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Uppsala, November, 2021

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Report

on the dissertation presented by **Shpilman Aleksei Aleksandrovich** termed "*Analysis and Computer Modeling of Microtubule Structures*" for degree of Candidate of Technical Sciences.

The goal of this thesis is to study microtubule structures from different aspects using computer analysis and modelling. The thesis is divided into four main parts 1) Microtubules and methods of analysis and modeling of their systems, 2) Methods of image analysis and imitational modeling and 3) Results of the analysis and modeling of microtubule systems. 4) Discussion of the results of image analysis and imitational modeling of microtubule systems. The author uses different approaches addressing both the dynamic, geometry, and self-assembly of the microtubule structures. The rich methodological approach involves analysis of microtubule network radiality via computer vision methods as well as modeling of microtubule network dynamics in cells geometry and modeling of microtubule structures assembly *in vitro*.

Important initial work was to create data sets of images of microtubule systems from CV1 cells under different concentration of stabilizing agents for the training of convolutional deep neural networks. The works has continued with several advanced steps of training deep neural networks. This has been essential to classify these image towards various architectures that are important for the microtubule function. The work proceeded with development of a computer model that recreates dynamics of the microtubule system inside of a cell of a complex geometry. This work has then enabled the author to perform experiments *in silico* with images of cells of variable geometry in order to study the effect of different geometries on the microtubule system. The author has subsequently developed a computer model of the assembly of the microtubule structures *in vitro* in a quasi-three-dimensional space. This model can consider both the microtubules and motor proteins in uniquely accurate manner. Overall, this has enabled an *in silico* modelling of many structures that are displayed *in vitro*.

It is notable that the authors have created a dataset and performed analysis of images of microtubule systems using both image analysis techniques and convolutional neural networks. The deep convolutional neural networks together with transfer learning seem to perform best for the task of classification of these images. Moreover, the work also describes creation of a computer program that allows modeling of the cell geometry including the dynamic and complex microtubules. The results suggest that using this approach it is possible to reproduce fairly complex phenomena that are observed *in vivo*.

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Furthermore, the author developed a model of microtubules self-organization in a quasi-three-dimensional space. This model seems to be able to reproduce many of the important structures.

This work is overall novel and may have useful application for other structures depending on further development. The thesis is based on several publications that many are published in proceedings to important international conferences. Overall, the work shows high level of innovation and creativity. The biological relevance is also clarified and this work provides a solid foundation for work on the structures of microtubule but also has general international value outside of the field of microtubule. Some of the highlights include presentation of a novel algorithm based on the cluster analysis of the brightest pixels. Moreover, the deep learning approach for the microtubule image classification is novel and may have applications for different problems. The computer model of dynamic cellular microtubules shows intricate effects of cellular geometry on the dynamic and state of the microtubule network which is very interesting. Overall the unique dataset that were created allow for testing various computer vision methods that can be used for further methodological development.

I also present some remarks for further developments of these concepts and for future publications. The work could be aided by clearer benchmarking and discussion of the competing and alternative approaches. More effort could be set to perform direct comparative experiments and clarify the state-of-the-art within the field. It is also recommended to understand and describe the strength and weaknesses of the particular data sets and try to receive access to additional data sets in order to further strengthen the argumentation and to better understand the limitations of the approaches.

Overall, this is a novel, well written, interesting and innovative thesis with substantial amount of high quality experiments. Based on this assessment, I am pleased to recommend that this work is awarded with a degree of Candidate of Technical Sciences.

Best regards

09.11.2021

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