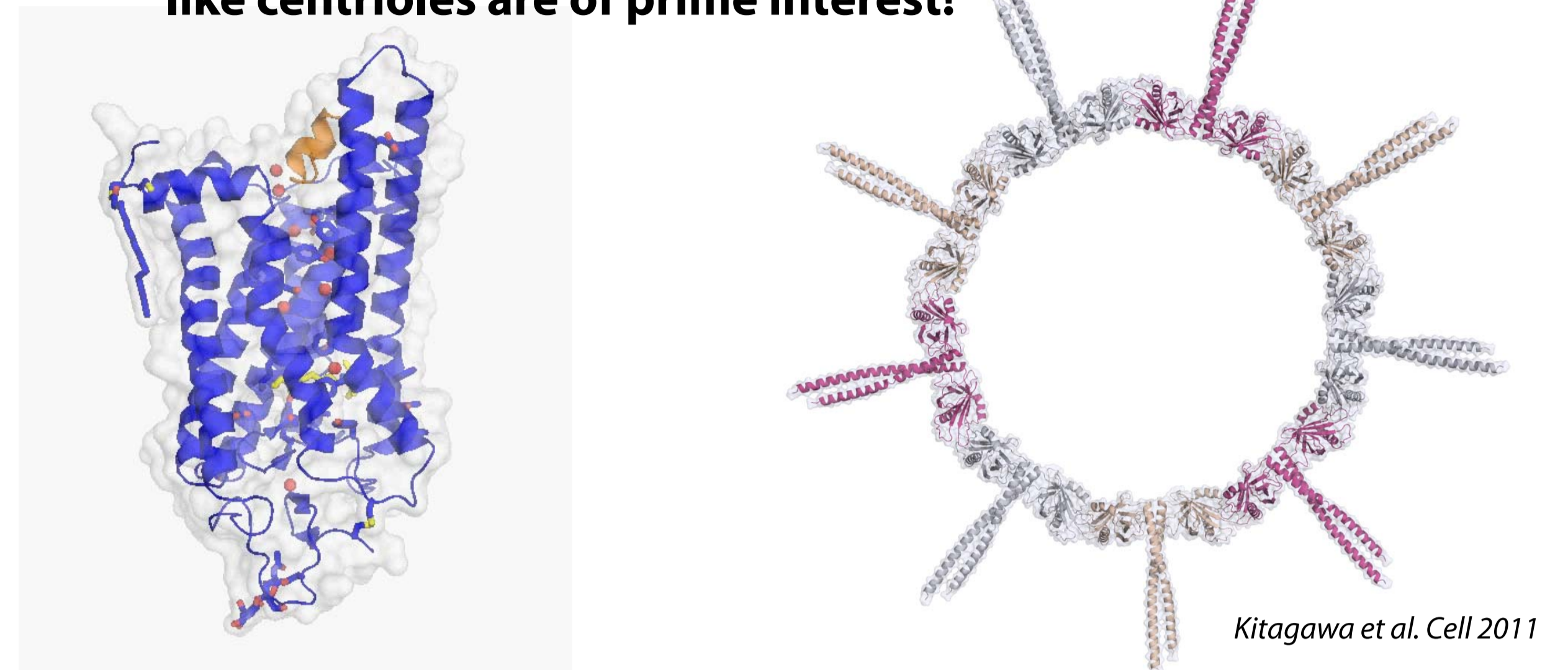


## Femtosecond analysis of protein nanocrystals and supramolecular complexes

Valérie Panneels, Ching-Ju Tsai, Xiao-Dan Li, Guido Capitani, Michel Steinmetz and Gebhard Schertler

Membrane proteins (MPs) represent key components of cell membranes, about one fourth of the human proteome and 60% of the drug targets. We are interested in learning about the different conformations a MP can adopt in response to interacting molecules.

