ACCOUNTS of chemical research

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# Nanomechanical Molecular Devices made of DNA Origami

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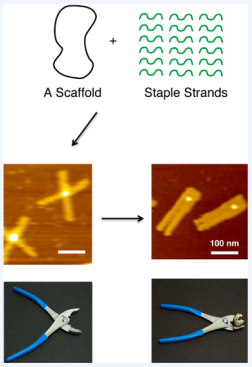
**CONSPECTUS:** Eight years have passed since the striking debut of the DNA origami technique (Rothemund, P. W. K. *Nature* **2006**, *440*, 297−302), in which long single-stranded DNA is folded into a designed nanostructure, in either 2D or 3D, with the aid of many short staple strands. The number of proposals for new design principles for DNA origami structures seems to have already reached a peak. It is apparent that DNA origami study is now entering the second phase of creating practical applications. The development of functional nanomechanical molecular devices using the DNA origami technique is one such application attracting significant interest from researchers in the field. Nanomechanical DNA origami devices, which maintain the characteristics of DNA origami structures, have various advantages over conventional DNA nanomachines. Comparatively high assembly yield, relatively large size visible via atomic force microscopy (AFM) or transmission electron microscopy (TEM), and the capability to assemble multiple functional groups with precision using multiple staple strands are some of the advantages of the DNA origami technique for constructing sophisticated molecular devices.




This Account describes the recent developments of such nanomechanical DNA origami devices and reviews the emerging target of DNA origami studies. First, simple "dynamic" DNA origami structures with transformation capability, such as DNA origami boxes and a DNA origami hatch with structure control, are briefly summarized. More elaborate nanomechanical DNA origami devices are then reviewed. The first example describes DNA origami pinching devices that can be used as "single-molecule" beacons to detect a variety of biorelated molecules, from metal ions at the size of a few tens of atomic mass number units to relatively gigantic proteins with a molecular mass greater than a hundred kilodaltons, all on a single platform. Clamshell-like DNA nanorobots equipped with logic gates can discriminate different cell lines, open their shell, and bind to their target. An intelligent DNA origami "sheath" can mimic the function of suppressors in a transcription regulation system to control the expression of a loaded gene. DNA origami "rolls" are created to construct precisely arranged plasmonic devices with metal nanoparticles. All of their functions are derived from their nanomechanical movement, which is programmable by designing the DNA sequence or by using the significant repository of technical achievements in nucleic acid chemistry. Finally, some studies on detailed structural parameters of DNA origami or their mechanical properties in nanoscale are discussed, which may be useful and inspiring for readers who intend to design new nanomechanical DNA origami devices.

## ■ INTRODUCTION

It might be reasonable to claim that the invention of DNA origami technique marked a new epoch in the field of structural DNA nanotechnology based on the programmed assembly of branched DNA helices.[1,2] Since writing our first review featuring the DNA origami technique merely 3 years ago in 2010,[3] more than 100 papers focusing on DNA origami have been published, a publication number that continues to rise. Although quite a few early studies focused on new proposals or improvements to the design principle of DNA origami structures, the current trend toward interdisciplinary applications of DNA origami structures not only in nanoengineering but also in biorelated chemistry and medical fields, is becoming increasingly notable. The nanoarraying of nanomaterial, such as individual protein molecules or metal nanoparticles using DNA origami as pegboards,[4] and the challenges for medical applications, such as the development of drug delivery systems,[5] are some of the popular research topics in the field.

On the other hand, one of the most attractive topics in the field of structural DNA nanotechnology has been the development of nanomechanical DNA devices.[6] Various elegantly designed DNA devices such as rotatory devices,[7,8] DNA tweezers,[9] DNA scissors,[10] and DNA walkers have been constructed.[11−14] Probably due to these successes, early DNA origami structures showing mechanical movements were hybrids of dynamic conventional DNA machines and static DNA origami.[15−19] In this Account, we would like to define "nanomechanical DNA origami" as "DNA origami structures that show programmed mechanical movement of their body consisting of the scaffold and the staples", and we focus on reviewing such "dynamic" DNA origami structures to provide hints for researchers seeking to design useful nanomechanical molecular devices.

