站在巨人的肩膀上
美國工作經驗分享

成功大學 分醫所 生涯講座
紀盈志 (Ying-Chih Chi)
Principal Scientist at Pfizer
Yingchih.Chi@gmail.com
12. 05. 2022

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美國工作經驗分享

計劃趕不上變化
船橋頭自然直？

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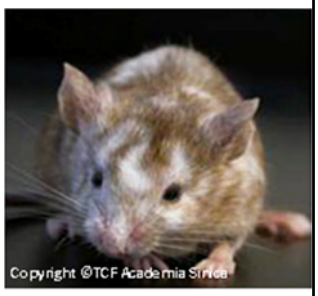
About Me – My career path

FJU - Biology

NCKU – Institute of Molecular Medicine



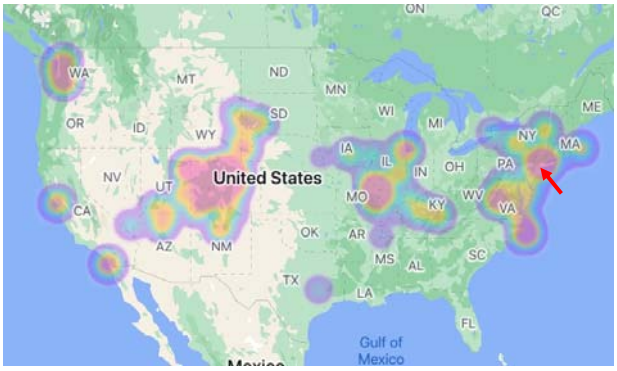
Academia Sinica – Transgenic core facility

University of Colorado Anschutz Campus

About Me – My career path

- **Parkinson's Disease:**
  - **University of Colorado Anschutz Medical Campus, CO**
    Ph.D. student in Biochemistry and Molecular Genetics
    Residue His50 plays a key role in protecting αSynuclein from aggregation at physiological pH
- **Pneumonia Infection:**
  - **University of Colorado Anschutz Medical Campus, CO**
    Postdoctoral fellow
    Understanding the catalytic mechanism of *Streptococcus pneumonia* IgA1 protease and the development of the neutralizing antibody
- **Mammalian Histone deposition:**
  - **University of Colorado Anschutz Medical Campus, CO**
    Postdoctoral fellow
    Understanding the molecular interactions among mammalian CAF-1, DNA and histones

About Me – My career path



Columbia University, NY

- **Management of Cryo-EM facility:**
  - **Columbia University, NY**
    Associate research scientist / Assistant director
    Managing all aspects of Cryo-EM facility to perform day to day functions and participate in collaboration projects

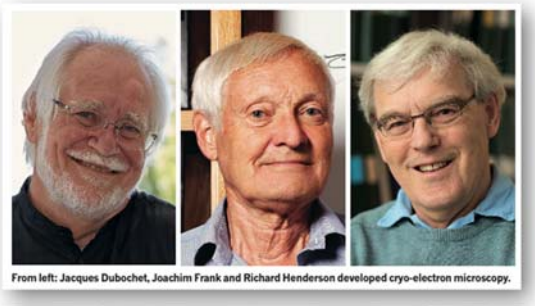
About Me
Career path

Pfizer, MO

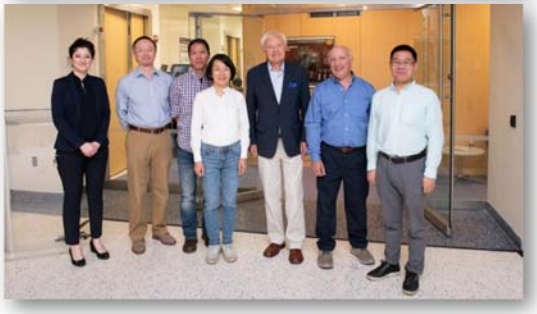
- **Research scientist in biopharma company**
  - **MO**
    Principal Scientist
    Managing Cryo-EM instruments and participle in drug development activities

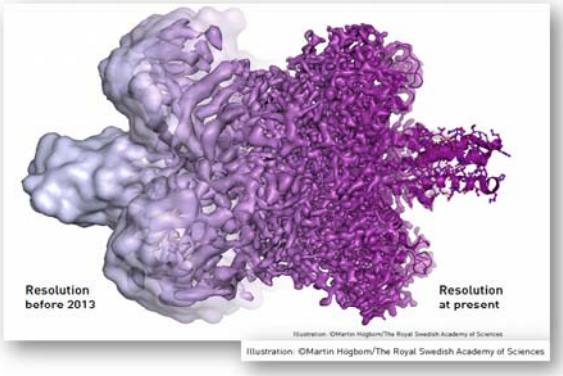
Questions?

