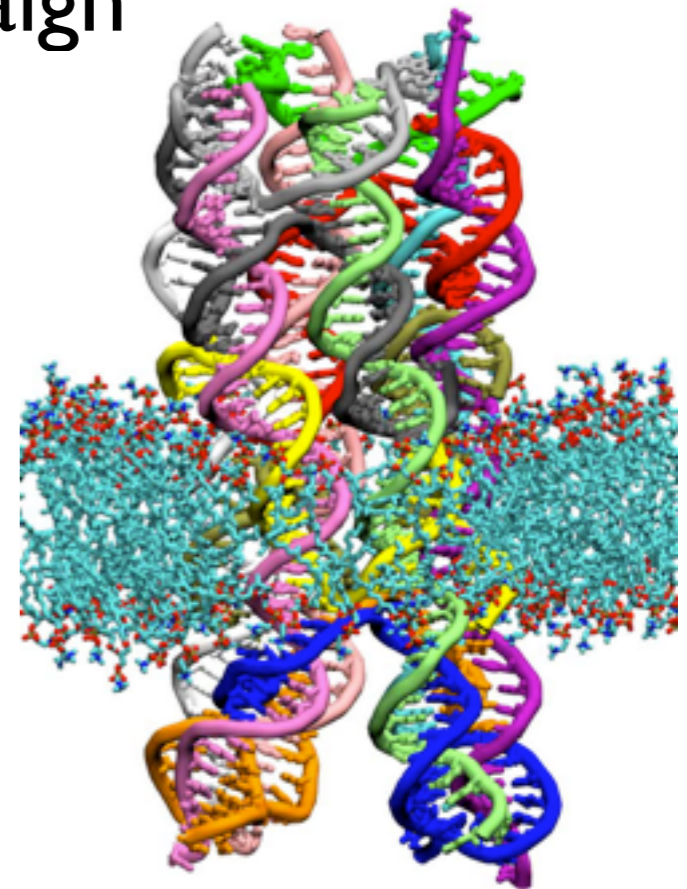
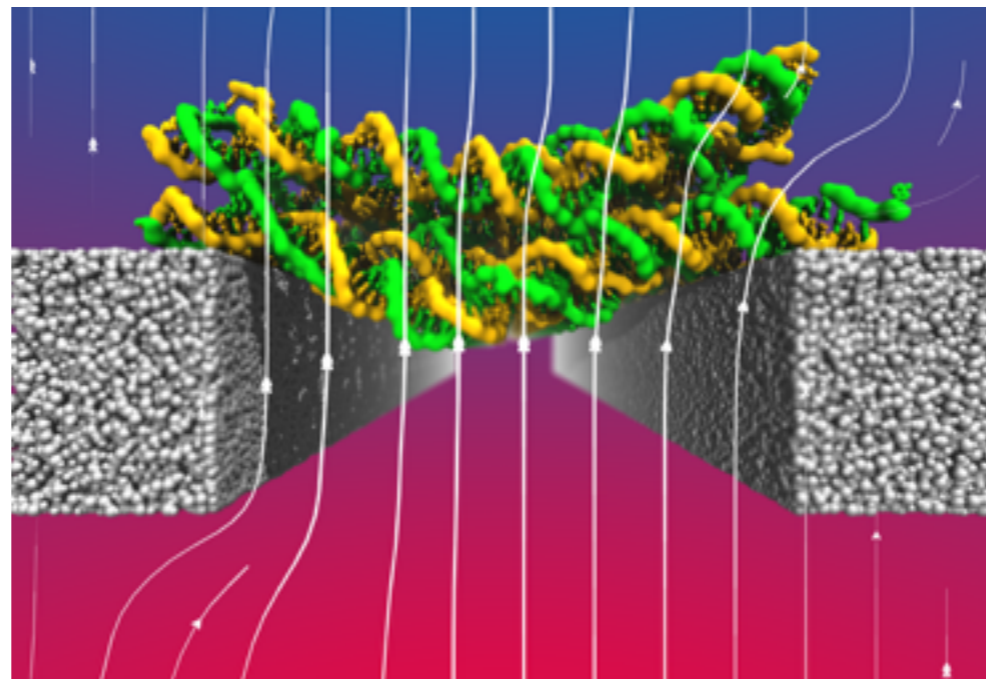
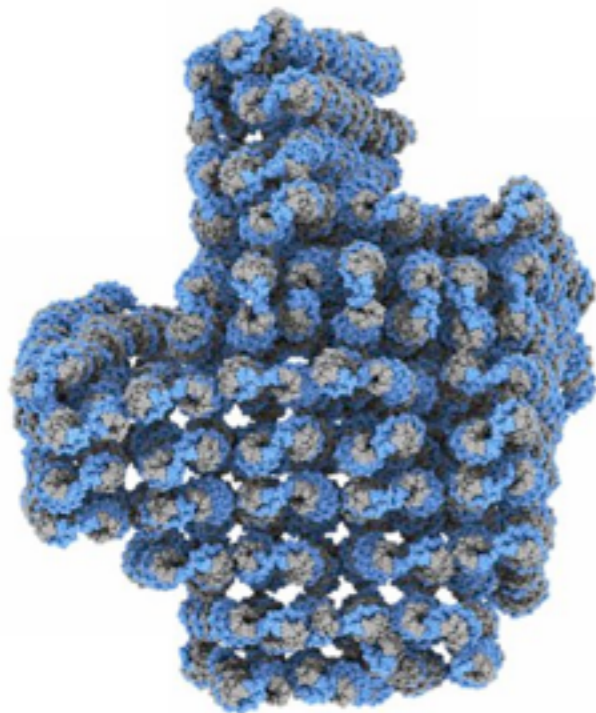


# Molecular Dynamics of DNA Origami

Aleksei Aksimentiev, Physics  
University of Illinois at Urbana-Champaign



# DNA origami

Scaffold: long ssDNA

Staple: short (17~50 bp) ssDNA, connecting different parts.

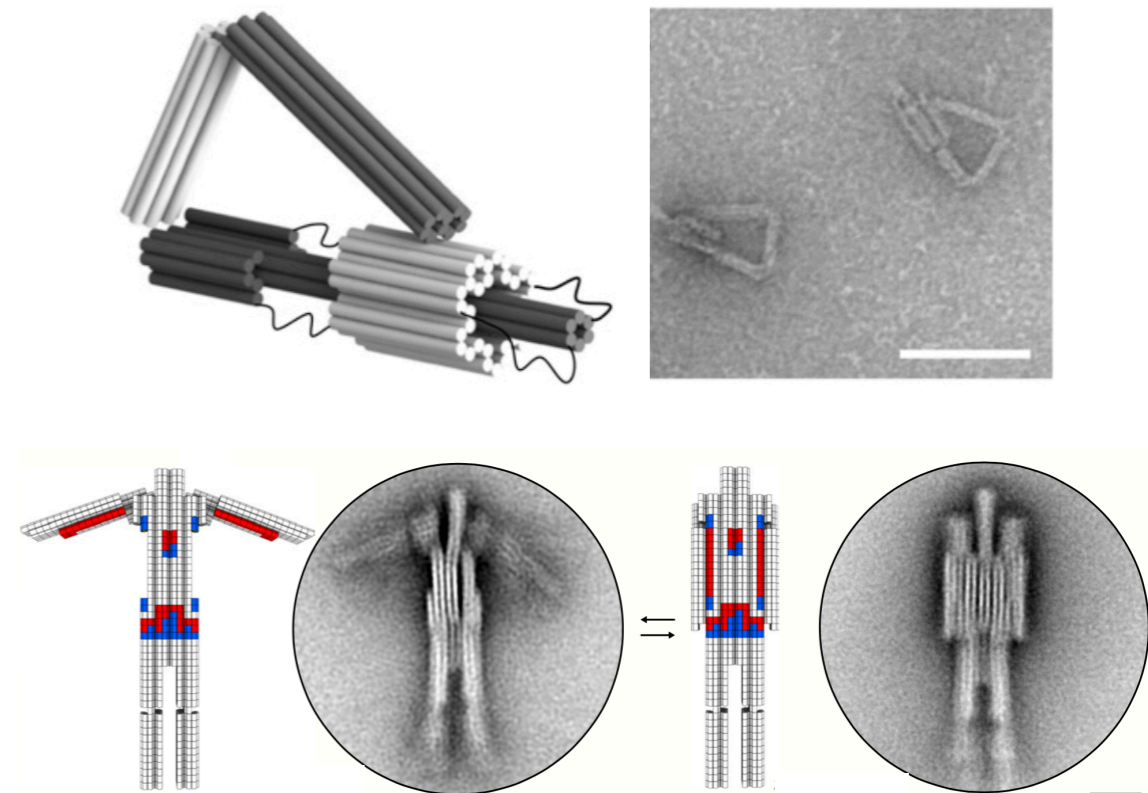
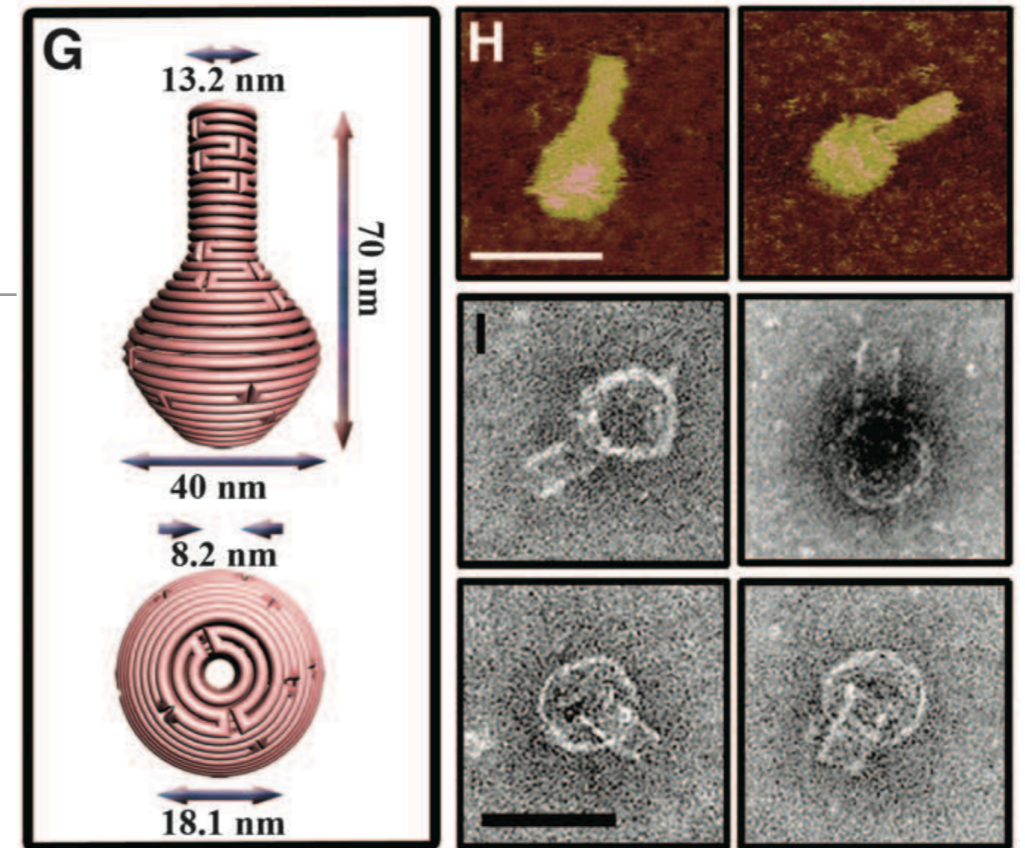


Video credit: Shawn Douglas

Han, Dongran *et al.*, *Science*, 2011, 332 (6027), 342-346.

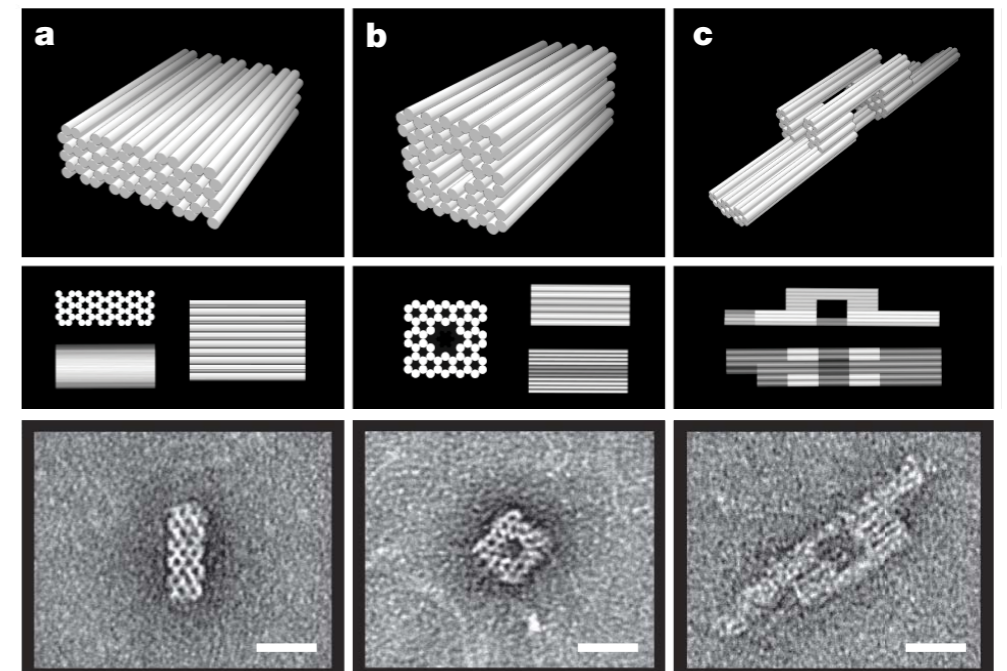
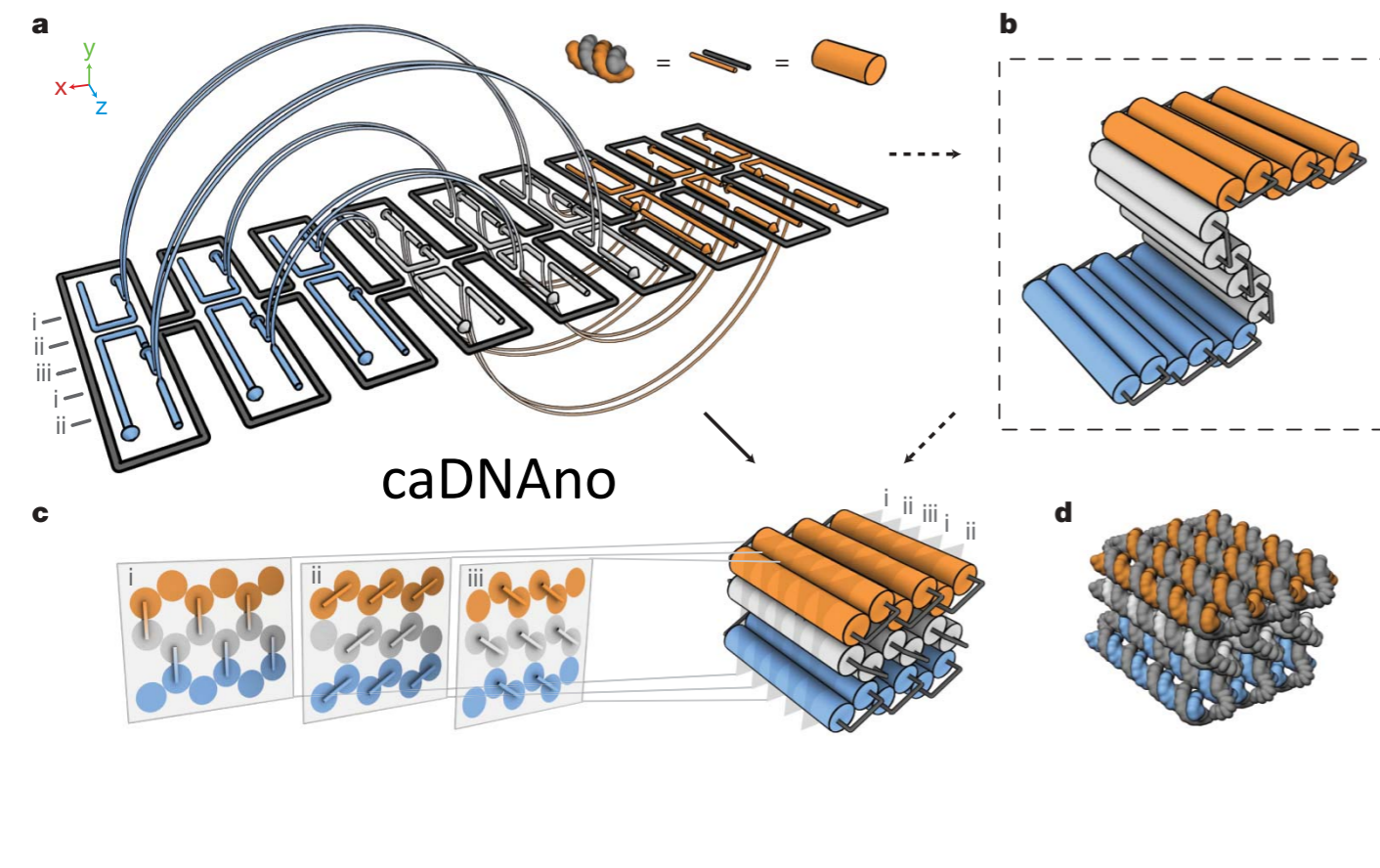
Marras, Alexander E. *et al.*, *Proc. Natl. Acad. Sci. USA*, 2015, 112 (3) 713-718

Gerling, Thomas *et al.*, *Science*, 2015, 347 (6229), 1446-1452.

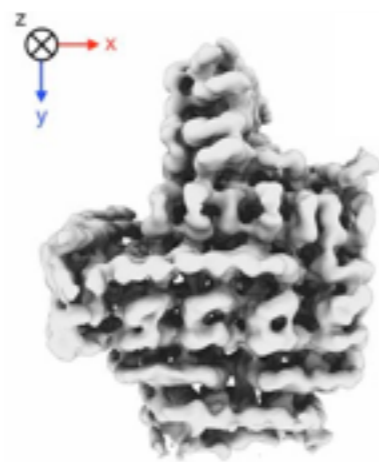
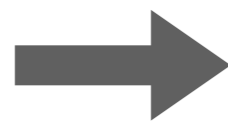


# Design and characterization of DNA nanostructures

Computer-aided design of DNA origami with caDNAno (Shih group, Harvard U.)



