Biosciences Directorate
Lawrence Livermore National Laboratory
P.O. Box 808, L-441, Livermore, CA 94551

November 11, 2005

Systems Biology / Microbiology Faculty Search
Department of Biology
Indiana University
Jordan Hall 142
1001 E 3rd Street
Bloomington, IN 47405-7005

Dear Sir / Madam,

I am very pleased to write a letter of support for Dr. Erszebet Ravasz, as she applies for the tenure track position in systems biology at the Department of Biology and the Biocomplexity Institute at Indiana University, Bloomington. I know Dr. Ravasz from my time at the University of Notre Dame, where I was a postdoc and she was a graduate student in the group of Prof. Barabasi. Already from the start of our two years of overlap, Dr. Ravasz impressed me very much with her depth of knowledge, her quick grasp of new topics and her enthusiasm.

Although we did not collaborate on a common project, I had the chance to closely follow the development of her research prowess through our participation in group meetings and one-on-one discussions. In addition to presenting her own research projects clearly and succinctly, Dr. Ravasz was actively participating by frequently giving important comments and suggestions on other projects. This was very much appreciated by the rest of our group. During this time, Dr. Ravasz' research efforts were focused on uncovering common themes in the topological organization of biological networks, a line of research that resulted in several highly cited publications. The most notable of these was published in the journal *Science* with Dr. Ravasz as the lead author (*Science* (2002) 2**97**, 1551).

This was not her first high-visibility publication, however. Already as an undergraduate student, Dr. Ravasz spearheaded an effort to understand the collective behavior of people as seen in the spontaneous synchronization of clapping after concerts. Not only did she devise the methods for
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how to conduct field measurements, but she also was the lead investigator on the subsequent analysis and modeling efforts. Not surprisingly, the resulting research paper was published in the journal *Nature* ((2000) **403**, 850). This spectacular success of an undergraduate project is representative of Dr. Ravasz' early scientific maturity and innovative thinking.

Dr. Ravasz' research interests during the last couple of years have continued in complex systems. In particular, she has focused on understanding the mechanisms behind protein folding. Approximately a month ago, I had the opportunity to visit Los Alamos National Laboratory and attend a presentation by Dr. Ravasz on her latest results on using network theory to understand the development of protein structures that contain stable folds. As was very evident from her impressive talk, Dr. Ravasz has continued to push the limits of network methods and developing novel approaches to probe the properties of complex systems.

Dr. Ravasz is not only an accomplished researcher. This last year, she has also gained experience in serving as a mentor for a graduate student. She is well liked and have clearly been able to communicate well with the student.

In summary, I consider Dr. Ravasz to be an extremely strong candidate, and I enthusiastically support her application for a tenure track position at IU Bloomington, Department of Biology and the Biocomplexity Institute. I believe that she will be a significant addition to an already strong program.

Sincerely,

Eivind Almaas, Ph.D.
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DEPARTMENT OF PHYSICS

November 15, 2005

Professor Yves Brun
Systems Biology/Microbiology Faculty Search
Department of Biology
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Bloomington IN 47405-7005

Dear Professor Brun:

It is a pleasure to write a letter of recommendation for *Erzsebet Ravasz, Ph.D.,* who is applying for a position in your institution. Erzsebet has been working with me for four years, during the PhD studies, but I had known about her two years before she joined my group—in fact, we have coauthored a *Nature* paper before meeting. I had made special efforts to hire her—she was very highly recommended. During a brief visit to her undergraduate institution I was told by one of her former professors, that in every five-six years they have a very exceptional student, and it is rarely a woman. This time, however, Erzsebet is the one. I can attest that he was right.

In the past eight years I have had three quite extraordinary students: Istvan Daruka, who is now faculty in Hungary, Reka Albert, who is faculty at Penn State, and finally, Erzsebet. She is an unusually smart person, who can handle any tool and technique with amazing ease, nothing staying in her way to solve a problem. She is incredibly fast as well; an overnight project of her would take a week for an average student. She thinks, and takes the best approach one could find. These qualities are at the basis of her extraordinary track record as well: she has played a key role in some of the most important projects in my group, work that has lead to a *Nature* and a *Science* paper, and several other publications.

