Molecular mechanics of DNA bricks: in situ structure, mechanical properties and ionic conductivity

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Abstract

The DNA bricks method exploits self-assembly of short DNA fragments to produce custom three-dimensional objects with subnanometer precision. In contrast to DNA origami, the DNA brick method permits a variety of different structures to be realized using the same library of DNA strands. As a consequence of their design, however, assembled DNA brick structures have fewer interhelical connections in comparison to equivalent DNA origami structures. Although the overall shape of the DNA brick objects has been characterized and found to conform to the features of the target designs, the microscopic properties of DNA brick objects remain yet to be determined. Here, we use the all-atom molecular dynamics method to directly compare the structure, mechanical properties and ionic conductivity of DNA brick and DNA origami structures different only by internal connectivity of their constituent DNA strands. In comparison to equivalent DNA origami structures, the DNA brick structures are found to be less rigid and less dense and have a larger cross-section area normal to the DNA helix direction. At the microscopic level, the junction in the DNA brick structures are found to be right-handed, similar to the structure of individual Holliday junctions (HJ) in solution, which contrasts with the left-handed structure of HJ in DNA origami. Subject to external electric field, a DNA brick plate is more leaky to ions than an equivalent DNA origami plate because of its lower density and larger cross-section area. Overall, our results indicate that the structures produced by the DNA brick method are fairly similar in their overall appearance to those created by the DNA origami method but are more compliant when subject to external forces, which likely is a consequence of their single crossover design.

1. Introduction

The self-assembly property of DNA has transformed nanotechnology by offering a potentially disruptive route to manufacturing of tailored nanomaterials [1]. Although conventional nanomaterials, such as carbon nanotubes [2], gold nanoparticles [3] or silicon nanowires [4], have become indispensable components of a variety of engineered systems [5], assembly of such materials into functional units continues to present a considerable challenge. The Watson–Crick hybridization of complementary DNA strands has offered a route to programmable assembly of inorganic components [6, 7], promising exciting developments in the area of bioengineering applications [8].

Building on the pioneering studies that introduced DNA self-assembly as an engineering tool [9, 10], the DNA origami method [11] has kick started the field by offering a simple, practical, and versatile approach to producing DNA nanostructures. The DNA origami technique employs a collection of short DNA strands
to bring together distant fragments of a long DNA strand (scaffold), folding the latter into a prescribed geometrical shape, figure 1(A). The earliest forms of DNA origami were two-dimensional plates of various shapes [11]. The method was subsequently expanded to permit assembly of complex three-dimensional (3D) structures [12, 13]. The functionality of such DNA origami nanostructures can be further enhanced by the addition of auxiliary chemical groups, such as thiol groups, which bond easily to metallic nanoparticles [14]. The functionalization allows conventional nanomaterials to be assembled in a pre-determined manner [8, 14]. However, the typical yield of the DNA origami method is relatively low compared to many chemical processes, likely because of the numerous kinetic traps in the self-assembly process of DNA [15, 16].

The DNA brick method has emerged as an alternative to the DNA origami method for assembling custom 3D DNA nanostructures [17]. The DNA brick nanostructures are made entirely from short DNA oligos, figure 1(B), which increases the yield of the self-assembly reaction and makes it possible to use the same library of DNA strands to produce a broad range of custom 3D shapes [17]. Conceptually, the architecture of a DNA brick object is similar to that built using LEGO® building blocks. The basic building unit of the DNA brick method is a 32-nucleotide oligomer folded back upon itself in a horseshoe shape, figure 1(C). The four eight-nucleotide parts of the DNA brick are used to connect neighboring bricks through complementary hybridization interactions, figure 1(C). The central 16-nucleotide fragment of the strand (that includes the crossover) is defined as the ‘head’ whereas the two terminal eight-nucleotide fragments of the strand are defined as the ‘tails’. Each head connects to the tails of two different bricks; the same head-to-tail direction of the bricks is maintained throughout the structure. The folded oligos stack together like $1 \times 2$ LEGO® blocks, staggering in all three orthogonal directions. Under ideal conditions, each brick is connected to four other bricks [18]. As a consequence of their design, the DNA helices in DNA brick structures are connected via single-strand crossovers, in contrast to DNA origami where the connections are realized via a two-strand exchange, a Holliday
junction (H), figure 1(D). Thus, DNA brick and DNA origami structures can have the same overall shapes but differ substantially by the internal connectivity of their constituent parts.

