Jelena Stajic

# Research Statement

My research has been characterized by

- diverse research topics
  - genetic regulatory networks (biological physics)
  - compact polymer configurations (statistical, biological physics)
  - superfluidity in ultracold Fermi gases (atomic, condensed matter physics)
  - high temperature superconductivity (condensed matter)
- extensive collaboration with experimental groups
  - R. Martin (NIH): modeling the expression of the multiple antibiotic resistance (*mar*) gene circuit
  - J. Thomas's group (Duke University): interpreting data on the heat capacity of ultracold atomic gases
  - T. Lemberger's group (Ohio State University): analyzing penetration depth measurements in the high temperature cuprate superconductors

Although diverse, my research interests share a common thread: in each physical system, the interaction between its elementary parts (fermions in Fermi gases and high temperature superconductors, genes in regulatory networks) leads to non-trivial collective phenomena (superfluidity and superconductivity, adaptation to environmental conditions). In my postdoctoral work, I have completely dedicated my efforts to biological physics, studying the design principles of genetic regulatory networks. In the future, I intend to be on the lookout for new and exciting areas of research concerned with collective behavior in natural systems; in particular, I would like to be able to use my background in many-body and statistical physics to study biological systems. I believe that my demonstrated potential for forging collaborations with both theorist and experimentalist colleagues render me an excellent candidate for working in a collaborative, interdisciplinary environment. In what follows, I give a detailed description of my research accomplishments and plans. I include a short description of my work in ultracold quantum gases in order to convey the nature of my thesis work.

**I. Genetic regulatory networks.** The functioning of genetic regulatory networks is a central question of modern molecular biology. In these networks, two genes are connected if the product of one regulates (positively or negatively) the expression of the other. They can be studied at several different levels; one is to organize genes into circuits that perform a certain function in the cell, such

as responding to environmental signals. The influence of the architecture of these circuits on their function can then be analyzed in order to infer the design principles.

In collaboration with my postdoctoral supervisor Michael Wall, I am studying two genetic circuits in *Escherichia coli*. The lactose utilization circuit (*lac* operon) is interesting as it has been observed to exhibit bistability when induced with an artificial inducer, TMG. The aim of our study is to establish whether the natural system (which responds to lactose) exhibits bistability, as is often assumed despite the lack of experimental support. A collaboration with experimentalist colleagues from LANL is planned to verify our predictions. If the natural circuit is found to be bistable, the question remains whether memory effects or switching behavior, both results of bistability, are important to its function and why. The other system of interest, the *mar* circuit, has been studied extensively due to its importance in elucidating the mechanisms which make bacteria resistant to adverse environmental conditions. It is one of few examples of positive autoregulation in *E. coli*, generally regarded as less stable than the much more frequent negative autoregulation. We have constructed a well-motivated mathematical model which yields results in good agreement with dynamical expression data provided by R. Martin and J. Rosner at the NIH. Since our dynamics analysis suggests that the circuit would have a faster response if it lacked the positive autoregulation, it remains a mystery why this feature is a favorable evolutionary adaptation.

My future research in this field will involve both network and molecular level approaches. On the network level, one of the burning questions is how to perform reverse engineering given the high throughput expression data available today. Another question concerns the so called network "motifs", i.e. patterns of gene regulation which seem to occur in real networks significantly more often than in random ones. Is this frequency due to their particularly favorable dynamic properties as it has been proposed or perhaps to the fact that many of them respond to the same signal? On the molecular level, the traditional way of modeling gene regulation (using Hill's functions) is outdated given the level of detail available today on the events involved in the initiation of transcription. My research will seek new approaches: one is to use rule based modeling of binding events, thus taking into account the formation of all possible complexes of transcription factors, their ligands, different components of the DNA polymerase and the DNA itself.

**II. Compact polymer configurations.** Many polymer physics systems (e.g. folded proteins in biological systems) have compact configurations which are described well by self-avoiding lattice walks that visit every lattice site once and only once (Hamiltonian walks). A better understanding of the properties of Hamiltonian walks (HWs), such as the connectivity constant $\omega$ (i.e. the effective coordination number), could lead to progress in explaining the behavior of these systems.

In collaboration with S. Elezovic-Hadzic from the University of Belgrade, we investigated three families of fractal lattices: Sierpinski (2-D and 3-D) and n-simplex lattices. We computed the asymptotic behavior of the number of HWs for several members of these families, using a combination of analytical, computer enumeration and renormalization group methods. If the polymer collapse transition is possible on a given lattice, these dense walks, or equivalently folded proteins which they model, are "delocalized", i.e. favor configurations in which the number of pairs of monomers neighboring in space while far removed along the polymer chain is significant. Importantly, the scaling relations for the number of HWs do not follow the well-known form characteristic of homogeneous lattices,

which has thus far been assumed to hold for fractal lattices too. These conclusions were drawn from the results on the lattices studied; further investigation is necessary to test their generality and assess their significance for real physical systems.

