

Thesis Changes Log

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PhD Program: Life sciences

Title of Thesis: Positive selection in parallel evolution

Supervisor: Prof. Georgii Bazykin

The thesis document includes the following changes in answer to the external review process.

Comment from Prof. Hahn:

I would like to see a bit more detail related to my comment 5 in the original review of the thesis. In particular, in your response you provide a mathematical way to understand $dP: M/M+N$. I want to understand why "N" here in dP is so different from the divergent sites counted in the original method. Is there a reason that counting it your way leads to better measures of parallelism and selection?

Answer:

Now probabilistic approach is added to demonstrate differences between the methods. It is described at the beginning of Chapter 3 (sections 3.2.4 and 3.2.5, pages 35-42).

In brief, I would say that P test, applied to AC substitution type, normalizes rate of parallel (A,C)(AC) substitutions by rate of single (A,C) substitutions. Negative selection at nonsynonymous sites can only decrease the number of AC_AC patterns comparative to the number of AC single substitutions.

Traditional test, applied to AC substitution type, normalizes rate of parallel (A,C)(A,C) substitutions by rate of different divergent substitutions: (A,C)(A,T), (A,C)(A,G), (A,C)(C,T), (A,C)(C,G) and (A,C)(T,G). If negative selection constraints allow parallel substitutions, but prohibit divergent, it will decrease the denominator for nonsynonymous sites and thus give higher rate of nonsynonymous parallel evolution, than for synonymous.

Comment from. Prof. Kondrashov:

I would like to see a very short discussion on what factors other than positive selection for parallel non-synonymous substitutions could explain $P > 0$. If no such factors come to mind, I think that it would be sufficient to discuss how ruggedness of the landscape does not influence this pattern.

Answer:

I expect that Prof. Kondrashov meant explanations for $P > 1$. I added discussion of possible causes of adaptive parallel evolution at the end of Chapter 3 (Discussion section, second and third paragraphs from the end, page 67). Explanation of reasons, for which P test can not give values higher than one under purely negative selection are added to the beginning of Chapter 3 (sections 3.2.4 and 3.2.5, pages 35-42).