FYZIOLOGICKÝ ÚSTAV AV ČR

Posudek školitele disertační práce Mgr. Daniela Šmíta
"Analysis of dynamical interactions of axon shafts and their biophysical modelling"

Školitel:
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The dissertation of Mr. Šmít presents a systematic analysis of the phenomenon of "axon zippering" and of its biophysical mechanisms. This phenomenon was very rarely examined in the previous literature, and was never studied systematically. Thanks to Mr. Šmít's work, this novel type of axon-axon interaction is now characterized, and its functional significance for neural development can now be investigated in future studies. A long article with the main results of the thesis is currently in press (and expected to appear before the defense date) in the prestigious interdisciplinary journal eLife (IF 8.303). The importance of Mr. Šmít's work is confirmed by the highly positive evaluation this paper received from eLife's editors and reviewers. A second paper (with a methodological contribution) already appeared in BMC Biophysics. In both these papers, Mr. Šmít is very deservedly the first author. He also successfully presented his results from this project at two international and two domestic conferences.

The project was developed since the very beginning in close collaboration with prof. Alain Trembleau at Université Pierre et Marie Curie. Experimental work was carried out in Paris, while the data analysis and mathematical modeling took place principally in Prague. This is reflected in the double doctorate (cotutelle) arrangement under which Mr. Šmít's research was carried out. The cotutelle was directly supported by a special stipend awarded by the French Embassy in Prague, which allowed Mr. Šmít to spend 4 months per year in prof. Trembleau's laboratory, during three consecutive years (2012-2015).

The extent of the work carried out by Mr. Smit is remarkable. He quantitatively analyzed a collection of about 30 video (time-lapse microscopy) recordings of a developing axonal network, which involved a painstaking segmentation of the individual images and the tracking of the developing geometry of the network. He personally took part in experiments in which the axon networks were manipulated by micropipettes, and he recorded the results of Biomembrane Force Probe experiments allowing to measure the mechanical tension in the axons. To carry out an efficient analysis of such experiments, he implemented a software package (BFPTool) that can be useful also to other biophysics labs; the software was publicly released on GitHub and an accompanying methodological article was published in BMC Biophysics. He implemented a detailed mathematical model of the dynamics of axon zippers, which helped us to establish that the axon zippering was controlled by a competition between mechanical tension and axon-axon adhesion. He carried out numerous calculations in order to analyze various biophysical aspects both on the level of individual axons or axon bundles and on the level of the networks formed by zippers.

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All these aspects of Mr. Šmít's research are described in detail in chapters 2 to 4 of the thesis. I wish to draw attention also to the carefully written Introduction (chapter 1), which summarizes both the neurobiological and the biophysical aspects of the background for the project. The thesis is rather long, but this reflects the amount of work carried out by Mr. Šmít.

In conclusion, I value very highly the work that Mr. Šmít carried out during his Ph.D. study. The obtained results, and the thesis itself, demonstrate that he successfully completed an interdisciplinary scientific training in biophysics and neurobiology. He showed capability to carry out highly original research and to function in the international scientific community. I therefore enthusiastically recommend that his dissertation thesis is admitted for defense.

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