Erzsebet's main work focused on understanding the modularity of complex networks. This was one of our more time consuming projects, taking almost two years to complete. We asked the following question: there is ample evidence that complex networks are scale-free. Yet, there is indication that they are modular, that is, they are sprinkled with small groups of nodes that are very highly linked to each other. The problem was that it looked impossible to marry these two concepts: we could not figure out how could a scale-free network, which is held together by hubs, be made of relatively isolated groups or modules. Our first idea was an obvious one, followed by

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many other groups: let us try to locate the modules or groups using clustering algorithms applied directly to the network topology. Yet, after trying many ideas, we were not pleased with the results: while we could cluster the networks, we simply did not understand how good the clustering was. In particular, an important drawback of clustering algorithms was (and is) that they cluster everything you provide them. We, on the other hand, wanted to answer a more fundamental question: does it make sense to cluster the network? Are there really clusters and modules in the system? How are they reconciled with the scale-free topology? Erzsebet has performed a heroic job methodically convincing us that simply performing the clustering will not solve our problem, and that the different clustering methods are largely equivalent. We have never published this aspect of the work, as we did not think that by simply applying clustering methods we are understanding the system. The breakthrough came only about a year after we started working on the problem, when we realized that reconciling the hubs and the modules requires the network to have a hierarchical architecture. Also, the final piece of the puzzle emerged when we understood that the scaling of the clustering coefficient could help us distinguish hierarchical from non-hierarchical networks. This finding allowed us to establish the hierarchical nature of a large number of real networks, from biological systems (published in *Science*) to communication and other non-biological networks (published in *Physical Review E*). This result is now a basic piece of the network literature, and most networks are simultaneously checked for their scale-free and hierarchical nature. Erzsebet's perseverance, as well as her ability to process a huge amount of data and information in a very short time, was indispensable to the success of the project. With many other students we would have been probably forced to drop the project before completion, considering the project's overall complexity and difficultly.

Erzsebet's strength is her unusual smartness, which makes her interested in a large number of problems. This is, however, a bit of a drawback as well: she occasionally gets lost in one of her research interests, requiring me to refocus her work on specific tracks. I think she would really thrive in a truly interdisciplinary and challenging environment, where I could see her immersing herself in many interesting collaborations.

During her postdoctoral studies at Los Alamos National Laboratory, Erzsebet has focused on understanding the energy landscape of proteins using a complex network representation of their configuration space. She found that configuration networks are similar to high-dimensional lattices with forbidden regions embedded in them. However, results from a molecular dynamics sampling of a protein's configuration network indicate that these networks are scale-free, at odds with the picture suggested by high-dimensional lattices. She showed that the observed scale-free nature of the protein configuration space is due to the way molecular dynamics simulations sample the space. She is currently using molecular dynamics simulation data to verify her modeling assumptions, as well as a simple physical model with beads and sticks to uncover the importance of steric constraints in the foldability of a sequence. Thus her work in the past year has familiarized her with another big subject in biological physics: protein folding, a knowledge that will be extremely useful in the long run for her career.

Erzsebet is a very outgoing person, always on the move. She loves to travel and does so with the same energy that she devotes to her work. I highly recommend her in your attention—I would frankly be happy to hire her back, and I am sad that she has to leave. Her dream is to return to Romania as faculty, which she is guaranteed to succeed. Yet, I am not sure that she will actually do that in the end—considering her unparalleled energy she will probably accept a faculty job in the USA. I think considering her record the question will not be if she can do that, but rather, if she wants to stay in this country. If she does, I do not doubt that she will succeed at it.

Do not hesitate to contact me if you have any additional questions.