Transmission electron microscopy and/or atomic force microscopy validates the design



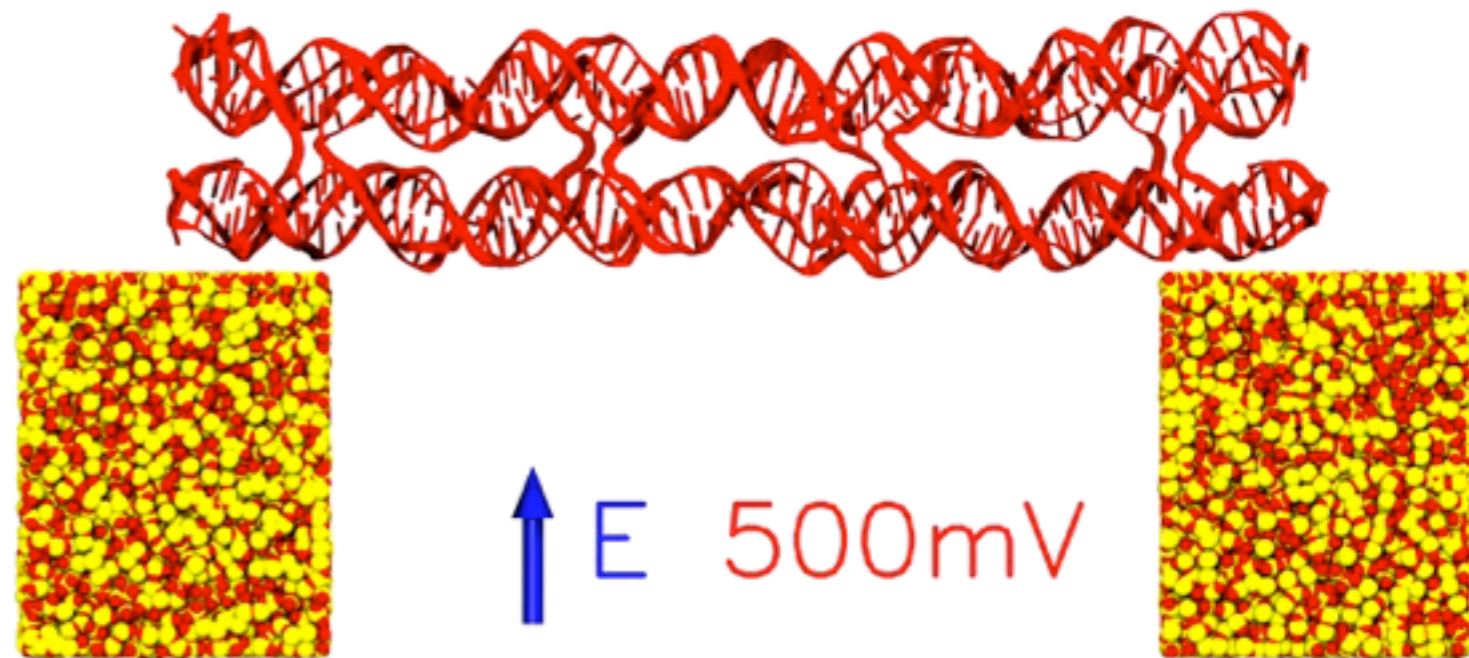
Cryo-EM reconstruction, the only experimentally derived structural model

# All-atom molecular dynamics simulations of DNA nanostructures

Massive parallel computer

Blue Waters (UIUC): ~200,000 CPUs

Atoms move according to classical mechanics ( $F=ma$ )



Time scale: ~ 0.1-100  $\mu\text{s}$

Length scale: 10K - 100M atoms or ( $< 50 \text{ nm}$ )<sup>3</sup>

Time resolution: 2 fs

Spacial resolution: 0.1 Å

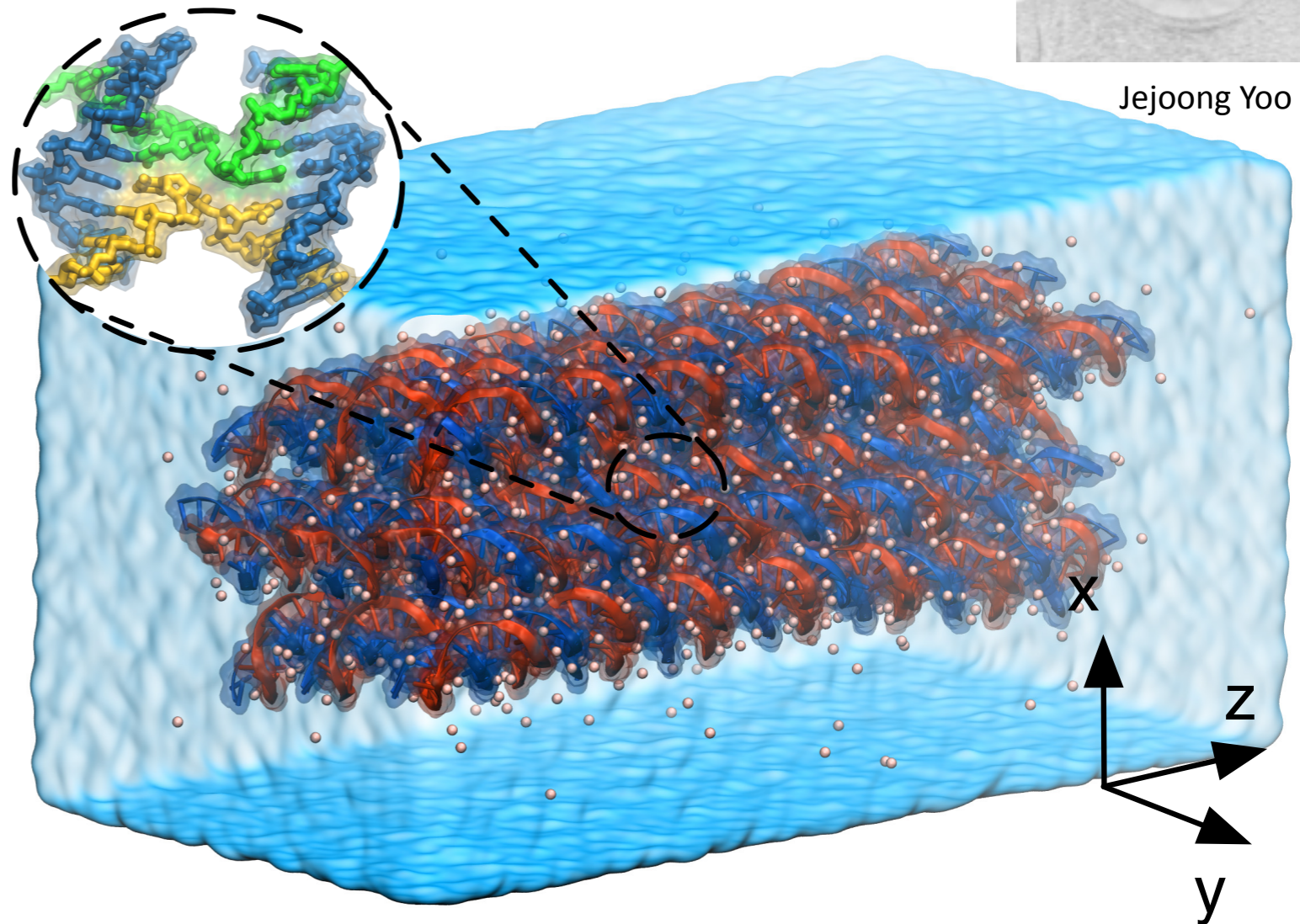
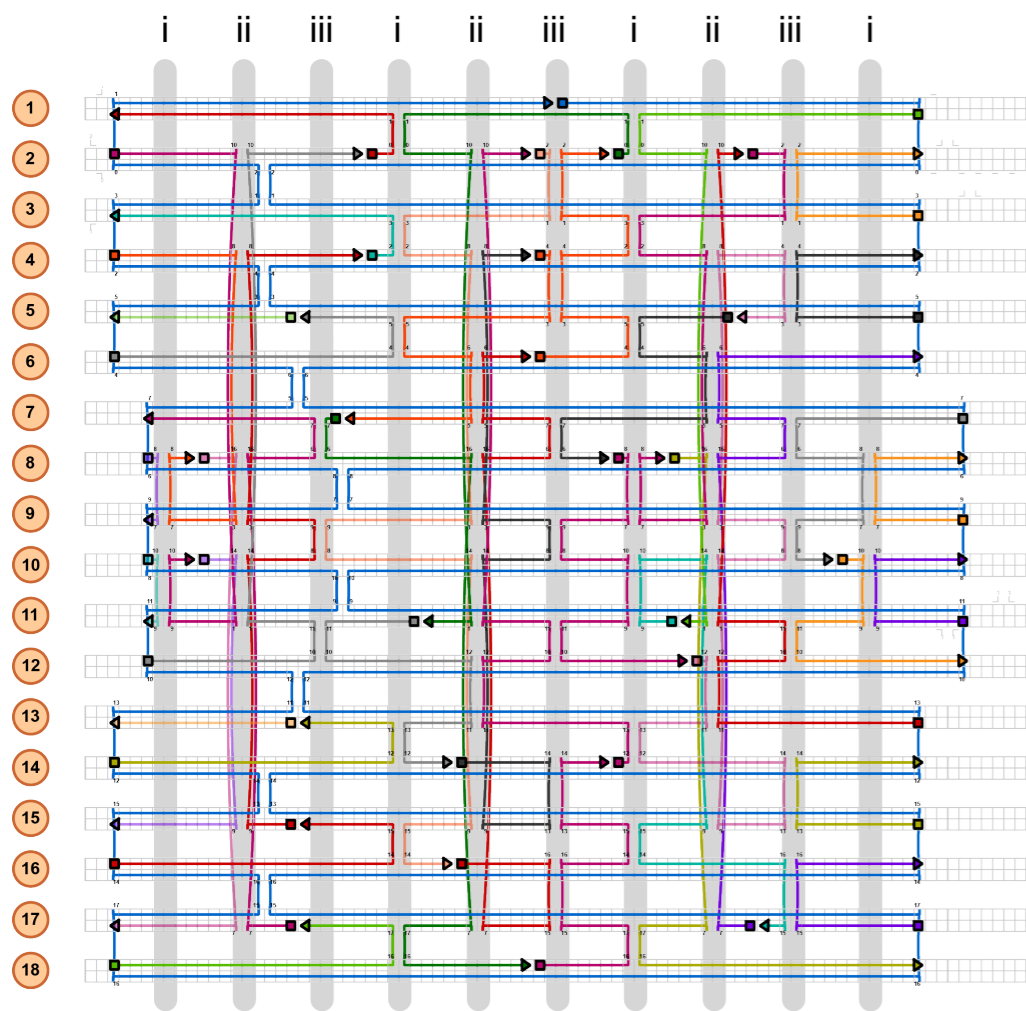
Interaction between atoms is defined by molecular force field

*ACS Nano* 9:1420-1433 (2015)

# From caDNAno to all-atom



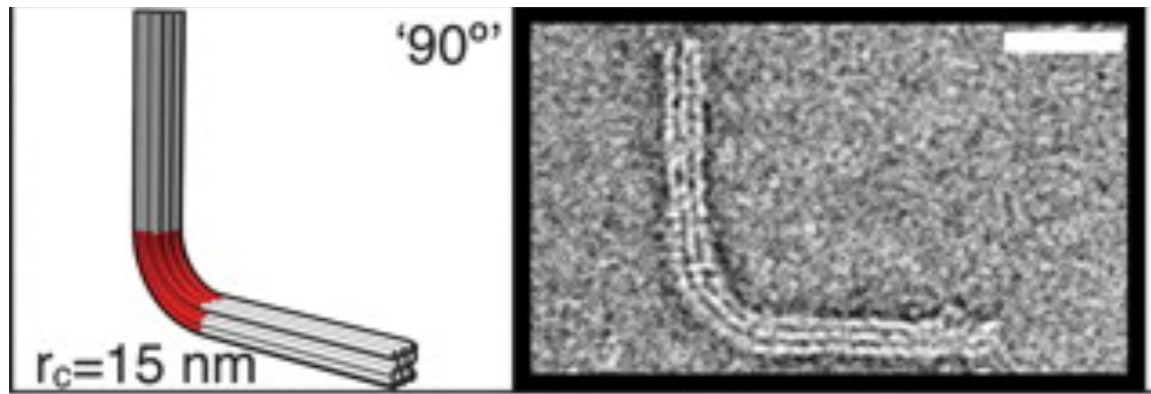
Jejoong Yoo



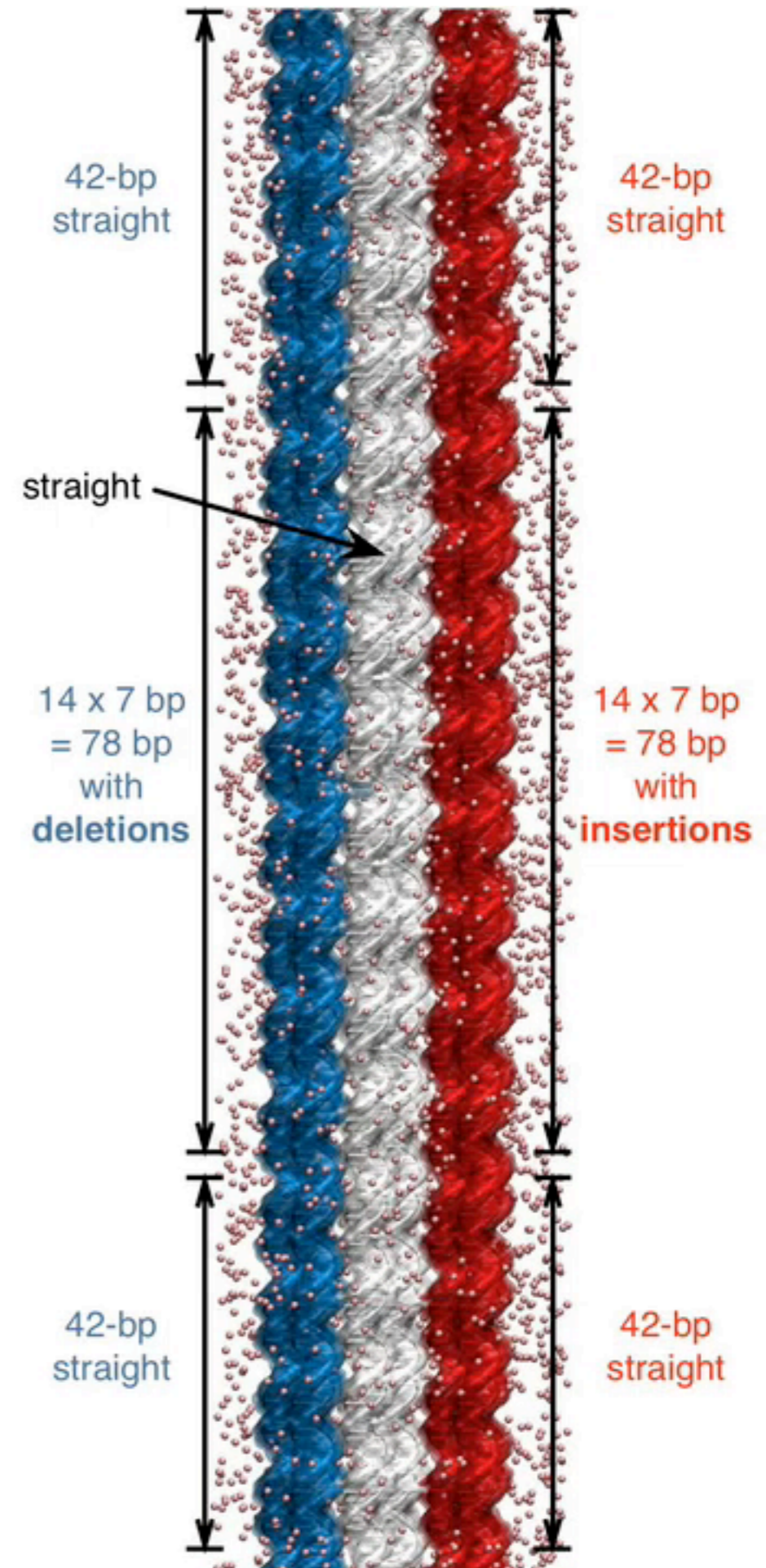
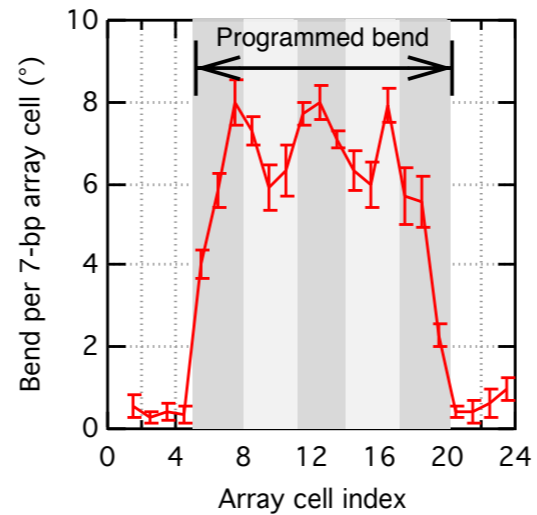
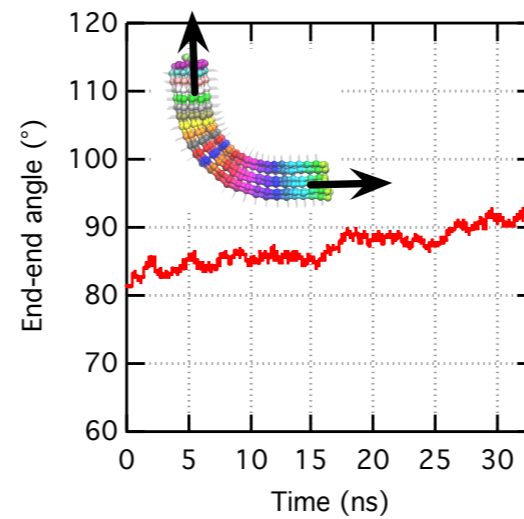
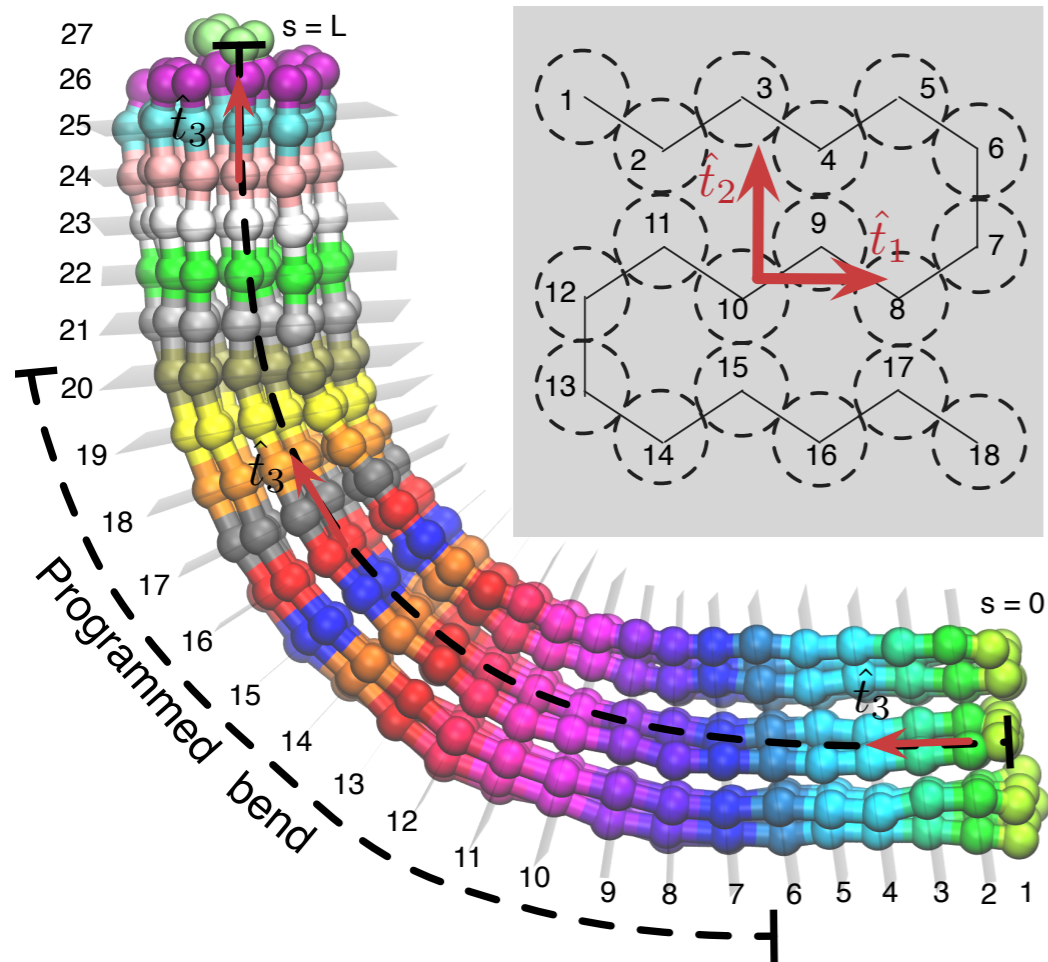
- caDNAno returns topology (json) and sequence (csv) information.
- **cadnano2pdb.pl** combines json and csv files into a PDB file.

