

- Sensitive dN/dS ( $\omega$ ) models can “zoom-in” on small fractions of alignments
- Those could (should\*) be real biological features indicative of accelerated evolutionary rates
- But they can (and often appear to be) artifacts due to MSA/sequence quality issues
- These apparent issues remain even after applying current state-of-the-art

MSA/filtering tools (e.g. PRANK, PREQUAL) in this space

- Need a method to separate the signal from the noise
- What are some obvious evolutionary features of the noise?
- We developed this method out of necessity, because the signal was being overwhelmed by the noise in high-throughput screens for selection.

- Let's examine another example (from Zoonomia), where we downsample the genes down to 16 species (using **treemer**)
- Two genes that show evidence of episodic positive diversifying selection
  - One likely “real”
  - One likely “not real”
  - How can we tell?