Completing Our First Decade of Biological Physics Conferences

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The 5th International Conference on Biological Physics (ICBP) was held 23–27 August 2004 at Chalmers University of Technology & Göteborg University, in Göteborg, Sweden. The first meeting in Szeged in Hungary 1993 attracted about 100 participants. The 2nd meeting in Munich, in Germany 1995, was attended by 150, and the 3rd meeting in Santa Fe, in USA 1998, by some 180. Seven hundred came to the 4th meeting in Kyoto, in Japan 2001, 500 from the host country. About 270 were expected to come to Sweden for this 5th meeting. However, 537 participants were attracted to Göteborg, 435 from 43 foreign countries, thus doubling the number of participants from non-host countries. Fifty-three lecturers were invited, 516 poster abstracts were submitted and 50 selected for oral presentation [1]. Future conferences in this series will show whether this increase corresponds to a genuine expansion of biological physics or if it was just a result of effective advertising. It is likely, however, that biological physics has now become acceptable also to core physicists. That would be an important new trend in itself.

The meeting, which was organized by Clas Blomberg,¹ Mats Jonson² and Leif Matsson, was divided into 12 different symposia covering, in principle, all areas of biological physics. *Adrian Parsegian's* opening presentation emphasized molecular assembly and protein-DNA interaction under osmotic stress conditions of crowding that obtains in viruses and in cells. Here, forces of stress and hydration dominate not only the work of macromolecular packing but also the specificity and kinetics of molecular association. *William Moerner's* optical explorations of single molecules also focused on molecular interaction, revealing characteristic times under varied conditions, a concept elaborated by many others. Following the theme of macromolecular kinetics, *David Nelson* showed how sequence heterogeneity could create plateaus and jumps in unzipping of DNA and RNA under the denaturing force of optical tweezers. *Cees Dekker* spoke of DNA translocation through pores in layered nano-structures and of a new technique to fabricate such structures.

Single-molecule associations and processive kinetics were formulated by *Michael Fisher*, who described the progress of a motor protein along a molecular fibre, a process driven by the binding and subsequent hydrolysis of ATP. *Kenichi Yoshikawa* demonstrated that a giant DNA molecule exhibits all-or-none switching in the genetic activity accompanied by transitions between elongated coil and folded compact states, whereas abrupt changes in activity disappear with short DNA. *Gerd Nienhaus* presented a spectroscopic study of a novel fluorescent protein and how it can be used to study intracellular processes. By photo-polymerization of micrometer size particles of special shapes that permit complex manipulations in the optical trap, e.g., torsional manipulation of bio-molecules, *Pal Ormos* showed how the level of control of optical tweezers could be extended.

In the session on charge transfer, *Sven Larsson* took electronically excited states in Photosystem II as an example of delocalized states in a finite system. *Serge Aubry* introduced a new model for the study of electron transfer in photosynthetic reaction centers. How to obtain novel insight into peptide dynamics was described by *Josef Wachveitl*. He incorporated a molecular photo-switch into an octa-peptide and used 60 fs pulses to initiate dynamics which was followed using transient spectroscopy. Ultrafast kinetics was also used to probe recombination of the NO ligand to heme iron in a work presented by *Paul Champion*. In another talk on proteins, *Jens Ulstrup* presented scanning tunneling microscope data for electron transfer proteins forming a monolayer on a surface. *Thorsten Koslowski* introduced methods known from solid state chemistry to describe charge transfer in DNA.

David Walt described experiments performed in nano-capsules at the end of a bunch of optical fibres, with measurements that allow individual monitoring of reactions at the scale of a nanoliter. *Wolfgang Knoll* described efforts to create and probe artificial membranes, a step towards a general class of biosensors. *Steven Boxer* described a tethered vesicle system which can be used to create membrane protein arrays and whose dynamics may lead to emergent properties, and *Owe Orwar* spoke about networks of nano-fluids and the control of chemical reactions in such systems. *Jürgen Köhler* showed how the spectral dynamics of the absorptions from individual pigments of a chromo-protein provide information about the organization of the energy landscape of the protein in tiers that can be characterized by an average barrier height, and that a clear correlation is observed between this height within a distinct tier and the time scale of the spectral fluctuations. *John Nagle* reported a new non-crystallographic use of synchrotron x-ray scattering to obtain more information about bio-membrane structure than from traditional crystallographic methods. *Lilian Costa* explained how single-molecule force spectroscopy can provide an understanding of the interaction between regulatory proteins and DNA.

In the session on structure and dynamics of biomolecules, *Hans Frauenfelder* showed that proteins are not isolated systems but are intimately connected to their surroundings. Large-scale motions in the protein follow alpha fluctuations in the

solvent; interior motions can be controlled by beta fluctuations in the protein's hydration shell. These relations are interpreted in terms of a hierarchically organized energy landscape. *Jane Clarke* explained how mechanically sensitive proteins can act as force receptors and how the energy landscape is affected by application of an external force. *Peter Wolynes* discussed how energy landscape theories can provide incentives to make new experiments and carry out difficult computer simulations addressing protein folding mechanisms. General mechanisms of how small proteins fold were described by *Alan Fersht*. *Eugene Shakhnovich* presented a unified statistical-mechanics based theory of protein folding and evolution, and *Yurii Krupyanski* discussed equilibrium fluctuations in myoglobin and lysozyme. *Frank Jülicher* discussed cellular oscillations during mitosis of mechano-sensory cells and described how these behaviours emerge from the collective interplay of cellular components. *Marileen Dogterom*, *Jack Tuszynski*, and *Miljko Sataric* presented nonlinear models of microtubules, and *Samuel Safran* gave a talk on the shape and fluctuations of red blood cells.