Programming DNA self-assembly into a complex 3D shape is a task beyond the capabilities of manual design [19] and hence is commonly carried out with the help of an automated design tool. The first such tool was the original program used by Rothemund to create the 2D origami structures [11]. Developed to aid the design of 3D origami, the caDNAno program has a graphical user interface and can automatically generate the nucleotide sequences of the staple strands required to realize a target structure [19]. The caDNAno program, however, only helps to design the structures; it neither predicts the equilibrium solution structure of the design nor its physical properties. A number of computational methods have been developed to make such predictions [20–23], including the CanDo program [24] that can predict equilibrium structures and fluctuations of DNA origami within the framework of continuum mechanics. All-atom explicit solvent molecular dynamics (MD) simulations can provide, perhaps, the most complete physical description of self-assembled DNA nanostructures [21], albeit at a high computational cost. Using a coarse-grained representation in MD simulations considerably extends the time scale of the MD method [22], permitting simulations of the actual self-assembly process [16].

Here, we report the results of all-atom MD simulations of several solvated DNA nanostructures realized via both the DNA brick and DNA origami assembly methods. Following our previous study of the in situ structure, mechanical properties and ionic conductivity of DNA origami [21, 25], we investigate here the equilibrium structure, structural fluctuations and the response to external electric field of DNA brick objects. Analysis of our MD trajectories allows us to directly compare the properties of the objects realized via the two design strategies, elucidating the effect of their internal connectivity.

2. Results and discussion

To enable direct comparison of the DNA origami and DNA brick structures, we designed DNA origami and DNA brick representations of the same object—a 128 base pair long 4 × 4 DNA rod, figure 2(A). The designs were chosen to be identical in terms of their initial conformations, the nucleotide locations in the initial structures and the nucleotide sequence, differing only by the pattern of crossovers, figure 2(B), and the structure of the rods’ ends. The structure building procedures are described in detail in methods; supplementary figure S1 provides the caDNAno designs of both structures. The caDNAno designs were converted to all-atom representations and merged with aqueous solution of 50 mM MgCl₂, a concentration close to optimal for DNA bricks assembly [17]. The systems were then equilibrated for 5 ns with all heavy DNA atoms constrained to their initial coordinates, allowing Mg²⁺ ions to penetrate the DNA structures and neutralize the DNA charge. The structures were then equilibrated for another 30 ns with the constraints gradually released. The systems were then simulated unrestrained for another 135 ns each. Supplementary table S1 provides a summary of all simulations performed.

2.1. In situ structure and conformational fluctuations

Over the course of the MD simulations, the two DNA structures maintained their overall structure, undergoing minor deformations. Figures 2(C) and (D) illustrate the conformations of the two structures at the end of the MD trajectories. Both structures have not collapsed or separated into individual strands, and have taken the expected conformation similar to the ideal design, along with the expected twisting seen in the DNA structures built using the square lattice design [13], with the DNA brick structure appearing to have twisted slightly less. The amount of the overall twist about the helical axis of the rod (the z-axis) was ~39° over 112 base pairs in the DNA origami structure and ~37° over 112 base pairs in the DNA brick structure. Although the overall amount of twist is very similar in the two structures, the DNA origami rod visually appears to have a larger twist along the z-axis in figures 2(C) and (D) because of the non-monotonic dependence in the DNA brick structure’s cross section along the z-axis (figure 2(J)). The final conformations of the two structures appear largely similar, but differ in the structures of their ends. The two ends of the DNA origami structure are staggered and frayed by the same amount whereas the two end of the DNA brick structure appear distinctly different. The asymmetric appearance of the DNA brick structure is a direct consequence of its design, figure 2(B) and supplementary figure S1.

