

VitroJet

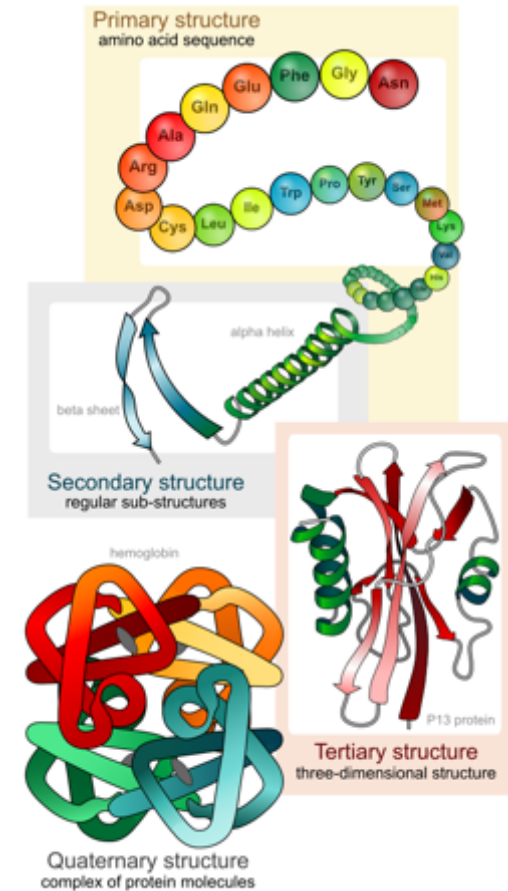
Next generation sample preparation for cryo-EM

Introduction

- Government budgets for health care all over the world are increasing due to a **growing demand for the aging population** (e.g. heart disease, cancer, diabetes, tuberculosis and neurodegenerative diseases)
- Healthcare costs grow substantially faster than the GDP which is **not sustainable** → **major breakthroughs** in the development of new medicines and treatments for diseases are **needed**.
- Root cause of these diseases lies in disrupted processes in our cells, which are governed by **proteins**, the **molecular machines** inside the cells.

Molecular machines: proteins

- Proteins: macromolecules consisting of one or more long chains of amino acids of which the **3D structure** determines the **function**.
- Malfunction of these proteins (in other words **deviations in the 3D structure**) is the **root cause of many diseases**.
- **Understanding the 3D structure** is the key to **targeted drug design**.

