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DNA Computing and Molecular Programming

22nd International Conference, DNA 22
Munich, Germany, September 4–8, 2016
Proceedings
Preface

This volume contains the papers presented at DNA 22: The 22nd International Conference on DNA Computing and Molecular Programming. The conference was held at Ludwig-Maximilians-Universität (LMU) in Munich, Germany, during September 4–8, 2016, and organized under the auspices of the International Society for Nanoscale Science, Computation and Engineering (ISNSCE). A one-day Symposium on RNA-Based Information Processing was held after the main conference on September 9, 2016. The DNA conference series aims to draw together mathematics, computer science, physics, chemistry, biology, and nanotechnology to address the analysis, design, and synthesis of information-based molecular systems.

Papers and presentations were sought in all areas that relate to biomolecular computing, including, but not restricted to: algorithms and models for computation with biomolecular systems; computational processes in vitro and in vivo; molecular switches, gates, devices, and circuits; molecular folding and self-assembly of nanostructures; analysis and theoretical models of laboratory techniques; molecular motors and molecular robotics; studies of fault-tolerance and error correction; software tools for analysis, simulation, and design; synthetic biology and in vitro evolution; applications in engineering, physics, chemistry, biology, and medicine.

Authors who wished to orally present their work were asked to select one of two submission tracks: Track A (full paper) or Track B (one-page abstract with supplementary document). Track B is primarily for authors submitting experimental results who plan to submit to a journal rather than publish in the conference proceedings. We received 55 submissions for oral presentations: 16 submissions in Track A and 39 submissions in Track B. Each submission was reviewed by at least four reviewers. The Program Committee accepted 11 papers in Track A and 18 papers in Track B. This volume contains the papers accepted for Track A. In addition, we received 95 poster submissions for Track C.

We express our sincere appreciation to our invited speakers: Matthew Cook, Monika Heiner, Yan Liu, Pekka Orponen, Rebecca Schulman, and Bernard Yurke and invited tutorial speakers Thomas Ouldridge, Paul W.K. Rothemund, and Nadrian C. Seeman. We especially thank all of the authors who contributed papers to these proceedings, and who presented papers and posters during the conference. Finally, the editors thank the members of the Program Committee and the additional reviewers for their hard work in reviewing the papers and providing constructive comments to the authors, as well as for taking part in enthusiastic post-review discussions.

June 2016

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Invited Speakers
Can Excitonic Quantum Computers be Constructed by DNA Assembly of Chromophore Networks?

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Abstract. Fluorophores have been employed extensively in DNA nanotechnology, principally in donor-acceptor combinations, enabling Förster resonant energy transfer (FRET) to be used for applications, such as monitoring hybridization reactions and monitoring DNA nanomachine functions. FRET is an energy non-conserving process in which a bundle of energy, referred to as a Frenkel exciton, is transferred from the donor fluorophore to the acceptor. The characteristic length scale at which FRET sets in is called the Förster radius and is typically about 5 nm. If the donor and accepter are brought to within less than 2 nm of each other, the energy transfer can occur in an energy conserving manner referred to as coherent FRET. A Frenkel exciton, undergoing coherent FRET exchange among a cluster of chromophores, spreads out over the cluster in a wave-like manner, referred to as a quantum walk. Frenkel excitons also exhibit particle-like aspects and are best viewed as fully quantum mechanical entities. One manifestation of particle-like behavior is that, when two excitons encounter each other, they can experience a two-body interaction that gives rise to quantum mechanical phase shifts. In order for this to happen the chromophores must possess a permanent electric dipole moment and this requires the chromophores to be asymmetric. These two properties of Frenkel excitons – their wave-like behavior and their two-body interaction – are sufficient to enable universal quantum computation. I will describe how these two features can be exploited to implement a complete set of quantum gates for universal quantum computation. Quantum computing, regardless of its embodiment, is a race against decoherence, the process by which the wave-like behavior is destroyed. Chromophores, residing in buffer and attached to DNA, are in an environment highly susceptible to this process. It remains to be seen whether the decoherence rate can be reduced enough to enable Frenkel excitons to perform universal quantum computation by undergoing a many-body quantum walk over a network of chromophores attached to a DNA scaffold.
From One, Many: Programmably Reconfigurable, Multiscale Materials Built with DNA

Rebecca Schulman
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Materials within living systems have complex structure that constantly reorganizes in order to continue to function reliably as the environment changes. Commonly, this structure arises because a simple set of components is reorganized by sensors and activating agents into many different forms. For example, tubulin can be organized into cilia, fibrous networks or machines such as the spindle, and the extracellular matrix, an extended matrix composed of a relatively small number of principle protein components, is continually growing and being digested and remodeled in response to interaction with cells within a tissue. The ability to reuse simple components in different materials allows for rapid reorganization and allows material to have structure across many different length scales.