Figure 2(E) shows the root-mean-square-deviation (RMSD) of the DNA atoms from their initial coordinates with hydrogen atoms excluded. The structures gradually approached a stable plateau after the constraints were fully removed. The relatively high RMSD of 10 Å can be partially attributed to the initial expansion of the DNA structures from their ideal design [21, 26]. Indeed, the RMSD computed relative to the final conformation was considerably lower, as low as 4–6 Å when the terminal array cells were excluded, supplementary figure S4(A). Figure 2(F) shows the percentage of base pairs that were broken during the MD runs. In both systems, the
amount rose gradually with time, but was less than 3%, on average, in agreement with the results of our earlier study [21, 26]. A considerably smaller amount of broken base pairs was measured when terminal array cells were excluded from the analysis, supplementary figures S1 and S2(B).

Figures 2(G) and (H) characterize the local integrity of the two DNA structures by treating the individual array cells as separate regions and showing the percent of broken base pairs per region. End regions, such as array cells 1 and 16, were found to have a considerably higher fraction of broken base pairs (>7%) compared to the internal regions, where the percent remained below 5%. The DNA brick structure, figure 2(H), had the highest concentration of broken base pairs in array cell 16 than any other regions, which results from the crossover density lower than average in that region that produced visible fraying of the helices, figure 2(D). Most of the bases from the broken base pairs remain stacked and do not extrude from the helices.

Overall the local structure of the internal regions of both DNA structures (origami and bricks) remained stable. The total percentage of broken base pairs fluctuated around ~2.5% at the end of the run (figure 2(F)), with most of the base pair separations being concentrated at the ends of the rods. However, reversible
deformations of the local structure can also take place [21]. The most notable example of that in the present set of simulations is in the region shared by array cells 13 and 14 in the DNA origami structure, figure 2(G). At ~100 ns, the fraction of broken base pairs reaches ~5%. Unlike at the edges, the base pairs in these array cells are constrained by the surrounding structures, and are able to be partially repaired over time.

Overall, the DNA brick structure appeared to be larger and less dense than its DNA origami equivalent. The average inter-axial distance in the DNA origami and DNA brick structures was 24.7 and 25.5 Å, respectively, figure 2(I). The inter-axial distance was computed as the distance between the centers of mass of two base pairs of the same base index from the neighboring DNA helices. The distances were averaged over the entire structure (excluding array cells 1 and 16) and over the respective MD trajectories. In agreement with the inter-DNA distance, the cross-sectional area of the DNA brick structure, 59.8 nm², was considerably larger than that of the DNA origami, 53.5 nm², figure 2(I). This implies that neighboring DNA helices are bound weaker in DNA bricks than in DNA origami, which is consistent with the brick structures having about half the number of crossover connections compared to DNA origami, figure 1(D).

2.2. The structure of interhelical junctions
A self-assembled DNA nanostructure maintains its 3D shape because of the lateral connections between its DNA duplexes, which we refer to here as interhelical junctions. In both DNA origami and DNA brick structures, the interhelical junctions are found at the crossover planes. While having approximately the same number of junction points per array cell, figure 2(B), the two structures differ considerably by the actual geometry of the junctions. The DNA origami junctions are laterally connected via two DNA strands per junction, arranged in a cross-like configuration known in biology as the HJ, figure 3(A) (left). In the DNA brick structures, the junctions are realized by one DNA strand per junction, figure 3(A) (right), which makes a DNA brick structure to have, on average, half of the interhelical connections of a DNA origami structure. Traditional HJs in solution ([MgCl₂] ~10 mM) have been shown to have a right-handed conformation characterized by a ~60° interhelical angle [27, 28]. Nevertheless, HJs in DNA origami structures were found to adopt a slightly left-handed conformation because of the geometrical constraints imposed by the neighboring DNA helices [21, 29]. Similar constraints must also apply to DNA brick junctions, however, their microscopic structure has not been characterized prior to this study.

