Less Is More: An Adaptive Branch-Site Random Effects Model for Efficient Detection of Episodic Diversifying Selection

Martin D. Smith,[1] Joel O. Wertheim,[2] Steven Weaver,[2] Ben Murrell,[2] Konrad Scheffler,[2,3] and Sergei L. Kosakovsky Pond*,[2]

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- Best-in-class power
- Able to detect episodes of selection, not just selection on average at a branch
- Does not make unrealistic assumptions for tractability, improves statistical behavior

- Sample size is ~sites, branch level rate estimates could be imprecise
- Cannot reliably estimate which individual sites are subject to selection
- Exploratory testing of all branches leads to loss of power for large data sets (multiple test correction)

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- Fix the tree; estimate and fix some of the nuisance model parameters that are shared by all branches
(GTR biases, frequency counts)
- Fit a simple baseline model (one ω per branch); use this model to get initial guesses for all other parameters
- Perform a greedy step-up procedure (like forward variable selection in regression models, but not as statistically bad)
- For each branch (longest first) try two ω rate classes, then three ω rate classes etc, until no more goodness-of-fit improvement (AIC-c)
- Fix the number of rates and move on to the next longest branch
- Perform selection testing on the overall model (different number of ω classes on branches), using the likelihood ratio test
- Each branch specified a priori (could be all branches)
- Appropriate multiple testing correction