The Nobel Prize in Chemistry 2017 : Cryo Electron Microscopy



From left: Jacques Dubochet, Joachim Frank and Richard Henderson developed cryo-electron microscopy.



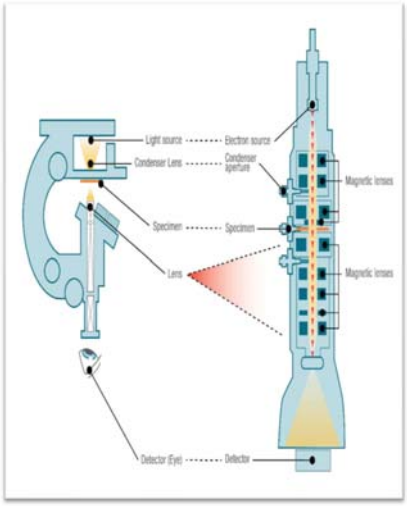


Krios G3i GatanK3 Falcon3 | Krios G3i GatanK3 Falcon3 | Krios G3i GatanK3 Falcon3 | Krios G2 Gatan K3 Falcon3 | Glacios Gatan K3 Falcon3 | F20 Gatan K2 | T12 Ceta

What is CryoEM?

Transmission Electron Microscope (TEM)

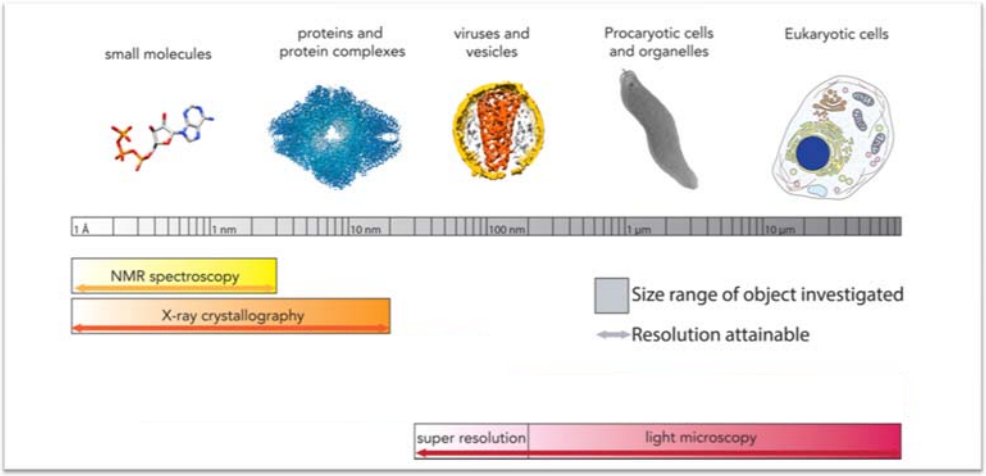
Light microscope



https://www.thermofisher.com/blog/atomic-resolution/seeing-with-electrons-the-anatomy-of-an-electron-microscope/

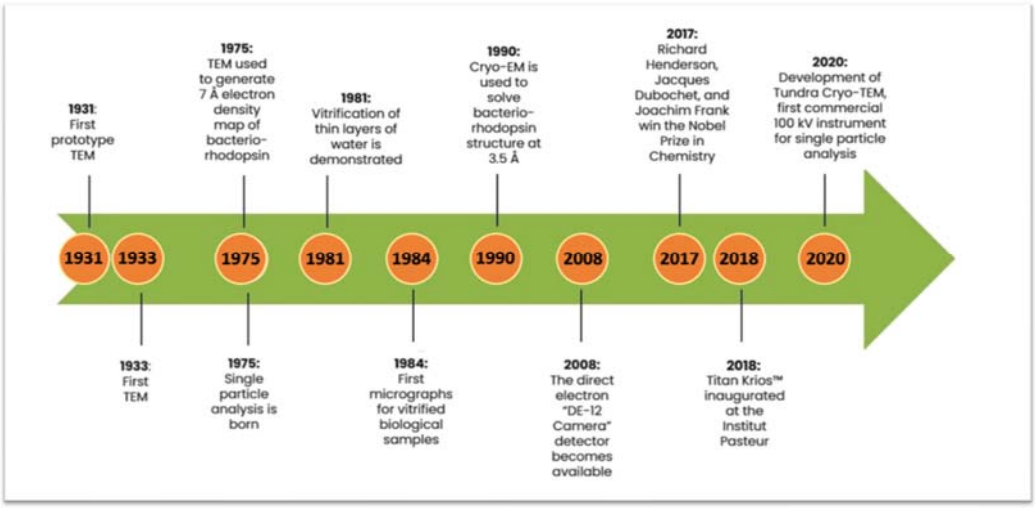
	Light microscope	Transmission Electron microscope (TEM)
Illumination	Light	Electron beam
Magnification	500x to 2000x	100kx to 500kx
Sample thickness	5um or thicker	0.2um or thinner
Sample environment	Ambient air	High vacuum
Lens	Optical lenses	Electromagnetic lenses
Sample preparation	N/A, Stained, or Labelled	Negative stained, or Frozen (Cryo)

