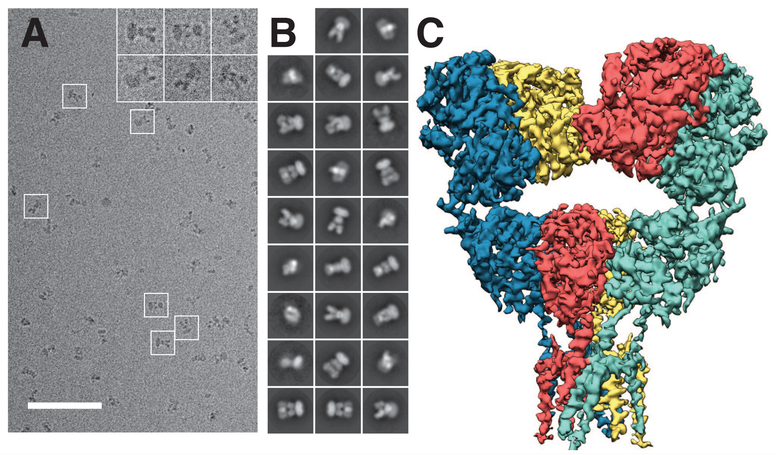
Cryo-cell: a freezable fluid cell for cryo-electron microscopy

TEAM: Eric Furfine[3], Jungwon Park[2] and Joel R. Meyerson[1]

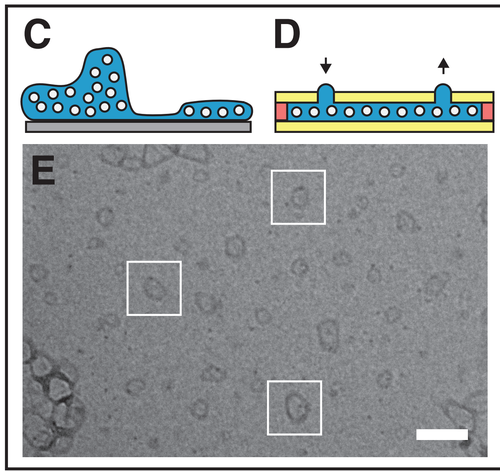
1. Brandeis University, Department of Biochemistry / Howard Hughes Medical Institute
2. Seoul National University, Department of Engineering
3. Furfine Biotechnology / OH2 Biotechnologies / Mosaic Biosciences

PROBLEM STATEMENT: Cryo-electron microscopy (cryo-EM) is emerging as the preferred method to determine 3D protein structures in biomedical research and drug discovery. The method's importance was acknowledged with the 2017 Nobel Prize in Chemistry. Before a structure can be obtained, proteins must be frozen in a thin layer of ice. Problems associated with this "sample preparation" are widely considered the major bottleneck to realizing the full potential of cryo-EM.

PRODUCT SOLUTION: Aiming to address this bottleneck we successfully prototyped and tested the "Cryo-cell" which uses a nanofabricated fluid cell to obviate the need for the current "blotting" technology and reduce the amount of protein needed by 1,000-fold. The Brandeis SPROUT and NSF I-Corps programs have supported prototype development and research to establish a market for the device. We anticipate the mature incarnation of the Cryo-cell will help breach current problems in cryo-EM, open new scientific opportunities, and accelerate the current broadening of the cryo-EM market into the "mainstream".



A. Example cryo-EM image of frozen GluR proteins. Inset shows two-fold magnified protein images (100 nm scale).
B. Two-dimensional averages of the same protein shown in (A). Averages composed of a few thousand protein images.
C. Cryo-EM structure of GluR.
Figures adapted from Meyerson et al. 2014 *Nature*, and Meyerson et al. 2016 *Nature*.



C. Illustration of cross section through cryo-EM sample prepared with traditional method, with water (blue), protein (white), and support material (gray).
D. Illustration of cryo-cell section, with water (blue), protein (white), top and bottom chamber materials (yellow), and spacers (red). Arrows indicate inlet and outlet ports for loading sample.
E. Cryo-EM image acquired with fluid cell prototype showing virus preparation (white boxes) (100 nm scale).

MARKET AND MARKET NEED
- academia
- pharmaceutical industry (e.g. Novartis, Phizer, Genentech)
- sample preparation and optimization
- repeatability and reproducibility
- reduced operation cost and expertise

COMPETITION
- Thermo Fisher Vitrobot
- Leica EM GP
- Gatan CP3
- CryoWriter
- Spot-it-On

TIMELINE (6 months)
- refined prototype
- test new prototype features
- benchmark against competing technology
- pursue licensing / additional funding