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

Dear Faculty Search Committee Members,

I am writing to apply for the position of assistant professor advertised in the issue of Nature. I believe that my extensive research experience in computational materials and biochemistry, my teaching experience, and interdisciplinary academic preparation provided me with the necessary background for a successful faculty career.

I am currently a postdoctoral fellow at the National Cancer Institute investigating the structure function relationship and tertiary structure prediction of nucleic acids via molecular modeling. I am also actively involved in nanobiology studies of the design and development of functional nanodevices and sensors constructed from RNA molecules. I received a PhD in Materials with emphasis on Computational Materials Engineering with a PhD minor in High Performance Computing Applications from the Pennsylvania State University in 2002. My doctoral research was on the multiscale modeling of the underlying processes of laser interaction with organic matter. I developed a novel model simulating chemical reactions in large-scale molecular dynamics simulations of dynamic non-equilibrium processes. For this research I received several awards including the Best PhD thesis award from Penn State. As a postdoc at Penn State, I initiated the project on the study of the degradation and laser ablation of polymers which was funded by the National Science Foundation. The results of my work have been published in highly ranked scientific journals.

The focus of my research program is on the development of advanced computational technology for multiscale modeling of biomolecules and biomaterials and application of this technology for investigation of various research areas in photochemistry and photobiology, such as

- structure-function relationship of biomolecules and biomaterials as a result of exposure to radiation;
- mechanisms and drug design of photosensitizers;
- dynamic non-equilibrium processes in biotissue undergoing processing by high-power laser pulses.

The ultimate goal of my research program is to understand the radiation damage of biotissue at the molecular level so that better cancer therapy and treatment methods can be developed. For the proposed projects I anticipate to obtain funding from Basic Energy Science at the Department of Energy and National Institutes of Health.

I expect that my research ideas will find a good match with the current experimental and theoretical programs at Indiana University. I believe that collaborations are crucial for success of research projects and will allow me to verify and enhance models and perform direct calculations of experiments. Within the Biology Department, I would be delighted to collaborate with Dr. Jim Drummond on the effects of DNA mismatch processing and with Dr. Patricia L. Foster and Dr. Miriam E. Zolan on DNA repair studies. I also envision collaboration with Dr. Tuli Mukhopadhyay on the structure function investigations of RNA viruses.

I have experience in supervising students' research projects and teaching courses at both the introductory and upper level. Based on this experience I am confident that I have the skills necessary to teach general undergraduate and graduate courses as well as more advanced courses in the area of Computational Biomaterials.

I expect that my research program will complement and strengthen the ongoing efforts within the Department of Biology and the Biocomplexity Institute. I have enclosed my curriculum vitae, statements of teaching and research interests, and selected publications for your review. I also asked Dr. Bruce Shapiro (National Cancer Institute), Prof. Barbara Garrison (Penn State University), Prof. Leonid Zhigilei (University of Virginia), and Prof. Ruth Nussinov (Tel Aviv University and National Cancer Institute) to send letters of reference to the Search Committee. I welcome the opportunity to discuss my qualifications with you in greater detail. Please phone or e-mail me at the numbers on this letterhead if you have questions. Thank you for your time and consideration.

Sincerely,

Dr. Yaroslava Yingling

Research Interests

Yaroslava G. Yingling

Interaction of radiation with biomolecules and biotissue

My research interests focus on multiscale modeling of the interaction of radiation with biomolecules and biotissue pertaining to cancer treatment and diagnostics. My specific research projects fall into three categories. In the first category are the studies of radiation induced damage of DNA and RNA molecules and the cellular response to this damage in cancer and normal cells. The second area involves photochemical and biophysical interactions of DNA and RNA molecules with the photosensitizers. The third area entails the development of a coarse-grained model to investigate the ablative photodecomposition of biotissue. I plan to design and perform atomistic simulations to examine specific aspects of the radiation-absorption conditions and also design a mesoscopic model to describe large biological macromolecules and ultimately biotissue. The ultimate goal of my research is to understand the radiation damage of biotissue at the molecular level so that better cancer therapy and treatment methods can be developed.