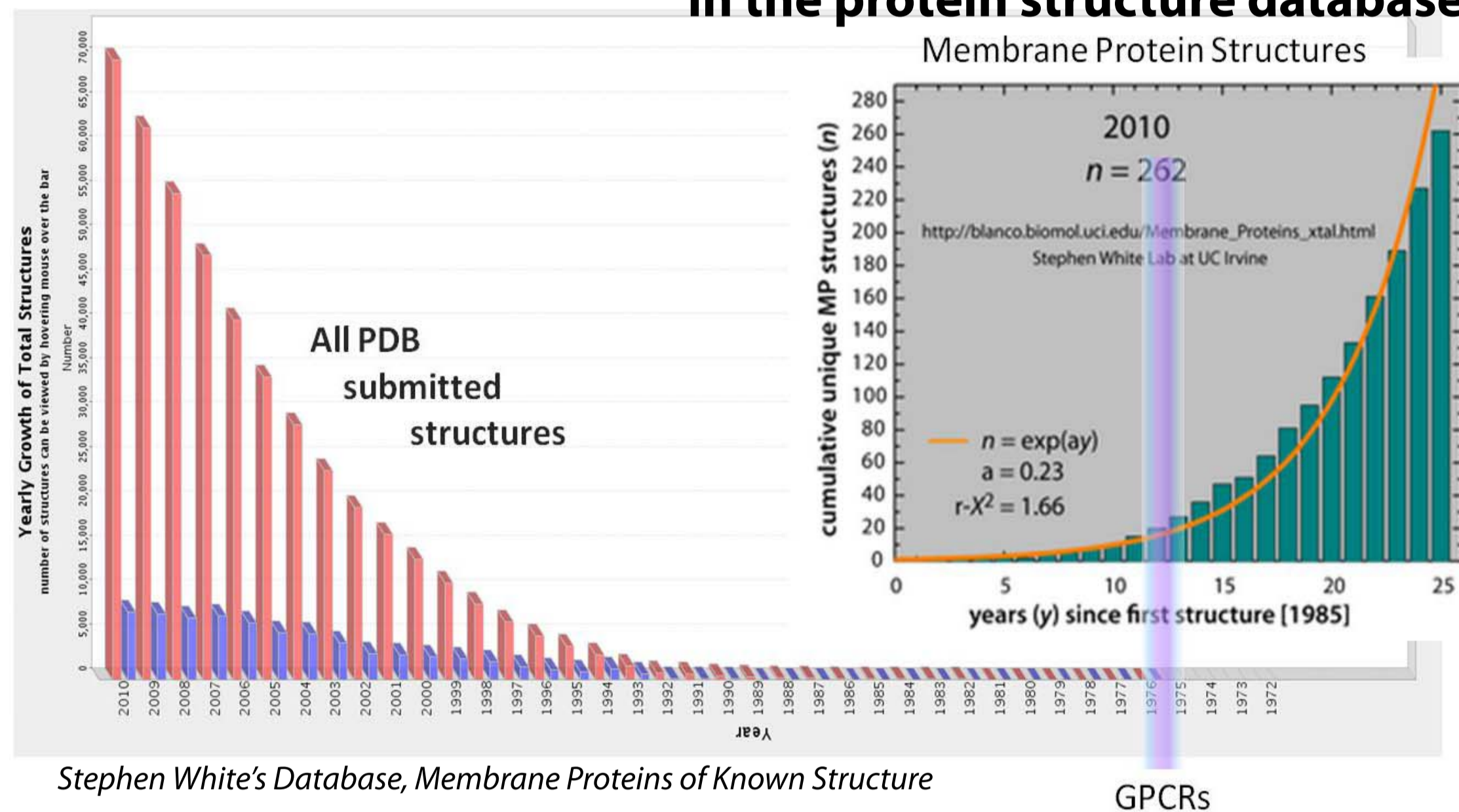
### Membrane proteins like GPCRs and transporters and supramolecular complexes like centrioles are of prime interest!



