

Supplementary Information

De novo design of DNA origami with a generative diffusion model

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Supplementary Notes

Supplementary Note 1. Denoising diffusion probabilistic model (DDPM) for DNA origami nanostructures

1. DNA structure representation

A DNA origami structure can be defined by its base-pair coordinates, represented as 3D central coordinates denoted by $\mathbf{x} = [\mathbf{x}_1, \dots, \mathbf{x}_N]^T \in \mathbb{R}^{N,3}$, where each $\mathbf{x}_n$ corresponds to the central coordinates of a base pair. We treat all base pairs within the DNA structure equally, akin to a point cloud, with the objective of capturing a distribution over DNA conformations and reconstructing it through DDPM as described in below.

2. Diffusion probabilistic model preliminaries

Diffusion models^{1,2}, a recent and promising addition to the deep generative model family, have garnered interest for their capacity to produce high-quality samples via a straightforward training regimen. These models encompass two fundamental processes: the forward process and the backward process. Drawing inspiration from the second law of thermodynamics, the forward process gradually introduces noise to the initial data across numerous diffusion steps. Eventually, after T steps, the data transitions into pure noise. This diffusion process can be depicted as a Markov chain:

$$q(\mathbf{x}_{1:T}) = \prod_{t=1}^T q(\mathbf{x}_t | \mathbf{x}_{t-1}) \quad (1)$$

where $\mathbf{x}_0$ represents the original data and $\mathbf{x}_t$ denotes the perturbed data at diffusion step t . The transition for each step is formulated as:

$$q(\mathbf{x}_t | \mathbf{x}_{t-1}) = \mathcal{N}(\mathbf{x}_t | \sqrt{\alpha_t} \mathbf{x}_{t-1}, \beta_t \mathbf{I}) \quad (2)$$

where β_t is the predetermined noise schedule, and $\alpha_t = 1 - \beta_t$. It's worth noting that, in the forward process, $\mathbf{x}_t$ for any given step t can be directly sampled using $\mathbf{x}_0$ using a closed-form expression denoted as $\bar{\alpha}_t = \prod_{i=1}^t \alpha_i$:

$$q(\mathbf{x}_t | \mathbf{x}_0) = \mathcal{N}(\mathbf{x}_t | \sqrt{\bar{\alpha}_t} \mathbf{x}_0, (1 - \bar{\alpha}_t) \mathbf{I}) \quad (3)$$

In the backward process, a natural approach is to reverse the steps employed in the forward process with the aims of reconstructing the original data from pure noise. To accomplish this objective, a denoising process is suggested to approximate the true backward transition $q(\mathbf{x}_{t-1} | \mathbf{x}_t)$ by learning a Gaussian model:

$$p_\theta(\mathbf{x}_{t-1} | \mathbf{x}_t) = \mathcal{N}(\mathbf{x}_{t-1} | \mu_\theta(\mathbf{x}_t, t), \Sigma_\theta(\mathbf{x}_t, t)) \quad (4)$$

Instead of forecasting $\mathbf{x}_{t-1}$ from $\mathbf{x}_t$ directly at each step t , DDPM suggests that predicting the injected noise yields superior outcomes, and the mean $\mu_\theta(\mathbf{x}_t, t)$ can be expressed as:

$$\mu_\theta(\mathbf{x}_t, t) = \frac{1}{\sqrt{\alpha_t}} \left(\mathbf{x}_t - \frac{\beta_t}{\sqrt{1 - \bar{\alpha}_t}} \epsilon_\theta(\mathbf{x}_t, t) \right) \quad (5)$$

$\epsilon_\theta(\mathbf{x}_t, t)$ is the denoising neural network utilizing a straightforward loss function:

$$\mathcal{L}(\theta) = \mathbb{E}_{t, \mathbf{x}_0, \epsilon} \left\| \epsilon - \epsilon_\theta(\mathbf{x}_t, t) \right\|_2^2 = \mathbb{E}_{t, \mathbf{x}_0, \epsilon} \left\| \epsilon - \epsilon_\theta \left(\sqrt{\bar{\alpha}_t} \mathbf{x}_0 + \sqrt{1 - \bar{\alpha}_t} \epsilon, t \right) \right\|_2^2 \quad (6)$$

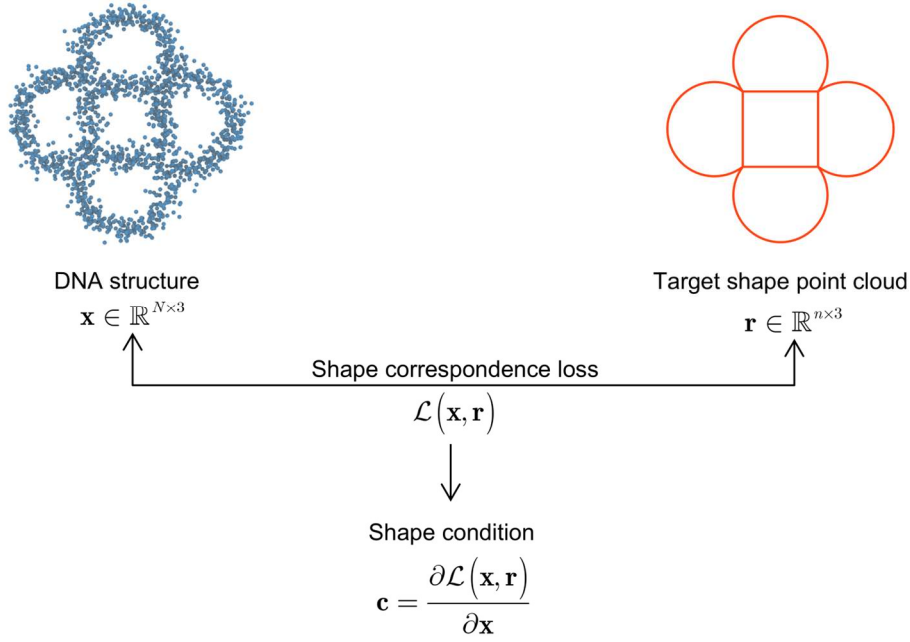
where $\epsilon \sim \mathcal{N}(\mathbf{0}, \mathbf{I})$. In practice, t in the loss function typically uniformly sampled from the range of diffusion steps. Regarding the covariance $\Sigma_\theta(\mathbf{x}_t, t)$, DDPM simplifies matters by setting it as untrained time-dependent constants, i.e., $\Sigma_\theta(\mathbf{x}_t, t) = \sigma_t^2 \mathbf{I}$. Where $\sigma_t^2 = ((1 - \bar{\alpha}_{t-1}) / (1 - \bar{\alpha}_t)) \beta_t$. Finally, $\mathbf{x}_{t-1}$ can be sampled from $p_\theta(\mathbf{x}_{t-1} | \mathbf{x}_t)$ as below:

$$\mathbf{x}_{t-1} = \frac{1}{\sqrt{\alpha_t}} \left(\mathbf{x}_t - \frac{\beta_t}{\sqrt{1 - \bar{\alpha}_t}} \epsilon_\theta(\mathbf{x}_t, t) \right) + \sigma_t \mathbf{z} \quad (7)$$

where $\mathbf{z} \sim \mathcal{N}(\mathbf{0}, \mathbf{I})$ is the Gaussian noise.

3. Conditional DDPM

We prioritize the development of conditional DDPM models to address objective of the inverse design problem. In the previous study³, a classifier-free diffusion model was introduced for conditional data generation by sampling from the conditional distribution $p(\mathbf{x}_t | c)$, where c denotes the label assigned to each data sample. In our approach, the model is instead conditioned on the target shape $\mathbf{r} \in \mathbb{R}^{n,3}$ as the conditioning variable.



Supplementary Figure 1. Shape correspondence condition. Molecular graphics were generated using UCSF Chimera25, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.

Given that base pairs within a DNA structure and a point cloud derived from a target shape are distinct entities, we adopt an optimal transport-based conditioning strategy⁴. Specifically, we use the Wasserstein distance to infer cross-domain correspondences between objects from the internal geometric relations within each object. This relational property makes it applicable even to unaligned objects with different structures and scales^{5,6}.

The optimal transport loss in the inner sampling loop was given by

$$\mathcal{L}(\mathbf{x}, \mathbf{r}) = \sum_{i,j} K_{ij}^W(\mathbf{x}, \mathbf{r}) \|\mathbf{x}_i - \mathbf{r}_j\| \quad (8)$$

where Wasserstein optimal couplings K_{ij}^W is computed through the Sinkhorn algorithm⁴. As a result, the loss remains both computationally efficient and differentiable, making it suitable for direct use during sampling.

$$\mathbf{c} = \frac{\partial \mathcal{L}(\mathbf{x}, \mathbf{r})}{\partial \mathbf{x}} \quad (9)$$

We refer to the gradient condition information from the shape correspondence loss between DNA structure $\mathbf{x}$ and target shape $\mathbf{r}$ as shape guidance. This condition information will be integrated into each base-pair feature of DNA structure, which yields the diffusion process as follows.

$$q(\mathbf{x}_{1:T}) = \prod_{t=1}^T q(\mathbf{x}_t | \mathbf{x}_{t-1}, \mathbf{c}_{t-1}) \quad (10)$$

where $\mathbf{c}_{t-1} = \partial \mathcal{L}(\mathbf{x}_{t-1}, \mathbf{r}) / \partial \mathbf{x}_{t-1}$

The denoising neural network become $\epsilon_{\theta}(\mathbf{x}_t, t, \mathbf{c}_t)$ utilizing a straightforward loss function

$$\mathcal{L}(\theta) = \mathbb{E}_{t, \mathbf{x}_0, \mathbf{r}, \epsilon} \left\| \epsilon - \epsilon_{\theta}(\mathbf{x}_t, t, \mathbf{c}_t) \right\|_2^2 = \mathbb{E}_{t, \mathbf{x}_0, \mathbf{r}, \epsilon} \left\| \epsilon - \epsilon_{\theta}(\sqrt{\bar{\alpha}_t} \mathbf{x}_0 + \sqrt{1 - \bar{\alpha}_t}, t, \mathbf{c}_t) \right\|_2^2 \quad (11)$$

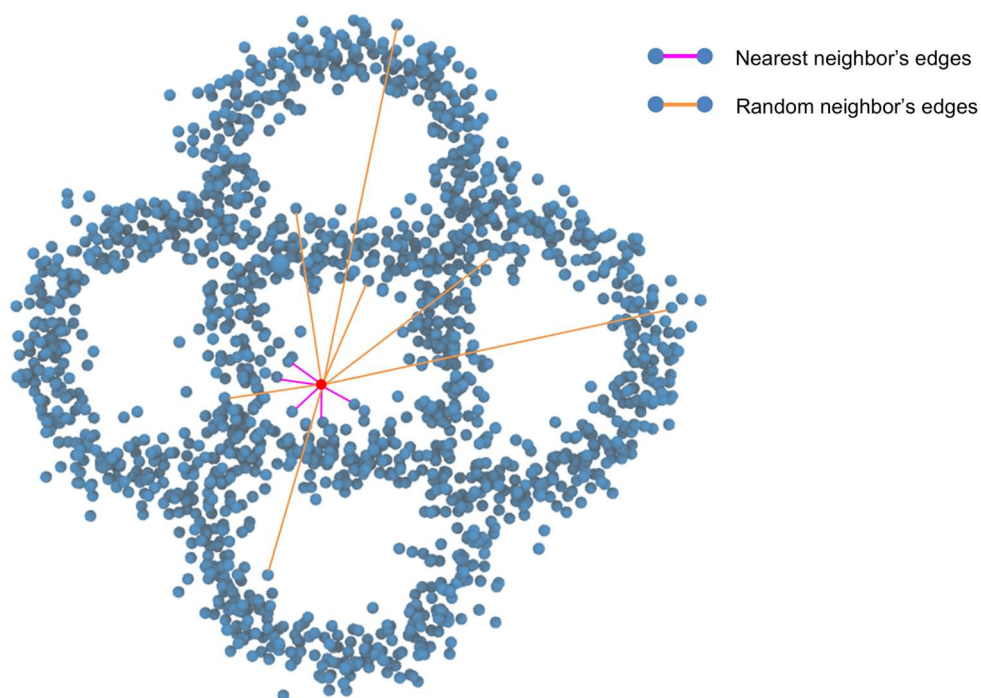
and the resulting data sampling process is given below.

$$\mathbf{x}_{t-1} = \frac{1}{\sqrt{\alpha_t}} \left(\mathbf{x}_t - \frac{\beta_t}{\sqrt{1 - \bar{\alpha}_t}} \epsilon_{\theta}(\mathbf{x}_t, t, \mathbf{c}_t) \right) + \sigma_t \mathbf{z} \quad (12)$$

Supplementary Note 2. Denoiser architecture

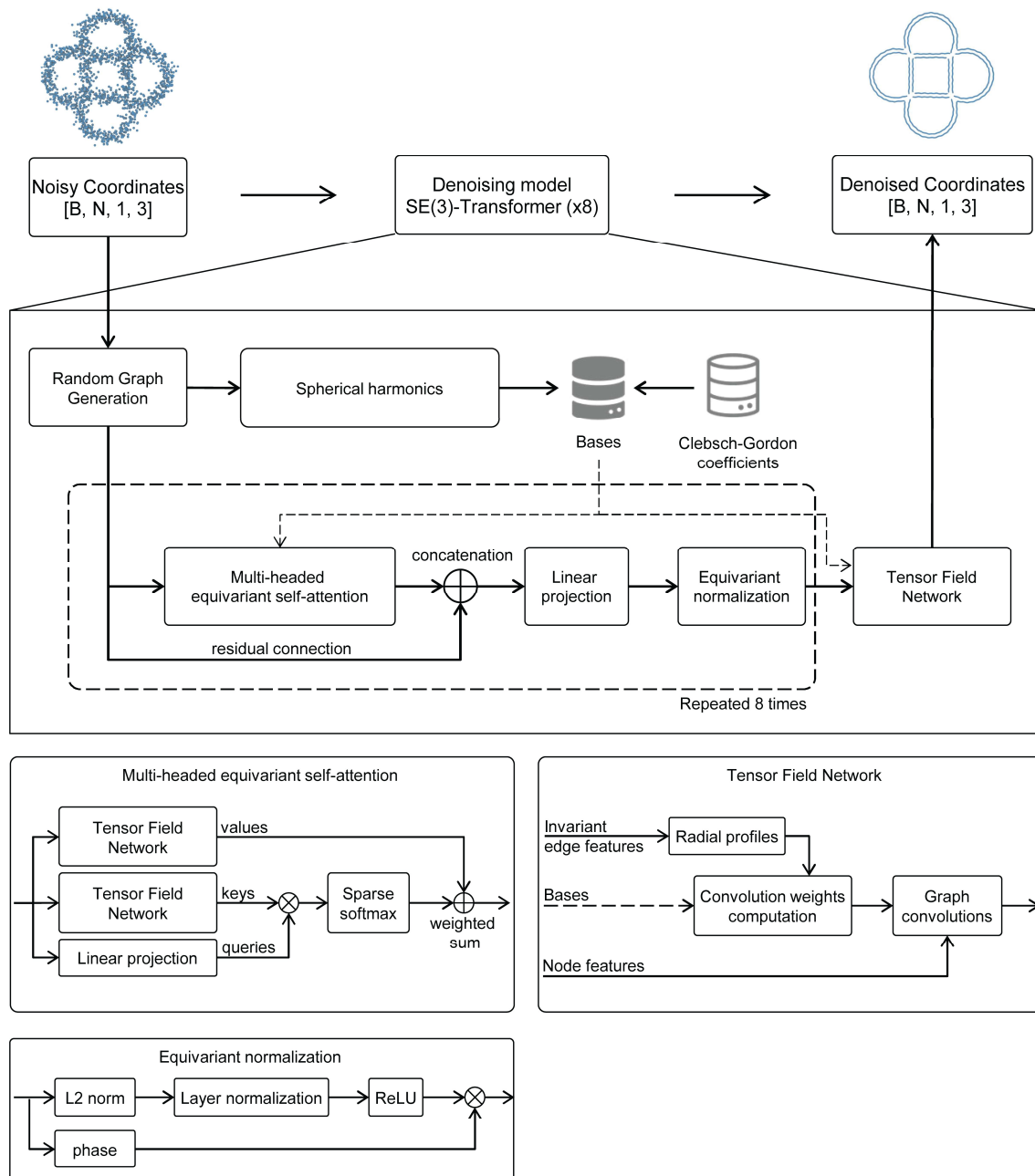
1. Scalable graph Transformer using random graph neural networks

We construct scalable graph Transformer models for DNA base-pair systems using randomly sampled graphs that capture both short- and long-range interactions. Given a DNA structure represented as a point set $\mathbf{x} \in \mathbb{R}^{N \times 3}$, we define the corresponding graph $\mathcal{G}(\mathbf{x}) = (\mathcal{V}, \mathcal{E}(\mathbf{x}))$ with $|\mathcal{V}| = N$, where $\mathcal{V}$ and $\mathcal{E}(\mathbf{x})$ denote the node and edge sets, respectively. Here, the edge set $\mathcal{E}(\mathbf{x})$ is stochastically determined from the input structure $\mathbf{x}$. To randomly sample edges without duplication, we adopt a distance-based propensity function and perform weighted selection using Gumbel Top-k sampling⁷ (Supplementary Fig. 2). We build a hybrid graph in which each node is connected to its 25 nearest neighbours and 15 additional edges sampled according to an inverse cubic propensity function. As a result, both short- and long-range interactions are incorporated into the graph at appropriate rates.



Supplementary Figure 2. Random graph generation. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.

2. Tailoring SE(3)-Transformer for denoising DNA coordinates

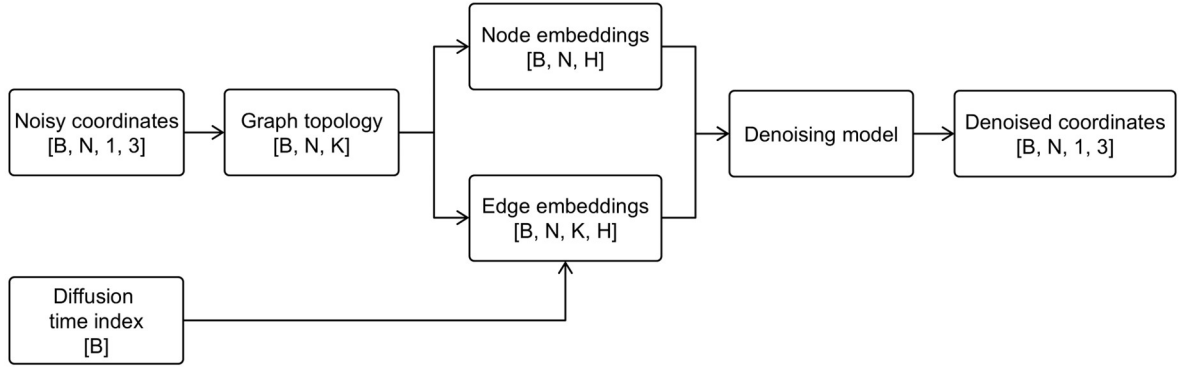


Supplementary Figure 3. SE(3)-Transformer denoiser. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.

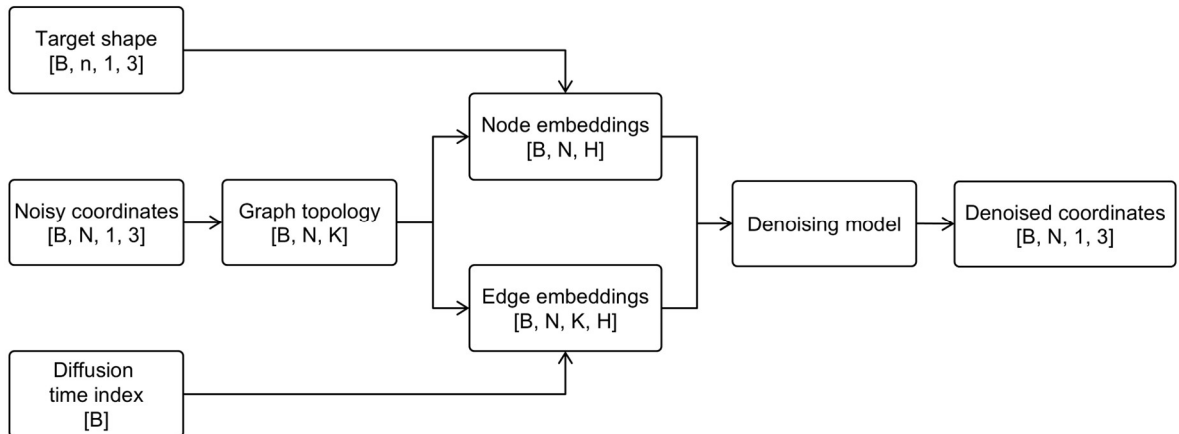
Implementation of DDPM requires choosing an architecture for the neural network ϵ_θ introduced in Supplementary Note 1. In this section we describe generative diffusion model for DNA origami,

which corresponds to the choice of ϵ_θ as a translation and rotation equivariant graph neural network tailored to modelling DNA structure backbones. Our denoising model include 8 SE(3)-Transformer layers

We present our adaptation of the SE(3)-Transformer, customized for DNA origami architecture and DDPM by selecting specific edge and node characteristics. To model base-pair interactions, we depict the structure using a random graph, as shown in Supplementary Note 3. Every node within the graph is labelled with an index, denoted by $n = 1, \dots, N$; representing a base pair. We associate each node with coordinates $\mathbf{x}_n \in \mathbb{R}^3$. For each pair of nodes n, n' , which were generated by a random graph function, we define an edge and associate it with edge features $a_{nn'} \in \mathbb{R}^D$



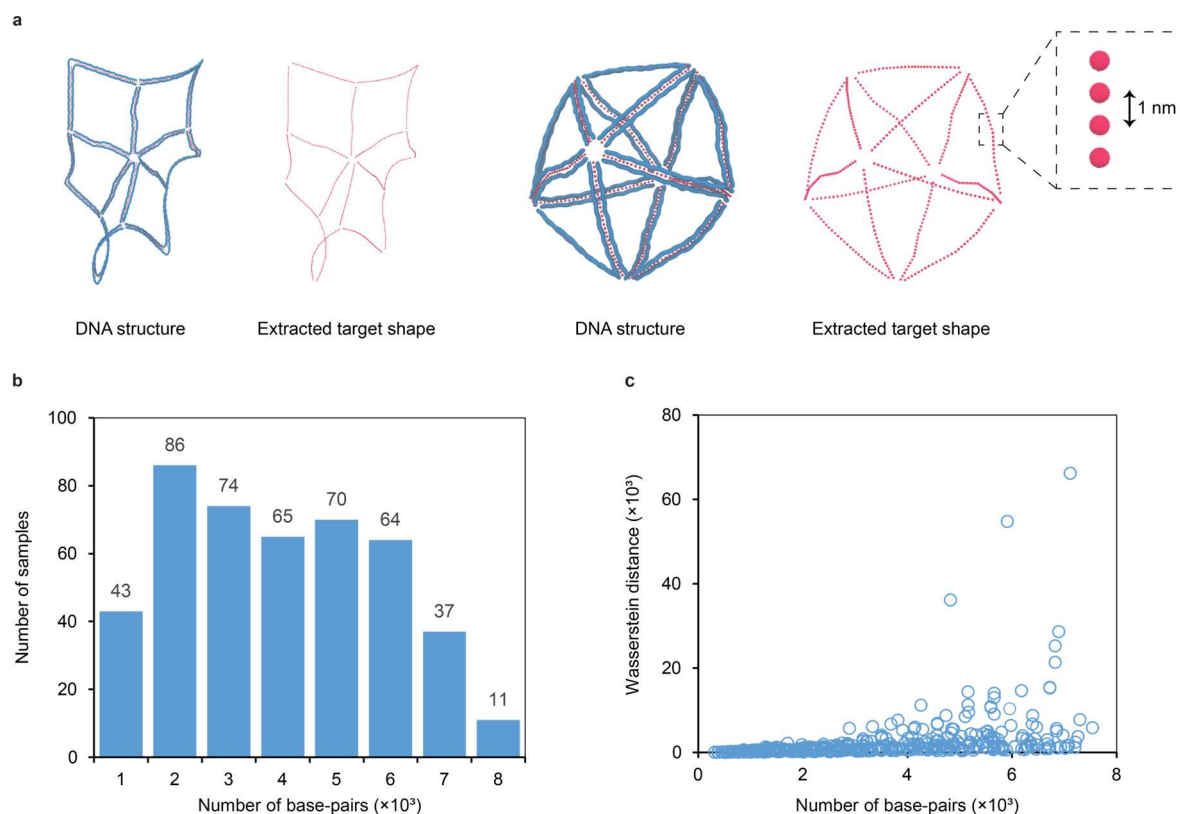
Supplementary Figure 4. Unconditional denoiser.



Supplementary Figure 5. Conditional denoiser.

Supplementary Note 3. Training

Training dataset. Our training dataset comprises 450 wireframe DNA structures sourced from ATHENA⁸. Each design is accompanied by two key pieces of information: the structure configuration in equilibrium and the corresponding shape pattern. To obtain the configurations in equilibrium, we employed the multiscale computational model, SNUPI^{9–11}, which can provide the three-dimensional shape of DNA origami structures quickly at near-atomic resolution. From the structure configuration, the shape patterns are extracted from central line of each substructure, represented as 3D point clouds. Within each substructure, pattern points partition the central line into segments of approximately equal length, around 1 nm each. The number of base pairs of designs ranges from around 300 to 7,000.



Supplementary Figure 6. Training data generation. **a**, DNA structure training data set generation. **b**, Training data set distribution analysis. **c**, Training data set shape correspondence analysis in comparison with random point cloud. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.

Algorithm 1 Training algorithm of generative diffusion model for DNA origami**Input:** Training dataset, The probability of unconditional training p_u **Output:** The learned reverse model ϵ_θ 1. **Repeat**2. Sample $\mathbf{x}_0, \mathbf{r} \sim q(\mathbf{x}_0, \mathbf{r})$ 3. Sample $t \sim \text{Uniform}(\{1, \dots, T\})$ 4. Sample $\epsilon_t \sim \mathcal{N}(0, \mathbf{I})$ 5. Compute shape correspondence loss $\mathcal{L}(\mathbf{x}_t, \mathbf{r})$ using equation (8)6. $\mathbf{c}_t = \begin{cases} \partial \mathcal{L}(\mathbf{x}_t, \mathbf{r}) / \partial \mathbf{x}_t & \text{with probability } 1 - p_u \\ \emptyset & \text{with probability } p_u \end{cases}$

Randomly discard conditioning information to train unconditionally

7. Take a step of gradient descent on θ with the following gradient

$$\nabla_\theta \left\| \epsilon_t - \epsilon_\theta \left(\sqrt{\bar{\alpha}_t} \mathbf{x}_0 + \sqrt{1 - \bar{\alpha}_t} \epsilon_t, t, \mathbf{c}_t \right) \right\| \text{ using equation (11)}$$

8. **Until** converged

Optimization. We trained generative diffusion model for DNA origami on two Nvidia A100 80GB using the Adam optimizer¹² with hyperparameters $lr = 10^{-4}$, $\beta_1 = 0.9$, and $\beta_2 = 0.999$. We trained for 300,000 steps using batch size 2 for approximately 2 weeks. We implemented all models in PyTorch and did not perform hyperparameter tuning.

Supplementary Note 4. Sampling

With a learned reverse ϵ_θ , the DNA structure $\mathbf{x}_0$ can be generated from reverse diffusion process.