Research Background. My research experience includes the multiscale investigation of photochemical, photothermal, and photomechanical processes in various organic and polymeric materials and the atomistic modeling of structure-function relationship of nucleic acids.

My PhD thesis research involved investigations of the underlying processes resulting from the laser ablation of organic materials. Laser ablation is a complex collective phenomenon that includes processes occurring at different length and time scales and involves millions of atoms. Moreover, the photon absorption event by organic molecules can lead to the occurrence of photochemical processes, which create free radicals participating in various chemical reactions. I have developed a novel coarse grained chemical reactions model (CGCRM) which allows the detailed study of various chemical processes in large-scale molecular dynamics (MD) simulations. The model adopts physically and experimentally based parameters, such as the vibrational relaxation time, or the probabilities and exothermicities of photochemical reactions, and accounts for all phases of laser ablation. The results from my simulations elucidated the roles of photochemical, photothermal, and phototmechanical processes on laser ablation phenomena in chlorobenzene material. I also investigated the effects of volatility of matrix and analyte molecules on laser ablation processes. For this project, I received the Best 2003 PhD thesis award from the Materials Research Institute at PSU.

During my postdoctoral work at Pennsylvania State University, I modeled the interaction of UV light with polymeric materials. I have successfully applied the CGCRM methodology to the modeling of a more complex problem such as large-scale simulations of amorphous polymeric materials degradation due to both chemical and photophysical processes. I have designed a polymer sample model that was represented by the intertwined network of bead-and-spring polymer chains and the corresponding force field with the physical and chemical properties of poly(methyl methacrylate) (PMMA). PMMA is used in spacecraft materials, thin films, bone replacements, cement spacers, and various dental materials. An original algorithm has been designed to represent a low flux of various energy photons and oxygen atoms on the surface and

applied to the study of the influence of low earth orbit environment (LEO) conditions. LEO conditions present particular challenges as the synergetic combination of an aggressive atomic-oxygen bombardment with solar UV radiation lead to degradation of technologically important materials. The results from the model identified primary degradation processes in polymeric materials and essential mechanisms for laser ablation of polymers.

In my current postdoctoral work at the National Cancer Institute, I concentrate on the atomic-level study of the structure-function relationship of RNA molecules. I have performed a detailed molecular modeling investigation of the wild-type human telomerase RNA domain. Telomerase, a ribonucleoprotein enzyme complex, is an ideal target for cancer therapeutics and diagnostics because it is active in all major types of cancers but not in most normal cells. I have depicted that two-base mutations, occuring in dyskeratosis congenita, lead to a change in the dynamical function of the telomerase RNA pseudoknot domain by stabilizing the hairpin domain and disrupting the formation of a pseudoknot helix. Moreover, I was able to solve a complex and dynamic three-dimensional structure of the wild-type telomerase RNA pseudoknot via purely molecular modeling. I have also conducted studies involving the use of RNA sequences as a building block for nanodevices and the interactions of a metabolite with the riboswitch.

My research background gives me unique skills for tackling the complex issue of radiation damage of healthy and abnormal tissue, the detailed understanding of which will lead to improvements in cancer drug design and radiation treatment.

Future Research.

In my future research, I will combine my past research experiences and concentrate on the modeling of photochemical modifications of biomolecules and biomaterials due to radiation exposure. Biotissue is a complex system and, therefore, the analysis has to be done at different levels of details, from an accurate atomistic modeling of nucleic acid damage to interactions between sets of more complex biomolecules and to the development of large-scale models of multi-level molecular complexes as tissue. Therefore, I plan to concentrate on three research areas:

- Atomistic investigations of radiation damage of nucleic acids and damage response in normal and cancer cells;
- Molecular modeling of the effects and advantages of various photosensitizers on nucleic acid structure and function;
- Multiscale studies of laser-tissue interactions.

