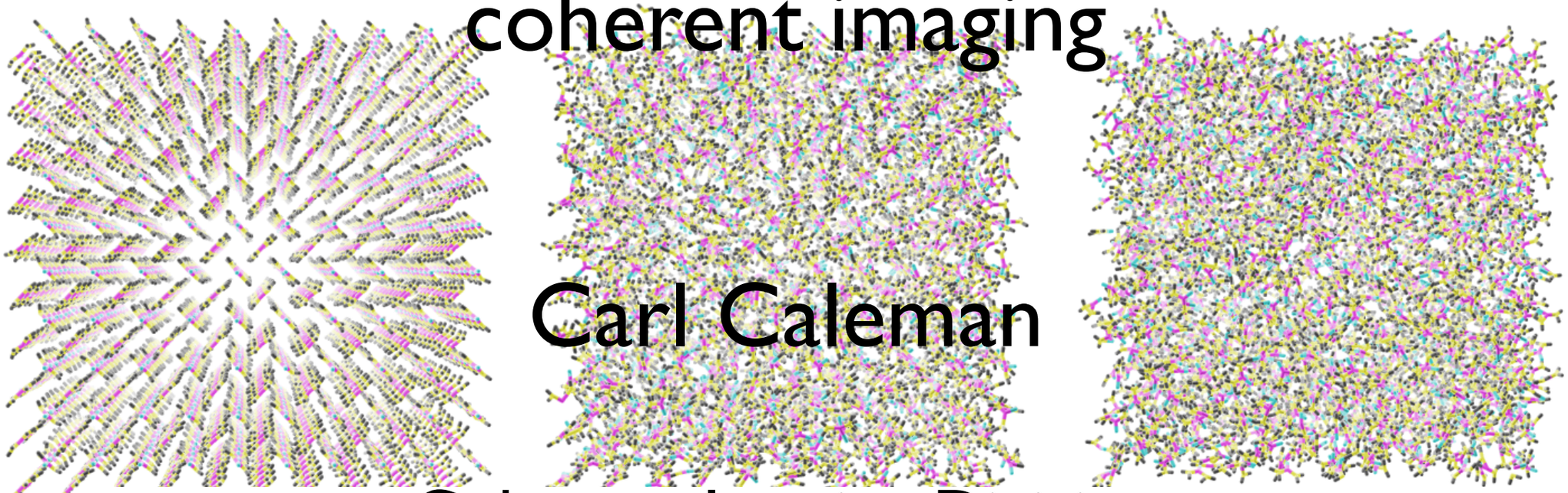
Computational challenges in coherent imaging



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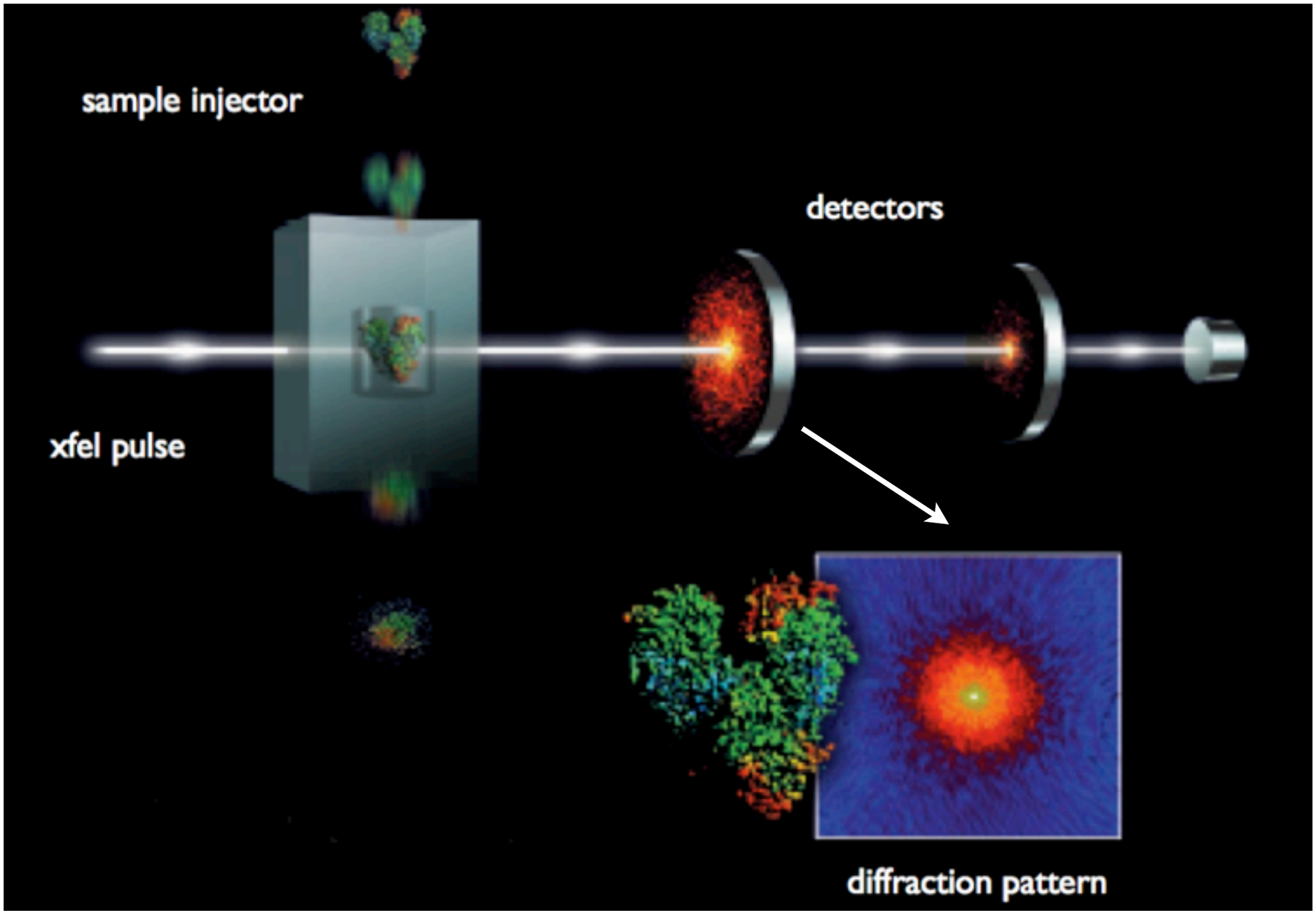
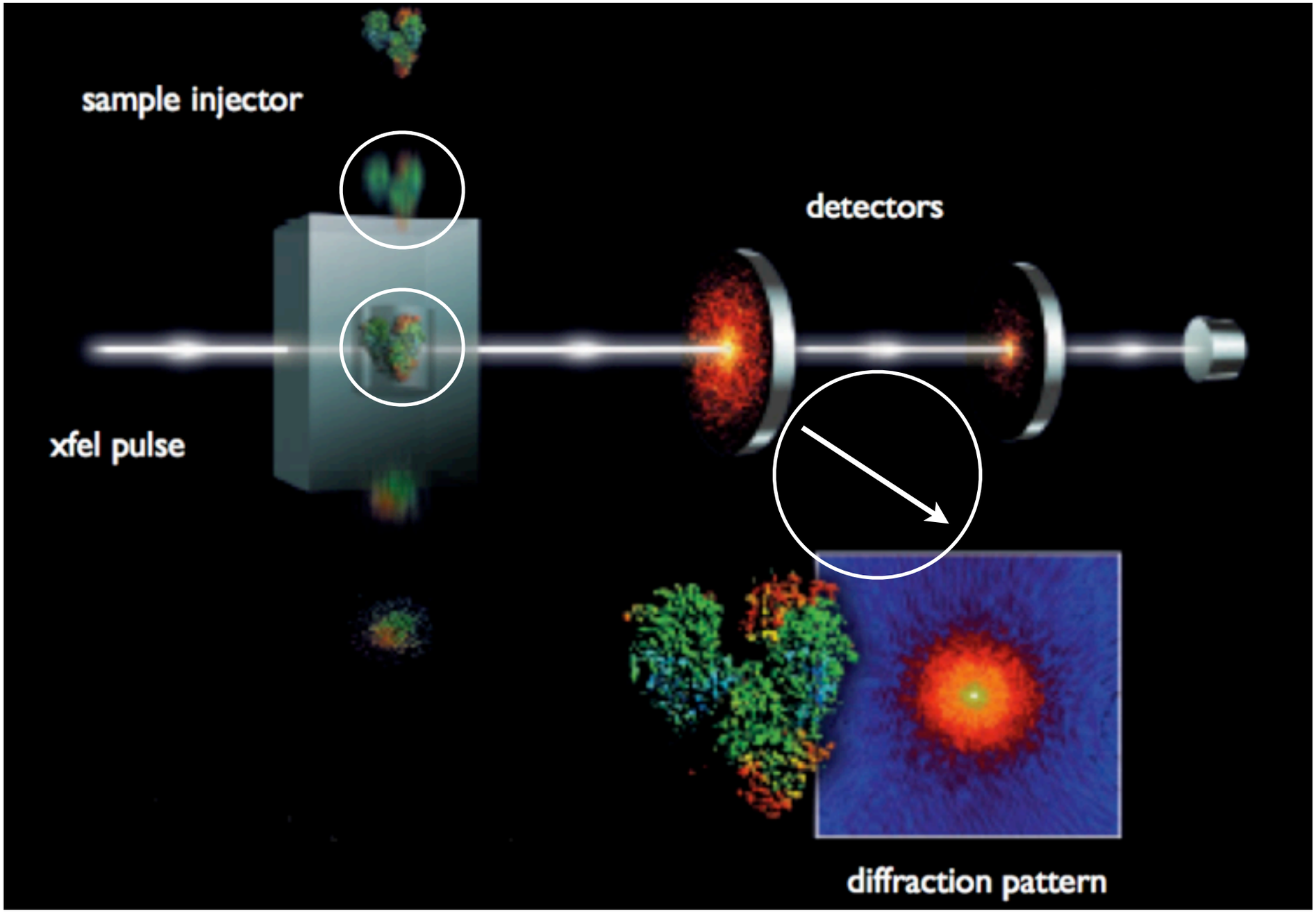
Outline