Why we need CryoEM?



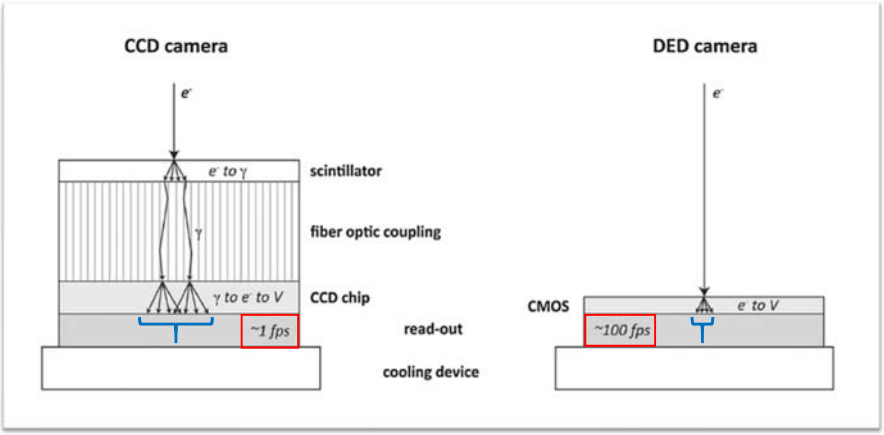
Biochem Soc Trans **46**, 807–816 (2018).

CryoEM – 40 years of development

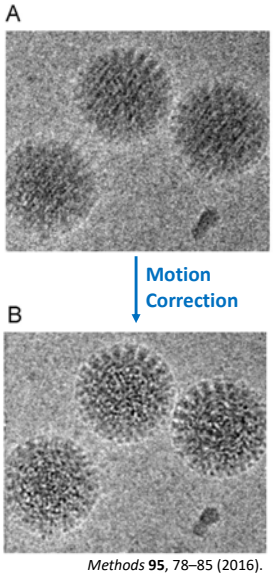


https://bitesizebio.com/62839/history-of-cryo-electron-microscopy/

Direct electron detector (DED): One of the driving force of the cryoEM resolution revolution

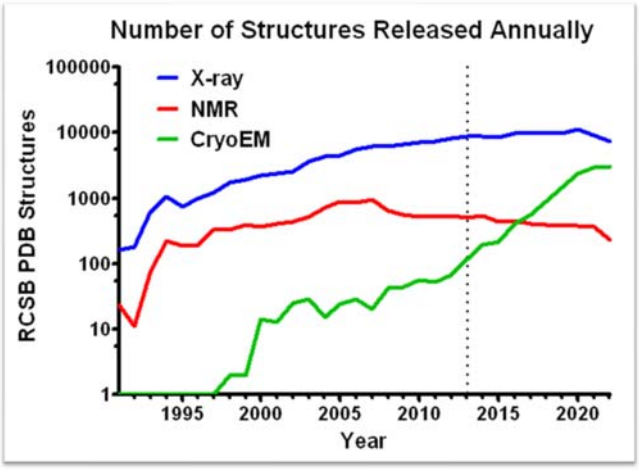


Annals of Anatomy - Anatomischer Anzeiger **217**, 82–96 (2018).

