ChemPubSoc Europe

DOI: 10.1002/cbic.201600289

CHEMBIOCHEM Editorial

Toward Applications for DNA Nanotechnology—More Bricks To Build With

Hendrik Dietz*[a]

In the quest toward gaining control over the molecular scale, this special issue provides more bricks and tricks for building with nucleic acid molecules. Twelve Communications, five Full Papers, and three Reviews are presented to string everything together and to provide a perspective. The issue covers a broad range of topics including crystals, hydrogels, interlocked architectures, gold nanoparticles, enzyme scaffolding, covalent crosslinking and chemical ligation inside nanostructures, and objects based on xeno nucleic acids. Strategies for the productive use of hierarchical self-assembly techniques and the use of gold-nanoparticle-DNA conjugates are discussed in the review articles.

Several groups were concerned with enhancing the durability of DNA-based objects by introducing additional covalent bonds after assembly. Zhang and Paukstelis (DOI: 10.1002/cbic.201500610) studied nornitrogen mustard as a potential agent for covalent interstrand crosslinking; they could confirm such activity in the context of DNA crystals, which makes them more durable for potential applications as diffraction host matrices. Whether such activity also holds for other DNA constructs, remains to be seen. Kalinowski et al. (DOI: 10.1002/cbic.201600061) and also De Stefano and Gothelf (DOI: 10.1002/cbic.201600076) both studied the possibility for chemically ligating colocalized 3′ and 5′ strand termini within preformed DNA objects. Kalinowski et al. successfully performed phosphoramidate ligation, while De Stefano and Gothelf relied on disulfide chemistry. Altogether, covalent interstrand and terminal linkages will help to expand the window of conditions for which DNA nanostructures can maintain their shape.

Koßmann et al. (DOI: 10.1002/cbic.201600039) focused on the problem of facilitating the integration of protein-based functional groups into DNA-based objects and report an engineered halo-based oligonucleotide binding (HOB) protein that offers improved coupling to chlorohexane-modified oligonucleotides, which enables a path for the efficient and site-specific immobilization of desired protein groups on DNA nanostructures by fusing those groups to the HOB protein.

Taylor et al. (DOI: 10.1002/cbic.201600136) report entirely new types of bricks for building objects based on synthetic genetic polymers, also known as xeno nucleic acids (XNA). A series of previously reported objects such as tetrahedra and octahedra were elaborated "wholesale"—as the authors put it—in XNA. XNA expands the palette of chemical diversity for nucleic acid nanotechnology and opens the door toward engineering complex functionalities, such as molecular recognition or catalysis. Beyond the canonical B-form double helix, Tripathi and Paukstelis (DOI: 10.1002/cbic.201500491) determined crystal structures from quite unusual parallel-stranded homoduplexes, which could also become a new type of brick to build with in DNA nanotechnology.

Moving away from precisely controlled structures toward materials that are already considered for tissue engineering and drug delivery, Jiang et al. (DOI: 10.1002/cbic.201500686) and Kandatsu et al. (DOI: 10.1002/cbic.201600088) report on DNA-based hydrogels. Jiang et al. report hydrogels that form from a single multi-domain DNA oligonucleotide. Characteristics such as melting temperature, viscoelasticity, and the release of molecules and particles trapped in the meshes of the gel could be programmed by tuning the sequences of the particular domains. Kandatsu et al. report a light-switchable hydrogel by introducing a photo-responsive base within the gel-crosslinker segments. Multiple gel-sol transitions triggered by illumination with two different wavelengths are shown. These two studies show the direct connection between the particular design of DNA molecules and the properties of macroscopic materials.

Arranging multiple enzymes in close proximity has the potential to enhance the overall activity of a cascade reaction. Liu et al. (DOI: 10.1002/cbic.201600103) integrated a three-enzyme pathway onto DNA scaffold structures to study the effect on the cascade reaction. The turnover rate depended less on the inter-enzyme distance, but more on the relative arrangement. A triangular scaffold gave the highest activity. Overall, this study provides new tricks for using DNA nanostructures productively for the enzymatic production of chemicals. Li et al. (DOI: 10.1002/cbic.201600052) drew an unexpected connection between DNA walkers, cell growth, and carbon nanotubes. The authors explored the potential for using a DNA walker to control the kinetics of release of a drug that is released from fuel strands on carbon nanotubes owing to walker activity. The released molecules sept into the medium and reduced the growth rate of a particular cancer cell line. This study indicates an interesting direction in which dynamic DNA devices can be used as timers for the release of chemical agents.

Other articles in this issue are concerned with various applications for DNA-conjugated gold nanoparticles, the interactions of polyethylene-glycol molecules and DNA aptamers,

[a] *Prof. Dr. H. Dietz*
Technische Universität München
Walter Schottky Institut, Physik Department
Am Coulombwall 4a, 85748 Garching bei München (Germany)

This manuscript is part of a Special Issue on DNA Nanotechnology.

DNA-based tubes and yarns, and a DNA-origami based prototype for a comparative binding assay. A series of studies deals with interlocked architectures. Valero et al. (DOI: 10.1002/cbic.201500685) studied "stopper" objects to constrain the motion of DNA macrocycles on linear DNA tracks. Wu et al. (DOI: 10.1002/cbic.201600036) report DNA sequences for making symmetric or asymmetric three-ring DNA catenanes. Li et al. (DOI: 10.1002/cbic.201600071) also report three-ring DNA catenanes. Interlocked architectures may be considered for devices whose functions require that certain domains in such objects move in particular, but unconstrained ways, relative to the rest of the object.

The issue at hand itself may be considered as a self-assembly experiment. The submissions clearly reflected a trend: Application development has moved toward the center of the stage in the field of DNA nanotechnology. Questions such as making DNA objects more durable or how to integrate or position functional groups have become increasingly relevant. The studies in this issue provide new bricks to build with, and also fresh ideas on how or what to build. Enjoy reading!

Hendrik Dietz
Guest Editor