Self-assembling DNA templates for programmed artificial biomineralization

Enrique C. Samano,*ae Mauricio Pilo-Pais,b Sarah Goldberg,b Briana N. Vogen,a Gleb Finkelsteinb and Thomas H. LaBean*acd

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Complex materials with micron-scale dimensions and nanometre-scale feature resolution created via engineered DNA self-assembly represent an important new class of soft matter. These assemblies are increasingly being exploited as templates for the programmed assembly of functional inorganic materials that have not conventionally lent themselves to organization by molecular recognition processes. The current challenge is to apply these bioinspired DNA templates toward the fabrication of composite materials for use in electronics, photonics, and other fields of technology. This highlight focuses on methods we consider most useful for integration of DNA templated structures into functional composite nanomaterials, particularly, organization of preformed nanoparticles and metallization procedures.

1. Programmed assembly of DNA nanostructures

Our current ability to create complex DNA nanostructures via designed self-assembly owes much to the confluence of early efforts to build periodic matter for crystallography[1] with the concept of DNA-based computing.[2] Development of concepts and materials for computation by molecular self-assembly.[3,4] has led to widespread success of DNA-based nanotechnology and the great diversity of DNA building blocks, architectures, and geometries described in the past decade [ref. 5–10 and other literature cited therein]. Fig. 1 gives a very brief survey of the variety of construction strategies and superstructures produced by programmed DNA assembly. It should be noted that other nucleic acids have also been applied as molecular construction materials,[11,12] but to a lesser extent than DNA. Although, other materials,
Fig. 1  Schematic drawings and AFM images of DNA nanostructure building blocks and lattices. (a) Double-crossovers forming 2D-DNA crystals,\(^{23}\) (b) DNA Holliday junction arrays using rhomboid tiles,\(^{24}\) (c) DNA grid assembled from \(4 \times 4\) cross-tiles,\(^{7}\) and (d) DNA triangle tiles with flexible junctions.\(^{9}\) All scale bars are 300 nm.

Sarah Goldberg
Sarah Goldberg obtained her PhD in Condensed Matter Physics from the Weizmann Institute of Science in 2009. Her work focused on the long-range order of the vortex lattice in type II superconductors. Currently, she is a postdoctoral researcher at Duke University, developing nanoscale elements for electronic and plasmonic applications.

Gleb Finkelstein
Gleb Finkelstein obtained his PhD in Physics from the Weizmann Institute of Science in 1999. Following postdoctoral work at MIT, he moved to Duke University, where he is now an Associate Professor. His group works on a range of subjects in condensed matter physics and nanoscience.

Briana N. Vogen
Briana Vogen received her PhD in Chemistry from Duke University in 2010. She is currently a postdoctoral researcher at Duke in the laboratory of Prof. LaBean. Her research interests include designing and patterning surfaces for potential applications in DNA nanotechnology.

Thomas H. LaBean
Thomas H. LaBean earned his PhD at the University of Pennsylvania in 1993. He studied the folding properties of arbitrary-sequence proteins expressed by randomized, synthetic DNA libraries. He then moved to Duke University and studied de novo protein design, and then worked on DNA-based molecular computation. He now studies self-assembling biomolecular nanostructures as a Research Professor at Duke University.
including polypeptides, offer alternative molecular assembly systems. Our understanding of the rules of nucleic acids assembly (dominated by Watson–Crick base pairing) far outstrips our current ability to design self-assembling polypeptide systems from scratch. High-resolution structural DNA nanotechnology employs both building blocks and assembly tags made of DNA, so DNA is both “bricks and mortar” in these nanoscale assemblies; by contrast, some lower-resolution nano-assemblies use DNA only as “mortar” in the directed-assembly of other nanomaterials.

This highlight will not discuss “DNA as mortar” developments nor active, responsive DNA connectors, but will focus on more complex, “smart” assemblies and their use as templates upon which other “dumb” materials (i.e. materials typically not associated with molecular recognition) can be organized. One family of “smart” DNA assemblies used as templates is the DNA origami structures. These are typically 2D-nanostructures based on the 7249-base, single-strand M13 bacteriophage genome that is folded in a programmed and precise manner by means of about two hundred specific, complementary “staple” strands of synthetic DNA. As an extension to these 2D templates, 3D DNA nanostructures have tremendous potential to organize materials in 3D, encapsulate and release drugs, regulate the activity of encapsulated proteins, and selectively cage nanomaterials.

