MASSACHUSETTS INSTITUTE OF TECHNOLOGY

BIOLOGICAL ENGINEERING DIVISION

DOUGLAS A. LAUFFENBURGER
Director
56-341
Cambridge MA 02139
617-252-1629 (telephone)
617-258-0204 (fax)
lauffen@mit.edu (email)

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Prof. Rob de Ruyter van Steveninck
Chair, Biocomplexity Search Committee
Department of Physics
Indiana University
Swain West 165
Bloomington, IN
Telephone: 812-855-6857

Dear Prof. de Ruyter van Steveninck:

I am extremely pleased to write in strong support of the application of **Dr. Ivan Maly** for a faculty position in biocomplexity at Indiana University. Dr. Maly is undertaking postdoctoral research work in my group, having joined us following completion of his PhD under the direction of Prof. Gary Borisy at Northwestern University. I am tremendously impressed with Ivan's intellect, knowledge, technical skills, and innovative thinking, and view him as a superb candidate for great success in an independent academic research and teaching career applying computational modeling methods to problems in cell biology. He clearly ranks with the best of my previous graduate students and postdocs who now hold tenured or tenure-track academic positions in this field, such as Jennifer Linderman (Professor, University of Michigan), Dan Hammer (Professor, University of Pennsylvania), Anand Asthagiri (Assistant Professor, Cal Tech), and Stas Shvartsman (Assistant Professor, Princeton University). Accordingly, I have every expectation that Ivan will prosper at any first-rate academic institution interested in his research program directions.

Ivan came to my laboratory having gained strong expertise in analysis of cytoskeletal dynamics from a quantitative biophysical perspective, and expressing the goal of learning about cell signaling dynamics from a quantitative biochemical perspective. His objective in establishing his own independent research program is to investigate, using computational modeling approaches in collaboration with experimental investigators, how biochemical signaling and biophysical cytoskeletal processes operate together in integrated fashion. This

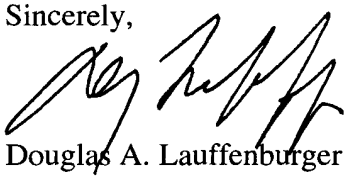
is a terrific direction to build a program toward, and I think Ivan is exceptionally well poised to undertake this with great success. His specific project efforts here have focused on two major topics: autocrine signaling circuits (in collaboration with Steve Wiley at Pacific Northwest National Laboratory along with myself), and cell signaling responses to mechanical stress (in collaboration with Roger Kamm here at MIT and Rich Lee at Harvard Medical School). Both topics involve interesting and complex spatiotemporal dynamics of EGF receptor signaling pathways which appear to play key roles in cell migration and cell growth. Medical applications of this work range across wound healing, epithelial morphogenesis, cancer, and cardiac tissue remodeling. Ivan has done a superb job of identifying important features of particular questions inherent in these problems which can be addressed powerfully using his strong computational skills – which include nonlinear ordinary and partial differential equation analysis as well as stochastic, Monte Carlo-type simulation methods. His first paper with me, recently accepted for publication in Biophysical Journal, examines whether an autocrine EGF receptor signaling circuit could be responsible for directionally-persistent cell migration; this concept was speculatively raised based on intriguing data from some earlier experimental work from our laboratory (Maheshwari et al., J. Cell Biol. [2001]) but had not been explored in terms of quantitative analysis of an underlying model for the positive and negative feedback loops – and their potential spatial localizations -- existing in the EGF receptor pathway. Ivan's analysis and results are tremendously exciting, and have spurred me to pursue this problem with a vigorous new set of experiments. This is, of course, the sort of outcome one always hopes for with theoretical/computational work – that it will not only interpret previous experimental observations but also further generate a next round of experimental studies to be undertaken, to continue to move the particular field of inquiry forward. Ivan's second paper here (now under review at Nature), in collaboration with Roger Kamm's group and also Jeff Drazen's at Harvard School of Public Health, achieves similar interpretive and predictive success; it describes how autocrine EGF receptor circuits may be crucially involved in proliferative responses of lung airway epithelial cells to compressive stresses. Here, Ivan served as the theoretical analysis contributor to a largely experimental effort. These two initial papers from Ivan's work here to date thus demonstrate two complementary facets of his talents: he can serve effectively as the lead investigator or as a supporting collaborator with experimental scientists. Both of these talents are important for building a successful program in computational cell biology, and in my experience here Ivan has proven to exhibit them splendidly. There will be at least two more papers to come before he finishes here, one on autocrine/paracrine EGF receptor signaling in cardiac myocyte growth and the other further development of the lung epithelial cell story.

Regarding personal qualities, Ivan is not only exceptionally bright but has an engaging intellect. He is someone who enjoys the give-and-take of science at its best, and can trade ideas with enthusiasm and respect rather than rancor and defensiveness. I

thoroughly enjoy our discussions, in which I must admit he more often than not gets the best of me! As I noted above, Ivan gets along well with others in the laboratory at all levels and from all backgrounds.

Overall, I can offer a most enthusiastic possible recommendation of Ivan Maly to you for your position. He is truly first-rate, and I expect him to become a leading figure in the field of computational biology.

Sincerely,



Douglas A. Lauffenburger
Whitaker Professor of Bioengineering
Biological Engineering Division,
Department of Biology, and
Department of Chemical Engineering