- What do we do?
- Reconstruction and data analysis
- Interaction of Xray Free-electron pulses with matter
- Samples in vacuum
- Computational demands

What do we do?


sample injector
detectors
xfel pulse
diffraction pattern

What do we do?


sample injector
detectors
xfel pulse
diffraction pattern

Reconstruction and data analysis

LETTER

doi:10.1038/nature09748

Single mimivirus particles intercepted and imaged with an X-ray laser

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LETTER

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Femtosecond X-ray protein nanocrystallography

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X-ray crystallography provides the vast majority of macromolecular structures, but the success of the method relies on growing crystals of sufficient size. In conventional measurements, the necessary increase in X-ray dose to record data from crystals that are too small leads to extensive damage before a diffraction signal can be recorded[1–3]. It is particularly challenging to obtain large, well-diffracting crystals of membrane proteins, for which fewer than 300 unique structures have been determined despite their importance in all living cells. Here we present a method for structure determination where single-crystal X-ray diffraction 'snapshots' are collected from a fully hydrated stream of nanocrystals using femtosecond pulses from a hard-X-ray free-electron laser, the Linac Coherent Light Source[4]. We prove

the irradiance (or power density) of focused pulses from a hard-X-ray FEL such as the Linac Coherent Light Source (LCLS), USA, would be sufficient to produce diffraction patterns at near-atomic resolution[6].

We demonstrate here that this notion of diffraction before destruction operates at subnanometre resolution, using the membrane protein photosystem I as a model system, and establish an approach to structure determination based on X-ray diffraction data from a stream of nanocrystals[6,8]. Membrane proteins have a central role in the functioning of cells and viruses, yet our knowledge of the structure and dynamics responsible for their functioning remains limited. Photosystem I is a large membrane protein complex (1-MDa molecular mass, 36 proteins, 381 cofactors) that acts as a biosolar energy converter in the process of

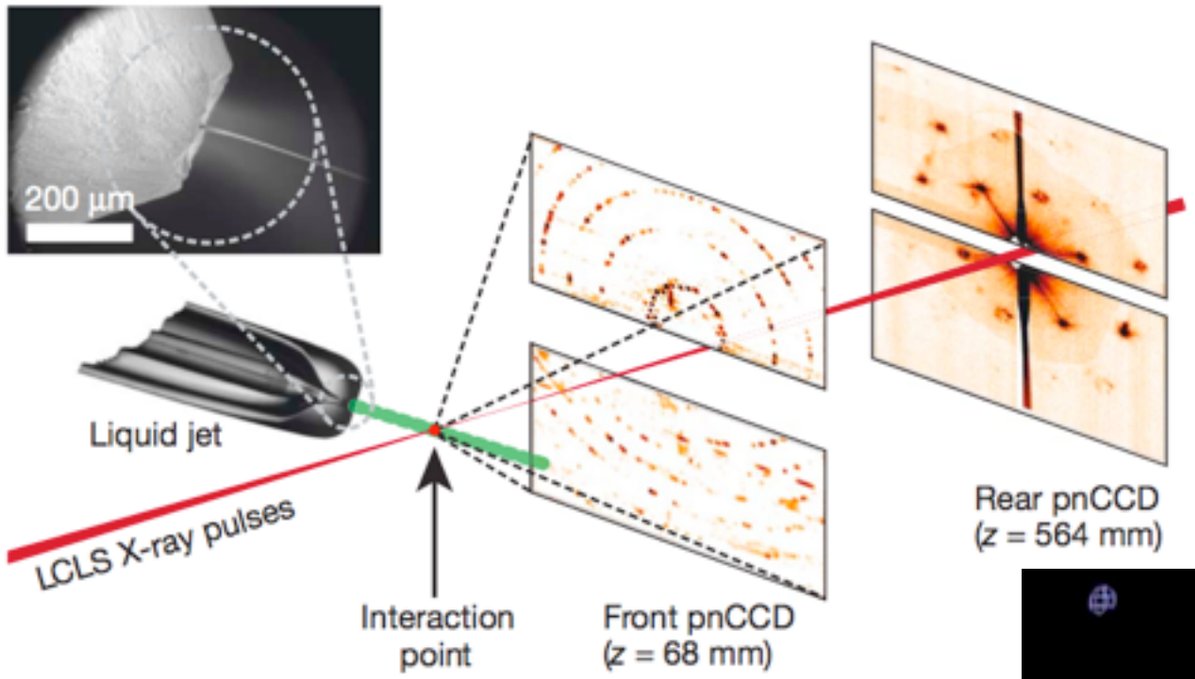
copies.

