

Teterina, Yana A

From: Uli Jentschura [ulj@tqd1.physik.uni-freiburg.de]
Sent: Monday, January 19, 2004 7:30 AM
To: Teterina, Yana A
Cc: Curry, Errissa M
Subject: RESENDING Sergej Aksenov letter of reference

To Whom It May Concern

This letter concerns the evaluation of the research profile of Dr. Sergej Aksenov, now working at the University of Cambridge (United Kingdom), Department of Anatomy. It is a pleasure to write this letter of recommendation for Sergej, because I can personally vouch for his enormous programming skills, his intuitive grasp of the essentials related to a scientific problem, and his ability to work in a team of researchers diligently and with an excellent sense for the demands of cooperative research.

Dr. Aksenov has repeatedly proven his ability to work on a variety of subjects related to the mathematical modeling of biological processes. Details can be found in his curriculum vitae which I am sure he has already submitted to your laboratory. I would only like to mention his work on a stochastic model of a cluster of chemoreceptors in *Escherichia coli*. There are only few people in the world who master both: special functions, complex mathematical models and molecular biology at the same time: Sergej is one of them.

In addition, Dr. Aksenov has shown in the past an extraordinary ability to adapt to new situations, and to new countries and environments. He is truly an international person, and his loveable character and his extreme sense for cooperativity make him an ideal candidate for a lecturer position.

Dr. Aksenov has been working with me in the past on a project related to numerical algorithms for the calculation of a specific mathematical function known as the Lerch transcendent. We have been cooperating over large distances, and it has been a true pleasure to see the project emerge and be completed to perfection by Sergej.

I have personally been involved in cooperations with a number of scientists from different countries: among them Peter Mohr, Jean Zinn-Justin, Paul Indelicato, Krzysztof Pachucki, Savely Karshenboim, Valerij Serbo, and Ilya Ginzburg (USA-France-Russia).

As I learned from my past experience, cooperations are not always easy. With Sergej, it has always been a true pleasure to work and to discuss. His diverse abilities in different areas, his tremendous sense for working in a team and his tremendous commitment to the problem at hand should make him the ideal candidate for the open position.

In the case of any further question, please do not hesitate to contact me at Tel. +49 (761) 203 5956 or Tel. +49 (761) 503 1436 (evening hours) European time for any further information I can provide.

I wish Sergej luck in his new workplace, and may his efforts be crowned with as much pleasure in working, and with as much success as they have always been in the past.

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January 16, 2004

Professor James A. Glazier
Director, Biocomplexity Institute
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Dear Professor Glazier,

Subject: Recommendation of S.V. Aksenov

I am writing this letter of recommendation at the request of Dr. Sergei V. Aksenov, who I understand is applying for a faculty position. I have known Sergei since August 1997, when he was a graduate student working at the Joint Institute for Nuclear Research in Dubna, Russia. It was then that we met at a meeting in Sofia, Bulgaria (Destobio: International Conference on Deterministic and Stochastic Modelling of Biointeraction). After both giving talks on mathematical models of gene regulation, we started a conversation that ultimately led to a long-distance collaboration over a period of about a year (from late 1997 through early 1999).

The research problem that we addressed together relates to bacterial gene circuits involving a cascade of two regulator proteins. In these circuits, a regulator protein senses a signal and in response influences the expression of a second regulator gene, the product of which then influences expression of a set of effector genes, encoding proteins that carry out some function, such as metabolism. Our goal was to understand the functional implications of this genetic regulatory circuit design. The approach that we took was to compare "cascaded" or "two-step" circuits with "one-step" circuits involving only a single regulator protein. We formulated mathematical models for one- and two-step circuits and *a priori* criteria for functional effectiveness, such as stability, robustness, and temporal responsiveness. We then imposed constraints on parameters in the models to ensure one- and two-step circuits being compared were as much alike as possible. We required parameters unrelated to transcriptional control to have identical values in the models for alternative circuits, and we required alternative circuits to produce the same steady-state input-output behavior. Sergei discovered that one- and two-step circuits have few functional differences. At the end of the day, the only notable, inherent difference we could find was in temporal response. As intuition suggests, a two-step circuit responds more slowly to a signal than the equivalent one-step circuit. Sergei presented these results in a talk at the International Symposium on Power-law Modeling of Biological Systems held in Oeiras, Portugal. Work on this project did not progress to a publication, largely because of a lack of funding, which limited the time both of us were able to devote to it during the course of our collaboration, and then because of Sergei's moves to Michigan and Cambridge, where he took up new problems as a postdoc.

Sergei's sound analysis and commitment to our project were outstanding and exceeded my expectations, especially given that we had no funding whatsoever for it. The time he devoted to the project was his own free time, and he did the far greater portion of the work involved, including the first draft of a manuscript, which was nicely written.

I am confident that Sergei's work with me will soon reach fruition in the form of a publication. I have recently received funding to study design principles of bacterial gene circuits, and it is now evident that studies of two-step circuits are critically needed. Work in 2002 of Alon and co-workers, published in *Nat. Genet.*, indicates that one- and two-step circuits are among the most important classes of gene circuits (or network motifs) in the genetic regulatory network of *E. coli* (and probably other bacteria). Compared with our theoretical understanding of one-step circuits [Wall, Hlavacek & Savageau (2004) *Nat. Rev. Genet.* **5**, 34-42], we know little about two-step circuits. I believe that Sergei's analyses provided valuable preliminary data for my grant proposal, and we here in Los Alamos have started to extend his studies and have obtained interesting new results that complement those already obtained by Sergei.

Sergei's first language is not English, so a comment on his English proficiency is perhaps in order. During our collaboration, we communicated mainly through email. I encountered no difficulties in corresponding with Sergei. I can say the same about our face-to-face conversations. I consider him to speak, write, and read English at an adequate to high level of proficiency for scientific purposes. In addition, I can say that it has always been a pleasure to work with Sergei and share his company.

Based on my experience, I can say that Sergei is deeply committed to and capable of using mathematical and computational methods to better understand biological systems. I would think that he has a bright future ahead of him.

Sincerely,

William S. Hlavacek