Standfuss et al. Nature 2011

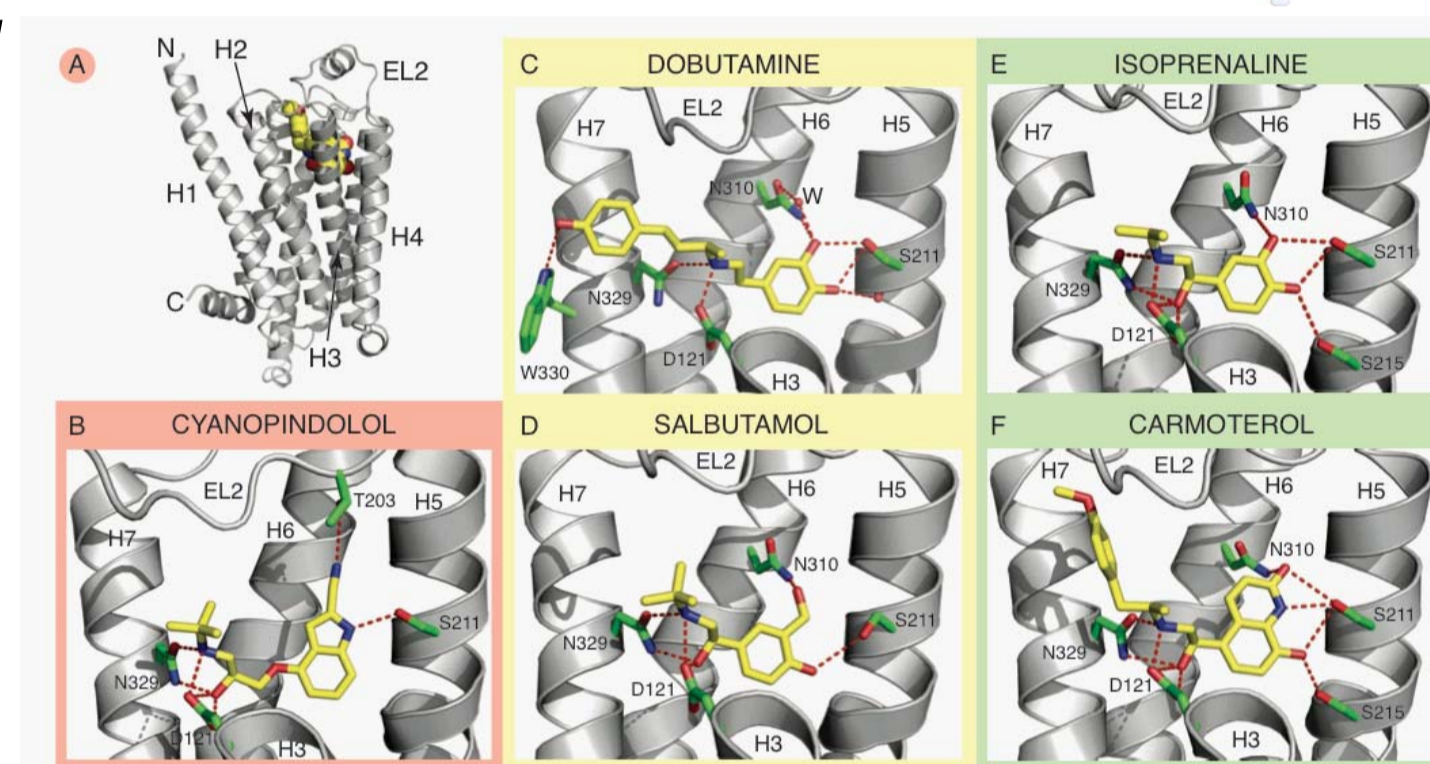
Kitagawa et al. Cell 2011

### Membrane proteins (MPs) are still underrepresented in the protein structure database pdb



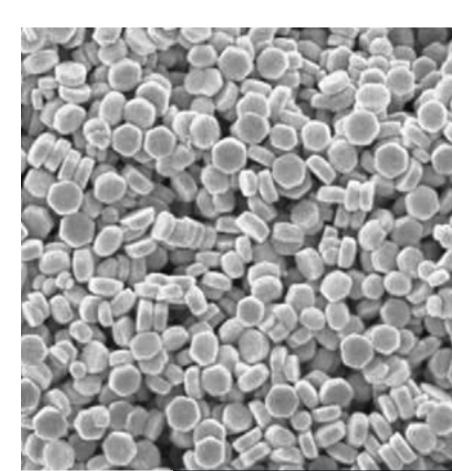
Stephen White's Database, Membrane Proteins of Known Structure

