Based on the likelihood ratio test, there **is** evidence of *episodic diversifying* selection in this dataset (p=0.000).

BUSTED analysis (v4.0) was performed on the alignment from /Users/sergei/Dropbox/Talks/VEME-current/data/HIV-sets.fas using HyPhy v2.5.40. This analysis **did not include** site-to-site synonymous rate variation.

Suggested citation: Gene-wide identification of episodic selection, Mol Biol Evol.

32(5):1365-71, Synonymous Site-to-Site Substitution Rate Variation Dramatically Inflates False Positive Rates of Selection Analyses: Ignore at Your Own Peril, Mol Biol Evol. 37(8):2430-2439

threshold	10	Update			
16 sequences in the alignment	•	288 codon sites in the alignment	•••	1 partitions	^
26 median branches/par used for testing	rtition 🗬	3 classes non-synonymous rate variation		None synonymous rate variation	
0.0 p-value for episodic diversityfing selectio	+ +	13 Sites with ER≥10 for positive selection	4	N/A:N/A Multiple hit rates (2H:3H)	Ф

Alignment-wide results

Evidence ratio

AIC-c Params. Rate distribution Model Rate plot Log (L) -2039.96 4170.83 Unconstrained model 45 **Tested ω** 0.5596 (86.941%) 0.9885 (10.960%) 96.09 (2.0981%) Mean = 2.611, CoV = 5.24220 40 60 80100 Constrained model -2078.31 4245.48 44 Tested ω 1.000 (14.819%) 1.000 (20.229%) 1.000 (64.952%) Mean = 1.000, CoV = NaN 73

Gene-wide selection analysis using a branch-site method (BUSTED), HIV-1 env

hyphy busted --srv No --alignment data/HIV-sets.nex --starting-points 5

Produces *HIV-sets.nex.BUSTED.json* file View in http://vision.hyphy.org/BUSTED or https://observablehq.com/@spond/busted

BUSTED inference

- Because BUSTED is a random-effects method, it pools information across multiple sites and branches to gain power
- The cost to this pooling is lack of site-level **resolution**, i.e., it is not immediately obvious which sites and/or branches drive the signal
- Standard ways to extract individual site contributions to the overall signal is to perform a post-hoc analysis, such as empirical Bayes, or "category loading"
- For BUSTED, "category loading" is faster and experimentally better
- Can also compute exploratory evidence for selection support along individual branches at specific sites