



## FEATURE

# An Interview with Sergey Bezrukov

S. Bahar

Sergey Bezrukov has played a major role in the development of biological physics (and biophysics!) over the past two decades. His work connects molecular biophysics and nonlinear dynamics, providing a bridge among interdisciplinary scientific “islands”. THE BIOLOGICAL PHYSICIST spoke with him recently about his research, his thoughts about interdisciplinary science, and his future plans.

*What led you to your work in interdisciplinary science in general, and biological physics in particular?*

Quite often the origins of an interest are hard to trace... I think my first impulse towards biological physics came from reading Schrödinger’s book “What is life” which, in the Russian translation, was titled “What is life from a physicist’s point of view”. A sophomore at the St. Petersburg Polytechnic University at the time, I was fascinated by the book and deeply impressed by the intellectual powers of “a physicist”.

So, arriving to the US in 1990 I was not a newcomer to biological physics, but my career got a critical boost when I joined Adrian Parsegian’s lab at the NIH. The greatest place for a physicist interested in biology, the lab was just then electrified by the emerging discovery of hydration forces in macromolecular and membrane arrays and,

more generally, by the role of water in conformational equilibrium of molecules and supra-molecular structures. What rewarding surroundings to be in! The experimental strategy of the lab was to watch a system’s behavior under osmotic stress induced by polymeric solutes so as to understand the fundamentals of the molecular hydration and involved interactions. Adrian managed to attract many bright young scientists – Josh Zimmerberg, Igor Vodyanoy, John Kasianowicz, and Don Rau – just to name a few.

At the famous lab seminars, the so-called Wednesday “chocolate talks” – the adjective reflecting Adrian’s passion for the Aztecs’ invention – one could eat kilos of chocolate and listen to the finest scientists from around the world. Even more important, because of the extremely informal style of the seminar, it provoked intense, sometimes heated discussions with the speakers, not always allowing them to proceed to the end of their talks. For me this was particularly valuable, as most of the invitees’ names I knew from their papers but did not associate them with real people, nor had I any idea how they think on a “real time scale.”

I greatly enjoyed the atmosphere, picked up the ideas fast, and built on them by incorporating approaches developed back in St. Petersburg. Indeed, there we had been

studying large-scale conductance fluctuations in electrolyte solutions using micron-sized capillary channels in quartz glass. The whole configuration was very close to that of a standard Coulter counter – a device proposed by Wallace Coulter in 1953 to count and to size particles by their transient occlusion of a micron-size channel. We were trying to increase the sensitivity of the method by applying noise analysis to the conductance fluctuations rather than just time-resolving events. By doing this, we were able to extend it to “counting” micellar particles.

Adrian’s lab had impressive experience with mesoscopic ion channels, such as the voltage-dependent anion channel from the outer mitochondrial membrane (Josh), alpha-hemolysin (John), and alamethicin (Igor). In essence, these channels are miniaturized versions of the capillary channel that we had worked with in St. Petersburg. So, the idea to extend the Coulter principle to the molecular level of a single ion channel came quite naturally. Our first publication on the subject appeared in the Tokyo “noise conference” proceedings in 1991. By 1994 it matured into a *Nature* paper with Igor and Adrian. The idea was further developed by many authors around the globe and, I am sure, it is among the major seeds that later grew into the modern nano-sensor boom.

*In the community of non-linear physicists you are mostly known by your work on stochastic resonance in ion channels. What was the driving motive to undertake this study?*

Well, this time inspiration came from Frank Moss of the University of Missouri at St. Louis. In 1994, while attending the Annual Biophysical Society meeting in New Orleans, Igor and I went to the evening lecture given by Frank on stochastic resonance in sensory biology. Frank was talking about stochastic resonance in the crayfish mechanoreceptor

and, being a superb speaker and the leader of the field, he completely captured our imagination. The line of our reasoning was straightforward: ion channels underlie sensory transduction, so why not look at them as candidates for stochastic resonators? After some intense work which, by the way, even included designing a noise generator based on amplification of Nyquist’s resistor noise, we were able to demonstrate that voltage-dependent ion channels are indeed stochastic resonators.