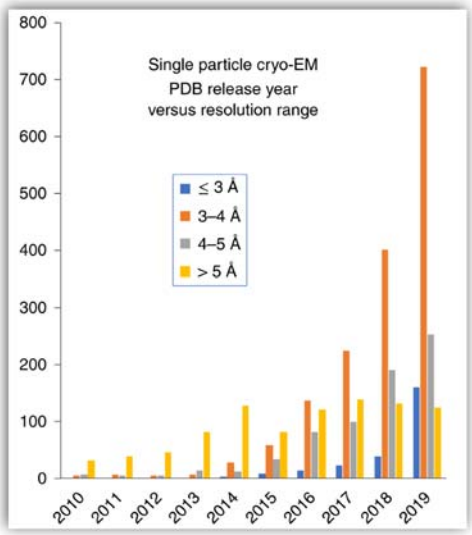


Methods **95**, 78–85 (2016).

CryoEM is on the rise

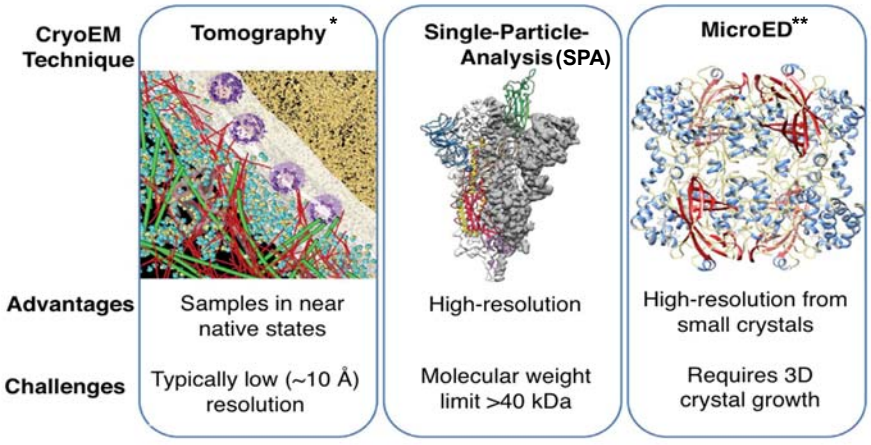


RCSB PDB data



Nat Methods **18**, 156–164 (2021).

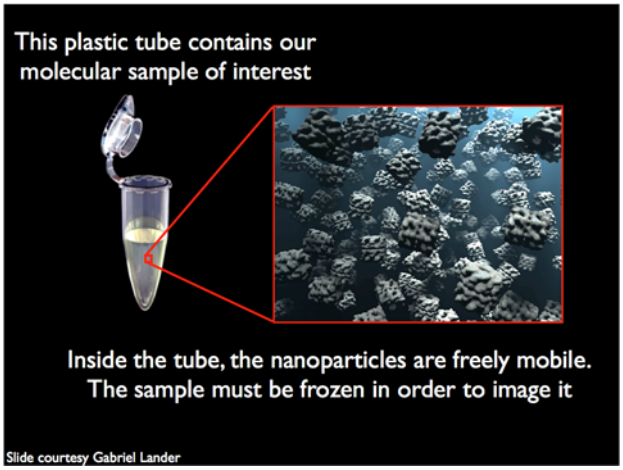
Current CryoEM applications



Current Opinion in Structural Biology 64, 51–58 (2020).

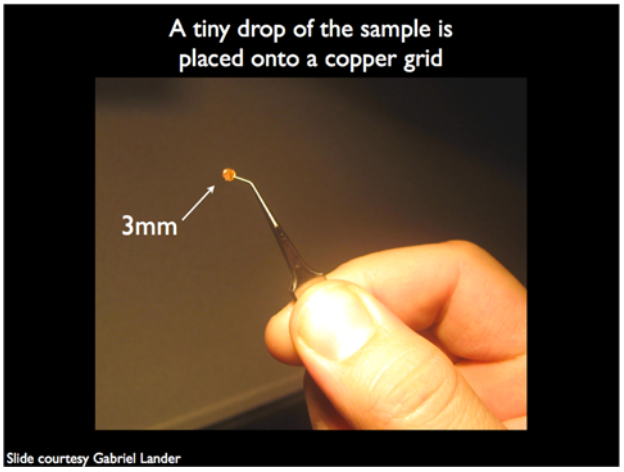
* cryo-electron tomography (CryoET)
** Microcrystal electron diffraction (MicroED)