GPCRs

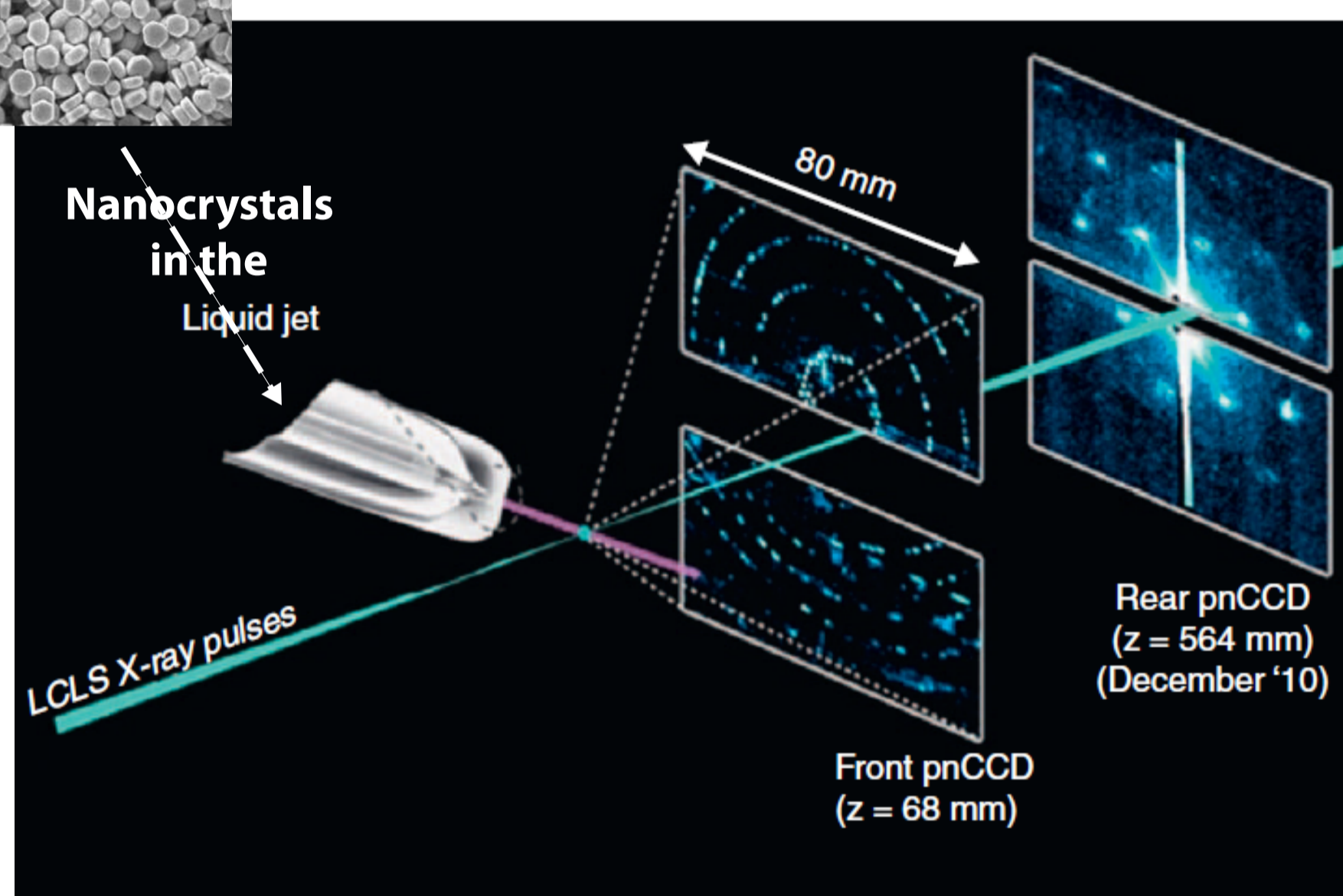


Warne et al. Nature 2011

