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Professor Rob de Ruyter van Steveninck
Biocomplexity Faculty Search Committee
Biocomplexity Institute
Indiana University

Dear Professor Steveninck,

The purpose of this letter is to confidentially evaluate the qualifications of Dr. Plamen Christov Ivanov for a faculty position.

I first met Dr. Ivanov when I was a guest of his colleagues at the University of Sofia during July 1991. At that time he had a Master of Science degree in theoretical solid state physics and was working toward his Ph.D. degree. He impressed me with his quick grasp of new ideas, and his clear exposition of his own research. Therefore I contacted him in Spring 1993 with the idea of inviting him to do work as a part of our research group focusing on applications of statistical physics to complex physiological systems. He completed his PhD in Biophysics as my student in 1998 and since then has been a very active research associate in our group.

Dr. Ivanov is dedicated, energetic, and extraordinarily creative and his performance has earned my highest recommendation. Almost from the day he arrived, he has consistently shown himself to be a researcher of great ability. In his very first year here, he initiated an original research program, focusing on the question of whether there is information in heart rate fluctuations that could usefully distinguish healthy from diseased hearts. Dr. Ivanov introduced the theory of wavelets in our Center in 1994, a time when this theory was mainly an abstract mathematical construction and its potential for physical and biological applications was not widely appreciated. He mastered the theory and practical aspects of this technique, and his work, based on wavelet theory and Hilbert transform resulted in a publication in the journal *Nature* **383**, 323 (1996). This work became the object of a great deal of interest. It has triggered follow-up studies and has collected 100 citations to date. It is described also in *Science News* **150**, 196 (1996) and in *Dallas Morning News* (Discoveries Section) (Sept. 30, 1996). Dr. Ivanov's findings provide important information on the mechanism of cardiac regulation and are considered a breakthrough. His novel approach of adapting abstract mathematical concepts to extract hidden information from complex signals, has received a strong positive response from researchers in a wide range of fields (from meteorology to oil recovery) suggesting that the approach he developed finds broad application.

Dr. Ivanov has also recognized that the scale invariant properties of the heart rate are not sufficiently simple to be described by a single scaling exponent. In a recent study he applied novel multifractal analysis techniques to heart rate data. Dr. Ivanov found that there is a much higher level of complexity associated with healthy human heartbeat dynamics than previously thought — i.e., fractals within fractals. Such multifractal complexity has not been observed in physiological systems, until the work of Dr. Ivanov. In particular, he found that healthy heartbeats display a complex set of multifractal properties, while heartbeats of people with congestive heart failure are simple fractals and are always much less varied. The discovery of mutifractality in the human heartbeat by Dr. Ivanov is a groundbreaking finding

because it changes our understanding of the neuroautonomic regulation of the heart, and opens new avenues of diagnosis. By knowing which exponents from the multifractal spectrum are lost in unhealthy hearts, one can possibly pinpoint which elements of the neuroautonomic regulation system are not working. These findings of Dr. Ivanov led again to a publication in Nature, where he is again the first author [*Nature* **399**, 461–465 (1999)]. The achievements of Dr. Ivanov in developing new techniques were also recognized by the American Mathematical Society, which selected his work for its media display for July 1999. This work was also featured in *Science Daily Magazine* and in the Science Section of the German newspaper *Sueddeutsche Zeitung*, July 6, 1999, and has been cited 113 times already. More recently Dr. Ivanov has shown that other physiologic systems also under neural regulation, such as the human gait, may not be characterized by multifractal complexity.

In the past nine years in the field of physiology Dr. Ivanov has studied the statistical properties and the mechanisms of control of human cardiac dynamics, respiration, sleep dynamics, locomotion, as well as the effects of endogenous circadian rhythms on physiologic function. He has also investigated conducting properties in low-dimensional disordered systems in the presence of spatial correlations with the goal of understanding the function and structute of biological macromolecules such as DNA and proteins. Currently Dr. Ivanov is investigating networks of functional synchronization between different neuronal groups and brain centers. He works on developing adequate approaches to quantify the complex topology and structure of these networks which may help our understanding of how information is transfered between different cerebral centers, and how different areas of the brain interact during physical and cognitive tasks. He has been invited to give lectures on this topic at the WE-Heraeus-Seminar on Synchronization in Physics and Neurosciences in Bad Honnef, Germany, December 2001, and at the International Workshop on Randomness and Complexity in Eilat, Israel, January, 2003.

Dr. Ivanov has also demonstrated his ability to write up long and careful accounts of his work, and he was invited to contribute to a Cambridge University Press book on wavelets (as the only contributor invited to cover biomedical applications of wavelets) in *"Wavelets in Physics"*, edited by H. C. van den Berg (Cambridge University Press, Cambridge, 1999)]. The book presents a selection of 12 review articles (chapters) covering the frontiers of wavelet theory application to fundamental fields in physics, each written by distinguished researchers. Dr. Ivanov has also been invited to contribute chapters to other books: *"The Science of Disasters: Climate Disruptions, Heart Attacks, and Market Crashes"*, edited by A. Bunde and H.-J. Schellnhuber (Springer Verlag, Berlin, 2002), *"Modelling Bio-medical Signals"* edited by G. Nardulli and S. Stramaglia (World Scientific, Singapore, 2002), and *"Processes with Long-Range Correlations: Theory and Applications"* edited by G. Rangarajan and M. Ding (Springer Verlag, Berlin, 2003). He was recently invited to write a review article for a special edition of the journal *Chaos* **11**, 641-652, (2001), devoted to various aspects of noise and fluctuations in physical and biological systems.