Each research area requires the development of the corresponding methodology. I plan to develop novel computational models, algorithms, and high-performance computing techniques.

Direct connection to experimental research is crucial for the success of the modeling interpretation and validation. Collaboration with computational research groups can lead to better model development and outcome. Therefore, I will be seeking collaborations with experimental and computational research groups whenever possible.

Next, I will describe each research project in detail followed by the methodologies that will be applied in these projects.

Project I.

(a) Radiation-induced damage of biomolecules

Radiation is a high-energy beam that is able to penetrate cells and change the properties of various molecules in different parts of the cell. Radiation is used to treat many types of cancer by shrinking the tumor, providing temporary relief of symptoms, or treating unoperatible malignancies. Because of new research and technical developments radiation therapy is now a rapidly advancing technique. However, the understanding of the mechanism controlling radiation response is not yet complete. The future improvement of radiotherapy and the development of other techniques, such as chemoradiation therapy and photodynamic therapy, are largely dependent on a better understanding of the complex and multiple processes controlling cell response to ionizing radiation.

The radiation induced modifications trigger chemical changes in the molecules that can lead to the formation of highly reactive free radicals. These changes can cause mutations in a cell's DNA or RNA, leading either to a cell death or to the cancer development. The possible radiation damage of DNA includes alterations in bases and sugars, single and double-strand breaks, DNA-DNA and DNA-protein crosslinking.[1] Moreover, radiation can produce water-derived radicals, which can react with nearby molecules resulting in scission of chemical bonds or oxidation of the DNA molecules. It it generally believed, that double strand breaks in DNA molecules play a pivotal role in cell killing and formation of genetic alterations.[2] However, the relative roles of various types of DNA damage in cells have not been clearly established. Most of the studies so far have been done on DNA molecules; however, it is likely that there will be significant damage to cellular RNA during radiation treatment. The significant damage to RNA also leads to apoptosis.[3]

Even though considerable research has been done on understanding the possible outcomes of DNA damage,[2] the characterization of the biological effects on a molecular level is far from complete. Moreover, the dynamical and structural response to radiation damage of RNA and DNA molecules is largely unknown. Because of my research background this area is especially fruitful to explore. I plan to examine the structural and dynamical details of various types of nucleic acid damage due to radiation and/or free radicals via atomistic simulations. The details of the applied methodology are explained in methods section. Different segments and sequences of DNA and RNA molecules will be used. The atomic coordinates for MD simulations can be taken from NMR, X-Ray studies or designed using available software. The significance of known types of radiation damage, including sugar and base modification, single and double strand breaks, inter and intra strand crosslinking, will be examined. The structural and dynamical changes of damaged nucleic acid will be compared with native molecules. I will start with 20-base pair duplex DNA oligonucleotides, which is chosen for comparison of results with the experimental findings of Harrison et al.[4] The research area will then be expanded to RNA molecules.

Expected outcome: The primary intent of this project is to understand the mechanism of nucleic acid radiation damage and its effect on structure, dynamics, and function of biomolecules. The doses prescribed to a tumor during radiotherapy are directly dependent

on the tolerance of the normal tissue in the radiation field. The understanding of the mechanism controlling the radiation response is crucial for local tumor control and minimizing the effects of radiation to the normal tissue. Moreover, the results received from this basic study will establish the core of my future simulations and model development.

(b) Radiation response

P53 tumor suppressor protein is a transcriptional activator that accumulates in response to radiation and other DNA-damaging agents and influences the cell's decision on repairing DNA damage or inducing apoptosis. In human cancer, the p53 gene is commonly mutated or deleted. Radiation therapy may be the ideal way to treat a tumor with a p53 mutation; mutations in p53 can jeopardize the efficient repair of damaged DNA. However, mutations in p53 may also lead to increased cell survival due to inability to induce apoptosis.

