Supplementary Material for "The Free-Energy Landscape of a Mechanically Bistable DNA Origami"

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S1. FURTHER RESULTS

A. Free-energy landscape without electrostatic repulsions

To explore the degree to which electrostatic repulsions contribute to the instability of the closed configuration, we re-computed the free-energy landscape but with the electrostatic interactions turned off (Figure S1). The free-energy penalties associated with smaller values of θ are somewhat reduced but the landscape still very clearly exhibits a single minimum corresponding to the open configuration.

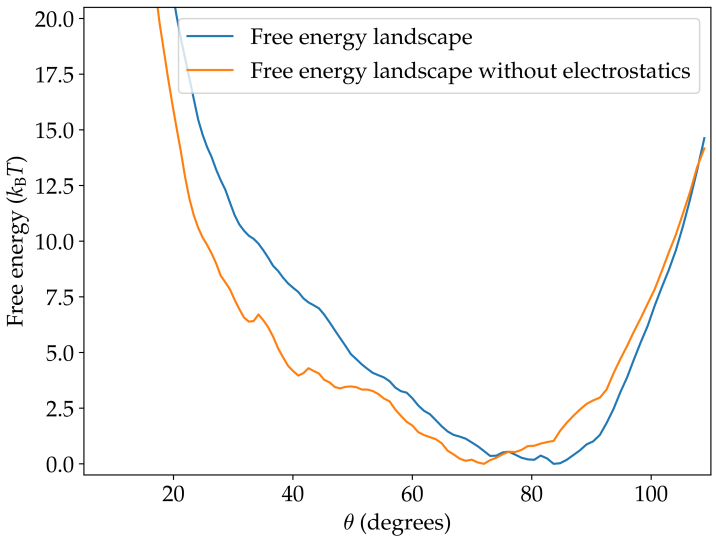

Figure S1: Free-energy landscape of the complete origami as a function of θ at $[Na^+]$=1 M and with the electrostatic interactions turned off. $T = 300$ K.

B. Free-energy landscape at different temperatures

To explore the degree to which the free-energy landscape of the origami depends on temperature, we re-computed the free-energy landscape at temperatures 20 K higher and lower than that used in the main text (Figure S2). The differences in the landscapes are of the order of the errors in the computations showing that the free-energy landscape experienced by the origami is essentially the same in the temperature range for which the fully assembled state is most stable. The relative invariance in the landscapes is perhaps unsurprising given that the temperature changes represent just a 7% change in the absolute temperature and that the physical properties of DNA and its assemblies that lead to the form of the landscape (e.g. persistence length of double-stranded DNA, interhelical repulsive interactions and interhelical spacing in DNA origamis [28]) show a modest dependence on temperature.

C. Free-energy contributions of each joint

The contributions from each joint to the free-energy landscape as a function of θ are shown in Figure S3. These were used in the computation of the lines in Figure 6 of the main text.

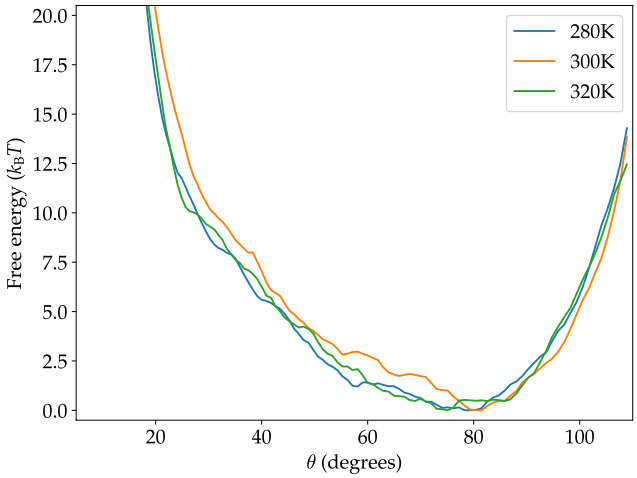

Figure S2: Free-energy landscape of the complete origami as a function of θ at [Na^+]=1 M at three different temperatures, as labelled.

