CHARLES UNIVERSITY IN PRAGUE
1st MEDICAL FACULTY
INSTITUTE OF PATHOPHYSIOLOGY
12853 PRAHA 2, U Nemocnice 5
Head: Assoc. Prof. Martin Vokurka MD, PhD

From: Prof. MUDr. RNDr. Petr Maršálek, PhD. <Petr.Marsalek@lf1.cuni.cz>,
To: Prof. MUDr. RNDr. Jiří Beneš, CSc. <BenesJi@volny.cz>,
Subject board chair: Medical Biophysics, Charles University in Prague.
Carbon Copies:
Karolína Soukupová <Karolina.Soukupova@lf1.cuni.cz>, graduate studies section,
Alain Trembleau <Alain.Trembleau@upmc.fr>, advisor,
Martin Zapotocký <Zapotocky@biomed.cas.cz>, advisor,
Daniel Šmít <Daniel.Smit@centrum.cz>, candidate.

Report on a PhD thesis submitted by Mgr. Daniel Šmít:
"Analysis of dynamical interactions of axon shafts and their biophysical modelling. / Analýza dynamických interakcí těl axonů a jejich biofyzikální modelování".

The thesis describes both experimental and theoretical exploration of unique phenomenon of axonal growth captured as *in vitro/ ex vivo* preparation and as a theoretical model.

Fulfillment of formal requirements
The candidate published together with co-authors two original papers in journals with registered (and high) impact factors, both of them as a first author. I did not find on one place in the thesis or in the thesis extended summary notes describing the individual contribution of the candidate. But both the first positions in the author list and the thesis itself with many painstakingly elaborated details indicate that the candidate invested into the thesis vast amount of work.
The thesis contains more than 256 pages, not including Table of Contents and Abstracts. The thesis adheres to the recommendations of the subject board and contains all the prescribed sections with abstracts, keywords, legal statements et cetera. Overall formal aspects, text formatting, figure preparations, and so on, are of excellent quality and much above the average. In particular, I should highlight the very good quality of Figures. Also the subtitles of text margins are nice and help reader in cross-referencing the text.

Methods and models
The thesis uses a well documented methodology. Uses of equations, physical and mathematical descriptions, numerical computations and statistical processing of the results adhere to good standards used in the field. I cannot comment that much on the experimental investigations, but it is my understanding that the main contribution of the candidate is the theoretical physical description of the subjects, as he comes from the field of theoretical physics.

Originality and novelty of results
The main topic and its mathematical and computational study are an original contribution of the candidate to the mechanics of developing, renewing, and regenerating *in vitro/ ex vivo* tissue preparation, which is a biological and theoretical model of what is taking place *in vitro/ in situ*. This is also demonstrated by publishing the two papers in prestigious international journals. Since these two manuscripts underwent a detailed peer review, this shows the acceptance of them by the academic community.

Minor comments, typographical errors, questions/ comments for the defense.
P. xi: Upper/ lowercase: Abstrakt v (č)eštině; Fig 1.12b: Question: Is the icon thereof a standard symbol of molecular motors in mechanical circuits, besides spring and dash-pot? Are there more symbols like this? Are there standard technical terms in the Czech language to denote these? P. 142, fig. 3.25 typo: ve(r)tex; P. 166 first line: repetition: neuronal neuronal.
While most of the thesis quite technical, I would also prefer to have parts with simplifications to guide me from simple to more complex. The thesis extended summary is very well prepared in this aspect. Regarding the thesis, it is hardly possible to read all the text. Finally, on page of the thesis 51 and Figure 1.13, I found the differential adhesion hypothesis, which sheds some light and gives a simple concept, what the highly technical preceding 50 pages are about.
Another question for the defense: Can you summarize in simplification, what is the relation between active and passive processes governing the axonal growth?

Conclusions
The candidate demonstrated his ability to work independently, produce results and present his work. The work is novel and is of high scientific merit. I recommend that the thesis is accepted in its current form. I recommend that after a successful public defense of the thesis,

Mgr. Daniel Šmít

is awarded the "Philosophiae Doctor (PhD)" degree, in the specialty of the medical biophysics.

signed

prof. MUDr. RNDr. Petr Maršálek, PhD.,
<Petr.Marsalek@LF1.cuni.cz>,
<Marsalek@PKS.mpg.de>,
cell phone: +420 777 009 314,
First Medical Faculty, Charles University in Prague
currently on leave at the
Max Planck Inst. for the Physics of Complex Systems,
Dresden, Germany.

Dresden, April 2017
Document no. PM-Rev-No-41-V2-2017