Sincerely,

Albert-László Barabási
Emil T. Hofman Professor of Physics

Dr. Zoltán Néda
Professor of Theoretical Physics

BABEŞ-BOLYAI University

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Recommendation letter for **Dr. Erzsébet Ravasz**

I am truly honored to write this recommendation letter in support of Dr. Erzsébet Ravasz's application for a tenure-track position in your Department. Without being unfair to my other students, I can state without hesitation that Erzsébet Ravasz is the most talented, gifted and pleasant student I have ever had. I consider myself fortunate to have had the opportunity to collaborate with her. Now that she has finished her Ph.D. studies with honors and had her first post-doc experience as a Director Funded Post-Doctoral Fellow at the Los Alamos National Laboratory, I feel that she has become a mature researcher with excellent professional qualifications and background. I am also proud that I was her undergraduate and Masters thesis supervisor, and I remember with pleasure the fun we had doing physics together.

I have known Erzsébet since 1997, the year she became my student in quantum mechanics and when we started to work together and collaborate. During her undergraduate studies at the Babes-Bolyai University in Cluj, Romania we greatly enjoyed doing physics together, and published interesting papers. We also had enlightening discussions on quantum mechanics and relativity theory. She made the computer simulation for many of our common projects, studied and analyzed the experimental data, and had several key contributions to our research. We studied and solved together many problems in the fields of stochastic resonance, synchronization in social systems and magnetization related phenomena. Results from our research were published in Nature and Physical Review E.

For our common work on spatial stochastic resonance in Ising models and Barkhausen noise, it was Erzsébet who wrote the simulation codes and ran the simulations. For the problems related to synchronization in human clapping, Erzsébet made all experimental measurements, data analyses and computer simulations. She also had many interesting observations and comments that led us to the final conclusion. These two papers (Nature and Phys. Rev. E) on synchronized human clapping got a remarkable media coverage: New York Times, BBC news, Discovery Channel News, Le Figaro, Népszabadság, South Bend Tribune, ABC News, etc. During our common work Erzsébet proved her excellent talent in programming and data analyzing. She was hard-working and her results were always trustworthy.

Beside her truly outstanding research activity, during her study years in Cluj, she earned excellent grades, and finished at the top the class in her major. Erzsébet was one of those very small numbers of students who obtained the highest grade (10) during my quantum mechanics exams. She won a prestigious bursary from our University for excellence in research. As an undergraduate student she spent several research periods abroad at KFKI-Budapest, INPG/LTPCM-France, Collegium Budapest (Hungary) collaborating with well-known scientist in theoretical and computation physics. Her professional knowledge, her quick and sharp mind and open personality were appreciated by all my colleagues. She is the only student who has ever received an immediate tenure track offer from our Department upon successfully finishing her Ph.D.

She continued her Master Studies in Theoretical Physics at the Babes-Bolyai University, and wrote her Master dissertation also under my supervision. During this period she began her collaboration with

Professor László Barabási, and became interested in the emerging field of random networks. Her research in this period focused on the study and modeling of social networks. During this research Erzsébet analyzed in various aspects huge social networks. The results of her Master dissertation were included in a scientific paper published in Physica A.

During her master studies she held problem-solving and discussion classes in quantum mechanics for our undergraduates in Cluj. Student appreciated her sharp logic, enthusiasm and excellent pedagogical skills. As my teaching assistant I had the opportunity to learn about her superb teaching abilities, elegant conflict resolution, open and pleasant way of interacting with students and patience with them. Groups that had problem-solving classes with other teaching assistants many times asked us to have her as the tutor for their group as well. She was always looking for new ways to approach a problem, new methods for getting students attention and getting them interested in physics.

She finished her Master studies at BBU in 2000, after which she continued her Ph.D. studies with Professor A.L. Barabási at the University of Notre Dame. Although I was sorry to loose her as a student, I recommended that she undertake Ph.D. studies under the supervision of my good friend Professor Barabási at Notre Dame. In this way she could work in the group that started the currently very active field of random networks, and could participate directly at the leading edge of this research field. She followed my advice and became part of this prestigious research team. She continued there her work in statistical and computational physics studying networks and modeling biological systems. At Notre Dame, Erzsébet demonstrated her ability to interact and collaborate with biologists in analyzing and interpreting huge biological datasets. Under the guidance of Professor Barabási she published important and highly cited papers in prestigious journals, such as Science, Phys. Rev. E, Physica A and the Journal of Bacteriology. She participated in many successful projects and gave several research seminars and lectures at conferences. She obtained her Ph.D. with honors in 2004, and received the Alumni Research Award for her research during her Ph.D. studies.