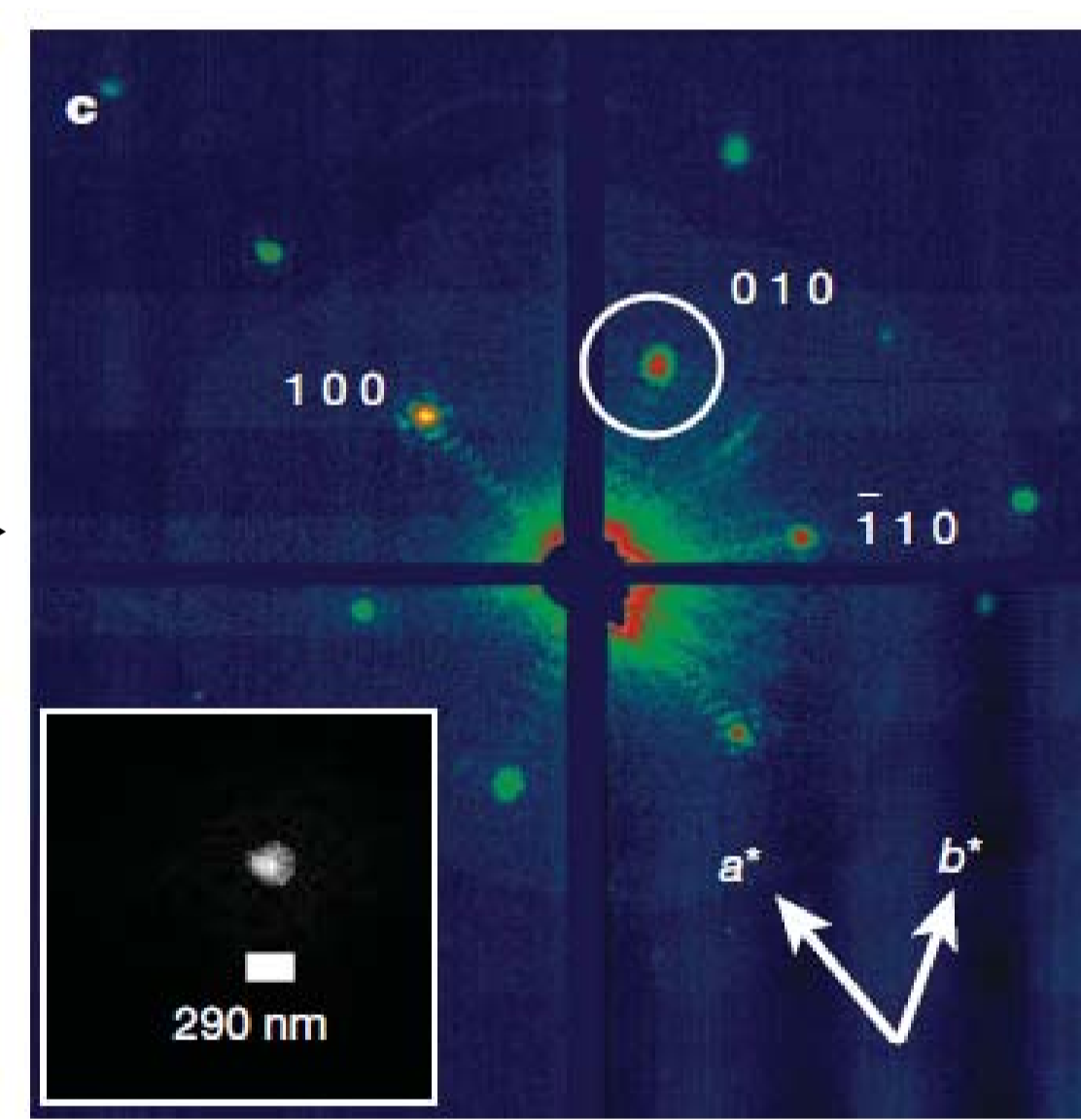
### Serial crystallography of protein nanocrystals



