Nanoscopic imaging of membrane proteins

"The starry heavens above me"

Telescope

Supported by AFOSR YIP program

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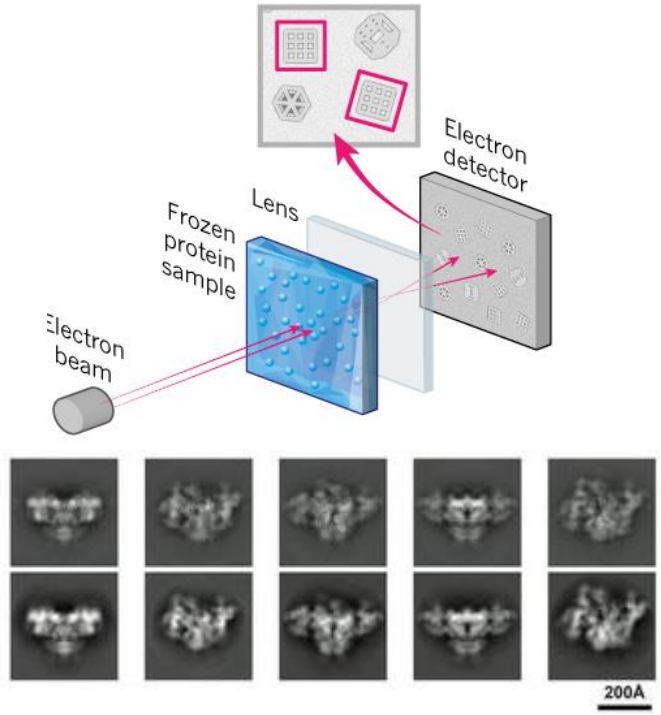
The disconnection between two Nobel prizes

Cryo-EM (2017, Chemistry) ***versus*** **Super-resolution OM (2014, Chemistry)**

single snapshots

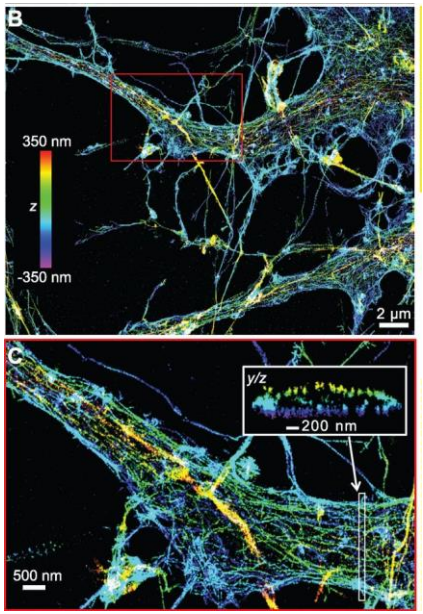
- ❑ nanoscale morphology
- ❑ no liquids, no dynamics



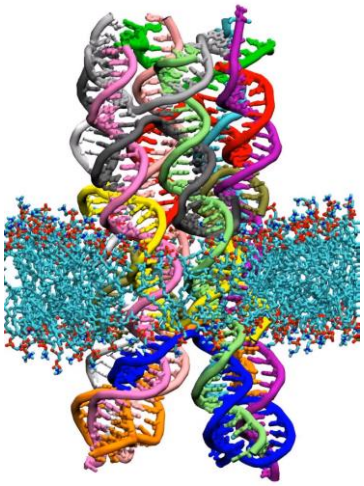
Nature (2015)

in vivo kinetics

- ❑ liquid, dynamics
- ❑ no nanoscale morphology



Needs MD simulation



Science (2014) ; J Phys Chem Lett (2015)

Structural biology

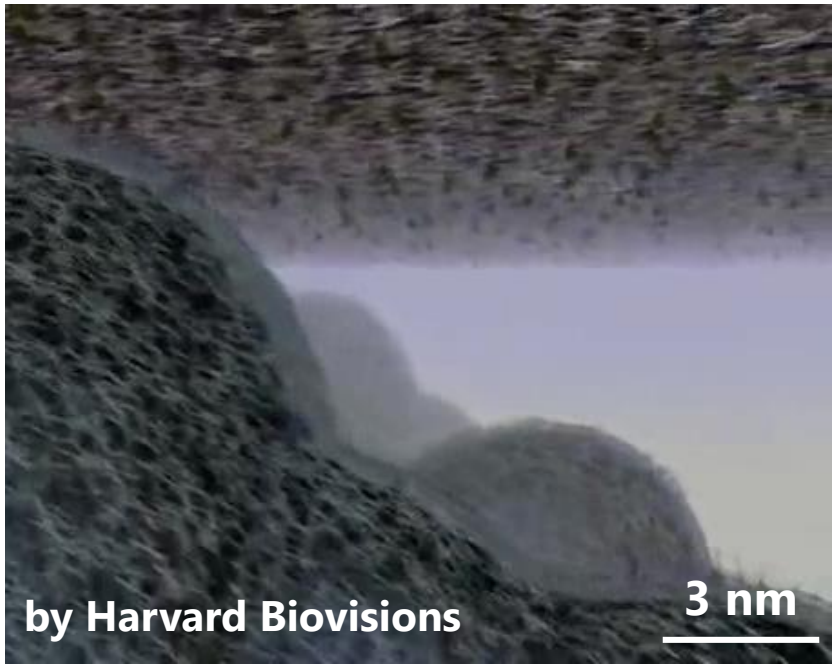
Biophysics

Our long-term goal: **structural biophysics**

Structural biology | **Biophysics**

Reconstruct the "elusive" at the nanoscale

- ❑ nanoscale morphology
- ❑ liquids, dynamics



Only an animation!

