Topical issue on Bio Macromolecules

Editorial

This EPJD topical issue is devoted to the emerging physical problems of an interdisciplinary field of research, focusing on the investigation of structure, dynamics and functioning of bio macromolecules. The choice of topic is motivated by increasing interest in the fundamental problems of the physics of bio macromolecules. The interdisciplinary character of these problems and their potential future applications in technology and medicine has stimulated many studies in this area. From a theoretical point of view, increasing computational capabilities alongside the development of new methods and approaches have allowed physicists to study large systems which were previously treated entirely with qualitative chemical and biological approaches. Experimentally, the development of very high resolution mass spectrometers and ion traps, versatile tunable lasers, new detectors and imaging techniques, NMR and atomic force spectroscopy have opened the way for new experiments on these biomolecules. These methods often provide direct information about the structure and dynamics of single biomolecules. Probably the best approach to pursue these studies in future is a combination of theory and experiment on the same model systems. Localising excitation and charges on these complex molecules and understanding their dynamics is a dream which could be accessible in the near future. Attempts in this direction have often proved very productive and have recently led to many interesting results and advances. Significant progress using this approach has come mainly from atomic and molecular physics, often combined with appropriate methods from condensed matter, nuclear, chemical and biological research. The physics of bio macromolecules is developing into a broad field of research, with many subfields and parallels with other research areas dealing with the structure, formation and dynamics of complex molecular systems. Cluster physics is one of the closest neighboring research fields. Discovering clustering phenomena and transferring the insights to bio macromolecular systems, and vice versa, could lead to essential breakthroughs in understanding biological and inanimate systems at the nanoscale. In this sense, the physics of bio macromolecules can be viewed as a subject of a newly emerging broader discipline, which may be called BioNano mechanics or BioNano science. This new discipline brings adjacent topics of physics, chemistry and biology into a common intellectual framework.

The physics of biomolecules has recently become a topical issue in many physical laboratories worldwide. This is because it became feasible to transfer the methodology, level of detail and accuracy of atomic and molecular physics research to much more complex biomolecular systems. Each year this trend involves more and more researchers, groups and physical laboratories worldwide. It is perhaps not realistic to cover all the aspects of the physics of bio macromolecules and to represent all the achievements in the field within a single topical issue of any journal. Thus, in this EPJ D special issue we focus primarily on several important directions in this exciting field of research, namely on the dynamics, spectroscopy and radiation damage of bio macromolecules and their functionality. This issue reports on the most recent advances achieved in these areas by a group of mostly European researchers focusing on the fundamental problems of bio macromolecule physics and their applications.

We introduce briefly each of these research directions.

Dynamics of Bio Macromolecules

Detailed knowledge of the dynamics of bio macromolecules is crucial for understanding of many biomolecular processes occurring in a cell environment. Although many of the key biological processes such as DNA opening, protein folding, membrane transport and photosynthesis have been identified long ago, in most cases a detailed understanding, in the physical sense, of the dynamics, interactions and functioning of biomolecules is still lacking and is the subject of intensive research. There is a huge number of different degrees of freedom in bio macromolecules, yet dynamical processes usually involve only a small part of the entire coordinate space of the system. Identification of the generalized coordinates relevant for a particular dynamical process is not always easy (neither theoretically nor experimentally), but this knowledge is often crucial in order to make significant advances in the process understanding. For instance,