*Sergey Bezrukov in his office at the National Institutes of Health.*

We first ran experiments with alamethicin channels. These channels mimic the “real” ion channels of neurophysiology in their voltage sensitivity (alamethicin’s gating charge is about five elementary charges) but differ from them in their opening-closing statistics. Alamethicin channels can be thought of as a large population of “real” channels in the limit of a low opening potential. The consequence is that, over a broad range of potentials, the relation between the holding potential and the average number of open channels is described by a nearly pure exponential function.

Our mathematical interpretation capitalized on this observation by analyzing the statistical properties of a Poisson wave of events with exponential dependence of their generation rate on applied voltage. This mathematical treatment was then extended to the general case of an arbitrary relation between the generation rate and the input signal. We showed that, in the limit of small signals and small noise intensities, noise-improved signal transduction is a quite general property of rate-modulated series of events. This generality probably explains why stochastic resonance has been seen in so many diverse systems.

Several years later Peter Hänggi's group in Augsburg did an impressive job of relaxing the limit of a low opening potential and gave a comprehensive theoretical treatment for "real" channels.

*What are your current research projects?*

I think that the most important project concerns the analytical theory of channel-facilitated transport, work done with Sasha Berezhkovskii of the Center for Information Technology at the NIH. There has been a lot of effort and progress around the world in the theoretical description of the channel-facilitated transport. However, current theoretical work mostly proceeds in the direction of combining the well-known "old" simple transport equations with "new" sophisticated numerical simulations.

Sasha and I realized, almost by accident, that effective analytical approaches in channel-facilitated transport are far from being exhausted. It started as a collaboration with Attila Szabo (NIDDK, NIH) where we developed a theory for particle number fluctuations based on a continuum model of particle dynamics in the channel. The analytical results were tested by careful numerical simulations. It turned out that our

analytical approach described fluctuations amazingly well, so, after a while, Sasha and I decided to explore the model further and apply it to transport problems.

Our theory, small fragments of which were recently published as two *Physical Review Letters* – one on the "up-hill" and "down-hill" passage time distribution equivalence and the other on a fluctuation theorem in membrane transport – takes into account both energetic and entropic effects in transport through the channels. The entropic effect arises as a natural consequence of complex, often irregular channel geometries. Using the continuum model we obtain analytical results for all of the main parameters of channel transport. For simple potentials and simple shapes we arrive at correspondingly simple algebraic expressions that provide crucial insights in channel-facilitated transport phenomena. As is frequently the case with diffusion and the consequent conditional probabilities, some of the results are totally counter-intuitive. This is exactly what adds excitement to our work and awakens audiences at public presentations.

*Is it difficult to be a physicist at the NIH?*

May I modify your question to "Is it difficult for a physicist to *get tenure* at the NIH?" A couple of years ago, a young post-doctoral fellow at the beginning of his NIH career raised this question during a ride from Dulles airport to the lab on our way back from an out-of-state meeting. My answer was: "No, not at all, NIH does appreciate physicists. Just get five publications into *Nature* and tenure is yours."

This is a joke, of course, though from real life. To be serious, to work at the NIH as a physicist is definitely a responsibility. NIH is a health research organization, so, enjoying the distinct privilege of working in this institution,

we have to connect with medical research. For example, several recent projects in my section dealt with the mechanisms of antibiotics transport, high-affinity blocking of anthrax pores, and drug-resistance of certain pathogenic bacteria.

Equally important is to be among the leaders in your field. The NIH environment is unique in many ways and conducive to excellent research. What I treasure most is that one is able to devote 100% of his time to research (no teaching), that funding is relatively stable (writing grant applications is not a must), and that there is a broad spectrum of excellent scientists on campus (from practicing medical doctors to “pure” abstract mathematicians) who are open to collaboration.

*You have been very active in organizing interdisciplinary science conferences – how do you feel that these have changed over the years and what impact have small conferences like UPoN had on biological physics?*

Yes, I did organize a number of “small” conferences, “small” compared to the annual meetings of the American Physical or Biophysical Societies. I think that conferences of this kind are important. There are two definitions of biophysics: biophysics in a broad sense – “*physics in biology*” – and biophysics in a narrow sense – “*physics of biology*”. For example, if you take a close

look at the Annual Biophysical Society meeting presentations, you’ll see that most participants just use certain physical instrumentation and the corresponding physics vocabulary. This is biophysics in the broad sense. You’ll find only a small fraction of presentations devoted to the physics of biological objects. So, the conferences that I organized were first of all limited to the “physics of biology” and, secondly, were biased toward topics that included the theory and practice of fluctuations as a major tool of learning.