- \* CHARMM36 force field
- \* Explicit water
- \* [MgCl<sub>2</sub>] ~ 10 mM
- \* NAMD
- \* 1 to 3M atoms
- \* 500 to 1,000 CPUs

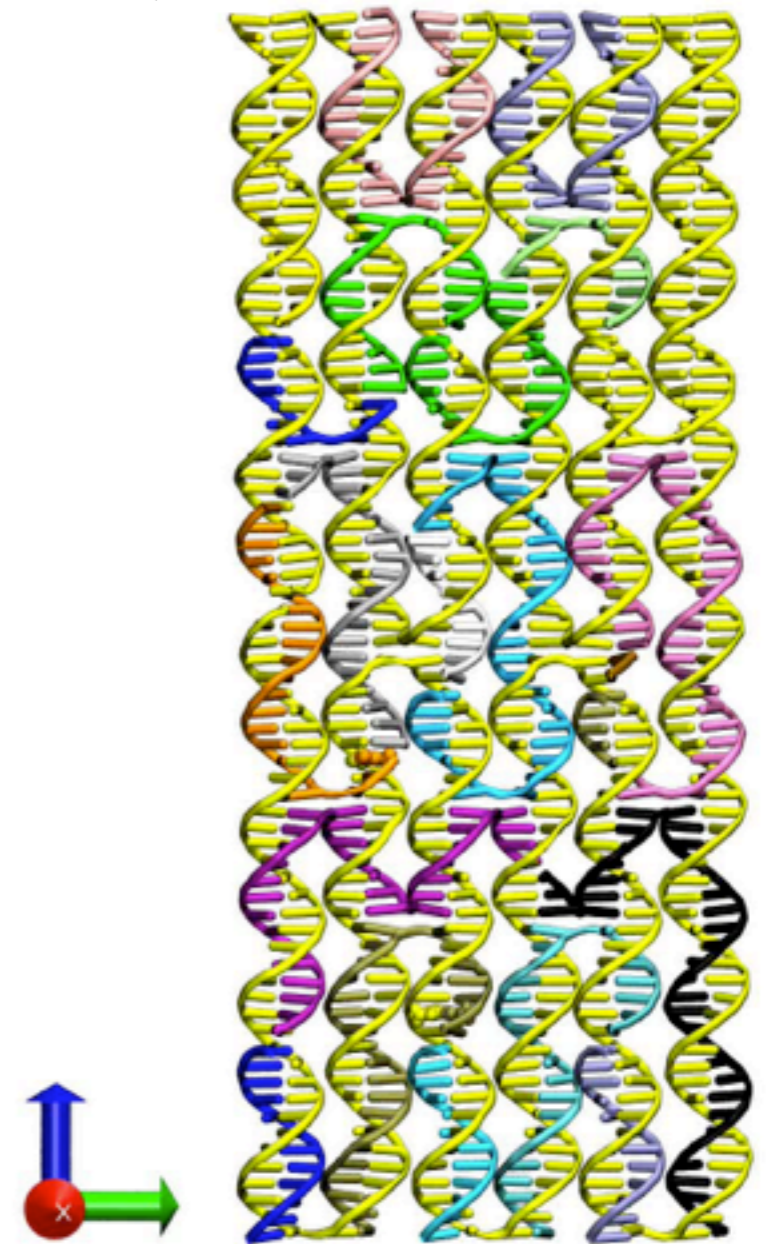
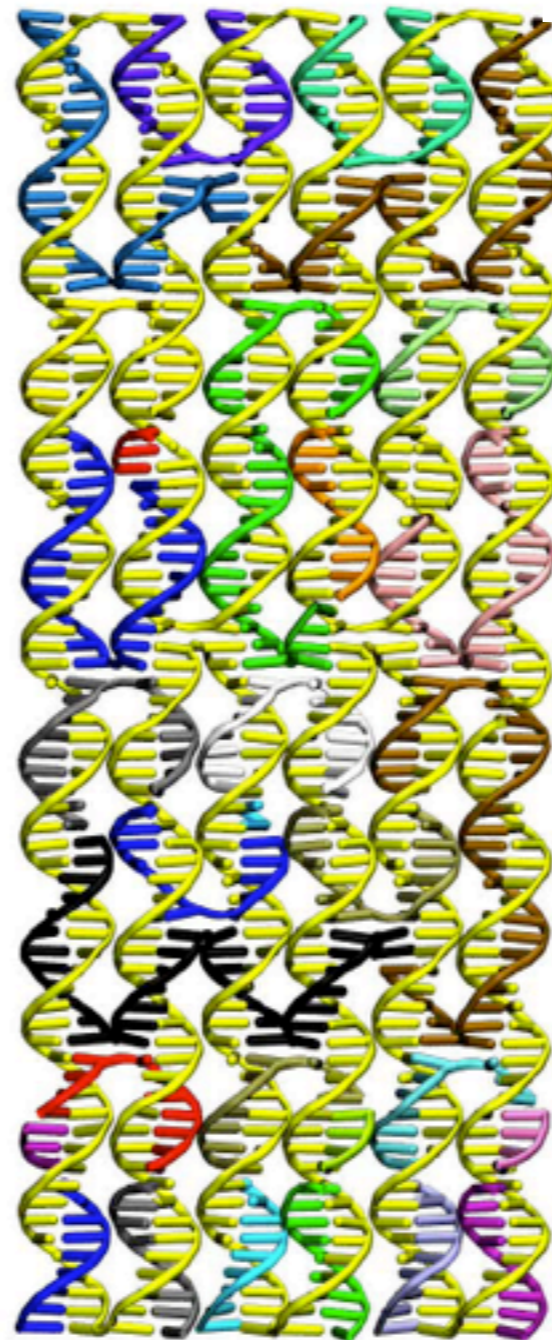
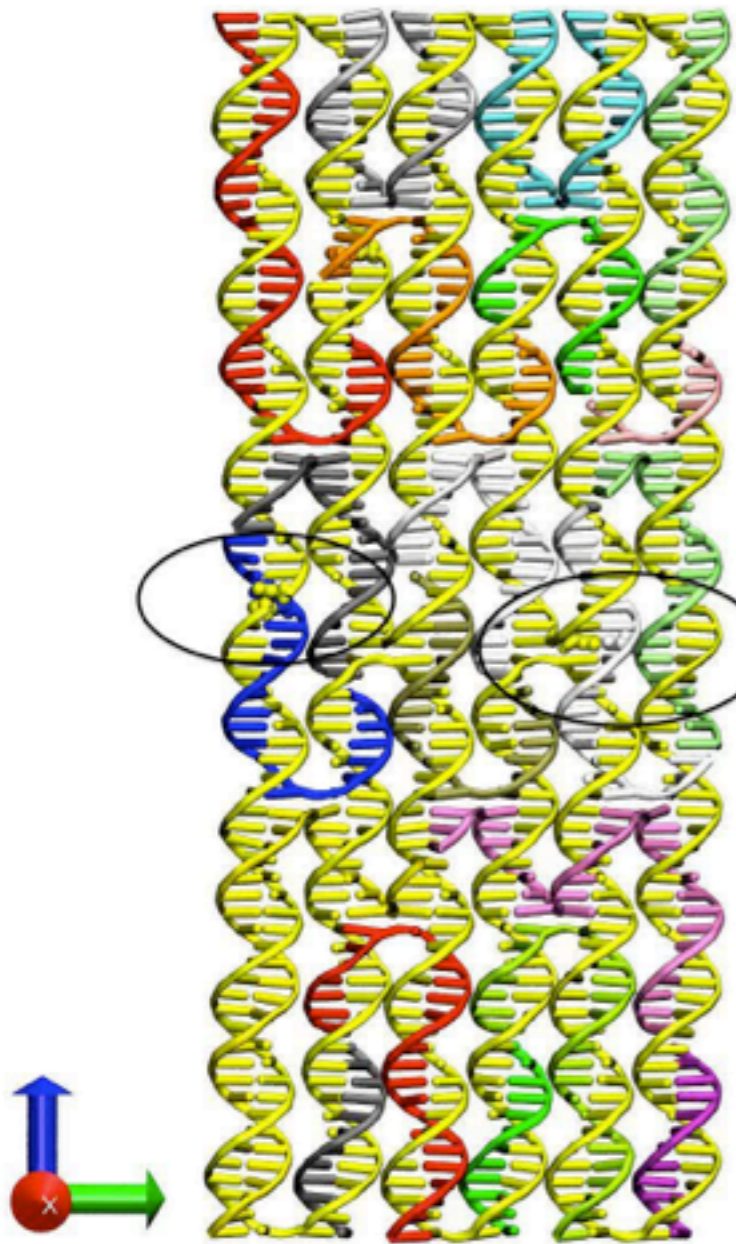
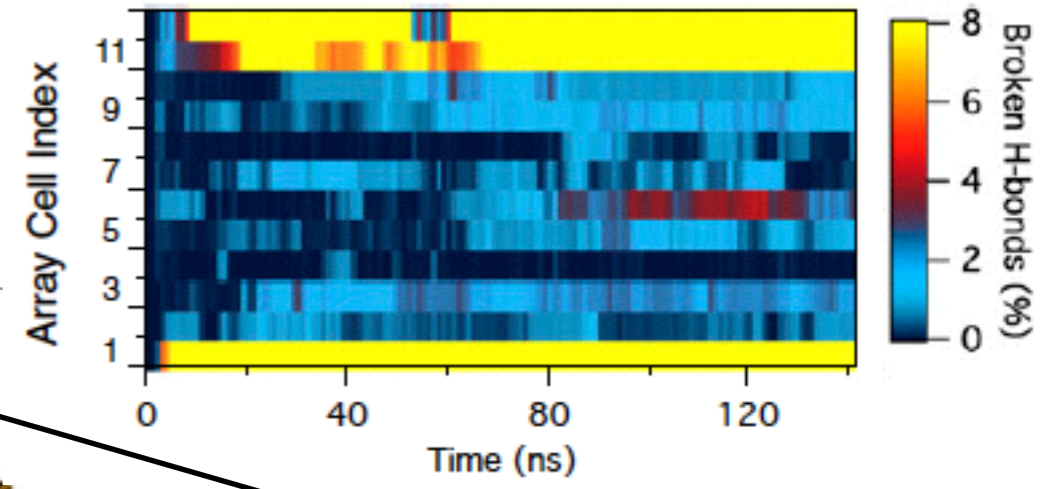
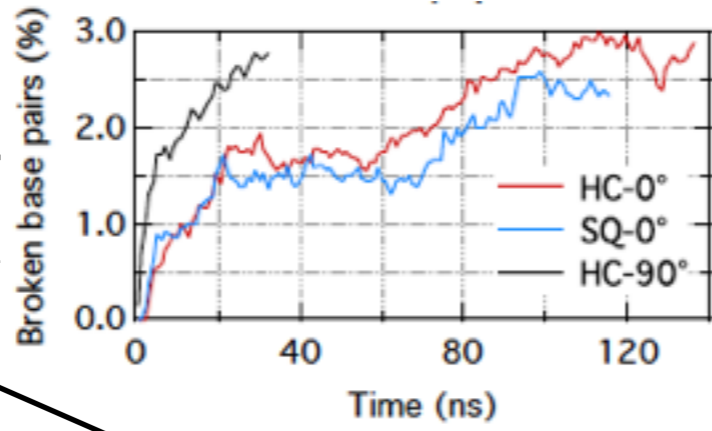
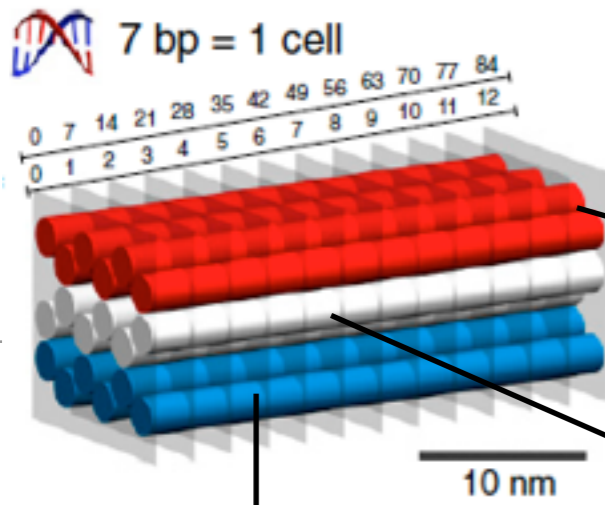
# All-atom MD simulation of L-shape DNA origami



Experiment  
Dietz, H. et al,  
*Science*, 325



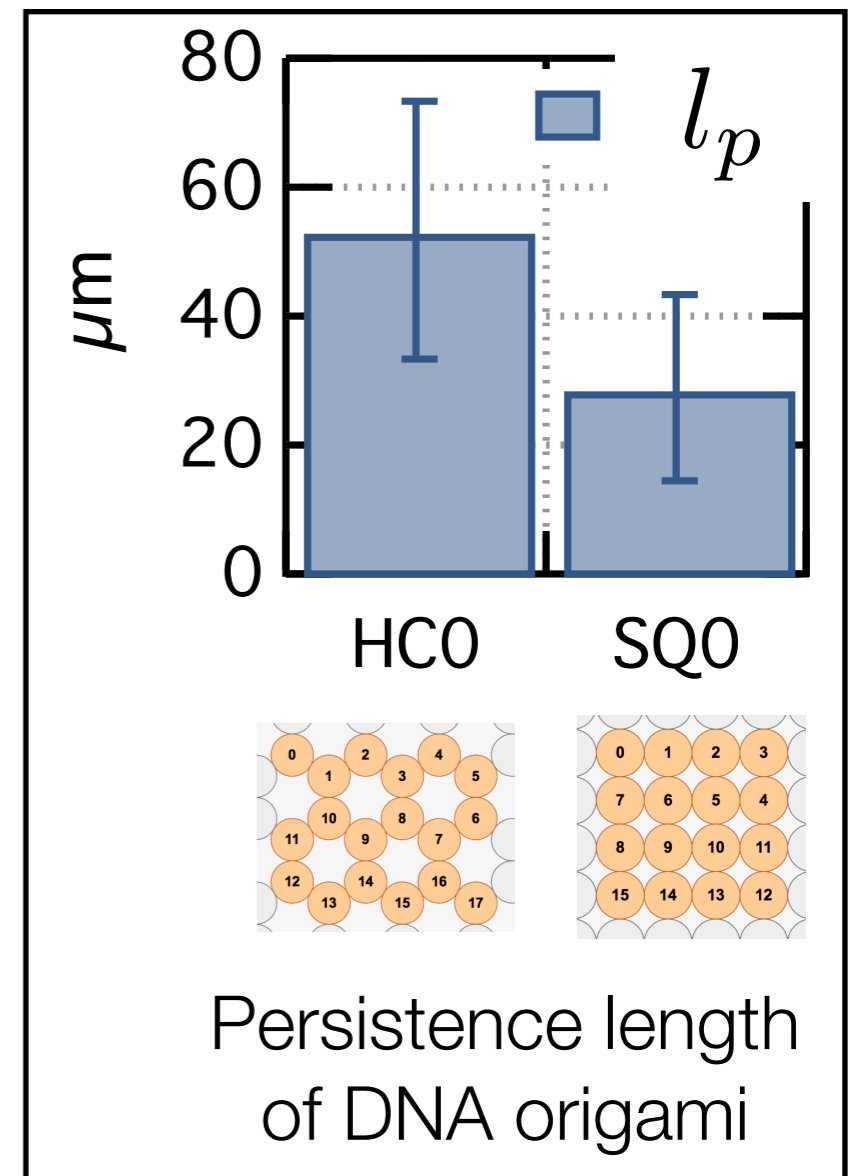
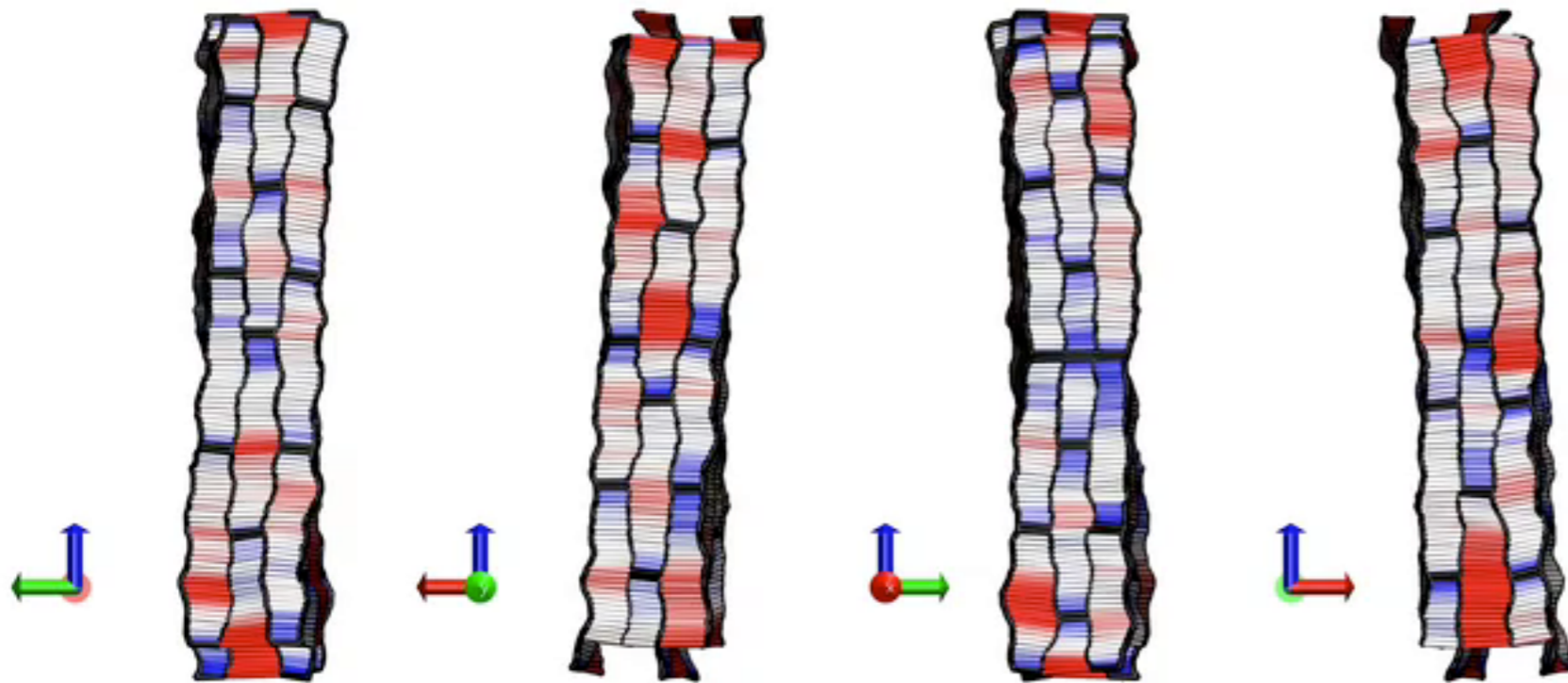
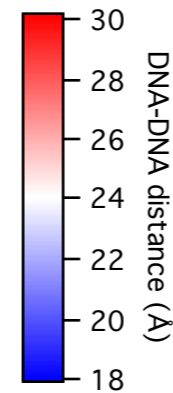
# Structural dynamics