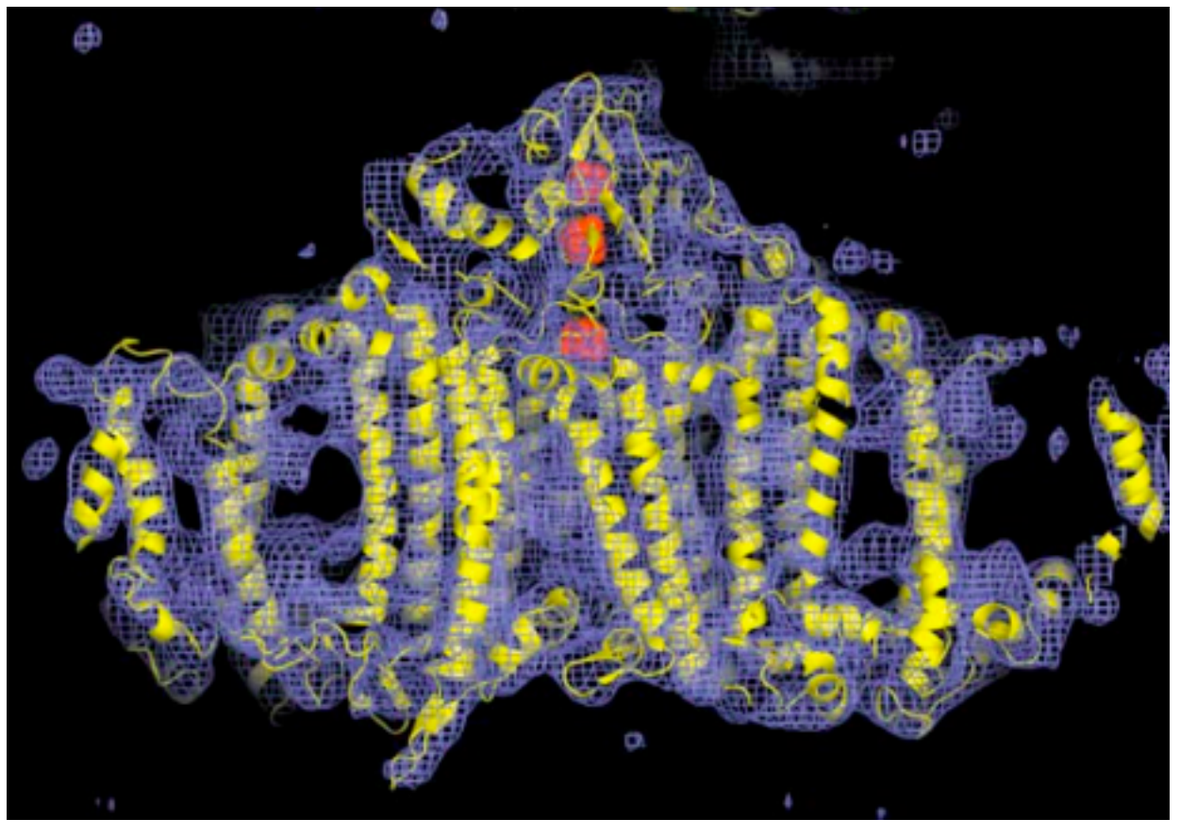
an X-ray free-electron laser, and bring together all the elements required for structural studies of single, non-crystalline objects.

Mimivirus (*Acanthamoeba polyphaga* mimivirus) is the largest known virus[6]. Its size is comparable to the size of the smallest living cells (in fact, the name mimivirus stands for 'microbe-mimicking virus'). The viral capsid (0.45 μm in diameter) has a pseudo-icosahedral appearance and is covered by an outer layer of dense fibrils[7,8]. The total diameter of the particle, including fibrils, is about 0.75 μm. Mimivirus is too big for a full three-dimensional reconstruction by cryo-electron microscopy[7] and its fibrils prevent crystallization. The genome[9] has 1.2 million base pairs (comparable to a small bacterium) and contains several genes previously thought to be present only in cellular organisms, including components of the protein translation apparatus. Mimivirus can be infected by a smaller virus, named a 'virophage'[10], which seems to be the first example of a virus behaving as a parasite of another virus[8]. Studies of mimivirus are causing a paradigm shift in virology and have led to renewed debates about the origin and the definition of viral and cellular life[11].

Figure 1 shows the experimental arrangement for imaging single virus particles. The sample injector, which uses aerodynamic focusing, was mounted into the CFEL-ASG Multi-Purpose (CAMP) instrument[12] on the Atomic, Molecular and Optical Science (AMO) beamline[13] at the Linac Coherent Light Source[5] (LCLS). We recorded far-field

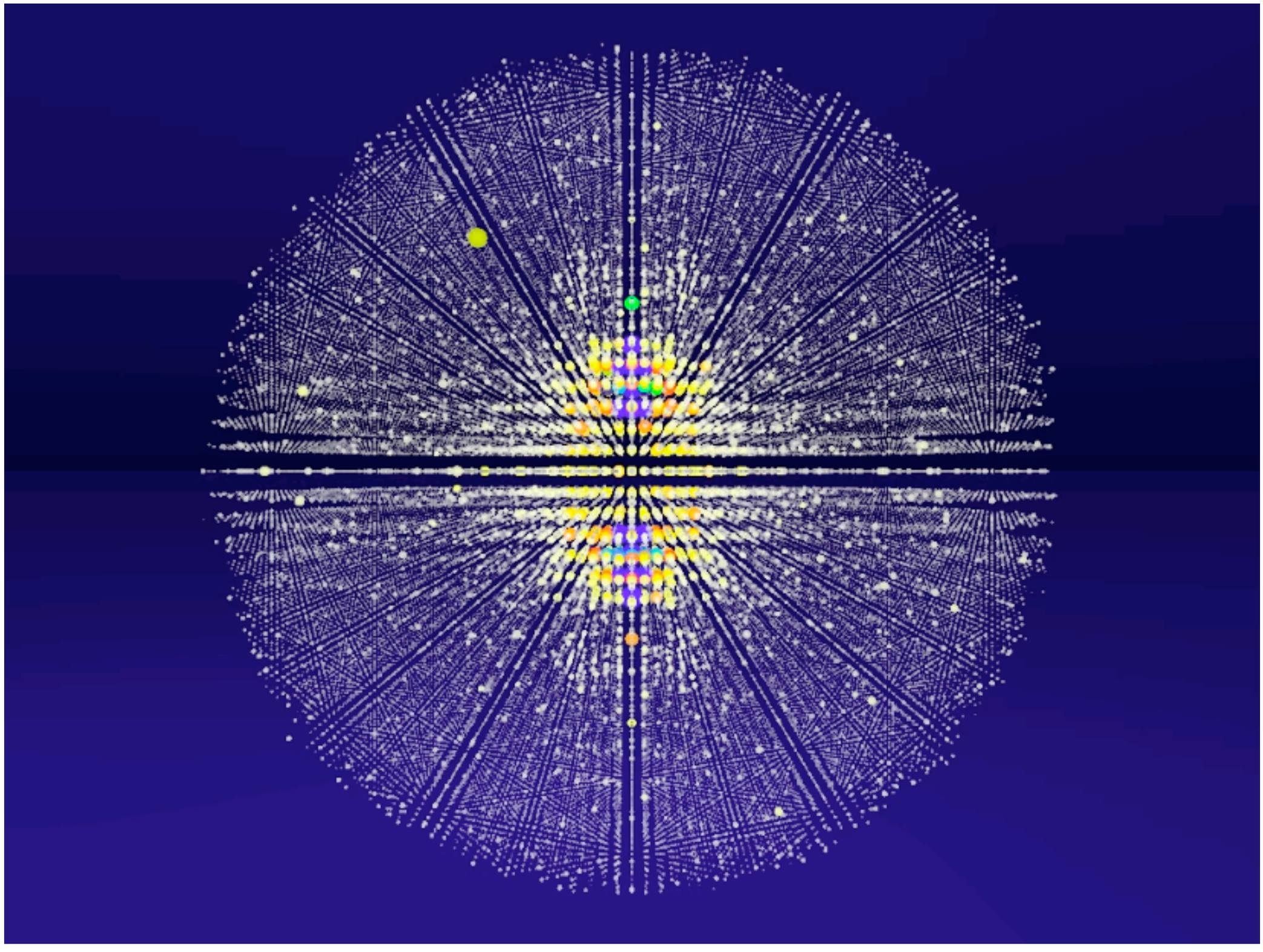
Femtosecond X-ray protein nanocrystallography