I will describe how we can use DNA to build dynamically reconfigurable materials on the micron to millimeter scales where the responses to inputs can be precisely programmed. The addition of one or combinations of DNA sequences can create large scale changes in the material, and these changes can alter a material’s form at length scales ranging from the nanoscale to the millimeter scale. Further, these materials can be continually reorganized in response to series of multiple inputs, suggesting a route to building materials that continue adapt in complex ways over time to their environment.
Petri nets offer a graphical & intuitive notation for biochemical reaction networks, such as gene regulatory, signal transduction or metabolic networks. Moreover, they may serve as an umbrella formalism combining different modelling paradigms, where each perspective contributes to a better understanding of the biochemical system under study. In this spirit of BioModel Engineering, we developed over the last two decades our unifying Petri net framework comprising the traditional time-free Petri nets (PN) as well as quantitative, i.e. time-dependent Petri nets such as stochastic Petri nets (SPN), continuous Petri nets (CPN), and hybrid Petri nets (HPN), as well as their coloured counterparts [1].

Coloured Petri nets permit, among others, the convenient and flexible encoding of spatial attributes, and thus the modelling of processes evolving in time and space, which are usually treated as stochastic or deterministic partial differential equations (PDE). In our approach, the discretisation of space on the modelling level, while traditionally the discretisation is left for the PDE integration methods [2].

Our framework is supported by a related Petri net toolkit comprising Snoopy, Charlie and Marcie. It has been applied to a couple of case studies. Those involving spatial aspects include the Brusselator model to explore Turing patterns [3], C. elegans vulval development, stochastic membrane systems composed of active compartments, Ca2+ channels arranged in two-dimensional space, phase variation in bacterial colony growth, and Planar Cell Polarity (PCP) signalling in Drosophila wing. Some of them will be sketched in this talk.

References

Computing Without Random Access Memory:
Cyclic Tag Systems for Proofs
and Interpretation

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Most simple models of computation that operate on one-dimensional information require some kind of lookup table to be used at each step of their operation. For example, Turing machines look up the next transition according to their state and the symbol they see on the tape. But in some settings, it is not clear how to achieve this random-access capability. Cyclic tag systems are suited to such settings, stepping steadily through a cyclic list rather than requiring random access. Since cyclic tag systems are universal (i.e. capable of simulating a Turing machine), their simplicity makes them an attractive route for proving that other systems are universal as well, and they have been used to prove universality of systems ranging from cellular automata to RNA oritatami. Their extreme simplicity even makes it possible for them to arise naturally in other systems; they have recently been discovered in a cellular automaton’s naturally occurring behavior. This talk will give a brief survey of these results.
DNA Nanotechnology: From Structural Design to Functionality

Yan Liu

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I will present the most recent work from our research group, which may include thermodynamics and kinetics of DNA tile based self-assembly processes, new designs of wireframe 2D and 3D DNA origami nanostructures, single stranded DNA and RNA origami based on paranemic crossovers and their applications in directed evolution of bivalent aptamers.
Three-dimensional DNA origami designs based on wireframe structures have recently evolved into an interesting alternative to the more established helix-packing designs: several alternative approaches exist [1–4], and functionalizations are beginning to emerge [5]. Wireframe designs are appealing both because they make more efficient use of DNA scaffold than helix-packing approaches, and because they seem to fold with higher yield and remain more stable in low-salt, physiological buffers conditions [2, 4].

Because of the inherent combinatorial complexity of wireframe designs, automation of the design process is a central task already for exploratory research, and even more so when aiming to make the methodology robust and generally available. Thus, computerised tools for aiding the process have been developed [2, 4], and lately also numerical modelling and simulation packages such as CanDo and oxDNA have introduced support for them.1

The theory underlying wireframe DNA origami design involves quite a number of interesting algorithmic and graph-theoretic ideas and challenges, including several open problems. In this talk, we discuss these underpinnings from the computer science direction, and also survey the current status of the design and modelling tools.