# Structural fluctuations reveal local mechanical properties

MD trajectories allow us to compute natural bending and torsion as well as persistence length

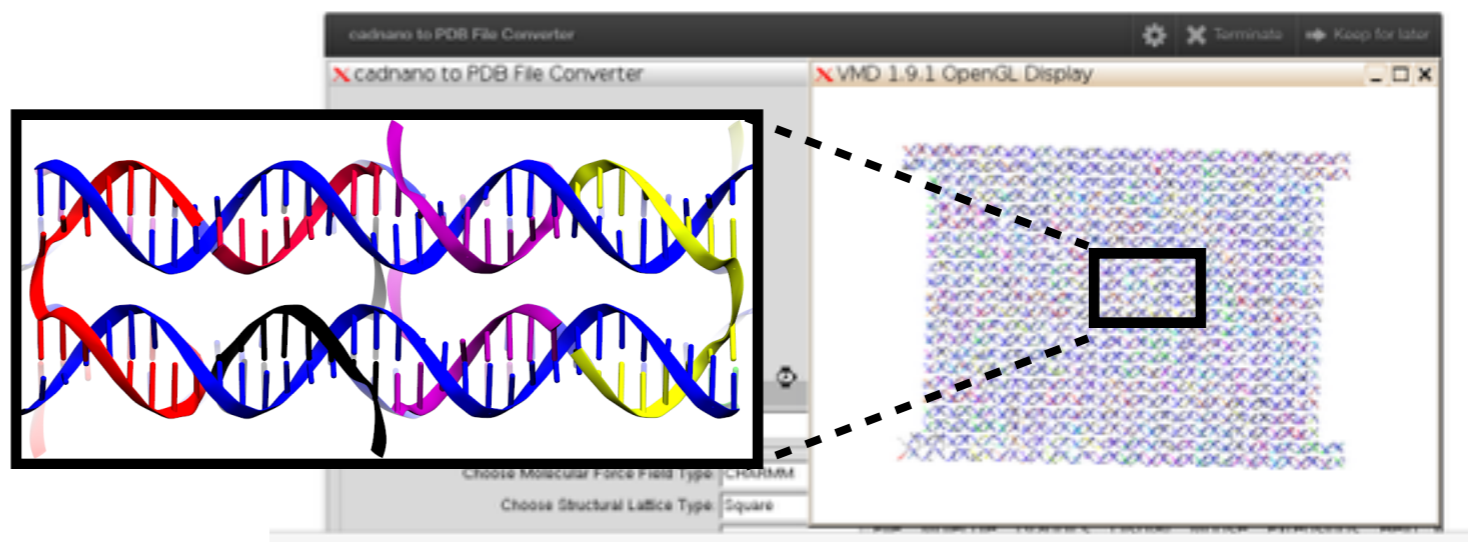
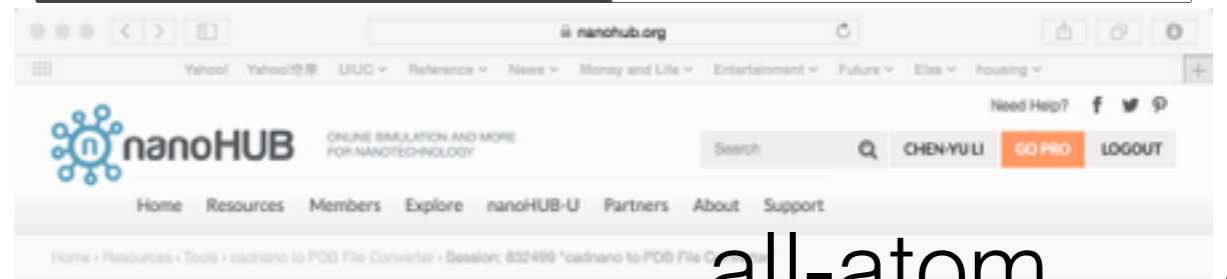
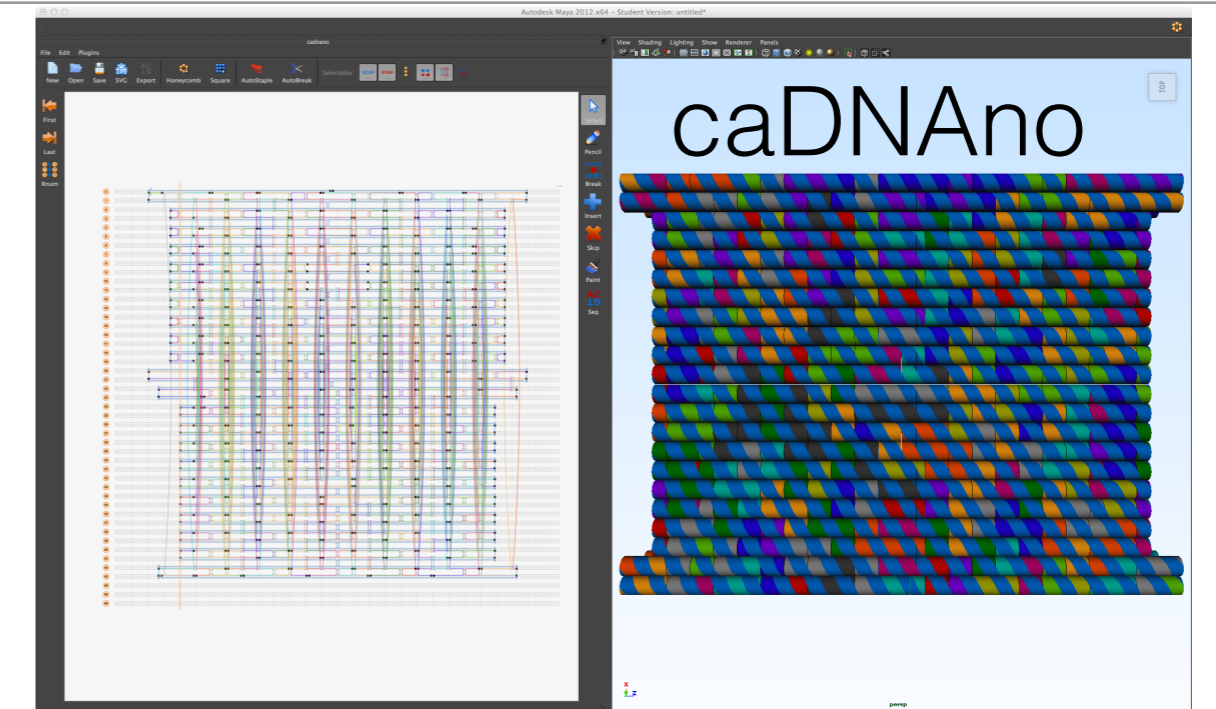
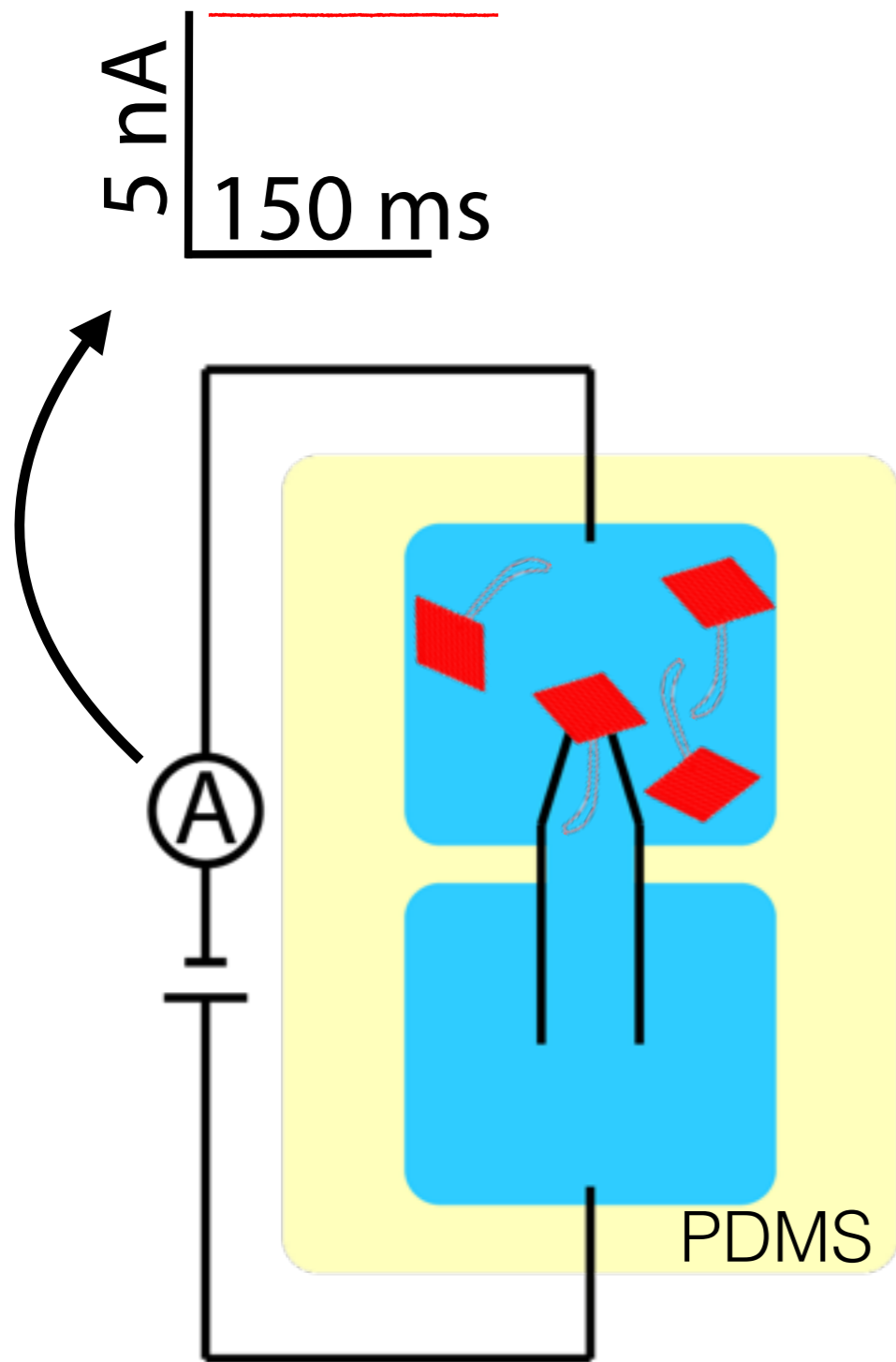
- Inter-DNA distance in color map
- Chicken wire frame represents center line of helices & junction



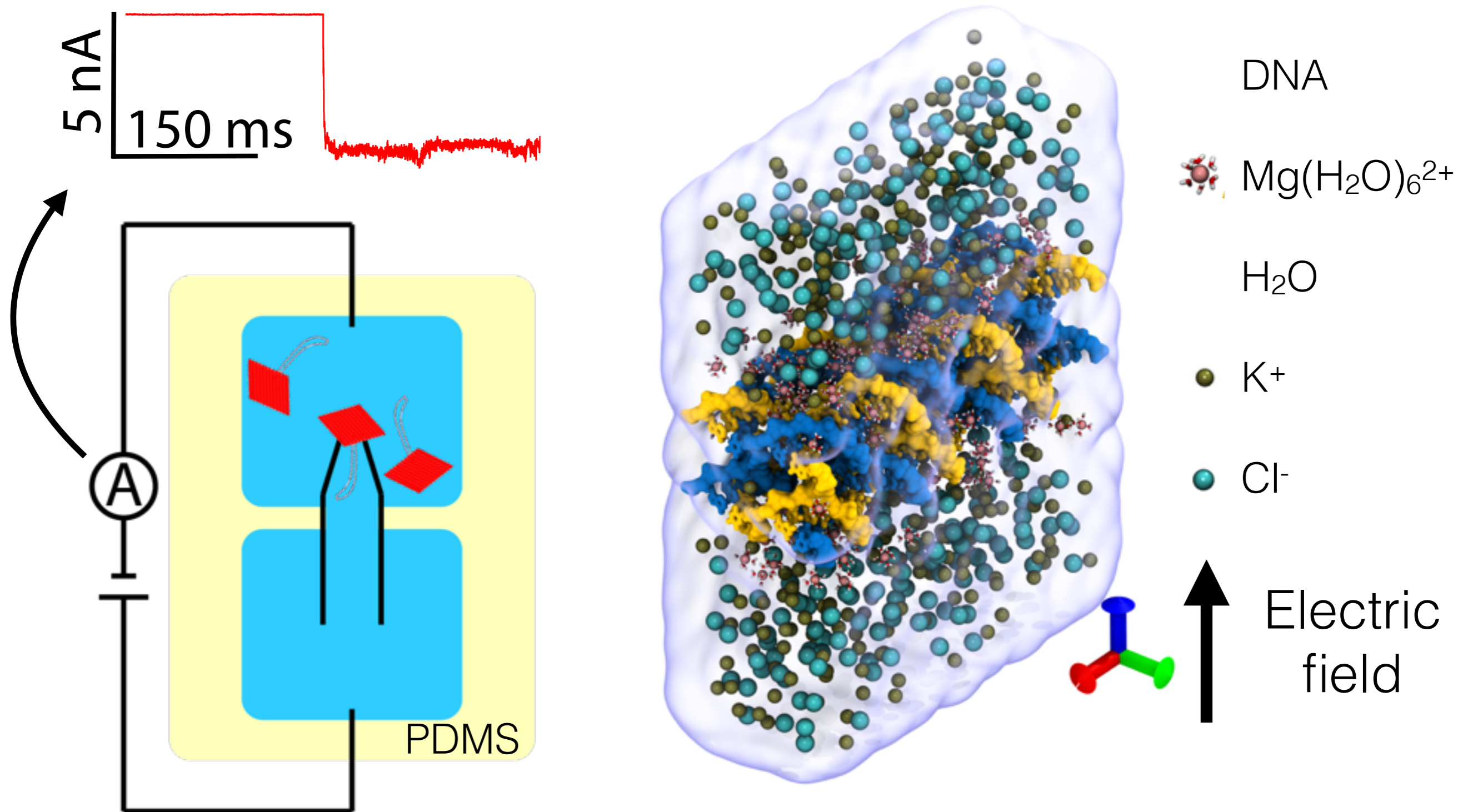
Our simulations predict higher rigidity for honeycomb-lattice design.



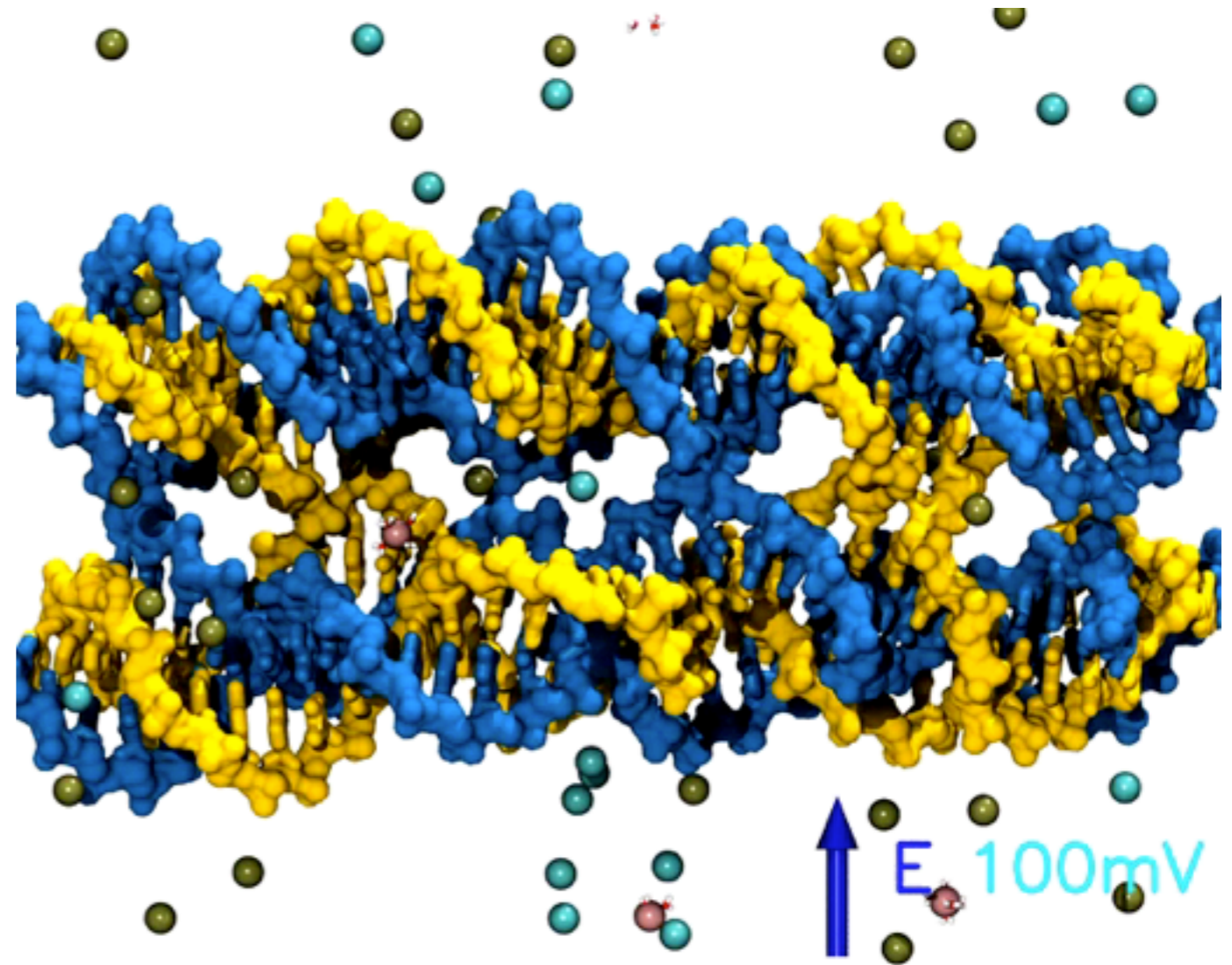
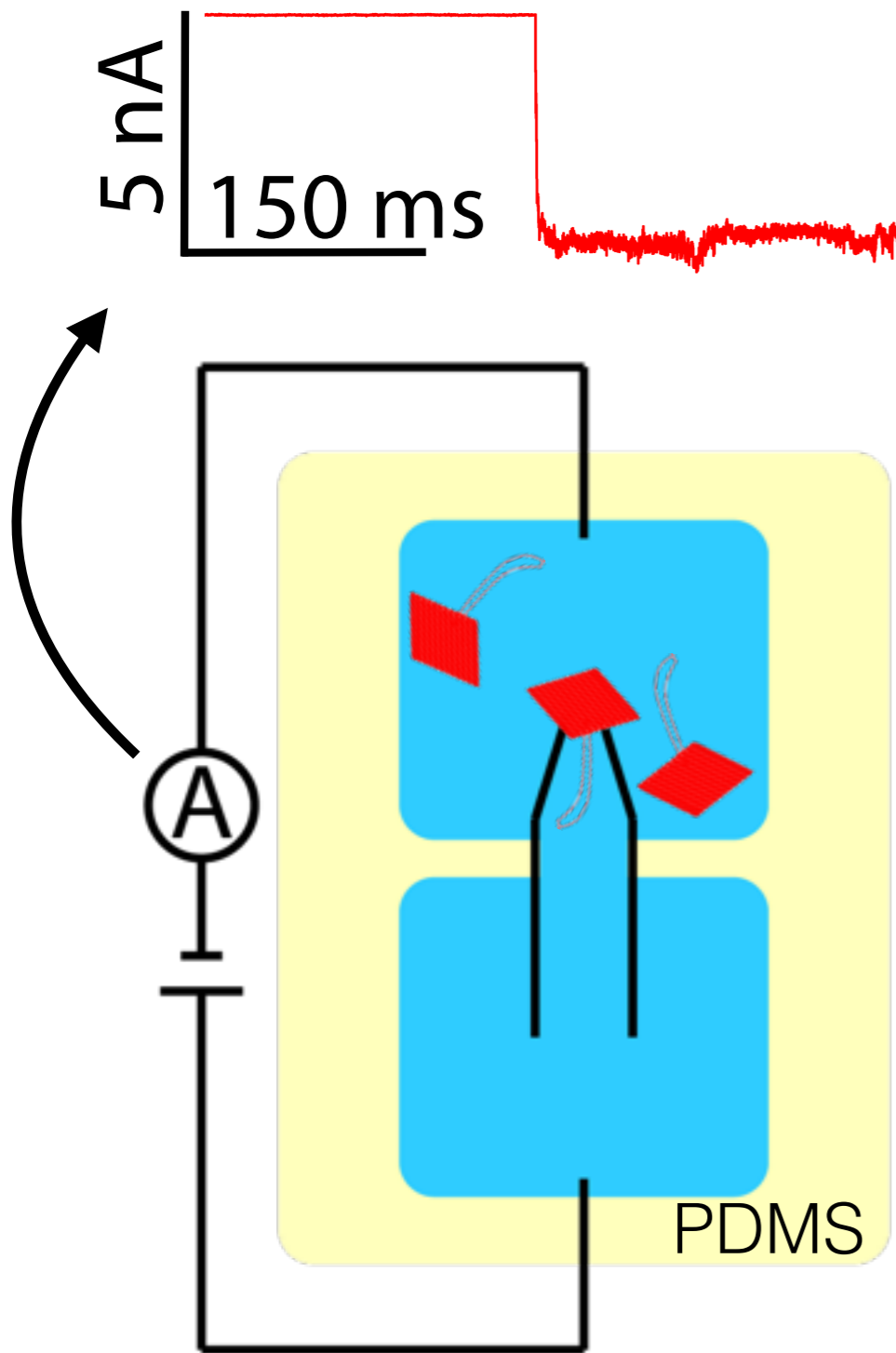
# MD simulation of DNA origami conductivity