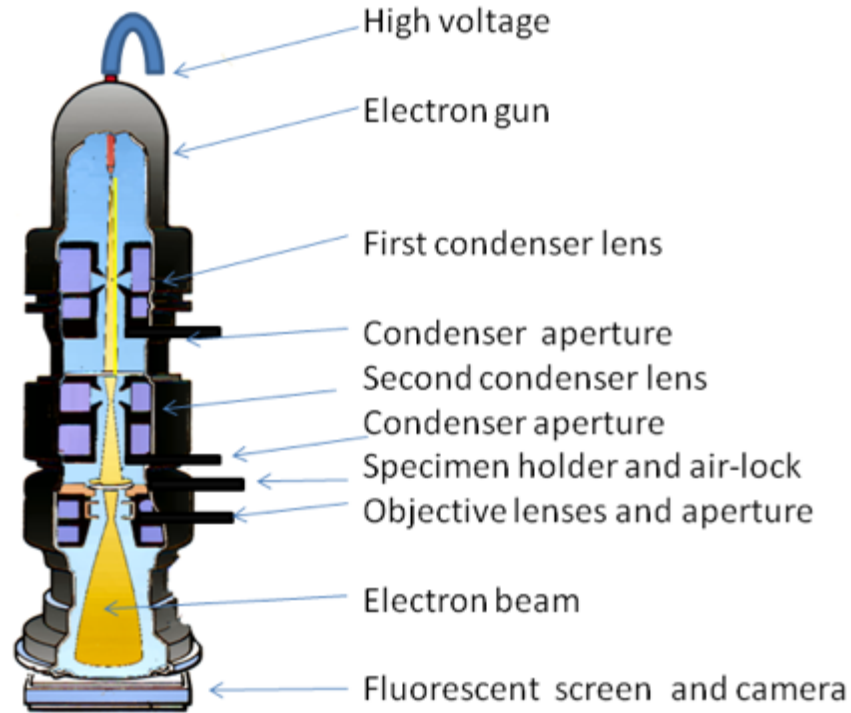


Molecular machines

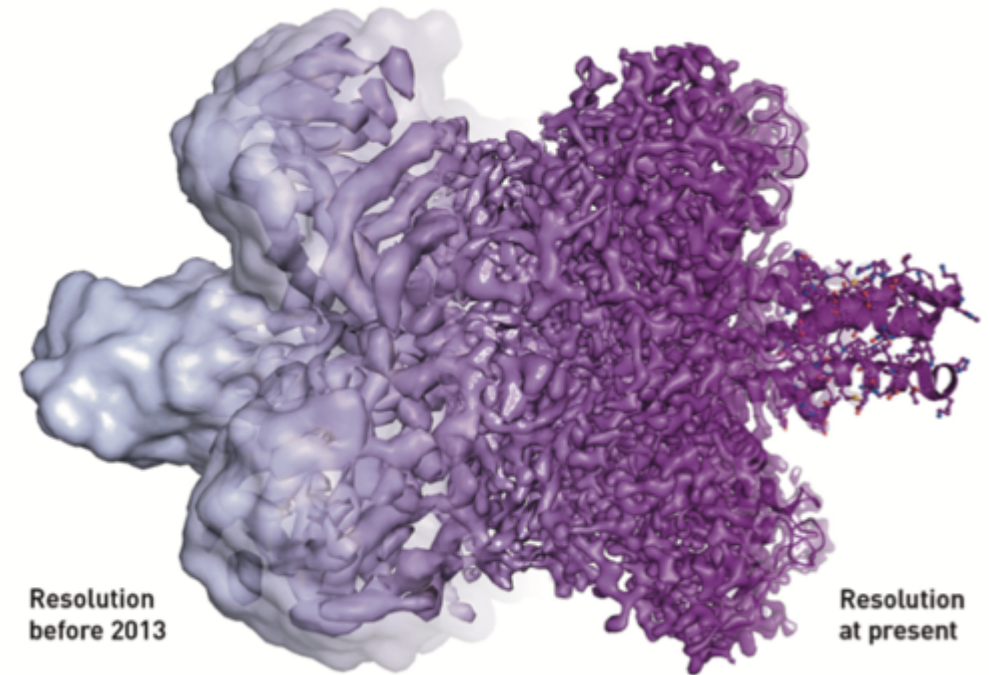


Motor protein transporting vesicle along microtubulus

Resolution revolution



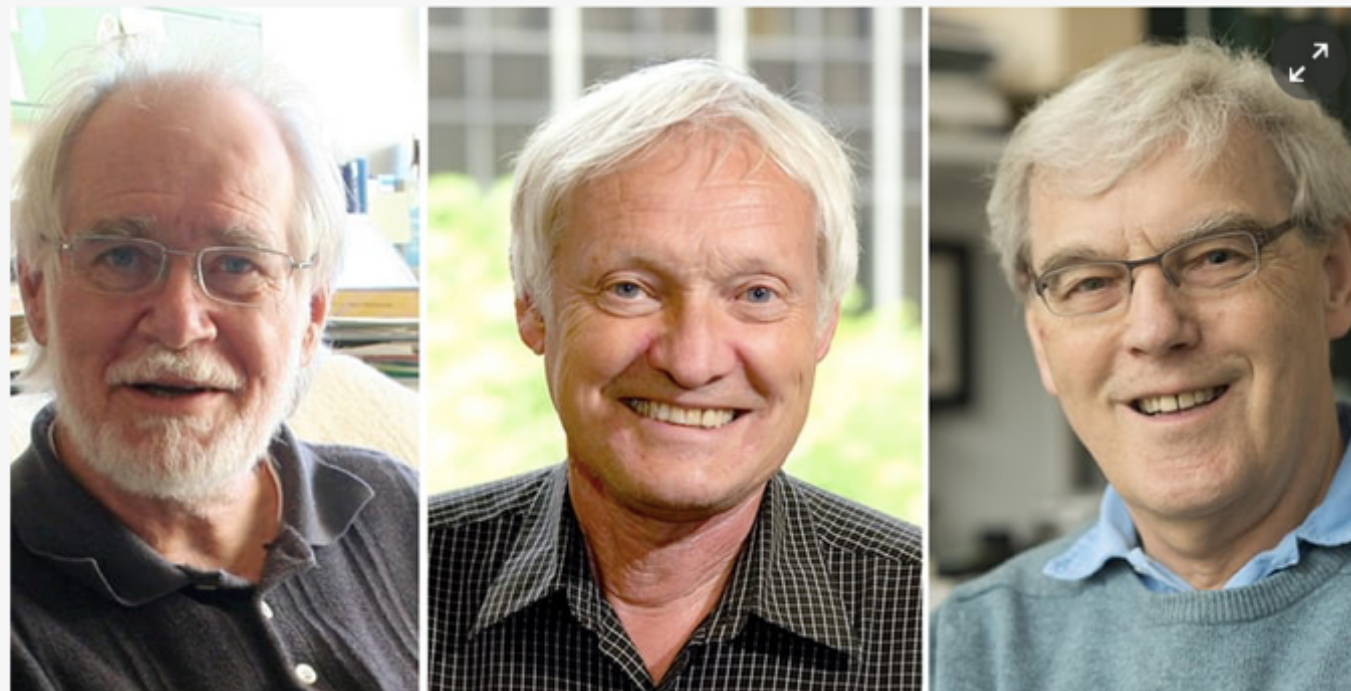