Why do we want nanocrystals? ADV. - they could be easier to grow than large single crystals  
- they are likely better ordered due for example to less long range disorder

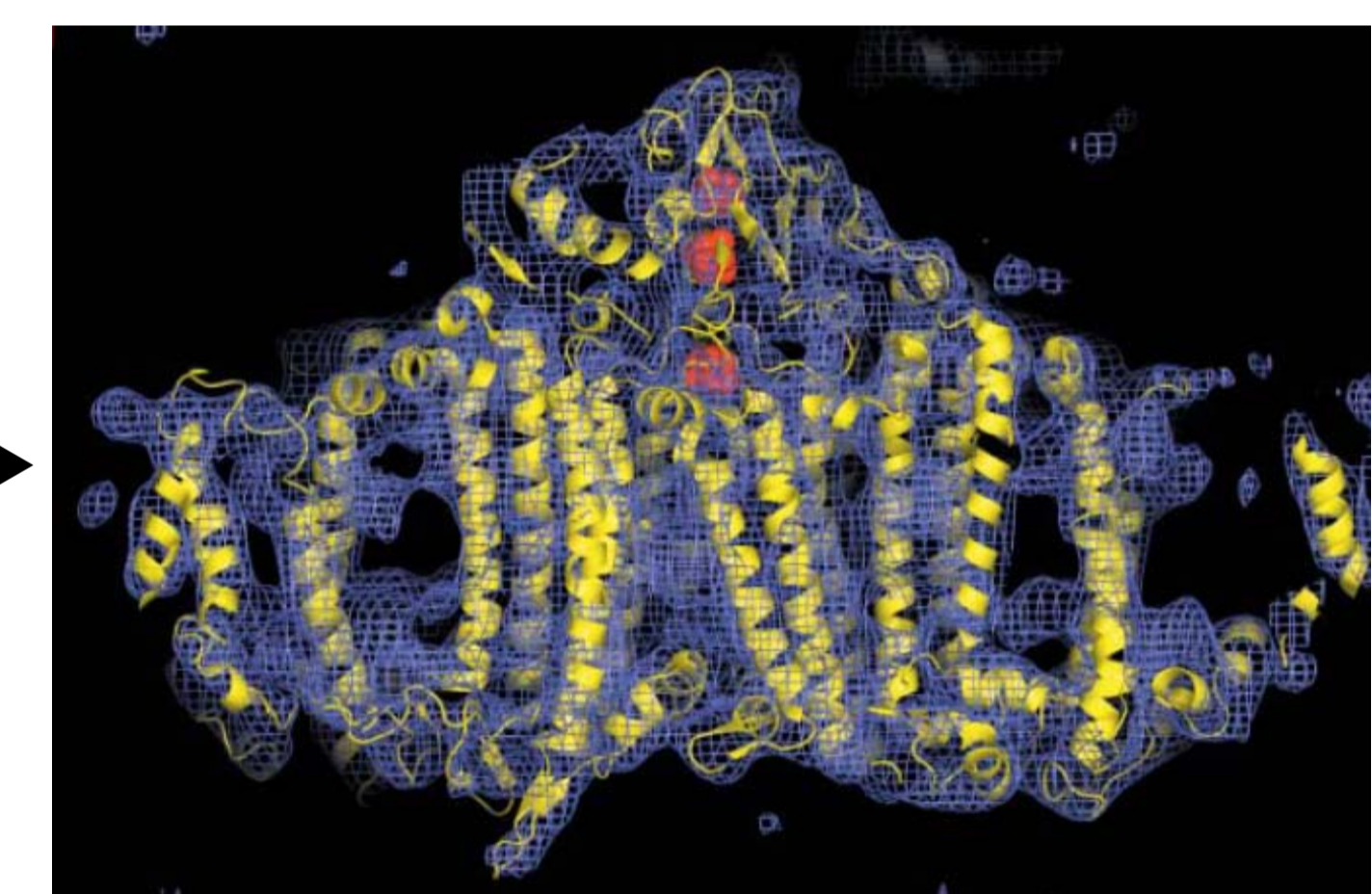


Fromme et al. Curr.Op.Struct.Biol. 2011



Chapman et al. Nature 2011

Electron density map of Photosystem I at 8.5 Å resolution, obtained by fs-crystallography



