BP 28: Molecular Recognition

Time: Friday 10:45–12:45 Location: PC 203

BP 28.1 Fri 10:45 PC 203

Influence of Sequence Correlations on Molecular Recognition — •Hans Behringer and Friederike Schmid — Fakultät für Physik, Universität Bielefeld, D-33615 Bielefeld

Equilibrium aspects of molecular recognition are investigated using coarse-grained models for the recognition process of two rigid biomolecules. To this end, a two-stage approach is adopted. First, the structure of the target molecule is fixed and learned by a probe molecule resulting in an ensemble of probe sequences. In a second step the recognition ability of the designed probe ensemble with respect to the chosen target sequence is tested by comparing the free energy of association with the previously fixed target structure and a different competing structure. Particular attention is paid to the influence of correlations in the hydrophobicity distributions on the recognition sites of the molecules on the recognition ability of the probe molecules.

Behringer, H., A. Degenhard, F. Schmid 2007, Coarse-Grained Lattice Model for Investigating the Role of Cooperativity in Molecular Recognition, *Phys. Rev. E* **76**, 031914.

BP 28.2 Fri 11:00 PC 203

Structure based prediction of protein-DNA recognition — Sahand Jamal Rahi[1], •Peter Virnau[2], Mehran Kardar[1], and Leonid A. Mirny[1,3] — [1]Massachusetts Institute of Technology — [2]Johannes Gutenberg-Universität Mainz — [3]Harvard-MIT Division of Health Sciences and Technology

Binding of proteins to specific DNA sites is central for several vital biological processes, such as regulation of genes, replication of DNA and repair of DNA damage. The challenge can be formulated as follows: Given the structure of a protein-DNA binding complex, predict sites in the genome which the protein recognizes, i.e., to which it binds with significant affinity. In this talk, we will discuss the predictive quality of atomistic force-fields in conjunction with molecular mechanics calculations and compare results with predictions from bioinformatics for the PurR protein-DNA complex. We will also compare binding energies derived from simulations with experimental binding energies for several amino acid and DNA point mutations.

BP 28.3 Fri 11:15 PC 203

The impact of defects on the binding affinity of surface bound oligonucleotide-duplexes — Thomas Naiser[1], Oliver Ehler[1], •Jona Kayser[1], Timo Mai[1], Wolfgang Michel[1], and Albrecht Ott[1,2] — [1]Experimentalphysik I, Universität Bayreuth, D-95440 Bayreuth, Germany — [2]Biologische Experimentalphysik, Universität des Saarlandes, D-66041 Saarbrücken, Germany

It is not fully understood how point defects and loop insertion affect the stability of DNA duplexes. This is for example of interest in the context of genotyping microarrays which base on the reduced binding affinity of non-perfect match duplexes. In order to study the complex problem of surface based hybridization in more detail, we performed array based hybridization experiments in simple and well controlled situations without competitive binding. The microarrays are produced in our lab using Light Directed Polymerization (LDP) of phosphoramedites on a dendrimer substrate. This technique provides a high flexibility in array design. We report a strong positional dependence of the influence of single base bulges and single base mismatches with increasing importance towards the middle of the strand. To explain the observed behavior we propose a molecular zipper. Direct comparison between binding affinities of DNA/DNA and RNA/DNA duplexes shows that for RNA/DNA purine-purine mismatches are most destabilizing whereas for DNA/DNA the affected base pair is the relevant parameter. We attribute these differences to the different structures of the duplexes (A vs. B form).

BP 28.4 Fri 11:30 PC 203

Physical-Chemistry Analysis of Microarray Data — •K. Myriam Kroll[1], Gerard Barkema[2,3], and Enrico Carlon[1] — [1]Institute for Theoretical Physics, KU Leuven, Celestijnenlaan 200D, B-3000 Leuven, Belgium — [2]Institute for Theoretical Physics, Universiteit Utrecht, Leuvenlaan 4, 3584 CE, Utrecht, The Netherlands — [3]Institute-Lorentz for Theoretical Physics, University of Leiden, Niels Bohrweg 2, 2333 CA Leiden, The Netherlands

DNA microarrays are comparably novel devices which allow to monitor the gene expression level of thousands of genes simultaneouly on a genome-wide scale. The underlying principle of these DNA chips is the hybridization process between surface-bound DNA sequences (probes) and the so-called target sequences (DNA or RNA) which are floating in solution. From the amount of hybridized targets, information about the presence of certain genes in solution can be extracted and conclusions concerning the gene expression level can be drawn. However, due to non-specific binding the measured signal contains a noisy background component which makes the data analysis and interpretation rather difficult. In this talk, we focus on the theoretical analysis of the publicly available data of microarray experiments performed on Affymetrix GeneChips. By combining well-established models from physical chemistry (Nearest Neighbor Model) and statistical mechanics, we construct a functional to predict the background intensity on every single spot on the chip. We then compare the results to other background subtraction schemes and show that our approach performs better on a global scale.