Transmission Electron Microscope



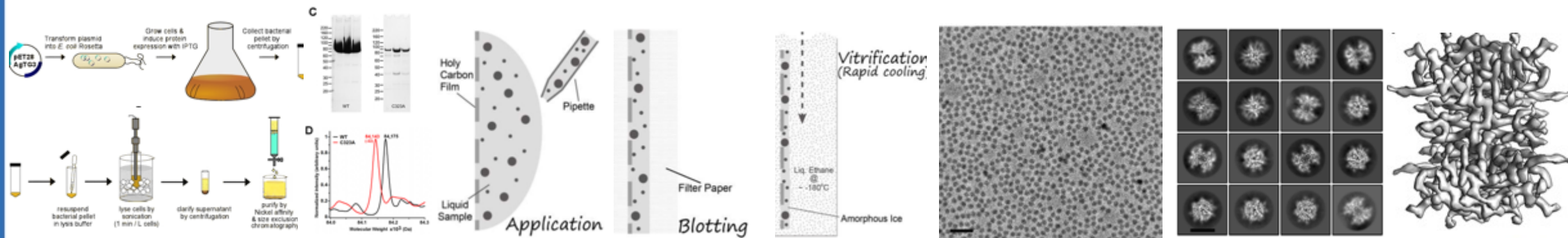
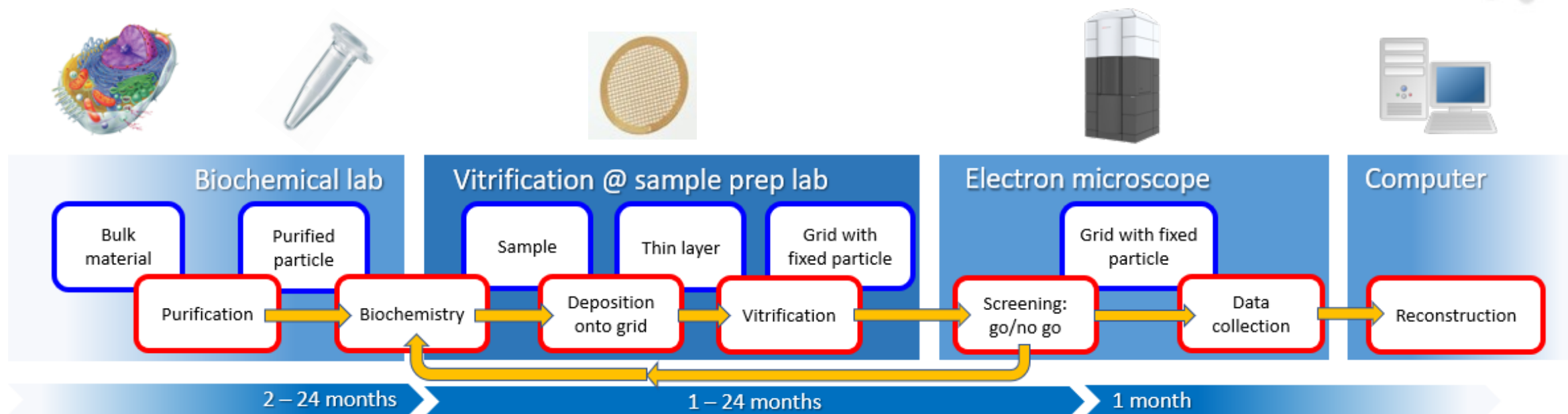
Jacques Dubochet, Joachim Frank and Richard Henderson win the 2017 Nobel prize in chemistry - as it happened