Algorithm 1 Unconditional sampling algorithm of generative diffusion model for DNA origami

Input: The learned reverse model ϵ_θ
Output: The base-pair coordinates of DNA structure $\mathbf{x}$

1. Sample number of base pairs for the generated DNA structure
2. Sample $\mathbf{x}_T \sim p(\mathbf{x}_T) = \mathcal{N}(0, \mathbf{I})$
2. **for** $t = T, T - 1, \dots, 1$ **do**
3. Shift $\mathbf{x}_t$ to zero CoM
4. Compute $\mu_\theta(\mathbf{x}_t, t)$ from $\epsilon_\theta(\mathbf{x}_t, t)$ using equation (5)
5. Sample $\mathbf{x}_{t-1} \sim \mathcal{N}(\mathbf{x}_{t-1}; \mu_\theta(\mathbf{x}_t, t), \sigma_t^2 \mathbf{I})$
6. **end for**
7. **return** $\mathbf{x}_0$ as $\mathbf{x}$

Algorithm 2 Conditional sampling algorithm of generative diffusion model for DNA origami

Input: The learned reverse model ϵ_θ , the target shape pattern $\mathbf{r}$
Output: The base-pair coordinates of the DNA structure $\mathbf{x}$

1. Estimate the number of base pairs N for the generated DNA structure corresponding to the shape pattern $\mathbf{r}$
2. Sample $\mathbf{x}_T \sim p(\mathbf{x}_T) = \mathcal{N}(0, \mathbf{I})$
3. **for** $t = T, T - 1, \dots, 1$ **do**
4. Shift $\mathbf{x}_t$ to zero CoM
5. Compute the shape condition $\mathbf{c}_t = \nabla_{\mathbf{x}_t} \mathcal{L}(\mathbf{x}_t, \mathbf{r})$ as described in Supplementary Note 2
6. Compute $\mu_\theta(\mathbf{x}_t, \mathbf{c}_t, t)$ from $\epsilon_\theta(\mathbf{x}_t, \mathbf{c}_t, t)$ using equation (5)
7. Sample $\mathbf{x}_{t-1} \sim \mathcal{N}(\mathbf{x}_{t-1}; \mu_\theta(\mathbf{x}_t, \mathbf{c}_t, t), \sigma_t^2 \mathbf{I})$
8. **end for**
9. **return** $\mathbf{x}_0$ as $\mathbf{x}$

Estimate the number of base pairs N for generated DNA structure corresponding to shape pattern

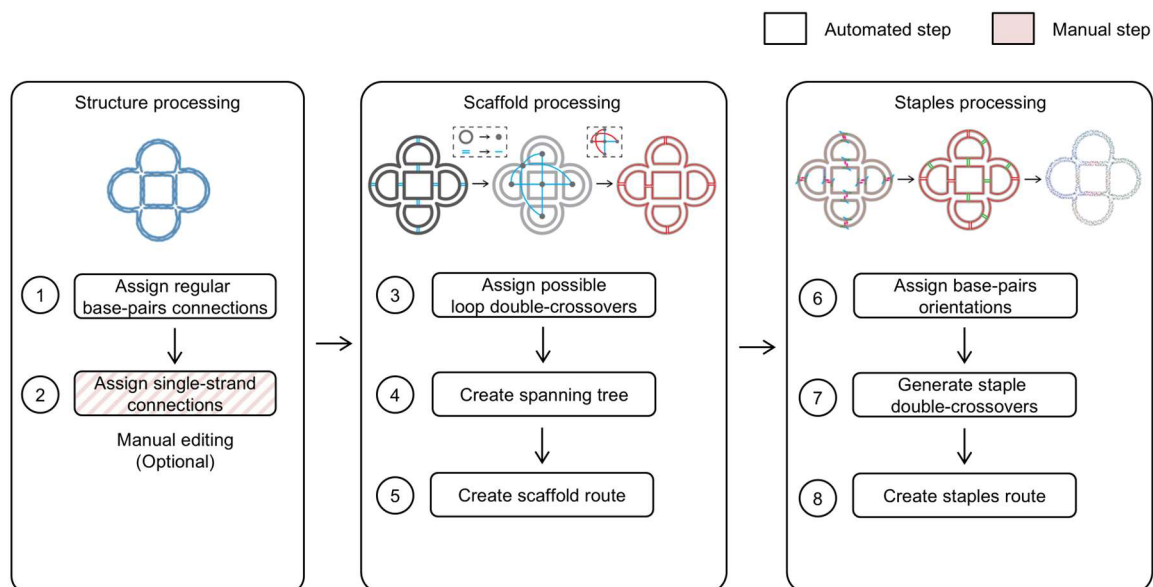
We first approximate the scaffold length equal to the total pattern length, and the number of paired nucleotides on the scaffold will be estimated as follows:

$$N \approx \frac{L}{0.34} \quad (13)$$

where L represent the total length of the target pattern.

Supplementary Note 5. Routing

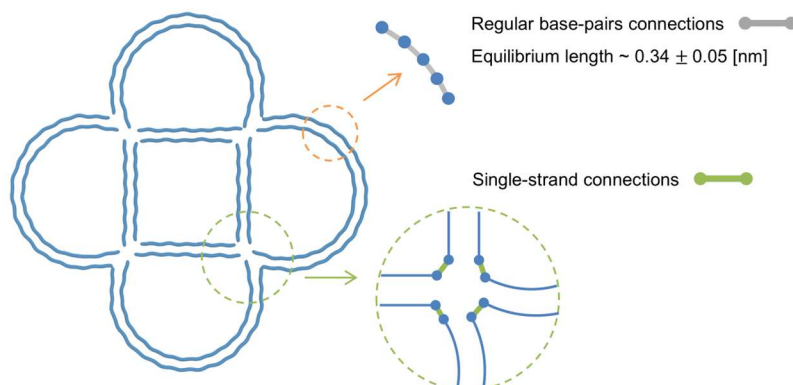
1. Routing methodology



Supplementary Figure 7. Routing pipeline overview. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.

We started routing pipeline with generated DNA structure from generative diffusion model for DNA origami.

Structure processing



Supplementary Figure 8. Staple routes processing. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.

Step 1. We create regular base-pair steps within helix by radius graph generation and ensuring a consistent base-pair bond length within the range 0.34 ± 0.05 [nm]. Additionally, we assign a distinct helix index to every base pair within the structure, enhancing its structural clarity and organization.

Step 2. The single-strand edges are created between two helices to facilitate the formation of closed loops. It is essential that all helices are interconnected continuously to form a singular closed loop. This process is automated by default, but manual editing by the user is also supported.

Scaffold route processing

Inspired by automated design programs^{8,13–16}, we have devised a similar algorithm aimed at generating scaffold routes across the entire structure. Interested readers are encouraged to explore the referenced works for further details

Step 3. The next step is to generate the loop double-crossovers as an intermediate step in the scaffold routing process. These double-crossovers are positioned between adjacent helices, typically near their centers. Each pair of loops can be linked by a single double-crossover.

Step 4. The provided structure is simplified into a dual graph, where nodes are closed loops and edges symbolize the loop double-crossovers.

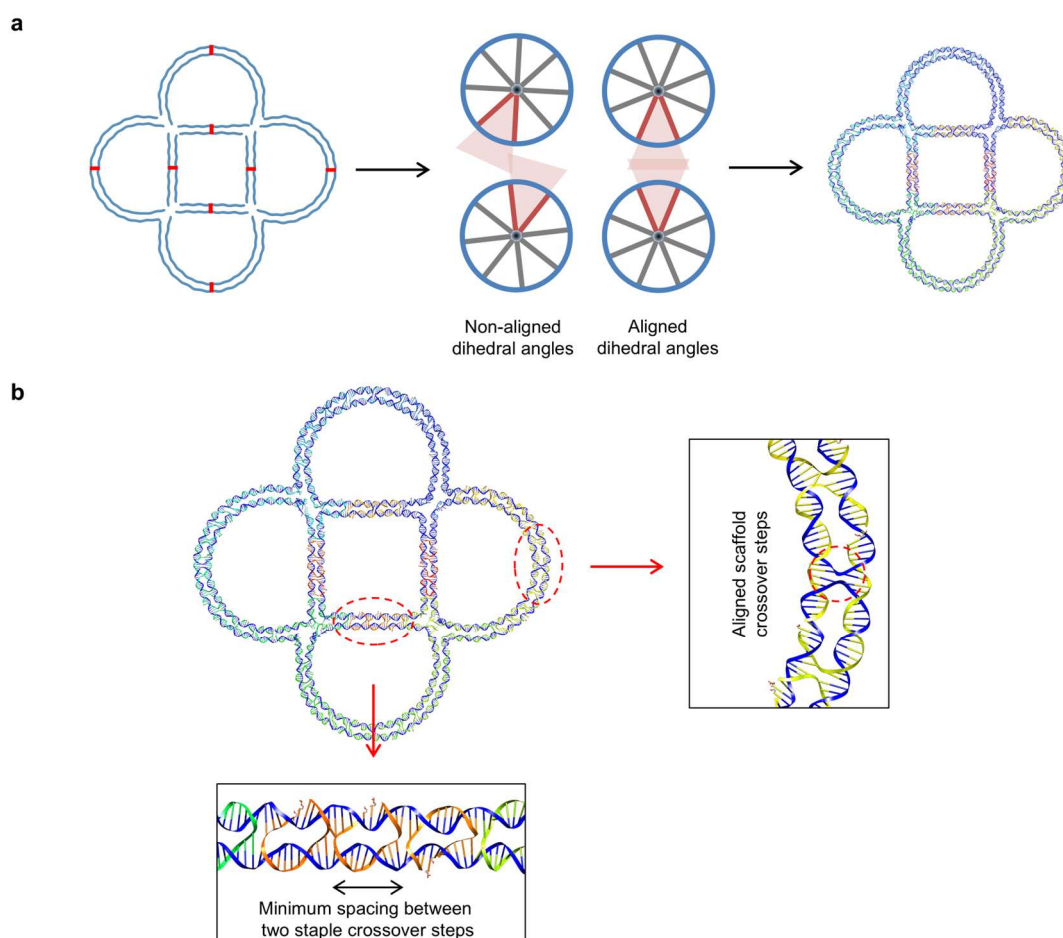
Step 5. The scaffold routing problem can be solved by computing a spanning tree of the dual graph of the loop-crossover structure. This process dictates the appropriate quantity and placement of all scaffold double-crossovers.

Staple routes processing

Step 6. To generate staple routes, each base pair is assigned a specific orientation following the 3DNA convention¹⁷. Initially, base pairs of loop double-crossovers are oriented with aligned dihedral angles to facilitate optimal double crossovers. Subsequently, the remaining base pairs within the same helices are assigned suitable orientations to establish helical structures resembling B-form DNA.

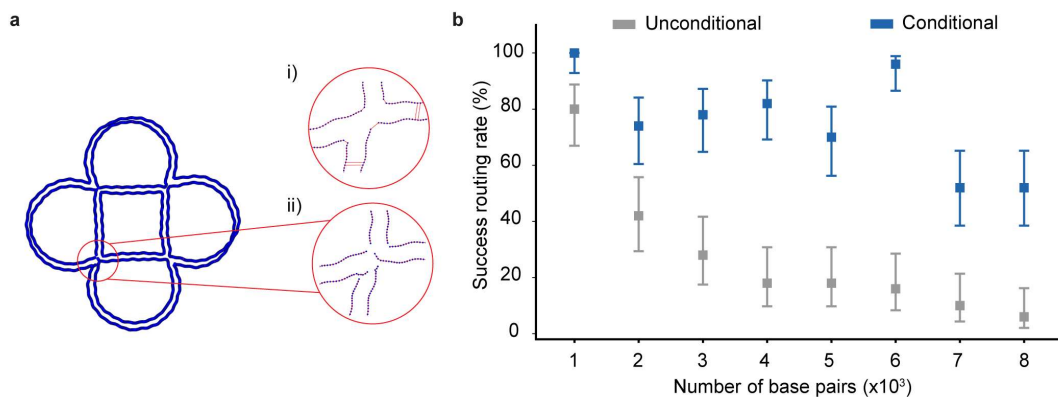
Step 7. Based on the assigned orientations of the base pairs, we derive the coordinates of the nucleotides on staples for the entire structure. The location of the staple double-crossovers was optimized in the structures to minimize the crossover bond length.

Step 8. Ultimately, the initial staple routes are extracted from the structure and automatically partitioned into shorter segments ranging from 20 to 60 nucleotides in length, with an average segment length of approximately 40 nucleotides.



Supplementary Figure 9. Staple routes processing. **a**, The process of aligning dihedral angles to optimize the structure. **b**, The arrangement of scaffold and staple crossover steps for staple sequence design. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.

2. Successful routing rate analysis



Supplementary Figure 10. Successful routing rate of DNA origami structures generated by generative diffusion model. **a**, Example of i) successful routing and ii) failed routing in automatic defining single-strand connections, **b**, successful routing rate of DNA structures, each point represents the success routing rate calculated from $n = 50$ independent sampling runs.

It should be noted that DNA origami datasets are inherently complex due to diverse folding patterns and significant variation in size, shape, and topology, and these factors pose challenges for generalizing this process. While the unconditional DDPM that learns to generate structures without external guidance can generate wireframe designs, it often struggles with large structures, frequently resulting in invalid strand routings. This limitation comes from the difficulty of learning a universal generative distribution from a relatively small and structurally simple dataset. However, a conditional diffusion approach, in which the generation process is guided by an explicit target shape or geometry, can improve the model performance. By narrowing the design space around a defined structural objective, this conditioning significantly enhances the likelihood of producing realistic and constructible DNA origami structures.

To evaluate the impact of target shape constraints on the DNA structure generation process via reverse diffusion, we synthesized 50 DNA structures with varying sizes (1,000 to 8,000 base pairs) using both unconditional and conditional generative diffusion model for DNA origami. Success or failure is typically determined during Steps 2 and 3 of the routing phase. The success of routing depends on whether the base-pair coordinate point cloud at the junction is correctly positioned (Supplementary Fig. 10a). Specifically, if the base-pair connections along certain edges are too long and extend beyond the junction, the system may fail to generate single-stranded connections automatically. If a single-

stranded connection fails at a junction in Step 2, the loop double crossover cannot form in Step 3, preventing all subsequent steps from proceeding. The successful routing rate, which measures the ability to generate valid DNA structures that can be fully routed into pseudo-atomic resolution DNA origami (Supplementary Fig. 10b).

In the unconditional case (gray bars), where no structural constraints were applied, the generated wireframe structures exhibited limited resemblance to the DNA structures in the training set (Supplementary Fig. 22). The success routing rate progressively decreased as the structure size increased, failing entirely for structures beyond 5,000 base pairs. This limitation is attributed to the inability of the small and simple training dataset to capture the full diversity of DNA origami designs, particularly for common structures exceeding 7,000 base pairs. Consequently, unconditional model struggles to generalize, even within specific structure types such as DX wireframe assemblies.

In contrast, conditional model (blue bars) significantly improves structural fidelity by enforcing target shape constraints during generation. The resulting DNA structures exhibit high correspondence to their intended target shapes, enabling successful routing into pseudo-atomic resolution DNA origami. For commonly designed DNA origami structures, the success routing rate remains above 50%, demonstrating the efficacy of shape-conditioned diffusion in guiding structure generation. The target shapes utilized in this experiment are detailed in Supplementary Table 2-3.

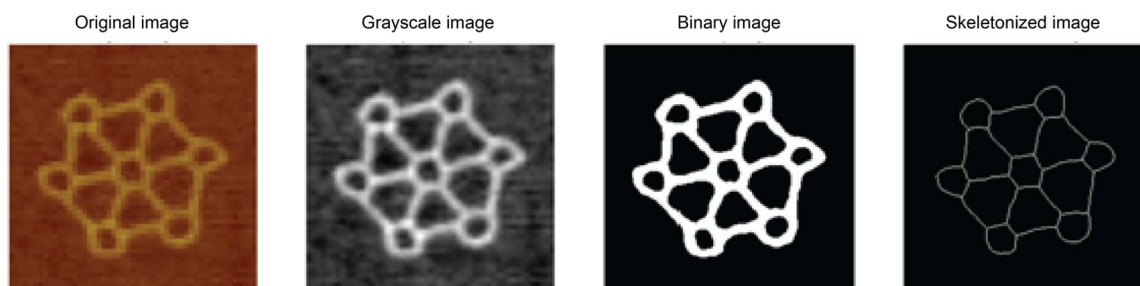
For each experimental setting, the success rate was calculated as the proportion of successful structures among $n = 50$ sampled structures. The corresponding 95% confidence intervals (CIs) were estimated using the Wilson score interval for a binomial proportion. Specifically, if k denotes the number of successful structures and $\hat{p} = k / n$ is the observed success proportion, the lower and upper bounds of the 95% CI were computed as

$$\frac{\hat{p} + \frac{z^2}{2n} \pm z \sqrt{\frac{\hat{p}(1 - \hat{p})}{n} + \frac{z^2}{4n^2}}}{1 + \frac{z^2}{n}}$$

Where $z = 1.96$ for the 95% confidence level. Wilson intervals were used because they provide more reliable coverage than the standard normal approximation, particularly for moderate sample sizes and proportions close to 0 or 1.

Supplementary Note 6. AFM image analysis

1. Contour line extraction



Supplementary Figure 11. AFM image processing pipeline for structural analysis.

The atomic force microscopy (AFM) image processing workflow begins with the acquisition of the original AFM image in .tiff format (left). To facilitate structural analysis, the image is first converted into a grayscale representation, where pixel intensities correspond to height variations in the AFM data. This transformation enhances contrast and reduces data complexity while preserving essential structural details.

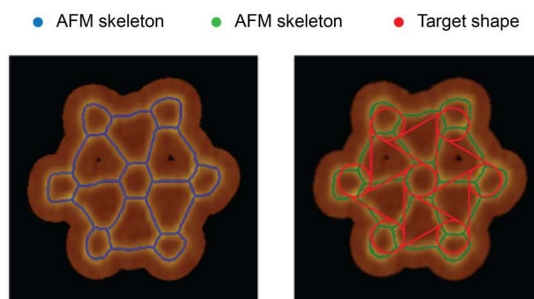
Next, a thresholding technique is applied to generate a binary image, segmenting the structure from the background by assigning pixel values of either 0 or 1. This binarization step effectively isolates the DNA nanostructure, removing background noise and improving feature extraction.

Finally, the binary image undergoes skeletonization, reducing the structure to its central lines while maintaining its topological characteristics. This step enables precise quantification of connectivity and geometric properties, facilitating further structural analysis. The skeletonized representation provides a simplified yet informative visualization of the DNA nanostructure, aiding in the assessment of its fidelity and integrity.

2. RMSD analysis

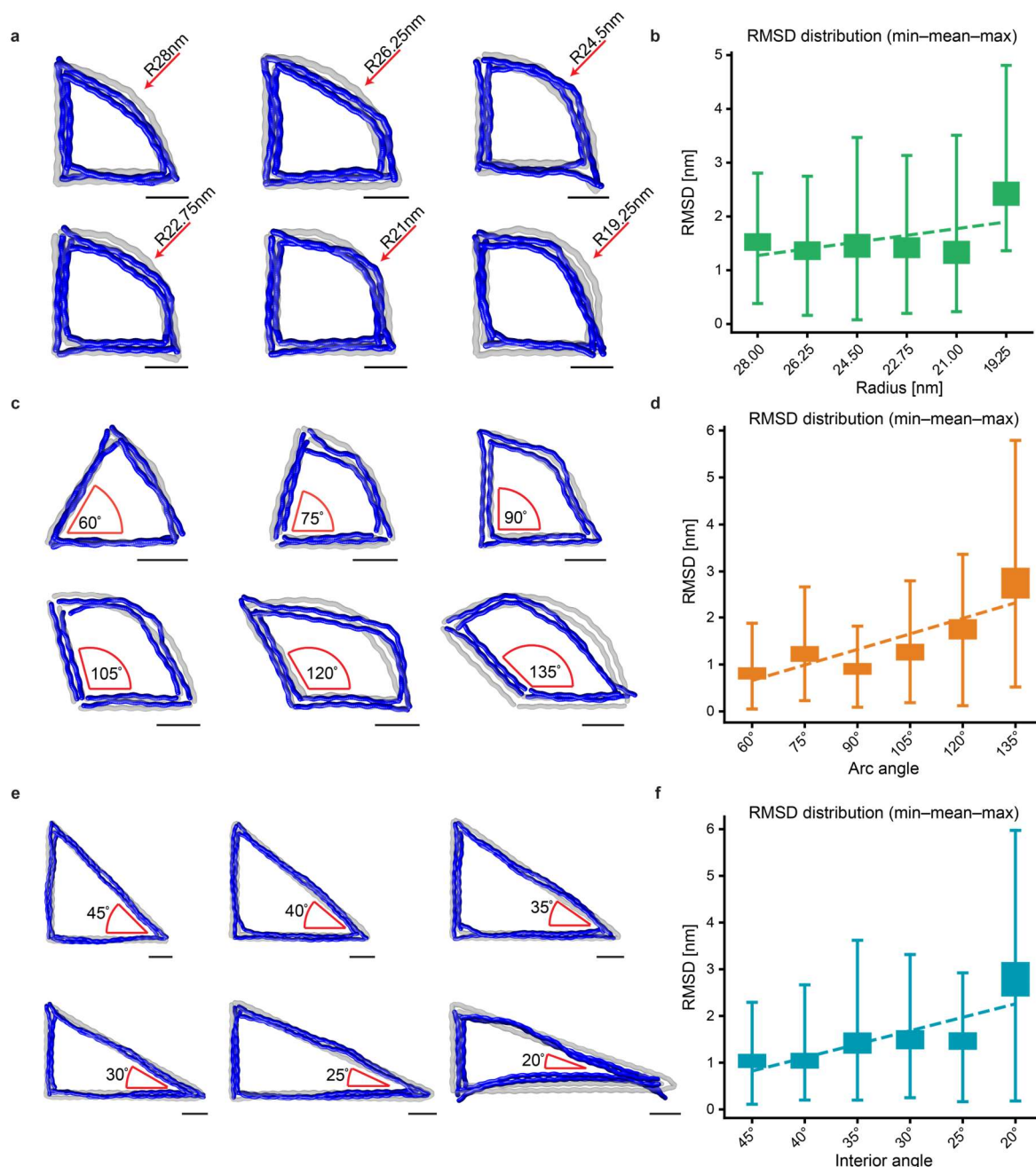
The extracted skeleton from the atomic force microscopy (AFM) image (left) is converted into a three-dimensional (3D) point cloud representation. This point cloud is then aligned with the corresponding target shape using the iterative closest point (ICP) algorithm, which optimizes the spatial transformation between the AFM-derived structure and the designed target (right).

Following alignment, the root-mean-square deviation (RMSD) is computed between the AFM skeleton point cloud and the target shape point cloud, providing a quantitative measure of structural fidelity. The aligned AFM image further illustrates the correspondence between the experimental and designed structures, enabling assessment of nanoscale deviations and deformations.



Supplementary Figure 12. Alignment of AFM-extracted skeleton with target shape.

Supplementary Note 7. Design recommendation for users.



Supplementary Figure 13. Effect of radius and length of curved edges and interior angles on design quality (RMSD). **a**, Design and predicted equilibrium overlays across curvature radii ($R = 28-19.25$ nm). **b**, RMSD dependence on curvature radius. **c**, Design and predicted equilibrium overlays across arc angles ($60^{\circ}-135^{\circ}$). **d**, RMSD dependence on arc length. **e**, Design and predicted equilibrium overlays across interior angles ($45^{\circ}-20^{\circ}$). **f**, RMSD dependence on interior angle. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.

Through simulations and experiments, we identified increased local structural fluctuations and geometric deviations, especially in designs with edges that are excessively long relative to the Euclidean distance between connected vertices and with abrupt angular turns at junctions. These deviations are not attributed to limitations of the generative model, but instead reflect intrinsic physical properties of 2HB-edge DNA wireframe nanostructures. Accordingly, this supplementary note provides practical design recommendations to improve structural stability and shape fidelity within our framework.

Edges that are excessively long relative to the Euclidean distance between vertices reduce shape stability during imaging of the nanostructures. Because such long edges necessarily involve increased curvature, both edge length and curvature may be expected to influence structural stability (Supplementary Fig. 13a–b). To decouple the effects of edge curvature and edge length, we fixed the curvature radius and increased only the arc angle (Supplementary Fig. 13c–d). In these configurations, the edge length increased without altering curvature, and the RMSD increased with edge length, indicating that excessive edge length contributes to geometric deviation. In contrast, our empirical observations suggest that high curvature itself is reliably generated by our framework. For example, the outer rings of the hexa-chiral structure (Supplementary Fig. 35) exhibited high fidelity to the target geometry despite pronounced curvature.

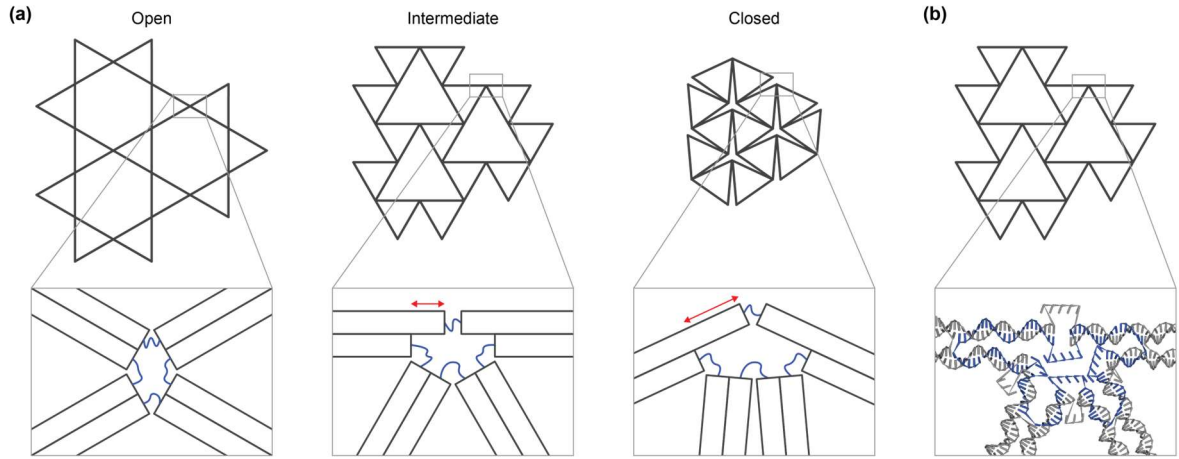
Additionally, distortion at abrupt angular features can be primarily attributed to electrostatic repulsion between closely positioned DNA edges combined with the mechanical compliance of flexible junctions. Consistent with this interpretation, RMSD analysis of triangular structures with systematically varied vertex angles revealed the highest mean RMSD for triangles with a 20° vertex angle (Supplementary Fig. 13e–f). Such sharp angular turns destabilize local junction regions, resulting in reduced local fidelity to the target geometry.

Based on these analyses, we recommend the following design strategies:

- (1) avoid excessively long curved edges relative to the shortest distance between vertices by introducing additional edges to suppress local structural fluctuations;
- (2) avoid overly sharp corners when possible, or replace them with finite-radius rounding (fillets);
- (3) when sharp turns are required, introduce local reinforcement or constraints, such as increased local connectivity and short supporting edges; and

(4) use SNUPI simulation outputs as a feasibility check to guide iterative refinement of physically challenging regions.

Supplementary Note 8. Intermediate-state design for transformable structures



Supplementary Figure 14. Junction design in the rotating triangle auxetic structure. a, Schematic illustration of cylinder models of open, intermediate, and closed state. **b,** Detailed view of an actual junction in the intermediate state showing unpaired scaffold and staple strands.

Our framework generates continuous duplex structures at junctions by default (Supplementary Fig. 14). As a result, the cylindrical duplex length at each junction is determined by the relative positioning of adjacent edges, while the ssDNA length is computed from the distance between the 5' and 3' ends of the scaffold and staple strands at the end of each duplex. Since our framework strictly follows the input design, geometric irregularities at the junctions naturally arise, resulting in differences in optimal duplex lengths and corresponding ssDNA lengths between open and closed states.

To minimize the energy costs associated with conformational transitions, we intentionally designed certain transformable structures in an intermediate state. Given that dsDNA resists compression and tends to bend or buckle under axial load¹⁸, we model it as effectively incompressible. Consequently, the majority of the energy cost during transformation is attributed to the elongation of connecting ssDNA segments. Assuming that ssDNA behaves as a Worm-Like Chain (WLC) polymer, the energy cost of its deformation is estimated based on the elongation of these segments.

The force–extension relationship of the WLC model is given by^{19,20}:

$$F_{WLC} = \frac{k_B T}{L_p} \left[\frac{1}{4 \left(1 - x / L_c\right)^2} - \frac{1}{4} + \frac{x}{L_c} \right] \quad (14)$$

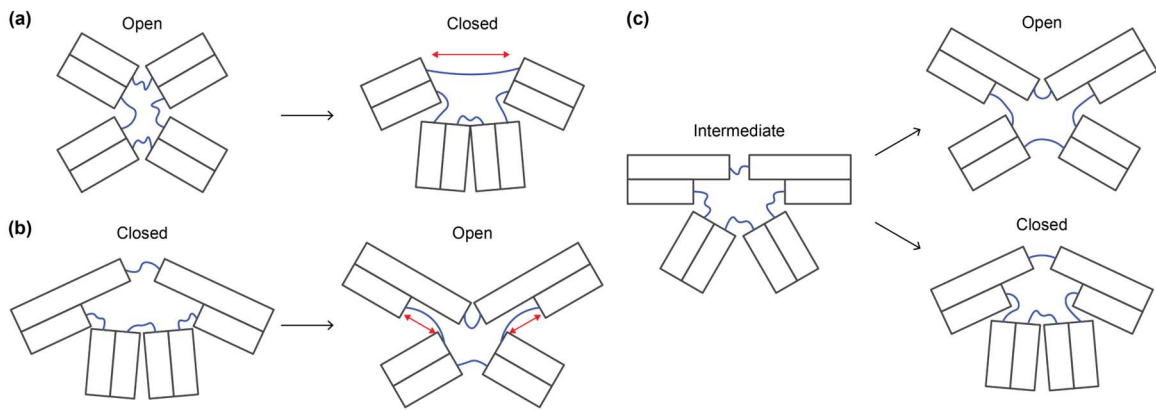
where k_B is the Boltzmann's constant, T is the temperature, L_p is the persistence length of ssDNA, L_c is the contour length, and x is the end-to-end extension. The corresponding energy cost can be computed by integrating F_{WLC} .

$$E(x) = \int F_{WLC}(x) dx \quad (15)$$

The required elongation in the direct transformation (e.g., open to closed) exceeds that of a partial transition (e.g., intermediate to open). Given the convex and strictly increasing nature of the WLC energy function,

$$E(x_{open \leftrightarrow closed}) > E(x_{intermediate \leftrightarrow open}) \text{ or } E(x_{intermediate \leftrightarrow closed}) \quad (16)$$

Thus, achieving both open and closed states from intermediate state through two smaller transitions is energetically more favorable than undergoing a single large conformational change.