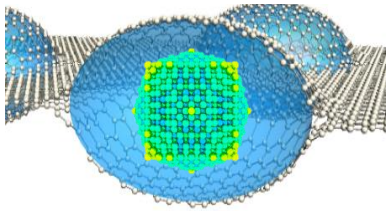
The trick to create a small liquid wrap in the Chen group

Funded projects on ***artificial materials***

Nat. Commun. 8, 761, (2017); ***ACS Nano*** 10, 9801 (2016); ***Acc. Chem. Res.*** 50, 1125 (2017); ***ACS Nano*** 10, 7323 (2016). ***Nano Lett.*** 17, 3270 (2017); ***Curr. Opin. Solid State Mater. Sci.*** invited (2018); ***Macromol. Rapid Commun.*** Accepted (2018).

Our technical core: liquid-phase TEM

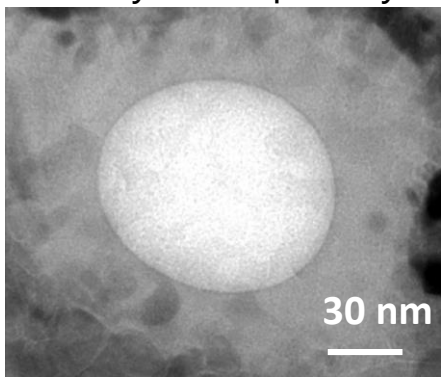
Graphene sandwich

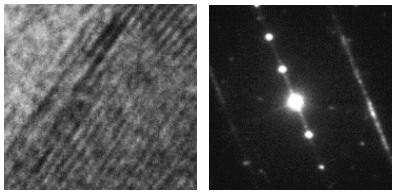


high resolution,
analytical capability

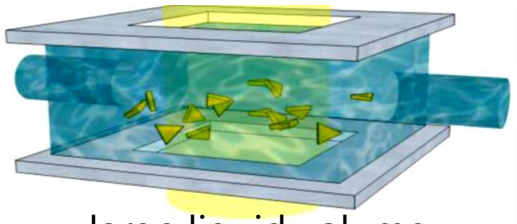
Small angle X-ray scattering

Electron tomography



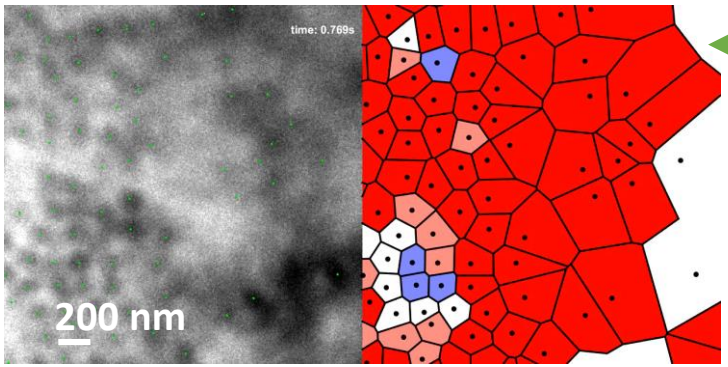


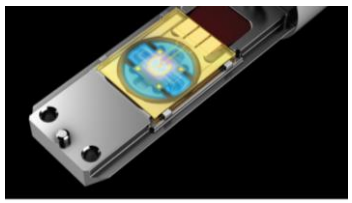
Microfabricated chamber



large liquid volume,
collective behaviors, external stimulation

Optical microscop





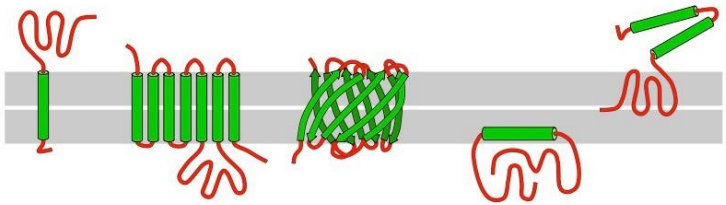
The non-trivial extension to biological samples

Challenges

- ❑ Sensitive to high-energy electron beams
- ❑ Inherently lower contrast
- ❑ Irregularly shaped and (often) heterogeneous

AFOSR-YIP Objectives

Why membrane proteins?



- ❑ Wide relevance
- ❑ Large in size
- ❑ Need to stay in lipids
- ❑ Hard to probe using X-ray crystallography or SSNMR

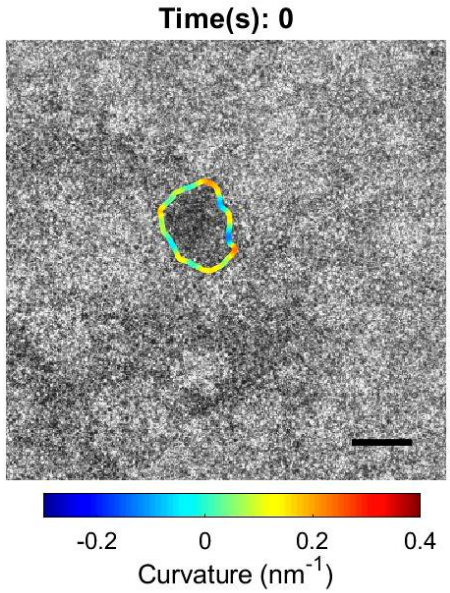
Structural biophysics: first movie of membrane protein fluctuation

Structural biology | **Biophysics**

Johnny Smith

Reconstruct the "elusive" at the nanoscale

- ❑ Atomic or nanometer resolution for morphology, element mapping
- ❑ liquids, dynamics (currently 10^{-3} s resolution, pushing to molecular scale)



(Chen group, unpublished) No longer an animation!