This year's prize has been awarded for developing cryo-electron microscopy for the high resolution structure determination of biomolecules in solution

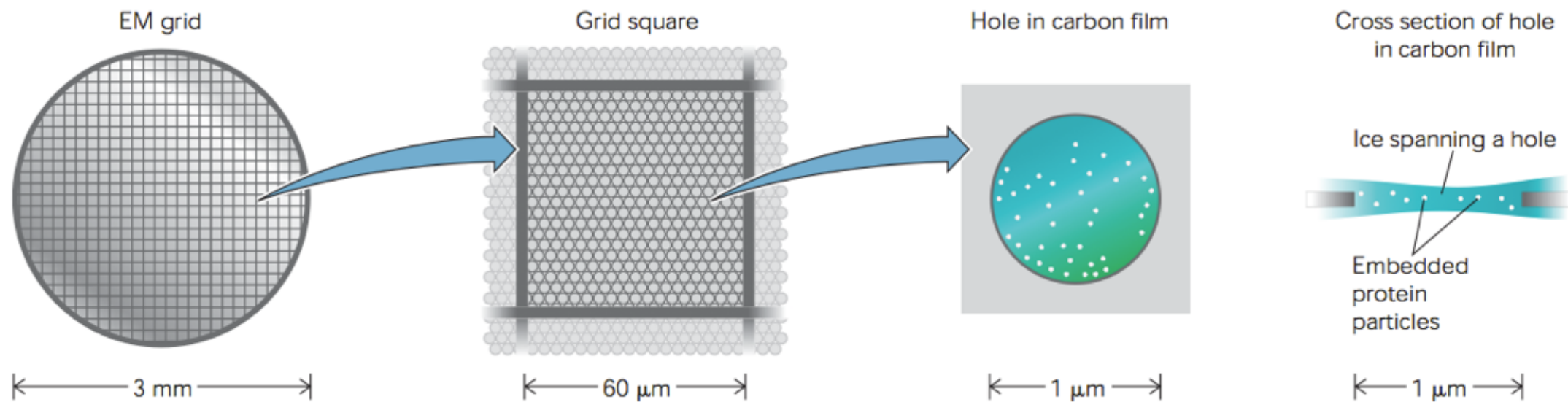
- [Nobel prize in chemistry awarded for method to visualise biomolecules](#)