Braun and co-workers first constructed and tested a conductive nanowire from silver nanoparticles nucleated upon viral DNA via an electroless deposition method. They later improved this method by employing a sequence-specific “molecular lithography” approach to selectively metallize a dsDNA template. They used an aldehyde-based reducing agent on λ-DNA molecules to grow silver clusters. The silver clusters were utilized as seed particles to nucleate more silver or gold around them and the electrical properties of the resulting wires were measured. They employed the same technique to fabricate a DNA-templated carbon nanotube field-effect transistor. They also demonstrated the ability to provide aldehyde derivatization of DNA in a sequence-specific manner as a means of more accurately localizing metal deposition. They envisioned a multi-step self-assembly process for the preparation of nanoelectronic components and circuits using DNA templates, and summarized their experience on the

2. Metallization of DNA templates

The literature reports several procedures for modifying and converting DNA templates into functional electronic nanostructures; i.e., nanowires, transistors, etc. Nucleation and growth of metal clusters on viral DNA, by the localization of an aqueous reducing agent, is the main approach to metallization of DNA templates. Metallic nanowires templated on viral DNA frequently display a lack of crystallinity and uniformity and instead show coarse grained morphologies. DNA origami structures are quite robust and stiff and are currently being developed as scaffolds to improve the fabrication of nanowires and other optically and electronically active nanostructures.

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fabrication of electronic circuits and components based on DNA in an excellent review. Recent literature also reports the production of conductive silver nanowires with controlled width using DNA nanostructures.

Metallization of λ-DNA with other metallic particles using similar methods has also been reported, including cobalt, palladium, platinum, and metals using similar methods has also been reported, including cobalt, palladium, platinum, and platinum alloys. Metalized forms of DNA have been used for electrostatic assembly of metallic wires, as shown in Fig. 2(a). More complex nanostructures require a higher degree of control on nanoparticle placement, and therefore may utilize more complex DNA templates, such as nanogrids constructed from a repeating tile or scaffolded DNA origami.

The particles that provide the basic units of any metallic nanostructure must be functionalized with a particular biological or chemical linker that enables their specific positioning within the DNA template. Mirkin and Alivisatos independently pioneered the functionalization of gold nanoparticles using thiol-labeled oligonucleotides. Gold nanoparticles can be self-assembled within the DNA scaffold by means of complementary binding to organize structures with nanometric accuracy. Alivisatos further demonstrated the attachment of discrete numbers of oligonucleotides to gold nanoparticles in a controlled manner utilizing either gel electrophoresis or HPLC purification steps. These methods have recently been extended to dithiol-capped oligonucleotides which reportedly offer superior gold–DNA attachment.

Using different functionalization methods, nanoparticles of assorted sizes and materials have successfully been attached to various DNA templates to build a wide variety of structures in two and three-dimensions (for related reviews, see ref. 6 and 52). The focus in this highlight is on 2D structures of metallic nanoparticles because they are most readily utilized for initial electronic and photonic applications. Regular, large scale arrays of gold nanoparticles, in which the underlying template is a DNA nanogrid composed of a small number of DNA sequences, have been reported by a number of groups, as shown in Fig. 3(b). DNA origami has recently provided a template for arbitrary metallic structures; for instance, a self-similar chain of gold nanoparticles as shown in Fig. 3(c). Placement and positioning of metallic nanostructures on a useful substrate, like silicon, for electronic and photonic applications are highly important. Controlled placement of a basic metallic structure on a silicon substrate has been recently demonstrated utilizing DNA origami, as shown in Fig. 3(d).

4. Vision for future artificial biominalization

The future of biomolecular assembly for the fabrication of functional nano-electronic and photonic devices is very...
bright. Development of construction methods incorporating the placement of preformed nanomaterials with the chemical deposition of addition inorganics, as outlined in the sections above, offers high probability of creating significant advances in massively parallel fabrication of useful devices and circuits. Combining these techniques with location specific docking of the DNA templates on silicon substrates, as demonstrated in ref. 56, will serve to bridge the gap between bottom-up and top-down fabrication methods, and allow bionano-assembly steps to be fully integrated with conventional microfabrication processes. Future research will also focus on expanding the repertoire of inorganic materials available for incorporation, including semiconductors and dielectrics, as well as moving to the use of 3D DNA templates for patterning.

One possible process for integrating the described methods is outlined in Fig. 4. The particular structure shown would serve as a single-electron transistor and could be used in properly designed circuits to represent computational bits (1 or 0) by gating one electron at a time. Such structures would vastly reduce energy requirements and heat buildup compared to conventional micron-scale, lithographically defined devices. Besides single-electron transistors, the described scheme could be adapted to the fabrication of other electronic devices, resonators, metamaterials, waveguides, and sensors, among others. Whether or not this particular envisioned biofabrication process ends up being used in the manufacture of computing and communication devices, harnessing some aspects of artificial, programmable bio-mineralization appears to be a promising path toward the production of complex, functional nanostructures.

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