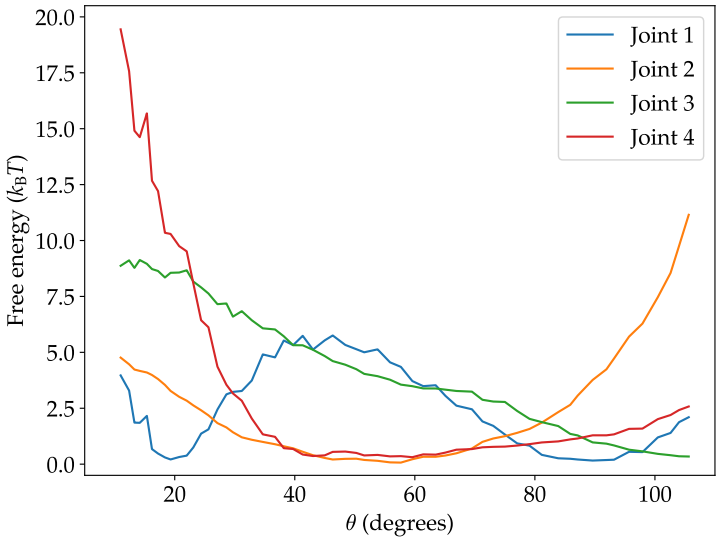

Figure S3: Free-energy contributions of each joint to that of the complete origami as a function of θ.

S2. SIMULATION DETAILS

We used the latest version of oxDNA (available at https://github.com/lorenzo-rovigatti/oxDNA) which supports an external harmonic potential that acts on the distance between the centres of mass of two groups of nucleotides.

Simulations were performed at 300 K using a Langevin thermostat. The time-step used was 0.005 in the internal simulation units of the oxDNA code, which corresponds to 15 fs.

A. Generating starting configurations

We converted the caDNAno design files of the origamis into oxDNA format using the tacoxDNA package [47]. The converted configurations are then rearranged manually in oxView [48] so that they are closer to their designed geometries.

The rearranged configurations cannot serve as starting configurations for molecular dynamics simulations because

of nucleotides experiencing large forces due to particle overlaps or extended bonds. Therefore, the potential energy of these configurations is first minimized for 200 steps using a steepest-descent algorithm, and then the configurations are relaxed in a molecular dynamics simulation using a modified backbone potential for 10^6 steps. After that, the extended bonds have typically returned to their normal lengths, and the configurations are ready for simulation using the standard oxDNA force field. All designs were equilibrated for a further 10^8 steps, corresponding to about 1.5 µs.

B. Free-energy landscape

We used umbrella sampling [49] to calculate the free-energy landscape as a function of the order parameter R, defined in Figure 2 of the main text. Specifically, R was defined as the distance between the centres of mass of two groups of nucleotides, which consist of the nucleotides at positions 259–273 on helices 0–9, and at positions 231–245 on helices 10–19, respectively. To obtain the landscape as a function of θ, the values of R and θ were tracked in each window of the umbrella sampling simulations. θ was defined as the angle between the two vectors in Figure 2 of the main text. Specifically, the first vector was defined as the vector pointing from the centre of mass of the nucleotides at positions 196–210 to that at positions 259–273 on helices 0–9, whereas the second vector was defined as the vector pointing from the centre of mass of the nucleotides at positions 147–161 to that at positions 231–245 on helices 10–19. The nucleotide positions and helix indices are defined in the caDNAno design in Figure S4.