Following the 2002 “Unsolved Problems of Noise” conference at NIH’s Bethesda campus, I received hugely enthusiastic feed-back. The conference was well-advertised and attracted a lot of NIHers. Several conference participants later won NIH grants and I hope that their presentations at the conference helped them in this respect. As for the impact, I think that small conferences generally have much greater effect “per capita” than large ones. The format of a well-organized small conference is more catalytic for intellectual advances just because of higher brain concentration.

*What are your plans for the future?*

Well... to stay a biophysicist in the narrow sense who explores “what is life from a physicist’s point of view.”

# PRL HIGHLIGHTS

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Emmanuel Tannenbaum

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See Also: Phys. Rev. Focus

**Dynamic range of hypercubic stochastic excitable media**

Vladimir R. V. Assis and Mauro Copelli

Published 31 January 2008 (7 pages)  
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**BRIEF REPORTS**

**Inconspicuous structural coloration in the elytra of beetles *Chlorophila obscuripennis* (Coleoptera)**

Feng Liu, Haiwei Yin, Biqin Dong, Youhua Qing, Li Zhao, Serge Meyer, Xiaohan Liu, Jian Zi, and Bin Chen

Published 17 January 2008 (4 pages)  
012901

**SPECIAL DBP ANNOUNCEMENT**

# **DBP BUSINESS MEETING**

**The DBP Business Meeting  
will be held  
at the March APS Meeting  
in New Orleans**

**from 5:45 to 6:45 pm  
In MCC Room 208  
Tuesday March 11, 2008**

**Don't miss it!**



## **SPECIAL DBP ANNOUNCEMENT**

# ***STUDENT TRAVEL GRANTS AWARDED***

Twenty-one students have been awarded Student Travel Grants ranging from \$100 to \$400 to help defray their expenses in traveling to the March Meeting. The total amount awarded this year is \$4000. The recipients, along with their universities, academic departments, and the sessions in which they will be presenting, are listed below. Congratulations!

**Svetlana Postnova**, U Marburg, Physiology, *B16*  
**Ross Brody**, U Maine, Physics, *V17*  
**Jessica Zimmerlin**, U Mass, Polymer S&E, *P16*  
**Yongxing Guo**, Brown, Physics, *P16*  
**Aphrodite Ahmadi**, Syracuse U, Physics, *X40*  
**Chih-Kuan Tung**, Princeton, Physics, *X40*  
**David Liao**, Princeton, Physics, *J16*  
**Patrick Hann**, Rowan U, Physics, *S16*  
**Kun-Chun Lee**, U Penn, Phys & Astrophys., *L16*  
**C. Zang**, G. Washington U, Physics, *W16*  
**Matthew Raum**, Virginia Tech, Physics, *H16*  
**Robert Forties**, Ohio State U, Physics, *V40*  
**Kevin Johnson**, U Mo-Columbia, Physics, *B17*  
**Nathan Dees**, U Mo-STL, Physics/Neurodynamics, *J17*  
**Aonan Tang**, Indiana U, Physics, *B16*  
**Ranjani Narayanan**, U FL, Physics, *D17*  
**Yanxin Liu**, Florida Intn'l, Physics, *D17*  
**Xiaoja Tang**, U GA, Physics, *D16*  
**Lam Nguyen**, Florida SU, Physics, *W25*  
**Ronald Benjamin**, UAB, Physics, *L16*  
**Allison Heath**, U TX, Systems Biology, *D16*

## **SPECIAL DBP ANNOUNCEMENT**

# ***CALL FOR NOMINATIONS of DBP Members for 2008 APS Fellowship***

On behalf of the 2008 DBP Fellowship Committee, this is to invite the nominations of some of your well-qualified colleagues to be considered for the elections to APS Fellowship this year.

With 2008 membership count of 1881, the DBP will be permitted to sponsor up to 9 qualified candidates for the elections. Hence your attention for this process is most important so that the Division of Biological Physics (DBP, not to be confused with DPB) can be better represented within the APS.

I would like to point out that I discovered a very senior world-famous colleague, Prof. Britton Chance, being overlooked by the entire APS community until 2007. Incidentally, Prof. Chance was awarded our Biological Physics Prize by the APS in 1987. It is quite likely that there could be some extremely qualified biological physicists still being overlooked. You may find out their status being a Fellow or not, directly from APS online directory. However equally importantly, please understand that any premature nominations of male or female candidates alike, are not desirable. These cases in all likelihood will be dropped. Please exercise your professional, rather than emotional, judgment as well as you can.

