

FEL on internal branches of Spike finds most selected sites, including many known to be of functional significance

Codon	Partition	alpha	beta	LRT	Selection detected?
5	1	0.000	19.047	2.891	Pos. p = 0.0891
12	1	0.000	20.331	2.990	Pos. p = 0.0838
18	1	0.000	19.108	2.886	Pos. p = 0.0893
138	1	0.000	26.726	2.738	Pos. p = 0.0980
367	1	0.000	44.298	9.049	Pos. p = 0.0026
439	1	0.000	34.504	4.989	Pos. p = 0.0255
452	1	0.000	30.455	5.519	Pos. p = 0.0188
477	1	0.000	23.695	4.327	Pos. p = 0.0375
501	1	0.000	38.294	3.319	Pos. p = 0.0685
570	1	0.000	21.078	3.049	Pos. p = 0.0808
614	1	0.000	22.071	3.101	Pos. p = 0.0783
681	1	0.000	18.297	2.820	Pos. p = 0.0931
1176	1	0.000	21.975	3.040	Pos. p = 0.0812

`hyphy fel --alignment data/spike.fas --tree data/spike.tree --branches Internal`

More accurate testing via parametric bootstrap

- P-values for MEME/FEL etc are derived from asymptotic approximations (large N)
- Not clear how well these hold for smaller and low-divergence datasets
- Can use a **much slower** simulation based method to derive more accurate p-values at each site
- Can result both in improved power and lower rates of false positives