## ■ DNA ORIGAMI BOXES

In the history of DNA origami studies, 2009 was a memorable year, marking the invention of a variety of 3D DNA origami

**Special Issue:** Nucleic Acid Nanotechnology

**Received:** December 31, 2013
**Published:** April 29, 2014

   dx.doi.org/10.1021/ar400328v | *Acc. Chem. Res.* 2014, 47, 1742−1749

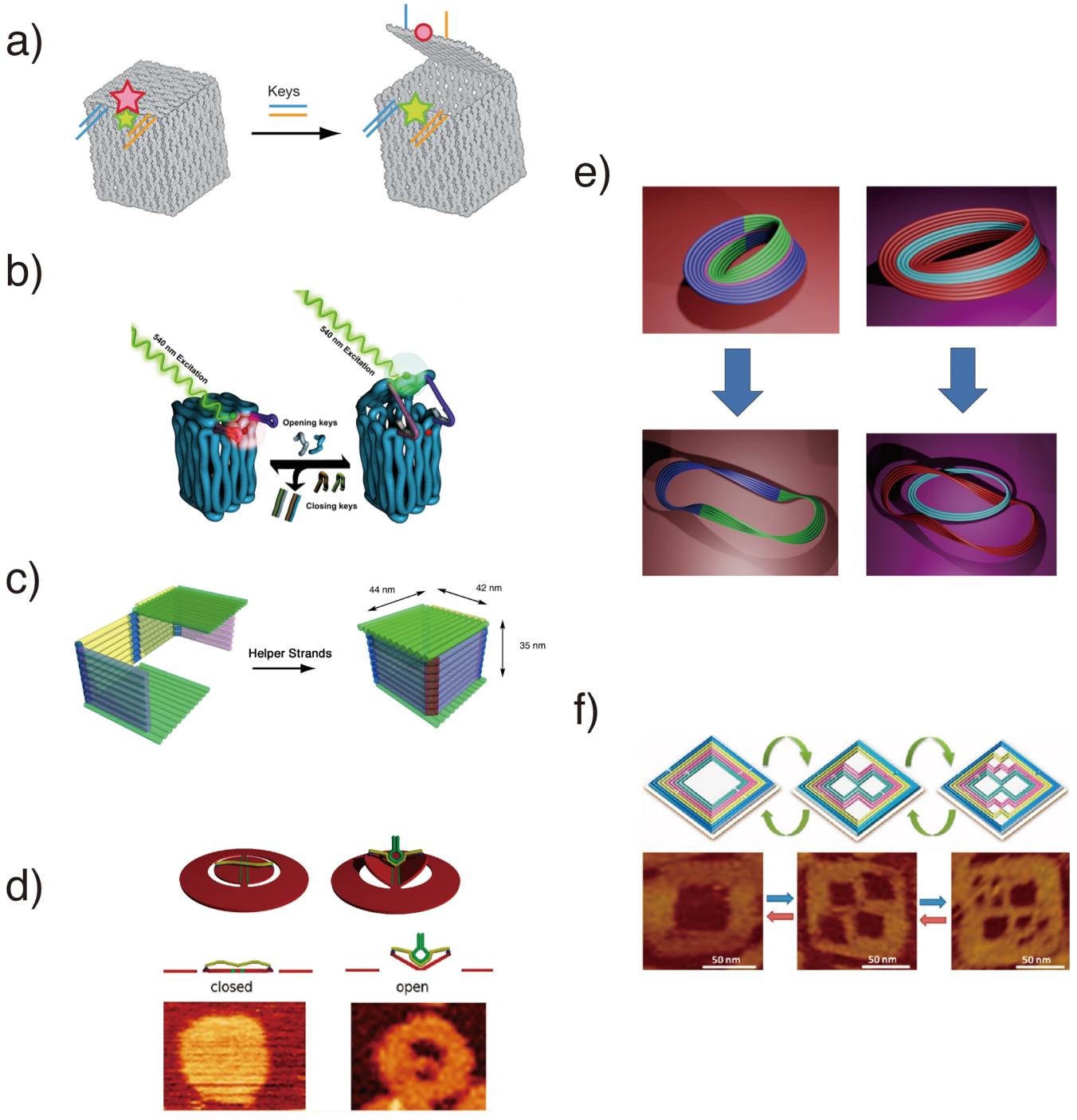



**Figure 1.** Simple "dynamic" DNA origami. (a) DNA origami box with controllable lid (Reproduced with permission from ref 20. Copyright 2009 Nature Publishing Group). (b) Smaller DNA origami box as a variation of (a) (Reproduced with permission from ref 25. Copyright 2012 American Chemical Society). (c) DNA origami box formed in two steps.[21] (d) DNA origami hatch (Reproduced with permission from ref 26. Copyright 2011 American Chemical Society). (e) "Fold and cut" of DNA origami Möbius strip (Reproduced with permission from ref 30. Copyright 2010 Nature Publishing Group). (f) Quasifractal structure controlled by a "fold-release-fold" strategy (Reproduced with permission from ref 31. Copyright 2012 American Chemical Society).

structures. Four independent hollow 3D DNA origami structures consisting of planar faces (two boxes,[20,21] one tetrahedron,[22] and prisms)[23] were reported and were accompanied by the impressive introduction of multilayer, honeycomb-lattice DNA origami design.[24] Among the four hollow 3D DNA origami structures, both DNA origami boxes were designed to achieve opening and closing mechanisms and thus can also be considered pioneering nanomechanical DNA origami devices.