To quantitatively characterize the conformations of the junctions in our DNA origami and DNA brick structures, we considered the center-of-mass coordinates of the eight base pairs near each junction, figure 3(A). Because of the asymmetric structure of the DNA brick junctions, we distinguish the 'bonded' (Z–Y–X′–W) and

![Figure 3: Geometric properties of interhelical junctions in DNA origami and DNA brick structures.](image-url)
The mechanical properties of a rod-like object can be determined by analyzing its structural fluctuations [30, 31]. To perform such an analysis on our DNA nanostructures, we represent their all-atom conformation in terms of local deformation tensors, following a method that we described previously [21]. The rod structures are described using a triad of vectors \( \{ f_i \} \) assigned to each array cell; the contour variable \( s \) spans the entire structure. The vectors are defined as orthogonal vectors between the corners of the idealized, structure, figure 4(A). Each of the three local generalized torsions \( \omega_i \) is defined as the torsion angle of the local triad per unit length with respect to the vector \( \hat{r} = \frac{df_i}{ds} = f_{ijk} \hat{r}_k = f_{ijk} \), where \( f_{ijk} \) is the Levi–Civita tensor [21, 30, 31]. For our rod-like objects, \( \omega_2 \) torsion describes twisting of the rods whereas \( \omega_1 \) and \( \omega_2 \) are related to bending.

Figures 4(B)–(D) characterize local trajectory-averages of generalized torsion \( \omega_{1,2,3} \) for DNA origami and DNA brick structures. The mean torsions \( \omega_1 \) (figure 4(B)) and \( \omega_2 \) (figure 4(C)) for both structures are near zero, with a slightly positive trend for \( \omega_2 \) in the case of DNA origami. \( \omega_3 \) (figure 4(D)) is notably higher for both structures, representing the axial twist that is visible in the final structures, figure 2(C) and (D). The amounts of axial twist vary periodically along the structure, with regions of positive and negative twist alternating every 3 or
4 array cells. Notably, the same regions in both structures twist by similar amounts, with the DNA brick object twisting slightly more in each direction, with the exception of array cell 10 where the twist is signifi-
cantly larger. The differences between the DNA origami and DNA brick structures. The scaffold strand of the DNA origami structure is shown in blue, all other strands are shown in unique colors. The blue semitransparent surface illustrates the approximate dimension of the simulation unit cell. Each system contains 1 M KCl and 50 mM MgCl$_2$, ions are not shown for clarity. The horizontal semitransparent cylinders are drawn to visually distinguish the top and bottom layers of the structures. In the direction of applied electric field the z-axis, the top and bottom layers are connected by four strands (green, purple, yellow, and red) in DNA origami and two strands (pink and orange) in DNA brick plates. Both DNA origami and DNA brick structures are effectively infinite within the x–y plane under periodic boundary conditions; periodic images of some strands along the y–z direction are shown to emphasize this point. The unit simulation cell contains four DNA helices, two helices per each layer. Supplementary figure S6 provides detailed schematic of the designs. (B) The x–y area of the DNA origami (top) and DNA brick (bottom) plates versus simulation time. The solid black lines indicate the moving average of the instantaneous x–y area values with a moving average window of 20 ns. The dashed lines indicate the trajectory–average values of the x–y area. (C) and (D) Ionic current density (panel C) and conductivity (panel D) versus transmembrane voltage of DNA origami (green) and DNA brick (blue) plates. (E) and (F) Reversible deformation of DNA origami (panel E) and DNA brick (panel F) plates produced by the applied electric field. Each panel, the top graph shows the duty cycle of the transmembrane bias; the bottom graph plots the average distance between the top and bottom layers of the plate. Data for the DNA origami plate in panels B–E were taken from our previous study [23]. (G) A representative conformation of a DNA brick junction under a 500 mV transmembrane bias. Individual strands are shown in unique colors. The arrows indicate the locations of joint breaks in the structure. A visible twist appears in the structure with respect to the junction. Reprinted with permission from Li C Y et al (2015 ACS Nano 9 1420–33). Copyright 2015 American Chemical Society.

