



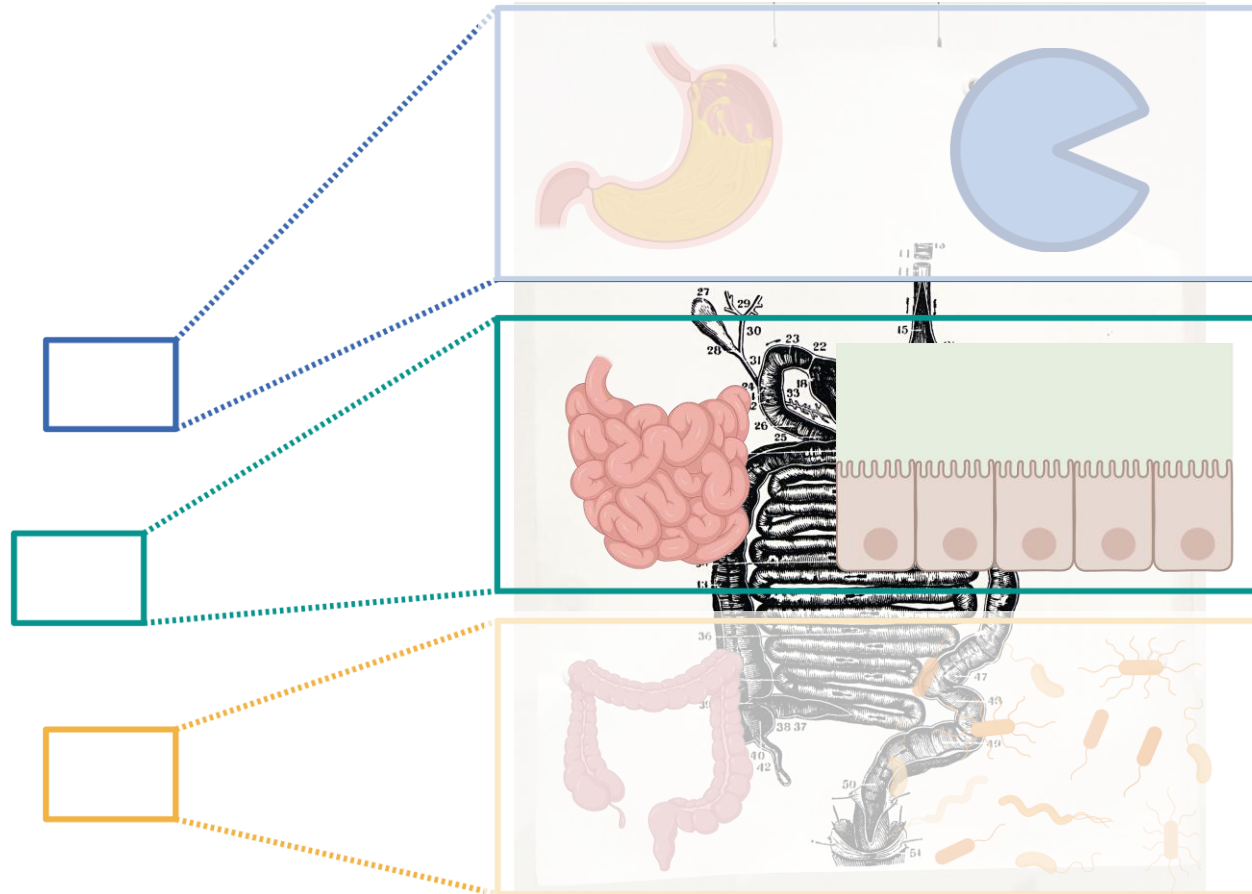
Impact of DNA origami shape, ligand, and ligand density on diffusion through intestinal mucus

Matteo Tollemeto
Technical University of Denmark (DTU)

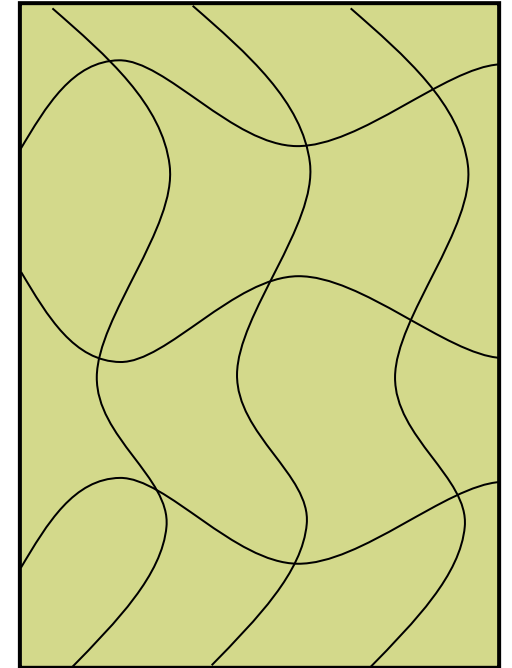
One day at the MoMA



The Gastrointestinal Tract & its barriers



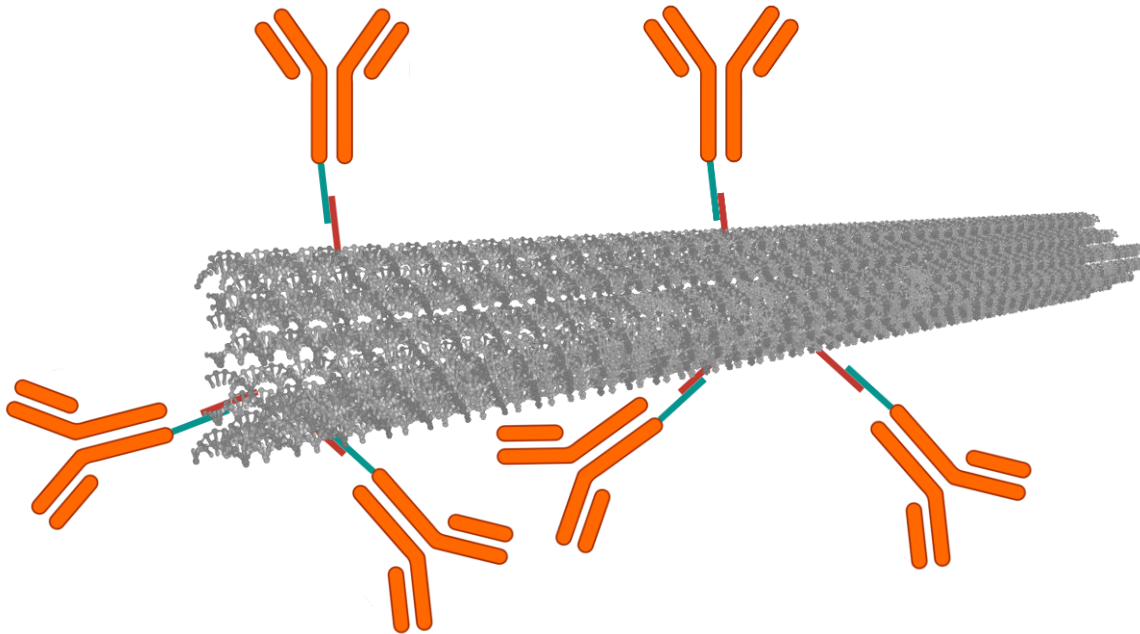
Mucus



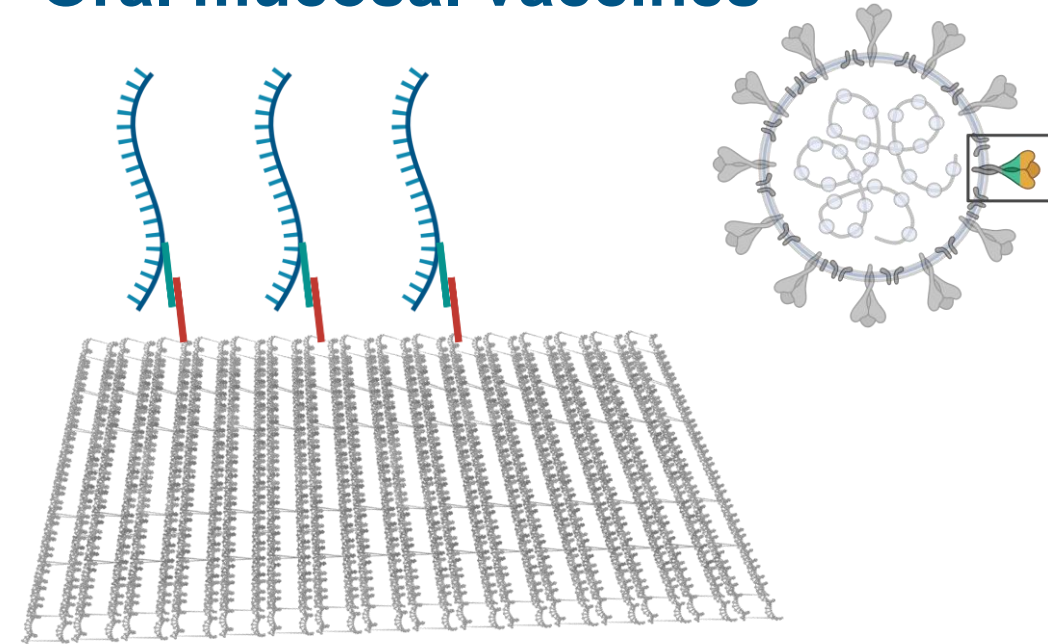
- Viscoelastic
- Pore size 200-1000 nm
- Negatively charged