The first DNA origami box was created by Gothelf and Kjems et al. (Figure 1a).[20] They divided the 7,249-nt M13 scaffold into six domains and folded each domain into six interconnected DNA sheets corresponding to the faces of the box. These faces were connected to each other at the vertices by the scaffold, and the angles between the faces were


dx.doi.org/10.1021/ar400328v | Acc. Chem. Res. 2014, 47, 1742−1749

controlled using a set of shortened staple strands joining the two faces. The resulting 42 × 36 × 36 $nm^3$ hollow box shape was thoroughly characterized by AFM, cryo-EM, and small-angle X-ray scattering (SAXS). This method revealed that there were both slightly convex and slightly concave faces in the structure due to differences in the design of these two groups of faces. The most notable feature of this box design was the dual lock−key system to open and close the lid of the box. To close the lid they attached two sets of complementary DNA strands to the lid and an adjoining face. The strands on the adjoining face had sticky-end extensions to provide a "toehold" for the displacement of the complementary DNA on the lid by an externally added "key" strand, which opens the lid. This selective lid opening was confirmed by measuring the fluorescence resonance energy transfer (FRET) between the fluorescent dyes attached to both faces.

The group later constructed much a smaller DNA origami box with dimensions of 18 × 18 × 24 $nm^3$ (Figure 1b), which corresponds approximately to 1/7 of the volume of the original DNA origami box.[25] To construct the structure, they used a 1983-nt scaffold, derived from a truncated pUC plasmid, and 59 staple strands. The small DNA origami box was characterized by gel analysis, dynamic light scattering (DLS), atomic force microscopy (AFM), and transmission electron microscopy (TEM). The lid control system was also improved, enabling the small DNA origami box to undergo multiple rounds of openings and closures in response to externally provided keys. The new lock-and-key system examined in this study used two long hairpin locks. Two opening keys bind to the two toeholds in the loops of the hairpins, and by strand displacement, unzips the two locks. An 8-nt overhang was introduced at the 5′-end of the opening keys, which can hybridize with the pair of closing keys to enable the removal of the keys. By adding opening and closing keys to the mixture in alternating cycles, up to three rounds of opening and closing cycles were achieved.

We also independently developed a box-shaped 3D DNA origami structure (Figure 1c).[21] Although the size is fairly similar to that of the box described above because the boxes share the same scaffold, the basic strategy used to construct this box was completely different. One difference was the right angles between the faces in our design from selecting appropriate positions for the crossovers connecting the faces. The crossovers in DNA origami are usually placed every 16 bp, which corresponds to 1.5 helical turns of DNA, to connect DNA helices at an angle of 180° and consequently to bundle them into a planar structure. In our box design, by contrast, the number of nucleotides between the crossovers at the edges of the faces was reduced to 8 bp, corresponding to 0.76 helical turns. Thus, the dihedral angle between the two faces next to the edge was uniformly fixed at 90° in a predetermined direction. Due to this strategy, the side of the DNA sheet that faces the inside of the box and the side that faces the outside is fully controlled. Another feature of the design is a two-step folding mechanism for future guest encapsulation. We designed the box to fold first into an open form composed of two units, each of which is made of three orthogonally connected faces. The complex then closes into a box shape, with nine helper strands to connect the three edges of the two units. The shape change from the open to the closed form was clearly imaged using AFM.

## A DNA ORIGAMI HATCH

Firrao et al. constructed a hatch-like DNA origami actuator capable of autonomous switchable motion (Figure 1d).[26] They designed and produced a circular DNA origami with an estimated diameter of 100 nm, consisting of an internal disk with a diameter of 60 nm and an external ring of 20 nm. The two semihalves of the internal disk are named "wings", which bend relative to the plane of the ring upon the hybridization of the keys. The external ring and the internal disk are connected at two diametrically opposite points via crossovers of the scaffold, and two lines of four-nucleotide single-stranded portions were introduced along the diameter to secure the flexibility of the wings to bend. The two opposite edges of the wings were bridged with a 120-nt long DNA oligomer named "probe", which complemented the loop region of a hairpin strand named "target", with a 18-bp GC clamp. The hybridization of the target with the probe generates a tensile force between the edges to pull the wings up from the plane. The actuation force was sufficiently large to overcome the electrostatic and van der Waals interactions between the wings and the mica substrate, as well as the stacking between the internal disk and the external ring. The authors estimated that the forces involved in the system are in the 10 pN range and that the DNA hybridization time is in the submillisecond range.