- 2.4. Comparison of the ionic conductivity
It has been experimentally shown that DNA origami plates are permeable to ions [33–35] and that their conductance can be affected by several factors, including their design [25, 36], the transmembrane voltage [25, 35], and the type and concentration of the electrolyte solution [25]. Tile-like DNA objects have been inserted into lipid bilayer membranes to mimic the function of biological ion channels [37–39], revealing substantial effects of the object’s architecture on the ionic conductance [40]. DNA brick plates can be potentially used instead of DNA origami for nanopore sensing measurements [33, 34], offering a larger design space and customization of the DNA sequence.
To investigate the ionic conductivity of the DNA brick plates and their response to the applied electric field, we designed an effectively infinite DNA brick plate to match the dimensions of the DNA origami plate that we have studied previously [25]. Both plates were composed of two layers of DNA duplexes submerged in aqueous solution of 50 mM MgCl₂ and 1 M KCl, figure 5(A). Supplementary figure S6 provides the details of both designs. Similar to the DNA origami plate, the DNA brick plate was equilibrated for ~400 ns allowing its cross section to change. Despite having the same initial dimensions, the DNA brick plate was found to have a higher cross section area than the DNA origami plate, figure 5(B). The conformation closest to the average was used to start the simulations under applied electric field. The ionic current simulations were performed following a previously described method [41, 42], under transmembrane bias of 100, 250 and 500 mV. Comparison of the ionic current density through the DNA brick and DNA origami plates indicates that the former is more permeable to ions. Consequently, the DNA brick plate has higher ionic conductivity, figure 5(D).

Previously, we have shown that DNA origami plates can be reversibly swelled by the electro-osmotic flow produced by the application of the electric field [25]. To investigate the response of the DNA brick plate to an alternating electric field, the plate was simulated under a transmembrane bias that was periodically switched between 500 to 0 mV. In comparison to the response of the DNA origami plate, figure 5(E), the DNA brick plate was observed to swell considerably more under a 500 mV bias, figure 5(F). Upon switching the transmembrane bias off, the DNA brick plate largely recovered its structure, however, the time scale of our simulations could be too short to achieve a full recovery. Closer examination of the DNA brick structure under the applied bias revealed that the interhelical junctions, because of their single bond structure, can act as swivel points for DNA duplexes, allowing the DNA helices to move about the bond, figure 5(G), which explains the larger swelling amplitude.

3. Conclusion

Using all-atom MD simulations, we have investigated the structure, mechanical properties and ionic conductivity of DNA bricks. In comparison to equivalent DNA origami structures, DNA brick structures were found to have a larger cross section and have a more relaxed structure on the interhelical junctions. Nevertheless, both structures appear to have the same overall twist about the helical direction, prescribed by the square lattice arrangement of the DNA helices utilized in both designs. The structure of the inter-helical junctions, however, is notably different, with the DNA origami structures having a left-handed crossing of the helices and the DNA brick junctions being the right-handed ones. In terms of mechanical properties, the two structures appear to be fairly similar, with the DNA brick structure being, on average, more flexible than the DNA origami one. Another notable consequence of their designs is the difference in the ionic conductivity of the DNA plates: the DNA brick plates were found to be more conductive. Responding to an external electric field, both structures have shown reversible swelling, although swelling of the DNA brick structures had larger amplitude and was not fully reversible on the time scale of our simulations. All of the above suggest that, while being fairly similar in appearance, the DNA brick and DNA origami structures can respond differently to external perturbations, such as mechanical deformation or applied electric field, with the DNA brick structures being more compliant.

