THE UNIVERSITY OF CHICAGO
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Dear Professor de Ruyter van Steveninck,

I just learned about the faculty position openings at the Biocomplexity Institute in Bloomington. I would be glad and honoured if you will consider me for such a position. Enclosed, please find my CV including a list of publications, the names of my references, a short description of my research activity and plans for further development.
Thank you for your time to read my application.

Looking forward to hearing from you,

Sincerely,

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Short Description of Research Activity

Diffusion phenomena - PhD research project

Modeling diffusive transport in crystals: diffusion of impurities in crystals, migration of color centers under electric field and phase separation by thermal annealing (embedded clusters).

Results:

1. The theory of the off-center diffusion (**A** in List of Publications).

The approach applies to non-central (off-center) impurities in crystals. (Usually, they form color centers in ionic crystals.) We relate the variability of the diffusion coefficient of off-center impurities to the degree of geometrical degeneracy of the off-center potential. We explained why diffusion coefficients of off-center impurities are usually larger than diffusion coefficients of on-centers.

2. In low dimensions, the off-center diffusion theory is relevant for describing the precursor regime of the coarsening process of embedded clusters (the Ostwald Ripening process). Our results show that, in the precursor regime of the coarsening process, the temporal increase of the average radius of the droplet obeys a 1/6-power law (see **B** in List of Pblications). There is a quantitative agreement between experimental results for coarsening silver clusters embedded in KCl lattice and our theoretical predictions.

3. We investigated the behavior of the interacting off-center impurities in solid matrices. The interaction among off-center impurities are highly cooperative phenomena and lead to a perturbation of the dielectric properties of the host matrix. Our study gives a theoretical validation of the experimental observation which shows that the decrease in the dielectric constant with the increase of impurity content occurs mainly due to the aggregation of the interacting off-center dipoles.

Atomic and molecular clusters

(**B** in List of publications)

a) The jellium correction on the critical condition of cluster fission within a Liquid Drop Model was derived. The approach gives a more accurate description of the critical size of a charged cluster and its characteristic fission barrier.

b) A semi-classical model of a fullerene based on a point ion approximation of the positive background was derived. The major benefit of considering the discrete nature of the fullerene cage is the proper scale at which we can get information about the electron density profile.

c) We investigated the mixing process in two different binary clusters. The first is that of single valence electron (coinage metal) atoms and transition metals with an open *d*-shell. We showed the delocalization of the d-electrons and their role in occurrence of magic numbers. In the second binary system, the coinage metal is replaced by an alkali one, and instead of a transition metal use is made of an electronegative element. The

nature of the chemical bonding, the distinction between metallic, covalent and ionic bonds and the degree of metallization of the doped clusters were investigated.

d) Based on a quasi-classical density functional treatment, we developed an analytic ansatz that allows us a direct visualization of both screening and Coulomb correlations in pure and mixed metallic clusters. We have shown that the effective electrostatic potentials for metallic clusters is subject to important Coulomb correlation effects which can be visualized at the proper scale by employing a discrete description for the positive background. The method is useful for a fast check of the effective potential to systems (clusters of heavy elements, for example) presently beyond the capability of more accurate approaches.

e) We analyzed the role of the proximity relation between two surface-melted clusters involved in inter-cluster mass-transfer and developed the theory of a precursor regime of the Ostwald ripening

Chemical reactions: dynamics on potential surfaces
(**C** in List of Publications)

a) We explore new links between various approaches of chemical reaction dynamics that may enhance our understanding about the system's relaxation on the characteristic potential surface (PS). Thus, by the mean of a transition state theory (TST) approach that includes metric contributions (these are integrated Jacobians of the coordinate transformation) to transition rates, we have shown how reaction coordinate path lengths affect the relaxation efficiency of a complex system. We intend to use the information so obtained to identify a way to enrich the precision with which we can characterize the ability of complex systems to relax, preferentially, to only a limited number of geometrical structures from the vastly larger variety that the system might exhibit.