The instructions, criteria and forms for the nominations are available on APS website, URL: <http://www.aps.org/programs/honors/fellowships/nominations.cfm>. All forms, the supporting information and recommendations for each nomination should be submitted electronically according to the instructions. New nominations for DBP-sponsored candidates and any updated information for the deferred candidates must be received by May 1, 2008, for the next reviewing cycle. The reviewing process is comprised of four stages. The final stage will end in mid-November at the APS Council Meeting. The announcements will be made by the APS Honor Program Office soon after the final conclusions.

For any questions, please contact the Fellowship Office directly at e-mail: [fellowship@aps.org](mailto:fellowship@aps.org), or telephone: (301) 209-3268.

Thank you very much for your attention.

Dr. Shirley Chan  
Secretary-Treasurer  
Division of Biological Physics

## **SPECIAL DBP ANNOUNCEMENT**

# ***ELECTION RESULTS***

The DBP election results are in. Out of 1883 ballots generated, 324 have voted online, and 11 paper ballots have been received. The percentage of participation is ~18%. For some unknown reason, this turnout is the lowest of the 5 elections I have prepared, both by counts and by percentage. To the best of my knowledge, the statistical mean of total vote counts still remains intact: 350 +/- 30.

Strangely, the DBP seems to have a "glass ceiling" of 400 votes cast, which remains unbroken even though DBP membership has increased over 60% in ~14 years. The only speculation I could come up with is that, perhaps over this period, the DBP has a similar core of actively participating members who really care about the future of the Division.

As the retiring Secretary-Treasurer, it is my sincere wish that more members will become actively involved and this "voting glass-ceiling" can be broken soon.

The individual counts show that **Herbert Levine** has been elected as the next Vice-Chair, over Angel Garcia. **Thomas Nordlund**, though running unopposed as the next Secretary-Treasurer, received extremely strong support from the voting members (over 90%).

**Timothy Newman** and **Daniel Cox** have been chosen as the new Members-at-Large, over Uwe Tauber and Mark Spano.

The Bylaws Amendments have been passed overwhelmingly, yes: 298 votes, no: 19 votes. The revised Bylaws will become effective after the DBP Business Meeting, to be held on Tuesday March 11, 5:45 p.m. - 6:45 p.m., Convention Center, Room 208, unless there should be a last-minute major objection from the attendees in this meeting. The new appointments of the mandated committees will follow the guidelines as described in the revised Bylaws.

On behalf of the Executive Committee, I would like to thank the Nominating Committee Members for identifying the slate of candidates to run for this round of DBP elections, and all those DBP members who have taken their time to vote.

Dr. Shirley Chan  
Secretary-Treasurer, Division of Biological Physics, APS




# Training Workshop

## Developing Multi-Cell Developmental and Biomedical Simulations with CompuCell3D

June 16th-20th 2008

Indiana University, Biocomplexity Institute, Bloomington, IN  
USA



**Background:** Modeling is becoming an integral part of contemporary bioscience. The Glazier-Graner-Hogeweg (GGH) model as implemented in the modeling environment, CompuCell3D allows researchers to rapidly build complex models of multi-cell processes in development and disease with user-selectable resolution, from sub-cellular compartmental models to continuum models of tissues. CompuCell3D's use of CC3D-ML, BioLogo and Python model-specification allows compact description of models for publication, validation and sharing. CompuCell3D is open source, allowing users to extend, improve, validate, modify and share the core software. For more information on the GGH and CompuCell3D, please visit: <http://www.compuCell3d.org/>

**Goal:** By the end of the week, participants will have implemented a basic simulation of the particular biological problem they work on. Post-course support and collaboration will be available to continue simulation development.

**Topics:** Introduction to GGH modeling. Applications of GGH modeling and overview of published work. Introduction to CompuCell3D. Python and BioLogo scripting. Basics of model building. Extending CompuCell3D. Building a basic simulation of your system.

