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INTRODUCTION TO THE SPECIAL ISSUE ON MEASURING & SOLVING SINGLE MOLECULES

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In this document, we present the articles of the Special Issue on measuring & solving single molecules. These include reviews and articles about the state-of-the-art experimental and mathematical methods and applications in life sciences, biophysics and materials science. Ways of solving pitfalls in this field are presented in various articles. This Special Issue can intrigue, inspire and help scientifically both young and established scientists working in this field.

Keywords: Solving single molecules; spectroscopy; FRET; AFM; quantum dots; ion channels; enzymes; molecular motors; ATPase; receptors; conjugated polymers.

1. Introduction

In biophysics, physics and chemistry, we can measure signals from single molecules at room temperature: biological ion channels (since the 70s), receptors and

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molecular engines (since the 90s), activity of enzymes and dynamics of biopolymers (since the 90s), quantum dots (since the 80s), are popular examples. This is a result of the never ending development of new measurement methods. Individual molecules are detected, measured and solved with spectroscopic methods (single-molecule fluorescence), mechanical manipulation (atomic force microscopy and optical traps), or ion channels measured with patch clamps. Yet, there are other methods: methods measuring diffusion and motion of individual molecules, combination of spectroscopy and force, etc.

Experiments involving individual molecules have made possible solving many molecular processes, identifying unique behaviors, and further utilizing these in applications. Here "solving the data" and "solving single molecules" refer to constructing the activity mechanism from the trajectory. In biophysics, there are processes that we can solve only when solving single molecules as other experimental and numerical approaches are not equally informative. Enzymes represent such an example (ion channels and structural dynamics of biological molecules are additional popular examples): only when solving individual enzymes, we can supply answers about accurate models on the enzymatic activity. In materials science, experimental projects involving individual quantum dots significantly help in advancing the scientific knowledge and the way quantum dots are used in applications.

These particular examples and their relevance to biophysics and materials science put the field of solving single molecules among the most important ones in biophysics.

2. The Articles in this Special Issue

The focus of this Special Issue[1–8] is on recent advances in measuring[3–7] and solving[1,2] single molecules. Every several years there is a special issue in this field[9–14] and a continuing flow of reviews.[15–18] The uniqueness of this Special Issue is in presenting reviews about very recent new experimental and mathematical results in the field, where the reviews also talk about problems that may arise in experiments and partial methods that analyze the trajectories, and ways that can enable us to solve these difficulties. The articles here are connected (this is specially designed): this Special Issue is built in a form of a coherent publication (say a book). This Special Issue can help young and established scientists getting in touch with the state-of-the-art research and developments in this field.

Here, we have articles about and in connection with: (1) enzymes,[1,2,3,4] (2) conformational dynamics and activity of biopolymers,[1,2,3,4] (3) motion of biopolymers,[7] (4) biological channels,[2] (5) AFM and optical traps (in Ref. 1, we talk about ways of solving also these experiments), (6) quantum dots,[5,6] (7) mathematical papers about solving idealized typical data, solving the noise in typical data, and about modeling the relevant processes.[1,2]

In summary, we present here 5 reviews and 3 research papers. The first article is a review (yet also presenting various new results) from Ophir Flomenbom about mathematical, statistical and numerical treatments required when solving single molecule trajectories.[1] The article from Fred Sachs and Chris Nicolai presents the QUB software that can extract the model from raw data, with a special focus on ion channels.[2] The review from Angel Orte and collaborators presents advances in FRET experiments including three-color FRET, yet also talks about ways that one should treat the trajectories and perform the experiments.[3] The article from Sune K. Jørgensen and Nikos S. Hatzakis is about enzymes: in the review the scientists talk about various measurement methods involving individual enzymes, new results about enzymes, and how these advance our views about enzymatic activity.[4] Mircea Cotlet and collaborators present synthetic ways to control blinking in quantum dots.[5] Andre Gesquiere and his group report on the effect of polymer chain on the morphology in conjugated polymer/fullerene composites quantum dots.[6] Hideaki Mizuno and collaborators use individual particle tracking to explore the dynamics of EGF receptors in various cell types.[7] The review from Sergey A. Menzikov presents a recently developed mechanism about the ATPse activity in neurons.[8] ATPase complexes are measured with individual molecule methods in many projects nowadays and can test any model.[19–25]

With reviews and research papers from life sciences, biophysics and materials science, the reader can find this Special Issue intriguing, inspiring and scientifically helpful.