In a normal cell, p53 participates in various processes of DNA repair and recombination by interacting with repair protein components and via various DNA-binding activities. The evolutionarily conserved core domain, for example, is involved in sequence-specific binding to promoters of p53-regulated genes and also interacts with internal regions of single-stranded DNA, three-stranded DNA substrates, and manifests a $3' \rightarrow 5'$ exonuclease activity.[5] Point mutations in this domain are the most frequent alterations in p53 found in human cancers. Moreover, it has been shown that the C-terminus of p53 alone is capable of DNA renaturation, DNA strand-transfer, and increases binding affinity for damaged DNA.[6]

Research studies over the last decade reveal that the p53 protein is crucial for cellular response to DNA damage.[7,8,9,10,11] Despite these studies, the biochemical basis for tumor suppression is still unknown. Moreover, the understanding of the p53 response mechanism to DNA damage at the molecular level is still not clarified.

The structures of three p53 domains have been solved and the atomic coordinates are available for MD simulations. Most of the p53 mutations that cause cancer are found in the DNA-binding domain. The crystal structure of a core domain of human p53 and a DNA binding site has been determined.[8] The atomic coordinates of the protein and the DNA will be taken as a starting point for molecular dynamics simulations. I will examine the effect of various types of DNA damage on the structure stability of the p53/DNA complex. I will then introduce known cancer mutations to p53 and compare the response of mutated p53 to various types of DNA damage. Other known p53-binding DNA sequences[8,9,10,11] can also be examined. The results will be compared to the experimental observations.

Expected Outcome: The primary intent of this project is to examine a possible role of p53 in the cellular response to radiation induced DNA damage. The specific goals are to analyze the contributions of the p53 domains to DNA binding and radiation damaged DNA; to evaluate the effect of known p53 mutations on complex stability and dynamics; and to examine the effects of various DNA radiation damage patterns on p53/DNA complex dynamics and stability. Understanding of the complex interactions between p53 and damaged DNA will provide insights into mechanisms of tumor development and may create new approaches for therapeutic interventions.

Given my expertise in molecular modeling and photochemistry I expect to complete this project in a relatively short time period.

Project II. **Photosensitizers and nucleic acids**

Photodynamic therapy (PDT)[12] uses the interaction of monochromatic light with a photosensitizer to destroy cancerous cells and tumors. During PDT a photosensitizer is injected into the tumor and absorbed primarily by cancer cells. Monochromatic irradiation of the tumor can then trigger selective photochemical reactions. The tumor is presumably destroyed due to the presence of singlet oxygen (generated via energy transfer from excited sensitizer to triplet oxygen) or various radical products (generated via electron transfer from excited sensitizer). As a result of the process DNA damage is observed.

The commonly used photosensitizing agent is porfimer sodium, which is a mixture of oligomers formed by ether or ester linkages of up to eight porphyrin units. Illumination of target tissues with 630 nm wavelength laser light induces a photochemical reaction that activates porfimer. This activation initiates a chain reaction, producing singlet oxygen, superoxide, and hydroxyl radicals, which lead to cellular damage and contribute to ischemic necrosis and ultimately tissue and tumor death. Porfimer PDT causes an increase in thymidine kinase mutants, DNA-protein crosslinks, and produces a light-dependent increase in DNA-strand breaks.

The main disadvantages of porfimer are weak absorbance at 630 nm, resulting in application of PDT to tissues of less than 1 cm, and persistent photosensitazion of the patient's skin that lasts several weeks after the therapy. Many new agents have been investigated with greater absorbance and higher diffusivity. The difference and advantages of binding and possible photocleavage of DNA of other photoagents, like rhodium, ruthenium, hematoporphyrin derivative (HPD),[12] and mixed-metal supramolecular complexes[13] will also be examined.

The extent and success of the tumor damage depends on the absorption and retention of photosensitizer in the tumor tissue. However, the reason for the localization of photosensitizers at abnormal tissue is not yet clear. Moreover, the issue of preferential photosentisizer binding to nucleic acids is crucial for drug delivery and further improvements of PDT. I plan to perform a series of molecular modelling investigations of nucleic acids/photosensitizer complexes. I will start with the crystal structure of a B-type DNA duplex with the porphyrin molecule which recently has been solved[14]. I will investigate the effect of bonded photoagent on the structure and dynamics of the DNA duplex. I will examine the effects of possible photochemical reactions on DNA structure.