Reversible wing movement was also achieved by making probe/target pairs not fully complementary. The addition of the "competitor", which perfectly complemented the target, selectively removed the target from the probe. This reversible movement was confirmed by observing FRET between a fluorescein attached to the edge of a wing and a quencher on the external ring. DNA origami structures have been recently applied to decorate solid-state nanopores or to open nanopores in lipid bilayers.[27−29] The hatch-like DNA origami actuators may be useful in such studies.

## "DYNAMIC" DNA ORIGAMI STRUCTURES REPRESENTING MATHEMATICAL FIGURES

Yan, Liu, and co-workers also reported "dynamic" DNA origami structures representing alternative topological figures.[30,31] The first example was a DNA origami Möbius strip, a topological ribbonlike structure with only one side, which can be transformed into either a circle or a catenane (Figure 1e).[30] They prepared a ∼100 nm DNA origami Möbius strip from 11 DNA helices, which was twisted 180° along its central axis and seamlessly connected back to itself. The overall length of the strip is ∼210 nm long and 25−30 nm wide. Amazingly, they demonstrated a topological transformation of Möbius strip at the molecular scale. The Möbius strip can be reconfigured into various topologies by "cutting" along its length at different positions. Yan, Liu, and co-workers performed this "cutting" by selectively separating selected DNA helices in the Möbius strip using a programmed strand displacement. The authors call this the "fold-and-cut strategy", which resembles Japanese Kirigami, a traditional art of paper cutting. They have beautifully shown the transformation of the DNA origami Möbius strips into double-sized supercoiled circles by "cutting" along the middle of the strips using AFM and TEM. They could transform the strips into catenanes by cutting along each strip's length approximately one-third of the distance of the strip's width.

The authors later proposed another "dynamic" DNA origami structure exhibiting reconfigurable quasifractal patterns (Figure 1f).[31] The rectangular DNA origami structure can alternate


dx.doi.org/10.1021/ar400328v | Acc. Chem. Res. 2014, 47, 1742−1749

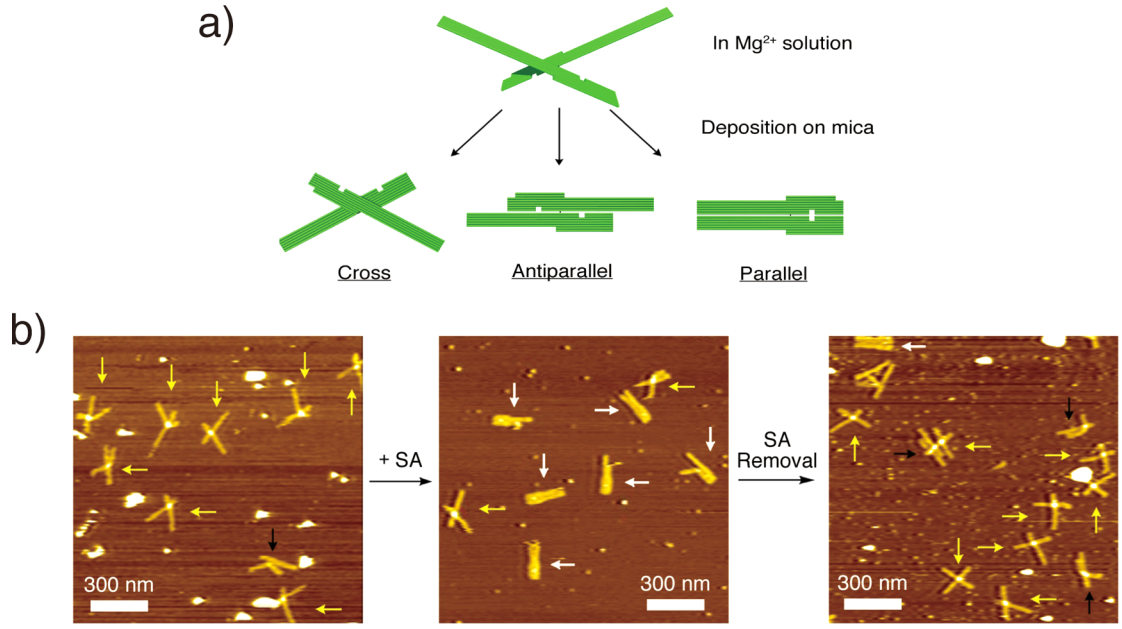



**Figure 2.** Nanomechanical pinching devices as "single-molecular beacon."[32] (a) DNA origami pliers and their three forms. (b) SA pinching by DNA origami pliers.

across three independent frames: an initial frame with one large square, a second frame with four medium squares, and a third frame with eight small squares and two medium squares. The authors applied a "fold-release-fold strategy," in which sets of unset strands are used to selectively remove sets of closure staple strands in the frames. Four sets of unset and closure sets were used to reversibly switch between the three frames.