After finishing her Ph.D. she had several post-doc opportunities and accepted the most prestigious one, the Director Funded Postdoctoral Fellowship at the Los Alamos National Laboratory. Here she continued her work in the field of random networks applying these in various problems in modern biology. Collaborating with Dr. Zoltán Toroczkai she obtained interesting results in the field of protein-folding and in understanding the hierarchical structure of important biological networks.

In conclusion, I find that Erzsébet has a wonderful talent for doing physics, science and teaching science in general. She is interested both in the classical problems of physics like basic quantum mechanics, relativity or field theory, as well as modern and active problems in statistical, biological and computational physics. She is an excellent programmer, hard working, quick thinker and has the ability to switch rapidly from one problem to another. Her broad general culture, friendly and extremely open personality makes her the perfect collaborator and colleague. The whole academic career and work of Erzsébet Ravasz recommends her as a mature and excellent researcher. Thus, I recommend strongly Dr. Erzsébet Ravasz for a tenure-track Position in Your Department. I am convinced that you will also find in her the friendly, trustable and professionally qualified colleague that you are looking for.

Sincerely Yours,
Dr. Zoltán Néda
Professor of Theoretical Physics

Center for Nonlinear Studies

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Los Alamos NATIONAL LABORATORY

November 7, 2005

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Dear Prof. Brun,

I am truly honored to be able to write this letter of recommendation in support of Dr. Erzsébet Ravasz's application for a faculty position in your department.

I have known Erzsébet since October 2004, when she joined the Center for Nonlinear Studies and the Complex Systems Group as a Director Funded Fellow. The Director's Fellow is a prestigious, two-year postdoctoral research award which gives the recipient unlimited freedom to develop and pursue her/his own research program. This fellowship is awarded based on a stringent competition in which candidates not only compete with others within their own field (such as physics) but also within all other fields represented at LANL, including chemistry, computer science and biology. In addition to a sizeable postdoc salary (in the range of $60,000-$75,000) the recipient also receives a considerable amount (about $20,000 per year) of additional funding in support of her/his research program development (usually used for travel to conferences, organizing conferences at LANL, hiring summer students for collaborative work and mentorship, etc.). In spite of the fact that this was the first postdoc position of Erzsébet, she won this award easily, with flying colors. The postdocs that usually win this award already have one or two previous postdoc appointments in their past, so they are more experienced with more publications and more citations than those that have just recently graduated. Erzsébet is one of those rare exceptions who could surpass the other, more seasoned postdoc applicants with her credentials. She just hardly graduated, and she already had about eight publications, with one article that appeared in Science and another article that appeared in Nature. In both cases she did the hard part of the work, and in the case of the Science paper, which is on metabolic networks, she also figured out the proper way of characterizing the network data, a key element of that publication. I know this first hand from her Ph.D. thesis advisor, Prof. Albert-László Barabási, who directed that work.

I have to confess, I felt extremely lucky that I could attract a postdoc of such caliber to Los Alamos. As currently the Deputy Director of the Center for Nonlinear Studies, a major part of my job consists in hiring excellent quality postdocs for various laboratory projects, and I'll have to say I have seen perhaps one more, similarly strong application out of the hundreds I processed in the past. That was of Jamil Abo-Shaeer, MIT student of the Nobel prize winner Wolfgang Ketterle (now at LBNL).

As a postdoc at LANL, Erzsébet fully lived up to her promising career. Here she decided to do a rather risky thing: she wanted to use networks theory to describe protein folding. This is a subject that neither her nor myself have been involved with in the past. In the competitive world of today, this is usually a bad idea, because of the constant publication pressure that young scientists are under. And indeed during her first year (basically until now) no significant publications came out, however, she did such a monumental amount of work on this topic, that it will guarantee several high quality publications in the near future, and possibly start a novel research trend in the area of protein folding networks.