I will continue this line of research by examining RNA/photosensitizers interactions. Porphyrin binds specifically to tRNA in the site that is important for maintenance of the tertiary structure. It has been shown that binding of porphyrine in the hinge region links RNA helices and photomodification occurs predominantly at G65.[15] A recent study provides details of the inhibition and additional binding sites of porphyrines with tRNA, precursor tRNA and M1 RNA.[16] I will then investigate the result of porphyrin on tRNA dynamics. The atomic resolution structures of tRNA and porphyrines are available. Possible binding sites of porphyrin will be examined and the porphyrin molecule will be docked into tRNA. The effect of porphyrin binding on tRNA structure will be examined and photochemical pathways and potential RNA damage will be revealed.

The development and introduction of new photosensitizers is a current and expanding research field. Other photosensitizers will be docked into the same location of DNA and RNA as porphyrins and the MD simulations will be performed and compared.

Collaboration with experimental groups working on drug development or photagents will be particularly productive in this project, as the combined effort will lead to faster progress and possible discovery of new and more effective anticancer drugs.

Expected Outcome: Understanding the modes of the binding of porphyrines to DNA and RNA and the factors that can affect that binding is of critical importance to improvements of PDT and future developments of other anticancer drugs and therapies. The specific goals in this project are: to examine the factors affecting the character of porphyrin binding and the impact that porphyrins' binding has upon the structure of DNA; to elucidate the mechanisms of porphyrin-induced DNA strand cleavage during laser excitation; to analyze the effect of bonded porphyrine on the stability and dynamics of tRNA and the effect of laser excitation on binding sites of tRNA; to evaluate the possibility of various chemical interactions between nucleic acids and porphyrine; to investigate the effect of other photoagents on nucleic acids structure and dynamics. The results from this project will aid in understanding the tumor-localization phenomena. Moreover, it is crucial for the drug design of DNA cleavers to understand at the molecular level all the different factors involved in their interactions with nucleic acids.

Project III. **Laser-tissue interactions**.

Laser light is used to surgically remove cancer or precancerous growths or to relieve symptoms of cancer on the surface of the body or on the lining of internal organs. Moreover, photoablation is one of the most successful techniques for refractive corneal surgery. Even though laser surgery has been extensively used, the understanding of the mechanisms of tissue ablation and the role of various tissue constituents is not complete. The success and optimization of current applications is strongly dependent on the complete understanding of the underlying processes.

Biological soft tissues are mostly comprised of a dense network of collagen and elastin fibers. Collagen is the most abundant protein in mammalian cells and the primary component of corneal tissue. A collagen molecule consists of three polypeptide chains arranged in a right-handed triple helix and held together by covalent cross-links. It is generally accepted that the peptide bond in polypeptide chains of collagen is the most probable absorber for 193 nm laser irradiation due to higher absorption coefficient.[17]

The examination of processes that result in laser irradiation of collagen fibrils and lead to material removal happens on time and length scales well beyond the current simulation techniques. I plan to develop a coarse-grained model of laser ablation of soft biotissue. Since collagen is a primary component of soft biotissue, an understanding of its role in UV photochemistry is a necessary step towards elucidation of laser tissue interactions. A development of a comprehensive and accurate multilevel model requires analysis of components at various levels of details. Next, I will highlight the necessary steps that will be performed in this project.