BP 28.5 Fri 11:45 PC 203

Switchable DNA layers - a versatile instrument for protein detection on a chip — •Wolfgang Kaiser[1], Erika Pringsheim[1], Jelena Knezevic[1], Kenji Arinaga[2], Shozo Fujita[2], Naoki Yokoyama[2], Ulrich Rant[1], and Gerhard Abstreiter[1] — [1]Walter Schottky Institut, Technische Universität München, Deutschland — [2]Fujitsu Laboratories Ltd., Atsugi, Japan

We present a new technique to detect label free protein targets by switchable DNA-layers. The concept is to "switch" surface bound DNA molecules by applying external AC fields. By varying the electrical field the DNA molecule changes its orientation from lying to upright and back, which is monitored in real-time by observing the fluorescence of a dye-label on the distal end of the DNA. Distance dependent energy transfer from the dye to the metal surface governs the fluorescence emission.

For the detection of proteins, the DNA is additionally functionalized with a chemical label which acts as a specific binding site for proteins. When proteins bind to this label, we observe a distinct shift in the switching behavior. At high switching frequencies DNA-protein-complexes can be discriminated from uncomplexed DNA due to their different hydrodynamic mobility. We present sensing experiments of streptavidin and antibiotin, and discuss the influence of the proteins' weight and hydrodynamic diameter (measured by dynamic light scattering) to the switching dynamics.

Switchable DNA layers make the determination of the hydrodynamic mobility / weight of proteins in a chip-compatible format possible.

BP 28.6 Fri 12:00 PC 203

Beyond modular structure in protein-interaction networks — Stefan Pinkert[1], •Jörg Reichardt[2], and Jörg Schultz[1] — [1]Dept. of Bioinformatics, University of Würzburg — [2]Institute f. Theoretical Physics, University of Würzburg

The availability of large-scale databases on protein-protein interaction (PPI) has lead to a surge of research for structure in this data and biological information following from it. The paradigm of these approaches is that the inner workings of the cell are organized into relatively independent modules. Researchers have hence been trying to discover biological information in PPI networks by looking for densely connected groups of proteins, so-called modules or clusters, which are only sparsely connected to the rest of the network. In this contribution, we show that this search for cohesive clusters in PPI networks falls short of the rich structure present in these data and can only represent a small portion of the biological information present in these networks. We introduce an analysis method which is able to overcome these limitations and apply it to the Human Protein Reference Database (HPRD). We provide an insight into the large scale organization of the human protein interaction network and discuss possible biases in the network coming from the combination of yeast-2-hybrid, in vitro and in vivo experiments.

BP 28.7 Fri 12:15 PC 203

separation of specific sequence oligonucleotides from a yeast genome using single primer abrupt termination PCR (SPAT-PCR) — •harish bokkasam — Department of Biological Experimen-

tal Physics, University of Saarbrücken, Saarbrücken, Germany

As a step towards gene expression analysis with short DNA fragments (20-50 bp), we develop a novel technique for fishing out a sequence specific oligonucleotide from a yeast genome. This method is based on SPAT-PCR, using a single primer and a temperature jump resulting in abrupt termination of the PCR cycle and interruption of the elongation of the primer on the RNA template. We design a complementary primer to select the specific sequence oligonucleotide (SSON). The intermediate product, consisting of the required SSON, excess primer and RNA template, is visualized and subsequently separated using gel-electrophoresis. The obtained SSON then serves as template for PCR amplification. The accuracy of this method can further be tested by using the obtained SSON as a target in array-based hybridisation experiments.

BP 28.8 Fri 12:30 PC 203

Stochastic dynamics of protein assembly — •Jakob Schluttig and Ulrich Schwarz — University of Heidelberg, Bioquant, BQ 0013 BIOMS Schwarz, INF 267, D-69120, Heidelberg, Germany

The growing interest in structure and dynamics of protein assemblies requires the development of computer time-efficient modelling methods. In our approach, we combine efficient methods from stochastic dynamics with molecular information derived from all-atom simulations. In order to bridge these two fields, we use the concept of an encounter complex, which denotes an intermediate state of mutual entanglement separating the spatially completely separated reaction partners and the bound state. The stochastic transport process preceeding the formation of the encounter complex is described with a Langevin equation. The effect of anisotropic proteins and anisotropic intermediates is studied using non-diagonal mobility matrices. Long-ranged (electrostatic) interactions can be taken into account using appropriate drift terms. We apply our methods to several cases of biological interest, including bi-molecular reactions like barnase-bastar and large assemblies like viral capsids.