Single-particle analysis (SPA) workflow

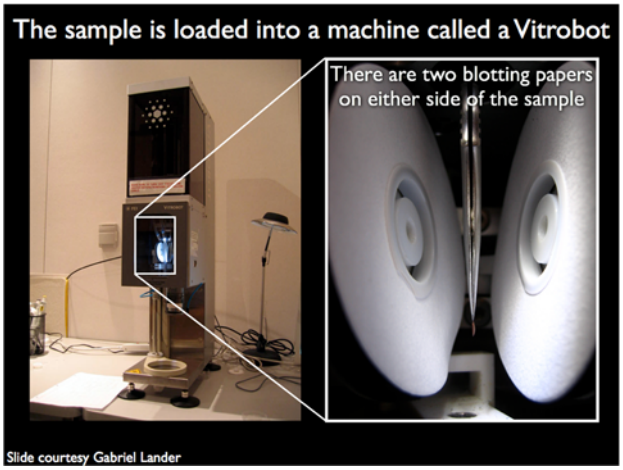


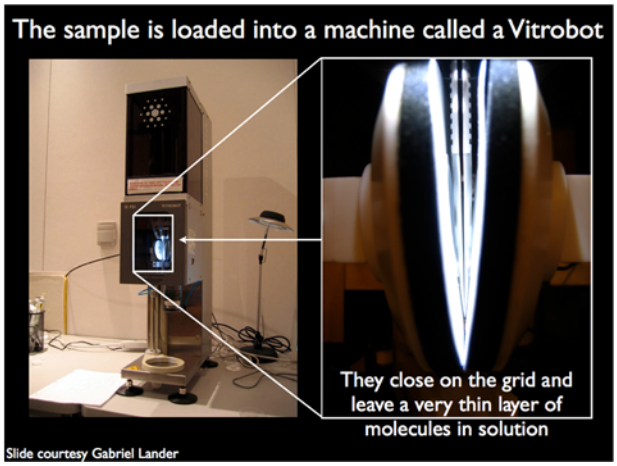
https://www.lander-lab.com

Single-particle analysis (SPA) workflow



Single-particle analysis (SPA) workflow





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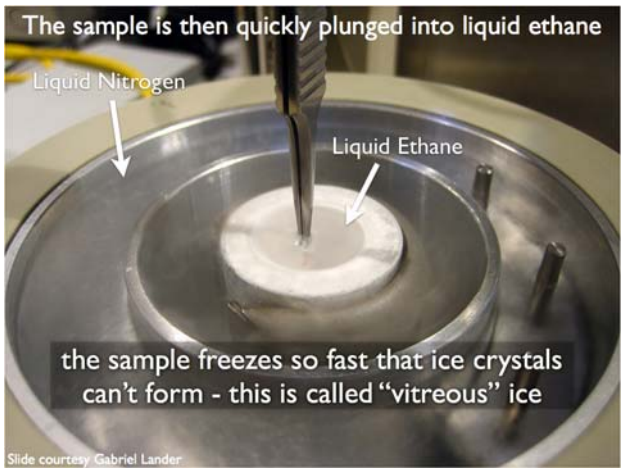
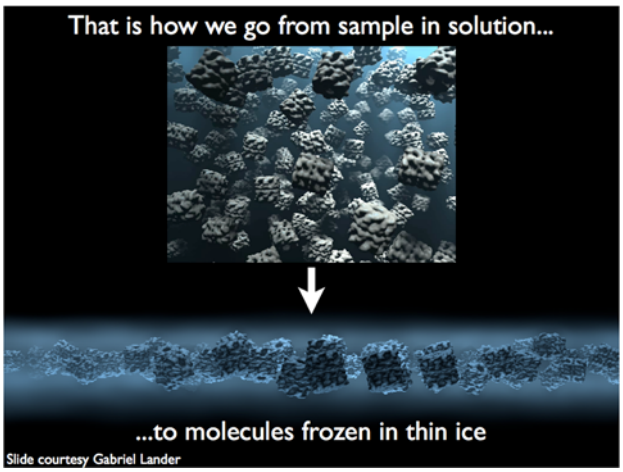
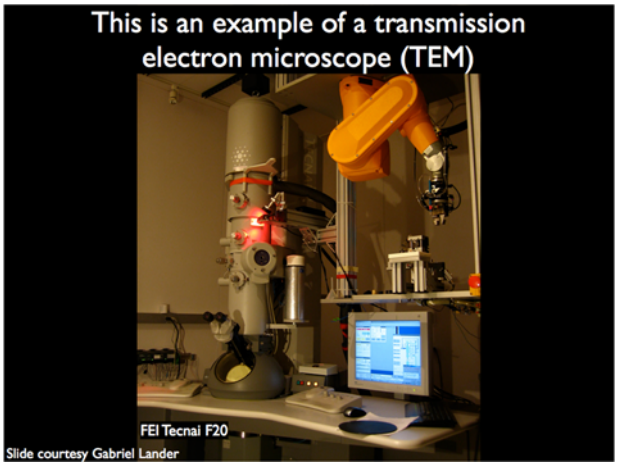
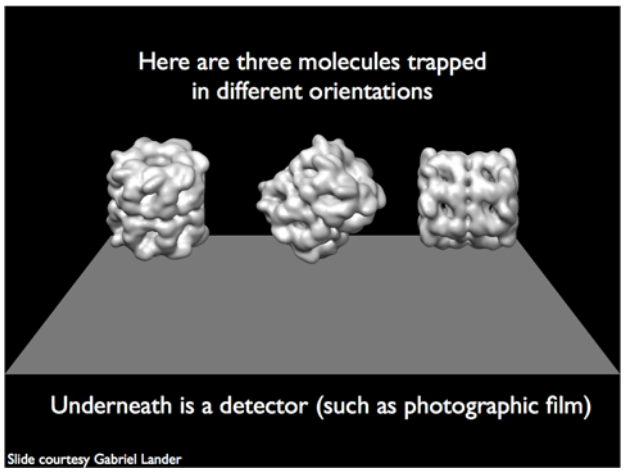


