

Jury Member Report – Doctor of Philosophy thesis.


Name of Candidate: Anastasiia Stoliarova

PhD Program: Life Sciences

Title of Thesis: Genomic patterns of epistasis at macro- and microevolutionary scales

Supervisor: Professor Georgii Bazykin

Name of the Reviewer:

<p>I confirm the absence of any conflict of interest</p> <p>Prof. Dmitry Ivankov</p> <p>(Alternatively, Reviewer can formulate a possible conflict)</p>	 <p>Date: 09-11-2021</p>
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The purpose of this report is to obtain an independent review from the members of PhD defense Jury before the thesis defense. The members of PhD defense Jury are asked to submit signed copy of the report at least 30 days prior the thesis defense. The Reviewers are asked to bring a copy of the completed report to the thesis defense and to discuss the contents of each report with each other before the thesis defense.

If the reviewers have any queries about the thesis which they wish to raise in advance, please contact the Chair of the Jury.

Reviewer's Report

Reviewers report should contain the following items:

- Brief evaluation of the thesis quality and overall structure of the dissertation.
- The relevance of the topic of dissertation work to its actual content
- The relevance of the methods used in the dissertation
- The scientific significance of the results obtained and their compliance with the international level and current state of the art
- The relevance of the obtained results to applications (if applicable)
- The quality of publications

The summary of issues to be addressed before/during the thesis defense

In the presented PhD thesis “Genomic patterns of epistasis at macro- and microevolutionary scales” Anastasia Stolyarova investigated evolutionary patterns arising due to epistasis at different evolutionary distances.

The thesis has a clear structure containing six chapters: Introduction (Chapter 1), Literature Review (Chapter 2), three chapters describing the obtained results (Chapters 3-5), and Conclusions (Chapter 6). The title of the dissertation reflects its actual content.

Chapter 3 is devoted to the consequences of epistasis on the intra-species level using as an object a hyperpolymorphic species *Schizophyllum commune*. Anastasia managed to find the inter-species evidence of epistasis as an excess of linkage disequilibrium between nonsynonymous alleles. To my knowledge, it is currently the only evidence of epistasis at the intra-species level.

Chapter 4 is devoted to the consequences of epistasis on the dense pool of evolutionary closely related species. Anastasia found several short bursts of nonsynonymous substitutions during the evolution.

Chapter 5 is devoted to the analysis of entrenchment and senescence in the course of evolution. Anastasia first obtained the results in the simulations and then demonstrated the found patterns in the evolutionary data. According to the results, entrenchment is coupled with sites under negative selection while senescence is observed for the sites under positive selection.

The organization of the Chapters 3-5 is typical for a publication: the chapters have Introduction, Methods, Results, and Discussion subsections.

I would stress a very high quality of the Introduction (Chapter 1) containing a comprehensive review of epistasis studies.

A couple of comments:

1. Page 17: Terms ‘smooth function’ and ‘simple function’ should be commented, at least. Better, they should be defined and commented.
2. On page 72, Anastasia writes “*The potency of any kind of selection increases with the amount of variation; for epistatic selection, however, this increase is expected to be faster than linear, because it depends on the number of possible allele combinations.*” On page 34, Anastasia writes “*At the same time, epistasis reduces the set of available evolutionary pathways ...*” These two factors seem to have opposite influence on the rate of evolution. However, on page 72 Anastasia mentions only one factor and does not discuss the other. The influence of reduced set of evolutionary pathways on the rate of evolution (or its irrelevance) should be commented.

However, these comments does not influence the overall high quality of the thesis. The results of the presented theses and corresponding publications are scientifically significant and comply with the international level and current state of the art. The work is perspective for fundamental research and may be potentially useful in the future for protein design. The publications are of high quality, the number of publications suits the requirements for a PhD thesis.

To summarize, I rate the PhD thesis of Anastasia Stolyarova as an important, of a high quality and scientifically significant.

Provisional Recommendation

I recommend that the candidate should defend the thesis by means of a formal thesis defense

I recommend that the candidate should defend the thesis by means of a formal thesis defense only after appropriate changes would be introduced in candidate's thesis according to the recommendations of the present report

The thesis is not acceptable and I recommend that the candidate be exempt from the formal thesis defense