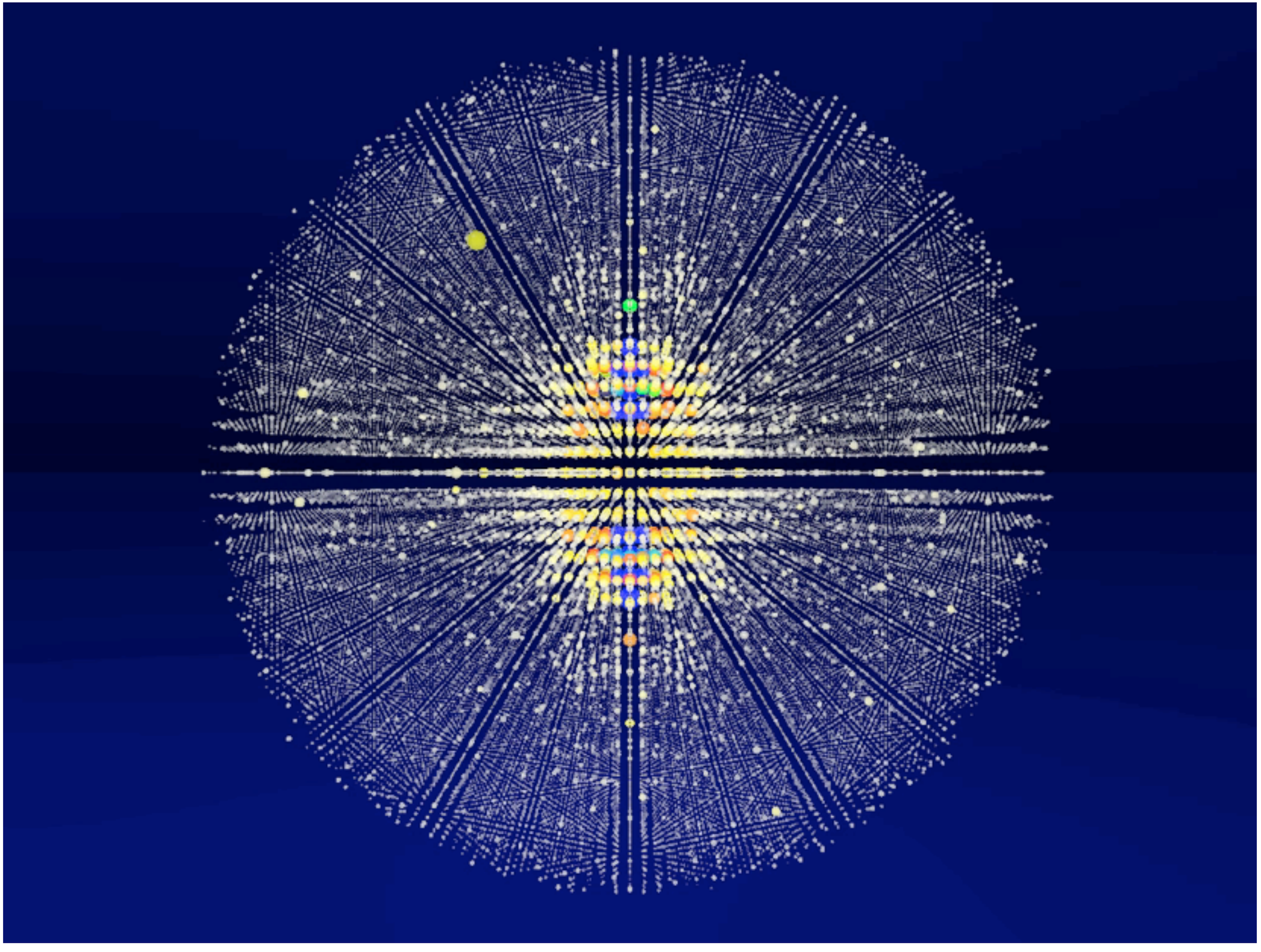


Chapman et al. Nature 470:73 (2011)

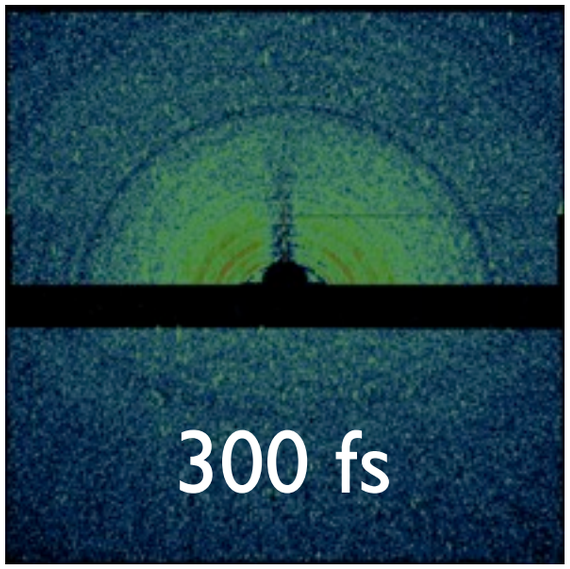
Femtosecond X-ray protein nanocrystallography

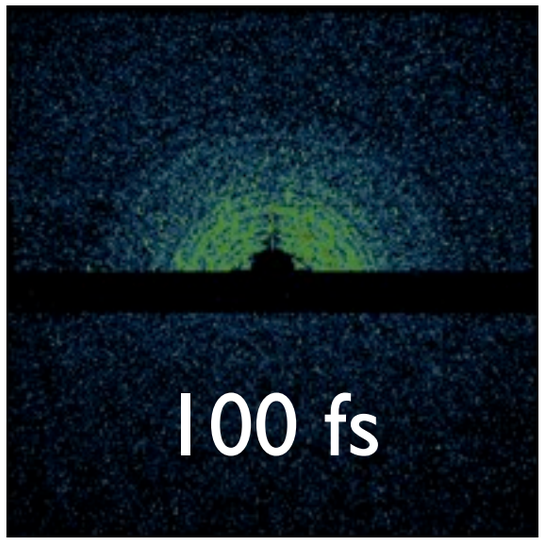


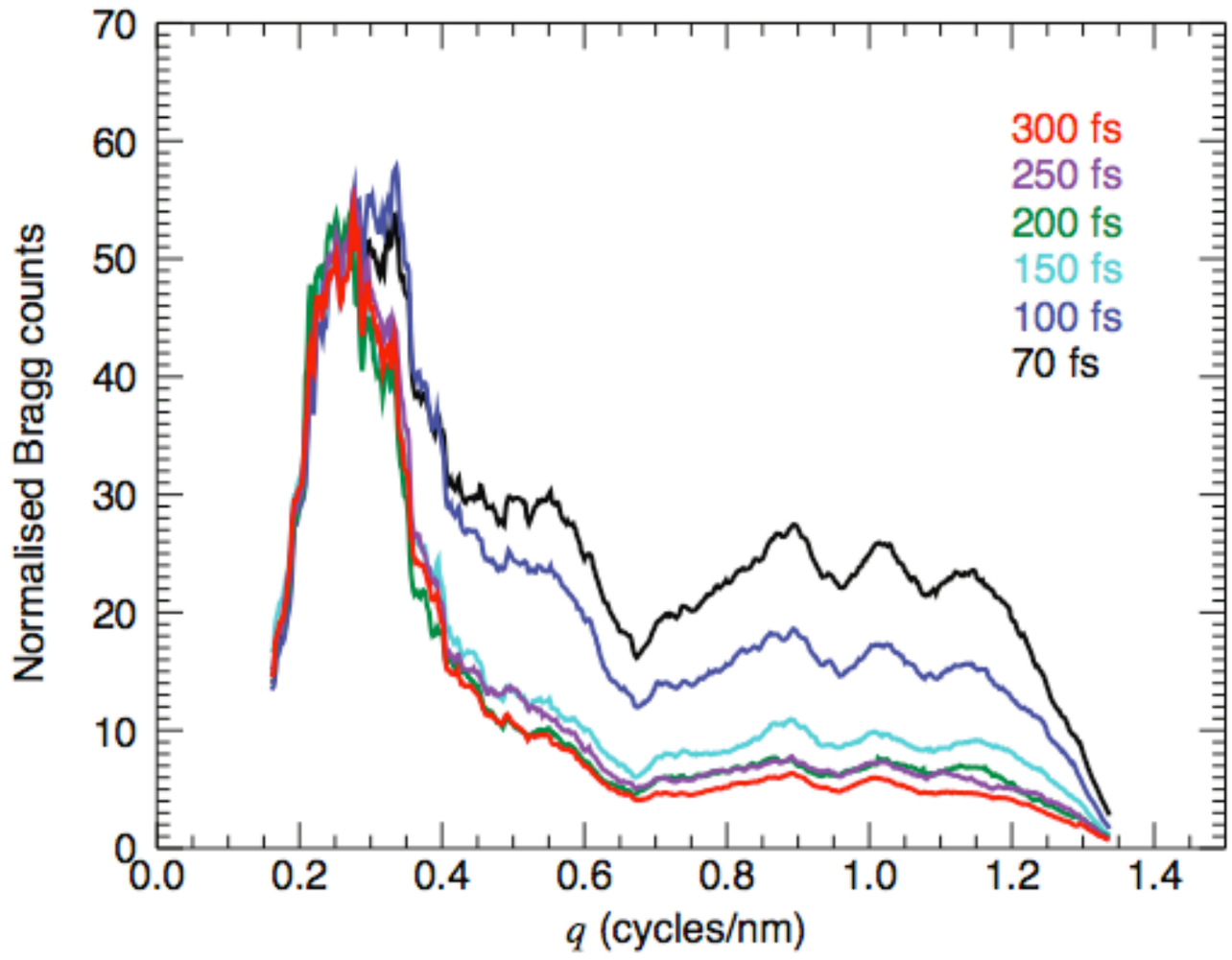
Femtosecond X-ray protein nanocrystallography