References


1 http://cando-dna-origami.org/, http://dna.physics.ox.ac.uk/
Invited Tutorial Speakers
Tutorial Abstract: Controlling Structure and Motion in Multiple Dimensions with DNA Information

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The essence of Structural DNA Nanotechnology is the combination of branched DNA molecules combined with interactions that can be prescribed by Watson-Crick base pairing. The key goals of the area include the production of objects, lattices and nanomechanical devices made from DNA, as well as controlling the positions of other materials. This approach began by producing structures needing only topological control, to generate knots, polyhedral catenanes, Borromean rings and, using L-nucleotides, a Solomon’s knot. By the middle 1990s, geometrical control was achieved, leading well-defined objects, often objects acting as tiles for 2D lattices. In the first decade of this century, the development of DNA origami by Paul Rothemund attracted many investigators to DNA nanotechnology, because of the ease of construction and the reliability of obtaining the product from an M13 single-stranded genome and 200–250 ‘staple strands’. Somewhat later, Peng Yin’s use of ‘DNA bricks’ led to 2D and 3D objects through a completely automated methodology.

Nanorobotics is a key area of application. We have made robust 2-state and 3-state sequence-dependent devices and bipedal walkers. We have constructed a molecular assembly line using a DNA origami layer and three 2-state devices, so that there are eight different states represented by their arrangements. All eight products can be built from this system.

One of the major aims of DNA-based materials research is to construct complex material patterns that can be reproduced. We have built such a system from DNA origami; it has reached 9 generations of exponential growth directly and 24 generations (with no apparent limit) in punctuated steps.

Wenyan Liu’s empirical rule states that the best arrays in multidimensional DNA systems result when helix axes span each dimension. We have self-assembled a 2D crystalline origami array by applying this rule. We used the same rule to self-assemble a 3D crystalline array. We initially reported its crystal structure to 4 Å resolution, but rational design of intermolecular contacts has enabled us to improve the crystal resolution to better than 3 Å. We can use crystals with two molecules in the crystallographic repeat to control the color of the crystals. We can change the color of crystals by doing strand displacement of duplex DNA; we can also color the crystals using triplex formation. When tailed in DNA, we can add semiconductors to the crystals, and follow their transitions by crystal color. The use of the crystals to host guests promises an approach to the organization of macromolecules in 3D. Diffraction of the crystals
offers a means to ascertain the successful construction of their targets and the characterization of their guests.

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On the Use of DNA Origami to Align Molecular Devices

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Over the last decade DNA origami has matured as a modular technique for self-assembling diverse components, from organic molecules to colloidal nanoparticles, into complex nanodevices. A second technique, “DNA origami placement”, allows such origami-templated devices to be precisely positioned within microfabricated structures at a resolution of ∼10 nm in x and y. This allows the integration of point-like or high-symmetry devices with on-chip electronics or optics to create hybrid structures which use self-assembled devices for their novel functional properties, and use microfabricated structures to interrogate the devices or wire them up into larger architectures. However, many devices of interest are highly asymmetric, and both their up-down orientation as well as their in-plane rotational orientation θ must be controlled. Alignment techniques based on mechanical flows, electric fields, and magnetic fields exist, but they typically align all devices in a single coherent orientation and cannot uniquely orient asymmetric devices such as diodes. Here we report extensions of DNA origami placement which allow high fidelity control over both up-down and rotational orientations: 98% of appropriately-functionalized DNA origami bind to a semiconductor substrate face-up, and over 98% of appropriately-shaped origami bind within ±7 degrees of a unique target orientation. To demonstrate orientation-dependent devices, we show that we can control the polarized emission of fluorescent dyes intercalated into DNA origami. Using the same system we show that we can maximize the coupling of fluorophores to a polarized mode of a photonic crystal cavity, and we construct an ultracompact polarimeter which incorporates over 3000 DNA origami devices having both unique and arbitrary orientations.
The Importance of Thermodynamics for Molecular Systems, and the Importance of Molecular Systems for Thermodynamics

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Abstract. Improved understanding of molecular systems has only emphasised the sophistication of networks within the cell. Simultaneously, the advance of DNA nanotechnology, a platform within which reactions can be exquisitely controlled, has made the development of artificial architectures a real possibility. Vital to this progress has been a solid foundation in the thermodynamics of molecular systems. In this tutorial, I will set out the fundamental ways in which thermodynamic principles determine what can be achieved with molecular networks, and at what cost. I will then discuss how, in turn, the need to understand molecular systems is driving the development of a new theory of thermodynamics at the microscopic scale.

Keywords: Thermodynamics · Molecular networks · Stochastic thermodynamics
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