Supplementary Figure 15. Conformational transitions from open, closed, and intermediate states. a and b, Direct transitions from open or closed states require large ssDNA elongation. **c**, Transitions from the intermediate state reduce elongation across ssDNA segments.

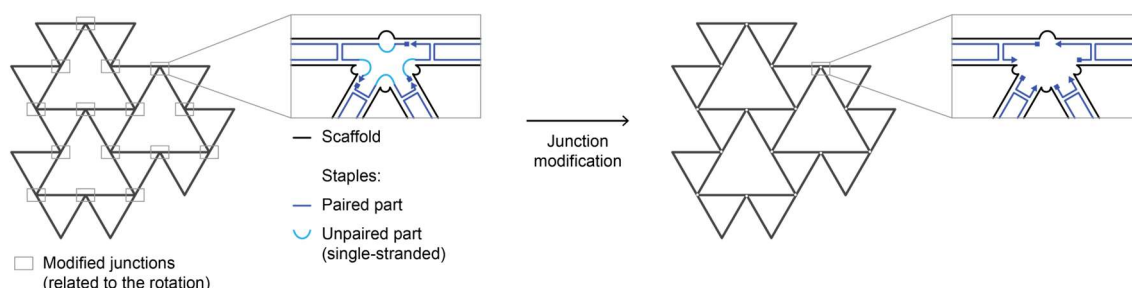
When the structure undergoes large conformational transitions (e.g., open to closed), the resulting displacement of the dsDNA segments necessitates substantial elongation of the connecting ssDNA strands due to geometric irregularities (Supplementary Fig. 15a, b). In contrast, when the transformation starts from an intermediate configuration, the positional shifts between junctions are smaller, thereby reducing the required elongation of the ssDNA strands and the associated energy cost. (Supplementary Fig. 15c).

While the energy cost of ssDNA elongation can be analyzed using the WLC model, a more fundamental limitation arises from the limited force generated by DNA hybridization of connector

strands. In configurations that demand significant elongation of the ssDNA linker, the energy barrier imposed by the WLC model may exceed what can be overcome by hybridization alone. As a result, such transitions may not occur because the hybridization cannot supply sufficient force to drive required elongation.

Supplementary Note 9. Junction modification for transformable structures

1. Junction modification method

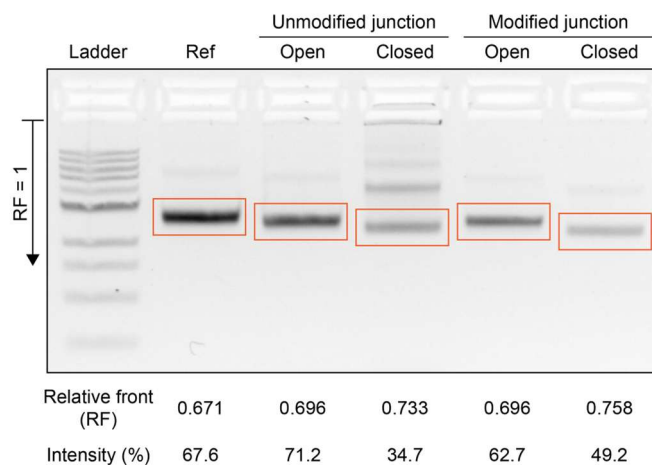


Supplementary Figure 16. Junction modification for creating flexible hinges.

Each junction consists of an unpaired single-stranded scaffold and staple segments (left). While this configuration is flexible enough to maintain an electrostatically repulsive open state in a static structure, it is still too rigid to allow free rotation and transition into a closed conformation. To improve structural adaptability, we modified the junctions by introducing gaps, reducing steric hindrance and enabling a more energy-efficient transformation. This was achieved by selectively cutting unpaired staple segments, effectively creating flexible hinges that lower the energy barrier for rotation.

Junctions are typically composed of two or three staples surrounding the junction, separated from edge staples by crossovers. Initially, the staples were connected to form a circular strand. Then, all unpaired segments were subsequently removed through modification, leaving only the single-stranded scaffold and generating a gap (right). This adjustment was expected to facilitate intra-structural rotational movement while preventing the unintended adherence of multiple structures.

2. Comparison of the quality of closed state between unmodified junction and modified junction



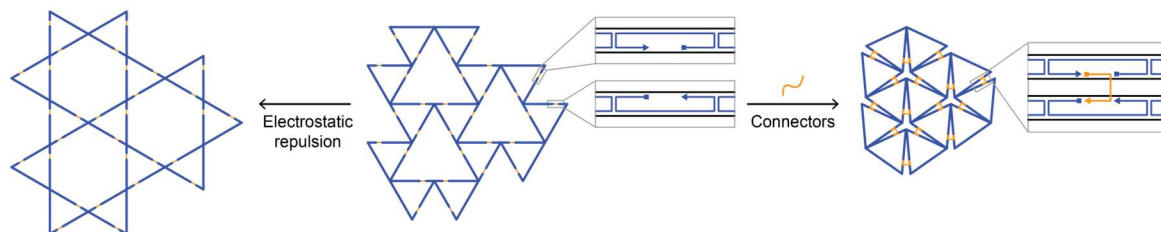
Supplementary Figure 17. Effect of junction modification to achieving closed-state of monomer. Representative gel electrophoresis image of rotating triangle auxetic structure. Relative front and intensity values correspond to the most mobile band in each lane. Uncropped gel images with molecular weight markers are provided in the Source Data and Supplementary Fig. 46.

To assess the structural impact of junction modifications, we compared the closed-state quality of structures with unmodified versus modified junctions. Unmodified junctions lacked defined rotational freedom, leading to unintended interactions among the neighboring structures. As a result, multimer formation increased, as evidenced by multiple bands in electrophoresis. This suggests that connectors or adhered to multiple structures, promoting aggregation rather than controlled rotation.

In contrast, closed structures with modified junctions exhibited a distinct monomer band with a higher relative front value (0.758) compared to the open state (0.696), indicating a more compact configuration with connectors. Since increased migration distance in electrophoresis typically correlates with increased structural compaction, this shift in band position further supports the successful formation of a denser conformation.

Supplementary Note 10. Connector design for shape transformation

1. Connector design

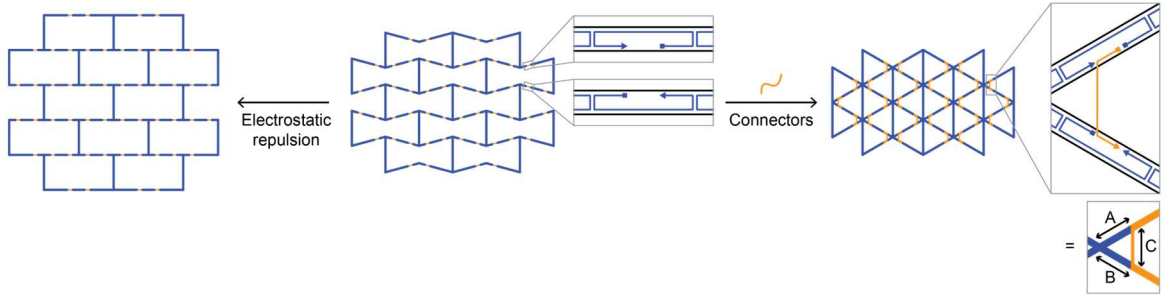


Supplementary Figure 18. Connector design to achieve closed state with rotating triangle auxetic structure.

To further induce a closed conformation, we considered two widely used strategies for reconfiguring DNA origami structures, namely overhangs and glue²¹ and connector strands²². Achieving the closed state requires connecting specific pairs of edges with high accuracy. However, our DX-edge structures are inherently flexible, and introducing gaps at the junctions further increased local flexibility. As a result, the overhang approach was unsuitable for establishing precise edge-to-edge connectivity, often leading to non-specific interactions within monomeric structures (data not shown). To address this limitation, we used connector strands with unique sequences tailored to each designated edge pair to improve connection specificity, introducing 8-nt gaps at designated positions. This structure contains 15 pairs of 8-nt gaps, with 15 distinct connectors designed to bind at specific locations. Each connector consists of 8-nt gap-filling sequences positioned on either side of a 3T spacer, forming a total length of 19-nt ([8-nt gap-filling sequence, one side] – [TTT] – [8-nt gap-filling sequence, other side]).

For the open-state structure, annealing and folding were performed with modified junctions and edges containing 8-nt gaps where connectors were absent. Although the structure was initially designed to remain in an intermediate state (middle), it naturally expanded into the fully open state (left) due to electrostatic repulsion. In contrast, the closed-state structure (right) was annealed and folded with connectors to bridge the gaps, stabilizing the compact conformation.

2. Extended connector design

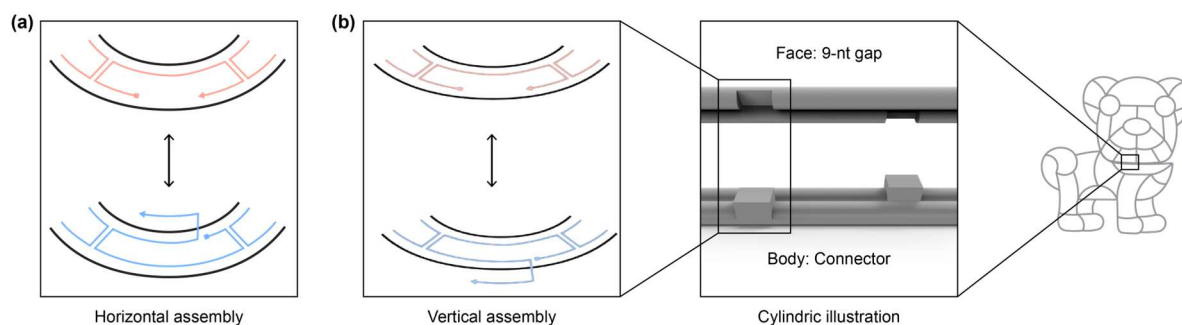


Supplementary Figure 19. Connector design to achieve closed state with rotating triangle auxetic structure.

Unlike the rotating triangle structure, the re-entrant structure requires a longer connector spacer due to a greater geometric distance between the connected edges. In the closed state of the rotating triangle, the connected edges nearly overlap, whereas in the re-entrant structure, the edges ideally maintain a 60° angle even when fully closed. Therefore, the spatial separation between the paired 8-nt gaps (connector sites) must be carefully considered.

Due to inherent geometric variation in the design output, the distance from a vertex to each 8-nt gap (A and B in Supplementary Fig. 19) varies between 18 and 31 base pairs. To estimate the required connector length at full closure, we calculated the theoretical distance between these two sites (C in Supplementary Fig. 19) using the following formula: $C(nm) = \sqrt{A^2 + B^2 - 2AB\cos 60^\circ}$. This calculation predicts a required spacer length of approximately $12.3 \text{ nt} \pm 1.31$, with an estimated range between 10 and 15 nt. Based on this result, we extended the connector spacer to 8T (shorter than estimated lower limit) and 16T (longer than estimated upper limit), resulting in total connector lengths of 24 nt and 32 nt, respectively. The final connector design for re-entrant structure follows the format: [8-nt gap-filling sequence, one side] – [3T, 8T, or 16T spacer] – [8-nt gap-filling sequence, other side].

Supplementary Note 11. Connector design for modularization

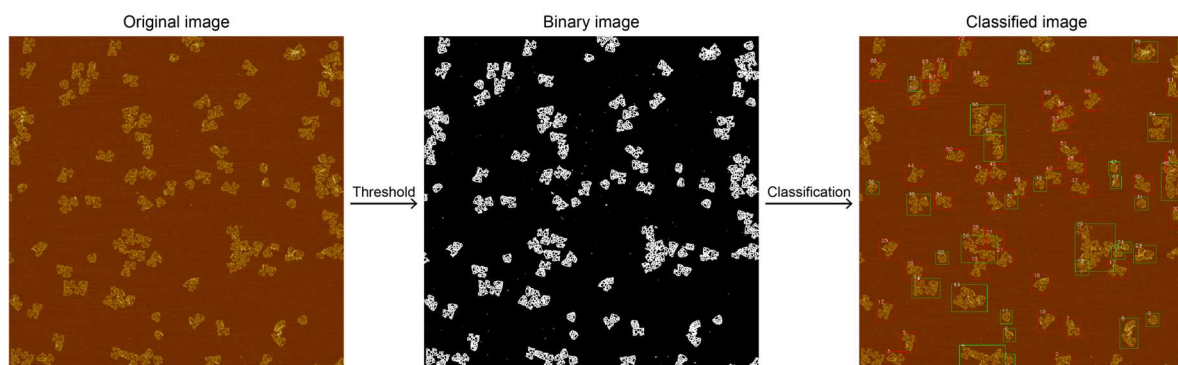


Supplementary Figure 20. Connector design to achieve modular assembly between dog face and body monomer. a, Schematic illustration of horizontal assembly and **b**, vertical assembly

To ensure effective dimerization between modules, we adopted a connector-based approach similar to previously reported designs^{21,23}. All four structures were modified to enable dimer formation by adopting vertical assembly instead of horizontal assembly to maximize the curvature-matching advantage of our framework. Horizontal assembly was avoided because the mismatch between the inner and outer curvature of the 2HB edges would likely introduce structural strain at the interface. Specifically, the face module includes 9-nt gaps at seven designated positions, whereas the body module contains 12-nt overhangs at corresponding positions. Each 12-nt overhang consists of a 3T spacer followed by a 9-nt gap-filling sequence complementary to the face module, while the overhang itself is extended from a staple strand of the body module. These complementary interactions facilitate precise module dimerization.

Due to structural constraints, vertical stacking was preferred over horizontal alignment. Although both modules share a common interfacial edge design, the intrinsic curvature differs between the inner and outer faces due to the asymmetry of the 2HB-based edges (Supplementary Fig. 20a). To accommodate this curvature mismatch and ensure optimal alignment, we assembled these modules vertically, forming an analogy to a square-latticed 4HB structure (Supplementary Fig. 20b).

Supplementary Note 12. Dimer yield estimation



Supplementary Figure 21. Yield estimation process.

To estimate the dimer yield from AFM images, each structure was first segmented and classified based on its pixel area. The original AFM image ($5\ \mu\text{m} \times 5\ \mu\text{m}$, $1024\ \text{px} \times 1024\ \text{px}$) was binarized, and the pixel area of each contour was computed. Contours intersecting the image boundary were excluded from analysis. The area-based classification threshold for dimers was set between 900 and 1400 pixels. This range was determined based on the observation that monomer structures typically exhibited an area of 500–600 pixels. Assuming an ideal dimer would have approximately double the area, the expected range would be 1000–1200 pixels. However, to account for structural variation due to conformational distortion during deposition, the cutoff was extended to 900–1400 pixels. The validity of this cutoff was confirmed by comparing automated classification with manual annotation across multiple images, yielding a classification accuracy exceeding 95%.

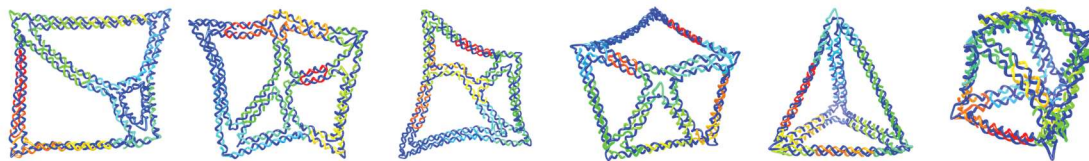
To visualize the classification, dimers and non-dimers were marked with red and green bounding boxes, respectively (Supplementary Fig. 21). The number-based dimer yield was then defined as the ratio of the number of dimers (red boxes) to the total number of structures (red + green boxes)²³. The associated standard error was calculated as $\sqrt{p(1-p)/N}$, where p is the number-based yield and N is the total number of classified structures, assuming p as a Bernoulli probability.

To account for the variation in structure size across images, the pixel-weighted dimer yield was also computed as $p_{px} = \sum n_i / \sum (n_i / p_i)$, where n_i is the number of dimers in image i , and p_i is the pixel-based yield in that image defined as the ratio of the pixel area of dimers to the total pixel area of structures²⁴. This formulation incorporates a weight based on pixel area by expressing the total number of structures as n_i / p_i , which effectively adjusts for the pixel area of all classified structures in image i .

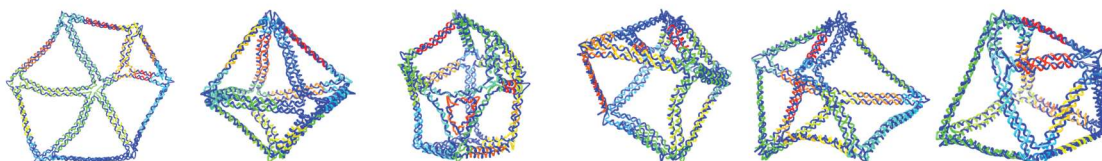
As a result, structures with larger pixel areas, such as aggregates, contribute proportionally more to the final yield, ensuring that the estimate reflects both the number and the relative size of the structures. The standard error for the pixel-weighted yield was similarly calculated as $\sqrt{p_{px}(1 - p_{px})/\sum(n_i/p_i)}$, assuming p_{px} as a Bernoulli probability as well.

Supplementary Figures

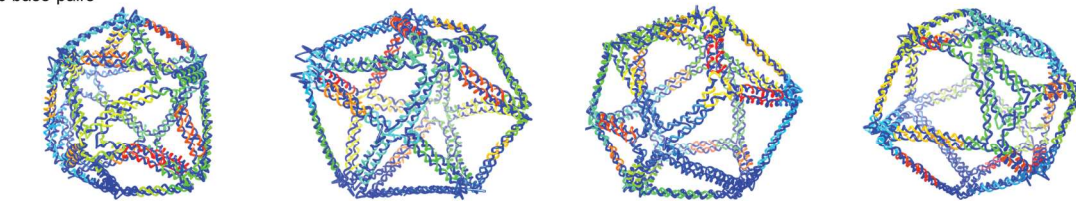
1000 base-pairs



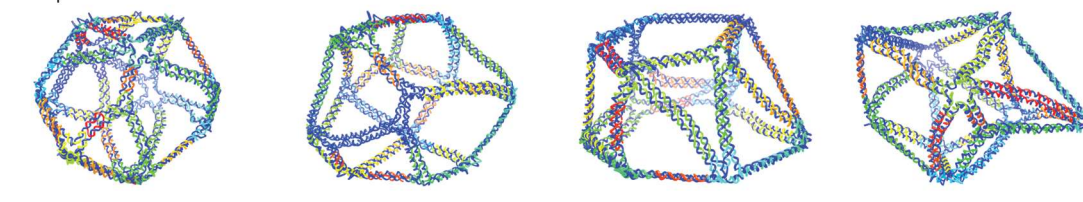
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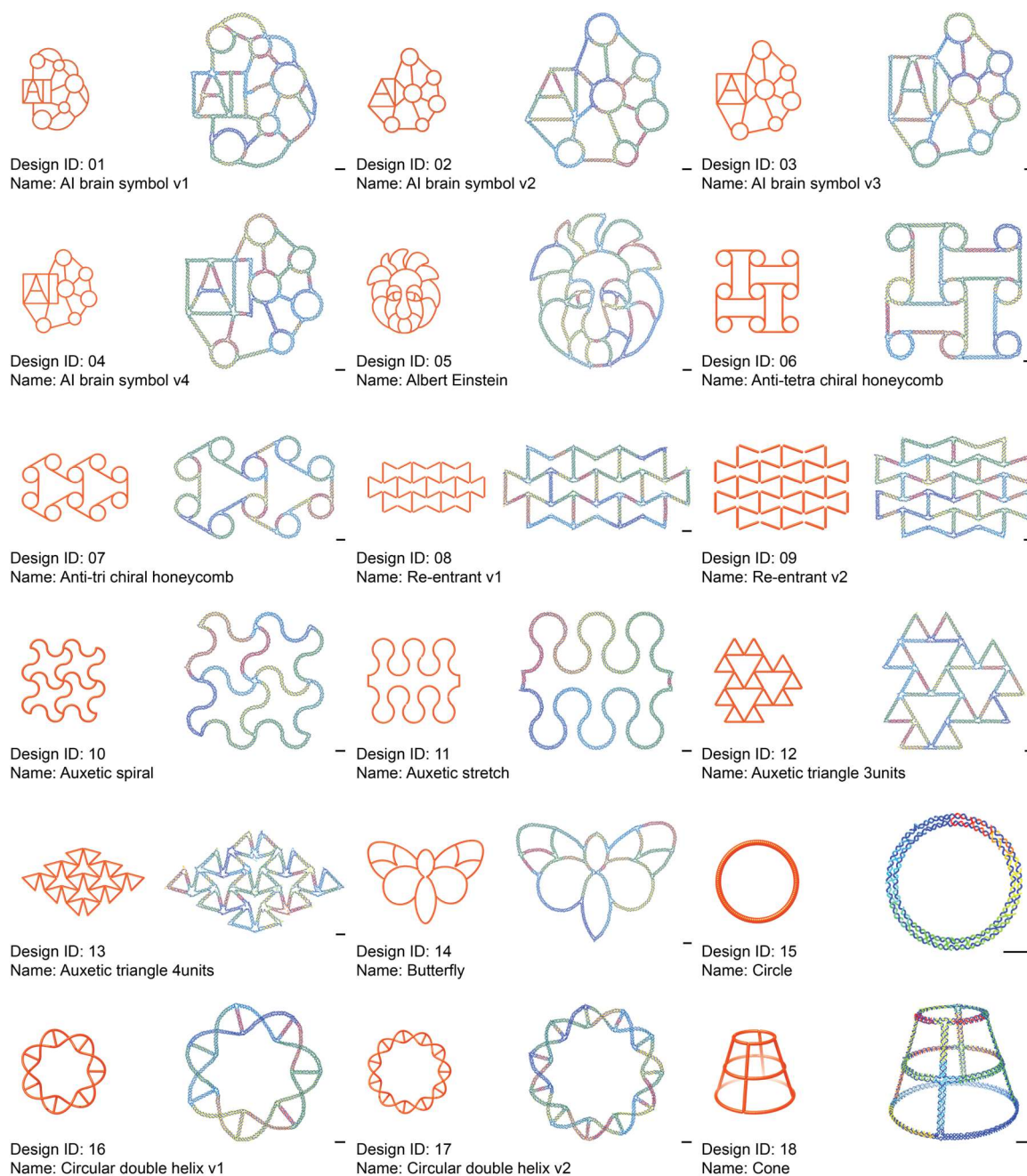
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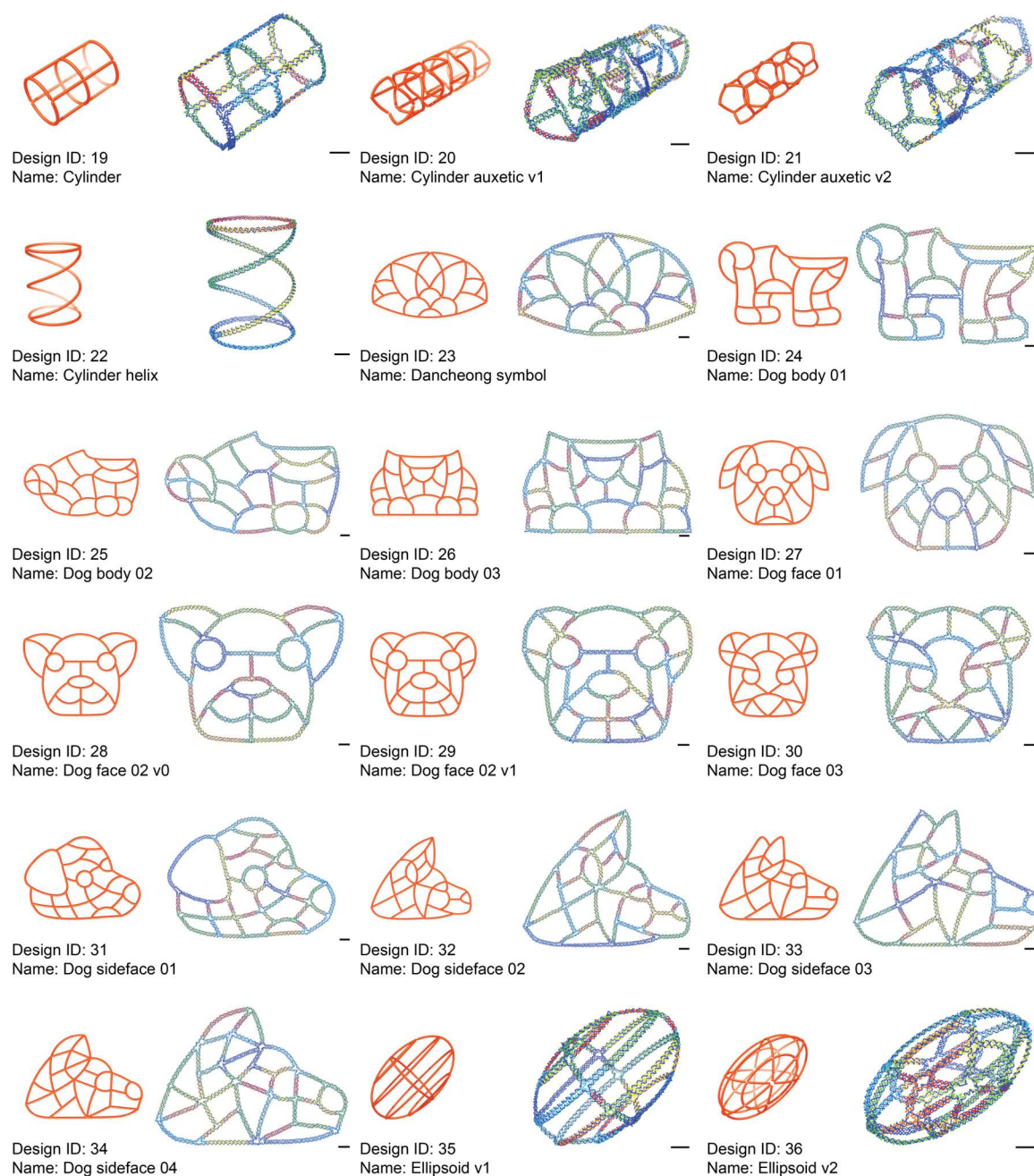
4000 base-pairs



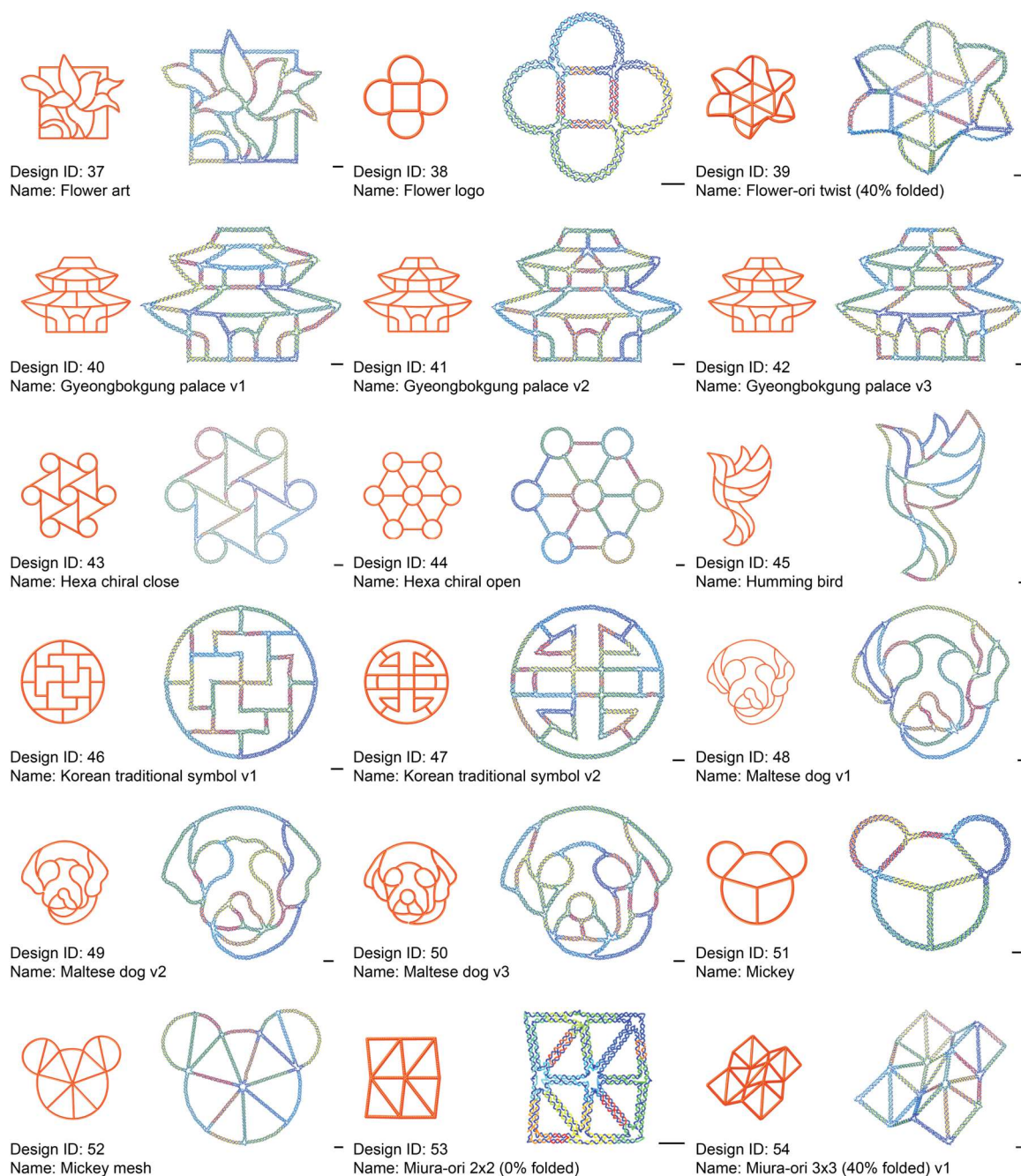
Supplementary Figure 22. Designs generated by unconditional DDPM. Scale bars, 10 nm. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.