## ■ DNA ORIGAMI PINCHING DEVICES

The first nanomechanical DNA origami devices with a specific function other than simple transformation were our "DNA origami pliers", which can be used as "single-molecule beacons" for the detection of biomolecules (Figure 2).[32] They consist of two ca. 170 nm long lever domains made of six parallel DNA helices. These levers are joined together at a fulcrum by an immobile Holliday junction. AFM measurements of DNA origami beacons require the latter's deposition on a mica surface. Three possible forms of origami beacons could adhere to a 2D surface (Figure 2a). The most feasible form is a "cross"-form, which directly represents the twisted solution structure of DNA origami pliers expected from a right-handed, antiparallel stacked X-structure of a DNA four-way junction with a small angle of 60°. The second feasible structure is an "antiparallel form", in which two levers are aligned in parallel on a plane but point in opposite directions. The third feasible form is a "parallel closed form", in which both levers are aligned in parallel in the same direction. Each lever has a small concavity of two helical turns long and two helices wide (ca. 7 nm × 7 nm), which serves as the jaws of the pliers to pinch the target molecule. When DNA origami pliers are in a parallel form, these concavities are placed next to each other to form a larger cavity, which accommodates the captured target fairly stably throughout AFM scanning.[33,34]

The DNA origami beacons used in this study sense various targets in a single-molecule manner using three independent mechanisms: "pinching", "zipping", or "unzipping". Pinching is used to capture and detect a single target molecule, which binds multiple ligands, in the jaws. For this purpose, two ligands are attached to each of the staple strands placed in the concavities (anchor strands) and cooperatively capture a single target molecule between the jaws. This intramolecular process triggers a shape transition of origami beacons from cross or antiparallel form to a parallel closed form, a process which can be visualized using AFM imaging or can be monitored in solution with spectroscopic analyses.

DNA pliers were first modified with a biotin group in each of the jaws (Figure 2b). The dominant species initially observed in AFM images in a buffer solution without target streptavidin (SA) were the DNA pliers in cross form (58% yield), a result consistent with the X-structure of the DNA four-way junction. However, when SA was added to the solution, the population of each form drastically altered. Approximately 58% of the DNA pliers were found in the parallel closed form in the presence of SA. A bright spot of 5 nm height corresponding to the expected diameter of the pinched SA molecule was found in the jaws of most parallel pliers. The biotinylated anchor strands could be selectively detached from DNA pliers after SA pinching using a DNA strand displacement technique with the aid of extra 8-nt toehold sequence on the anchor strands. The majority of DNA pliers was in cross form again, showing that the closing resulted solely from SA capturing.

Protein−ligand bindings are among the strongest biological interactions, and thus, selective pinching and detection of a protein is relatively easy. However, the single-molecular pinching of other targets that do not have such strong binding interactions may be difficult. A zipping mechanism, which involves multiple binding events, is the second detection mechanism of origami beacons appropriate for such targets. Here, multiple elements that bind together in the presence of the target are introduced to each of the levers, and cooperatively trigger the selective closing of the origami beacons. For example, $Na^+$ ion sensing is possible using G-quadruplex formation. Unzipping, the reverse process of zipping, is the third detection mechanism of origami beacons. The zipper elements for this mechanism are designed to bind together at the initial stage, and they selectively unbind in the