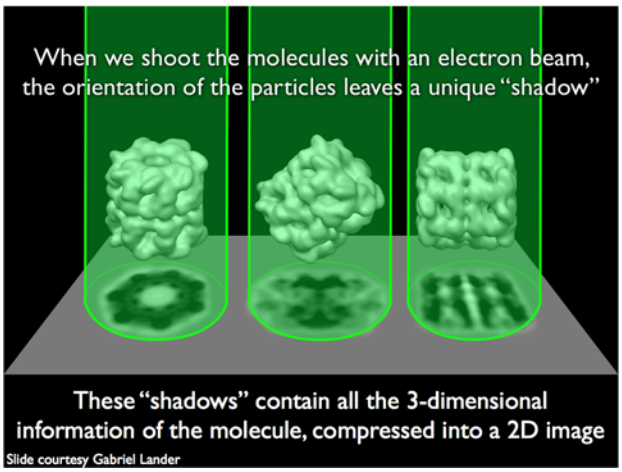


Single-particle analysis (SPA) workflow



Single-particle analysis (SPA) workflow





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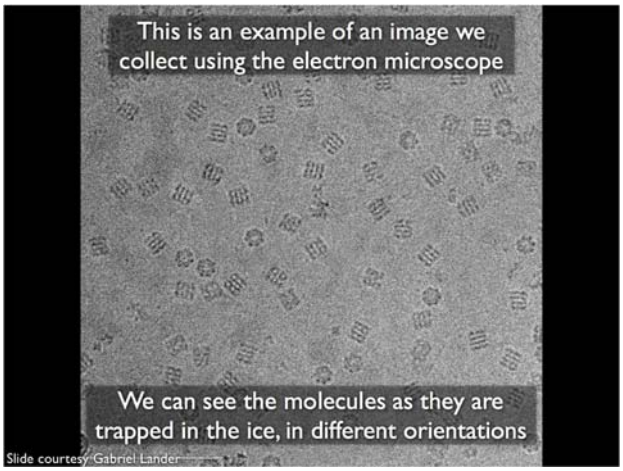
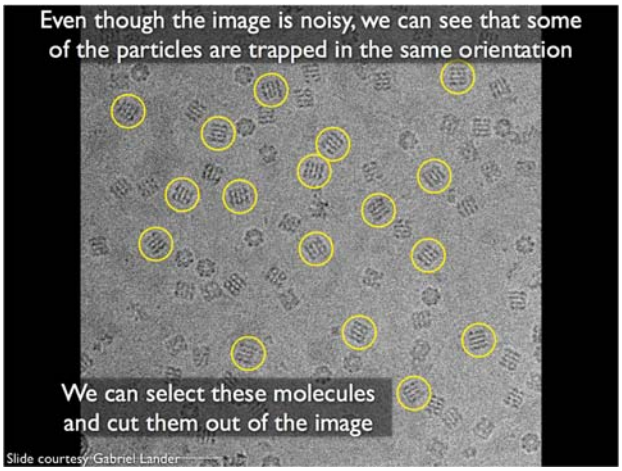
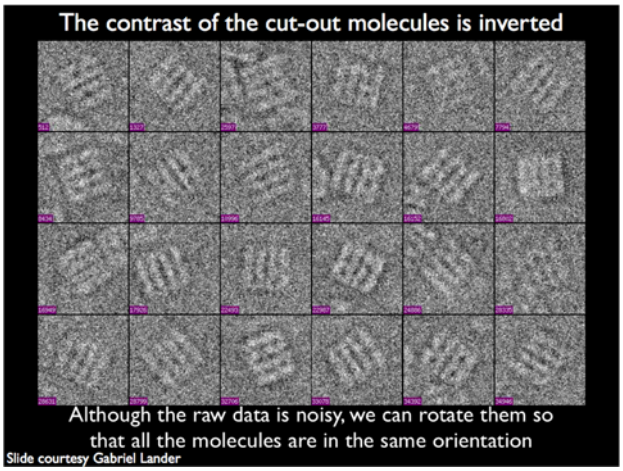
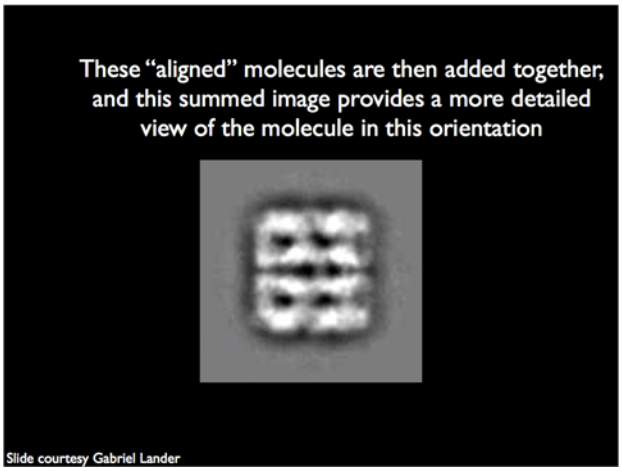