“Until it’s delivered, it’s not a drug”¹

Oral cancer therapy

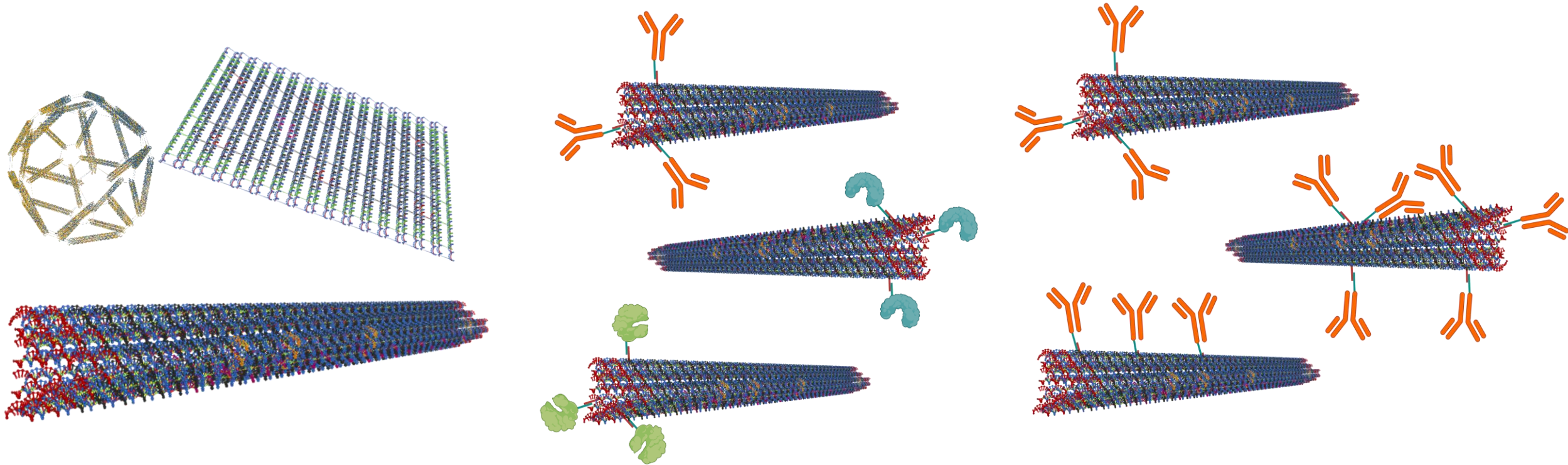


Oral mucosal vaccines



1- Prof. Samir Mitragotri

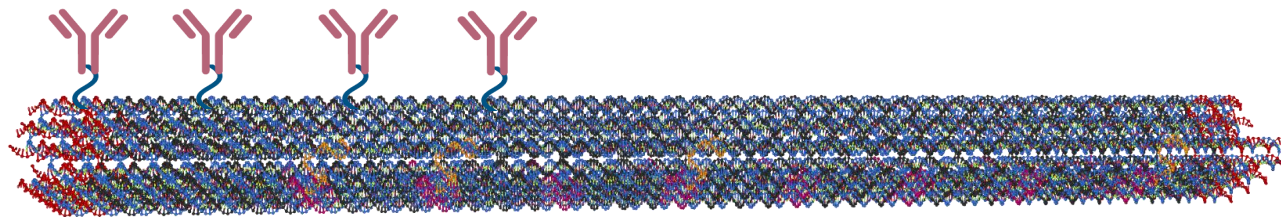
Impact of DNA origami **shape**, **ligand**, and **ligand density** on diffusion through intestinal mucus



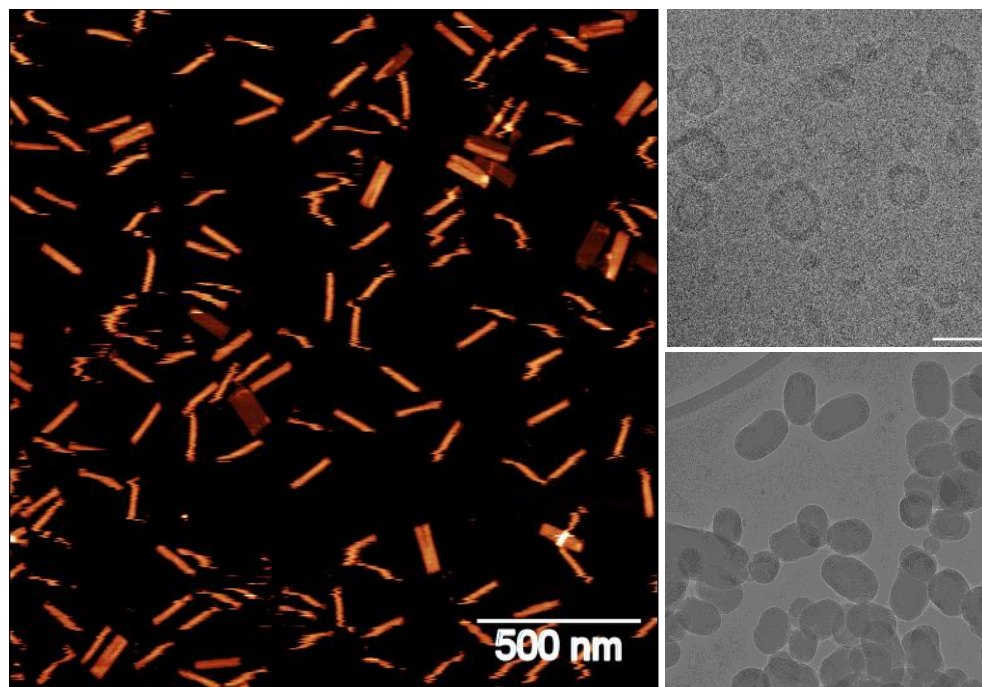
<https://www.biorxiv.org/content/10.1101/2025.04.25.650571v1> Accepted with minor revisions in Nano Letters

Why DNA origami?

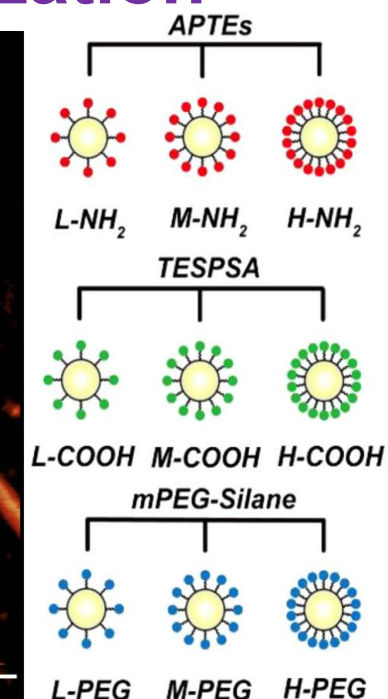
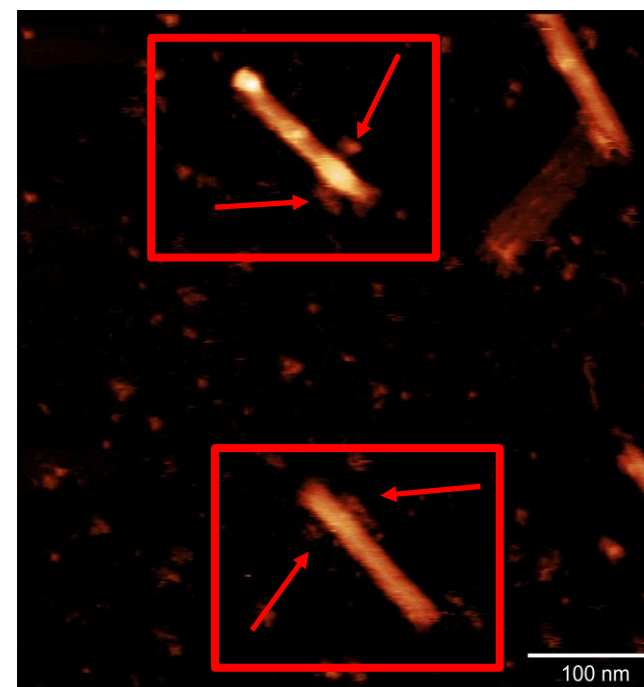
- Exact size & shape
- Exact position
- Exact number
- Simple chemistry