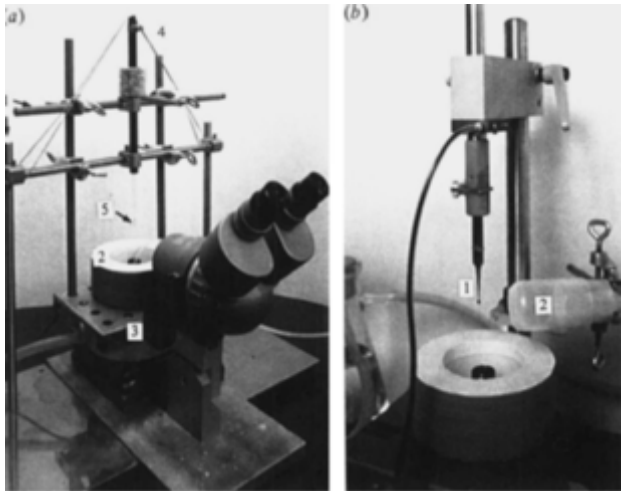
Workflow: single particle analysis



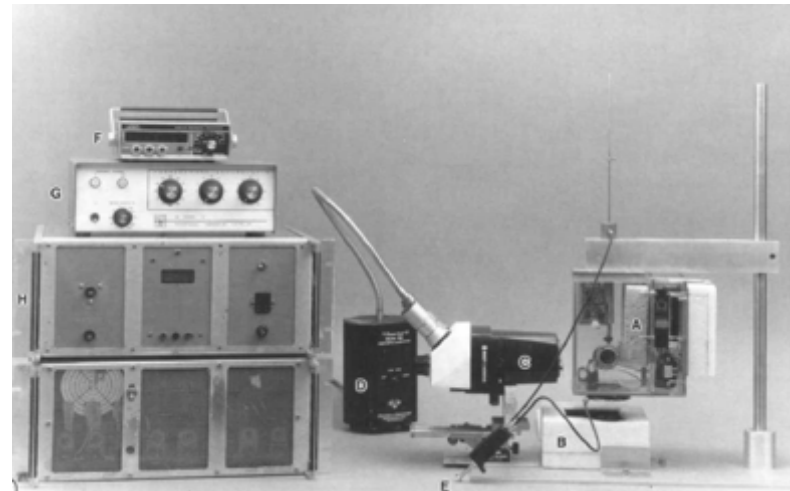
Sample preparation



Vitrification tools (1)



1981
Dubochet



1988
Talmon



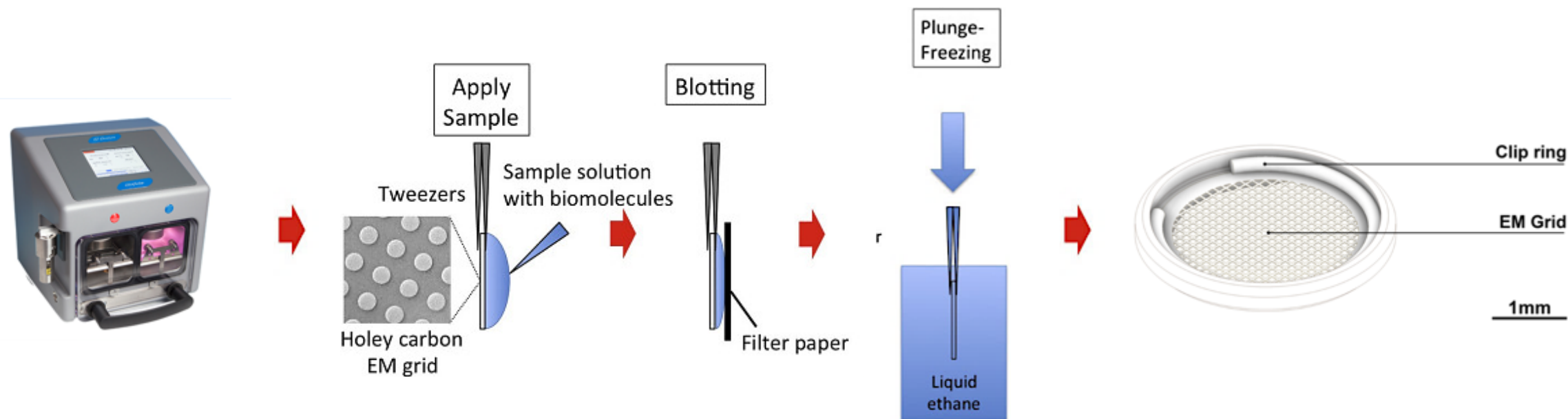
1999
Frederik



2005
FEI

Vitrification tools (2)

- Current sample preparation solution still rely on the methods established in the 80's which are limited with respect to efficiency and reproducibility.



Limitations

With the increasing demand on cryo-EM, sample preparation has become the major bottleneck that limits the true potential of cryo-EM.

- Limited reproducibility
- Operator dependency

Cryo-EM needs to shift from a “high content solution” to a “high throughput solution| to meet the societal demand.

CryoSol-World

- **Our goal:** establish cryo-EM as a high-throughput modality to enable breakthroughs in the development of new medicines and treatments for diseases.
- **Our focus:** reproducible high-quality sample preparation for cryo-EM.
- **Our background:** fluid dynamics, (plasma) physics, engineering, and biochemistry and sample preparation for cryo-EM (VitroBot).
- **Our leadership-team:** seasoned entrepreneurs with track record in (cryo-)EM.