this kind of situation is very typical in the investigation of protein folding, studies of nanoscale phase transitions occurring in bio macromolecular systems, description of thermodynamic and structural properties of biomolecules and their interactions with photons and charged particles (electrons, positrons, protons and ions). Examples of such investigations are presented in this topical issue of the EPJ D. From a theoretical point of view significant progress in generating detailed descriptions and analysis of dynamics of complex biomolecular systems became possible only recently due to increased computing power. However this development was also supported by significant experimental success. The number of experimental methods that allow monitoring of the dynamics of single bio macromolecules has increased significantly in recent years and is still growing. For example methods of NMR spectroscopy allow measurement of signals from interacting spins of atoms in unfolded proteins placed in some restricting media. In this way one can obtain valuable information about the details of unfolded protein dynamics and their structure. Although this information is extremely valuable for improved understanding of the biomolecular processes in a cell environment, so far it is not understood at a sufficient level of detail and is the subject of intensive investigation. Apart from NMR spectroscopy, there are many other experimental methods that allow monitoring of single biomolecule dynamics, e.g. fluorescence spectroscopy, AFM microscopy, optical and laser spectroscopy, Raman scattering, use of storage rings and collision techniques. We do not intend to cover all of these methodologies here, but want to draw the attention of our readers to the fact that this field of research has developed rapidly during recent years and is still far from its final state. We still expect much more to happen in the field. There is great demand for the knowledge generated in this field from the medical and pharmaceutical industries as well as from bionanotechnology and microelectronics.

The articles included in this EPJ D special issue address some of the questions mentioned above. The following articles illustrate the broad range of problems in the field open for the current and the future research:

- L.H. Andersen and A.V. Bochenkova, The photophysics of isolated protein chromophores
- F. Calvo and P. Poulain, Transitions between secondary structures in isolated polyanilines
- A.V. Yakubovich et al., Phase transitions in polypeptides: analysis of energy fluctuations
- J.H. Meinke et al., Computer simulation of proteins – thermodynamics and structure prediction
- M. Čubrovič et al., Semistiff polymer model of unfolded proteins and its application to NMR residual dipolar couplings
- G.F. Gribakin and C.M.R. Lee, Positron annihilation in large polyatomic molecules. The role of vibrational Feshbach resonances and binding

Spectroscopy and Radiation Damage of Biomolecules

The investigation of the mechanisms of radiation damage of bio macromolecules, in particular DNA and RNA molecules and their fragments, has recently become a highly topical issue due to the very successful application of energetic ion beams to the medical treatment of certain types of cancer, in particular brain cancer. For more than ten years, ion-beam cancer therapy has been successfully used clinically in Germany and Japan. Proton-beam therapy is performed in many more centres around the globe. Thousands of patients per year are being treated. These therapies appear to be a more favourable alternative to the conventional X-ray or γ photon therapy, also known as radiotherapy. Despite apparent experimental and clinical successes, a comprehensive understanding and description of a physical scenario of the cascade of processes occurring in a cell and in tissue is still missing. Thus in recent years significant effort has been made to understand in detail the mechanisms of interaction of charged particles (proton, ions and electrons) with biomolecules and to develop a comprehensive picture of physical processes occurring during the passage of energetic ions through biological tissue. This deep understanding of the processes is very important because the use for cancer treatment of new generations of beams of higher mass ions is planned in many countries in the future. It is also often referred to as hadrontherapy.

For many decades spectroscopic methods have been a very practical tool to monitor essential details of structure of various atomic and molecular objects. Recently UV spectroscopy of biomolecules has become a new emerging field. The development of electrospray ionization sources and ion traps renders possible very precise studies of photofragmentation of biomolecule cations and photodetachment and fragmentation of polyanions. Photofragmentation has been recently shown to be very specific, as compared to collision induced dissociation, in particular H loss and side-chain cleavage. These specific photodissociation processes could be used in the future during protein database searching. Photodissociation or photofragmentation is also a very efficient method to record the optical spectra of biomolecules, when the photon absorption leads systematically to the dissociation of the molecule. These spectra as well as the fragmentation channels compared to *ab initio* calculations may be used to determine the biomolecule conformation and could in future be used as probes of the conformation and consequently of biologic properties of the molecule, at least in specific cases.