Reproducibility



Functionalization

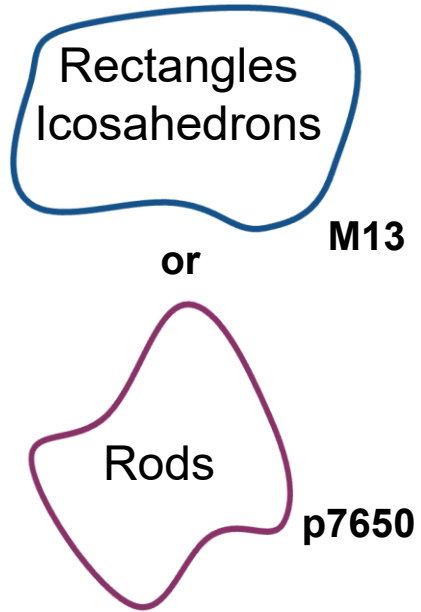


[10.1021/acsnano.2c11147](https://doi.org/10.1021/acsnano.2c11147)

DNA origami assembly

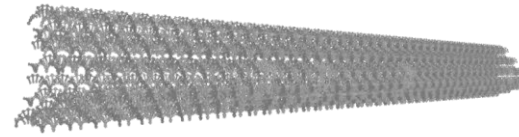
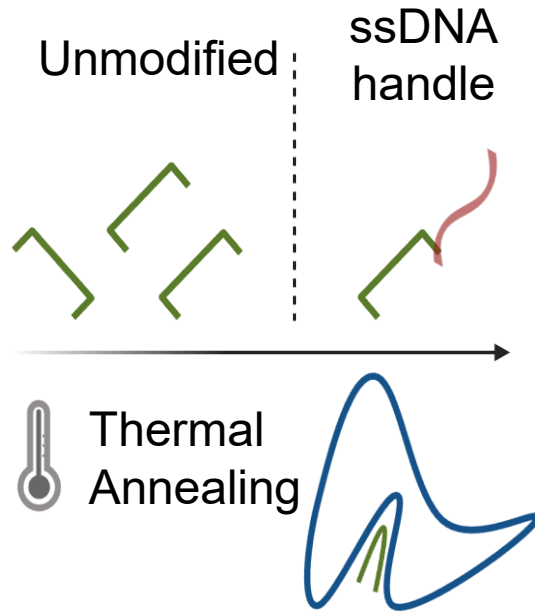
ssDNA Scaffold

ssDNA staples

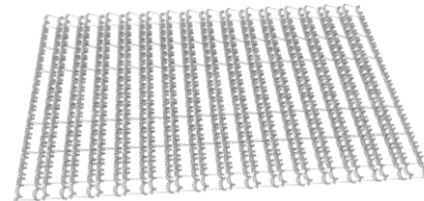


M13

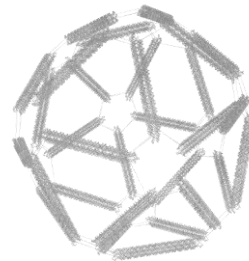
p7650



15 nm x 150 nm

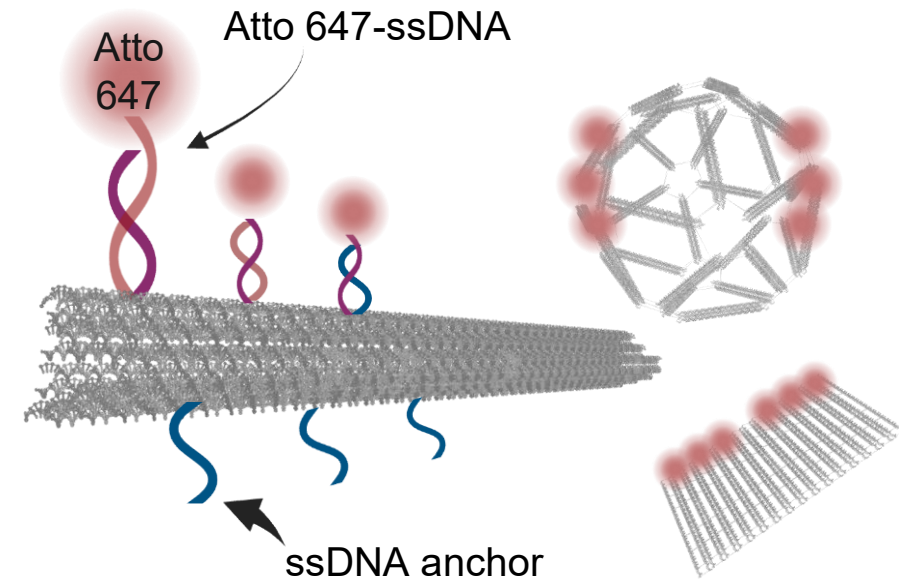


75 nm x 100 nm x 2nm

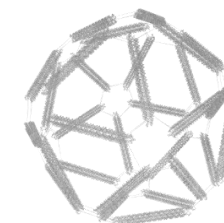
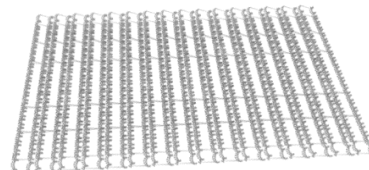
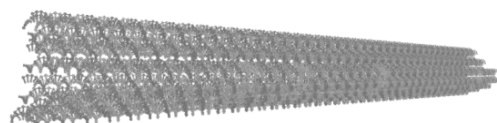
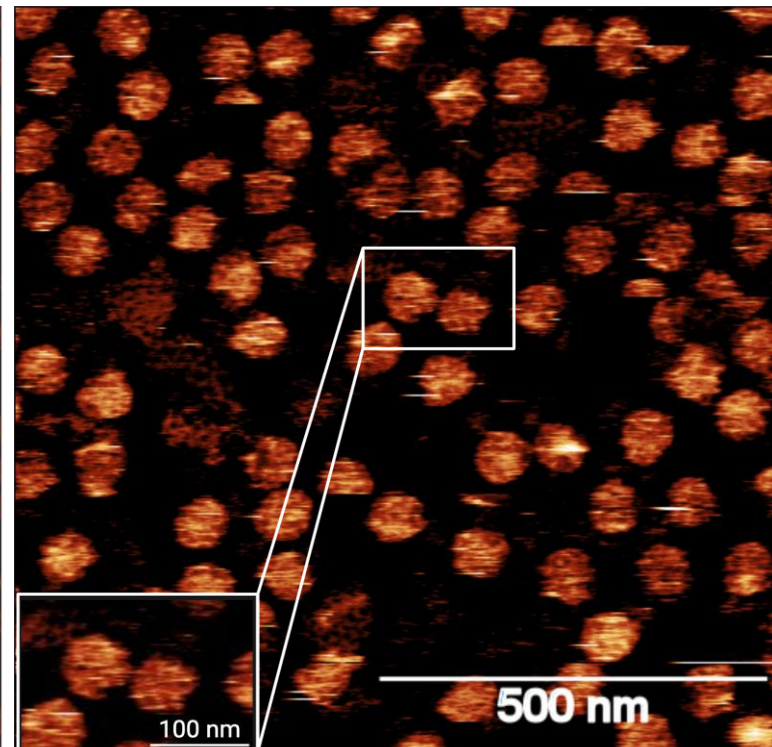
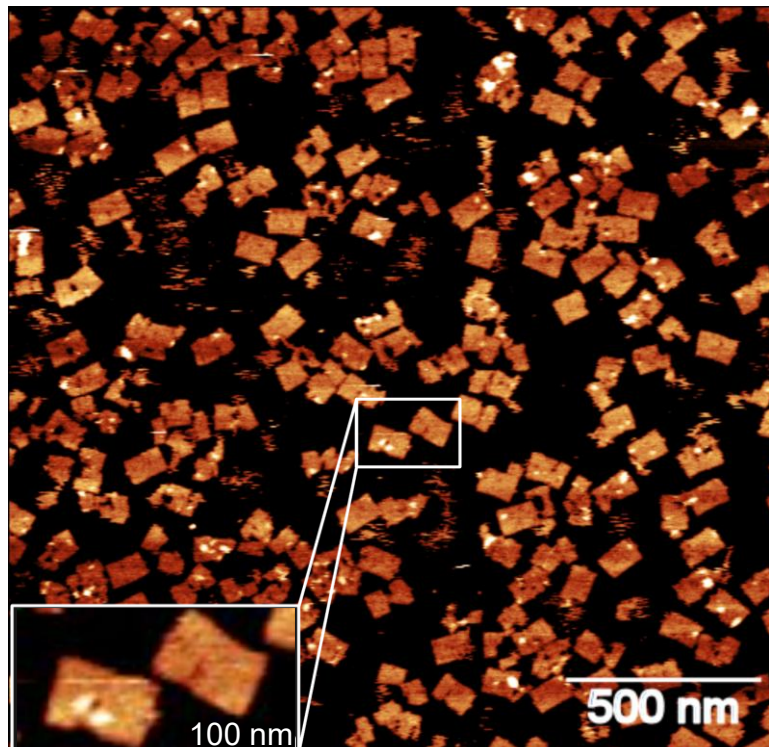
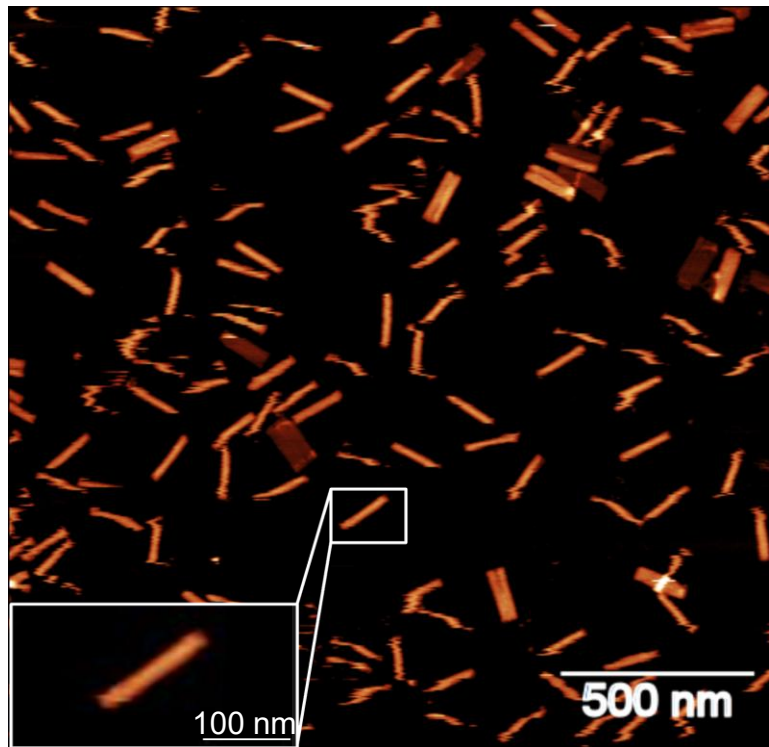