- In order to establish an accurate coarse-grained model a complete understanding of an atomistic force field and individual photochemical response is needed. Therefore, atomistic simulations of collagen molecules and their photo-induced interactions, including photothermal and photochemical processes, will be performed. The role of laser excitation of peptide bonds on atomistic level will be assessed. The three-

dimensional conformation of fibril forming triple helical collagen molecule has been determined by X-ray at atomic resolution and will serve as starting coordinates for atomistic molecular dynamics simulations.[18]

- The coarse-grained representation of collagen molecules will be developed and the force field parameters will be established. Collagen molecules tend to align parallel to each other forming the individual collagen fibrils. Collagen fibrils can assemble to form unidirectional fibers in tendons, two-dimensional layers in skin, or complex three-dimensional arrangements as in cartilage or cornea.[19] The details of the three dimensional structure of corneal collagen fibril have been revealed and will be taken into consideration for the sample development.[20] Each collagen molecule will be represented in our model by a flexible bead-and-spring model. It is then possible to construct a collagen fiber consisting of coarse-grained collagen fibrils. In a hydrated collagen material, the sample will include long collagen-like molecules surrounded by a matrix of coarse grained water molecules.
- A methodology representing absorption of a beam of photons by a coarse-grained sample will be designed. I have extensive experience in designing coarse-grained samples and developing various radiation conditions.[21,22]
- I will start from modeling an ablation of dry collagen films where a static absorption coefficient is suggested.[17] The goal here is to study the dynamics and effects of peptide bond and amino acids on collagen ablation at various laser fluences.
- Since corneal tissue consists of 78% water I will extend my research to the examination of photoablation of collagen in aqueous solutions. The tissue hydration is potentially important for the observed dynamic changes in tissue optical properties during ablation.

Expected outcome: The understanding of the collagen ablation process can lead to improvements in therapeutic and refractive procedures. The research activities in this project are focused on understanding fundamental processes associated with laser excitation, damage, and removal of collagen tissue. In order to understand more complex interrelationship defining the structure and function of biotissue it is necessary to consider not only collagen but also other components. A long-term project goal is the development of a model that can represent laser ablation of a complex biotissue, which include various biomolecules and components. The results from this project may lead to technical advancements in laser surgery and therapy allowing a reduction in the incidence of adverse events and better outcome for a patient.

METHODS

I will use a variety of computational methods and algorithms. Most of my studies will be based on the molecular dynamics (MD) technique, in which the time evolution of the molecular system is followed by numerical integration of the equations of motion. Numerous properties computed via MD simulations can be directly compared to experimental quantities. Moreover, MD simulations have proven to be a powerful tool for studying the functions of biological systems, providing structural, thermodynamic and dynamical information and revealing possible structure-function relationships.[23]

Atomistic molecular dynamics. Atomistic MD methods rely on the knowledge of accurate atomic coordinates of the molecules of interest, which can be obtained from NMR or X-ray studies. When an experimentally derived structure is not available, an

approximate 3D representation of a structure can be obtained using the developed software (S2S, RNA2D3D, InsightII) and further refined with MD.

Atomistic simulations using the Cornell force field will be performed whenever needed in order to examine in detail atomic motions and structural integrity following the radiation or free radical reaction. For the atomistic MD simulations, I prefer to use NAMD , AMBER , or CHARMM software packages.

Coarse-Grained approach: Phenomena like laser irradiation of biotissue demands a large system size (surface effects, absorption depth of light) and long time scales (laser pulse width, material relaxation). By foregoing atomic level detail and retaining only the essential structural information that describes the system, it is possible to model larger systems than those that can be modeled atomistically. The representation of collagen in my models will be based on the united atom approximation and the bead-and-spring approach. The chemical pathways of collagen photo irradiation will be investigated via atomistic simulations and if needed electronic structure calculations. The level of coarse grained approximations of collagen structure depends on its photochemical pathways. The force field parameters will be developed and fitted to represent the real properties of collagen such as cohesive energy, density, elastic bulk modulus.

Photodissociation of bonds and chemical reactions:

Starting conformations of damaged nucleic acids in atomistic MD simulations will be obtained by modifying the atomic structure to introduce strand breaks or covalent breaks in the backbones or bases. Partial atomic changes for modified residues can be determined by fitting the electrostatic potential energy of quantum electronic-structure calculations.