4. Methods

General MD methods. All MD simulations were performed using the NAMD program [43], periodic boundary conditions, CHARMM36 force field for DNA [44], the modified TIP3P model of water [45], and custom parameters for ions [46] based on the CHARMM force field [47]. All Mg²⁺ ions were simulated as Mg²⁺-hexahydrates [46]. During equilibration, the structure of the hexahydrates were preserved by harmonically restraining \((k = 5000\ \text{kcal mol}^{-1}\ \text{Å}^{-2})\) the distance between Mg²⁺ and water oxygen atoms to ~1.9 Å using the extrabonds function in NAMD. Our custom parameterization of Mg²⁺ ions was validated by simulations of competitive ion binding to DNA [48] and by simulations of DNA array systems [49]. These restraints prevented irreversible binding of Mg²⁺ to phosphate oxygens of DNA during initial equilibration [46, 48]. The van der Waals and short-range electrostatic energies were calculated using an 8–10 Å switching scheme. The long-range electrostatic interactions were computed using the particle-mesh Ewald scheme and the grid size of ~1.5 Å [50]. The integration timestep was 2 fs. Temperatures was held constant at 300 K using a Langevin thermostat [43]. Pressure was maintained at 1 bar using the Nosé–Hoover Langevin piston pressure control [51].

Assembly of the 4 × 4 DNA rod structures. The 4 × 4 DNA brick structure was designed in caDNAno [19] by stacking layers of bricks in a staggered pattern, similar to the brickwork layout seen in a brick wall. The first brick was placed with its head in array cell 1 and its tails in array cell 2; the 5’ branch of the brick was placed in helix 0 and the 3’ branch in helix 1, see figure 2(A) for array cells and helix numbering. The second brick was placed with its head and tails in the same array cells as the first brick, but with the 5’ branch in helix 2 and the 3’ branch in...
helix 3, completing the top row of the 4 × 4 structure, figure 2(A). To stagger the rows, the next brick was added one row down and one helix right, occupying array cells 1 and 2 of helices 5 (with 3rd end) and 6 (with 5th end); all bricks were placed to have the same head-to-tail orientation (along the z-axis) throughout the structure. Two 16-nucleotide half-bricks that had no crossovers were placed in array cells 1 and 2 of helices 4 and 7, completing the second row. The next row of bricks was built in the same way as the first row; the fourth row was identical to the second. To add the next layer of bricks (with heads in array cell 2 and tails in array cell 3), the previous layer of bricks was rotated, as a whole, by 90° clockwise with respect to the z-axis, bringing, for example, the brick that spans helices 0 (with 5th end) and 1 (with 3rd end) in array cells 1 and 2 to span helices 15 (with 5th end) and 8 (with 3rd end) in array cells 2 and 3. This procedure was repeated until array cell 15 was completed. To complete array cell 1, eight-nucleotide strands were added to helices 0, 3, 8, and 11, and 16-nucleotide strands were added to connect helices 1 and 2, 5 and 4, 7 and 6, 10 and 9, 13, and 12, and 15 and 14, making all DNA double stranded. Similarly, single-stranded DNA in array cell 16 was completed by adding eight-nucleotide strands to helices 0, 13, and 15, and 16-nucleotide strands to connect helices 1 and 6, 3 and 4, 5 and 10, 7 and 8, 9 and 14, and 11 and 12. The 4 × 4 square lattice DNA origami rod structure was designed using caDNAno and converted to the all-atom representation using a previously described method [21]. Supplementary figure S1 specifies the designs of the DNA origami and DNA brick representations of the 4 × 4 rod structure; supplementary tables S2 and S3 list the DNA sequences.