45 nm

DNA origami labelling

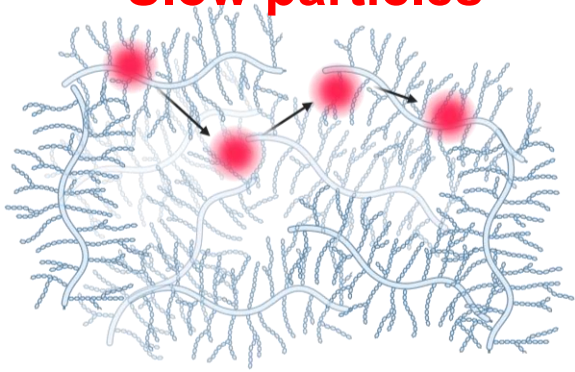


DNA origami

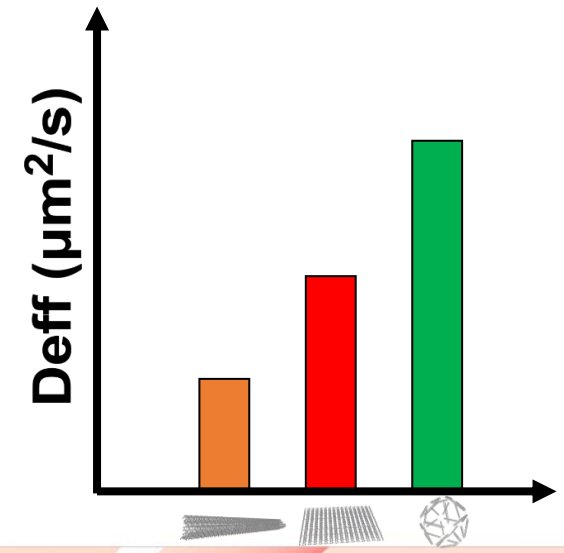
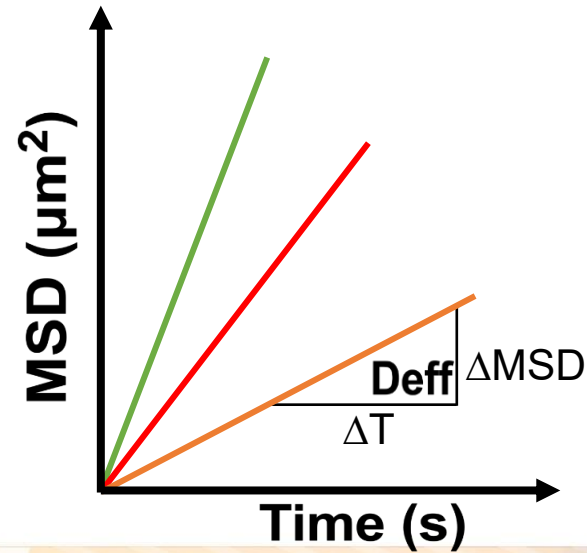
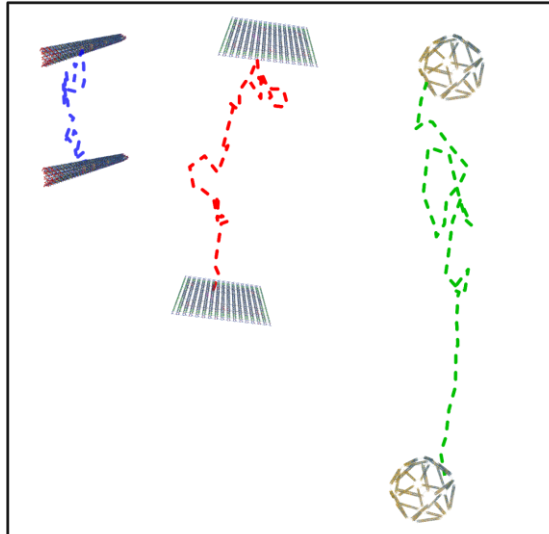
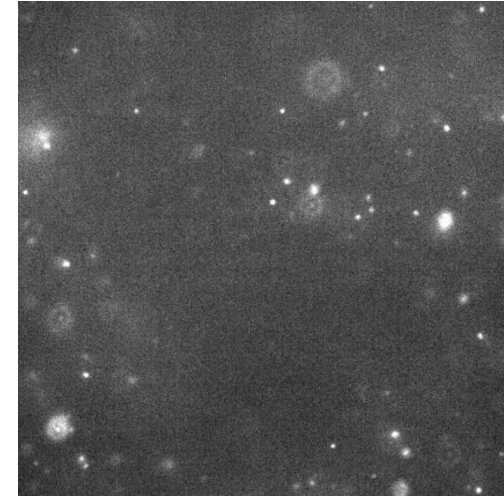
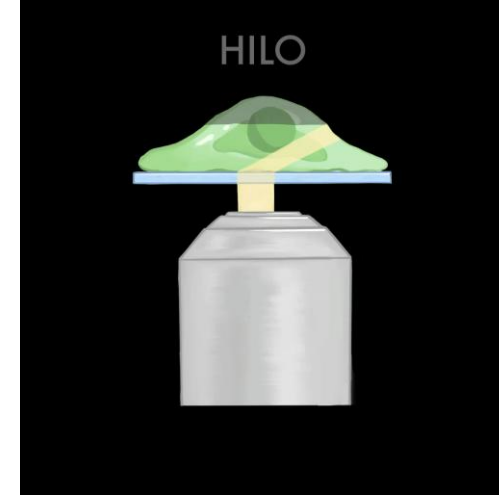
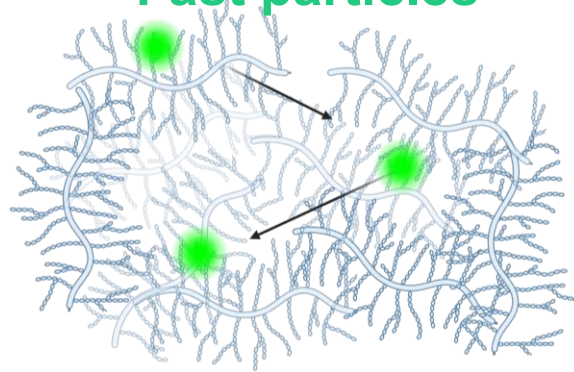


