


Allowing multi-nucleotide substitutions

- Some of the methods (e.g. BUSTED, aBSREL, RELAX) can extend substitution models to allow instantaneous double- and triple-“hits” (e.g. ACC to AGG)
- Sometimes multi-nucleotide changes along short branches at a single site can drive selection signal (possible false positives?)
- HyPhy includes a simple standard analysis for estimating alignment-wide multiple-hit rates.

JOURNAL ARTICLE

Evolutionary Shortcuts via Multinucleotide Substitutions and Their Impact on Natural Selection Analyses

Alexander G Lucaci, Jordan D Zehr, David Enard, Joseph W Thornton, Sergei L Kosakovsky Pond 

Molecular Biology and Evolution, Volume 40, Issue 7, July 2023, msad150, <https://doi.org/10.1093/molbev/msad150>

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Extra base hits: Widespread empirical support for instantaneous multiple-nucleotide changes

Alexander G. Lucaci , Sadie R. Wisotsky , Stephen D. Shank, Steven Weaver, Sergei L. Kosakovsky Pond 

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[See the preprint](#)

Examining multinucleotide substitutions

Site Substitutions



Evidence Ratio Thresholds

Use the sliders or input to specify the evidence ratio range of each respective model. For example, if three-hit substitutions with 3H+ support are defined as those occurring at sites with $ER(3H+:2H)>5$, set 3H+ range to a minimum of 5 but leave all other settings to their respective maximum ranges.

Use the **# of nucleotide changes** slider to specify the minimum number of substitutions to display.