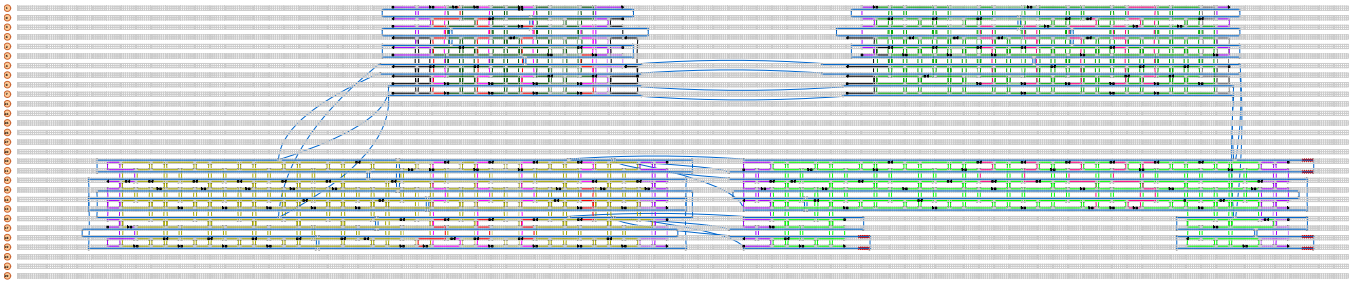

Figure S4: Full caDNAno design for the complete origami

We performed sets of simulations where the order parameter was restrained with a harmonic potential at the centre of each sampling window. The range of R values sampled was from $R = 12\,\text{nm}$ to $60\,\text{nm}$.

Before the umbrella sampling simulations, we prepared the starting configurations for each window using two pulling simulations. The order parameter of an equilibrated configuration was restrained at its original value (46 nm) with a harmonic bias potential of stiffness $k = 57.09\,\text{pN/nm}$.

In the first simulation, the equilibrium position of the harmonic bias potential was gradually reduced at a constant rate of 0.14 m/s, until it reached 12 nm. Configurations were outputted every 2×10^6 steps, i.e. when the traps had moved by 0.85 nm, resulting in a starting configuration for each window from the starting value of R to the final value of R, where neighbouring windows are separated by 0.85 nm.

In the second simulation, the equilibrium position was gradually increased at the same rate as the first simulation, until it reached 60 nm. Configurations were outputted at the same frequency, thus giving starting configurations for windows defined in a similar way as in the first simulation.

After the starting configurations have been prepared, the configuration in each window was restrained at the value of R corresponding to that window with a harmonic bias potential of stiffness $k = 11.42\,\text{pN/nm}$. Each window was equilibrated for 10^6 steps before a production run of 10^7 steps. R was outputted every 10^3 steps, giving 10^4 data points for each window. Using the biased probability distributions of R in each window, we used WHAM [40,50] to calculate the unbiased free-energy landscape of the system as a function of R.

A new set of production runs was then started from the last configurations of the previous production runs, and WHAM was performed on the new data points to calculate the free-energy landscape. This process was repeated three times. The resulting landscapes were very similar, thus confirming convergence.

In each umbrella sampling window, the value of θ was also recorded every 10^3 steps. Using the corresponding values of R, a quadratic relationship between R and θ was fitted and used to map the x-axis of the free-energy landscape from R to θ. The fitted relationship is $\theta = 0.015R^2 + 1.08R - 7.74$, with the coefficient of determination of the fit being 0.99. The data and the fit is shown in Figure S5.