VitroJet

Sample carriers



Supply cassette



Plasma cleaning



Sample



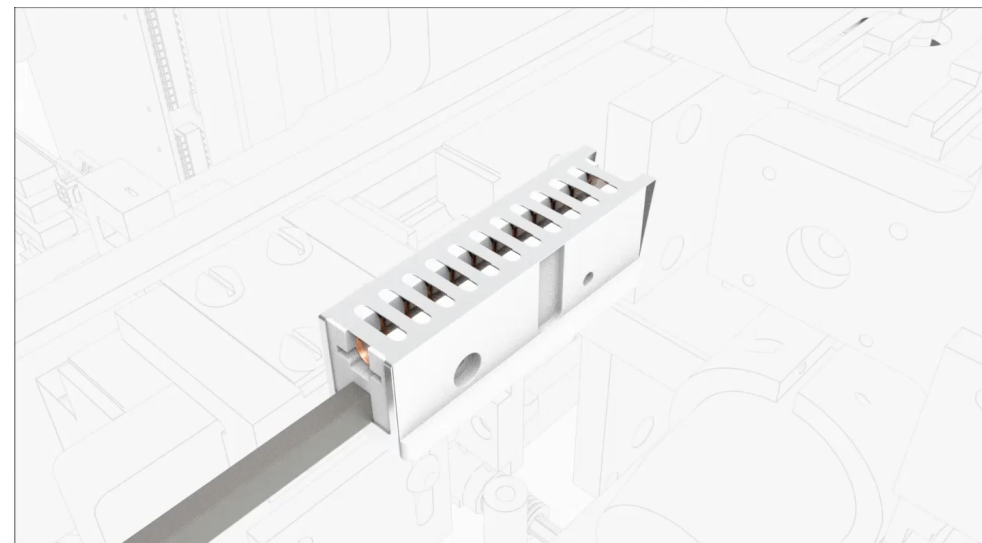
Sample deposition: pin printing



Jet vitrification



Storage cassette

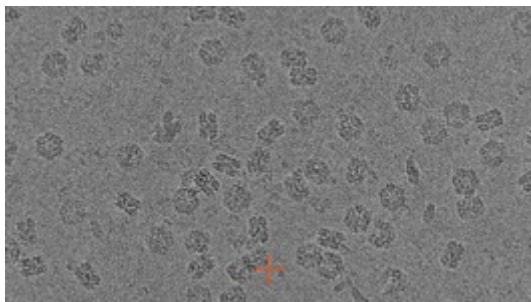


Microscope

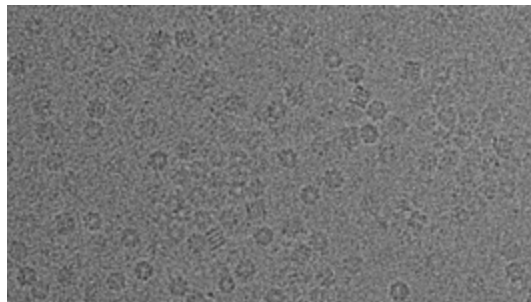


Proof of Principle (200kV)