# MD simulation of DNA origami conductivity



# MD simulation of DNA origami conductivity

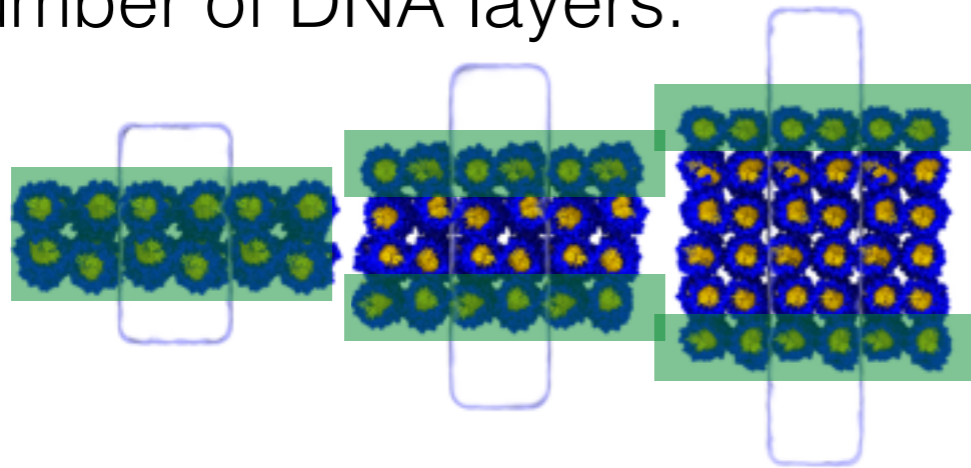


Instantaneous current:

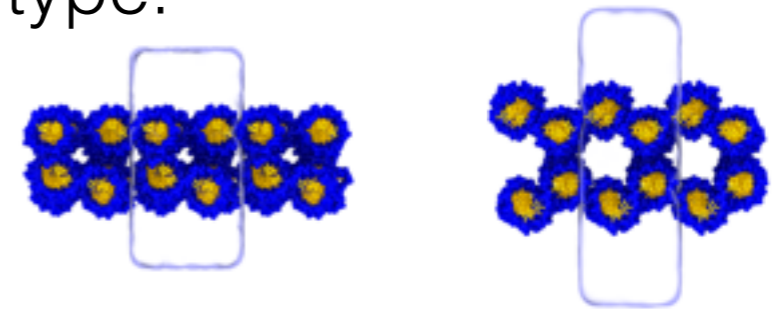
$$I(t) = \frac{1}{\Delta t L_z} \sum_{i=1}^N q_i (z_i(t + \Delta t) - z_i(t))$$

# Factors affecting ionic conductivity of DNA origami

Number of DNA layers:

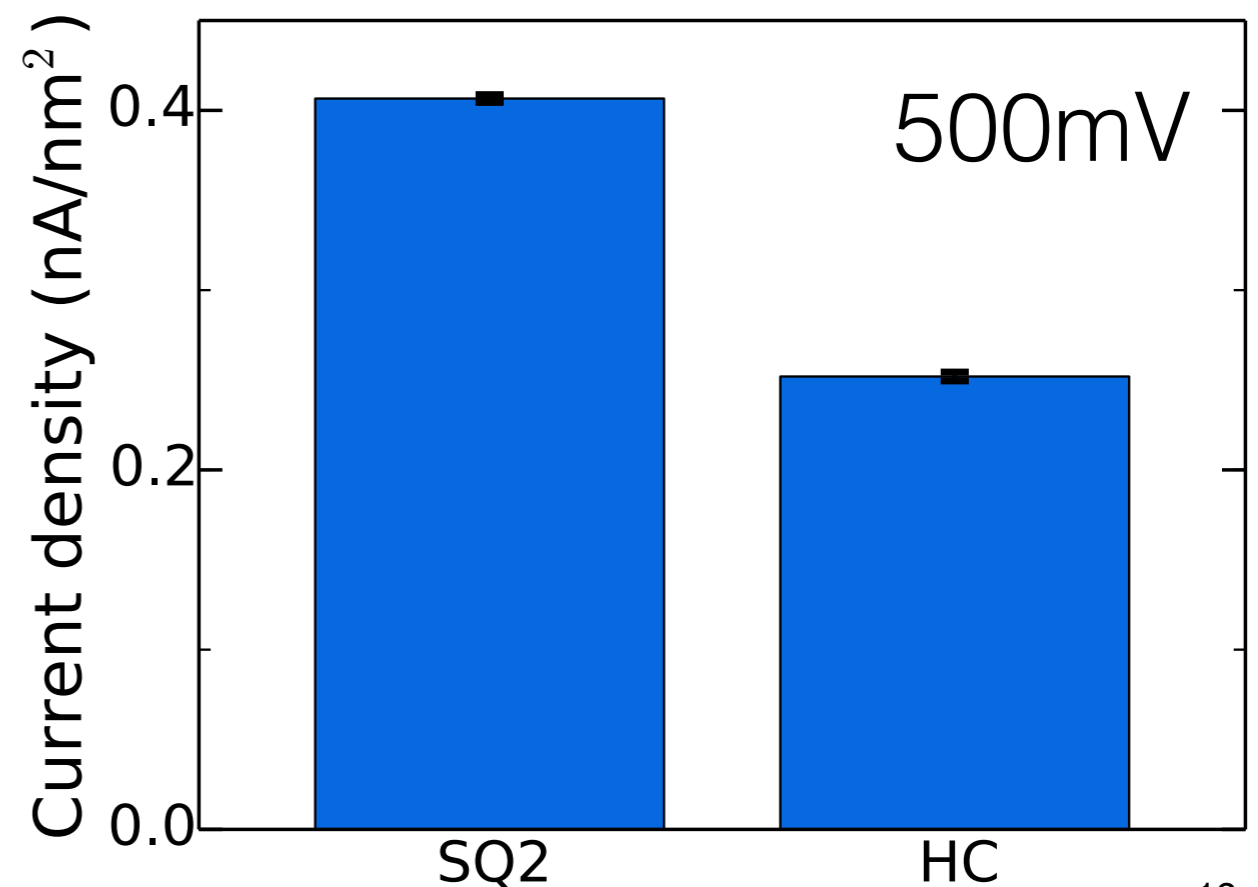
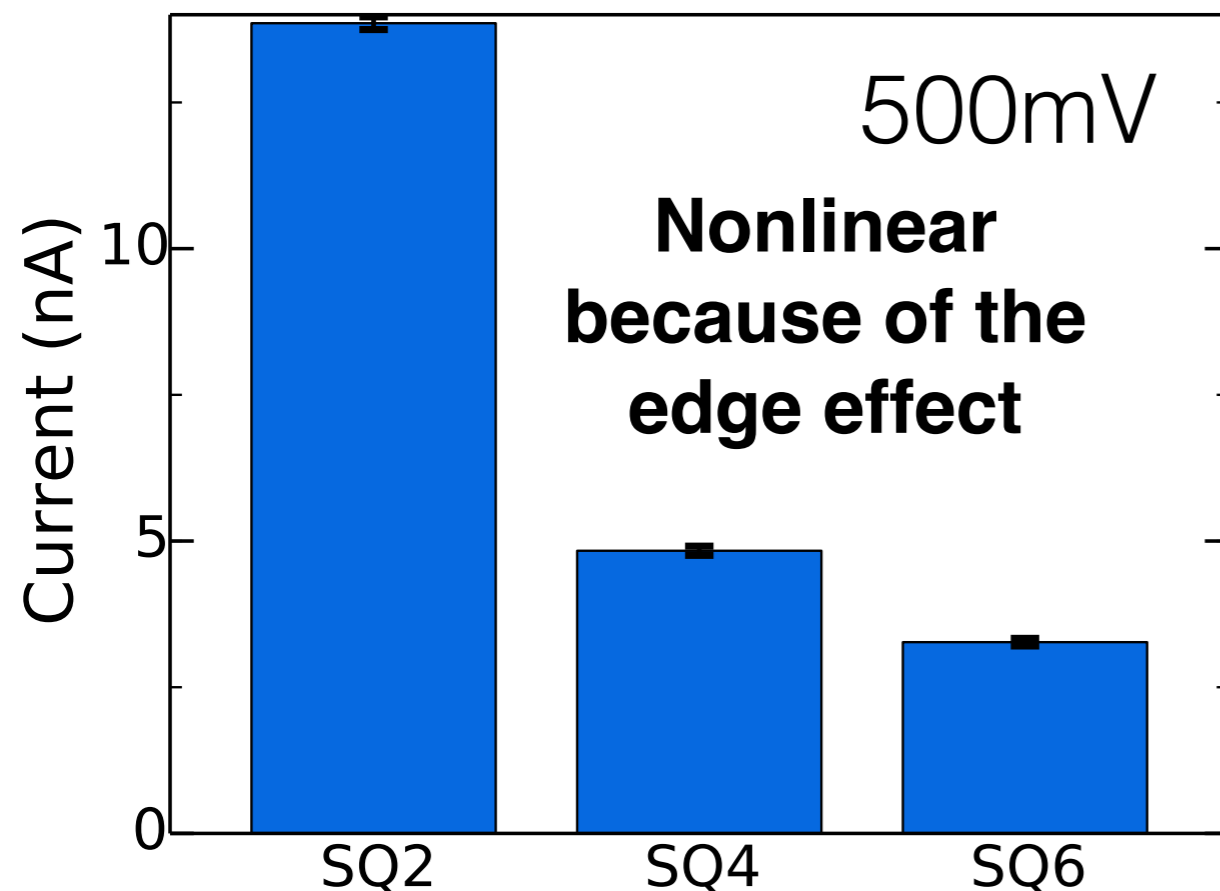


Lattice type:



**SQ2 has lower projected DNA density and a higher leakage current**

**More layer -> less leakage current**



# Effect of $Mg^{2+}$

# Higher $[Mg^{2+}]$ makes DNA origami less conductive.



Elisa A. Hemmig

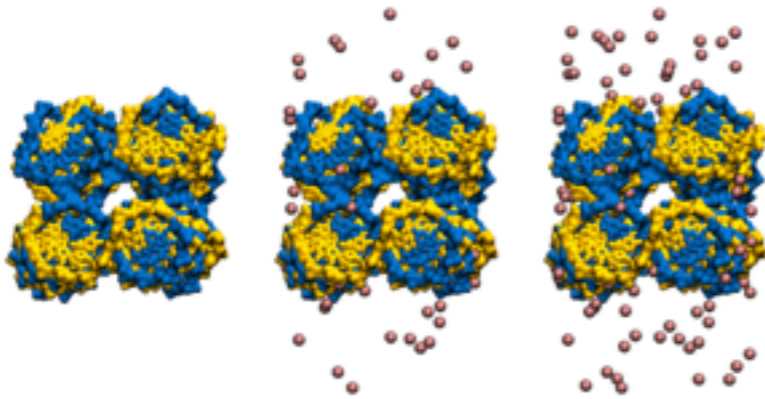


Silvia Hernández-Ainsa

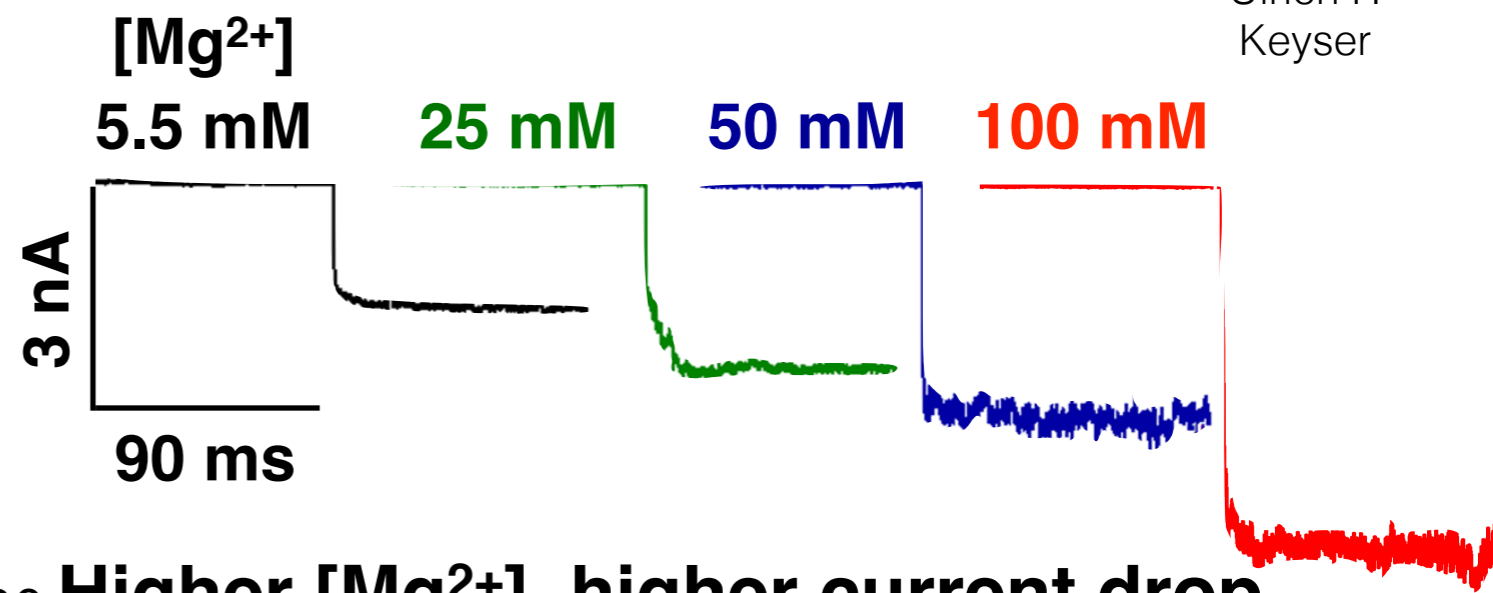
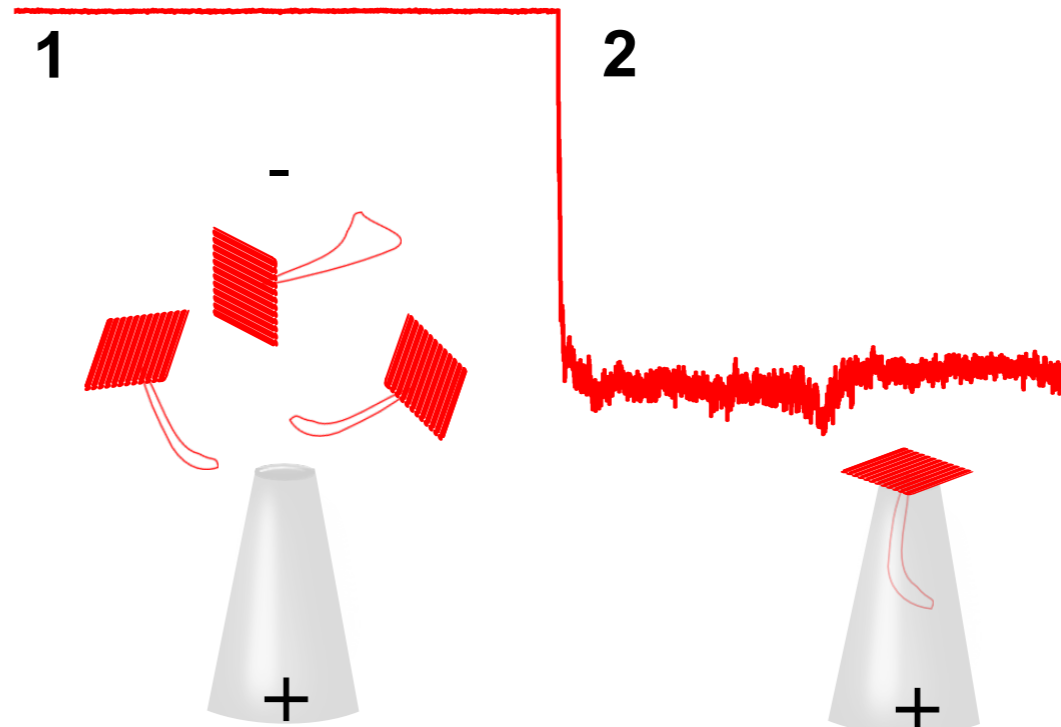
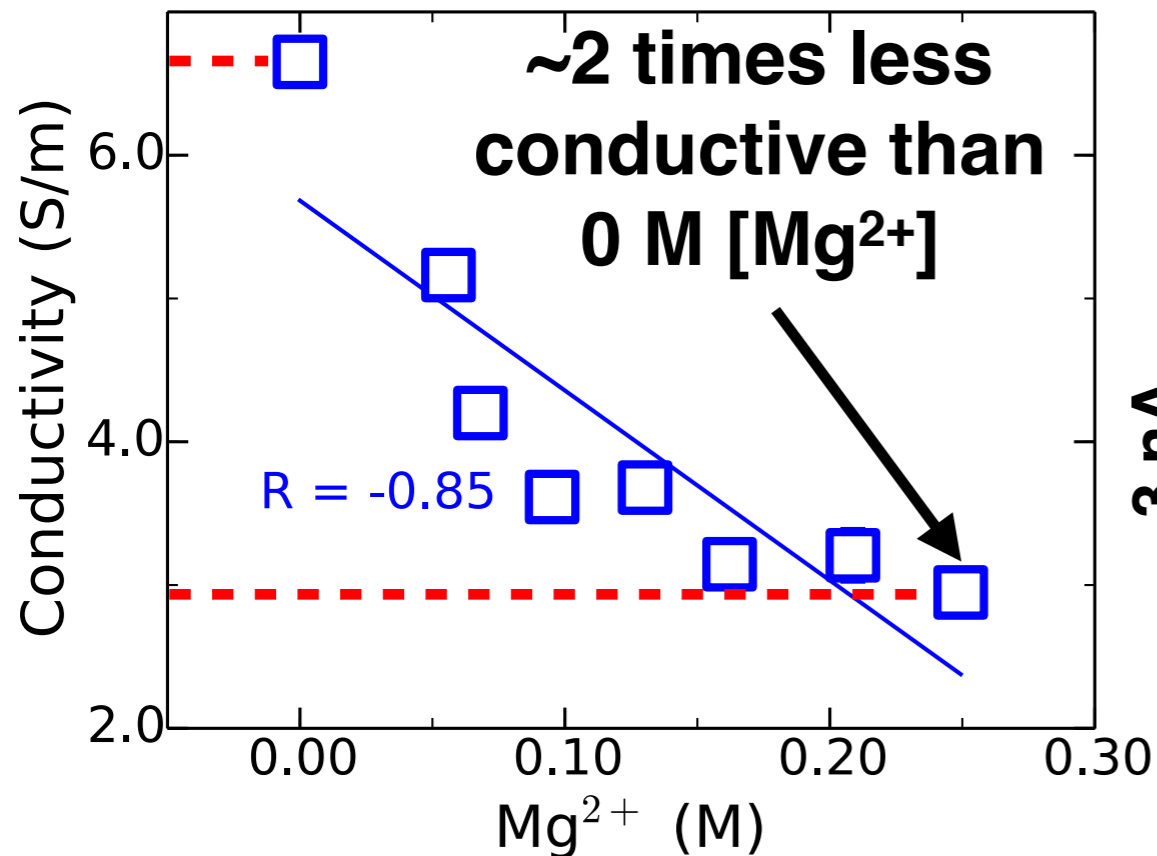