Femtosecond X-ray protein nanocrystallography



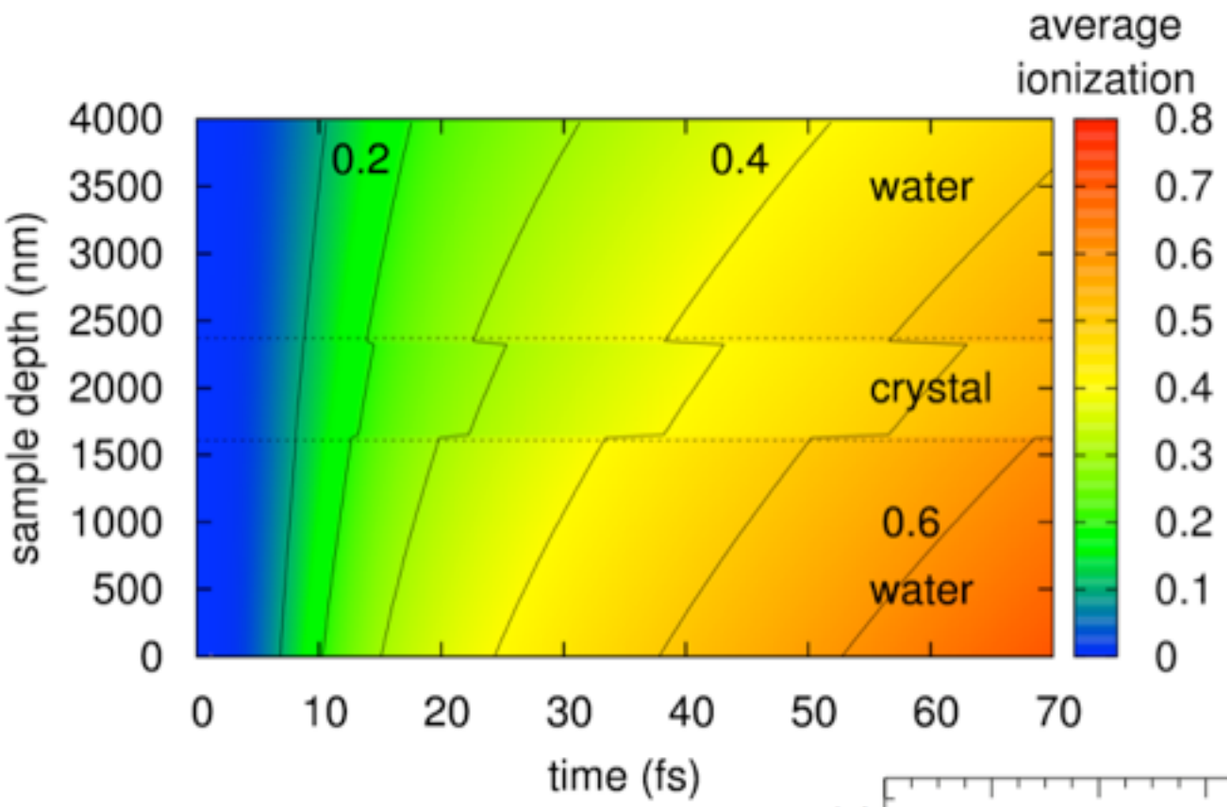


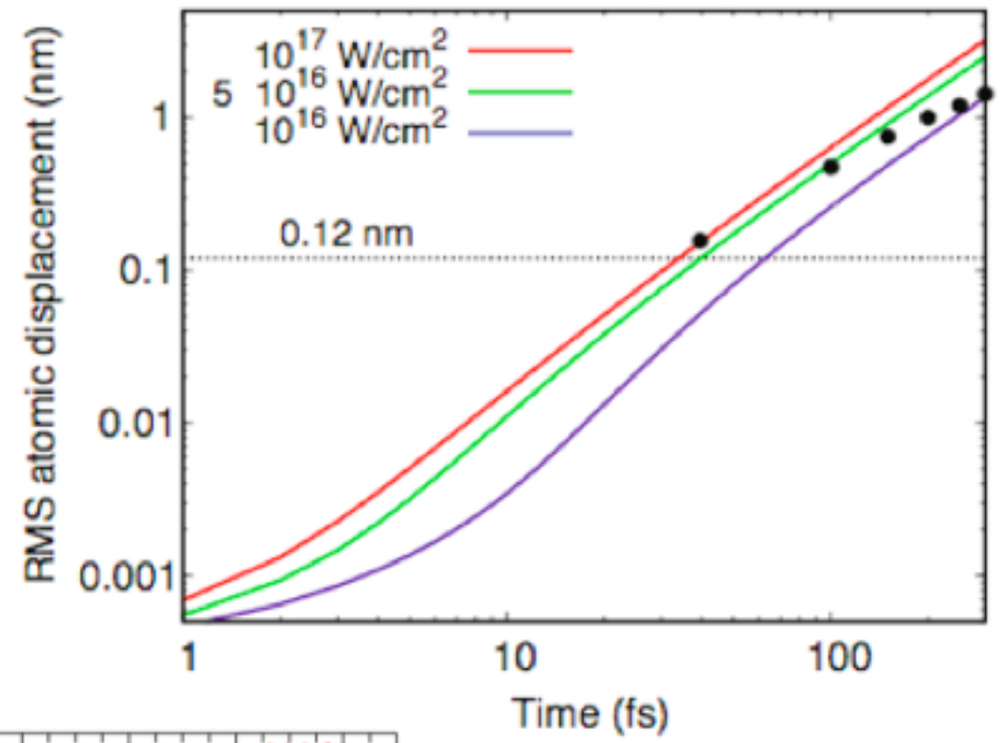


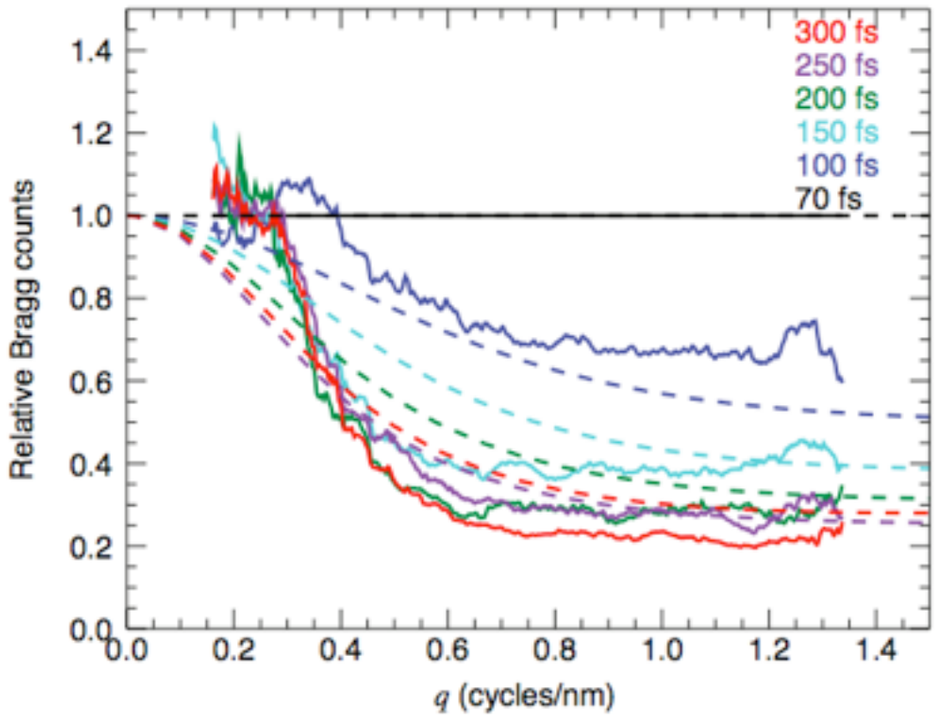
Plasma simulations (CRETIN) give ion and electron temperatures, and ionization rates.