Study framework

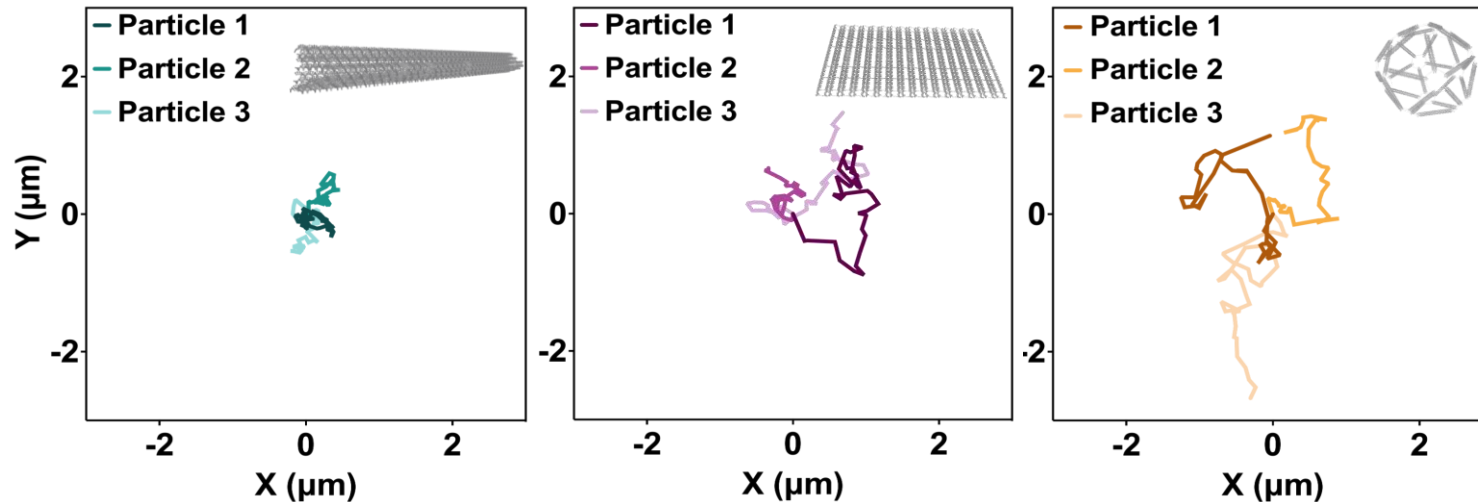
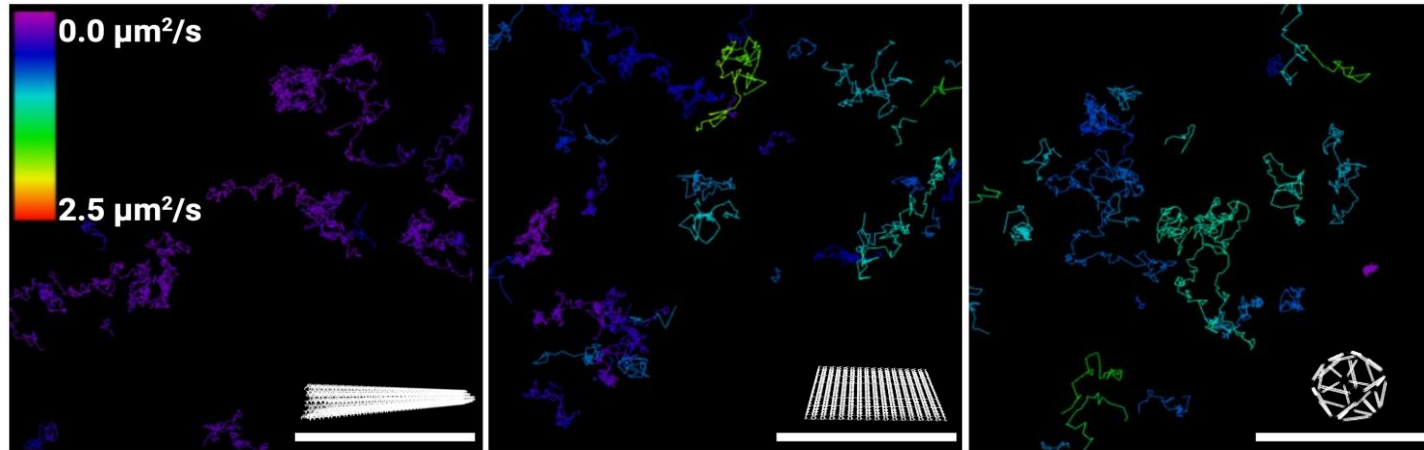
Mucoadhesion
Slow particles