**Format:** The workshop will consist of a limited number of lectures and extended hands-on computer tutorials.

**Instructors:** James A. Glazier, Maciej Swat, Benjamin Zaitlen, Abbas Shirinifard, Nikodem Poplawski, Randy Heiland (Biocomplexity Institute, Indiana University)

**Target Audience:** Experimental Biologists, Medical Scientists, Biophysicists, Mathematical Biologists and Computational Biologists from advanced undergraduates to senior faculty, who have an interest in developing multi-cell computational models, or learning how such models might help their research. No specific programming or mathematical experience is required, though familiarity with some modeling environment (e.g. Mathematica<sup>®</sup>, Maple<sup>®</sup>, Matlab<sup>®</sup>) and how to represent basic concepts like diffusion and chemical reactions mathematically, would be helpful.

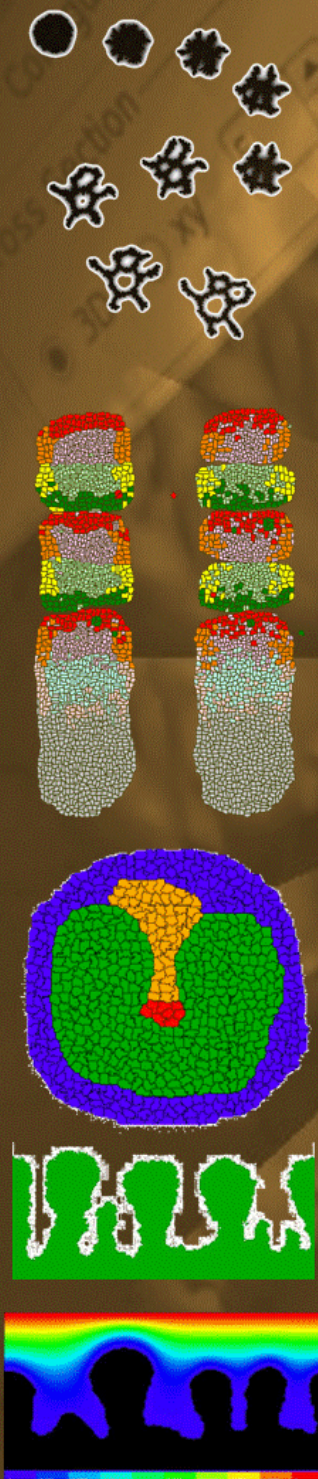
**Fees and Support:** The basic registration fee of \$500 will cover workshop participation, workshop materials and lunches. Partial support for registration, travel and hotel costs may be available.

**Application and Registration:** Enrollment is limited and by application only. To apply, please send a c.v., a brief statement of your current research interests and of the specific problem you would like to model. Students and postdocs should also include a letter of support from their current advisor. If travel support is being requested, please include a statement documenting need and amounts requested. Please submit all application materials electronically to Maciej Swat ([mswat@indiana.edu](mailto:mswat@indiana.edu)) by May 15th, 2008.

**Facilities:** Participants will have access to an OSX cluster and will be able to connect to the Internet using their own laptops.

**For More Information, Please Contact:** Maciej Swat ([mswat@indiana.edu](mailto:mswat@indiana.edu)).

Or visit: <http://www.compuCell3d.org>





## **JOB AD**

# **Two Postdoctoral Positions Oakland University**

Two postdoctoral positions will soon be available in an active lab where we study articular cartilage using multidisciplinary techniques, including microscopic magnetic resonance imaging ( $\mu$ MRI), polarized light microscopy (PLM), transmission electron microscopy (TEM), Fourier-transform infrared imaging (FTIRI), histology, biochemical treatment and mechanical characterization. The goal of this work is to determine a set of multidisciplinary parameters that describe the load-induced changes in osteoarthritic cartilage from animals at microscopic resolutions. Other research opportunities may be available depending upon the interests and background of the successful candidate.

The successful candidate for the postdoctoral position should have a PhD or equivalent in biomedical sciences, biophysics, bioengineering, or a related field. A solid background and previous experience in cartilage or other connective tissue is preferred. Working knowledge and skills with microscopic imaging instrument and image analysis will be an asset.

Oakland University is located in suburban Rochester, Michigan, in north Oakland County, which boasts one of the most picturesque campuses in the country. Our state-of-art lab instrumentation includes a  $\mu$ MRI system (Bruker AVANCE II NMR Console with a 7T wide-bore superconducting magnet and microimaging accessories), a mechanical system (EnduraTec ELF 3200), a PLM system (Leica DM RXP interfaced with two digital imaging systems), a FTIRI system (PerkinElmer Spotlight 300), and a number of histology and analytical chemistry equipments. Our web site contains more information regarding our lab and some of the recently completed cartilage projects.