**III. Ultracold quantum gases.** The past five years have seen astounding experimental progress in the field of dilute ultracold Fermi gases. In these systems the interaction strength between the fermions is tunable through Feshbach resonances, and a continuous crossover between the two limits, BEC (weakly interacting Bose gas) and BCS (weakly interacting Fermi gas), can be achieved by a simple magnetic field sweep. In addition, both Fermi and Bose gases can be loaded into optical lattices or confined in low dimensions, presenting an opportunity to study collective quantum phenomena in systems with virtually no disorder and under precisely controlled experimental conditions.

My thesis research with K. Levin at the University of Chicago aimed to describe superfluidity in Fermi gases. We developed a crossover theory based on the pairing fluctuation scenario which gives rise to both fermionic and bosonic excitations of the condensate. We concentrated on temperature effects in the superfluid phase, calculating many measurable properties of these systems such as the density of states, the critical temperature and the density profiles of the trapped gases. We demonstrated that these profiles can be used to infer temperature in the strongly interacting regime, where no reliable method for thermometry previously existed. Using this calibration, we were able to compare our calculations for the energy of the trapped gas with the thermodynamic measurements of J. Thomas's group. We found very good agreement, but more importantly, observed a power law change in energy vs. temperature very close to the point where we predicted superfluidity would occur. This was the most compelling evidence of a phase transition at the time and came after a year long effort of the entire atomic physics community to detect superfluidity in the strongly interacting regime. This research was published in Science magazine, and highlighted in Nature and Physics Today as an important breakthrough in studying the general phenomenon of superfluidity.

# Future research

The topics mentioned above represent my current research interests. I am naturally always open to their further broadening to make a connection with those of potential collaborators, especially experimental colleagues; I believe that a firm connection with experiment is key to success in theoretical pursuits. During my postdoctoral appointment I would like to further develop my interests in the following topics:

- Gene networks
- Signal transduction in prokaryots
- Pattern formation in biological systems, morphogenesis
- Noise in biological networks
- Neuroscience
- Protein folding

Jelena Stajic
Center for nonlinear studies, MS B258
Los Alamos National Laboratory
Los Alamos, NM 87545
(505) 665-3175 (office)
(505) 989-7289 (home)
jstajic@lanl.gov

Prof. J. Glazier
Director, Biocomplexity Institute
Department of Physics
Indiana University
727 East Third Street
Bloomington, IN 47405-7105

January 11, 2006

Dear Prof. Glazier,

I'm writing to apply for a postdoctoral position in the Biocomplexity Institute. I am currently a postdoctoral research associate in the Theoretical Division and Center for Nonlinear Studies of the Los Alamos National Laboratory. I obtained my Ph.D. in physics from the University of Chicago in September 2004 under the supervision of Prof. Kathryn Levin.

The topics of my thesis research were superconductivity and superfluidity in high temperature superconductors and ultracold Fermi gases (AMO and condensed matter physics); during my postdoctoral appointment I have dedicated my efforts to biological physics. My work in superfludity in Fermi gases centered on identifying signatures of superfluidity and establishing methods for thermometry in the strongly interacting regime (Phys. Rev. Lett. **94**, 060401 (2005); Science **307**, 1296 (2005)). In the studies of high temeperature superconductors, I analyzed their electrodynamic response aiming to identify the excitations that lead to the suppression of superconductivity (Phys. Rev. B **68**, 024520 (2003); Phys. Rev. Lett. **90**, 187003 (2003)). In my new field of interest, biophysics, I concentrate on elucidating the design principles of genetic regulatory networks, as well as the study of compact polymer configurations on lattices, thought to be relevant to the problem of protein folding (J. of Phys. A: Math. Gen. **38**, 5677 (2005)).

Although diverse, my research interests share a common thread: in each case the studied system exhibits collective behavior which cannot be understood from the properties of its elementary parts. My theoretical work is undertaken in the atmosphere of constant exchange of ideas with experimentalists and requires significant computational effort. During my future postdoctoral appointment, I plan to broaden my existing interests in biological physics to new fields, such as developmental biology, pattern formation in biological systems, neuroscience and signal transduction.

I'm enclosing my curriculum vitae and the statement of research interests. In my CV I have included the names and contact information for the following scientists familiar with my work: Dr. Michael Wall (postdoctoral advisor), Prof. Kathryn Levin (thesis advisor), Prof. Thomas Lemberger (an experimental collaborator) and Dr. Zoltan Toroczkai (supervisor). Thank you for your consideration.

Yours sincerely,

Jelena Stajic