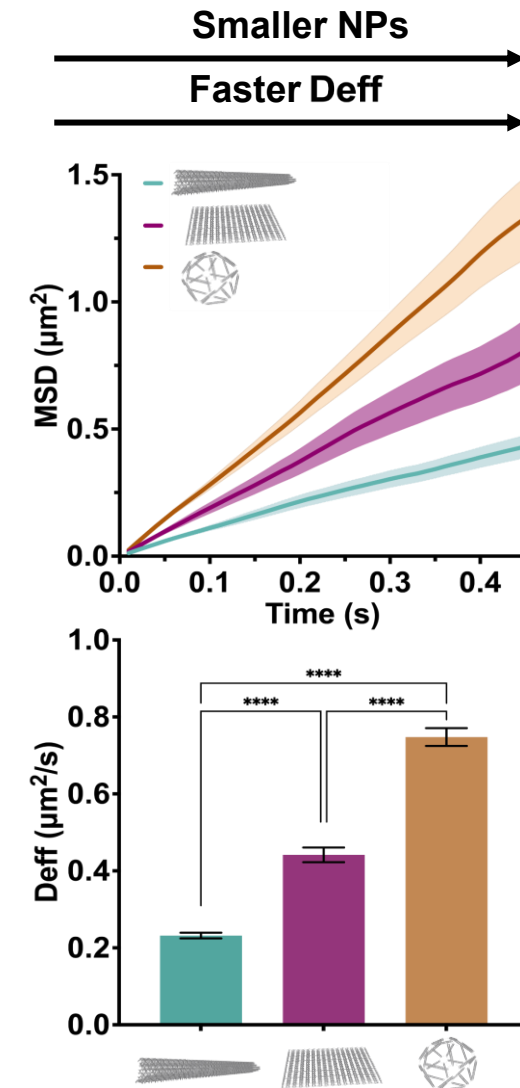
Mucopenetration
Fast particles



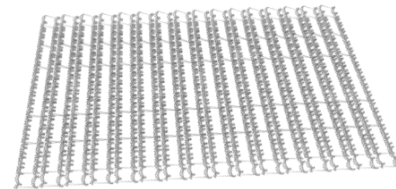
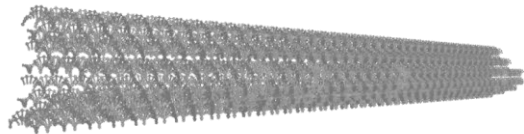
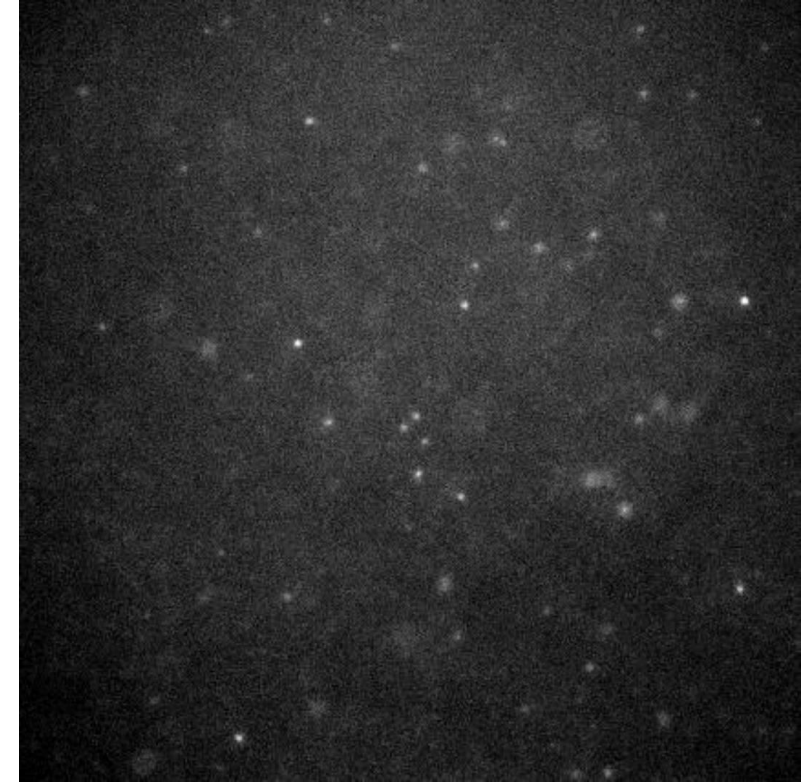
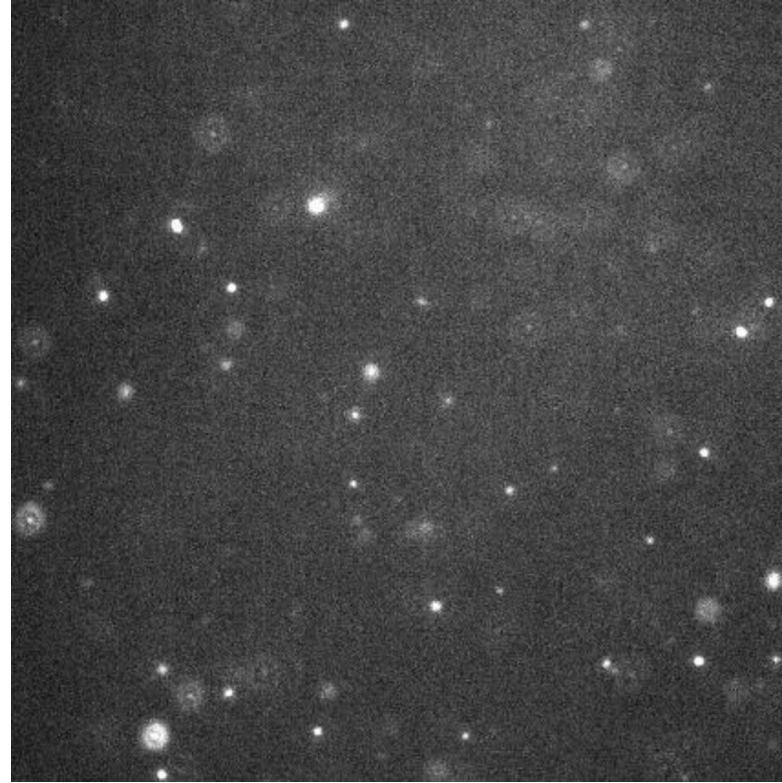
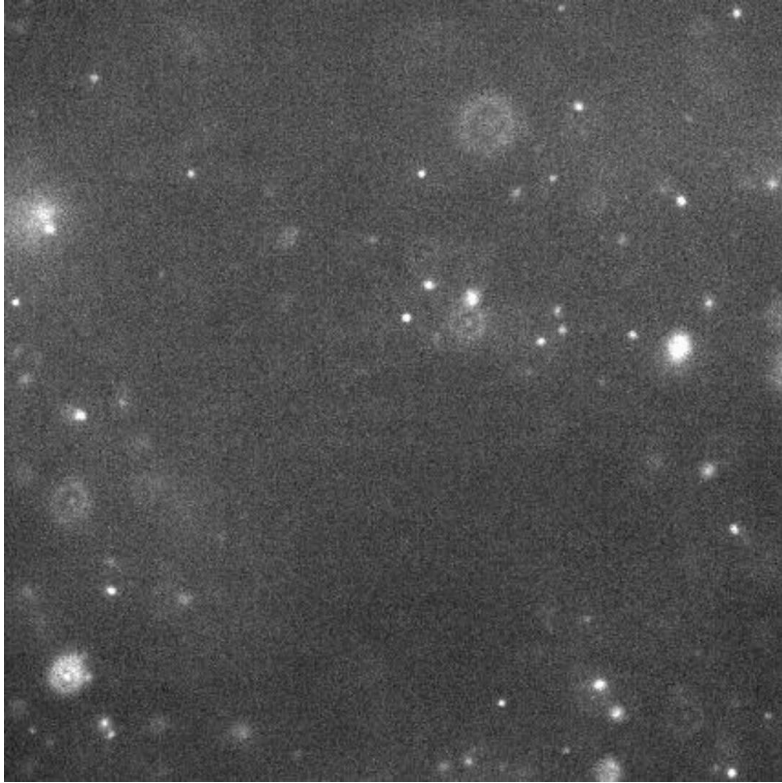
Shape effect



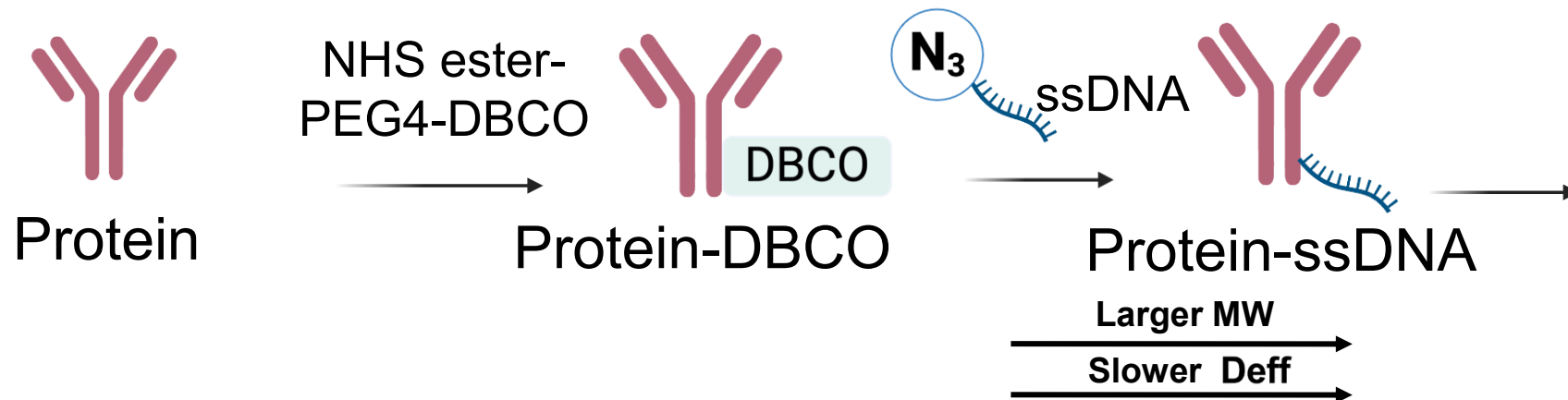
Scale bar: 5 μm



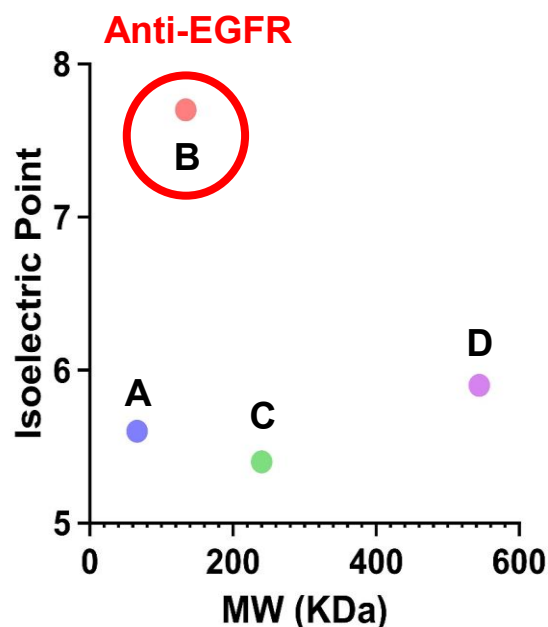
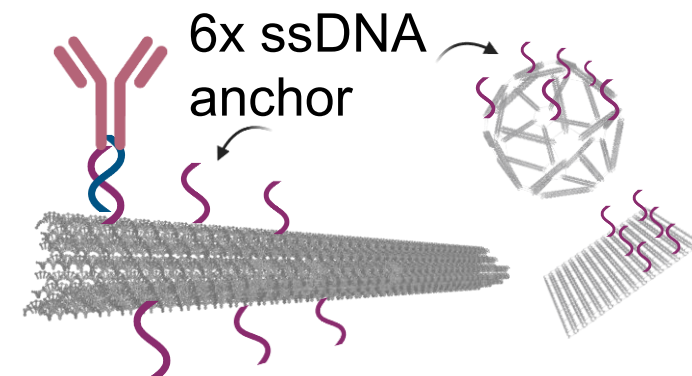
Shape effect