Dr. Ivanov is currently the key research associate in The Research Resource for Complex Physiologic Signals. This unique National Resource, of which I am one of the three leaders (with two others from Harvard and M.I.T.), is funded by the National Institute of Health (5 million US dollars for 5 years) with the mission to become a basis for biomedical research in the United States. The methods and techniques developed by Dr. Ivanov constitute a substantial part of the scientific program of this National Resource; he played a key role in the writing and preparation of this project, and he continues to make essential contributions to its ongoing research work in areas such as cardiac, respiratory, sleep and gait dynamics, functional networks in the brain, electron transport and conductivity in DNA. In January 2002 he wrote a new NIH grant proposal to study effects of circadian rhythms on physiologic function which was awarded in September 2002.

Dr. Ivanov's reputation as an expert in the field is shown by the fact that he has been invited to present his work at over fifty international conferences and forums in the last seven

years. He is regularly invited to serve as a reviewer and consultant referee for many scientific journals, including *Physical Review Letters*, *Physical Review E*, *Medical and Biological Engineering and Computing*, *IEEE Transactions of Biomedical Engineering*, *Fractals*, *Heart and Circulatory Physiology* and others. In addition, he has served on the Editorial Board of the journal, *Fluctuation and Noise Letters* in the period 2000-2003, and has worked on the organizational committees of several conferences and workshops.

Dr. Ivanov has considerable teaching experience as a teaching assistant for ten semesters of different courses in the Physics Departments of Boston University and the University of Rhode Island. I have also heard him discuss his research on many occasions: his seminars are models of clarity, and one always gains new insights by listening to them. Dr. Ivanov has fostered and mentored five graduate students and three junior post-doctoral researchers. He is a patient teacher, dedicated to his students and their development. His leadership and guidance has led to the development of significant new contributions.

Dr. Ivanov has guided graduate students Kun Hu and Zhi Chen along an extensive line of research related to estimating long-range correlations in nonstationary signals, which was enthusiastically accepted by the reviewers [*Physical Review E* **64**, 011114(19), (2001) and *Physical Review E*, **65**, 041107(15), (2002)] and has collected 43 citations to date. Dr. Ivanov has supervised Chung Lo, another graduate student, on a project related to quantitative analysis and modeling of the dynamics of sleep stage transitions during sleep — a work which attracted considerable attention [*Europhysics Letters* **57**, 625-631 (2002)]. This work was featured in *New Scientist*, vol.173, N.2331, p.38-40 and other media reports where the role of Dr. Ivanov in initiating and leading the project is clearly outlined. Currently Miguel Casa, a graduate student from UNED, Madrid and Ainslie White, a graduate student from Cambridge University, England are also working under Dr. Ivanov's supervision. In collaboration with Dr. Yosef Ashkenazy, a visiting postdoc from Israel, he has directed a project applying random walk theory to physiologic signal analysis (both heart rate and human gait) [*Physical Review Letters* **86(9)**, 1900–1903 (2001)]. In the last two years Dr. Ivanov has initiated projects with Jan Kantelhardt when the latter was still a student at the University of Geissen, Germany. As a postdoc at Boston University Dr. Kantelhardt continued to work with Dr. Ivanov on analysis and modeling of sleep regulation and sleep stage effects on heartbeat dynamics [*Phys. Rev. E* **65**, 051908(6), (2002) and *Europhysics Letters* **62**, 147 (2003)].

Dr. Ivanov's enthusiastic attitude and the quality of his work have attracted many researchers to collaborate with him and other members of our Center for Polymer Studies. Dr. Ivanov initiated contacts and projects with individual scientists and research teams from Potsdam University, Germany, the Center for Computer Science and Informatics, Amsterdam, the Philipps-Universitaet and Sleep Laboratory at Marburg, Germany, Educational Physiology Laboratory at the University of Tokyo, Japan, and Brigham and Women's Hospital, Harvard Medical School among others.

Dr. Ivanov is equal to the best of 71 Ph.D. thesis students and 81 postdoctoral fellows and research associates who have worked in my research group over the 31 years I have served on the faculties of M.I.T. and Boston University. This list includes individuals who are by now well established in leading institutions — e.g., Berker, Redner, Klein, Alstrøm, Selke, Family, Daoud, Ben-Avraham, Herzfeld, Milošević, Nakanishi, Rothschild, Bansil, Mantegna, Sciortino.

I support in the strongest terms possible his application for a faculty position.

Yours sincerely,

H. Eugene Stanley
University Professor; Professor of Physics (CLA); Professor of Physiology (MED)
Director, Center for Polymer Studies