dx.doi.org/10.1021/ar400328v | Acc. Chem. Res. 2014, 47, 1742−1749

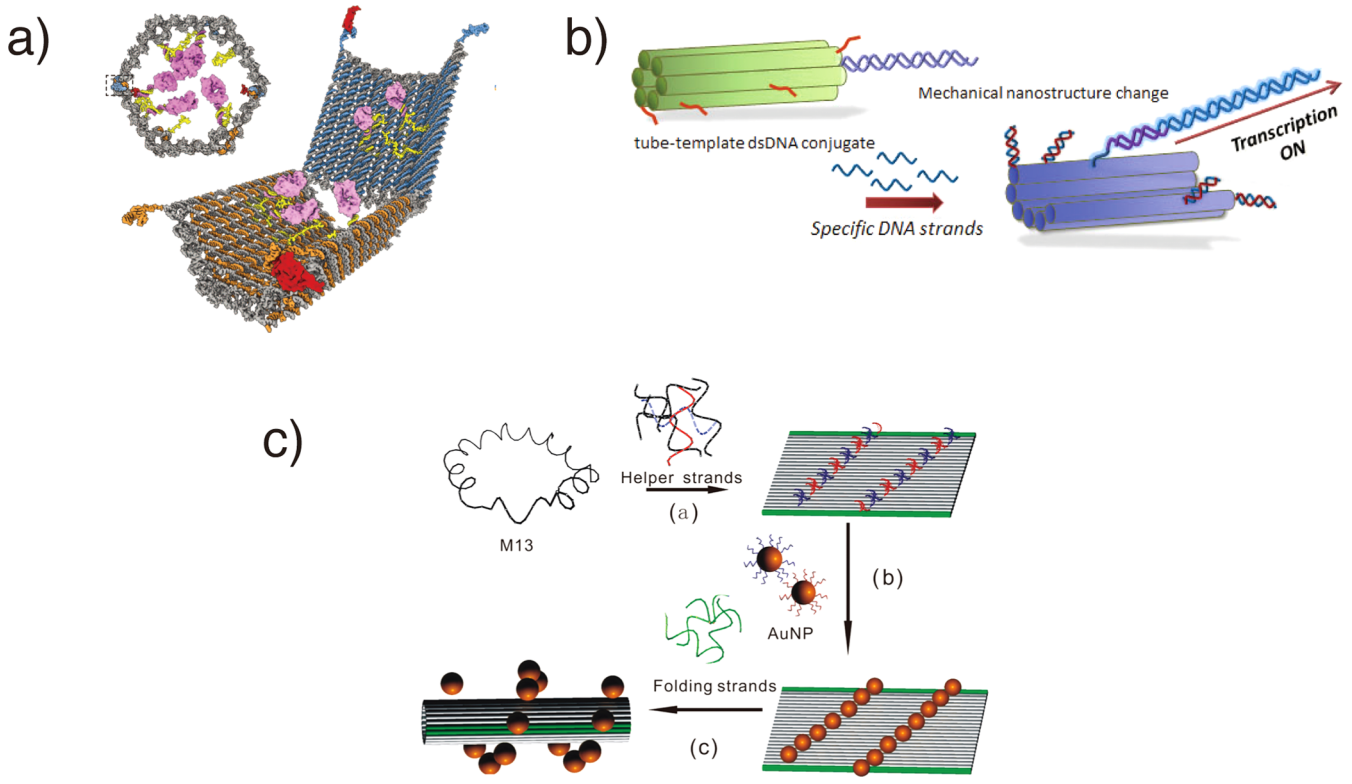



**Figure 3.** Other nanomechanical DNA origami devices. (a) DNA nanorobot (Reproduced with permission from ref 37. Copyright 2012 American Association for the Advancement of Science). (b) DNA origami "sheath" (Reproduced with permission from ref 38. Copyright 2012 American Chemical Society). (c) AuNP helical array on the DNA origami tube (Reproduced with permission from ref 40. Copyright 2012 American Chemical Society).

presence of target molecules. The presence of human microRNA (miRNA) could be clearly detected with origami beacons by using the unzipping mechanism.

The opening and closing of DNA origami pliers can be monitored in real time by labeling them with fluorescent dyes and observing the fluorescent signals. Dual-dye labeling of the pliers with a Texas Red and a fluorescein on one lever and BHQ-2 on the other lever enabled the real-time monitoring of the opening or closing of the pliers by observing which dye is located in front of the quencher.

Not only the existence of target molecules, but also the unique binding modes of bioorganic compounds can be analyzed using DNA origami pliers.[35] The invasive binding event of peptide nucleic acids (PNA) into a DNA duplex was observed by AFM imaging of the unzipping event of DNA origami pliers bearing target duplexes to the PNA invasion. The binding of neutral PNA to DNA is so strong that correctly designed PNA strands can invade into double-stranded DNA and replace DNA strands. The binding of PNA to DNA is extremely sequence selective to the extent that only a single mismatch with bis-PNA into the zipper elements completely inhibits the shape transition of the DNA origami pliers.

The shape transition of DNA origami pliers could also be detected with conventional agarose gel electrophoresis. The X-shaped open DNA origami pliers and unzipped invasion complex were clearly distinguishable from preclosed parallel DNA origami pliers by agarose gel electrophoresis, as the open pliers had significantly lower mobility.

The originally designed DNA origami pliers could only be switched between open cross and closed parallel forms or between open cross and closed antiparallel forms. Recently, we prepared a system for precise structural switching between all of the three forms of DNA origami pliers.[36] We redesigned DNA origami pliers to permit free switching between all three states, including parallel–antiparallel direct switching without taking the cross form. By the addition of one or two of four switcher strands to the solution, the hybridization and dehybridization of particular binder strands that fix the levers into predetermined state were selectively triggered according to their sequence. Circuit structure switching was even successful through all of the three states, in both of the two opposite directions, with the new design.