The resulting design was converted to an all-atom representation using the cadnano2pdb conversion script [21, 52], which places the DNA nucleotides according to the idealized geometry of a B-form DNA duplex. Following the conversion, each model was submerged in aqueous solution containing ~50 mM MgCl₂. We used the genbox program of the GROMACS package [53] to randomly place Mg²⁺ and Cl⁻ ions to add water to our models. The size of the water box was chosen such that a water buffer of 4 nm or more separated the periodic images of the DNA structures. The final dimensions of the solvated 4 × 4 DNA rod structures were approximately 15 × 15 × 56 nm³, the systems contained ~1.28 million atoms. The total number of phosphate groups was 4031 for the DNA origami rod and 3927 for the DNA brick rod. 2389 and 2337 Mg ions were added to the origami and brick rod systems, respectively; 747 chlorine ions were added to each system. Each ideal rod design contained 2048 base pairs. Following assembly, the potential energy of each system was minimized using the conjugate gradient method. The two systems were first equilibrated for 30 ns with all heavy atoms of the DNA bases harmonically restrained to their initial coordinates; the spring constants of the restraints were reduced from 0.5 to 0.1 and to 0.01 kcal mol⁻¹ Å⁻² every 10 ns. This gradual equilibration process allowed the DNA backbone to relax and the Mg²⁺ ions within the DNA rod structures and the radial distribution functions of Mg²⁺ ions within the DNA rod structures and the radial distribution functions of Mg²⁺ ions with respect to DNA phosphate groups indicate that the 30 ns constrained equilibration was sufficient for the ions to attain an equilibrium distribution within the DNA rod structures, supplementary figure S7.

Based on the above protocol, we developed a web tool for building all-atom DNA brick models of arbitrary geometrical shapes, the legoGen [54].

Assembly of the infinite DNA brick plate. To simulate the ionic conductivity of a DNA brick structure, we used the NanoEngineer-1 software to build the minimal unit cell of a DNA brick plate, periodic within the x–y plane. The minimal unit cell contained two DNA layers with two DNA duplexes in each layer. The DNA brick plate had the same initial dimensions, the same number of nucleotides, and the same nucleotide sequence as the DNA origami plate that we studied previously [25]. Supplementary figure S6 specifies the designs of the DNA origami and DNA brick plates; Supplementary tables S4 and S5 list the DNA sequences. The resulting NanoEngineer design of the DNA brick plate was converted to an all-atom representation using a custom nanoengineer2pdb conversion script. The all-atom model of the DNA brick plate was merged with a pre-equilibrated volume of electrolyte solution containing 50 mM MgCl₂ and 1 M KCl; the solution volume was taken from the equilibrated all-atom model of the solvated DNA origami plate [25]. The final system contained ~50,000 atoms; the electrolyte solution separated the periodic images of the plate along the z-axis. Upon energy minimization, the structure was equilibrated for 30 ns having all heavy atoms of DNA nucleotides harmonically restrained to their initial coordinates; the spring constants gradually reduced from 0.5 to 0.1 and to 0.01 kcal mol⁻¹ Å⁻² every 10 ns. To determine the equilibrium dimensions of the DNA brick plate system, the system was first simulated in the NPT ensemble for ~400 ns without applying any restraints. As a starting condition for our ionic current simulations, we chose a frame from the equilibration trajectory with the x–y cross-section area closest to the trajectory-average value. A transmembrane bias V was induced across the plate by applying a constant electric field E along the z-axis such that \( V = -EL_z \), where \( L_z \) is the length of the simulation in the direction of the applied field [41]. To prevent the DNA brick structures from drifting in the electric field, a harmonic constraint was applied to its center of mass using a spring constant of 1 kcal mol⁻¹ Å⁻². The simulations under applied field were performed in the constant number of atoms, constant volume and constant temperature ensemble.
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