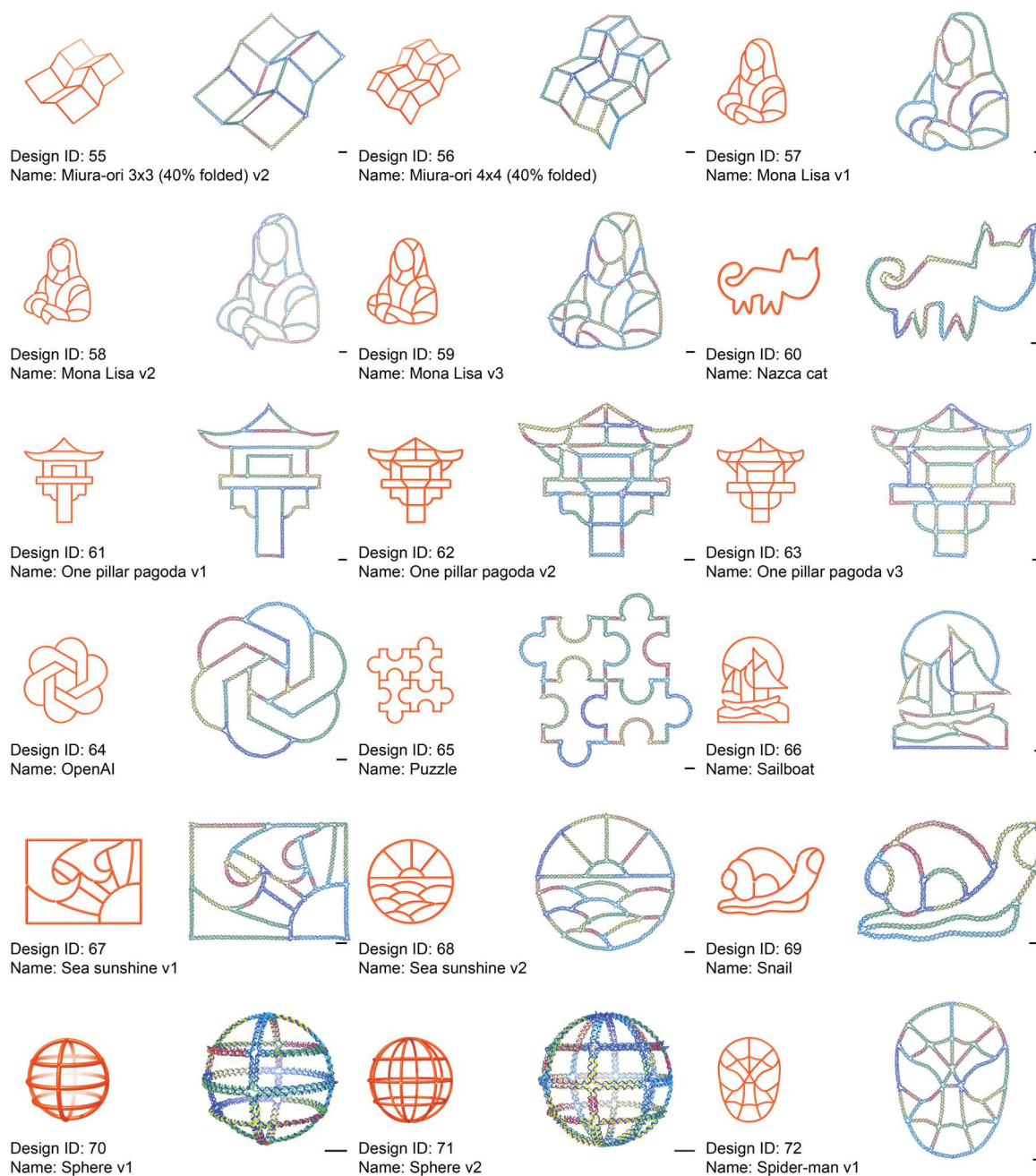
Supplementary Figure 23. Design gallery (continued). Scale bars, 10 nm. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.



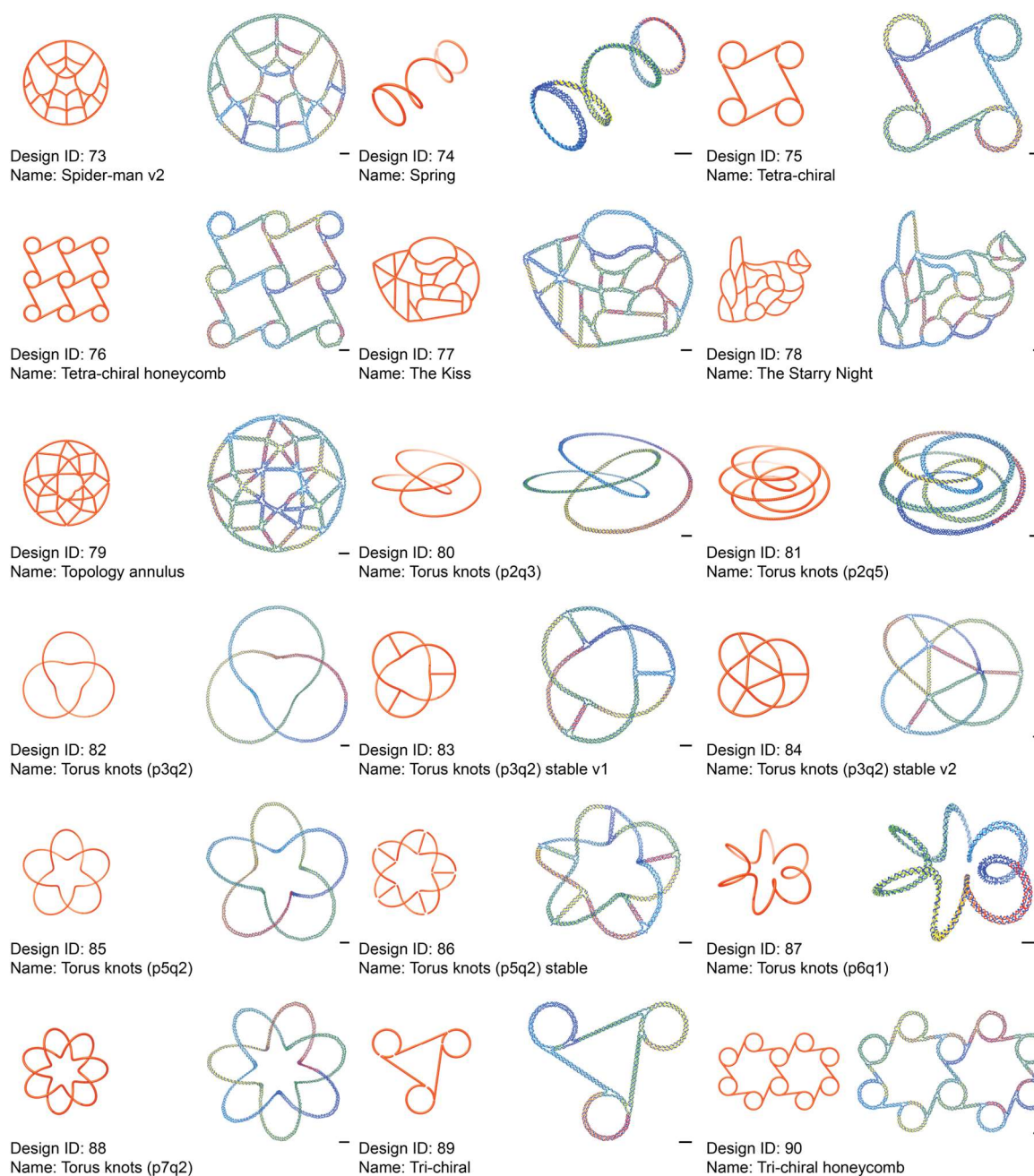
Supplementary Figure 23. Design gallery (continued). Scale bars, 10 nm. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.



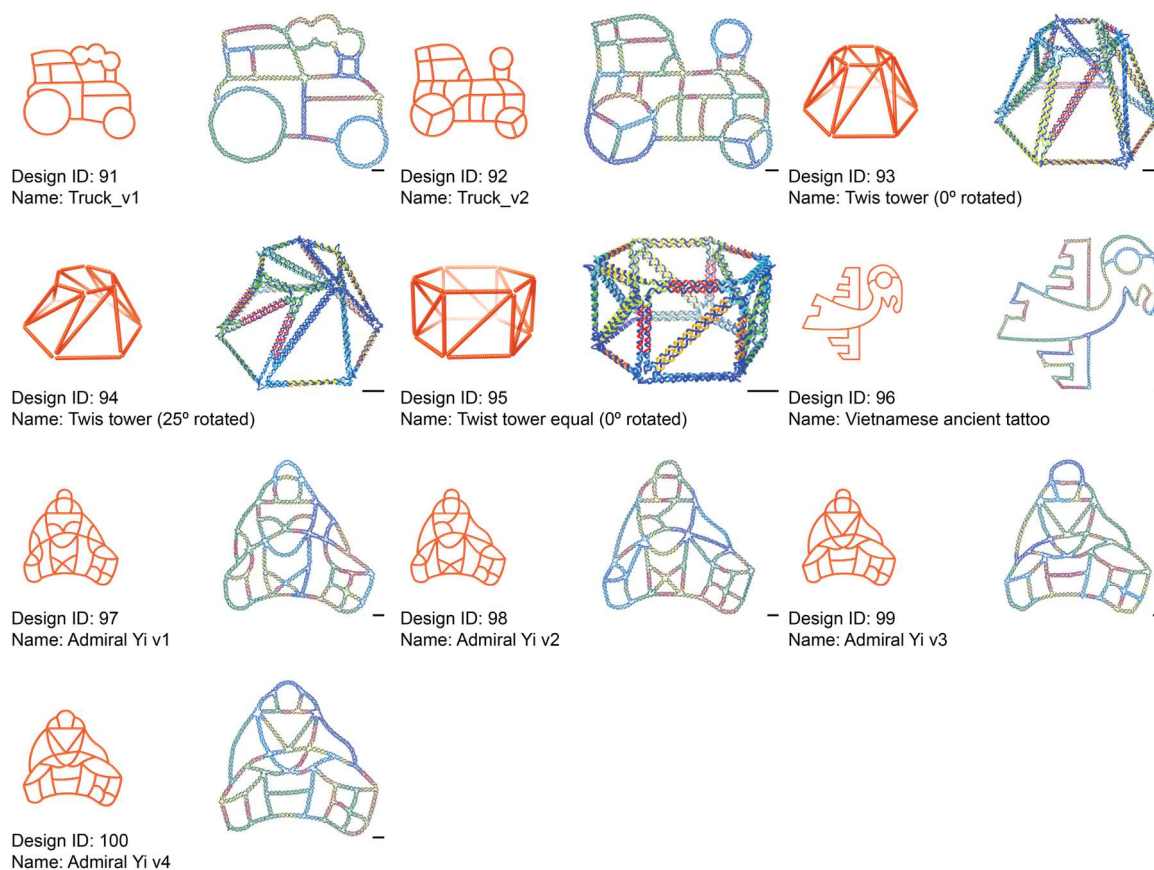
Supplementary Figure 23. Design gallery (continued). Scale bars, 10 nm. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.



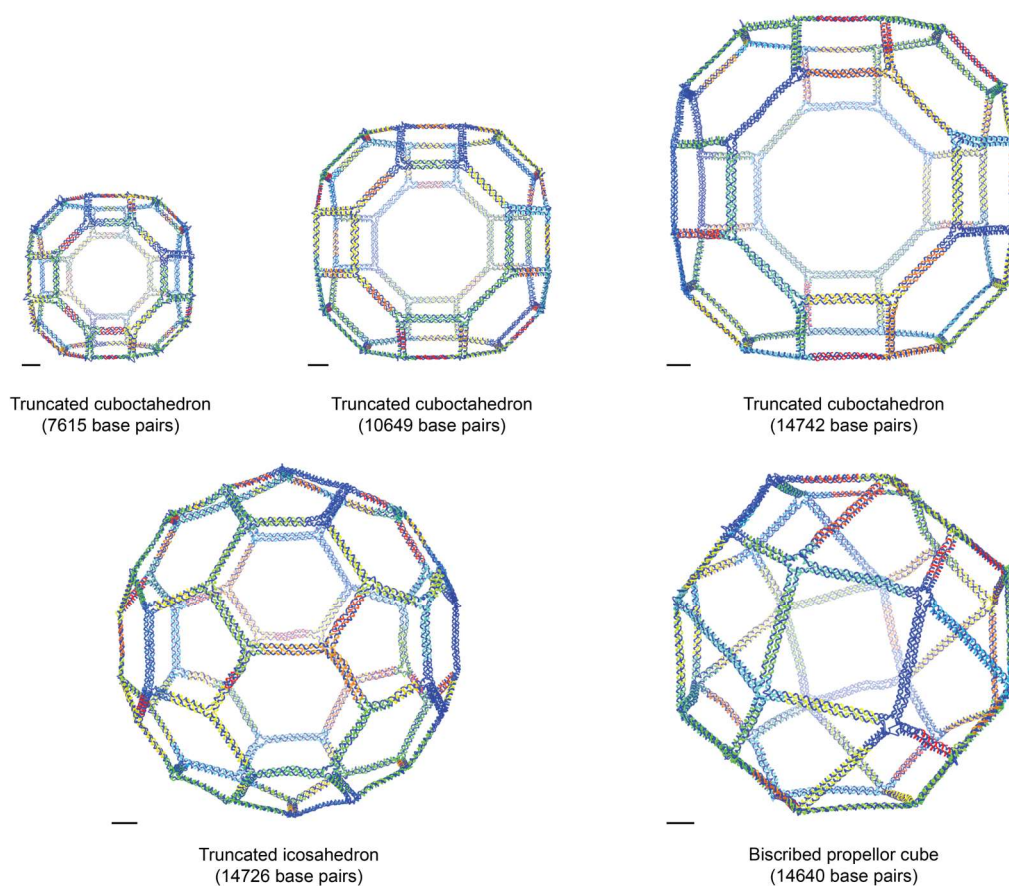
Supplementary Figure 23. Design gallery (continued). Scale bars, 10 nm. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.



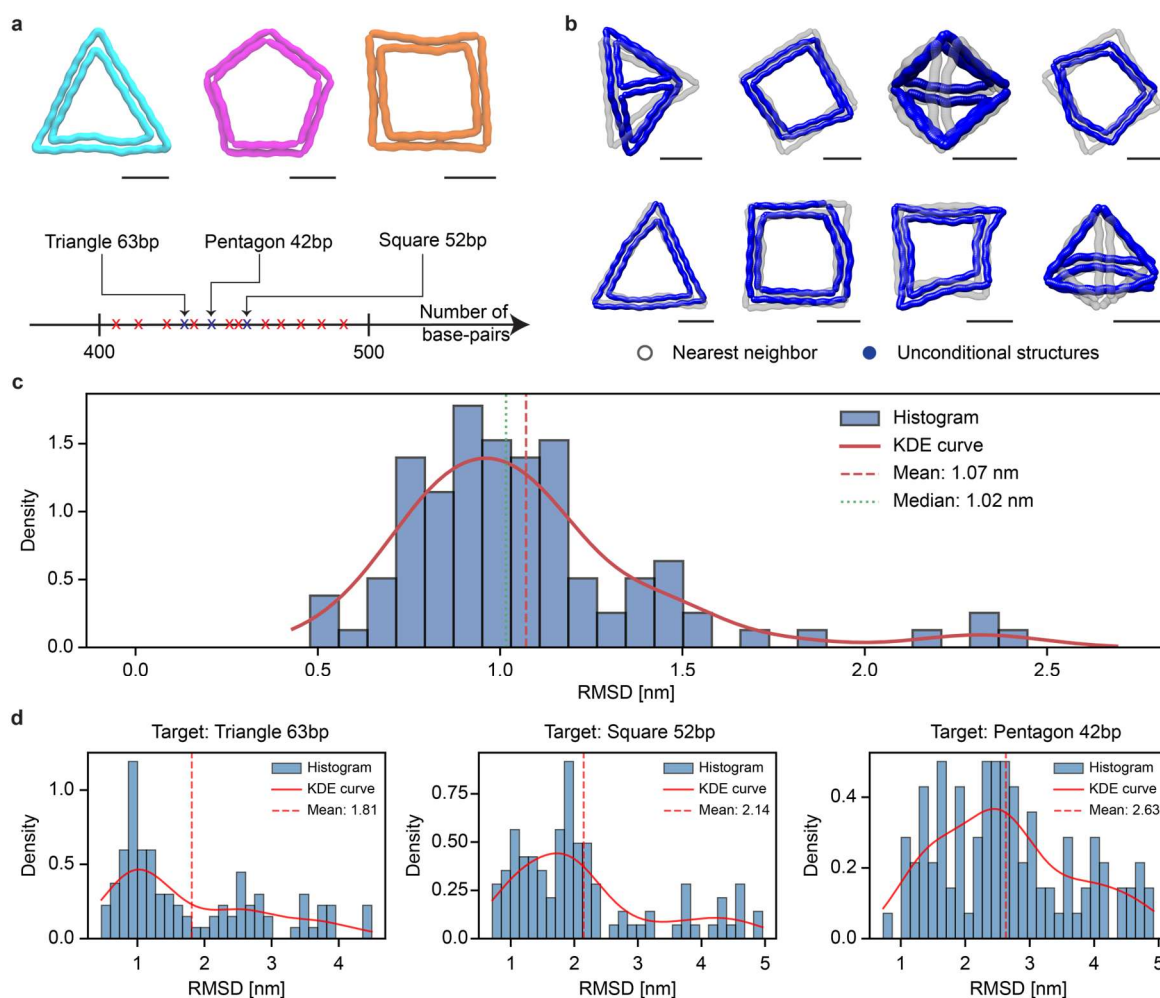
Supplementary Figure 23. Design gallery (continued). Scale bars, 10 nm. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.



Supplementary Figure 23. Design gallery (continued). Scale bars, 10 nm. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.

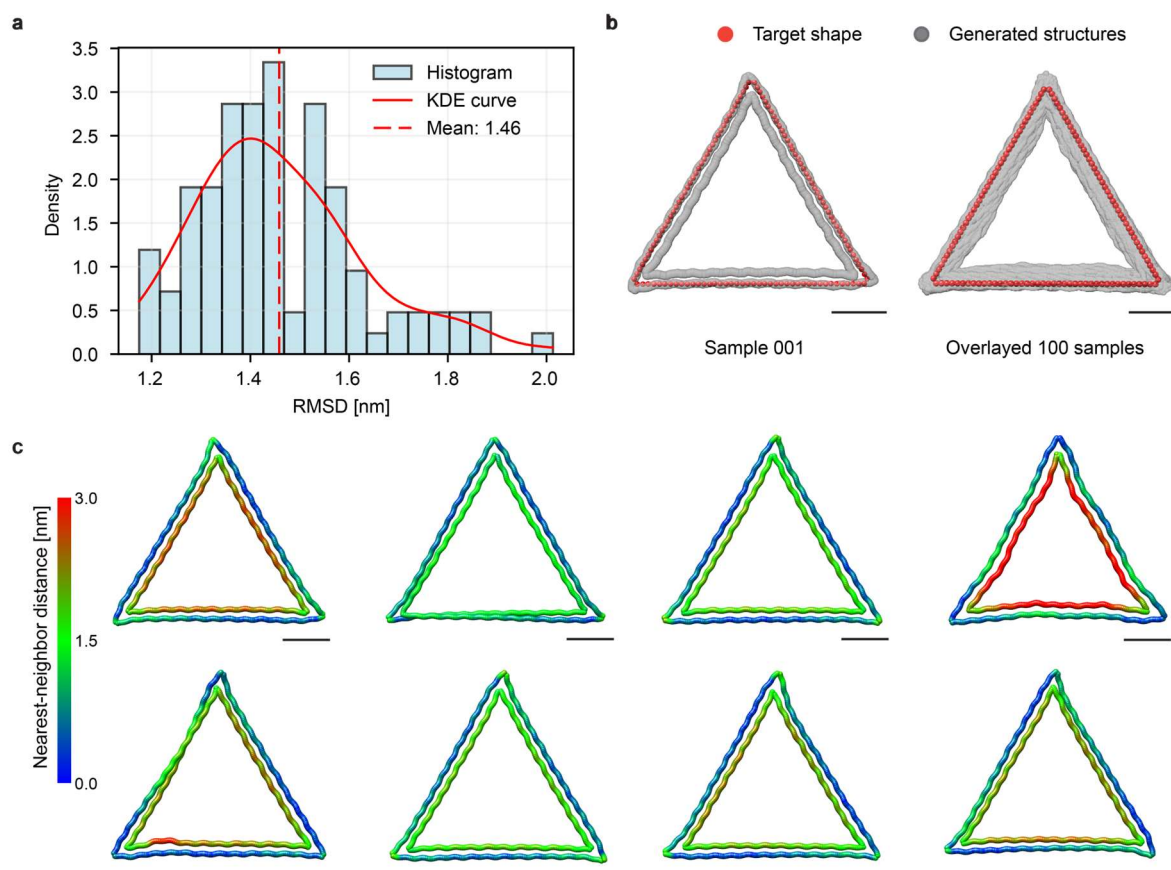


Supplementary Figure 24. Scalability of Generative SNUPI. Scale bars, 10 nm. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.



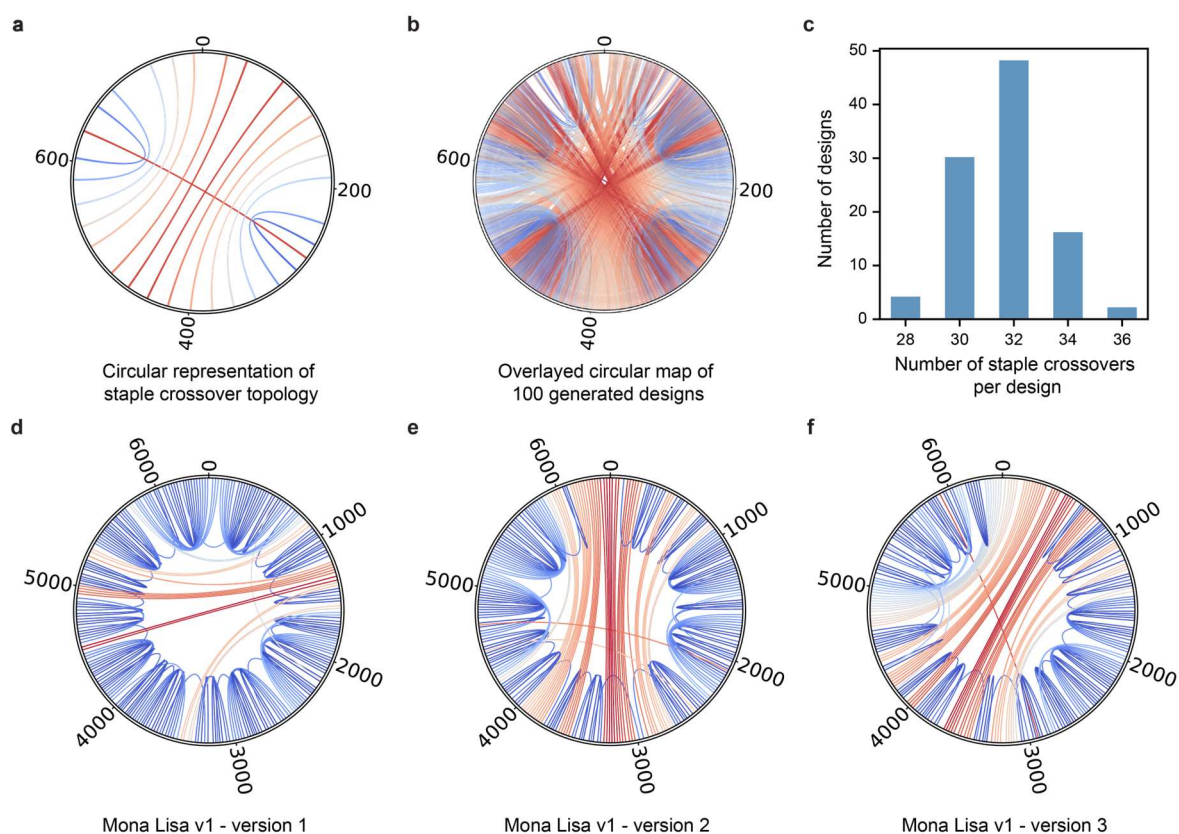
Supplementary Figure 25. Geometric similarity of unconditional generated samples to training set (Iterative closest point (ICP)-aligned RMSD).

a, Unconditional sampling regime in which 100 structures were generated in the 400–500 bp range. **b**, Representative unconditional generated structures aligned with nearest training set neighbor with lowest ICP-aligned RMSD. **c**, For each generated sample, 30 nearest generated structures matched by number of base pairs were selected and ICP-aligned RMSD was computed for each. The minimum RMSD was plotted as the nearest-neighbor distance. The distribution has mean of $\mu = 1.07$ nm and median of 1.02 nm. **d**, RMSD distributions between representative target families (triangle/square/pentagon) and 100 generated structures, with mean RMSDs of 1.81 nm, 2.14 nm, and 2.63 nm, respectively, indicating no near-zero collapse and consistent non-trivial geometric variability. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.



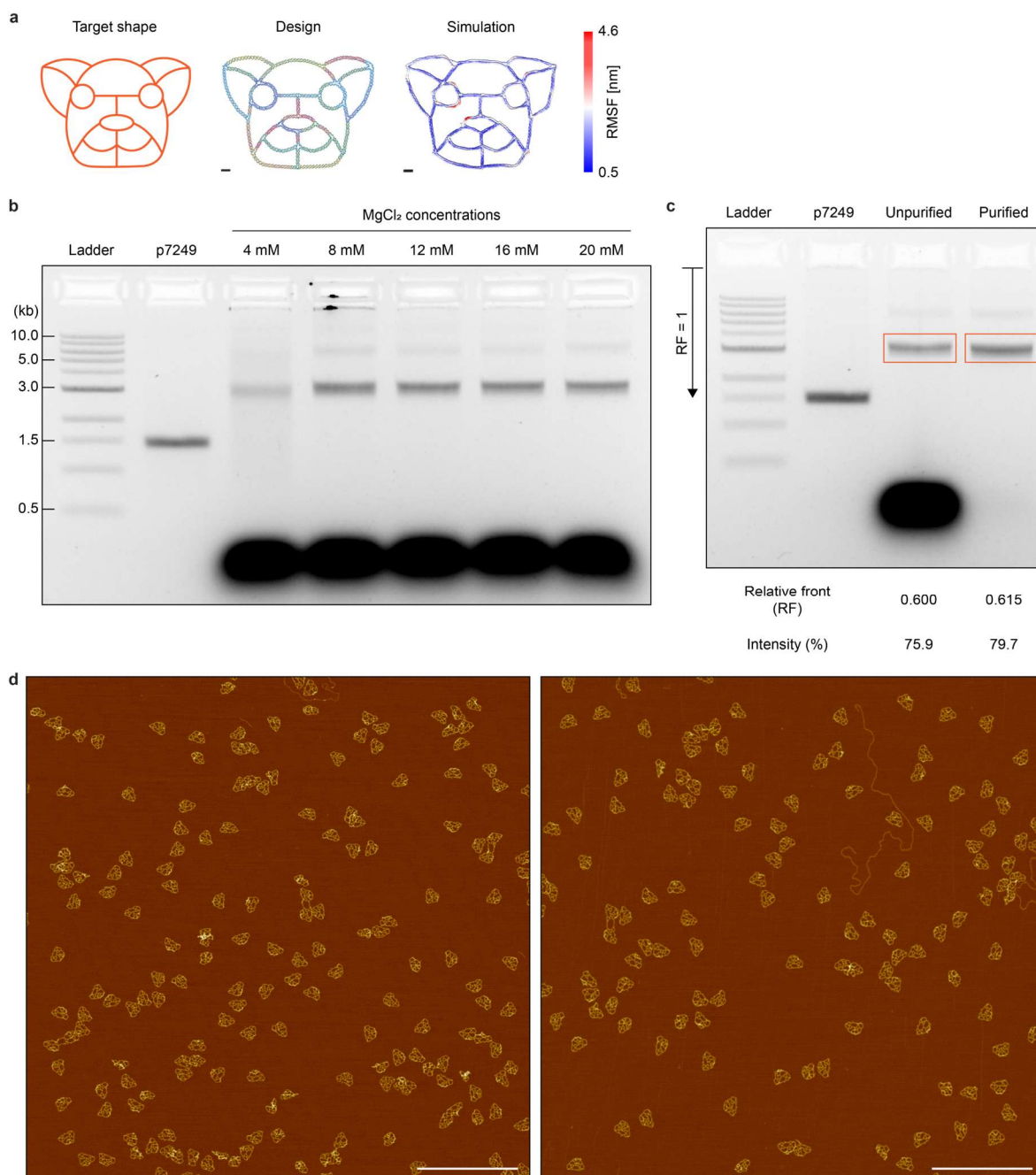
Supplementary Figure 26. Conditional sampling with both shape and number of base pairs fixed.

a, Histogram and KDE of RMSD between each generated structure and the fixed target shape after rigid alignment. The mean RMSD is 1.46 nm, indicating non-trivial variability rather than deterministic reproduction. **b**, Visualization of the fixed target shape (red) and generated structures (gray). Left: one representative sample. Right: overlay of all 100 generated samples, showing stochastic dispersion around the target shape and no collapse to a single identical configuration across random seeds. **c**, Eight representative generated structures colored by the nearest-neighbor distance to the target shape at each base pair, highlighting the distinct deviation patterns along the edges (blue = closer match, red = larger mismatch). Scale bars, 10 nm. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.



