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It is my great pleasure to wholeheartedly recommend the PhD. thesis of Štěpán Timr for defense.

Štěpán started working with me in 2011 within the realm of his Master thesis and has then continued his work in my group as a PhD. student. Currently, he has already handed his PhD. thesis and is expected to defend it in September 2017. Štěpán has gained extended scientific experience already during his undergraduate years, primarily via research summer schools at the Academy institute in Nove Hradky. In particular, he mastered there the technique of two-photon fluorescence microscopy and applied it to studies of membrane processes in living cells. I find it quite amazing that his undergraduate work resulted in two beautiful scientific papers, from which one was published in Nature Methods.

Štěpán came to my group upon recommendation of his summer school advisor and my colleague Dr. Josef Lazar. Apparently, Štěpán decided that he wants to broaden his knowledge and skills toward molecular simulations. As a result, “poor” Štěpán has been “caught” in-between our two groups doing both molecular modeling and experiments aimed at developing fast fluorescence techniques for detection of action potentials of neurons. The ultimate goal is to follow using optical techniques in real time the excitation transfer between nerve cells in the brain. We are at the very beginning of this long path, nevertheless,

Štěpán has already completed a “proof of principle” study showing that with the aid of molecular simulations we are able to precisely determine by two-photon fluorescence spectroscopy the actual orientation of a dye in a cellular membrane. This study, as well as another modeling study on cholesterol uptake in lipoprotein particles to which Štěpán contributed were both published in the Journal of Physical Chemistry B. In the last year of his PhD Štěpán fully focused on an ambitious project he himself devised, which aims at elucidating the role of recoverin in light adaptation in the rod cells during the vision process. An early success of this project is a paper published most recently in ACS Central Science describing the detailed molecular mechanism of anchoring of recoverin in the membrane via a myristoyl chain liberated upon calcium binding. During his PhD studies Štěpán also successfully completed a very demanding summer course in Biophysics and Computation in Neurons and Networks at Princeton University, where he broadened his horizon of modeling of neuronal processes.

Štěpán’s PhD thesis perfectly reflects both on the factual and formal sides the quality of his work and publications. Namely, after a thorough introduction to modeling of membrane systems it focuses primarily on two projects – modeling of the orientation of fluorescent probes in the membrane and of the molecular mechanism of the membrane-anchoring myristoyl switch in recoverin. On top of it, the thesis presents results of two other projects Štěpán participated on – modeling of membrane voltage and of cholesterol oxidation in lipoprotein particles. The corresponding four publications form an integral part of this high quality thesis.

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