The described research projects involve the development of an effective methodology that allows the study of explicit bond dissociation due to reaction with free radicals and the effect of energy transfer from the excited atom to the surrounding atoms during atomistic MD simulations.

Modeling of photochemical and photothermal reactions in coarse-grained models can be accomplished by the application of similar methodology that I have developed during my PhD thesis work with the necessary modifications.[21]

High performance computing. My experience in applications of high performance computing to scientific applications allows me to expand my models to larger time and space scales. I plan to implement advance algorithmic approaches and parallel computing environment in the design of my large-scale models.

My research interests are not limited by the described above topics and I have many more interesting research ideas for the future.

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YAROSLAVA YINGLING

STATEMENT OF TEACHING PHILOSOPHY

I believe that good teaching and learning progress can be achieved by active engagement of students' interests. It is important that students have clear understanding of the pragmatic utility of the study material for their future professional development. To achieve this goal I will use diverse approaches for different level of courses:

- In *introductory science courses* I will start with examples and then proceed to principles, use a variety of in-class demonstrations, hands-on activities, and references to everyday observations and experiences that would demonstrate the direct relevance of the course material and to the real-life problems that students will face in their future professional careers.
- For *advance undergraduate and graduate courses*, I will present recent achievements and current problems in the field of study, discuss the existing approaches and ideas, encourage students to read recent articles and to discuss their ideas. One of my main objectives will be to demonstrate that biological science is an active and vibrant field that has numerous fascinating applications and unresolved problems.

I believe that the purpose of science education is not simply to memorize a set of facts, but to develop a critical and analytical thinking and strong problem solving skills. Homework and practice problems encourage students to sharpen their problem solving skills and enhance their understanding of the fundamental principles of science. I think that working on independent projects is essential for development of critical thinking and communicating science ideas. Moreover, independent projects will encourage students to explore unresolved issues in the field and to promote scientific curiosity. Most of my courses will include term projects or papers which require independent literature search, writing, and class presentation.

Every student has a different mathematical background and abilities. Clear qualitative understanding of the material should precede mathematical formulation. The material should first be presented in a clear visualized form that grabs students' attention with possible real-life examples and analogies. A solid intuitive grasp should provide a basis for understanding of mathematical formalism describing a given phenomena or technique. I will make special efforts to explain approximations used in mathematical derivation so that students have clear understanding of the scope of applicability of resulting formulas and expressions.

Addition of computers-assisted learning to the curriculum can increase students understanding of biological science and make the process of education more interesting and enjoyable. I intend to develop courses/laboratories in computerized version with extensive use of multimedia and virtual reality.

Students will have to live in an environment that is growing more and more dependent on technology and will be faced with plenty important policy decisions concerning the environment, scientific research, energy, and technical development. Many of the students will not be scientists, however, the knowledge they obtain in my courses will help them to know more about physical processes in our surroundings, develop critical and analytical thinking and strong problem solving skills. This will give them an advantage in their future professional development and daily lives. These are guiding principles that permeate all of the courses that I teach.

Teaching Interests

I always enjoyed teaching. As an undergraduate student, I tutored high school, freshman, and sophomore students in physics and math. As a graduate student, I taught *General Chemistry*

laboratory for undergraduate students and *Computer Simulations for Physical Scientists* class for graduate students. I also designed and presented a short course on the use of parallel computing for graduate students. I taught individual lectures and given presentations and seminars. Also during my doctoral studies, I supervised a number of undergraduate research projects. As a postdoc, I run research projects where I mentored undergraduate and graduate students, visiting researchers, and postdocs.

These experiences have prepared me to teach a variety of classes at any level. I am prepared to teach a variety of courses in biological and physical sciences, such as introductory courses to general science and biology, biophysics, biological macromolecules, kinetics, thermodynamics. Also I can teach courses in computational sciences such as bioinformatics, molecular modeling, high performance computing applications, mumerical methods, optimization methods, computer languages. Furthermore, I would like to develop a course or a number of courses on the topic of *Computational Biomaterials Science and Engineering*.