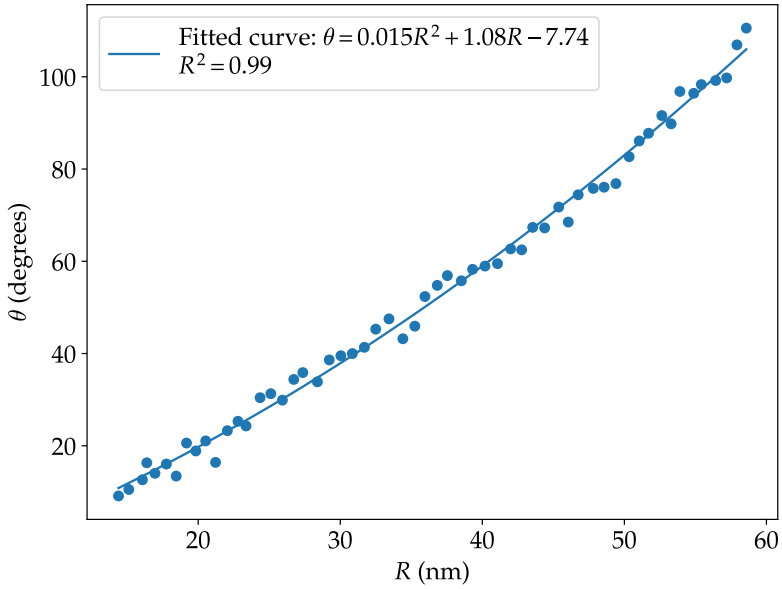

Figure S5: The mapping between the distance order parameter R and θ. The data points represent the average values of both for each umbrella sampling window and the line is a fit to this data.

C. Free-energy decomposition

We decomposed the free-energy landscape into four contributions associated with each of the four joints.

For joint 1, the origami design was modified from the original design by removing the nucleotides corresponding to the coupler and the crank blocks. The order parameter R_1 was defined as the distance between the centres of mass of two groups of nucleotides, which consist of the nucleotides at positions 147–161 on helices 10–19, and at positions 539–553 on helices 10–19, respectively. The nucleotide positions and helix indices are defined in the caDNAno design in Figure S6.

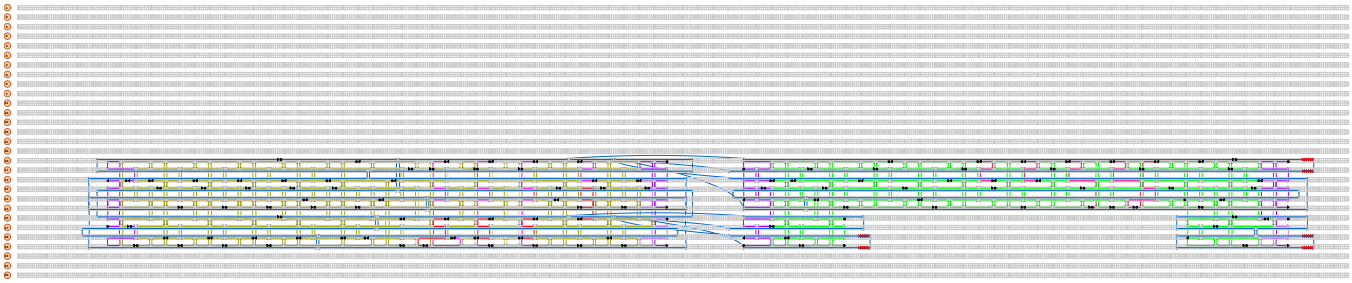

Figure S6: Full caDNAno design for the partial origami used for calculating the free-energy landscape of joint 1

For joint 2, the origami design was modified from the original design by removing the nucleotides corresponding to the coupler block. The order parameter R_2 was defined as the distance between the centres of mass of two groups of nucleotides, which consist of the nucleotides at positions 259–273 on helices 0–9, and at positions 231–245 on helices 10–19, respectively. The nucleotide positions and helix indices are defined in the caDNAno design in Figure S7.

For joint 3, the origami design was modified from the original design by removing the nucleotides corresponding to the crank block. The order parameter R_3 was defined as the distance between the centres of mass of two groups of nucleotides, which consist of the nucleotides at positions 413–427 on helices 0–9, and at positions 413–427 on helices 10–19, respectively. The nucleotide positions and helix indices are defined in the caDNAno design in Figure S8.

For joint 4, the origami design was modified from the original design by removing the nucleotides corresponding to the frame and compliant blocks. The order parameter R_4 was defined as the distance between the centres of mass of two groups of nucleotides, which consist of the nucleotides at positions 196–210 on helices 0–9, and at positions 539–553 on helices 0–9, respectively. The nucleotide positions and helix indices are defined in the caDNAno design in Figure S9. Part 1 of the landscape corresponds to the part where the joint points outwards and resembles the origami