## ■ DNA NANOROBOT WORKING WITH CELLS

The "DNA nanorobot" presented by Douglas et al. is another nanomechanical DNA origami device with a practical function directly linked to its movement (Figure 3a).[37] The autonomous DNA nanorobot consists of 96 oligonucleotide staple strands and a 7308 base pair filamentous phage-derived scaffold strand and is capable of transporting molecular payloads to cells, sensing cell surface inputs for conditional, triggered activation, and reconfiguring its structure for payload delivery. The DNA nanorobot takes the form of a hexagonal barrel with dimensions of 35 nm × 35 nm × 45 nm, and the barrel consists of two domains covalently attached in the rear with single-stranded scaffold hinges. Two pairs of partially complementary lock strands attached to the front edges noncovalently fasten the barrel. One of the two strands in a pair is an aptamer that responds to one of the three antigen keys related to specific cell lines and releases its complement to expose the payload. The initial closure of the barrel was successfully accomplished with the aid of two "guide" staples incorporated adjacent to the lock


dx.doi.org/10.1021/ar400328v | Acc. Chem. Res. 2014, 47, 1742–1749

sites that span the top and bottom domains of the device, which can be selectively removed using selective strand displacement.

The functioning of the nanorobot was first confirmed by loading the nanorobots with fluorescently labeled antibody fragments that bind an antigen presented on human cells. The opening of the nanorobots exposes the loaded antibody fragments and results in fluorescent labeling of the cells, which can be quantified by flow cytometry. Twelve payload attachment sites were arranged in an inward-facing ring in the middle of the barrel to enable different payload orientations and spacing. Typically two different kinds of DNA-bearing antibody fragment cargos were loaded after closing the barrel. Both the two aptamer locks and the two cargos accurately functioned as an AND logic gate, showing fairly selective binding to the target cells only in the presence of specific lock–key and payload–target combinations.

## DNA ORIGAMI "SHEATH" FOR TRANSCRIPTION REGULATION

A structural change of DNA origami can be also used to mimic the function of suppressors in a transcription regulation system. Endo and Sugiyama designed a six helix DNA origami tube to sheath a target dsDNA fragment (Figure 3b).[38] The standard design principle for the six helix DNA origami tube, i.e., arranging crossovers every 7 bp to connect adjacent duplexes at an angle of 120°, was adapted. A 900-bp dsDNA fragment containing T7 promoter sequence was prepared by PCR using a unique primer in which a portion complementary to the template and a portion corresponding to a staple strand for DNA origami tube were connected in series using an alkyl spacer unit. The alkyl spacer unit served as a terminator for the DNA polymerase reaction and left the staple strand portion single-stranded throughout the PCR cycles.[39] The six helix DNA origami tube was made of three 110-mer scaffolds and 8 staples strands. One of them was tethered to the PCR amplicon as described above, while another staple strand was modified with biotin using a linker with a disulfide bond for purification. Four of the staple strands were modified with a toehold at their ends. After formation of the six helix DNA origami tube, four DNA strands complementary to the toehold-modified staples were added to open the tube.

The sheathing of dsDNA template was performed by directly annealing the conjugate in the mixture containing the scaffold, the staple strands, and the template. The yield of the sheathing of dsDNA template was 50–60%, measured by gel electrophoresis. The tube–dsDNA template conjugate was then purified and separated from unbound dsDNA template using streptavidin magnetic beads, followed by cleavage of the disulfide bond using DTT to release the captured conjugate.

The activity of in vitro transcription using T7 RNA polymerase was analyzed by monitoring the expression level of the RNA transcript using agarose gel electrophoresis. Although complete inhibition of transcription with closed conjugate was not achieved, the transcription level of the open conjugate was 5.5-fold higher than that of the closed conjugate.

## ROLLING-UP A DNA ORIGAMI SHEET TO MAKE PLASMONIC AuNP ARRAYS

Ding et al. rolled a DNA origami sheet into a tube, constructing gold nanoparticle (AuNP) helical arrays (Figure 3c).[40] A rectangular DNA origami template composed of 24 DNA helices with dimensions of 90 nm × 60 nm × 2 nm was prepared following the standard protocol. In total, 45 of the staple strands arranged along two parallel diagonal lines were extended to tether capture strands for AuNP on one side of the sheet. Binding sites were arranged 16 nm apart, and three capture strands were used at each binding site to localize one AuNP (10 or 13 nm) there. The sequences of capture strands were switched alternatively between two different binding-site sequences to avoid nonspecific binding between neighboring binding sites. After the 2D DNA origami sheet was formed, AuNPs made functional with corresponding complementary DNA strands were added to position diagonal AuNP arrays on the sheet. The sequence of the two long sides of the rectangular DNA origami was modified to be complementary to that of the folding DNA strands. The addition of the folding strands triggered the rolling up of the rectangular origami sheet into a hollow DNA origami tube. Consequently, the AuNPs were arranged in a helical geometry on the hollow origami tube. Notably, CD spectra of AuNP helical arrays exhibited a characteristic peak-dip CD line shape in the vicinity of the plasmonic resonance of the AuNPs at approximately 525 nm, thus demonstrating a plasmonic chiral response.