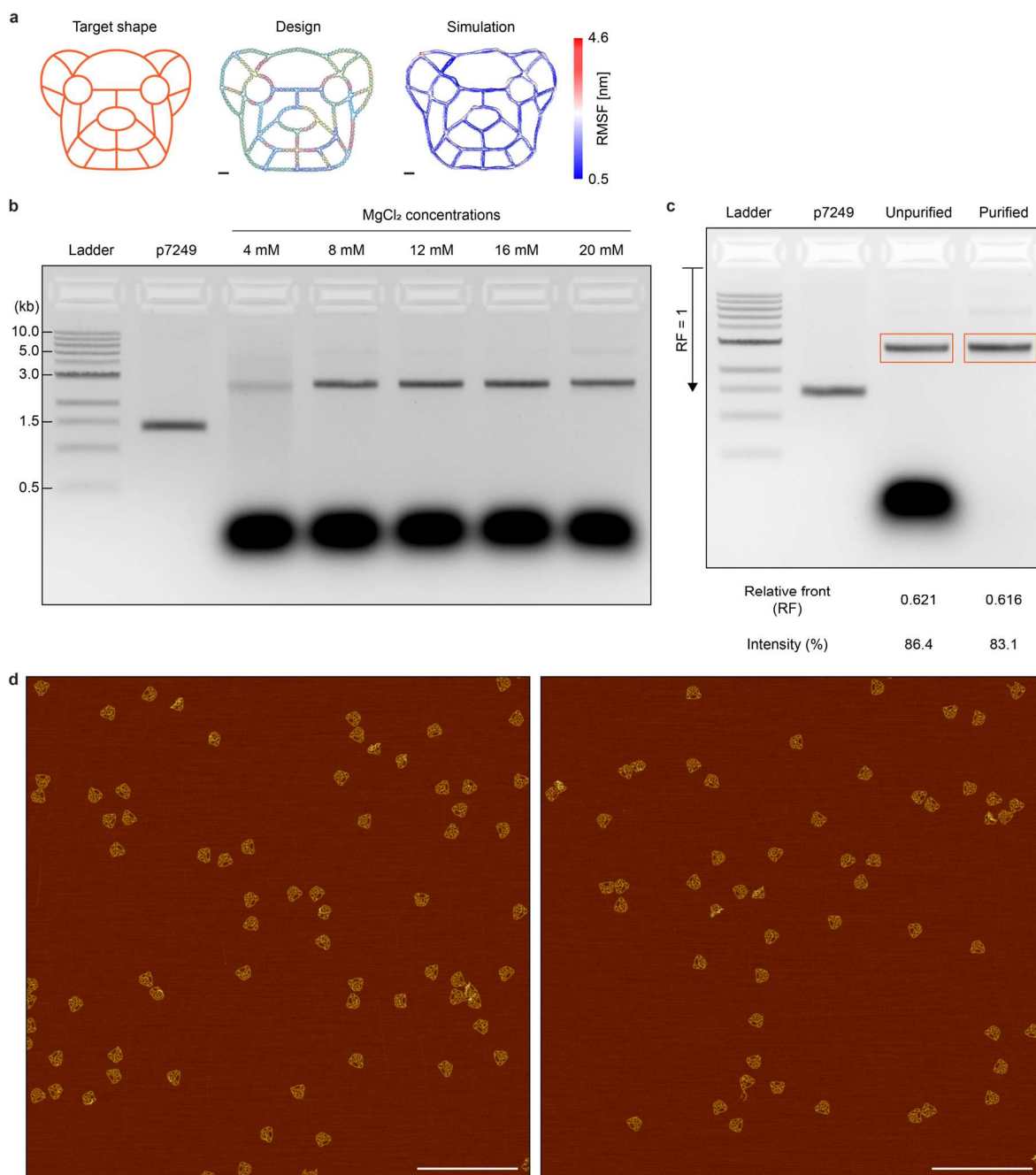
Supplementary Figure 27. Topology diversity from repeated generation under fixed target shape.

a, Representative circular map of staple crossover topology for one representative design from generated structure in Supplementary Fig. 26. **b**, Overlaid circular map of 100 generated designs for the triangle target shape shown in Supplementary Fig. 26 (both target shape and the number of base pairs fixed), showing the diversity of crossover distributions. **c**, Histogram of the number of staple crossovers per design across the 100 designs. **d–f**, Three representative routed designs for Mona Lisa_v1 using a standard ~7000-base scaffold, illustrating distinct crossover patterns despite the same target shape. Link color in the circular maps indicates crossover distance along the scaffold: blue, short-range; red, long-range (coolwarm colormap).



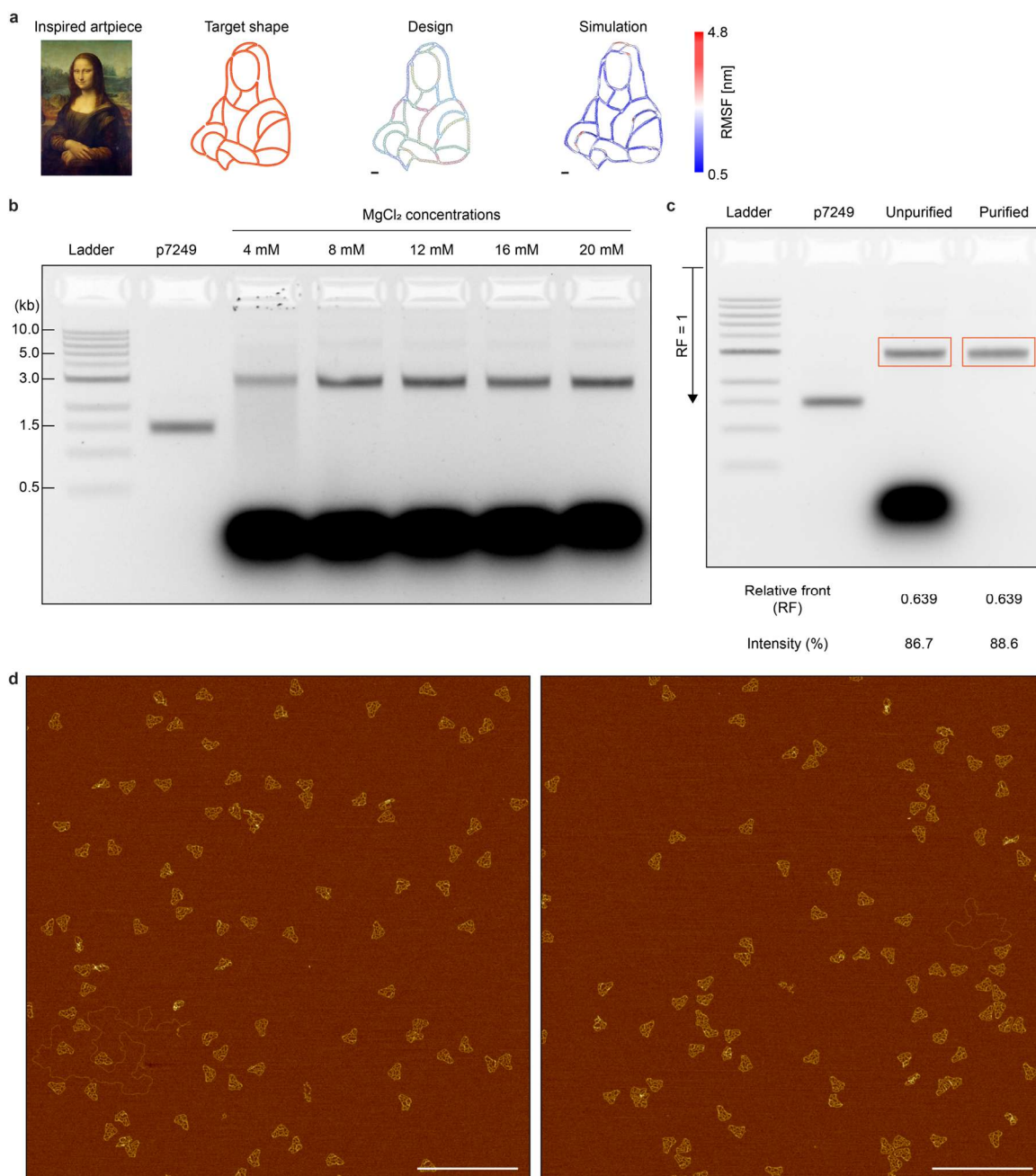
Supplementary Figure 28. Experimental results of dog face 1.

a, Target shape, pseudo-atomic model of the design, and SNUPI-based simulation result. (Scale bars, 10 nm) **b**, Overall structural quality under varying MgCl_2 concentrations (4 – 20 mM) and **c**, comparison of the structure before and after purification by ultrafiltration following annealing in 12 mM MgCl_2 , analyzed by gel electrophoresis. **d**, Representative AFM images of the structures (Scale bars, 1 μm). Uncropped gel images with molecular weight markers are provided in the Source Data and Supplementary Fig. 46. Gel electrophoresis experiments were repeated independently twice with similar results, and representative images are shown. AFM imaging was performed independently at least three times with similar results, and representative images are shown. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.



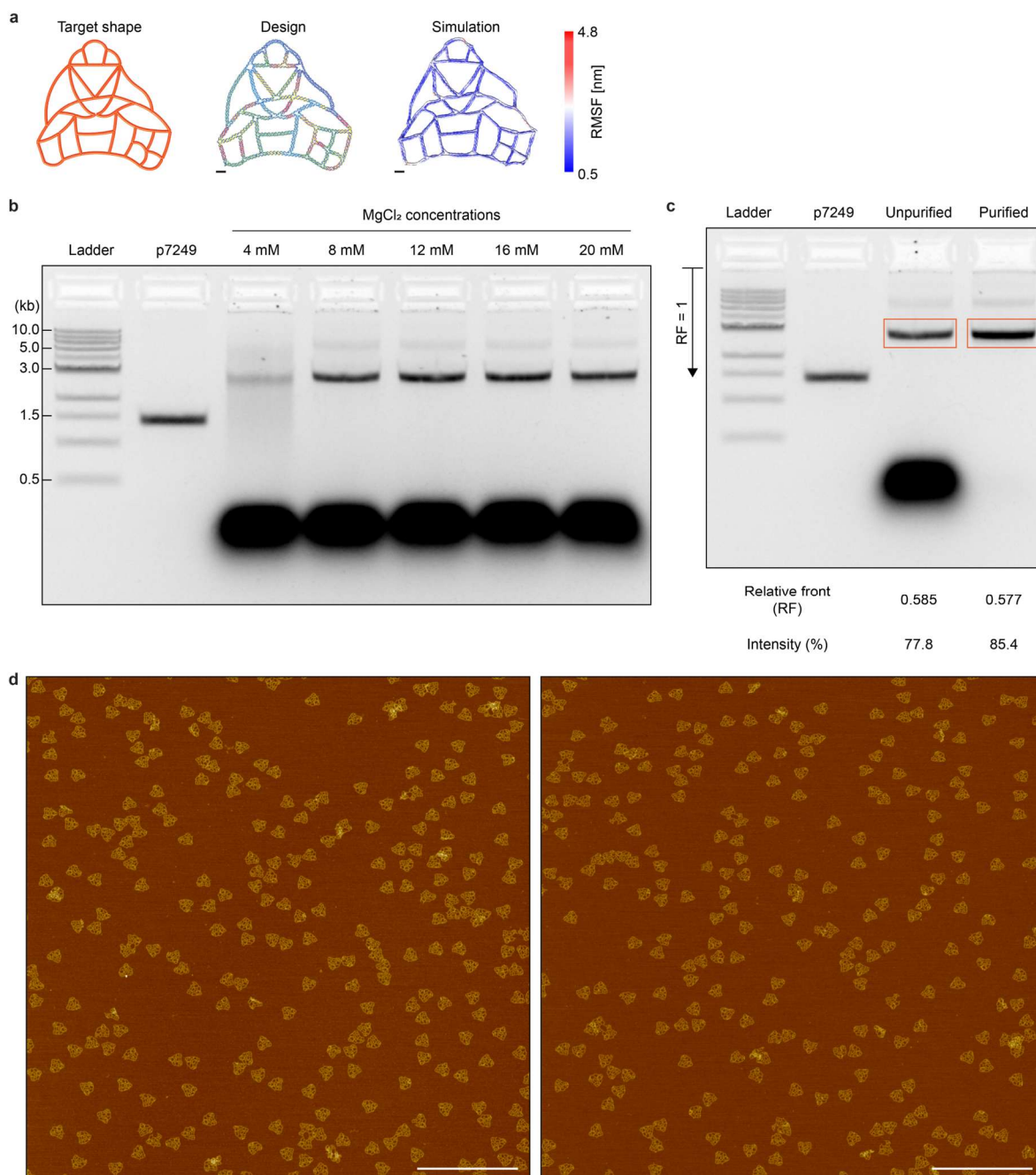
Supplementary Figure 29. Experimental results of dog face 2.

a, Target shape, pseudo-atomic model of the design, and SNUPI-based simulation result. (Scale bars, 10 nm) **b**, Overall structural quality under varying MgCl_2 concentrations (4 – 20 mM) and **c**, comparison of the structure before and after purification by ultrafiltration following annealing in 12 mM MgCl_2 , analyzed by gel electrophoresis. **d**, Representative AFM images of the structures (Scale bars, 1 μm). Uncropped gel images with molecular weight markers are provided in the Source Data and Supplementary Fig. 46. Gel electrophoresis experiments were repeated independently twice with similar results, and representative images are shown. AFM imaging was performed independently at least three times with similar results, and representative images are shown. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.



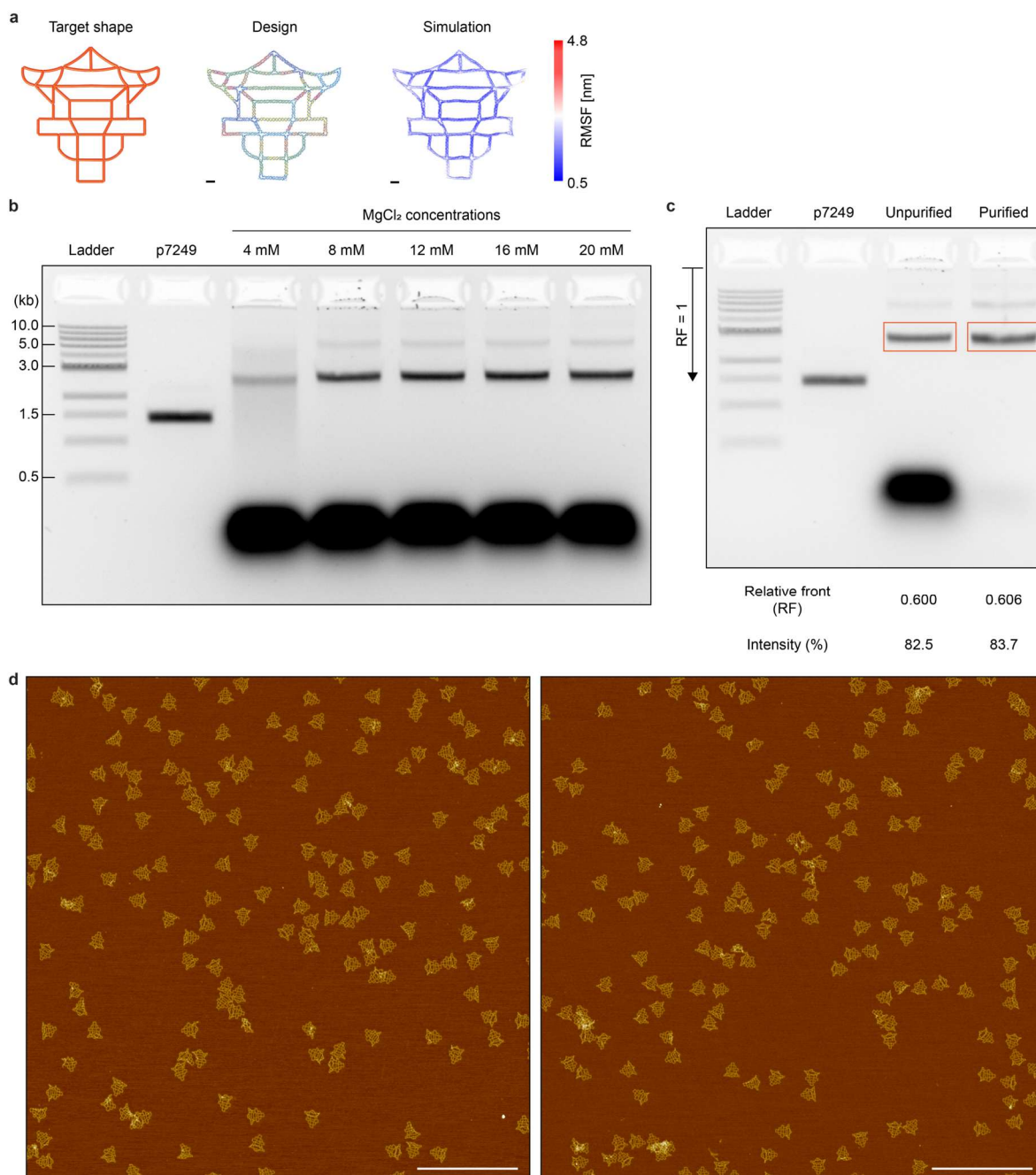
Supplementary Figure 30. Experimental results of Mona Lisa.

a, Inspired artwork “Mona Lisa” (Image courtesy of the Centre de recherche et de restauration des musées de France (C2RMF), via Wikimedia Commons. Public domain.), target shape, pseudo-atomic model of the design, and SNUPI-based simulation result. (Scale bars, 10 nm) **b**, Overall structural quality under varying MgCl_2 concentrations (4 – 20 mM) and **c**, comparison of the structure before and after purification by ultrafiltration following annealing in 12 mM MgCl_2 , analyzed by gel electrophoresis. **d**, Representative AFM images of the structures (Scale bars, 1 μm). Uncropped gel images with molecular weight markers are provided in the Source Data and Supplementary Fig. 46. Gel electrophoresis experiments were repeated independently twice with similar results, and representative images are shown. AFM imaging was performed independently at least three times with similar results, and representative images are shown. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.



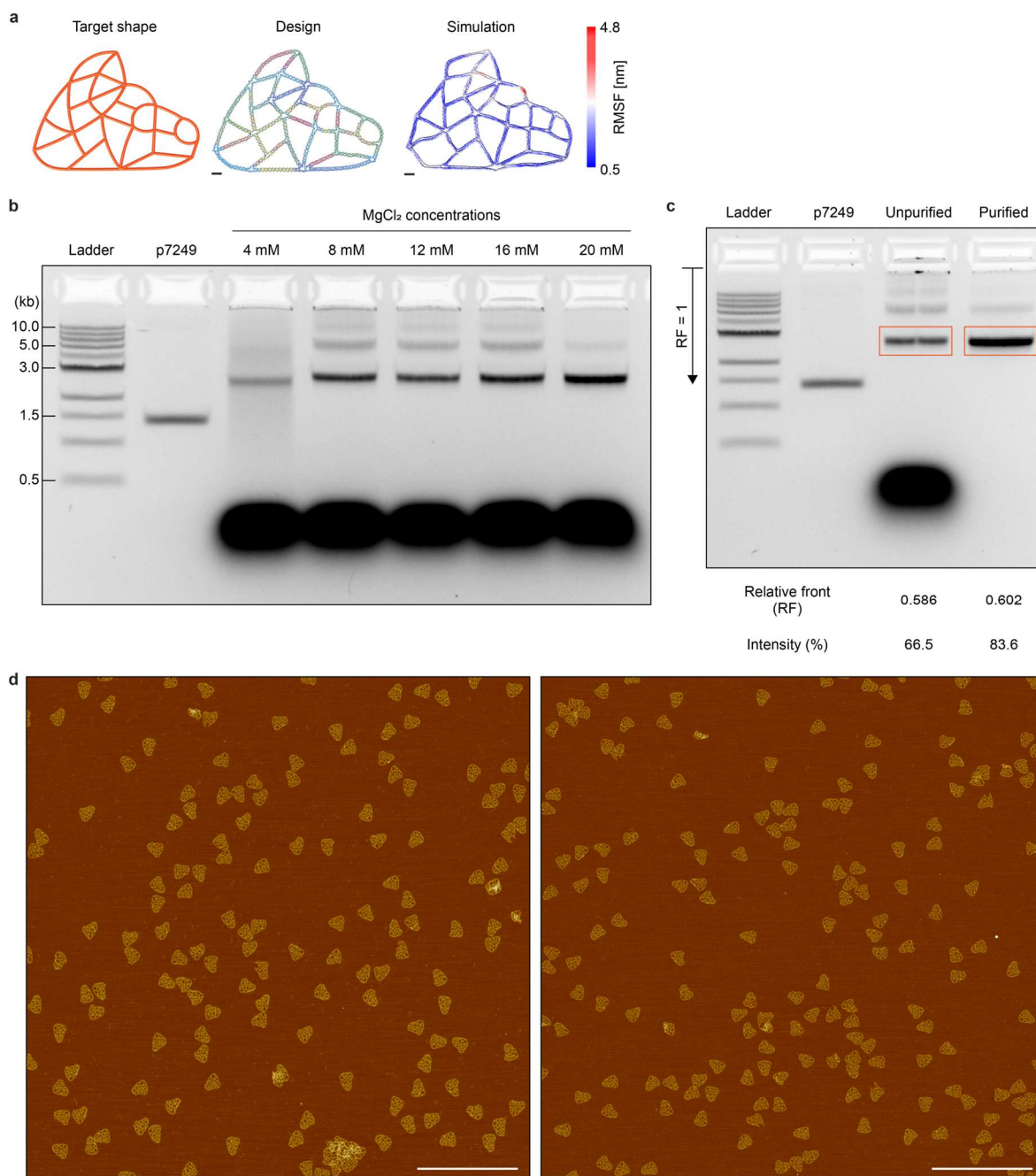
Supplementary Figure 31. Experimental results of Admiral Yi.

a, Target shape inspired by the statue “Admiral Yi”, pseudo-atomic model of the design, and SNUPI-based simulation result. (Scale bars, 10 nm) **b**, Overall structural quality under varying MgCl_2 concentrations (4 – 20 mM) and **c**, comparison of the structure before and after purification by ultrafiltration following annealing in 12 mM MgCl_2 , analyzed by gel electrophoresis. **d**, Representative AFM images of the structures (Scale bars, 1 μm). Uncropped gel images with molecular weight markers are provided in the Source Data and Supplementary Fig. 46. Gel electrophoresis experiments were repeated independently twice with similar results, and representative images are shown. AFM imaging was performed independently at least three times with similar results, and representative images are shown. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.



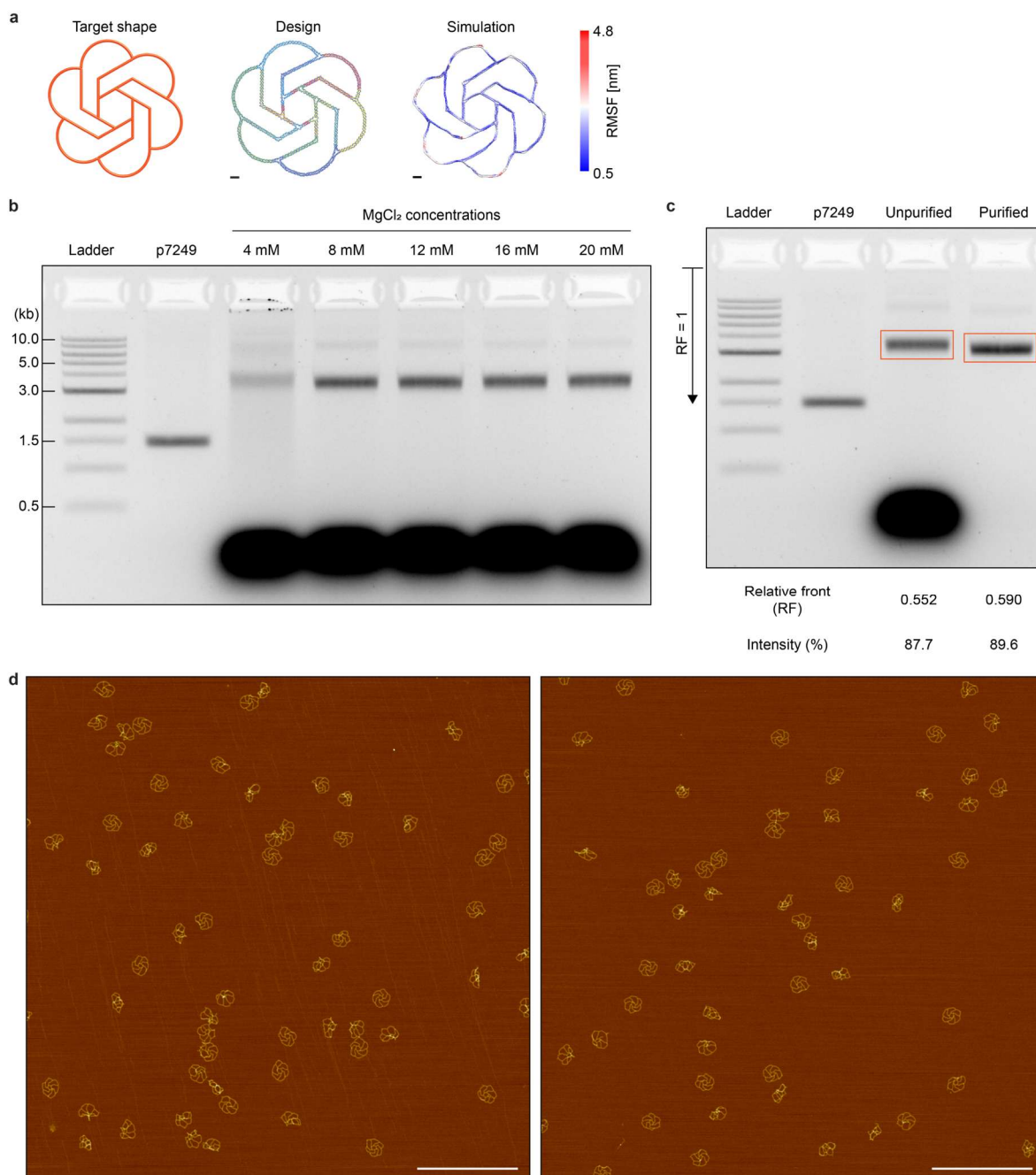
Supplementary Figure 32. Experimental results of Pagoda.

a, Target shape inspired by the architecture of “Chua Mot Cot”, also known as the One Pillar Pagoda, pseudo-atomic model of the design, and SNUPI-based simulation result. (Scale bars, 10 nm) **b**, Overall structural quality under varying MgCl_2 concentrations (4 – 20 mM) and **c**, comparison of the structure before and after purification by ultrafiltration following annealing in 12 mM MgCl_2 , analyzed by gel electrophoresis. **d**, Representative AFM images of the structures (Scale bars, 1 μm). Uncropped gel images with molecular weight markers are provided in the Source Data and Supplementary Fig. 46. Gel electrophoresis experiments were repeated independently twice with similar results, and representative images are shown. AFM imaging was performed independently at least three times with similar results, and representative images are shown. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.