Ulrich F. Keyser

SQ2, m13 sequence



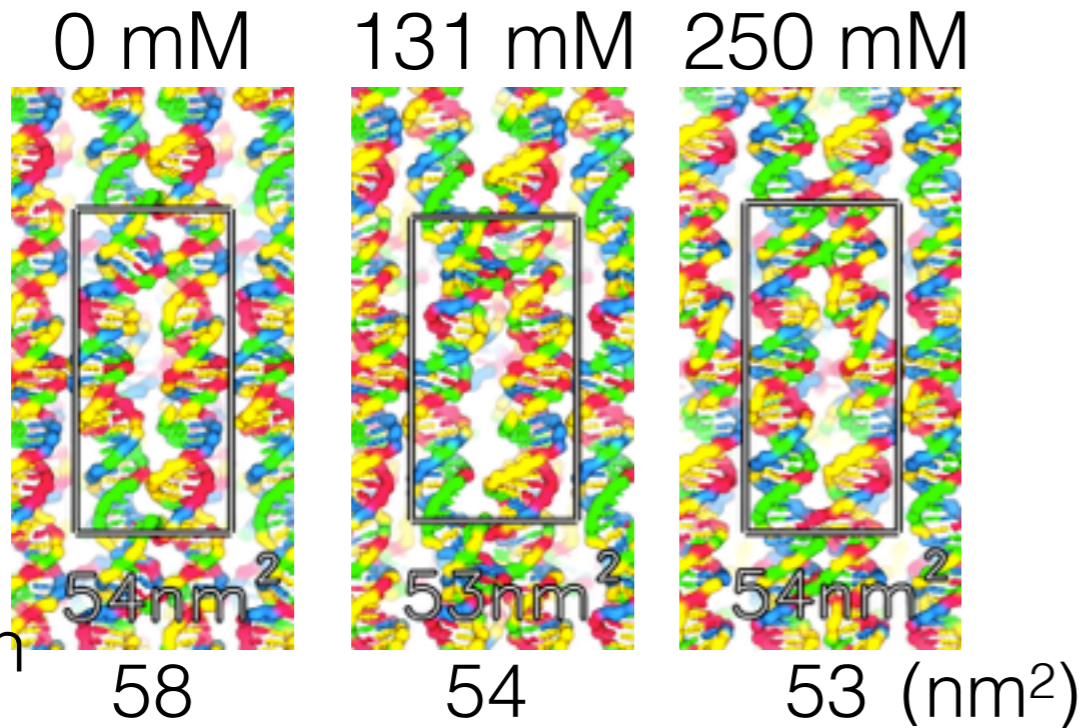
$[Mg^{2+}]$



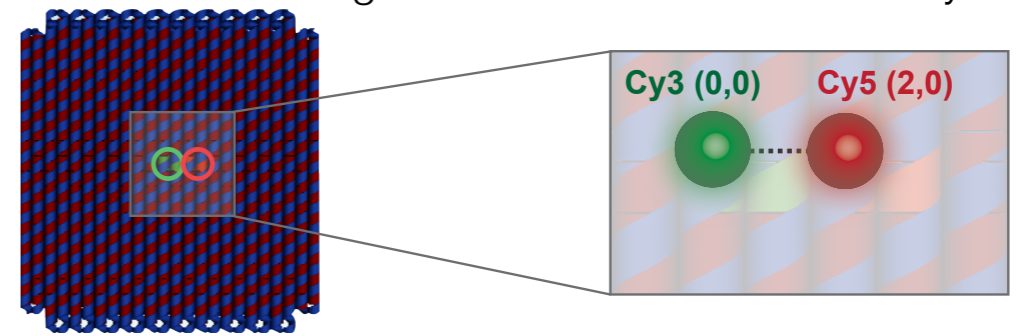
Higher  $[Mg^{2+}]$ , higher current drop.

# Mg<sup>2+</sup> makes DNA origami more compact, by screening the DNA-DNA repulsion.

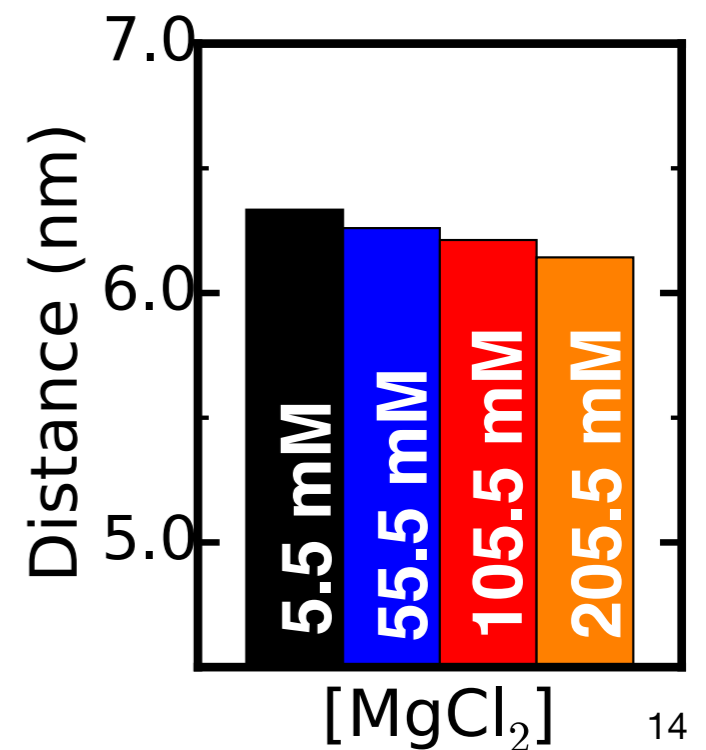
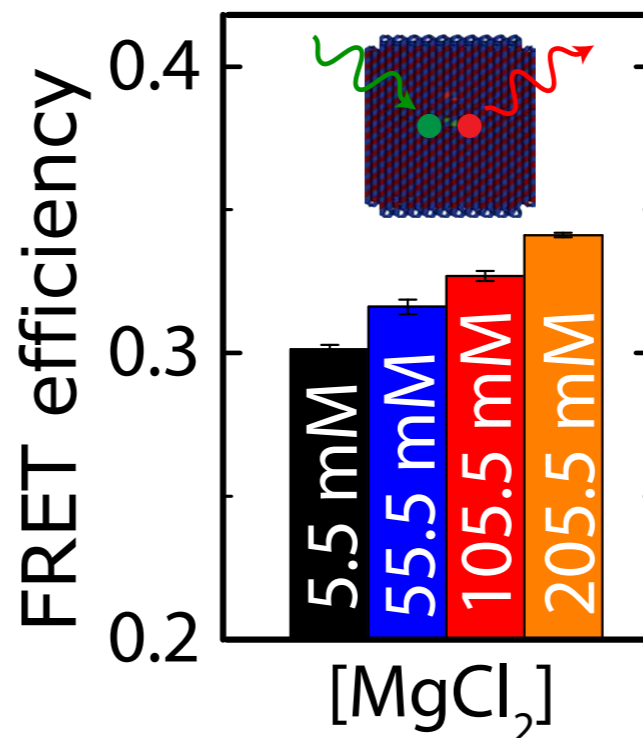
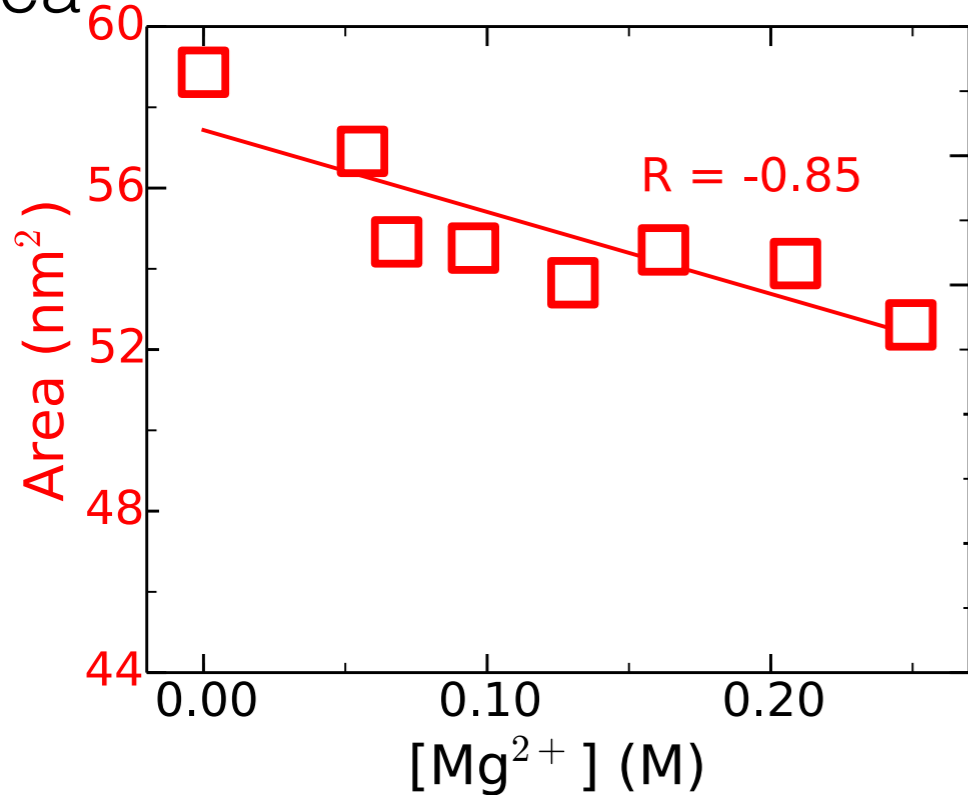
Mechanism of Mg<sup>2+</sup>



**FRET:**



**Higher [Mg<sup>2+</sup>], lower inter-DNA distance**



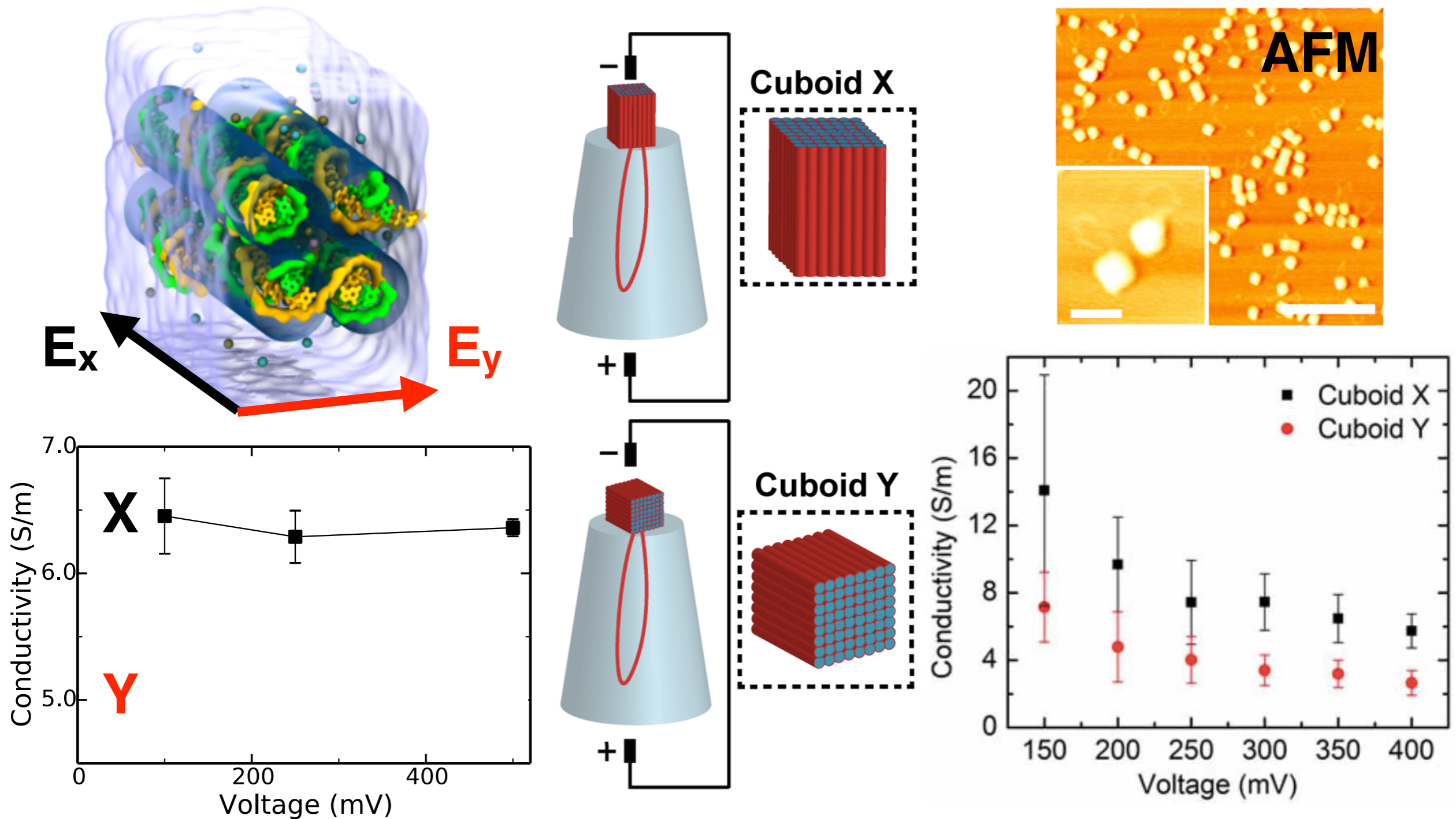
# Anisotropic conductivity



Jinglin Kong



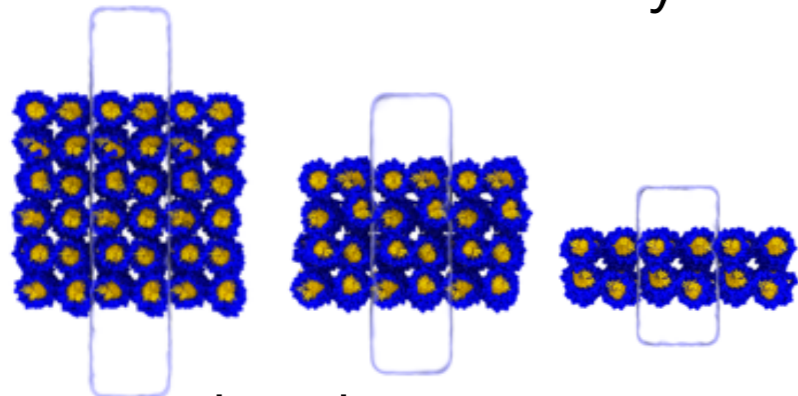
Ulrich F. Keyser



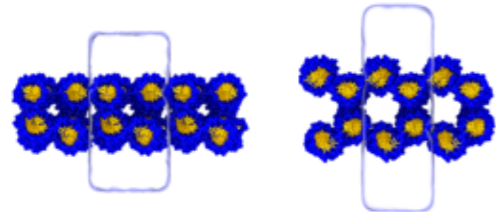
# Programmable ionic conductivity of DNA origami

## Structural design

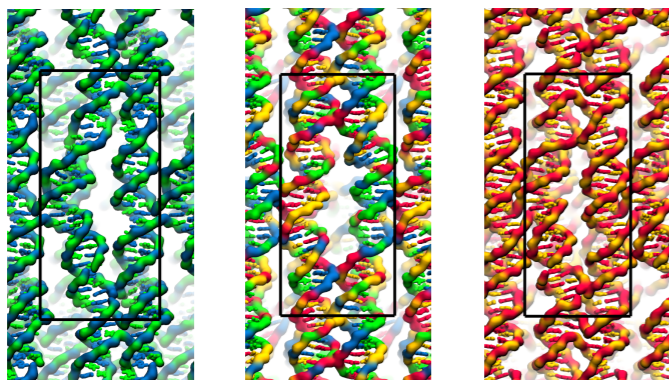
Number of DNA layers



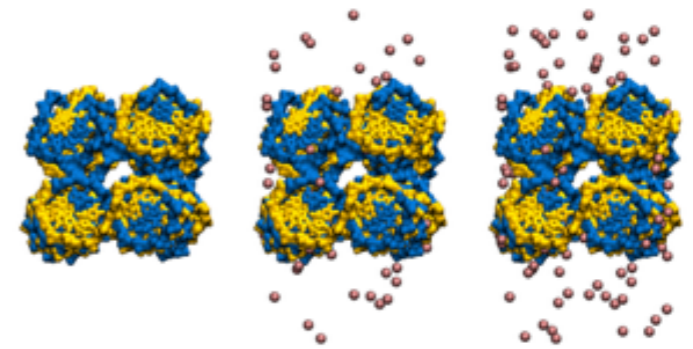
Lattice type



## Nucleotide content



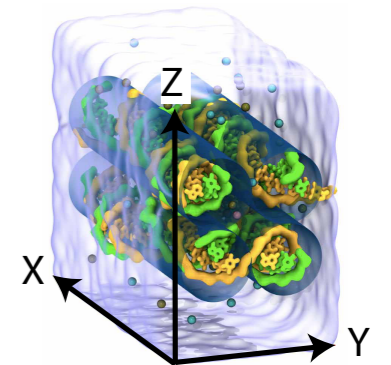
## Ionic environment



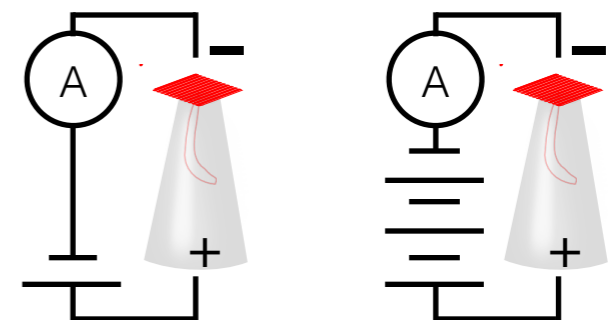
MD has  
Leak-proof  
predicting  
gates  
power!

