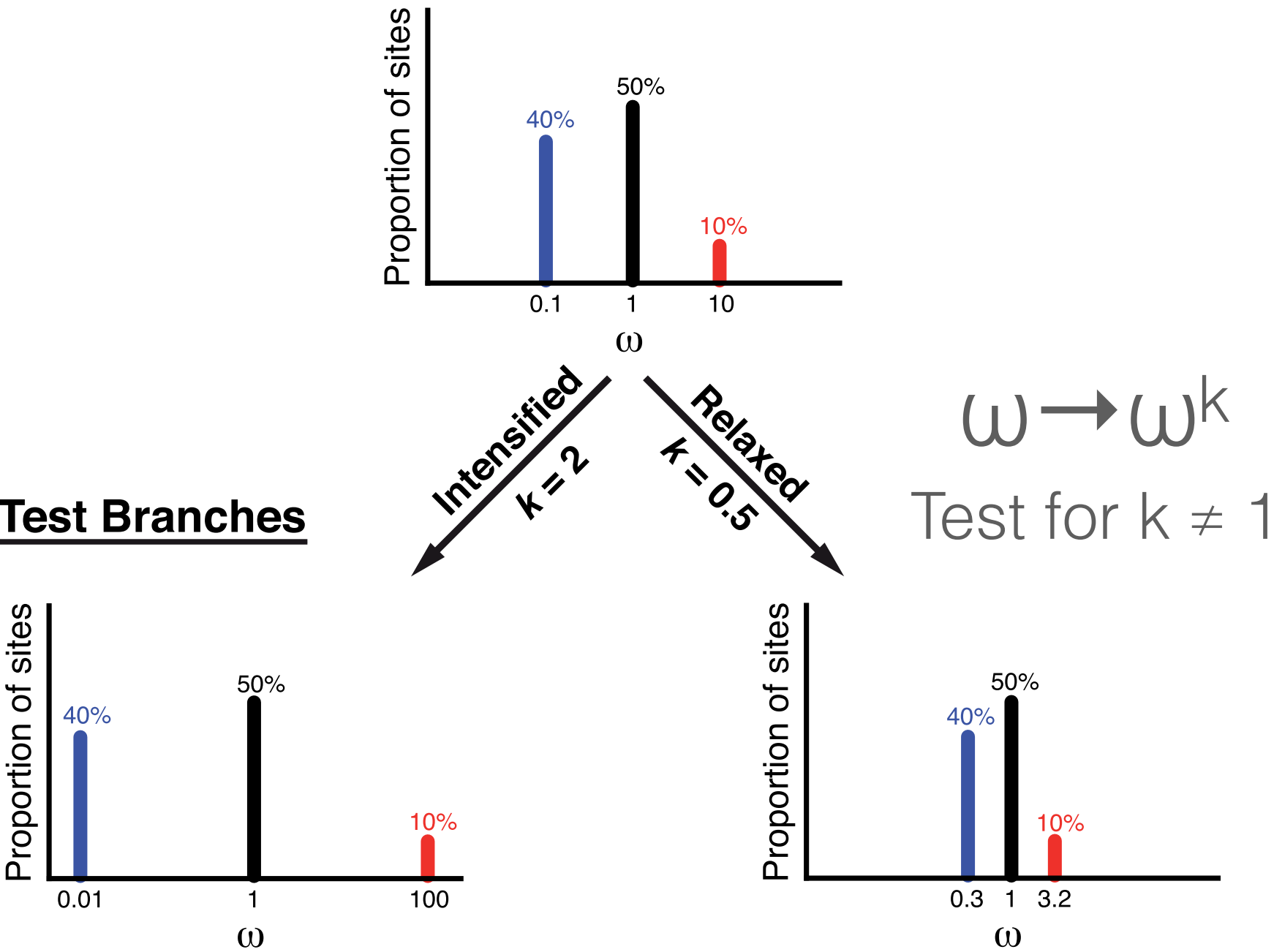


Table 1. Test for Relaxed Selection Using RELAX in Various Taxonomic Groups.

| Taxa | Gene/Genes | Test Branches | Reference Branches | <i>k</i> ^a | <i>P</i> -Value |
|--------------------------|------------------------------------|--|---|-----------------------|-----------------|
| <i>γ</i> -proteobacteria | Single-copy orthologs | Primary/secondary endosymbionts | Free-living <i>γ</i> -proteobacteria | 0.30 | < 0.0001 |
| | | Primary endosymbionts | Free-living <i>γ</i> -proteobacteria | 0.28 | < 0.0001 |
| | | Secondary endosymbionts | Free-living <i>γ</i> -proteobacteria | 0.61 | < 0.0001 |
| Bats | SWS1 | Primary endosymbionts | Secondary endosymbionts | 0.56 | < 0.0001 |
| | | HDC echolocating and cave roosting (pseudogenes) | LDC echolocating and tree roosting (functional genes) | 0.16 | < 0.0001 |
| | | LDC echolocating | Tree roosting | 1.07 | 0.577 |
| | M/LWS1 | HDC echolocating and cave roosting | LDC echolocating and tree roosting | 0.70 | 0.495 |
| | | Echolocating species | Tree- and cave-roosting species | 0.21 | 0.0005 |
| | | HDC echolocating | LDC echolocating | 0.84 | 0.427 |
| Bornavirus | Nucleoprotein | Endogenous viral elements | Exogenous virus | 0.02 | < 0.0001 |
| <i>Daphnia pulex</i> | Mitochondrial protein-coding genes | Asexual | Sexual | 0.63 | < 0.0001 |

^aEstimated selection intensity.