I will now briefly describe her results in order to illustrate its potential for future development and applications, and more importantly, Erzsébet's unparalleled industrious character. When she came to LANL, she come to my office and said that she would like to understand protein folding and that she has an idea on how to apply a networks approach to describe what might separate a protein with a funneled free-energy landscape from a bad folder amino acid sequence characterized by a spin-glass like free-energy landscape. The reason she talked to me about that was due to my previous mathematical work on gradient networks, which is a subgraph (usually a set of trees) of a substrate network selected by gradients of a scalar field distributed on the nodes of the substrate network. The general formalism I developed earlier for these structures seemed like a very natural way to describe conformational motions of a protein towards lower energy configurations when going from a denaturated state to the native state of the protein. This was a connection that she made. The substrate network is constructed by associating to a configuration a node on this network, and a transition via an elementary rotation around a peptide bond taking the protein from one configuration to another to a link of this network. Previous literature in protein folding has shown that such a discretization of conformational spaces is indeed possible due to the existence of a few local minima in the torsion energy (as a function of the dihedral angles) around a (peptide) bond. The gradient network is generated by identifying the directed edges on this conformational network along which the energy drop is the largest, from every node. The collection of these directed edges forms the gradient network. She then studied the properties of this network, and was able to show that they will have to be of scale-free character, thus recovering the observations by Rao and Caflish recently made (using molecular dynamics simulations) in the Journal of Molecular Biology, (2004) on certain peptides (like beta3s). The basic assumption that we made throughout this work was that the statistical properties of the conformational network topology and of the distribution of energies at the nodes will determine whether the free-energy landscape (under temperatures corresponding to physiological conditions) will have a funnel shape, or not. In order to understand however the conditions for funnels, one has to take into consideration the steric-constraints along the protein, which show up as forbidden regions in the conformational network. We then realized that funnels can indeed be achieved by side chain distributions that select (due to steric constraints) a certain type of conformational landscape as characterized by network topological measures related to assortativity and degree distribution. Erzsébet is currently testing our hypothesis by implementing a simple model using the same side chain distributions as used by nature (for some of the shorter proteins), which is quite an involved numerical work, but we hope that it will be finished in the following months. With the lessons learned about studying general statistical properties of conformational networks using statistically equivalent ball-chain models, and the correct energy distributions, she was able to not only recover the fact that the network observed by Rao and Caflish is scale-free, but it also led to the recovery of the same exponent (-2) reported by these authors. The networks representation of protein folding seems a rather promising avenue for future research, because it gives us the hope that based on this, novel and much faster numerical algorithms can be designed for protein folding, directly aiding biotechnology efforts, such as drug design.

Throughout the evolution of this project Erzsébet has shown an extraordinary initiative and very deep physical intuition. This work involved a lot of literature reading, learning, programming and thinking about rather unusual things, like conformation networks and their connection to real proteins. She has done a marvelous job in hardly more than a year's time! The reason behind this fast development is the fact that she almost immediately sees to the essence of the problems and quickly develops good questions in order to test her intuition.

The other hard to parallel quality of hers is that she implements problems numerically in an extremely short time, and they are also very high quality implementations. She has a very consistent code-check and debugging procedure, and thus with very high probability, her numerics are bug-free.

She is not a mathematical person, or a person that works things out using formulas. Her strengths are her intuition and industriousness. Her work output is several times of the average postdoc, she finishes things in a few days, while an average postdoc might take several times as long. However, her work intensity is inconsistent, high intensity work-periods are separated by low intensity or no-work ones. In average though, she still has a high output compared to the average postdoc. She has a passion for science, and as long as the research is exciting, she will be working on it with the highest intensity. She is very bright and has a very quick mind. Her thinking is very non-sequential, and during our discussions I often had to back-track and slow her down so I could follow what she was trying to say.

She has an extremely friendly, down-to-earth personality and she is ready to jump to help anyone in need, she has a very non-selfish character, a true team player.

I honestly believe that she would be an excellent addition to your faculty both as a researcher and as a person and friend.

Please do not hesitate to contact me if you have further questions.

Sincerely,

Zoltán Toroczkai,
Deputy Director,
Center for Nonlinear Studies
Los Alamos National Laboratory