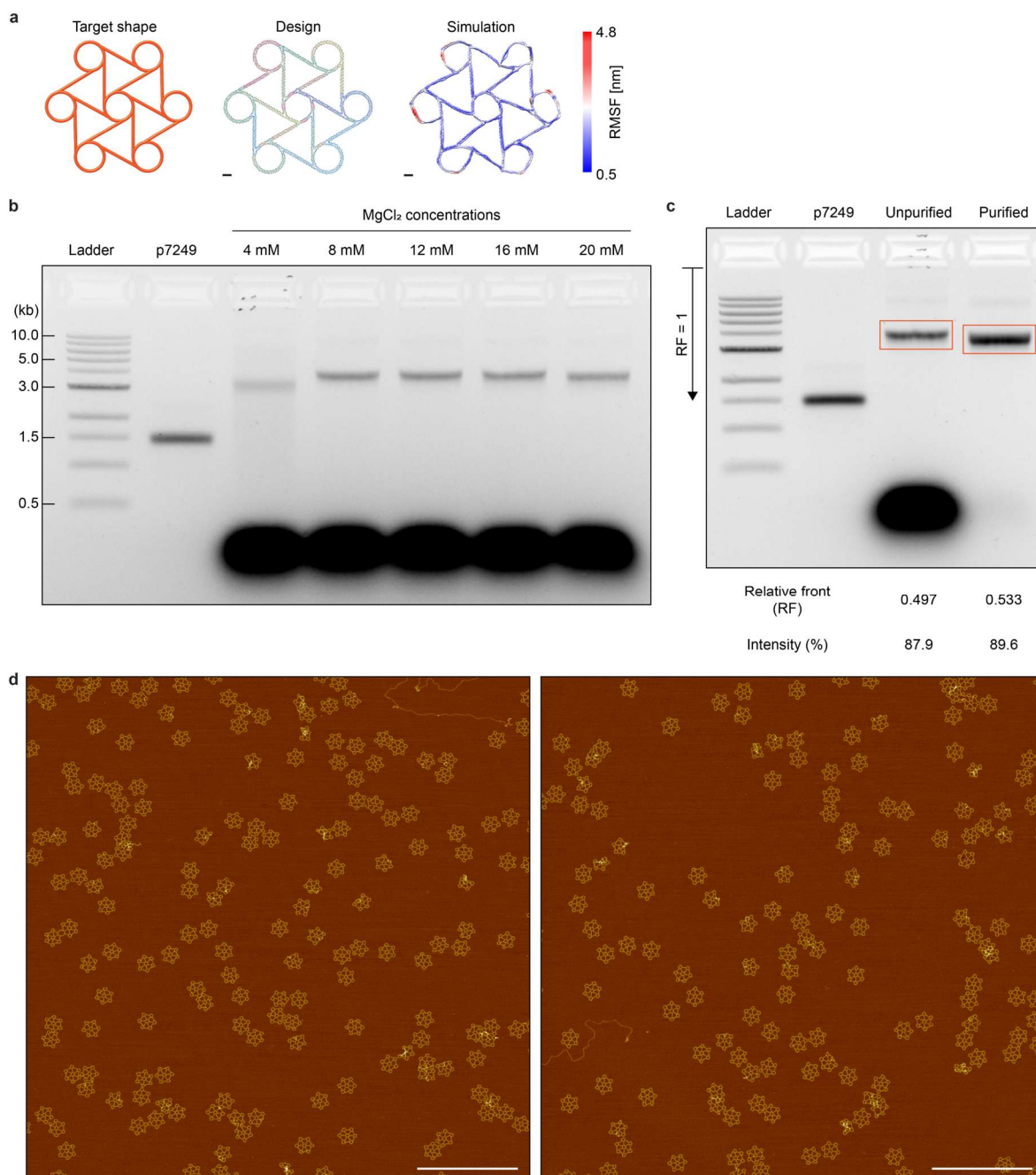
Supplementary Figure 33. Experimental results of dog side face.

a, Target shape, pseudo-atomic model of the design, and SNUPI-based simulation result. (Scale bars, 10 nm) **b**, Overall structural quality under varying MgCl_2 concentrations (4 – 20 mM) and **c**, comparison of the structure before and after purification by ultrafiltration following annealing in 12 mM MgCl_2 , analyzed by gel electrophoresis. **d**, Representative AFM images of the structures (Scale bars, 1 μm). Uncropped gel images with molecular weight markers are provided in the Source Data and Supplementary Fig. 46. Gel electrophoresis experiments were repeated independently twice with similar results, and representative images are shown. AFM imaging was performed independently at least three times with similar results, and representative images are shown. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.



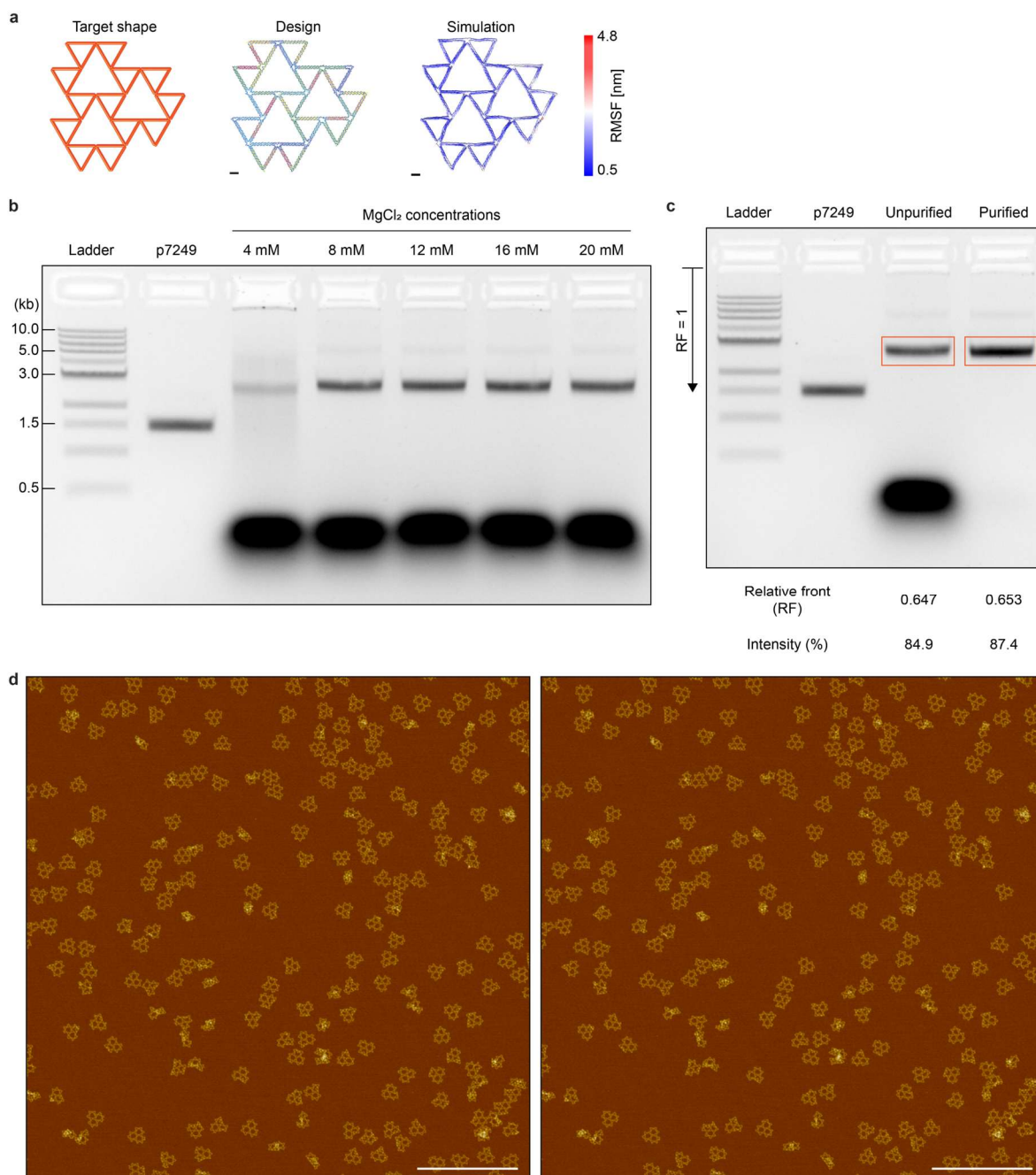
Supplementary Figure 34. Experimental results of the design inspired by OpenAI logo.

a, Target shape, pseudo-atomic model of the design, and SNUPI-based simulation result. Design inspired by the OpenAI logo (OpenAI is not affiliated with or does not endorse this work). (Scale bars, 10 nm) **b**, Overall structural quality under varying MgCl_2 concentrations (4 – 20 mM) and **c**, comparison of the structure before and after purification by ultrafiltration following annealing in 12 mM MgCl_2 , analyzed by gel electrophoresis. **d**, Representative AFM images of the structures (Scale bars, 1 μm). Uncropped gel images with molecular weight markers are provided in the Source Data and Supplementary Fig. 46. Gel electrophoresis experiments were repeated independently twice with similar results, and representative images are shown. AFM imaging was performed independently at least three times with similar results, and representative images are shown. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.



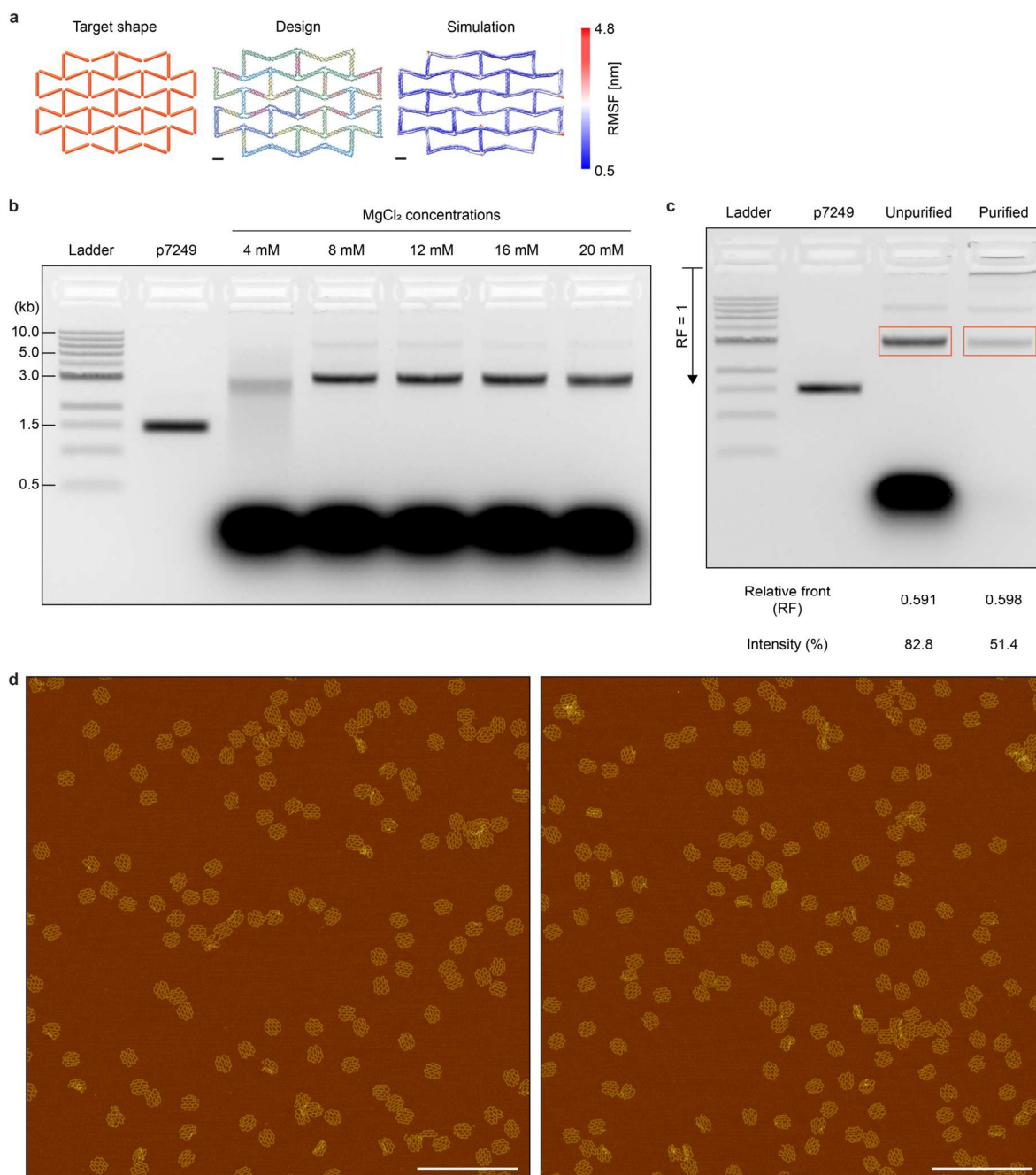
Supplementary Figure 35. Experimental results of hexa-chiral auxetic structure.

a, Target shape, pseudo-atomic model of the design, and SNUPI-based simulation result. (Scale bars, 10 nm) **b**, Overall structural quality under varying MgCl_2 concentrations (4 – 20 mM) and **c**, comparison of the structure before and after purification by ultrafiltration following annealing in 12 mM MgCl_2 , analyzed by gel electrophoresis. **d**, Representative AFM images of the structures (Scale bars, 1 μm). Uncropped gel images with molecular weight markers are provided in the Source Data and Supplementary Fig. 46. Gel electrophoresis experiments were repeated independently twice with similar results, and representative images are shown. AFM imaging was performed independently at least three times with similar results, and representative images are shown. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.



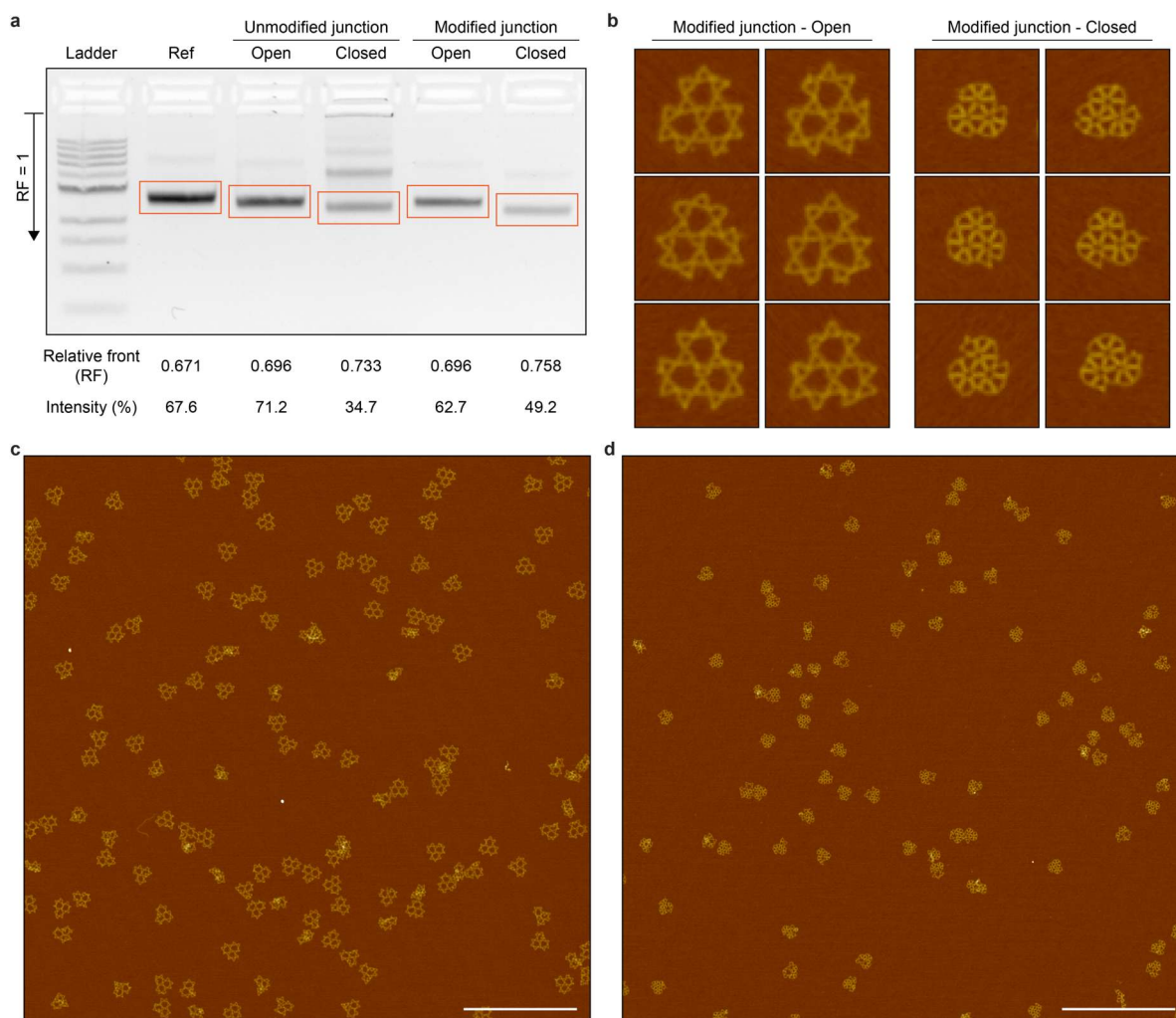
Supplementary Figure 36. Experimental results of rotating triangle auxetic structure.

a, Target shape, pseudo-atomic model of the design, and SNUPI-based simulation result. (Scale bars, 10 nm) **b**, Overall structural quality under varying MgCl_2 concentrations (4 – 20 mM) and **c**, comparison of the structure before and after purification by ultrafiltration following annealing in 12 mM MgCl_2 , analyzed by gel electrophoresis. **d**, Representative AFM images of the structures (Scale bars, 1 μm). Uncropped gel images with molecular weight markers are provided in the Source Data and Supplementary Fig. 46. Gel electrophoresis experiments were repeated independently twice with similar results, and representative images are shown. AFM imaging was performed independently at least three times with similar results, and representative images are shown. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.



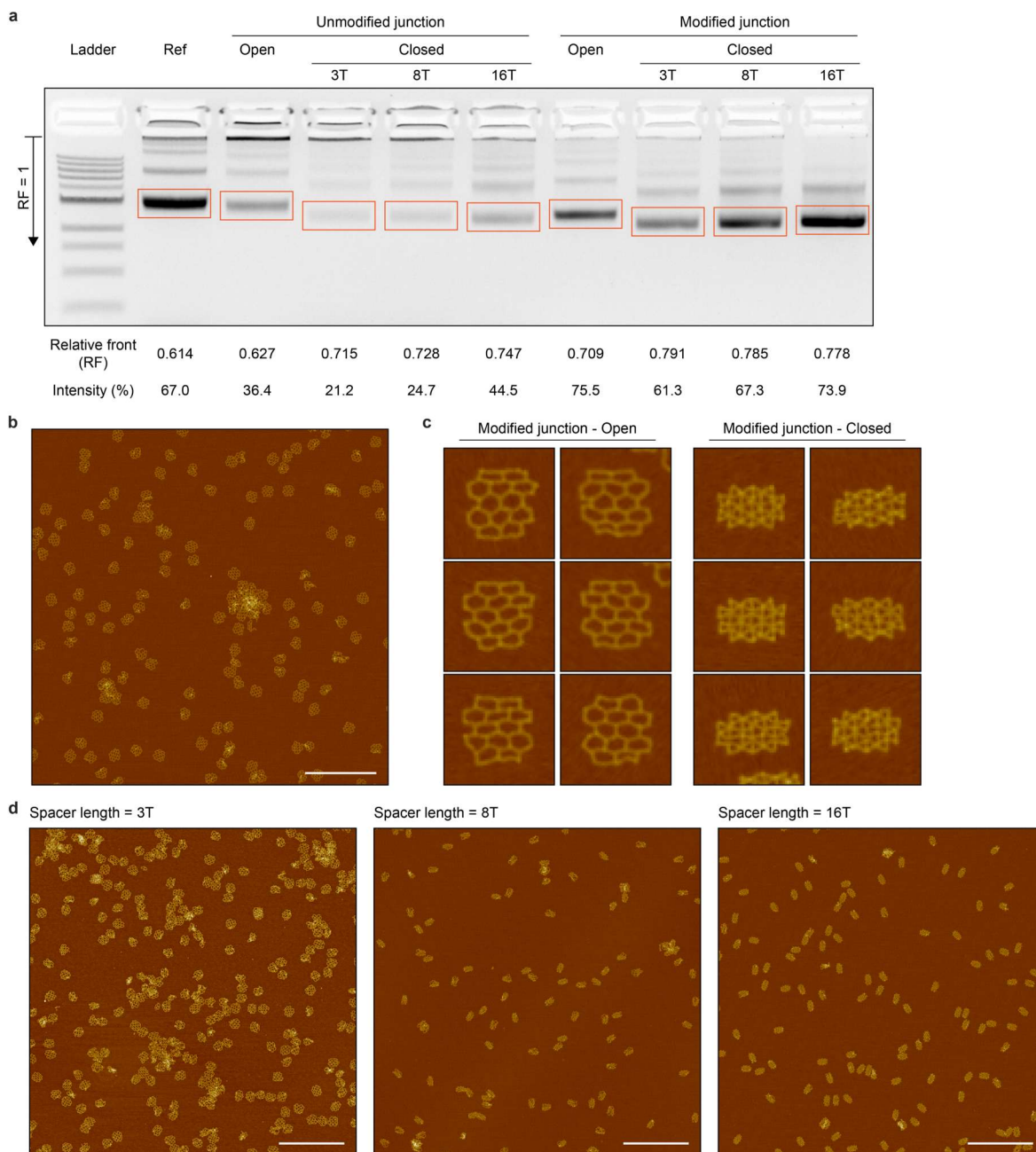
Supplementary Figure 37. Experimental results of re-entrant auxetic structure.

a, Target shape, pseudo-atomic model of the design, and SNUPI-based simulation result. (Scale bars, 10 nm) **b**, Overall structural quality under varying MgCl_2 concentrations (4 – 20 mM) and **c**, comparison of the structure before and after purification by ultrafiltration following annealing in 12 mM MgCl_2 , analyzed by gel electrophoresis. **d**, Representative AFM images of the structures (Scale bars, 1 μm). Uncropped gel images with molecular weight markers are provided in the Source Data and Supplementary Fig. 46. Gel electrophoresis experiments were repeated independently twice with similar results, and representative images are shown. AFM imaging was performed independently at least three times with similar results, and representative images are shown. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.



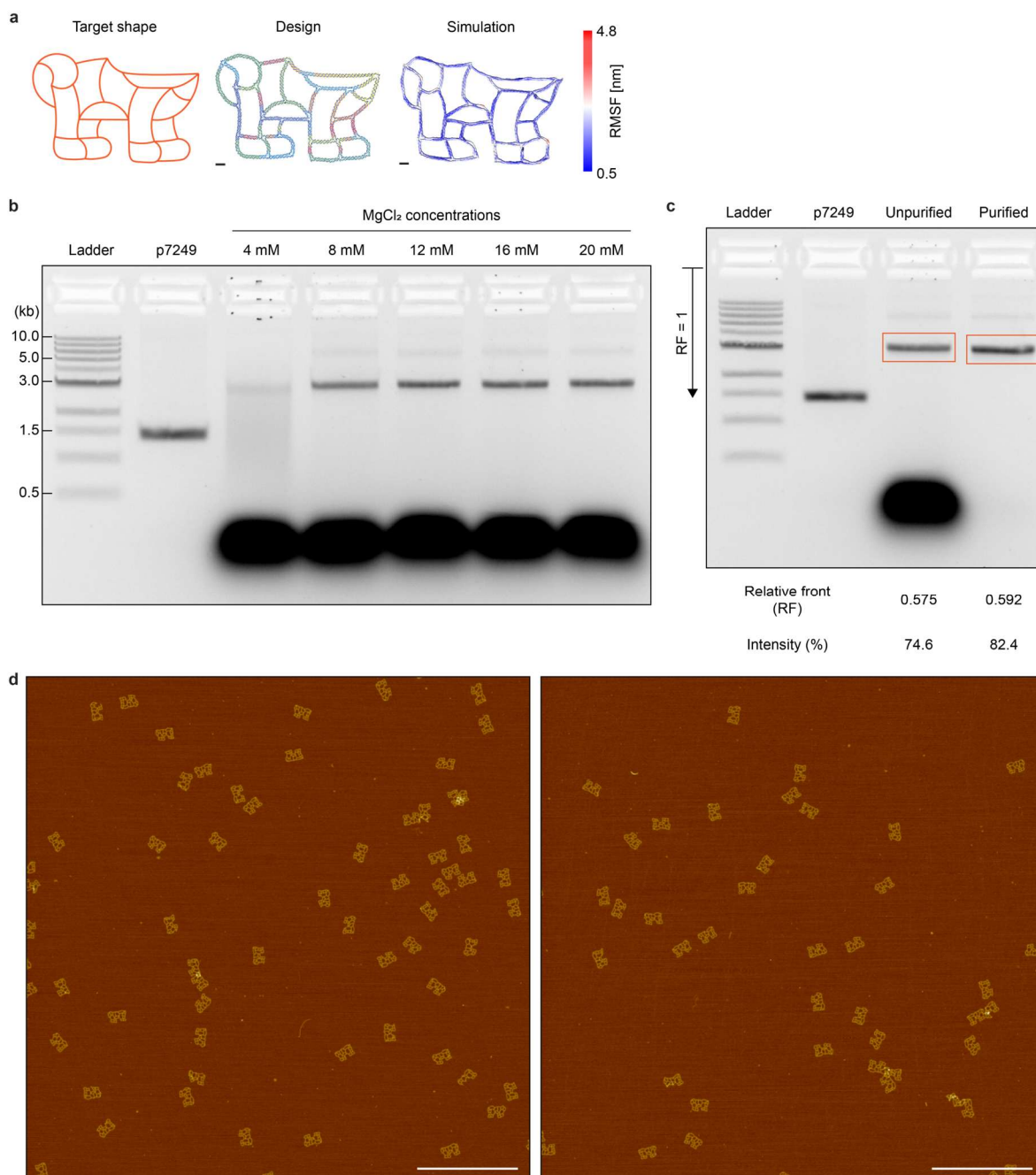
Supplementary Figure 38. Open and closed state of rotating triangle auxetic structure.

a, Comparison of overall structural quality in terms of band migration and monomer/multimer formation, analyzed by gel electrophoresis (*Ref*: reference structure without any modifications). Relative front and intensity value correspond to the most migrated monomer band. **b**, Representative cropped monomer images of open and closed states with modified junctions (image size 250 nm × 250 nm). **c**, Representative AFM images of open state and **d**, closed state with modified junctions (Scale bars, 1 μm). Uncropped gel images with molecular weight markers are provided in the Source Data and Supplementary Fig. 46. Gel electrophoresis experiments were repeated independently twice with similar results, and representative images are shown. AFM imaging was performed independently at least three times with similar results, and representative images are shown.



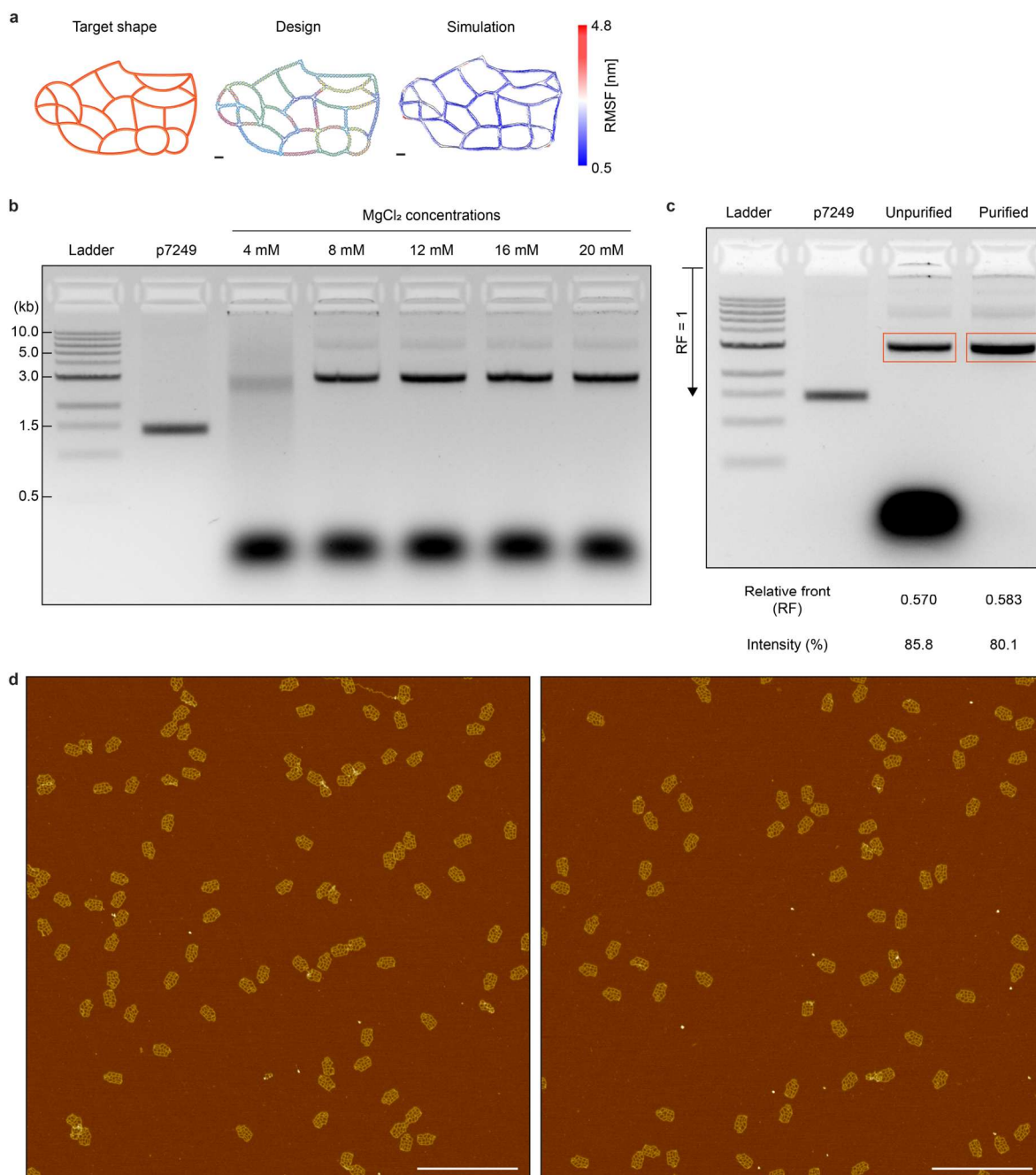
Supplementary Figure 39. Open and closed state of re-entrant auxetic structure.

a, Comparison of overall structural quality in terms of band migration and monomer/multimer formation, analyzed by gel electrophoresis (*Ref*: reference structure without any modifications; *3T*, *8T*, and *16T*: indicating the spacer length within the connector). Relative front and intensity value correspond to the most migrated monomer band. **b**, Representative AFM images of open state. **c**, Representative cropped monomer images of open and closed states with modified junctions (image size 250 nm × 250 nm). **d**, Representative AFM images of closed state with modified junctions (Scale bars, 1 μm). Uncropped gel images with molecular weight markers are provided in the Source Data and Supplementary Fig. 46. Gel electrophoresis experiments were repeated independently twice with similar results, and representative images are shown. AFM imaging was performed independently at least three times with similar results, and representative images are shown.