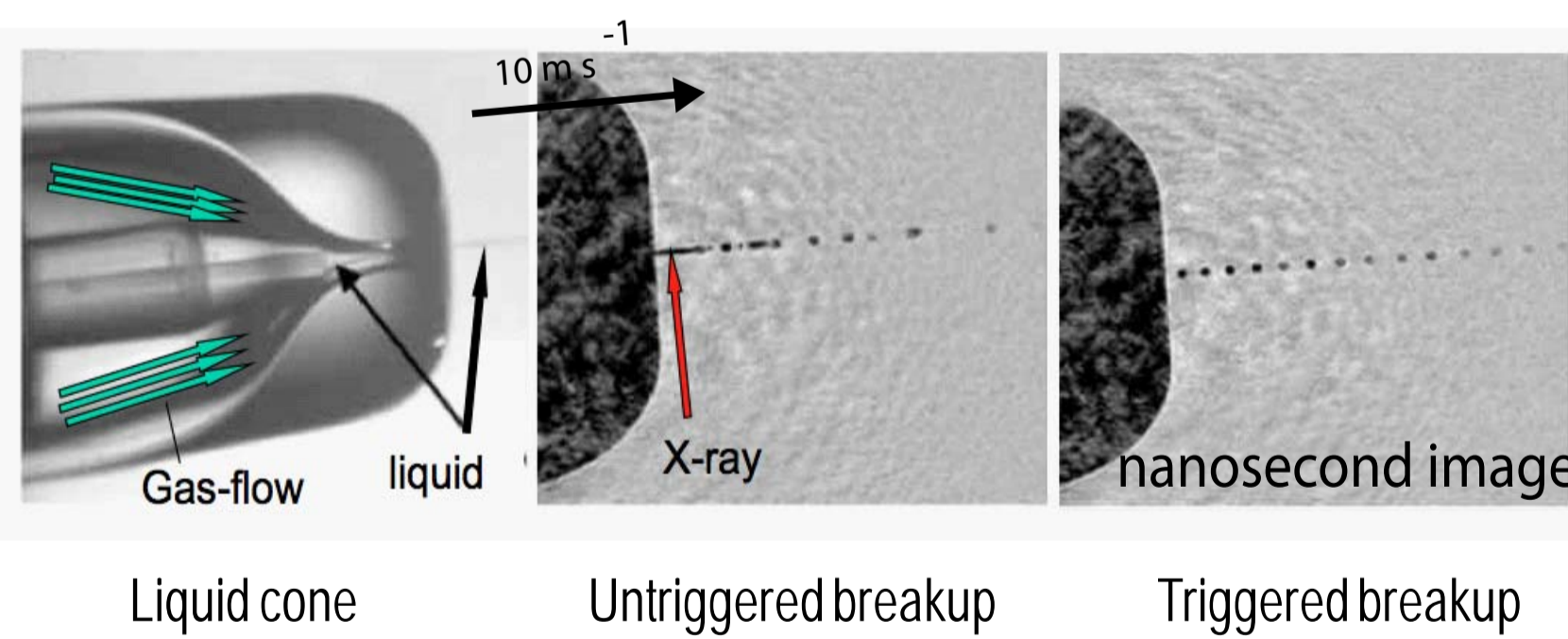
Chapman et al. Nature 2011

Serial single shots of thousands of nanocrystals on the principle of "diffraction-before-destruction"

ADV. - no time for radiation damage  
- diffraction on fully hydrated crystals

### Nanocrystals Delivery to the Beam

SPENCE GUN: Aerojet droplet source -triggered breakup (increases crystal hit rate), repetition rate of 120Hz