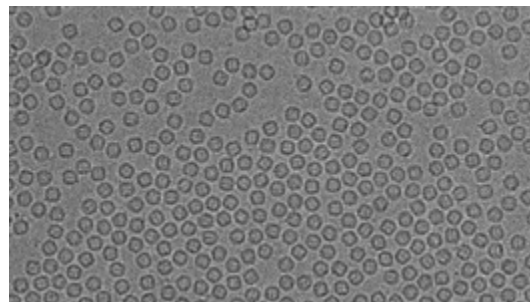
Wormhemoglobin 3.1Å



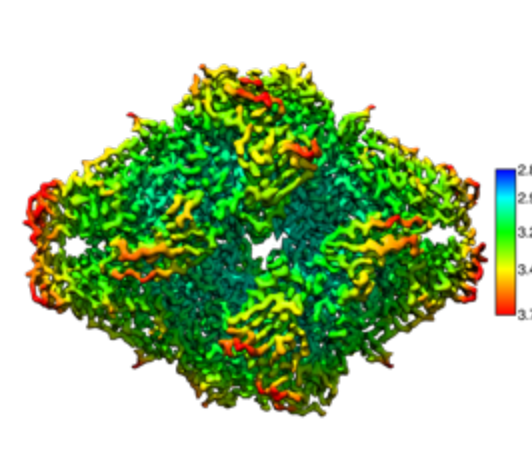
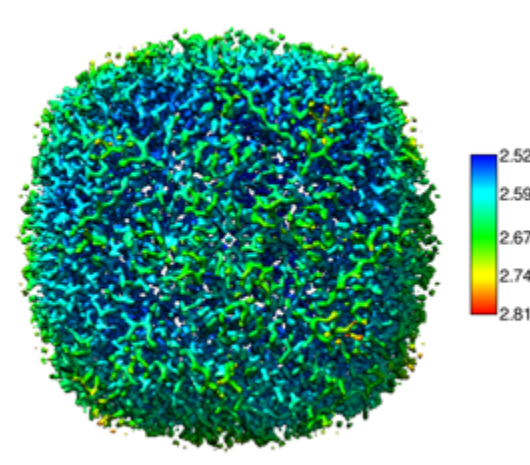
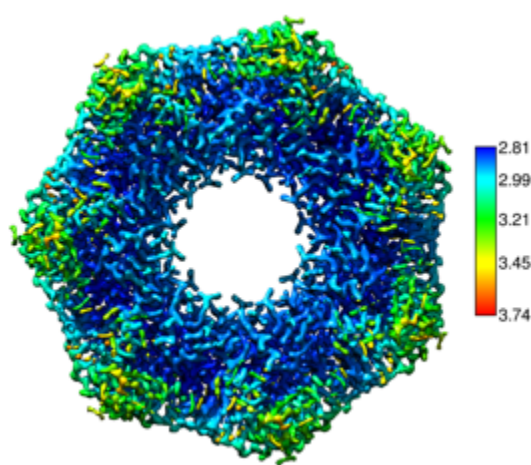
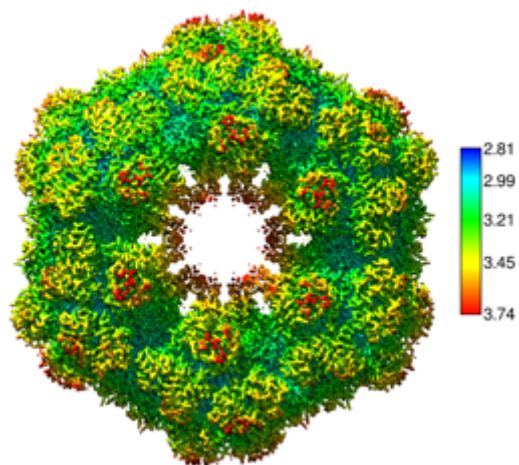
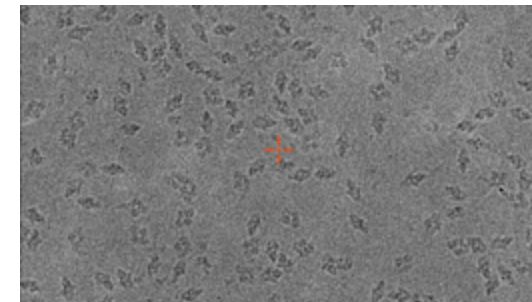
GroEL 2.9Å