## Electric field

Direction

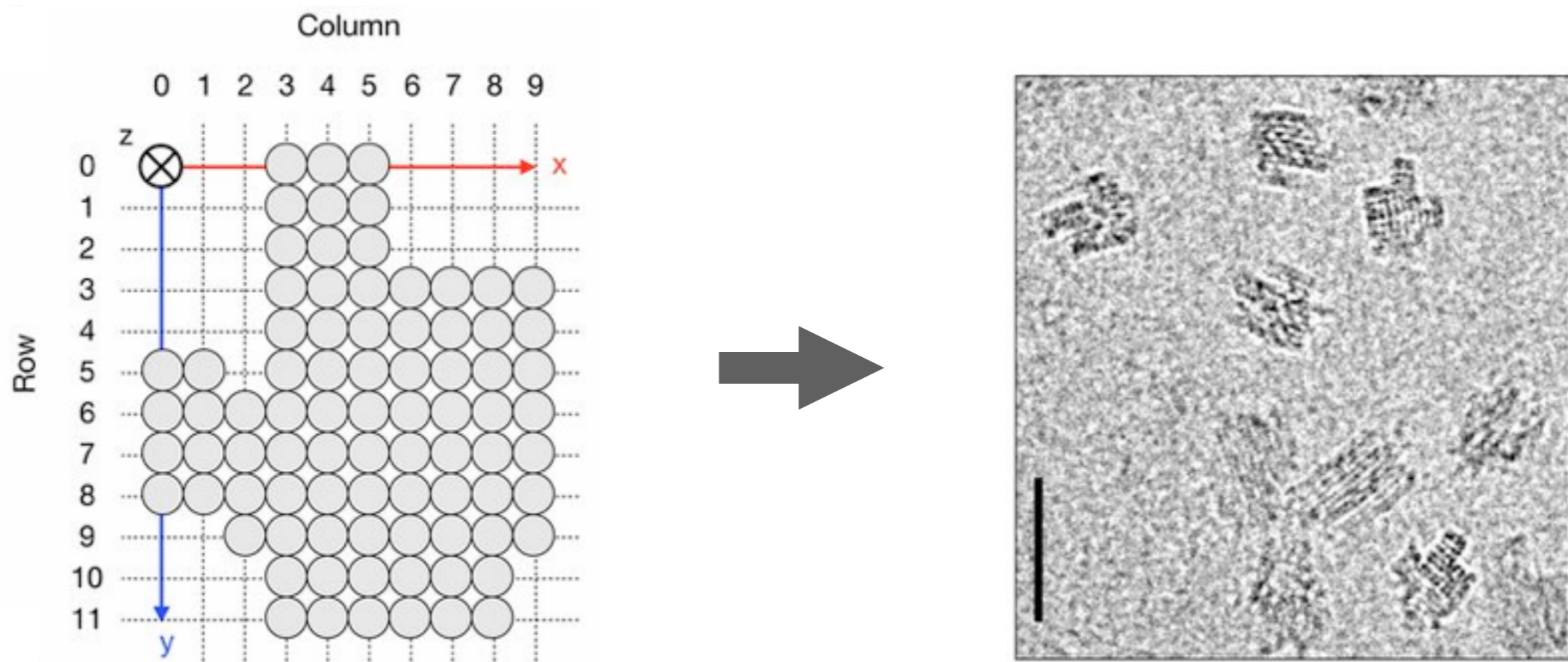


Magnitude



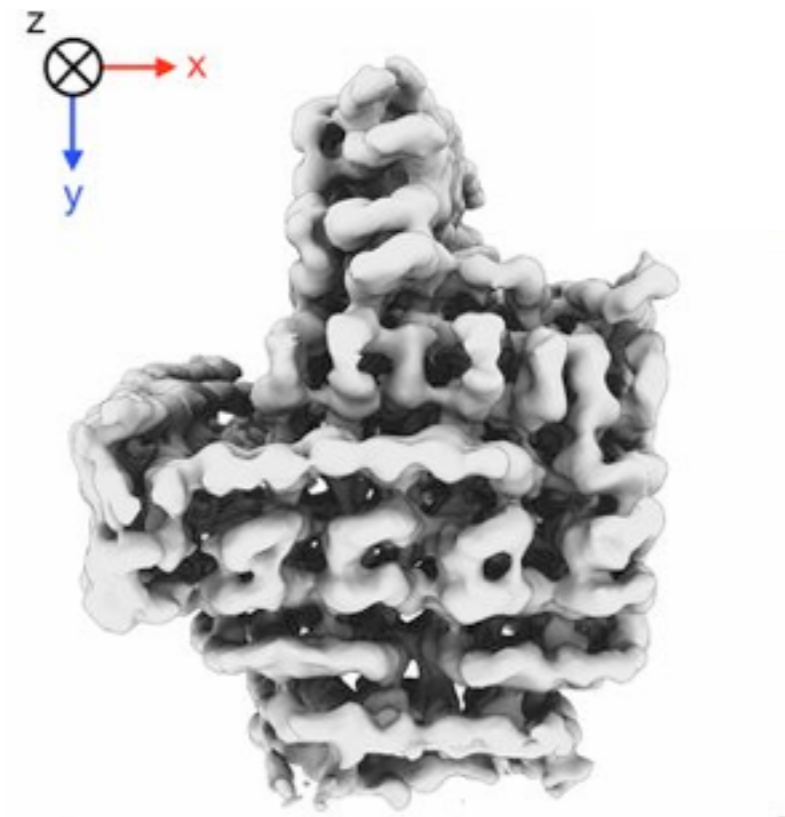
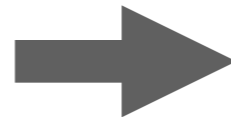
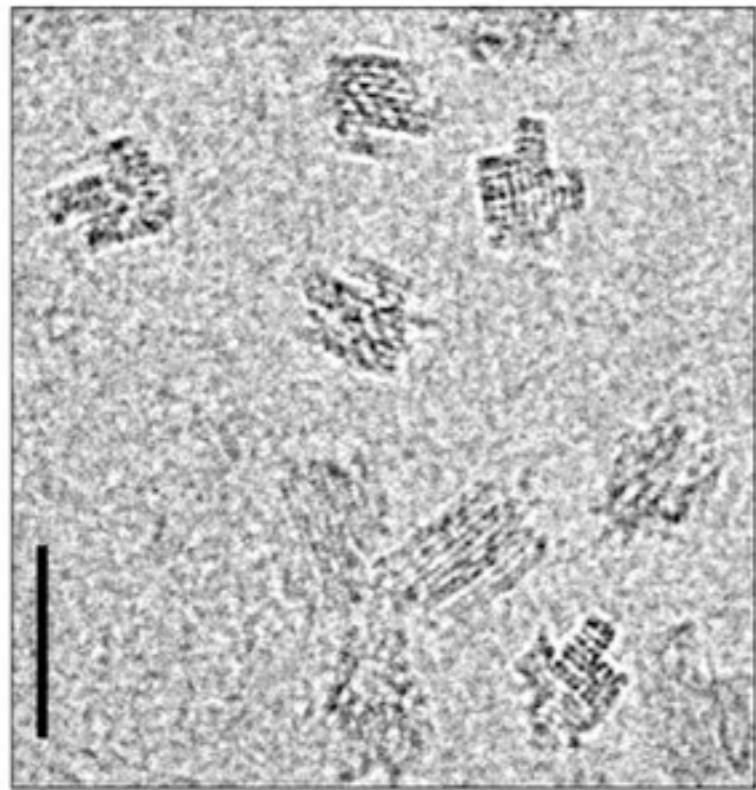


# Cryo-EM reconstruction versus all-atom simulation



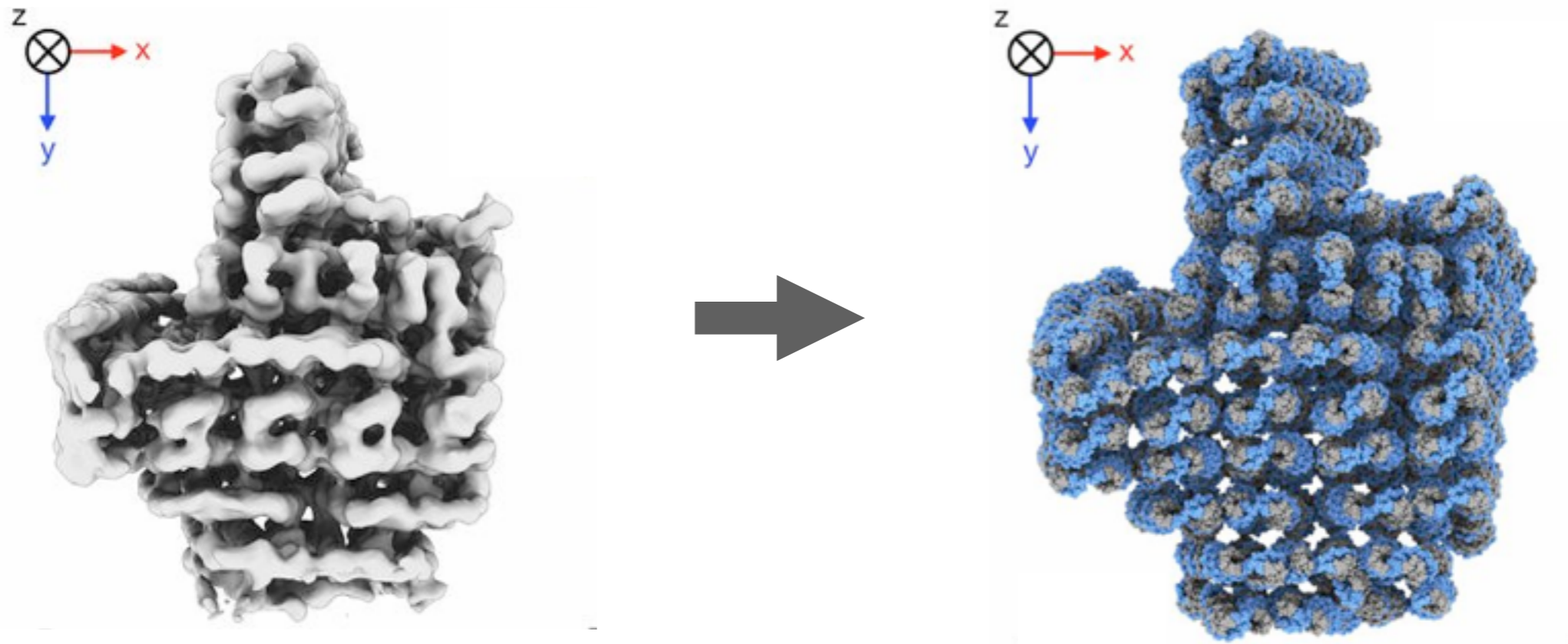
Bai *et al*, PNAS 109:20012 (2012)

# Cryo-EM reconstruction versus all-atom simulation



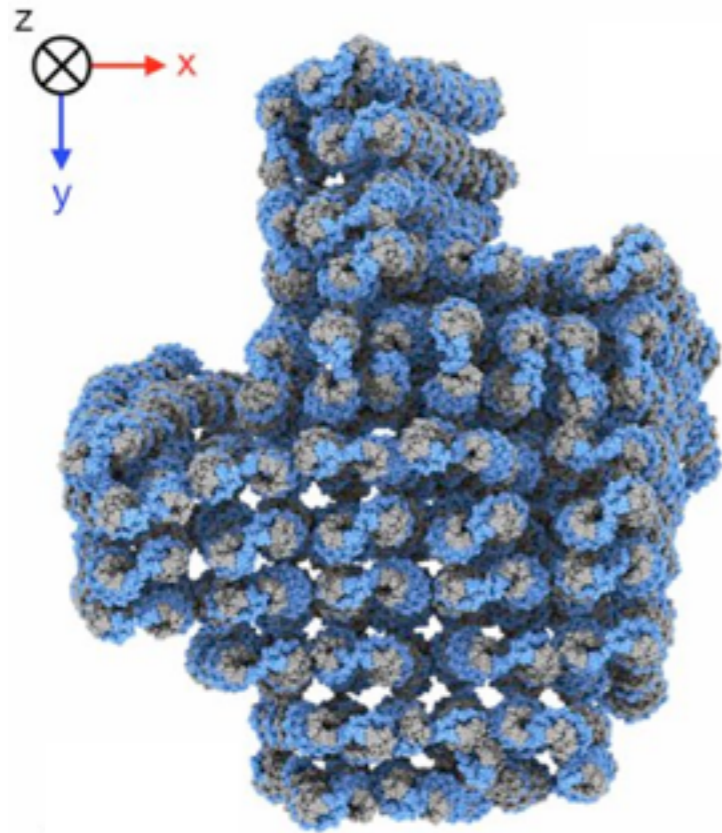
Bai *et al*, PNAS 109:20012 (2012)

# Cryo-EM reconstruction versus all-atom simulation

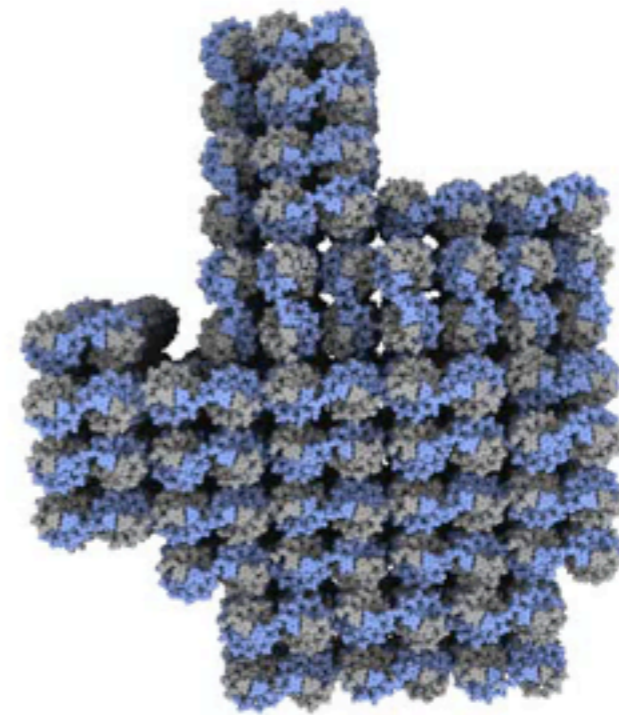


Bai *et al*, PNAS 109:20012 (2012)

# MD simulation of the cryo-EM object starting from a caDNAano design

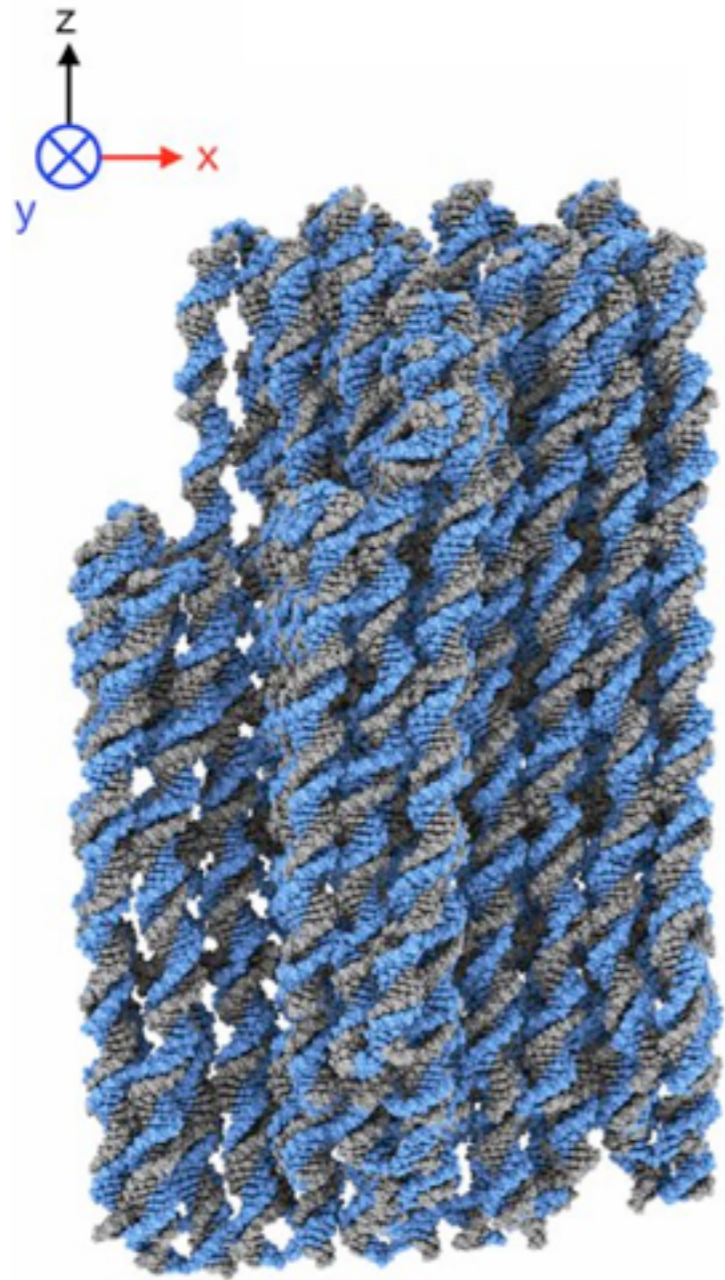


Bai *et al*, PNAS 109:20012 (2012)