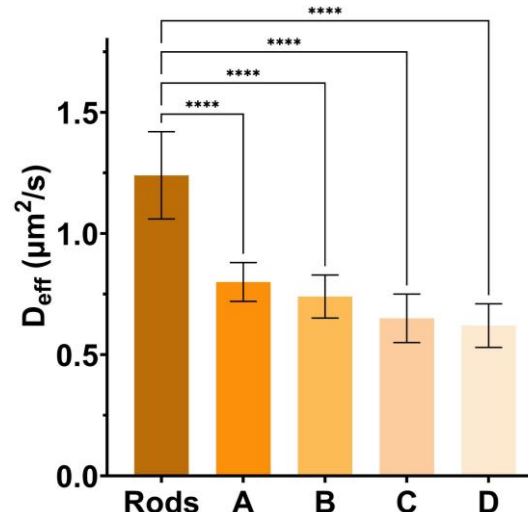
Ligand effect



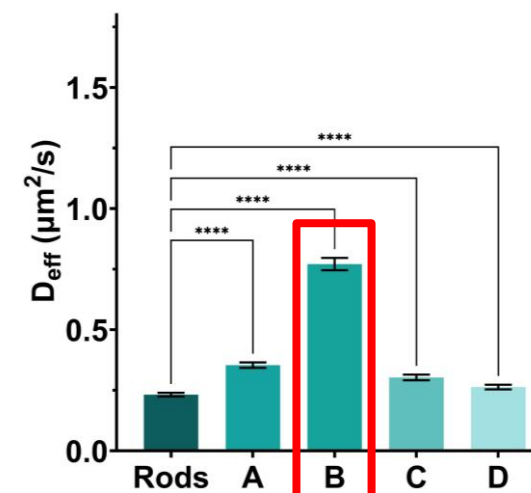
Expectations vs Reality
Glycerol vs *ex vivo* mucus



Inert viscous media

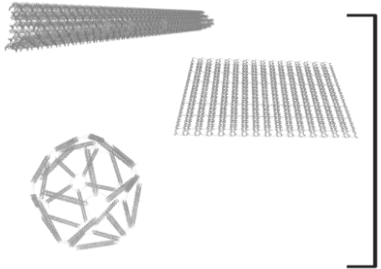


Mucus



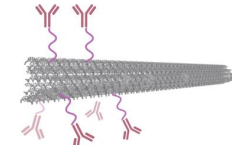
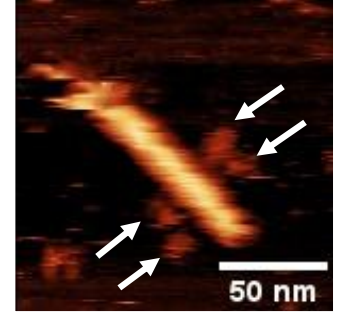
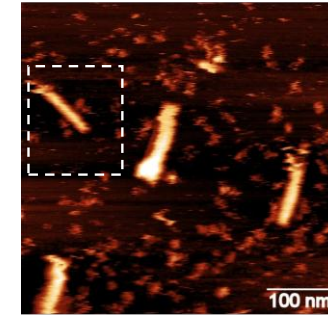
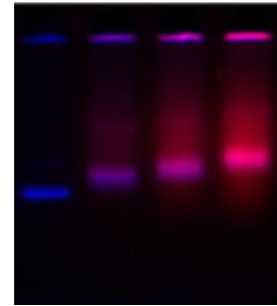
Density effect

Shapes

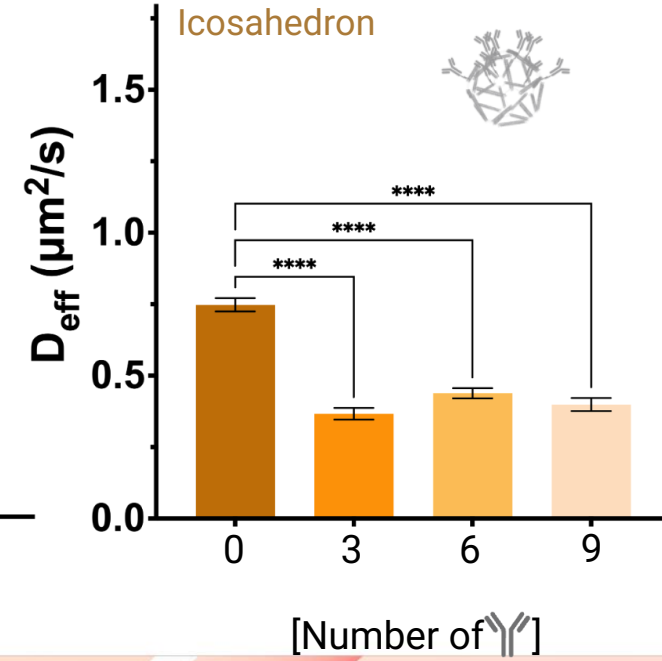
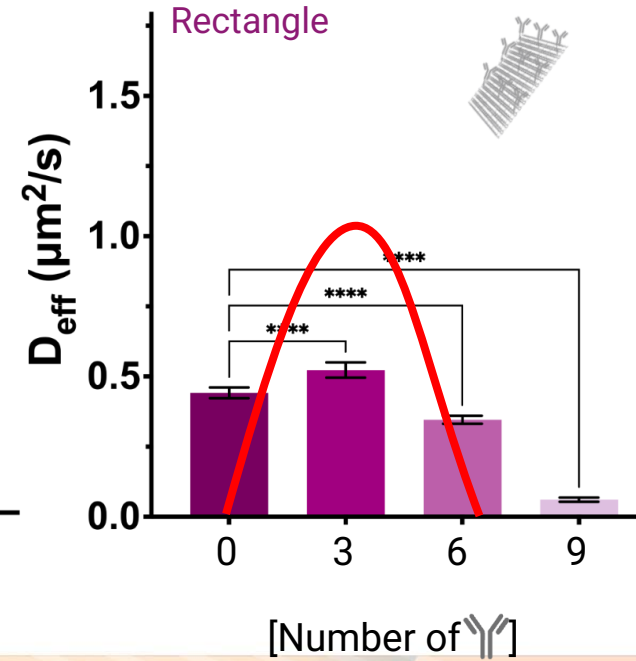
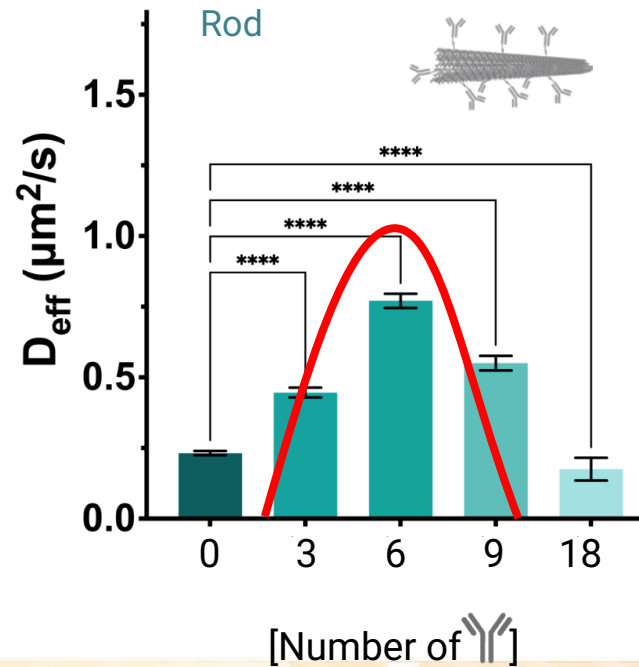
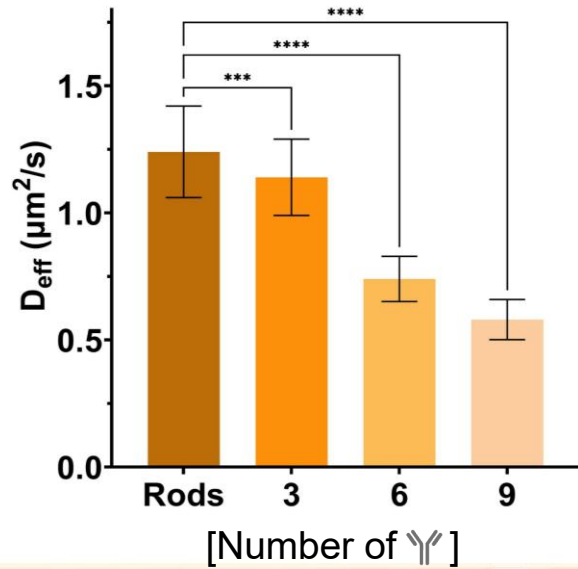