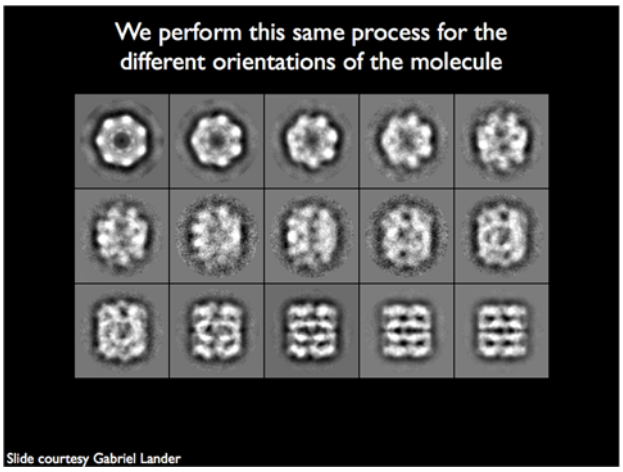


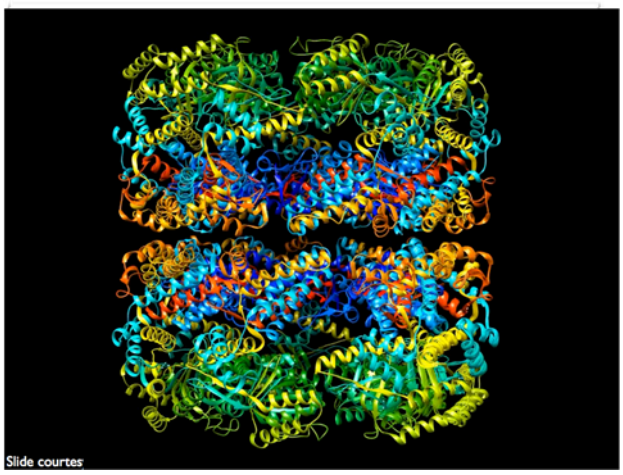
Single-particle analysis (SPA) workflow





Single-particle analysis (SPA) workflow

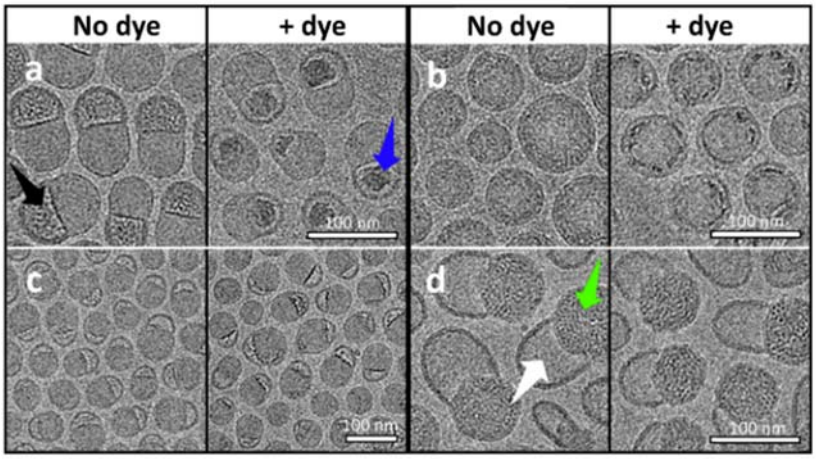




Single-particle analysis in drug discovery

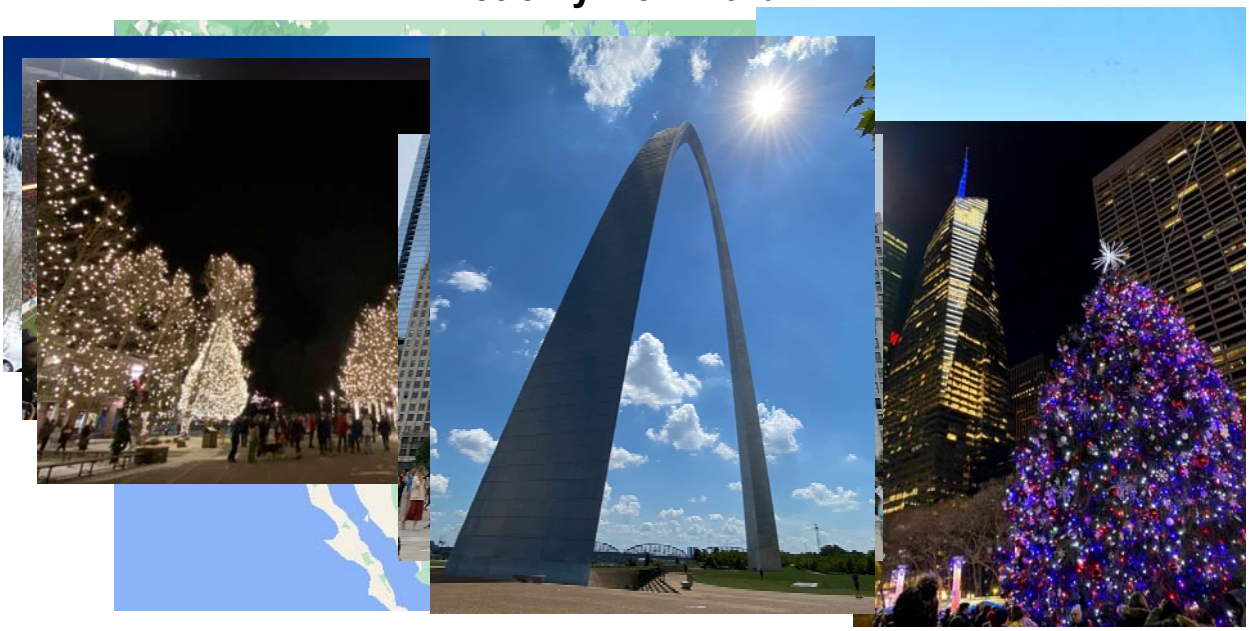
Science **367**, 1260–1263 (2020).

CryoEM in drug development



Biophys J **120**, 2766–2770 (2021).

Not only work hard



Questions?

Thank you!

Resource

The Jensen lab:

https://jensenlab.caltech.edu/courses/

Thermo Fisher:

CryoEM learning center

CryoEM 101:

https://cryoem101.org

EM University:

https://em-learning.com

3DEM mailing list:
http://3dem.ucsd.edu/mailinglist.shtm

CCPEM mailing list:
https://www.jiscmail.ac.uk/cgi-bin/webadmin?A0=CCPEM

https://twitter.com/VictorChangInst/status/1141128882797473793