b) We developed recently a model for the system's inter-basin motion (IBM). This approach is designed to study dynamics on a statistical sample of potential surface (PS) that can be reconstructed in basin regions with steep topographical patterns. Basically, we focused on the ability of the system to survey well-defined basin regions on the PS rather than monitoring single states belonging to that PS. The approach provides a practical method for computing escape rates from steep basins. We have found that the number of secondary minima in the monotonic sequences and their energies relative to that of the global minimum are the main factors that compete with each other to determine the escape rate of the system from that basin. These parameters are measures of the kinetics on the complex pattern of topography of the basin surface. Based on this approach we are able to diagnose and interpret kinetic.

c) Dynamics along two competing reactive pathways is analyzed in terms of a stochastic model. The approach allows one to diagnose this competition as a function of the energy of the intermediate relative to the barrier heights of the characteristic potential surface and values of the vibrational reactive modes.

Biodynamics
(**D** in List of Publications)

a) The incipient stage of the cellular cycle holds the key for understanding the way in which tumoral cells divide themselves. We developed a model for the growth factors-cell
receptors interaction and applied to tumoral dividing helper T-cells. The approach gives an insight of the physical aspects that go on at the interface between the membrane of tumoral cells and external cellular medium. In addition, it constitutes a useful tool for quantitative estimations of the dividing process.
b) We investigated the regulation of yeast cell flocculation and pointed out that the flocculation process might be controlled at the level of the expression of cell-surface activation abilities (lectin proteins).
c) We applied stochastic simulations to studying dynamics of conformationally constrained peptides in the presence of a nonideal contact with a thermal bath. The coupling of the system with the thermal bath is expressed in terms of a memory function. We show how the system-solvent coupling affects the propensity of relaxation towards the native state.
d) In folding amphiphilic molecules (molecules having both hydrophobic and hydrophilic parts, such as proteins), the role of the hydrophobes and water structured around them are most striking, and suggests that an internal field associated with the water distribution in the hydration shell be incorporated as an integral part of a many-body folding theory. Following the above approach we can investigate the hydrophobic hydration in terms of water structure which yields an effective permittivity of the surrounding medium. Thus, we can quantify the enhancement of coulombic interactions between charged groups of a protein upon hydrophobic caging of surrounding water. In addition, the model predicts a "red shift" in dispersion properties of "biological water" and successfully reproduces the trend of the excess heat capacity of salvation, a fingerprint for hydrophobic hydration.
e) Decisions on therapies and early treatment of wounded biological tissues can be improved by establishing a correspondence between unfolding of various vital proteins and clinical manifestation of the wound. We developed a theoretical approach for diagnosing the degree of damage of the tissue under thermal insult based on the prediction of the level of protein unfolding.
f) We established a quantitative relation between the degree of structural change of protein in injured and pathological tissues and the change of the transverse magnetic relaxation time (and the implicit contrast variability of MRI).

Plan of further developments

From scrutiny of previous theoretical results and experimental observations I plan to develop models of biological systems that aim at:

- **Explaining the role of the solvent in protein dynamics (folding, unfolding, refolding) and functioning;**
- **Elucidating the role of the hydrophobes in protein folding/unfolding and in the water-mediated interaction between unfolded proteins (aggregation).**

- Another line of research, which is very much depending on the possibility of developing inter-lab projects and collaborations, and for which, with my past experience of working in quite a few Labs, I have the potential to develop it, is **designing synthetic molecular chaperones**. Alteration of cellular proteins or organelles due to reactive chemicals or high-energy physical stresses represents the most common mechanism of tissue injury leading to tissue necrosis. Diseases such as myocardial infarction, cerebrovascular stroke, cerebral palsy, burns, electrical shock, and acute radiation poisoning are examples. The success of modern gene therapy also depends on repair of the cell membrane after insertion of new genetic material. When normal cellular repair functions are incapable of managing the cell injury, pharmaceutical intervention can be lifesaving. One of the newest and most exciting trends in biomedical research is to investigate strategies that restore cell membranes, organelles, and proteins to their native structure. Two specific projects have to be initially targeted in the effort of **designing synthetic molecular chaperones:**
    - Understanding the chemical and physical aspects of assisted refolding of proteins with synthetic polymers;
    - Understanding the physical chemistry of the interaction between synthetic polymers and cellular assembles.