- Plasma, continuum
- Assumes screened hydrogen model
- Follows electronic transitions between different bound states and bound-free transition explicitly in time

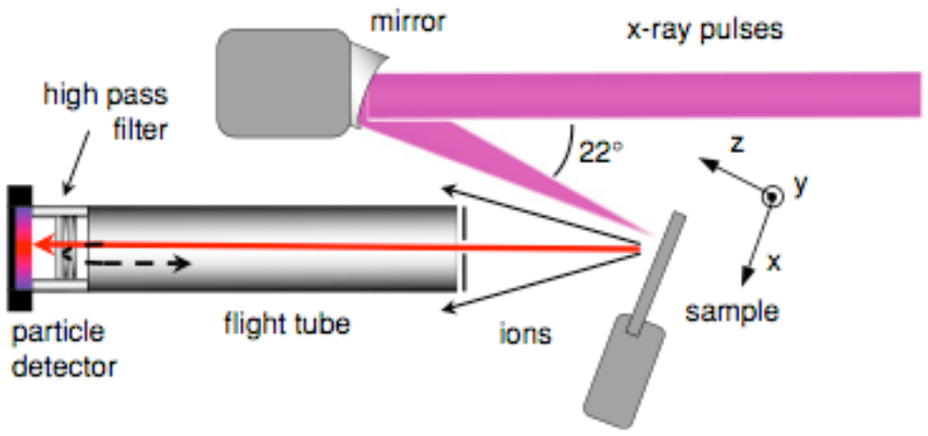
Interaction of Xray Free-electron pulses with matter