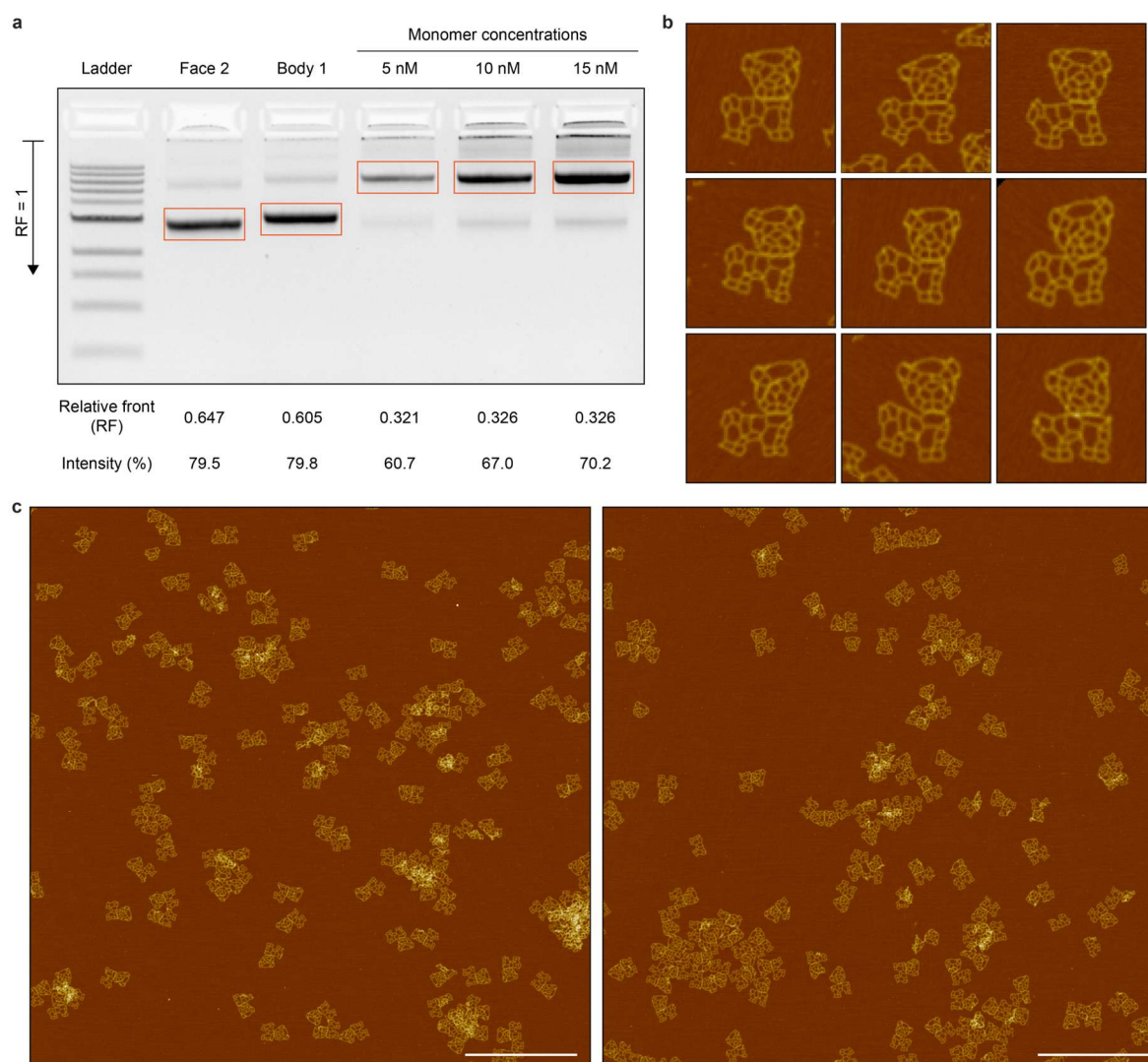
Supplementary Figure 40. Experimental results of dog body 1.

a, Target shape, pseudo-atomic model of the design, and SNUPI-based simulation result. (Scale bars, 10 nm) **b**, Overall structural quality under varying MgCl_2 concentrations (4 – 20 mM) and **c**, comparison of the structure before and after purification by ultrafiltration following annealing in 12 mM MgCl_2 , analyzed by gel electrophoresis. **d**, Representative AFM images of the structures (Scale bars, 1 μm). Uncropped gel images with molecular weight markers are provided in the Source Data and Supplementary Fig. 46. Gel electrophoresis experiments were repeated independently twice with similar results, and representative images are shown. AFM imaging was performed independently at least three times with similar results, and representative images are shown. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.



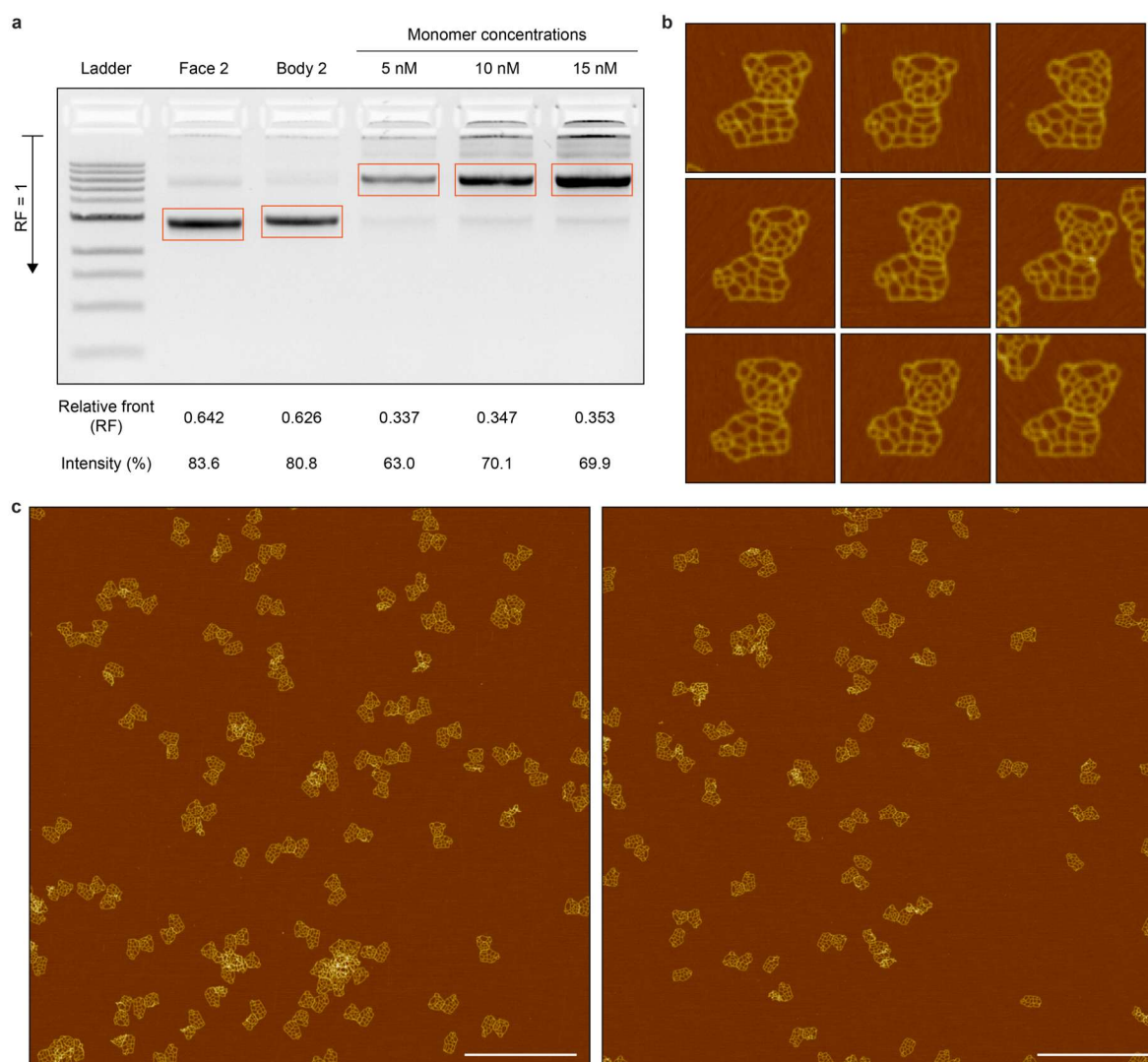
Supplementary Figure 41. Experimental results of dog body 2.

a, Target shape, pseudo-atomic model of the design, and SNUPI-based simulation result. (Scale bars, 10 nm) **b**, Overall structural quality under varying MgCl₂ concentrations (4 – 20 mM) and **c**, comparison of the structure before and after purification by ultrafiltration following annealing in 12 mM MgCl₂, analyzed by gel electrophoresis. **d**, Representative AFM images of the structures (Scale bars, 1 μ m). Uncropped gel images with molecular weight markers are provided in the Source Data and Supplementary Fig. 46. Gel electrophoresis experiments were repeated independently twice with similar results, and representative images are shown. AFM imaging was performed independently at least three times with similar results, and representative images are shown. Molecular graphics were generated using UCSF Chimera²⁵, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from NIH P41-GM103311.



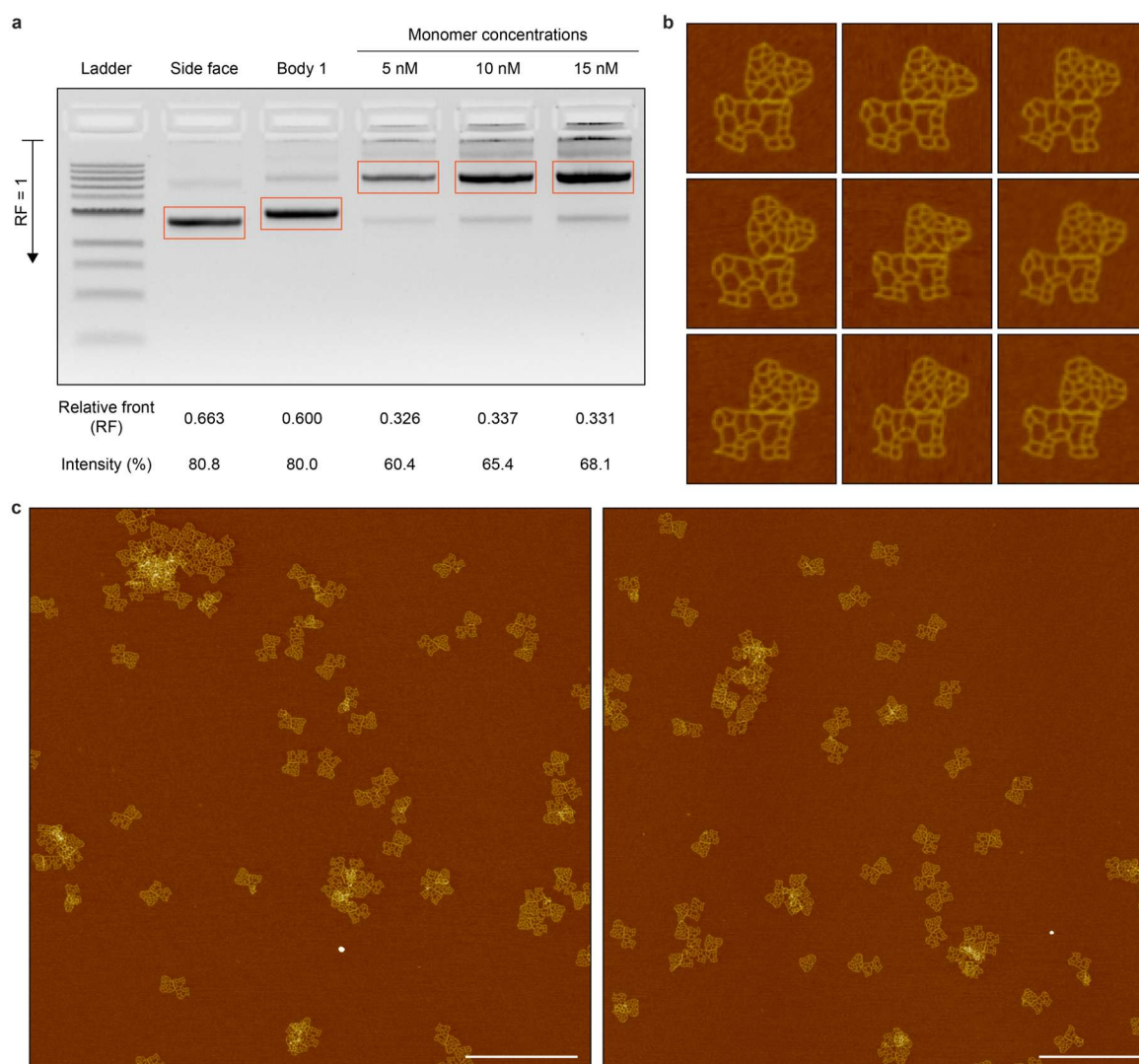
Supplementary Figure 42. Dimerized dog structure composed of face 2 and body 1.

a, Comparison of overall structural quality in terms of band migration and dimer formation, analyzed by gel electrophoresis (*Concentrations indicating the structure concentration when mixing two modules*). **b**, Representative cropped images of the modularized structure (image size 350 nm × 350 nm). **c**, Representative AFM images of modularized structure (Scale bars, 1 μm). Uncropped gel images with molecular weight markers are provided in the Source Data and Supplementary Fig. 46. Gel electrophoresis experiments were repeated independently twice with similar results, and representative images are shown. AFM imaging was performed independently at least three times with similar results, and representative images are shown.



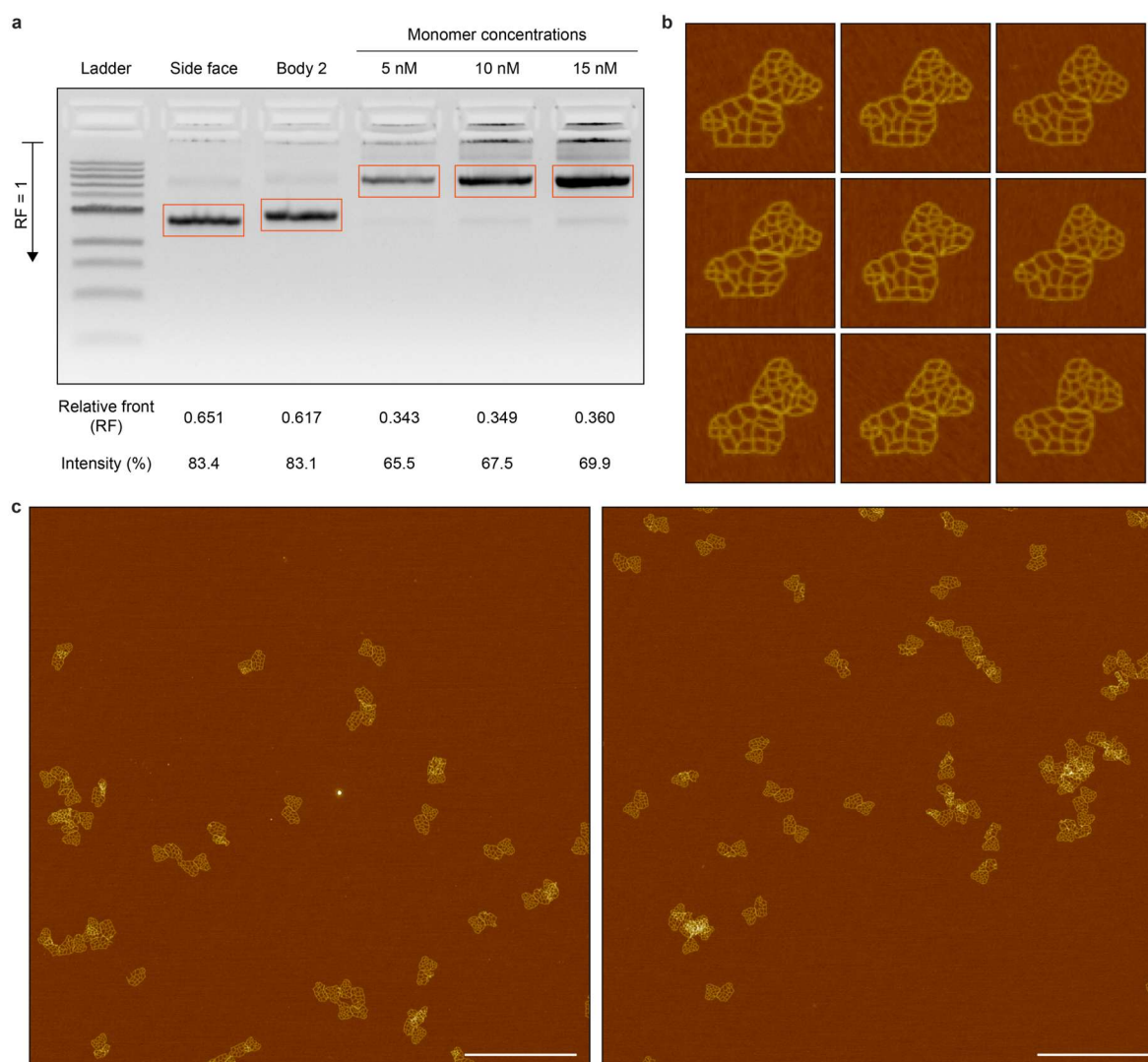
Supplementary Figure 43. Dimerized dog structure composed of face 2 and body 2.

a, Comparison of overall structural quality in terms of band migration and dimer formation, analyzed by gel electrophoresis (*Concentrations indicating the structure concentration when mixing two modules*). **b**, Representative cropped images of the modularized structure (image size 350 nm × 350 nm). **c**, Representative AFM images of modularized structure (Scale bars, 1 μm). Uncropped gel images with molecular weight markers are provided in the Source Data and Supplementary Fig. 46. Gel electrophoresis experiments were repeated independently twice with similar results, and representative images are shown. AFM imaging was performed independently at least three times with similar results, and representative images are shown.



Supplementary Figure 44. Dimerized dog structure composed of side face and body 1.

a, Comparison of overall structural quality in terms of band migration and dimer formation, analyzed by gel electrophoresis (*Concentrations indicating the structure concentration when mixing two modules*). **b**, Representative cropped images of the modularized structure (image size 350 nm × 350 nm). **c**, Representative AFM images of modularized structure (Scale bars, 1 μ m). Uncropped gel images with molecular weight markers are provided in the Source Data and Supplementary Fig. 46. Gel electrophoresis experiments were repeated independently twice with similar results, and representative images are shown. AFM imaging was performed independently at least three times with similar results, and representative images are shown.



Supplementary Figure 45. Dimerized dog structure composed of side face and body 2.

a, Comparison of overall structural quality in terms of band migration and dimer formation, analyzed by gel electrophoresis (*Concentrations indicating the structure concentration when mixing two modules*). **b**, Representative cropped images of the modularized structure (image size 350 nm × 350 nm). **c**, Representative AFM images of modularized structure (Scale bars, 1 μ m). Uncropped gel images with molecular weight markers are provided in the Source Data and Supplementary Fig. 46. Gel electrophoresis experiments were repeated independently twice with similar results, and representative images are shown. AFM imaging was performed independently at least three times with similar results, and representative images are shown.

Figure 4a. Face 1, Supp Fig 28c

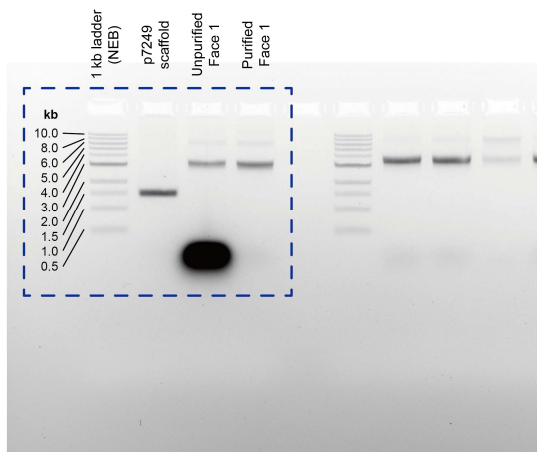


Figure 4a. Face 2, Supp Fig 29c

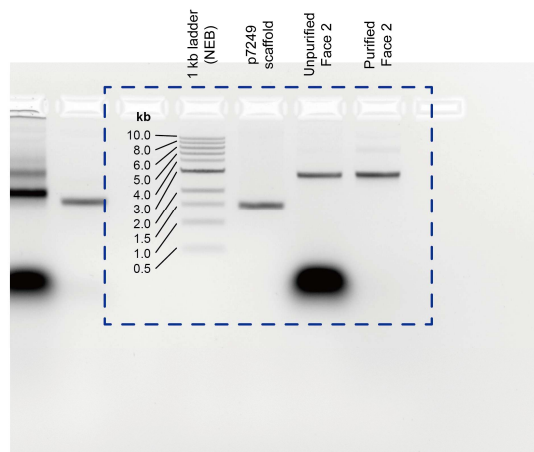


Figure 1c, Figure 4b (i), Supp Fig 30c

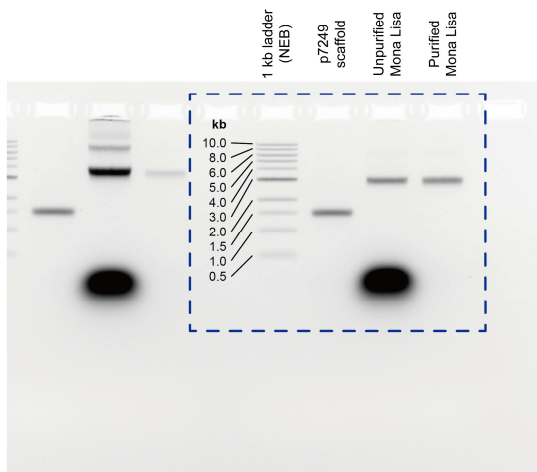


Figure 4b (ii), Supp Fig 31c

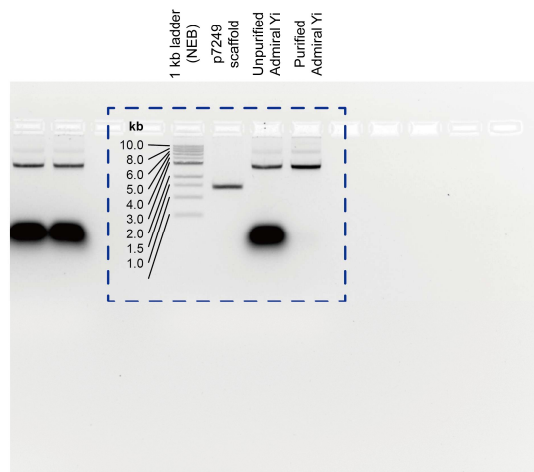


Figure 4b (iii), Supp Fig 32c

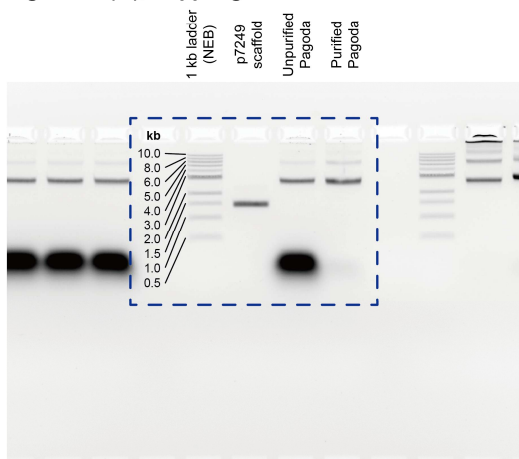
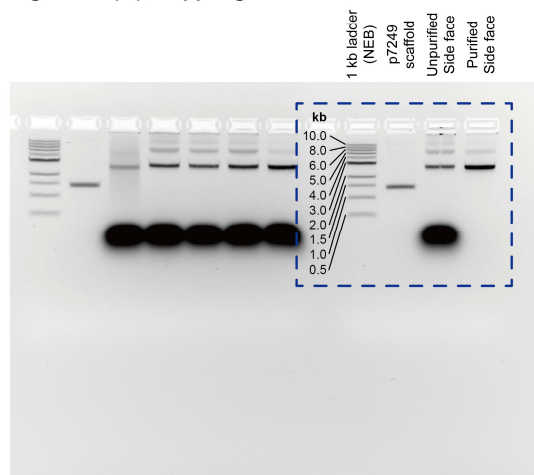


Figure 4b (iv), Supp Fig 33c



Supplementary Figure 46. Uncropped gel electrophoresis images (continued).

Figure 4b (v), Supp Fig 34c

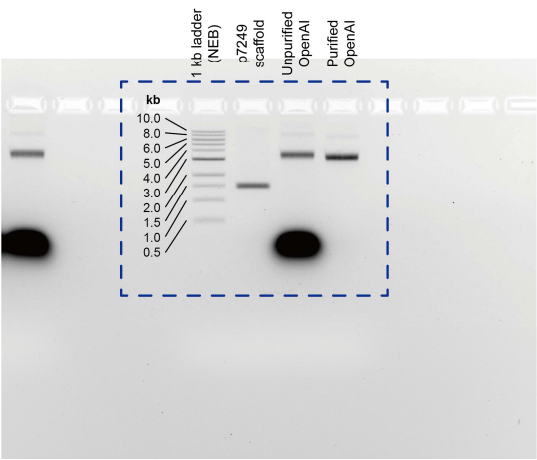


Figure 4b (vi), Supp Fig 35c

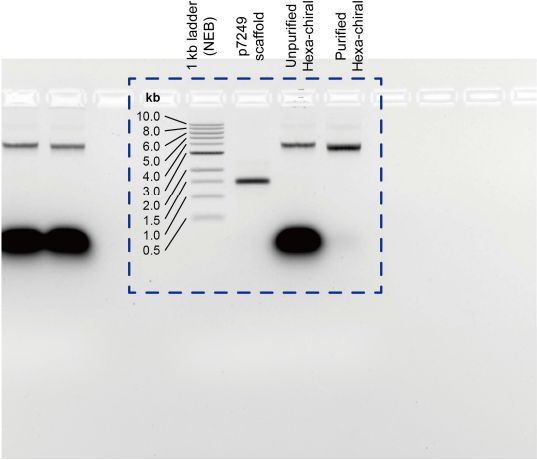


Figure 4b (vii), Supp Fig 36c

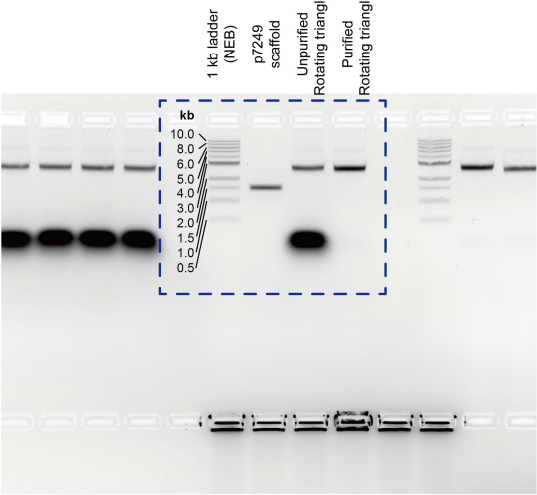
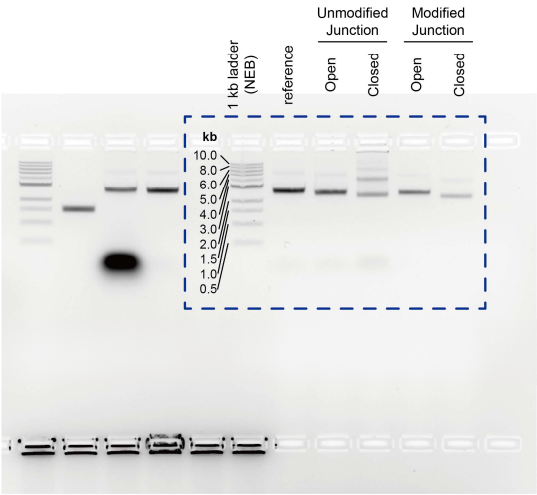


Figure 5a, Supp Fig 17, Supp Fig 38a



Supplementary Figure 46. Uncropped gel electrophoresis images (continued).