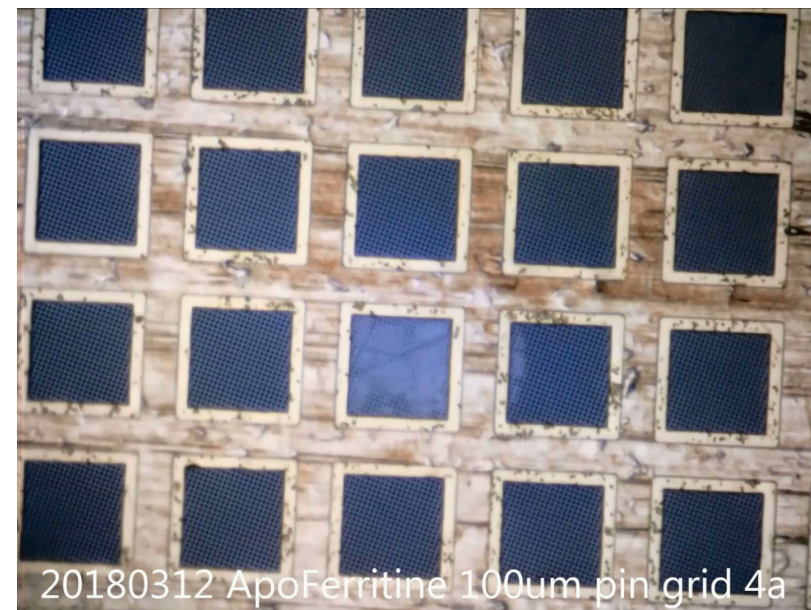
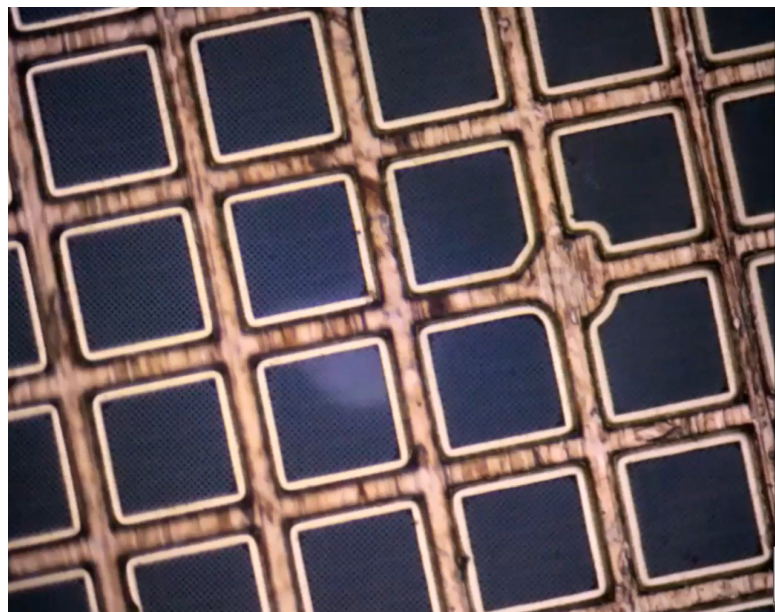
Apoferritin 2.5Å



β -galactosidase 3.1Å

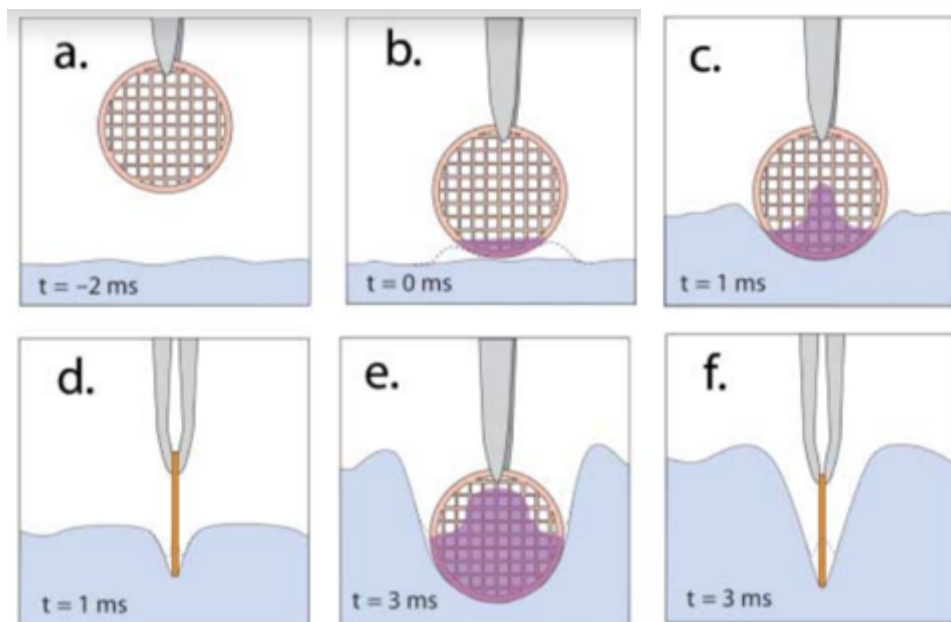


Core innovation: pin printing



Core innovation: jet vitrification

Kasas et al. 2018



Plunge vitrification



Jet vitrification

Next steps in R&D

- Optimization/further development key processes
 - Plasma cleaning
 - Pin-printing
 - Jet-vitrification
- Engineering pilot & commercial system
- Closely supporting pilot users in application development
- Expanding R&D team



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