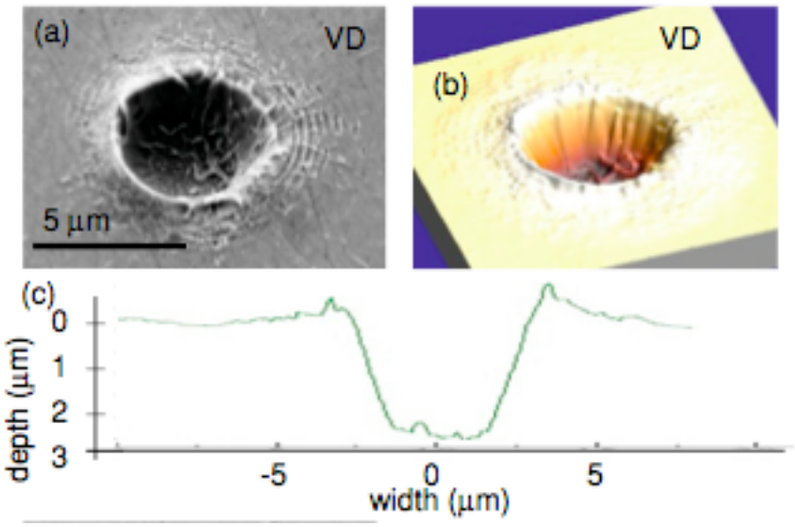


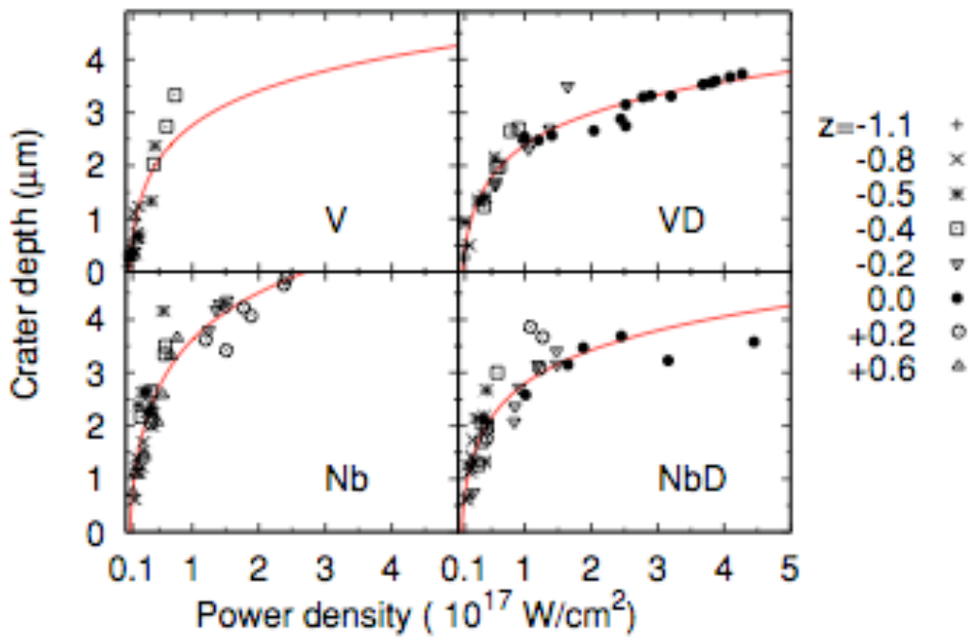




Interaction of Xray Free-electron pulses with matter





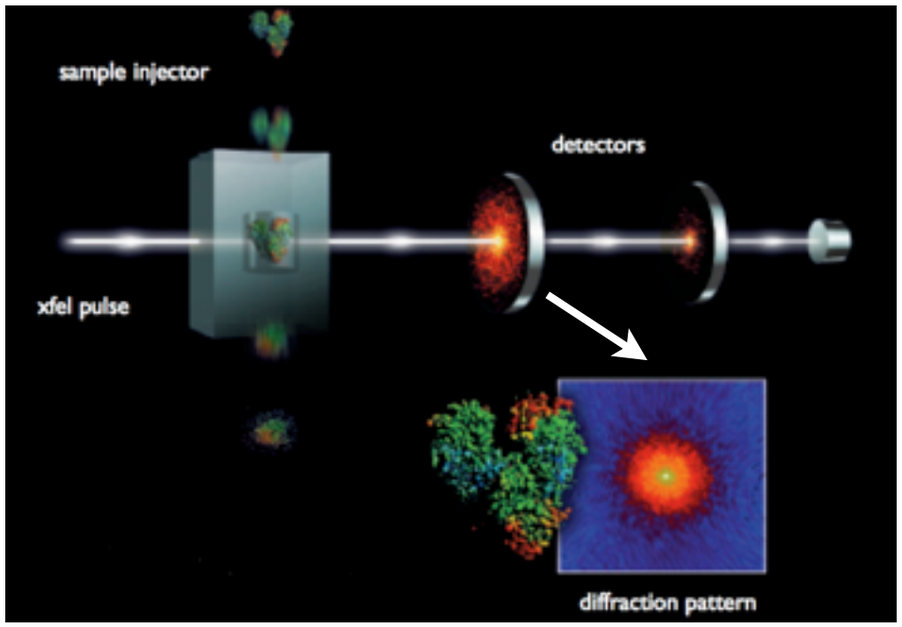


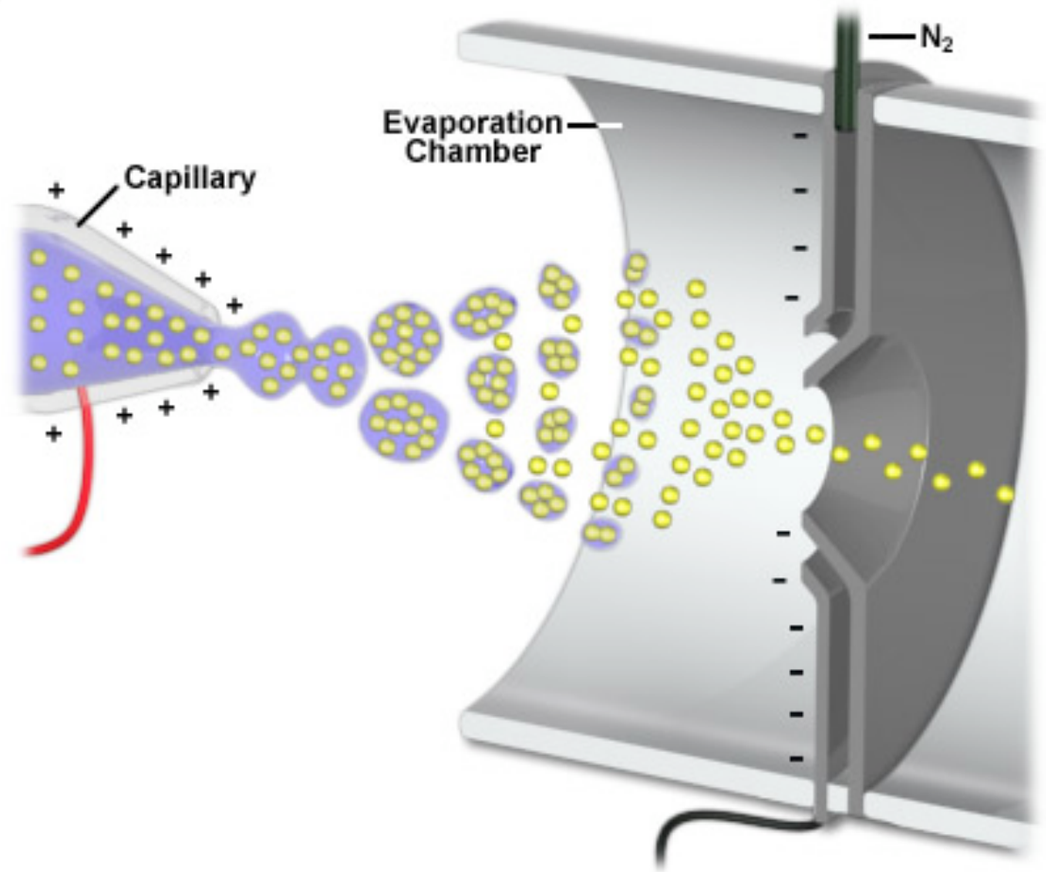
Andreasson et al. Phys. Rev. E 83:016403 (2011)

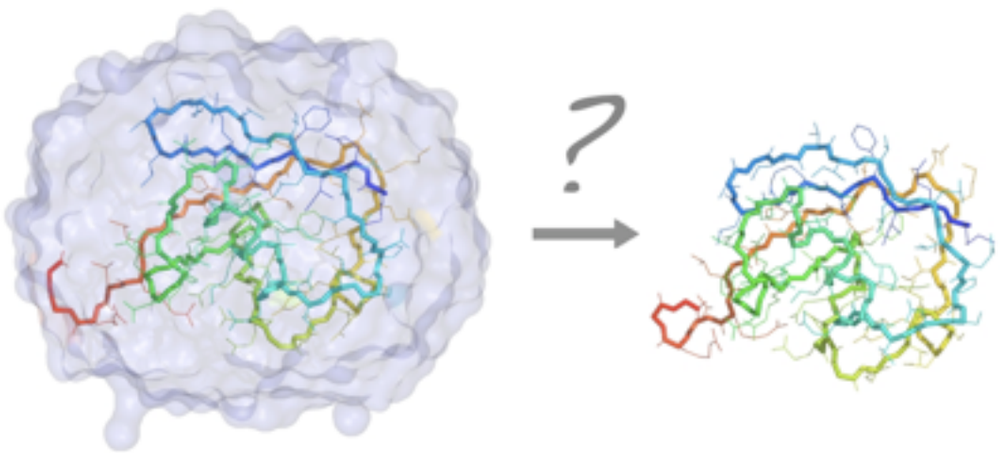
Molecular dynamics simulations (GROMACS)

- Classical force fields
- Newton's equation of motion
- Coulomb and Lennard-Jones potentials

