MUNI SCI Department of Mathematics and Statistics

Reviewer's evaluation of the dissertation thesis of Rimjhim Tomar

University: Charles University, Second Faculty of Medicine
Program, branch: Doctoral studies in Biomedicine, Biomedical informatics

Student's name: **Rimjhim Tomar**
Thesis title: *Statistical models of information processing in neuronal systems*

Reviewer's name: **Ondřej Pokora**
- institution: Department of Mathematics and Statistics, Masaryk University

The dissertation thesis of Rimjhim Tomar consists of five manuscripts in the area of mathematical modeling, mathematical and computational biology, and computational neuroscience. In general, the manuscripts deal with the (time-dependent) firing rate from several points of view. Under the so-called rate coding hypothesis (one of the neuronal coding hypotheses), the firing rate (number of generated action potentials per time unit) represents the intensity (strength) of a stimulus. The statistical and information-theoretical properties of the neuronal code are subjects of intense studies from different perspectives, and aims to advance the understanding of the nervous system and brain function through computational approaches. Hence, the research topic of this thesis is very current.

The included manuscripts are supplemented with chapters containing fundamentals of description of neuronal activity, measures of variability and randomness of neuronal activity, state-of-the-art mathematical models of a neuron, and briefly summarizing the most important results from particular manuscripts.

The manuscript *Review: Methods of firing rate estimation* was published in the *Biosystems* journal. It is a review of methods for firing rate estimation from experimental or simulated data, which is a necessity under the rate coding paradigm. Although there is nothing substantially new in the paper, the review is a well-written comprehensive overview of the classical and state-of-the-art methods. Rimjhim Tomar summarized the general concept of firing rate and time-dependent firing rate. The technical aspects and applications of several methods are accompanied by the original and recent references. Rimjhim Tomar is the sole author of this paper. The review has been cited nine times so far.

The manuscript *Variability and Randomness of the Instantaneous Firing Rate* published in the *Frontiers in Computational Neuroscience* focuses on the mathematical concept of instantaneous firing rate in order to analyze the variability and randomness of steady-state neuronal firing rate in different statistical models and experimental data recordings. The novel finding is that the relationship between the variability and randomness of interspike intervals and the instantaneous firing rate is not straightforward and unique and essentially depends on the choice of the mathematical model and probability distribution of the interspike intervals. This is an important result for saying that the properties of the instantaneous firing rate can be influenced by the improper choice of the model of neuronal firing. This could lead to refinements or improvements in methods of estimation of the instantaneous firing rate. Rimjhim Tomar is the first and corresponding author of the paper; the second author is the supervisor of the thesis.

The manuscript *A simple neuronal model with intrinsic saturation of the firing frequency* was published in *Biosystems*. The paper investigates whether and how the saturation of the firing rate (which is experimentally observed) may arise in four classical neuronal models without introducing the refractory period directly. The novel finding is that the inclusion of the reversal potential into the leaky integrate-and-fire model does not induce saturation of the firing rate and that the *two-point model with the reversal potential* is capable of mimicking the saturation phenomenon. Rimjhim Tomar is the first (and corresponding) of three co-authors. The paper has already been cited.

In the manuscript *Plant odor background may increase coding efficiency of moth pheromone receptor neurons*, firing rate estimation methods are used to quantify the coding efficiency of moth olfactory receptor neurons when subject to pheromone stimulation under volatile plant compound backgrounds. Based on the experimental data, the authors come to a new (surprising) finding that under higher concentrations of the volatile plant compound, the average neuronal response is suppressed but the coding efficiency of the signal can be raised. Rimjhim Tomar is the first of six co-authors.

In the manuscript *Effects of spike frequency adaptation on neural response variability*, the authors show that two broadly used neuronal models of spike-frequency adaptation (with after-hyperpolarization current and dynamic threshold) differ in their impact on the response variability (expressed by the Fano factor) of a neuronal network. This finding emphasizes the important role of the spike frequency adaptation mechanism for accurately modeling the variability of response in neuronal networks. Rimjhim Tomar is the first of three co-authors.

Summary: The research presented in the dissertation thesis of Rimjhim Tomar makes a significant contribution to the area of computational neuroscience, particularly to better understand the statistical and information-theoretical properties of the firing rate and coding efficiency. The first three included manuscripts have already been independently assessed within the peer review process and published in high-quality scientific journals. *Biosystems* focuses on the intersection of biology and systems theory with computational approaches, covering mathematical modeling, computational neuroscience, computer science, physics, and engineering. As of 2023, it has an impact factor of 2.0 and is ranked in the Q3 quartile in the fields of biology and of mathematical and computational biology. *Frontiers in Computational Neuroscience* has a strong reputation for publishing high-quality research related to computational models, simulations of neural systems, brain-computer interfaces, neural data analysis, and theoretical neuroscience. As of 2023, it has an impact factor of 2.1 and is ranked in the Q2 quartile in the field of mathematical and computational biology and in the Q3 quartile in the fields of neurosciences.

The manuscripts and dissertation thesis demonstrate a solid understanding of the state-of-the-art in the area of computational neuroscience and mathematical models of single neuron. The methodology is clearly and appropriately described in a way that allows reproduction. Rules of good scientific practice are also adhered to. All classical and current references are mentioned. The methods are presented clearly, with the appropriate description of the mathematical background, statistical analysis, and biophysical interpretation. The results are discussed in a broader scientific context, potential impacts on further research are also mentioned.

Notes and questions: I found the statement on the contribution of Rimjhim Tomar only for the second manuscript. Please specify your contributions for the last three manuscripts, too.

The overall structure and content of the unpublished manuscripts correspond to the common requirements of the scientific papers. After a bit of spellchecking and minor corrections in mathematical terminology, they would be ready for submission. What journals do you (co-authors) consider for publication?

In general, the usage of logistic regression in machine learning procedures is very common. In the *Plant odor background may increase coding efficiency of moth pheromone receptor neurons* manuscript, the concept of such a learning is used for subsequent predictions of the presence of a stimulus and evaluation of the efficiency metrics. Do you know any references where the same idea was used specifically on neuronal recordings? For predictions, a *threshold* to decide the zero/one response based on the estimated probability is typically used. Is it also this case? If yes, how did you choose the value of the threshold?

Conclusion: In her thesis, the student demonstrated creative abilities in the field of computational neuroscience and prerequisites for individual scientific work. I recommend that her dissertation thesis be admitted for defense. Rimjhim Tomar's contribution to the research is sufficient to award her with a PhD.

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