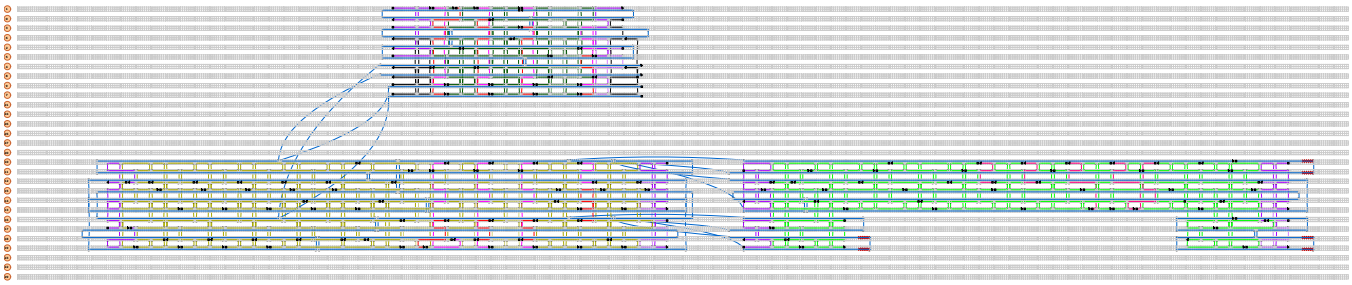

Figure S7: Full caDNAno design for the partial origami used for calculating the free-energy landscape of joint 2

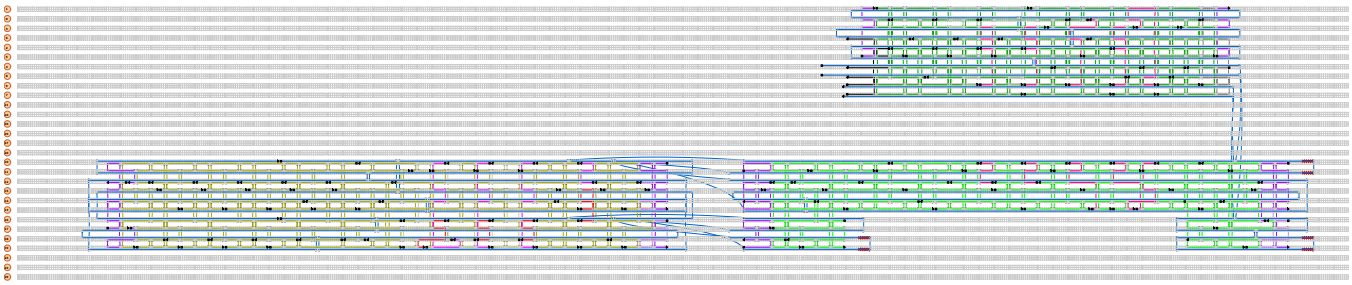

Figure S8: Full caDNAno design for the partial origami used for calculating the free-energy landscape of joint 3

in state S2, while part 2 corresponds to the part where the joint is folded inwards and resembles the origami in state S1. To calculate each sub-landscape we did not explicitly constrain the joint to point inwards or outwards. Instead, the portion of the landscape sampled was determined by the initial configurations, as for R_4 values corresponding to a bent joint, transitions between the two sub-landscapes are not feasible in the umbrella sampling simulations. For R_4 simulations corresponding to straight or stretched joints the two sets of simulations sample equivalent configurations.

