

Jury Member Report – Doctor of Philosophy thesis.

Name of Candidate: Bogdan Kirillov

PhD Program: Life Sciences

Title of Thesis: Uncertainty Quantification and Neural Network Interpretation for studying CRISPR mechanics

Supervisor: Assistant Professor Maxim Panov

Name of the Reviewer: Mikhail Gelfand

I confirm the absence of any conflict of interest

Date: 12-09-2023

Reviewer's Report

The problem addressed in the thesis, off-target activity prediction for CRISPR-Cas gene editing systems is of obvious practical relevance. The author suggests two interesting solutions that are intended to work as filters on the top of string search tools providing an initial, draft solutions. The developed methods are based on modern techniques and approaches not used in bioinformatic applications so far. At that, the results are quite novel. The provided benchmarks demonstrate that the developed methods outperform the current state-of-the-art programs or are at least as good, with explainability being an additional bonus.

The conclusions are clear and solid.

The structure of the thesis is traditional (Introduction - Review - Methods - three chapters on results - Discussion and Conclusions). The paragraphs in the chapters are well-structured and logical.

The review is well written with a smooth transition between the biological background and experimental details necessary to formulate the problem.

Previous research in the area of (off)-target identification is well summarized. Several general, relevant concepts (black box vs. white box systems, uncertainty quantification, interpretability, anomaly detection, etc.) are described well.

A strong feature of the text is that the main ideas are not only introduced formally, but also described at the level of the main underlying ideas.

The results are clear and described well. However, I would prefer a less autobiographical approach to Conclusions: instead of a passive mode "such and such methods were introduced" just highlight the performance and observations. It might be a good idea to separate the "subjective" conclusions (what has been done) and the "objective" ones (actual results and observations).

A more constrained style definitely would look better (e.g. in the first few sentences of the Abstract: "illusory simplicity", "limitless amounts", "immense pool"). However, this is a matter of taste. My other editorial remarks have been taken care of at the pre-defense stage.

The publication requirements are satisfied - two first-author papers in good journals (NAR, Sci. Rep.), four presentations at reputable international conferences (MCCMB, CRISPR, BelBI), of which two are immediately relevant to the thesis topic.

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