3. Concluding Comments and Additional Organizational Focus

3.1. *Ongoing discussions*

With this Special Issue, we arrange an ongoing Webinar where scientists can pose questions and answer these, debate, yet also present short videos about their projects. Please visit the webinar at: http://www.linkedin.com/groups/Webinar-about-Special-Issue-Measuring-5110327, and register (every scientist working in this field can register and participate in the Webinar). The webinar will form the basis of a conference that we plan to organize.

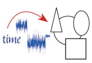
3.2. *More publication details of this Special Issue*

- New articles that are connected with this Special Issue will appear through 2014 in the online version of this Special Issue and at least one print issue (these articles may appear in various regular print issues). Every such article will have the Special Issue Comment.
- All articles in this Special Issue will have one free year with open access.

3.3. *The crew of editors in this Special Issue*

Chief Editor of this Special Issue: Dr. Ophir Flomenbom (born in 1974) holds a PhD degree in mathematical biophysics from Tel Aviv University, Tel Aviv, Israel, (2006) and a postdoctoral position experience at MIT, USA (2005–2008). Flomenbom founded a scientific company, Flomenbom-BPS Ltd (registered in 2009); please see http://www.flomenbom.net/. In the company, we deal with and solve scientific problems in biophysics and stochastic processes and related fields, e.g. socio-econo-physics. We also write software for scientists in these fields.

Editor of this Special Issue: Dr. Kelly Velonia, principal investigator, Department of Materials Science and Technology, University of Crete, Greece. Kelly Velonia holds a doctoral degree in Mechanistic Organic Chemistry from the University of Crete and held postdoctoral positions with the groups of Prof. R. J. M. Nolte (RUN, 2000 and 2002), and Prof. F. C. De Schryver (KUL, 2001). In 2004, she joined the Department of Organic Chemistry of the University of Geneva, Switzerland, as an Assistant Professor. In 2007 she was appointed Assistant Professor at the Department of Materials Science, University of Crete (tenure 2010).



Editor of this Special Issue: Dr. Mircea Cotlet, principal investigator, Brookhaven National Laboratory, NY USA. Mircea Cotlet obtained his PhD in Chemistry from Katholieke Universiteit Leuven in Belgium (2002). Following a short visiting postdoctoral stay in Harvard (2003) and a Director's postdoctoral fellowship at Los Alamos National Laboratory (2004–2006), he joined the Center for Functional Nanomaterials at Brookhaven National Laboratory where he is directing the Single Molecule Spectroscopy Effort (www.bnl.gov/sms). His interests are in synthesis and single particle characterization of energy relevant nanomaterials based on quantum dot.

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single molecule measure-ment is a renewal process; otherwise, the measurement is a nonrenewal process. Thus, without multiple conformational channels, a complex chain reaction as described in section IV or a photon emission process in section V is a renewal process although the rst passage time distribution is multiexponential and complicated.Â For example, the transition from the excited-state to the ground-state can occur through radiative decay, which is detected via emitted photons, or through nonradiative decay, which is not monitored. In the following, we consider four types of single molecule measurements illustrated in Figure 1 and the relevant transfer matrix expressions most closely related to these measurements. experiments to the single molecule level. The critical steps for a successful single molecule experiment. are discussed with a focus on FRET.Â Single-molecule fluorescence techniques are ideally suited to provide information about the structure-function-dynamics relationship of a biomolecule as static and dynamic heterogeneity can be easily detected. However, what type of single-molecule fluorescence technique is suited for which kind of biological question and what are the obstacles on the way to a successful single-molecule microscopy experiment? In this review, we provide practical insights into fluorescence-based single-molecule experiments aiming for scientists who wish to take their experiments to the single-molecule level. This Special Issue was launched to account for the rapid progress in the field of "Single Molecule Techniques". Four original research â€¦Â Technological advances in the detection and manipulation of single molecules have enabled new insights into the function, structure and interactions of biomolecules. This Special Issue was launched to account for the rapid progress in the field of "Single Molecule Techniques". Four original research articles and seven review articles provide an introduction, as well as an in-depth discussion, of technical developments that are indispensable for the characterization of individual biomolecules. Submit. Introductory Perspective. Introduction to the Special Feature on Single-Molecule Chemistry and Biology. Robert J. Silbey. Massachusetts Institute of Technology, 77 Massachusetts Avenue, 6-129, Cambridge, MA 02139.Â Single-molecule experiments thus will lead to a better understanding of how the mechanisms and dynamics seen in ensemble experiments are generated from dynamics and fluctuations at the molecular level. Theorists and experimentalists will work closely together to examine dynamics at the molecular level and the foundations of statistical mechanics.Â For several years, PNAS has published special feature issues on many cutting-edge research topics.