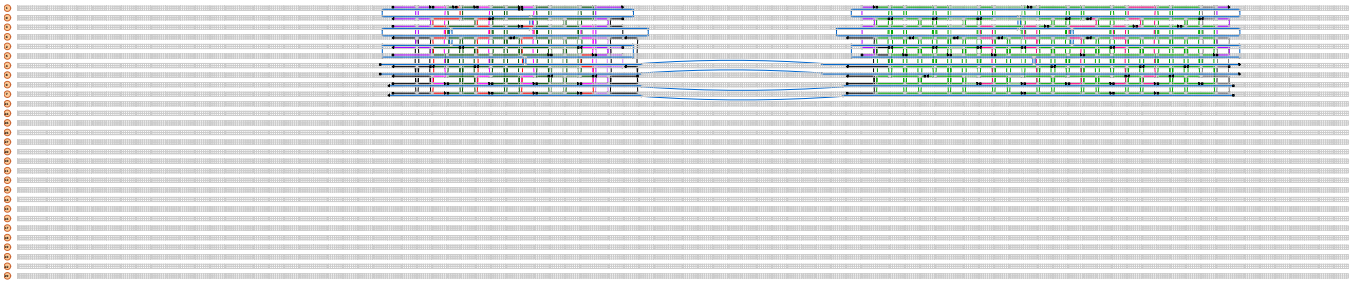

Figure S9: Full caDNAno design for the partial origami used for calculating the free-energy landscape of joint 4

For each joint, we performed a set of simulations where the order parameter was restrained with a harmonic potential in each sampling window. The sampling range of the order parameters was from 76–94 nm for joint 1, 12–60 nm for joint 2, 12–76 nm for joint 3, 68–86 nm for joint 4 (part 1), and 60–86 nm for joint 4 (part 2).

Umbrella sampling simulations were performed in a similar manner as those for the complete origami, with windows separated by 0.85 nm and the configuration in each window being restrained with a harmonic potential of stiffness $k = 11.42\,\mathrm{pN/nm}$. Each window was equilibrated for 10^6 steps before a production run of 10^7 steps. R_i was outputted every 10^3 steps, giving 10^4 data points for each window. Using the biased probability distributions of R_i in each window, we used WHAM [40,50] to calculate the unbiased free-energy landscape of the system as a function of R_i. The production runs were repeated three times with the landscapes obtained being similar.

To enable the transformation of the landscapes of the individual joints to be a function of θ, the values of R_i, the distance order parameters for the joints, were also measured in the umbrella sampling simulations of the complete origami. Figure S10 shows their variation with θ. The maxima in R_1 and R_4 occur when the crank and coupler blocks are collinear. The two parts of the joint 4 landscape correspond to different ranges of θ with a small region of overlap corresponding to when the crank and coupler blocks are approximately collinear. To generate a single landscape as a function of θ for joint 4, part 1 was used for $\theta > 53^\circ$ and part 2 for $\theta < 53^\circ$ and the two landscapes matched at that

point.

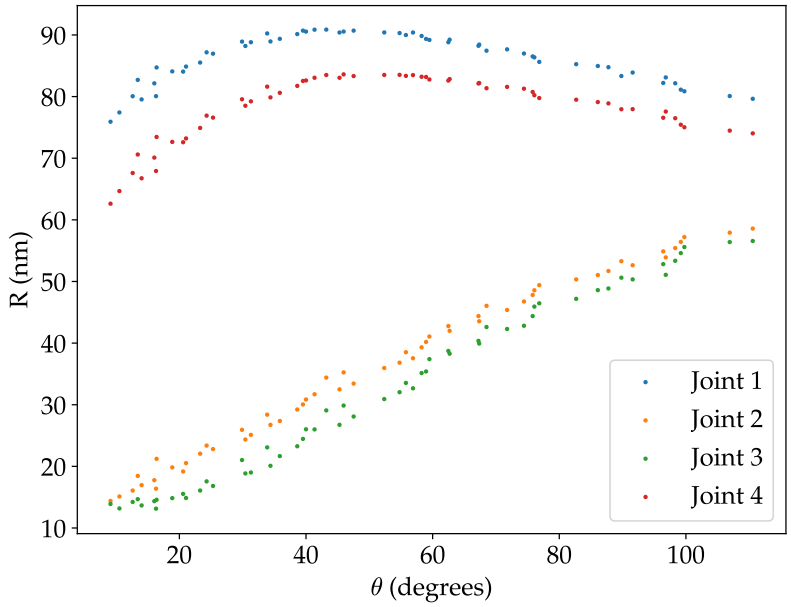

Figure S10: The mapping between the distance order parameters of the individual joints R_i and θ. The data points represent the average values for each umbrella sampling window of the complete origami.