The photodetachment of molecular polyanions is also a very elegant method to obtain UV absorption spectra of these molecules in the gas phase. In the near UV these spectra are due to chromophores such as tryptophan or

tyrosine and are very sensitive to their ionization state, allowing the localization of the negative charges in polyanions. In the future a very important challenge is to determine the dynamics and mechanisms for photofragmentation and photodetachment processes. Pump probe techniques and photoelectron spectroscopy are very promising. However, the challenge for experimentalists and theoreticians is that the time scale may extend from the femtosecond to the millisecond range depending on the processes involved. These emerging new spectroscopic methods are presented in several papers of this session of the special issue, particularly in papers by Grégoire et al. and Antoine et al.

Below are listed the articles which address specific problems of spectroscopy and radiation damage of biomolecules:

- E. Surdutovich et al., Ion-induced electron production in tissue-like media and DNA damage mechanisms
- S. Denifl et al., Electron impact ionization studies with the amino acid valine in the gas phase and (hydrated) in helium droplets
- S. Bari et al., Kinetic energy releases of small amino acids upon interaction with keV ions
- J.-F. Greisch et al., Collision induced dissociation of deuterium enriched protonated 2'-deoxyguanosine
- A. Giuliani et al., Electronic states of neutral and ionized tetrahydrofuran studied by VUV spectroscopy and ab initio calculations
- G. Grégoire et al., UV photoinduced dynamics in protonated aromatic amino acid
- R. Antoine et al., Electron photodetachment of trapped doubly deprotonated angiotensin peptides. UV spectroscopy and radical recombination
- V. Bernigaud et al., Ionisation and fragmentation of tetraphenyl iron (III) porphyrin chloride induced by slow multiply charged ion impact
- I. Baccarelli et al., Modelling dissociative dynamics of biosystems after metastable electron attachment: the sugar backbones

Bio Macromolecules in Action

Detailed understanding of the functionality of specific biomolecular species is obviously another very important direction in the field. There are many examples in biology that a certain biological function or a biological process is in fact driven by a specific molecule or by a specific biomolecular interaction. Indeed, many biological processes are driven by interactions between the molecular components of cellular machinery, commonly between proteins and their target molecules (generically termed ligands). Most of these processes portray a cascade of protein-ligand association/dissociation events, and thus, knowledge and control of their energetics and kinetics is of key importance in molecular biology, proteomics, and therapeutic research. One of the most remarkable examples of a protein-ligand system is that of antibody-antigens, which is involved in a fundamental recognition process during the body immune response. Although a tremendous amount of work has been devoted to the development of our knowledge of the immune response, understanding of this process on the molecular level is still in its infancy. Another very important example in which protein-ligand interactions play a key role concerns the design of drugs and detailed understanding of their functionality at the molecular level. This problem, which existed for a long time as a purely empirical or technological one, in recent years has received more and more theoretical attention. This is because modern computers are now sufficiently powerful to allow researchers to address meaningful questions which were previously insoluble. Modern experimental techniques also provide a lot of useful and detailed information stimulating greatly further theoretical work in this direction. This subfield of research is very broad and involves many open challenging problems and the research groups working on their solution. Here we do not have an opportunity to even mention most of them. Instead we present several prominent examples of investigations in which physical approaches towards the description of bio macromolecular systems have turned out to be very useful in the understanding of their functionality on the molecular level and in the elucidation of the bio macromolecule function and activity.

The following three articles of this EPJ D special issue address this type of problem:

- R.A. Broglia, Learning to design resistance proof drugs from folding
- M.T. Figge and M. Meyer-Hermann, Modeling receptor-ligand binding kinetics in immunological synapse formation
- I.A. Solov'yov and W. Greiner, Iron-mineral-based magnetoreceptor in birds: polarity or inclination compass?

To summarize, this EPJ D special issue presents a collection of essential contributions, up-to-date review and research reports in the above-mentioned fields. We believe these will be of significant value and interest for the interdisciplinary bio macromolecules research community. We also hope that this topical issue will attract attention to challenges in this field from non-specialists and will stimulate further effort and major breakthroughs within the research community.

The editors:

Prof. Dr. A.V. Solov'yov

Prof. Dr. M. Broyer