In the session on DNA dynamics, *Michel Peyrard* reviewed some mesoscale DNA models, their nonlinear dynamics, statistical physical properties, connection with experiments, and growing relevance in biology. Using the Peyrard-Bishop model for thermally induced DNA bubbles, *Kim Rasmussen* predicted the location of such sequence-independent transcription sites in DNA. Localized excitations and possible existence of conformational solitons in DNA were discussed by *Sergey Volkov*.

The perplexing discovery that living cells can count was reported by *Kendall Smith*, who showed that a replicating T cell requires a definite number of interleukin-2 receptor engagements to commit itself to DNA replication. Most likely this number corresponds to the quantal level of phosphorylation of intracellular regulators required for commitment, and the cell decides to initiate DNA replication as one spatially coherent unit if and only if a definite number of pre-replicative protein complexes (pre-RCs) have been previously bound to the double helix. As demonstrated by *Leif Matsson*, the non-equilibrium assembly of the quantal number of pre-RCs could be modelled as an order parametric Ginzburg-Landau type dynamics. After a spontaneous breakdown of symmetry this dynamics can explain why the DNA content of G_2 cells becomes exactly double that of G_1 cells. *Måns Ehrenberg* presented a novel theory of selective charging of tRNA isoacceptors when their common amino acid is rate limiting for protein synthesis along with corroborating experiments.

Alexei Kornyshev reviewed the Kornyshev-Leikin theory of helical macromolecules, through which pre-meiotic recognition of genes in homologous recombination could be understood. His collaborators *Dominic Lee* and *Aaron Wynveen* discussed torsional fluctuations and statistical mechanics of DNA assemblies.

By showing a simple neural network that specifically responds to brief particular dynamical patterns in natural speech, *John Hopfield* illustrated how unexpected computing capability could be obtained from a small amount of 'neural hardware'.

John Hertz showed how methods originally developed for spin glasses could be used to analyze the dynamics of neural networks in the neocortex. *Frank Moss* described how the paddlefish uses stochastic resonance to detect local electric fields, and *Eshel Ben-Jacob* presented a novel approach to analyze multi-channel recordings of cortical brain activity. *William Brownell* presented experimental data suggesting that the outer hair cells (OHC) in the inner ear of mammals are piezoelectric, leading to the hypothesis that bats, whales, and dolphins use OHC piezoelectric resonance directly in detecting the high frequency species-specific vocalizations used in echolocation. *Eors Szathmari* spoke about the assembly and dynamical stability of the earliest genomes, and the origin of life. In his talk on self-replicating protocells, *Steen Rasmussen* discussed the definition of life and possibilities of its origin.

It is not easy to summarize ICBP-2004. However, it is clear that the interface between biology and physics is steadily strengthening. Looking back to 1953, it becomes obvious that the structure of DNA would not have been discovered without the tools of modern physics. Today, molecular biology has approached a limit where the use of large computers and qualitative arguments do not suffice to explain all data and complex biological functions. Living matter is condensed matter; therefore, condensed matter theory is now required for a quantitative understanding. Indeed, judging from cellular-level analyses presented at this conference, one could say that the era of pathway quantification [2] has not only arrived but that it has also proven to be an instructive mode of physical thinking.

Ten to fifteen years ago biological physics focused mainly on sub-cellular phenomena such as protein folding, neural networks, and nonlinear waves in biological systems. Today biological physics also includes problems such as DNA replication and operation of the cell cycle machinery. We hope it will not be another fifty years before we know the dynamics of DNA in terms of molecular and condensed matter physics. This understanding is required to explain the relation between forces measured on a single DNA molecule and those in control of DNA replication. A description of DNA dynamics could be expected to be no less important for biological research than the discovery of the DNA structure. For instance, the enveloping dynamics of the cell cycle machinery and division of normal cells could lead to a better understanding of cancer. It could also provide clues to the definition of life, which appears to be a prerequisite in the search for the origin of life.

Biologists and physicists can now merge observations and ideas about collective phenomena in living matter. How, for example, do many identical protein complexes cooperate to allow induction of a biological function while a single complex cannot? Can physicists constructively confront the non-equilibrium chemical properties and biological functions of living matter? Considering the impact of the development of biosensors, medical imaging techniques, structure analysis of DNA and proteins – to mention just some successful uses of physics in biology, medicine and industry – biological physics is already “big physics” [3].

Notes

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References

1. See further references at <http://fy.chalmers.se/icbp2004> under Abstracts of Plenary & Symposium Lectures, Abstract Session A, and Abstract Session B.
2. Koshland, Jr., D. E.: The Era of Pathway Quantification, *Science* **280** (1998), 852–853.
3. Varmus, H.: The Impact of Physics on Biology and Medicine, *Physics World*, September 1999, 27–31.