Interested individuals should send their CV, statements of research experience and research interest, and the names, telephone numbers, and e-mail addresses of at least three references to:

**Professor Yang Xia**

Dept of Physics,  
Oakland University,  
Rochester, MI 48309, USA

**Tel:** 248-370-3420; **Fax:** 248-370-3408; **E-mail:** [xia@oakland.edu](mailto:xia@oakland.edu)

**Web:** [http://www.oakland.edu/~xia/XiaLab\\_index.html](http://www.oakland.edu/~xia/XiaLab_index.html).

*OU is an equal opportunity employer.*

## **JOB AD**

### **POSTDOCTORAL POSITION MD ANDERSON CANCER CENTER**

Applications are invited for a postdoctoral fellow position in the Department of Radiation Physics of the University of Texas (UT) MD Anderson Cancer Center to work on an exploratory research program on multiscale modeling of radiation response of biological systems. The position involves the development and application of computational methods for the modeling of the processes involved in the interaction of radiation with biological systems across different spatial and temporal scales. A good background in simulation and modeling of condensed matter or biological systems, interest in computational biological physics, experience in scientific programming, and high level of motivation for independent work is desired. Due to the interdisciplinary nature of the research, applications from candidates in all areas of computational science/engineering with interest in biomedical physics will be considered.

UT MD Anderson Cancer Center is renowned for its excellence in patient care, research and education programs. The candidates will have ample opportunities for interdisciplinary training to pursue an academic career in biomedical physics. Although it is primarily a research position, there will be opportunity to receive training in clinical medical physics. Interested candidates should send application materials by email to Ms. Cynthia M. Wyche (e-mail address: [cmwyche@mdanderson.org](mailto:cmwyche@mdanderson.org)). The application materials should include:

1. A letter of interest and current CV with names and contact information of at least two references;
2. An optional brief (no more than three pages) research proposal in the area of computation radiation biophysics that they would love to pursue.

The initial appointment will be for one year with possibility of renewals based on progress and availability of funds.

UT M.D. Anderson Cancer Center is a smoke free environment. We are an equal opportunity employer and we encourage qualified women and minority applicants. Applicants must be legally eligible to work in the United States.



## **JOB AD**

### **POSTDOCTORAL POSITION IBM WATSON RESEARCH CENTER**

A postdoc position is available immediately at IBM Watson Research Center (Yorktown Heights) in Dr. Yuhai Tu's group. We are looking for someone with strong background in physics (statistical, soft matter, nonlinear dynamics, etc.) and who is interested in working on biological problems. Specific subjects include studying complex biological networks, quantitative modeling of signaling pathways and molecular level understanding of biological devices, such as motors and switches.

Interested candidates should contact the PI (Yuhai@us.ibm.com) directly with their CV and 3 letters of recommendation.

## **JOB AD**

### **Software Developer/Research Associate/Post Doctoral Fellow Indiana University Biocomplexity Institute**

The Indiana University Biocomplexity Institute seeks a Research Associate or Post Doctoral Fellow to join in research on the development and improvement of Tissue Simulation Environment (compuccell3d.org). Rank is commensurate with experience. Two positions may be filled. Preferred skills and abilities include extensive experience in C++, Python, user interface design and implementation. Candidates should be able to interact with users, help prepare training workshops, and work in a small team environment with limited supervision. Opportunities include collaboration on new research projects and participation in publications with our scientists. Areas of interest include Monte Carlo methods, statistical mechanics, fluid dynamics, partial differential equations, mathematical modeling of biological systems, computer graphics visualization, and scientific software development. Skills in numerical modeling, graphics and visualization, or parallel programming are a plus, as is a strong (Masters or Ph.D.) scientific background. Technical writing and documentation experience are preferred. Applicant review will begin immediately and continue until positions are filled. Initial appointment will begin as early as January 7, 2008, and last one year with extension possible, subject to satisfactory performance. Send a CV and 3 letters of recommendation to Prof. James Glazier, Biocomplexity Institute, Indiana University, Bloomington, IN 47405, U.S.A. Indiana University is an Equal Opportunity / Affirmative Action employer.