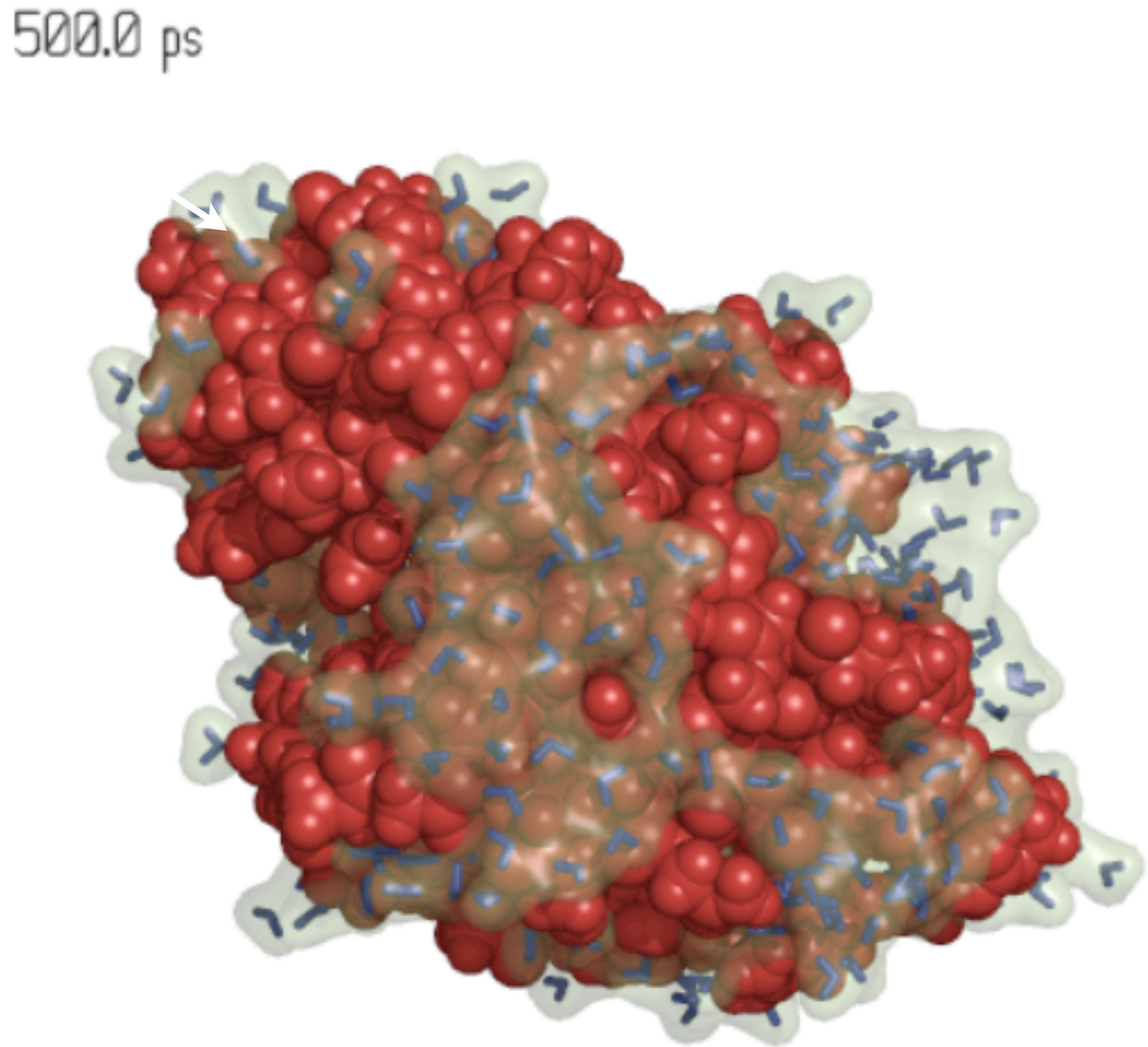
Samples in vacuum





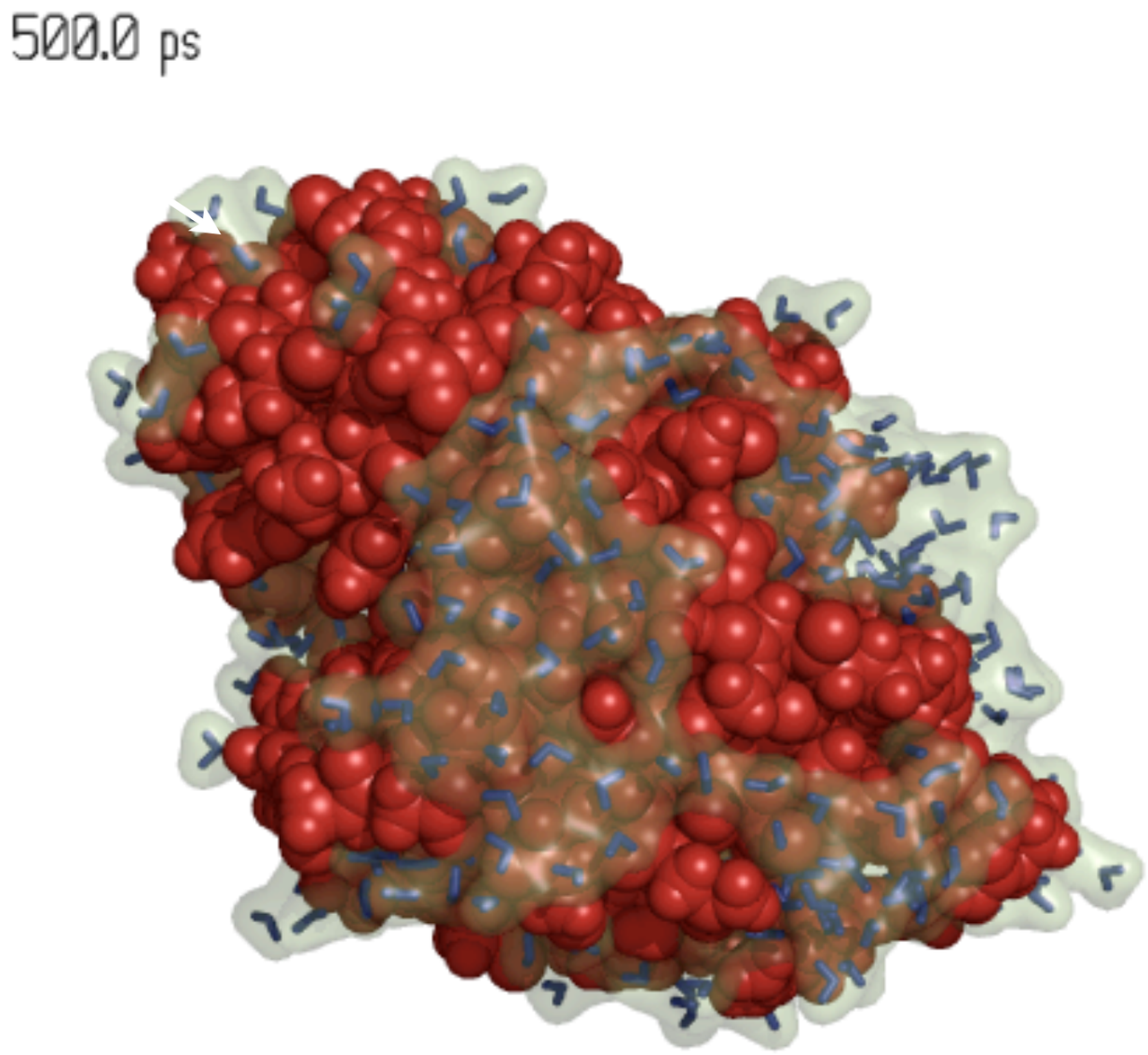


Samples in vacuum



Marklund et al. Phys. Chem. Chem. Phys. 11:8096 (2009)
Van der Spoel at al. Macromol. Bio. Sci. 11:50 (2011)

Samples in vacuum



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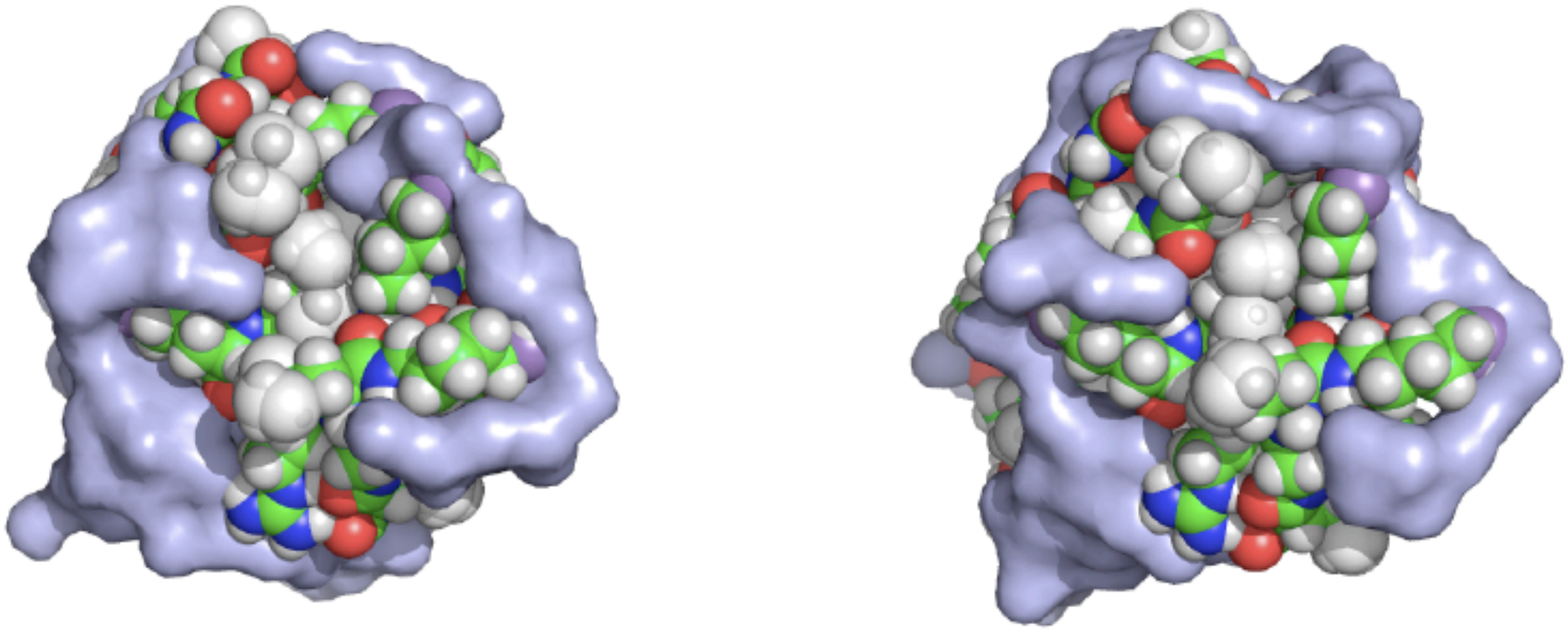
Samples in vacuum



Marklund et al. Phys. Chem. Chem. Phys. 11:8096 (2009)
Van der Spoel at al. Macromol. Bio. Sci. 11:50 (2011)

Computer demands

- Reconstruction and data analysis:
  - 100 fast CPU:s
  - Disc space (PB)
  - Gigabyte ethernet (fiber or infiniband)
  - 4 GB memory per core

- Plasma simulations:
  - 20 fast CPU:s
  - 8 GB memory per core

- Molecular simulations:
  - 1000 CPU:s
  - 1 GB memory per core
  - Fast communication

Acknowledgments

- Henry Chapmans group at CFEL
- Nanocrystallography collaboration
- David van der Spoels group

Thank you for your attention!