Figure 5g. Face 2 + Body 1, Supp Fig 42a

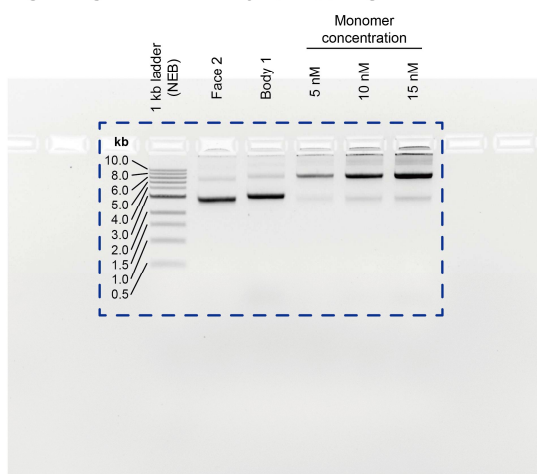


Figure 5g. Face 2 + Body 2, Supp Fig 43a

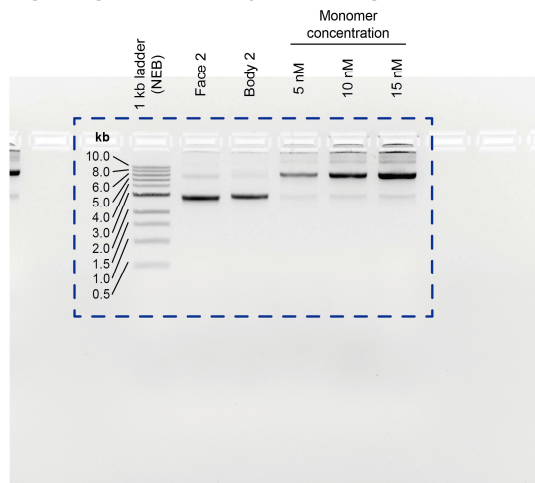


Figure 5g. Side face + Body 1, Supp Fig 44a

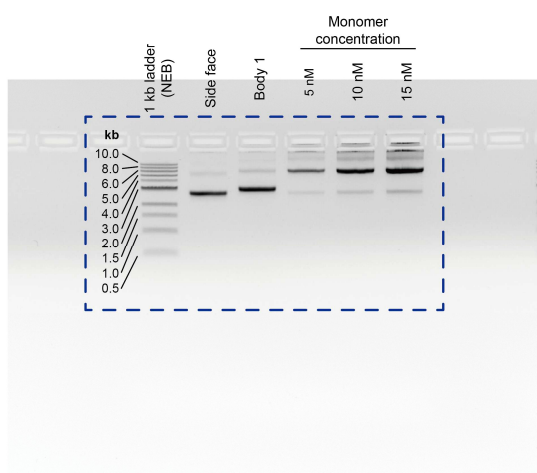
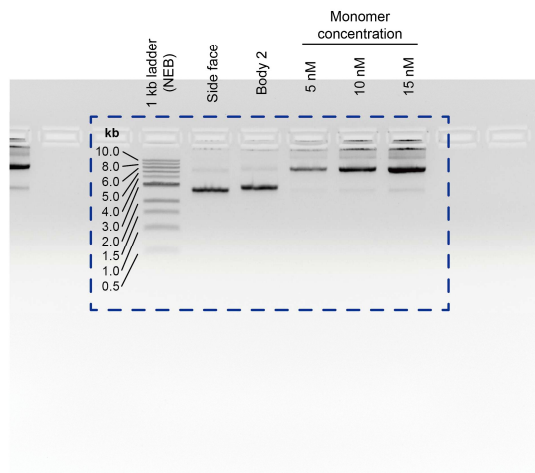
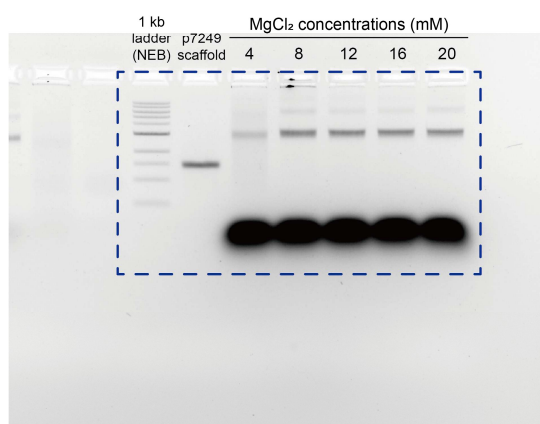


Figure 5g. Side face + Body 2, Supp Fig 45a

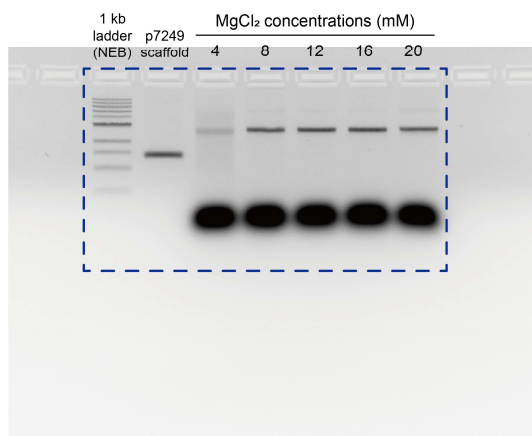


Supplementary Figure 46. Uncropped gel electrophoresis images (continued).

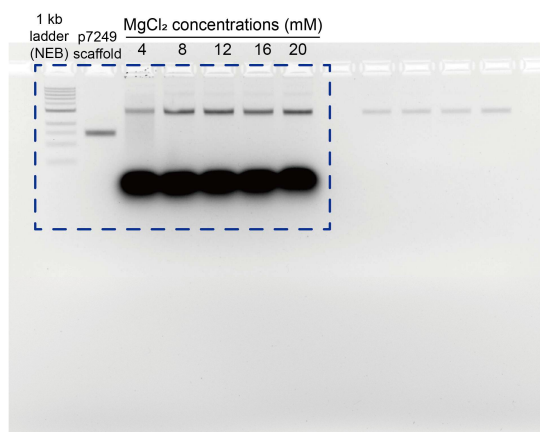
Supp Fig 28b



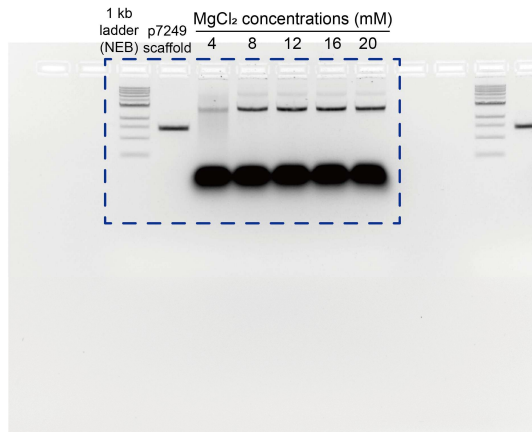
Supp Fig 29b



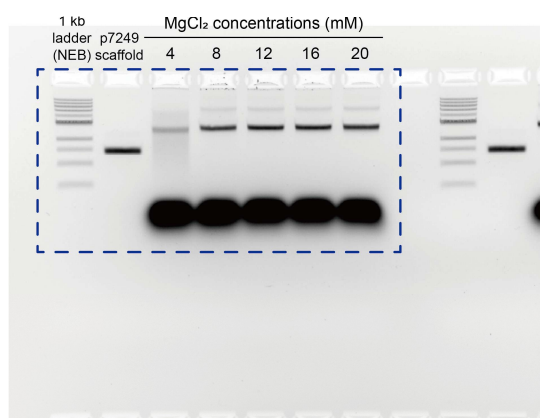
Supp Fig 30b



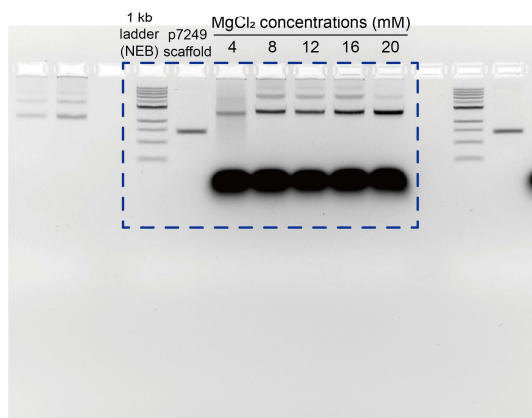
Supp Fig 31b



Supp Fig 32b

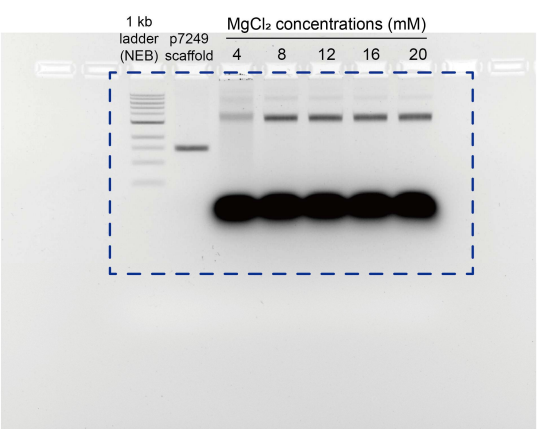


Supp Fig 33b

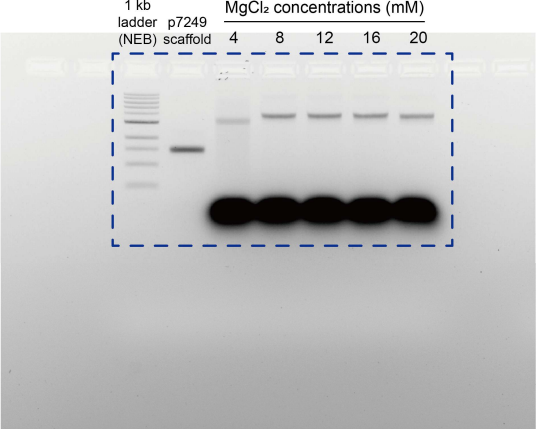


Supplementary Figure 46. Uncropped gel electrophoresis images (continued).

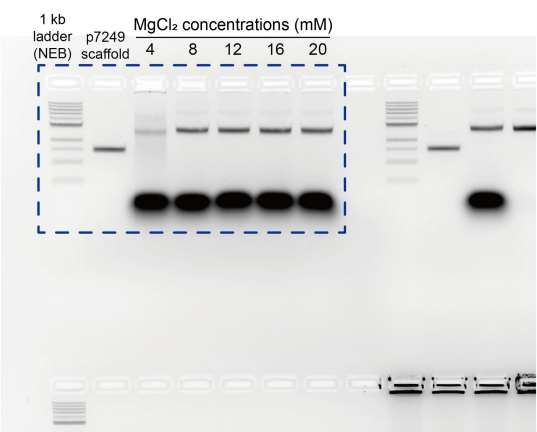
Supp Fig 34b



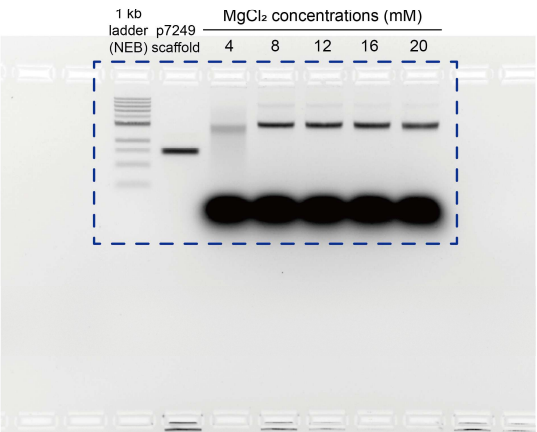
Supp Fig 35b



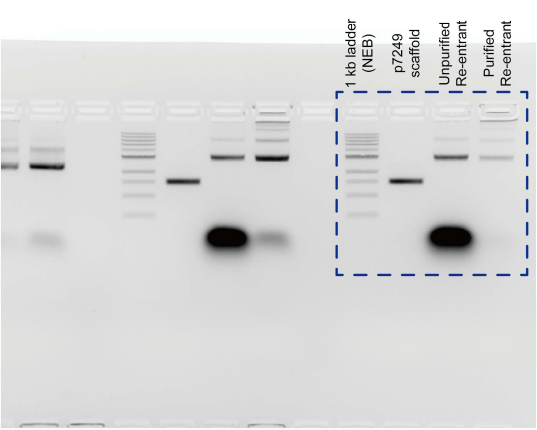
Supp Fig 36b



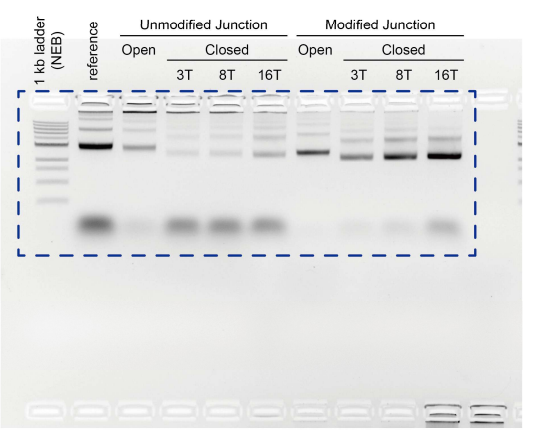
Supp Fig 37b



Supp Fig 37c

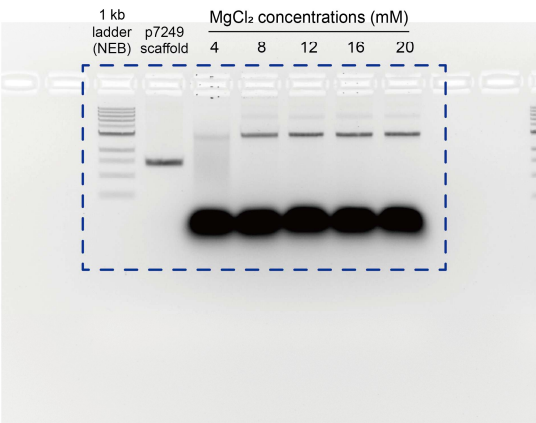


Supp Fig 39a

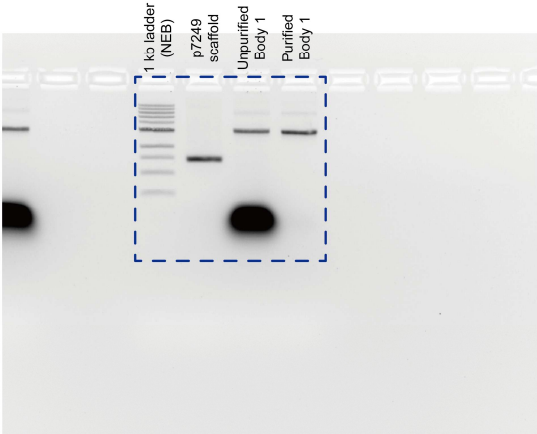


Supplementary Figure 46. Uncropped gel electrophoresis images (continued).

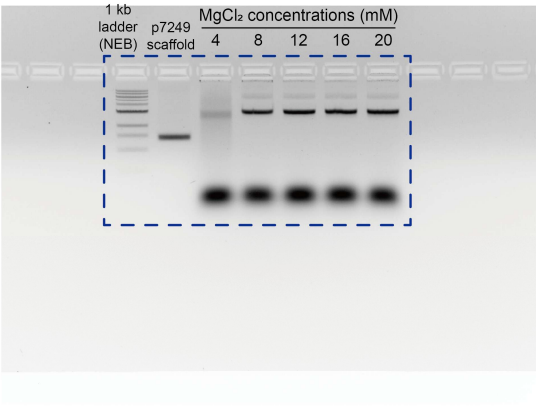
Supp Fig 40b



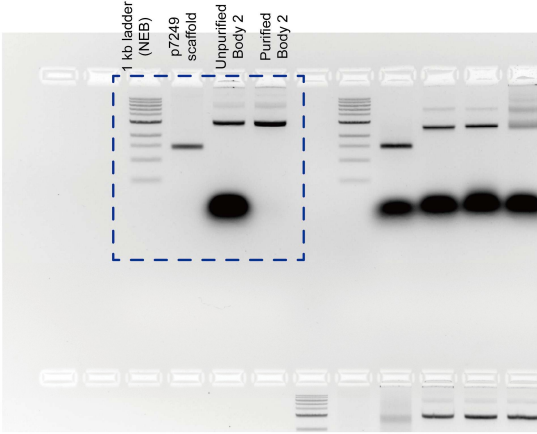
Supp Fig 40c



Supp Fig 41b



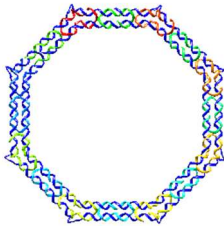
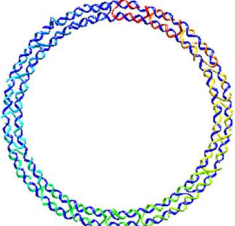
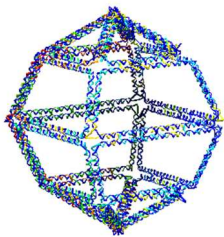
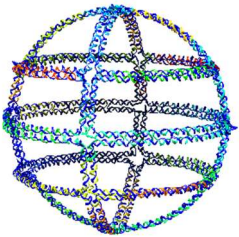
Supp Fig 41c



Supplementary Figure 46. Uncropped gel electrophoresis images (continued).

Supplementary Tables

Supplementary Table 1. Comparison of conventional 2HB-edge wireframe design methods with Generative SNUPI

	DAEDALUS [26]	PERDIX [14]	This study
Design method	Deterministic (Spanning tree algorithm)	Deterministic (Rendering dual graph and spanning tree algorithm)	Combined generative diffusion model and deterministic sequence design (similar to PERDIX)
Edge type	2HB	2HB	2HB
Input geometry	3D wireframe polyhedron	2D wireframe	2D or 3D wireframe
Edge constraints	Multiples of 10.5 bps	Arbitrary edge length (Minimum = 42bp)	Arbitrary edge length
Vertex angles	Uniform	Variable	Variable
Crossover regularity	Regular	Regular	Irregular
Edge curvature allowance	No	No	Yes
Example (2D) (Similar scaffold length)	N/A	Circle-like design (Segmented edge)  Scaffold length = 744nt	Circular design (Curved edge)  Scaffold length = 758nt
Example (3D) (Similar scaffold length)	Sphere-like design (Segmented edge)  Scaffold length = 5279nt	N/A	Sphere design (Curved edge)  Scaffold length = 4919nt
Input file type	PLY	PLY	SVG, PLY, STL, PT
Output file type	Sequence list (CSV), CanDo, BILD, PDB, caDNAno(JSON)	Sequence list (CSV), CanDo, BILD, PDB, caDNAno(JSON)	CanDo, BILD, oxDNA, PDB, PyTorch tensors
User interfaces	Command line based	Command line based	Command line based

Supplementary Table 2. Design gallery.

Index	Name	Number of base pairs	Wasserstain Distance [nm]	RMSD [nm]	Average RMSF [nm]
1	AI brain symbol_v1	6829	1.411	2.312	1.692
2	AI brain symbol_v2	6984	1.149	2.596	1.656
3	AI brain symbol_v3	6850	2.599	1.917	1.670
4	AI brain symbol_v4	6768	1.935	1.619	1.670
5	Albert Einstein	9031	3.074	2.444	1.706
6	Anti-tetra chiral honeycomb	6491	2.834	1.845	1.768
7	Anti-tri chiral honeycomb	6610	1.376	2.123	2.062
8	Re-entrant v1	6829	1.060	1.293	1.612
9	Re-entrant v2	6937	0.949	1.219	1.590
10	Auxetic spiral	6510	1.296	4.719	2.277
11	Auxetic stretch	7076	1.979	9.567	2.043
12	Auxetic triangle 3units	6810	1.191	1.259	1.560
13	Auxetic triangle 4units	6582	1.640	1.934	1.706
14	Butterfly	6207	2.072	2.189	1.696
15	Circle	752	0.730	1.783	1.736
16	Circular double helix v1	6907	1.013	2.702	1.944
17	Circular double helix v2	6967	1.178	3.580	1.795
18	Cone	4489	0.802	2.747	1.592
19	Cylinder	3290	0.704	2.816	1.808
20	Cylinder auxetic v1	7064	0.913	1.490	1.732
21	Cylinder auxetic v2	4419	1.133	2.322	1.833
22	Cylinder helix	4272	2.010	5.047	1.687
23	Dancheong symbol	6722	2.831	1.904	1.627
24	Dog body 01	6928	1.251	2.022	1.686
25	Dog body 02	6946	1.698	1.735	1.678
26	Dog body 03	6927	1.647	1.462	1.571
27	Dog face 01	6863	1.456	3.090	1.672
28	Dog face 02 v0	6875	1.901	1.664	1.689
29	Dog face 02 v1	6897	2.399	1.552	1.404
30	Dog Face 03	6886	3.299	1.878	1.627
31	Dog sideface 01	6936	2.769	1.960	1.647
32	Dog sideface 02	6848	1.307	1.627	1.729
33	Dog sideface 03	6927	6.396	2.208	1.638
34	Dog sideface 04	6957	2.525	2.230	1.624
35	Ellipsoid v1	6521	2.275	2.903	1.718
36	Ellipsoid v2	6860	3.055	2.130	1.752
37	Flower art	6939	3.850	1.757	1.689
38	Flower logo	1966	0.778	1.942	2.229
39	Flower ori twist (40% folded)	6996	4.797	1.618	1.632
40	Gyeongbokgung palace v1	6983	3.935	2.079	1.659
41	Gyeongbokgung palace v2	6921	3.090	1.919	1.628

42	Gyeongbokgung palace v3	7048	3.572	1.789	1.630
43	Hexa chiral close	6993	1.312	2.456	1.806
44	Hexa chiral open	6877	0.956	1.716	1.765
45	Hummingbird	6847	1.714	2.013	1.661
46	Korean traditional symbol v1	6715	0.902	2.049	1.381
47	Korean traditional symbol v2	6786	3.430	1.825	1.669
48	Maltese dog v1	7860	2.201	2.932	1.758
49	Maltese dog v2	6948	2.135	2.881	1.799
50	Maltese dog v3	6989	2.232	2.533	1.694
51	Mickey	2974	1.068	2.963	1.838
52	Mickey mesh	7073	3.739	2.129	1.554
53	Miura ori_2x2 (0% folded)	1851	1.240	1.659	1.658
54	Miura ori_3x3 (40% folded) v1	6953	0.878	1.812	1.662
55	Miura ori_3x3 (40% folded) v2	6848	3.241	1.370	1.532
56	Miura ori_4x (40% folded)	7105	1.112	1.592	1.663
57	Mona Lisa v1	6840	1.550	1.718	1.654
58	Mona Lisa v2	6958	1.720	1.756	1.727
59	Mona Lisa v3	6924	1.948	1.569	1.565
60	Nazca cat	3636	3.836	3.021	1.921
61	One pillar pagoda v1	6722	1.617	1.610	1.582
62	One pillar pagoda v2	6908	4.700	2.163	1.593
63	One pillar pagoda v3	6908	2.044	1.390	1.590
64	OpenAI	6974	0.933	2.738	1.779
65	Puzzle	6999	2.367	2.399	2.126
66	Sailboat	7967	1.544	2.750	1.690
67	Sea sunshine v1	6695	1.925	1.748	1.641
68	Sea sunshine v2	6817	1.932	1.693	1.711
69	Snail	4695	1.669	2.302	1.884
70	Sphere v1	4746	0.811	1.543	1.729
71	Sphere v2	6952	0.998	1.698	1.680
72	Spider-man v1	6989	1.683	3.405	1.645
73	Spider-man v2	6998	2.635	2.126	1.575
74	Spring	2894	1.909	5.622	2.031
75	Tetra-chiral	3199	1.713	4.267	1.788
76	Tetra-chiral honeycomb	6080	1.158	2.220	1.674
77	The Kiss	6869	2.376	2.126	1.567
78	The Starry Night	6852	2.704	1.795	1.689
79	Topology annulus	7399	0.929	1.581	1.619
80	Torus knots (p2q3)	7010	3.350	5.524	1.640
81	Torus knots (p2q5)	6962	8.804	3.960	1.798
82	Torus knots (p3q2)	5998	5.285	4.911	1.823
83	Torus knots (p3q2) stable v1	4027	1.226	6.997	1.853
84	Torus knots (p3q2) stable v2	6933	4.326	3.610	1.550
85	Torus knots (p5q2)	6973	2.198	4.090	1.764
86	Torus knots (p5q2) stable	5002	4.630	5.131	1.970

87	Torus knots (p6q1)	3003	0.857	4.465	2.139
88	Torus knots (p7q2)	7173	0.725	3.271	1.803
89	Tri-chiral	3011	1.256	2.715	1.761
90	Tri-chiral honeycomb	6639	1.356	2.000	1.765
91	Truck v1	5747	1.663	2.419	1.636
92	Truck v2	6946	1.520	1.958	1.787
93	Twis tower (0° rotated)	4878	1.926	2.690	1.779
94	Twis tower (25° rotated)	4618	2.126	2.303	1.659
95	Twis tower equal (0° rotated)	3838	3.702	1.066	1.718
96	Vietnamese ancient tattoo	7476	3.277	2.316	1.774
97	Admiral Yi v1	6830	2.921	1.518	1.695
98	Admiral Yi v2	6813	2.041	1.545	1.663
99	Admiral Yi v3	6918	3.181	1.737	1.700
100	Admiral Yi v4	6831	3.072	2.416	1.595

Supplementary Table 3. Unconditional success routing rate analysis

Number of base pairs	Success routing rate (%)
1000	80%
2000	42%
3000	28%
4000	18%
5000	18%
6000	16%
7000	10%
8000	6%

Supplementary Table 4. Conditional success routing rate analysis

Target Shape	Number of base pairs	Success routing rate (%)
Circle	1000	100%
Flower logo	2000	74%
Mickey	3000	78%
Cone	4000	82%
Sphere v1	5000	70%
OpenAI	6000	96%
Hexa-chiral close	7000	52%
Ellipsoid v2	8000	52%

Supplementary Table 5. Hyperparameters of generative diffusion model for DNA origami

Category	Hyperparameter	Value
Diffusion model	Linear noise schedule	$\beta_0 = 0.0001$ $\beta_T = 0.02$ $T = 500$
Graph Featurization	Node Features	Node Coordinates
	Edge Features	Relative Distance
	Number of edges per node, k	40
	Number of kNN edges	25
	Number of inverse cubic edges	15
Graph Neural Network	Number of SE(3)-Transformer layers	8
	Number of hidden degrees	2 (0,1)
	Number of hidden channels	32
	Number of attention heads	8
	Channels division	2
	Equivariant normalization	True
	Layer normalization	True
Total Number of Parameters		1.5M

Supplementary Table 6. Raw data of each modular structures

Five images were analyzed for each structure

	Number of dimers	Pixel area of dimer	Total number of structures	Total pixel area of structures	Number-based dimer yield (%)	Pixel-weighted dimer yield (%)
Face v2 + Body 1	38	45942.5	64	90742	63.5 ± 2.76	54.6 ± 2.65
	32	38143	54	81202		
	41	48780	72	94813		
	35	42443	51	75756.5		
	47	57207	63	83301.5		
Face v2 + Body 2	35	43216.5	49	70609	74.9 ± 2.60	63.3 ± 2.65
	35	43332.5	46	66402.5		
	49	59973.5	58	78505		
	43	52492.5	62	96564.5		
	47	55864	64	90749		
Side face + Body 1	54	60398.5	81	98839.5	65.3 ± 2.70	56.5 ± 2.62
	36	41027.5	58	76142		
	45	53363.5	62	87438.5		
	42	49489	63	74263.5		
	26	30633	47	79112.5		
Side face + Body 2	51	58081	74	94043.5	73.4 ± 2.37	59.0 ± 2.36
	38	46343.5	49	71674.5		
	53	62646.5	82	122464		
	57	67681	74	120159		
	57	67968.5	70	104388.5		

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