## PRECISE STRUCTURAL INFORMATION AND MECHANICAL PROPERTIES OF DNA ORIGAMI STRUCTURES

To design nanomechanical DNA origami devices with desired functions, accurate understandings of DNA origami structures and their mechanical properties are essential.

As predicted earlier, DNA origami structures designed following the original and standard principle, which approximates a helical pitch of B-form duplex to 10.67 nt for a canonical value of 10.5 nt, shows inherent distortions due to the unwinding of the helices.[41,42] Excellent previous studies have established expertise in how to offset such distortions. Modifying the number of nucleotides between the crossovers may be the most direct and basic method, although sometimes tedious. Another option involves introducing dumbbell hairpins to the origami surface to cancel local distortions.

More detailed studies on the actual DNA origami structures have been conducted by Dietz and co-workers using electron microscopes and multilayer DNA origami 3D structures as specimens.[43−45] They developed a 3D structure prediction platform for DNA origami designs called CanDo (computer-aided engineering for DNA origami) and are steadily updating it by reflecting actual structural information they obtain. According to their studies, rods consisting of a set of two-node beam finite elements with a stretch modulus of 1100 pN, a bend modulus of 230 pN nm$^2$, and a twist modulus of 460 pN nm represent B-form DNA helices very well. A nick between staple strands can be modeled by reducing backbone bending and torsional stiffness by a factor of 100, whereas stretching stiffness is retained. CanDo works with caDNAno,[46] an open-source DNA origami design software providing an intuitive and easy designing environment for nanomechanical DNA origami devices.

A report on the direct measurement of the mechanical properties of DNA origami structures has also been presented by Liedl et al., who used multilayer 3D DNA origami structures as specimens.[47] They used magnetic tweezers to control the stress on DNA origami structures. Three types of DNA origami structures, a 428 nm long six-helix bundle (6HB) with a single digoxigenin or biotin modification as an anchor, a 371 nm long 6HB with 18-helix bases carrying nine anchors at each end, and

a 478 nm long 4HB with 20-helix bases carrying ten anchors were prepared to bridge a 1 $\mu$m magnetic bead and the flow-cell substrate. The 4HB was prepared according to the square-lattice design principle. It was found that the single anchoring point in the first 6HB allows the bundle to swivel around the attachment point and does not withstand the application of torsional stress. The latter two bundles with multiple anchoring points behaved well according to the external force. They obtained bending persistent lengths of 740 ± 140 nm for the 4HB and 1880 ± 270 nm for the 6HB, thus corresponding to an increase in bending rigidity of 15-fold and 38-fold, respectively, compared to dsDNA. Similarly, obtained torsional persistence lengths were 390 ± 30 nm for the 4HB and 530 ± 20 nm for the 6HB. Compared to dsDNA, these values correspond to a 4.0-fold and 5.5-fold increase in torsional rigidity, respectively. This difference results from the connections between DNA helices in the bundles. These findings are in good agreement with the widely believed behaviors of 2D DNA origami sheets in solution: structures that are easily twisted and wound but stiff along the helical axis, properties worth noting for designing nanomechanical DNA origami devices.

## CONCLUDING REMARKS

Nanomechanical DNA origami device designs have evolved from DNA boxes capable of a single movement to a range of many devices with specific functions. Considering the advantages of the DNA origami technique, the integration of multiple functions in a single nanomechanical DNA origami device should be achieved in the near future.

Nanomechanical DNA origami devices are not only useful as independent molecular devices. An application of DNA origami beams to optical tweezers has also been recently reported.[48] Nanomechanical DNA origami devices should soon become essential tools in nanomechanics as well as in another emerging research field, namely the area of "molecular robotics",[49] closely related to the studies of artificial life, synthetic biology, and nanomedicine.

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The authors declare no competing financial interest.

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## ACKNOWLEDGMENTS

The authors acknowledge funding support from the Ministry of Education, Science, Sports, Culture and Technology, Japan (Grant-in-Aid for Scientific Research (S) (22220001), (B) (24350088), Grant-in-Aid for Scientific Research on Innovative Areas "Molecular Robotics" (24104004)), from PRESTO, JST, and from Kansai University (Subsidy for Supporting Young Scholars, 2012).

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