Ligand Density

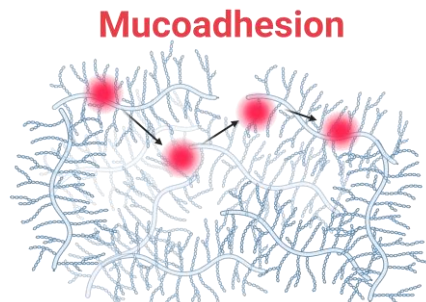
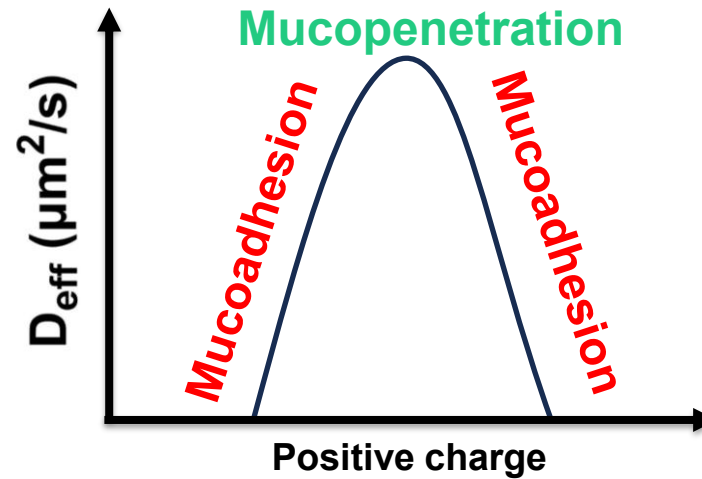
0x 3x 6x 9x



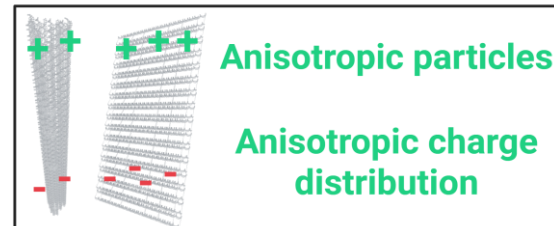
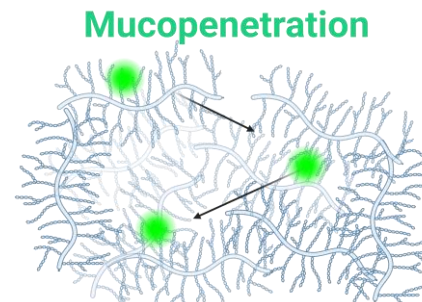
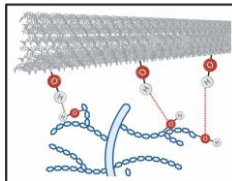
More
 Slower D_{eff}
 Inert viscous media



Take home message

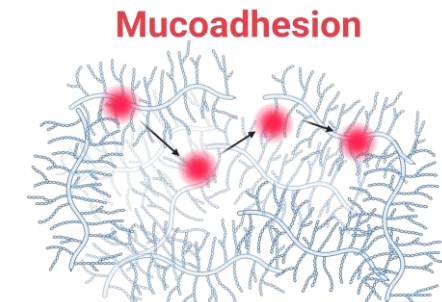


Hydrogen Bonding
Hydrophobic interactions

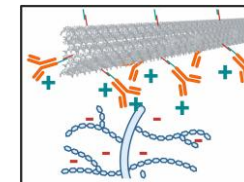


Anisotropic particles

Anisotropic charge
distribution



Electrostatic interactions

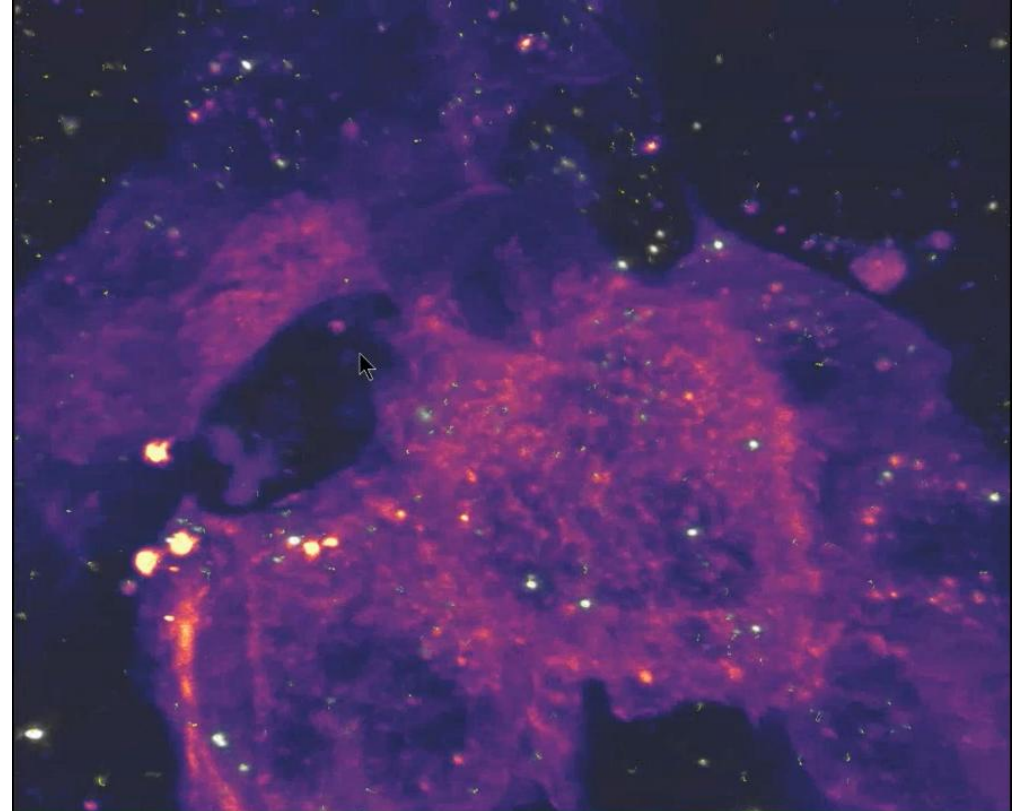
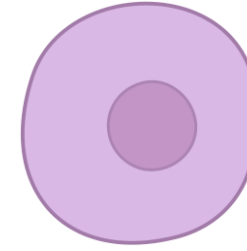
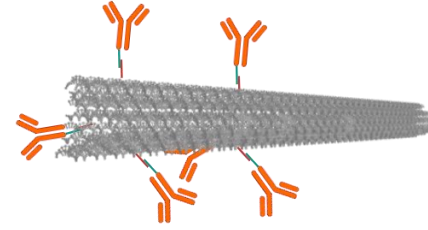
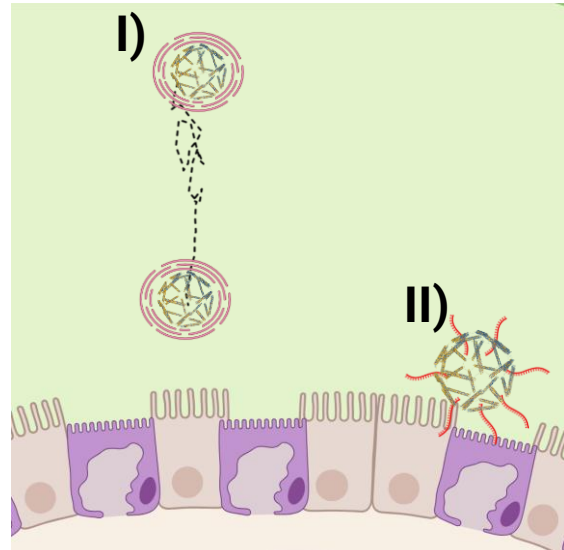
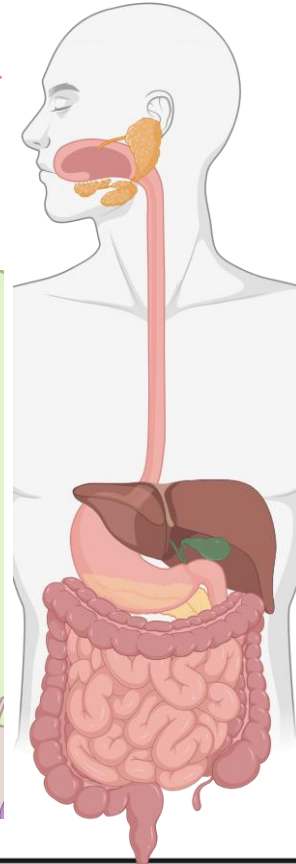
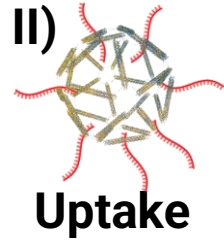
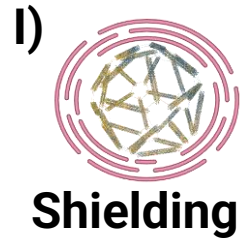


What's next?



Oral drug delivery

Particle design



Acknowledgements



Prof. Anja Boisen
IDUN group
DTU



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Bio-Organic Chemistry
TU/e

Assis.Prof. Tania Patino-Padial



M.Sc. Lars Paffen



PHILADELPHIA, PA
JULY 13-18, 2025

**NEXT-GENERATION
DELIVERY INNOVATIONS**