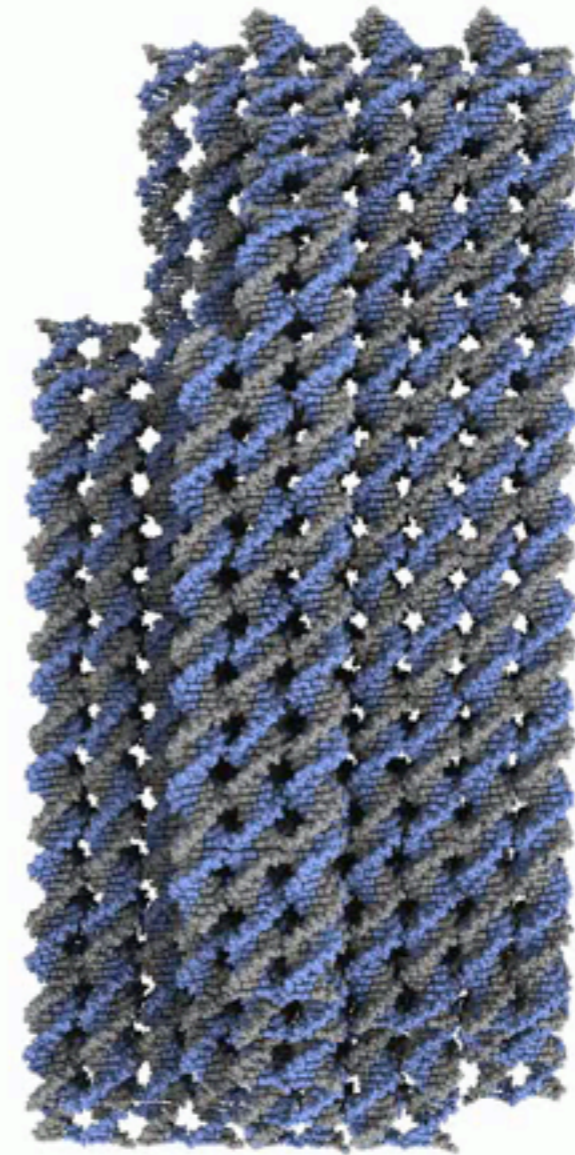


7M atom solvated model  
130 ns MD trajectory

# MD simulation of the cryo-EM object starting from a caDNAano design

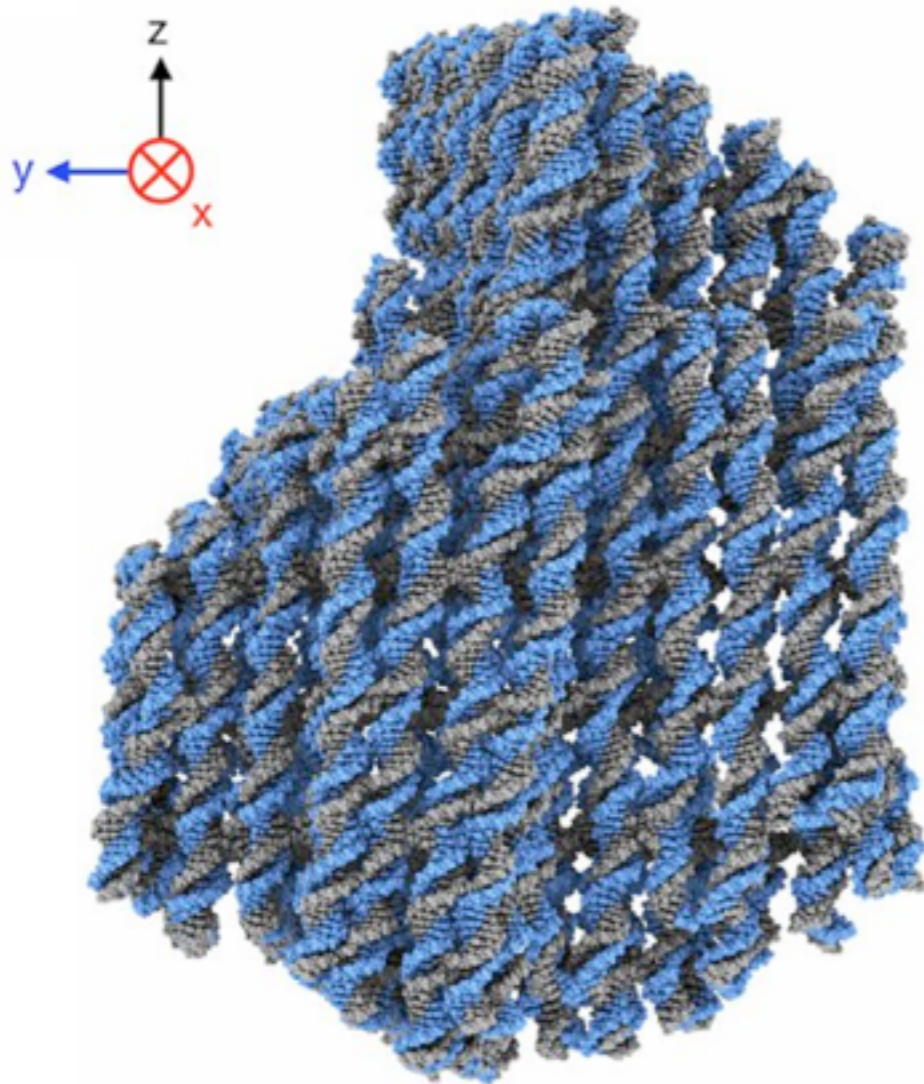


Bai *et al*, PNAS 109:20012 (2012)

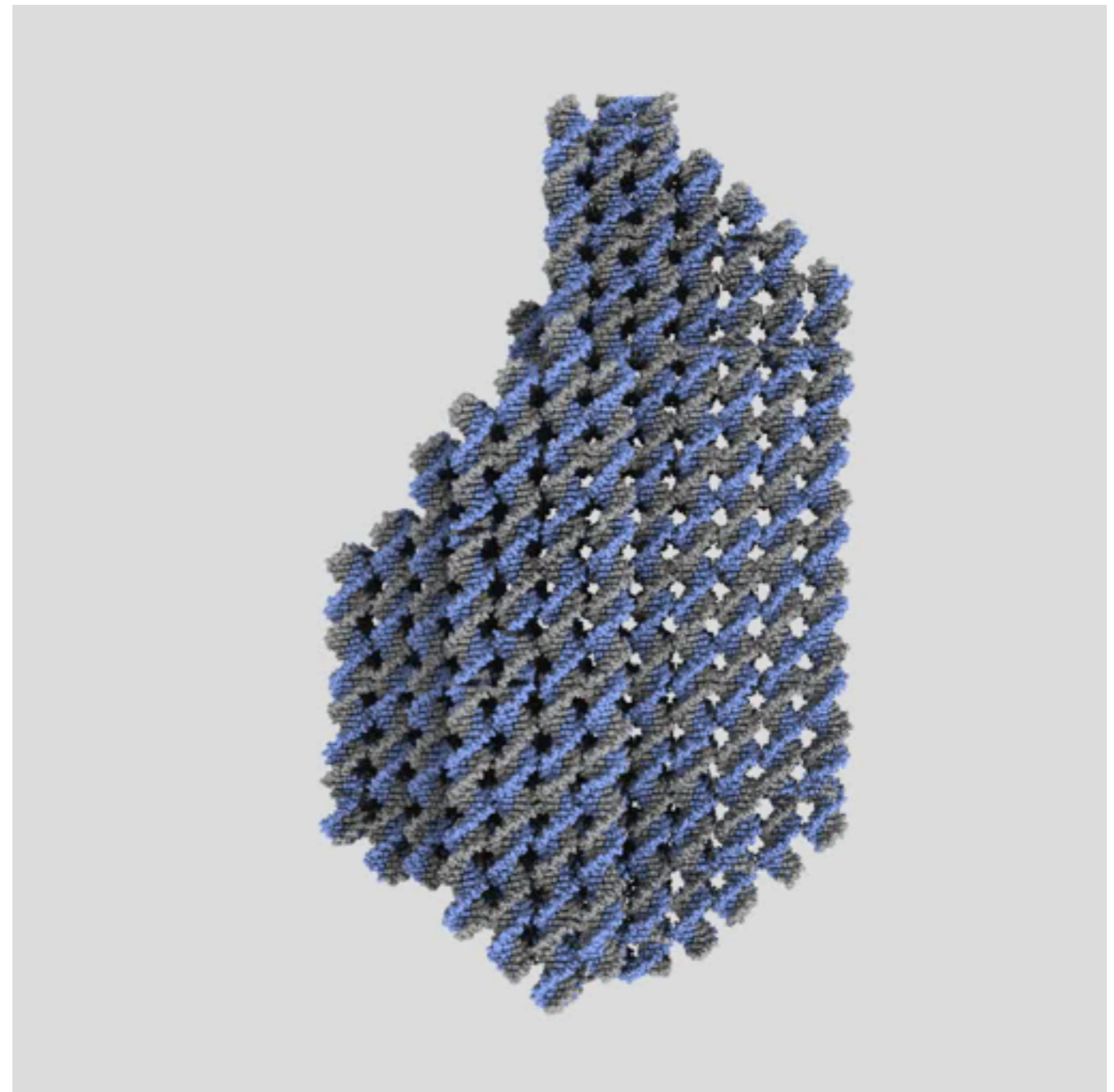


7M atom solvated model  
130 ns MD trajectory

# MD simulation of the cryo-EM object starting from a caDNAano design

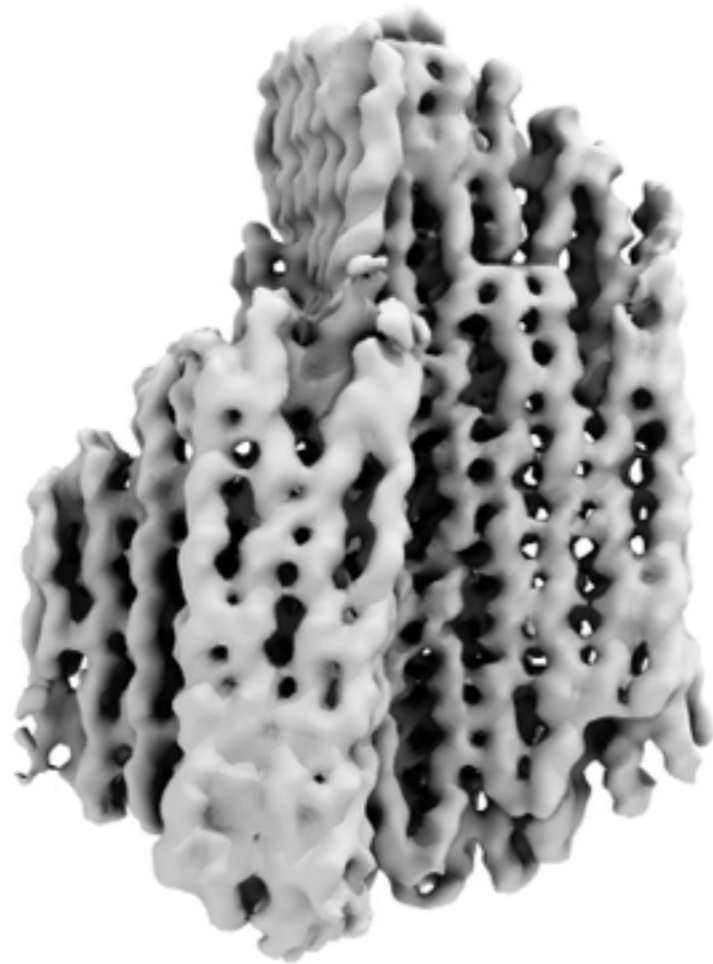


Bai *et al*, PNAS 109:20012 (2012)

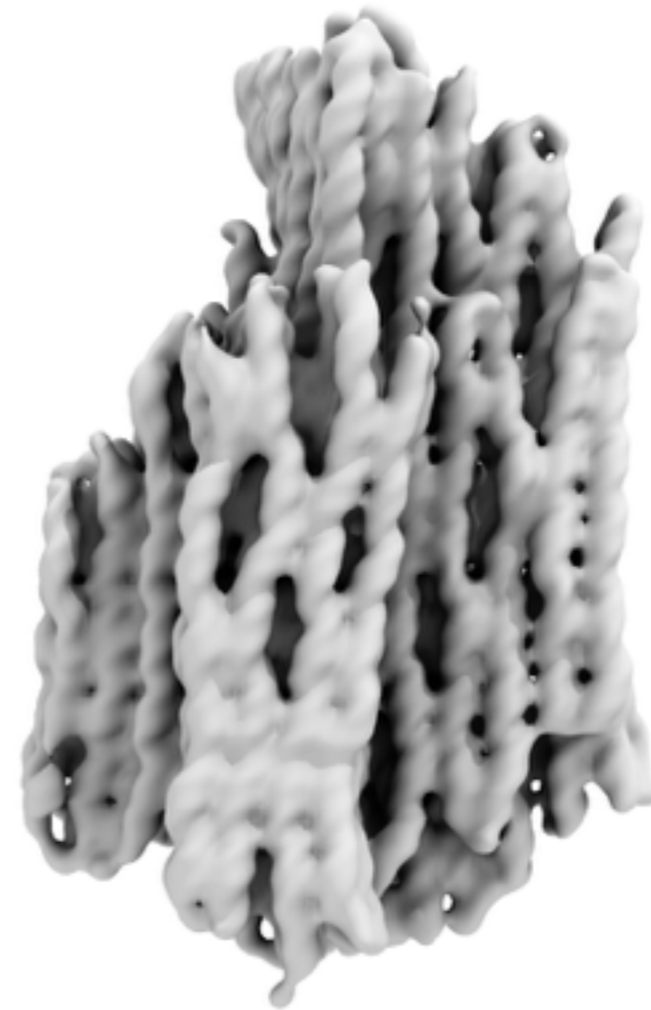


7M atom solvated model  
130 ns MD trajectory

Preliminary analysis indicates excellent agreement between the two methods

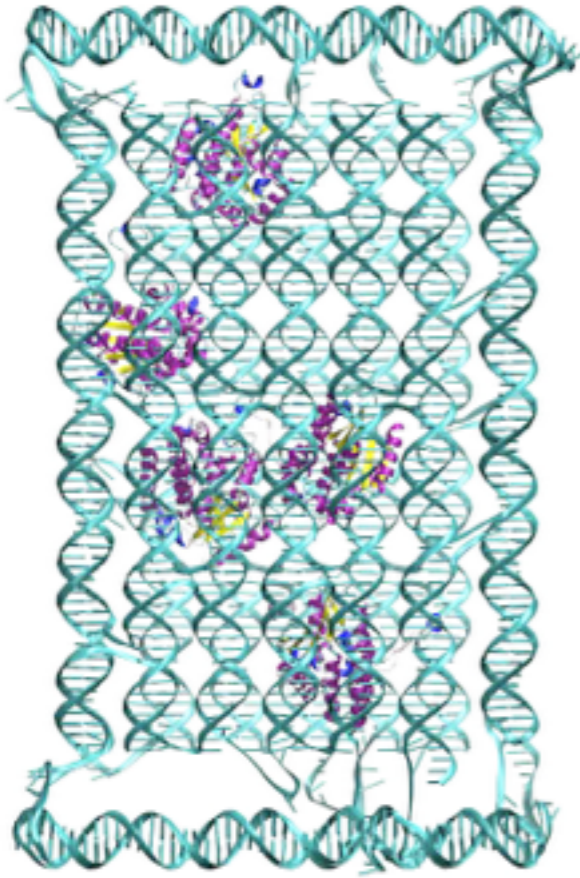


Cryo-EM reconstruction



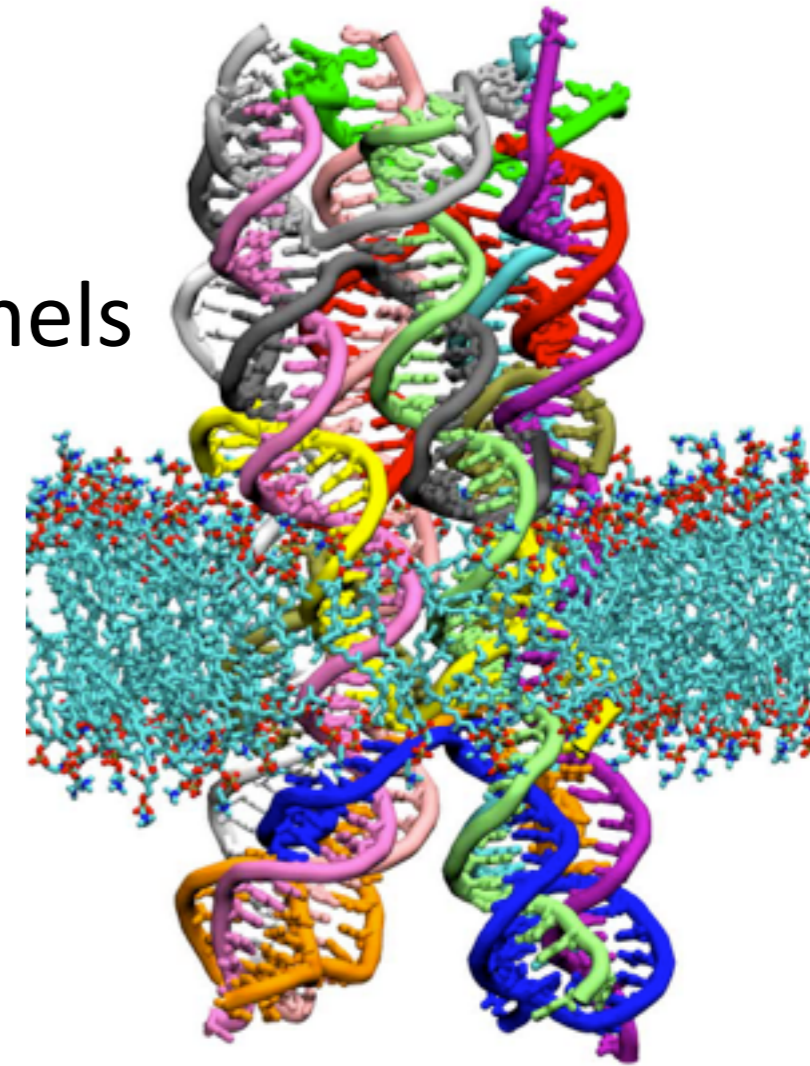
All-atom MD simulation

# Ongoing projects

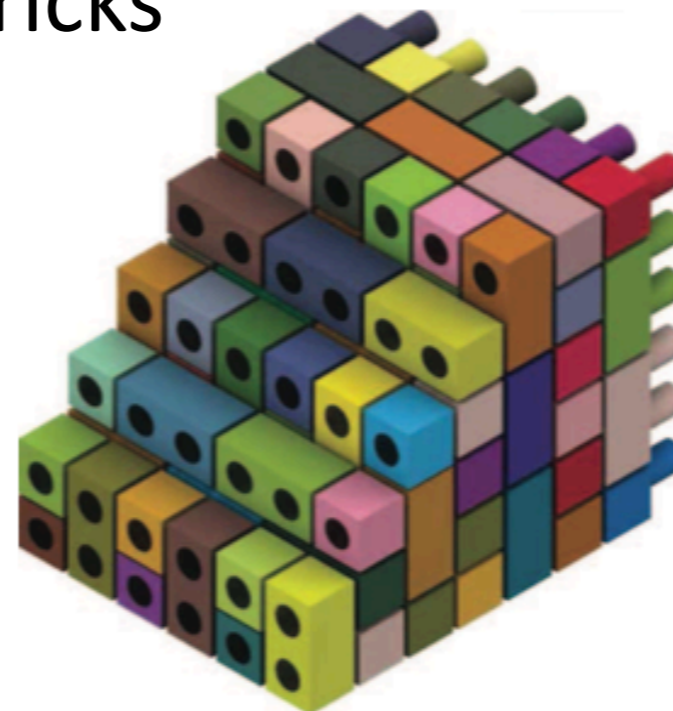
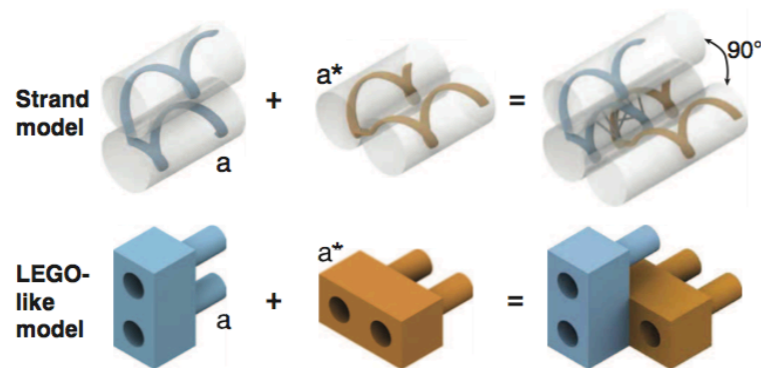


Locking  
nanocontainers

Ion channels



DNA bricks





# Acknowledgement

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Chen Yu Li



Dr. Jejoong Yoo



Dr. Chris Maffeo

## Collaborator (Keyser's group)



Dr. Ulrich F. Keyser



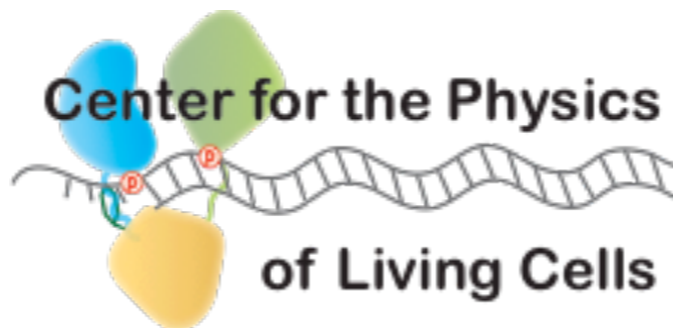
Dr. Silvia Hernández-Ainsa



Elisa A. Hemmig



Jinglin Kong



**XSEDE**

Extreme Science and Engineering  
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