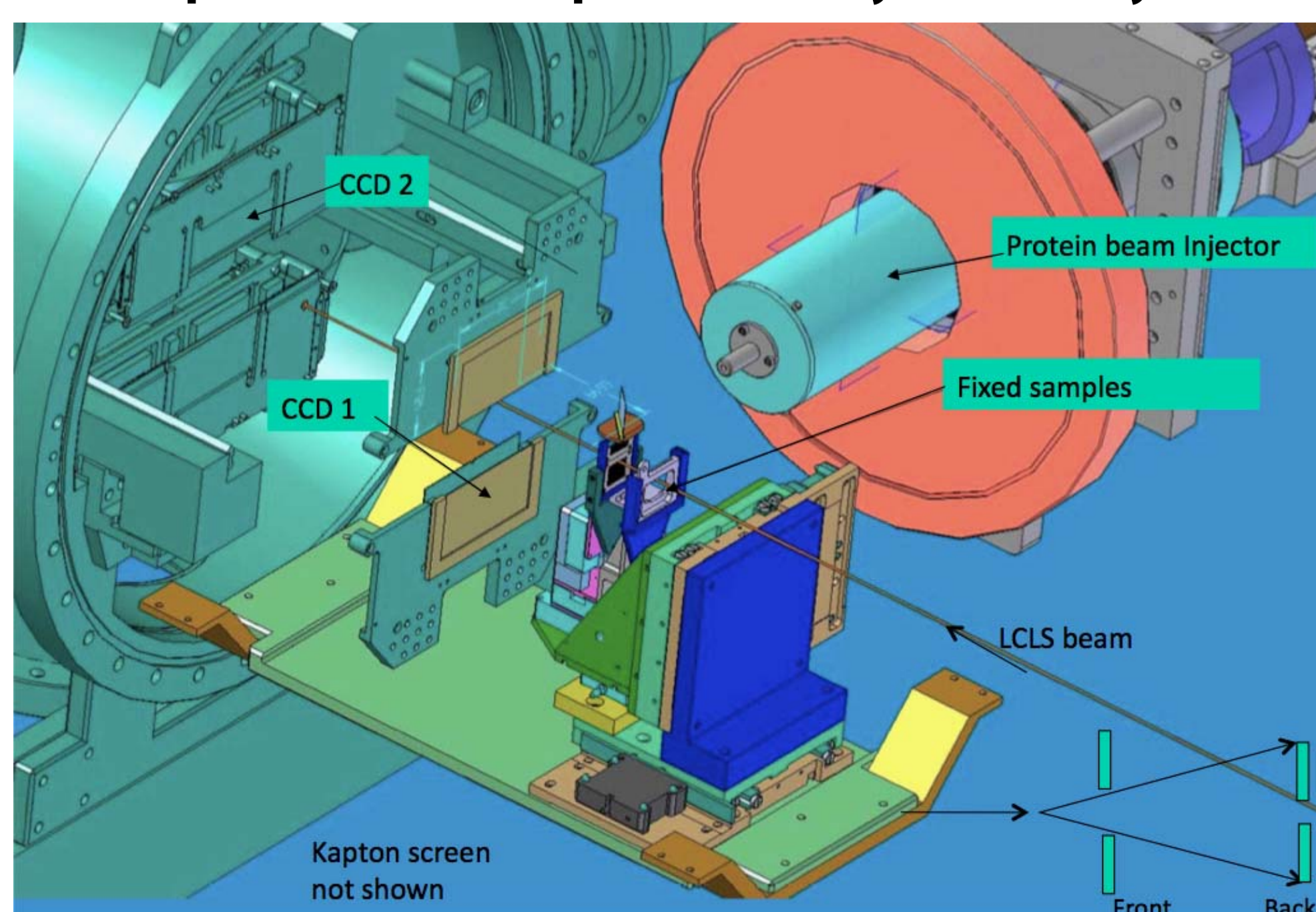


from John Spence, Shapiro et al. J.Synchrotron Radiation 2008

### Requirements on the X-ray beam parameters

Parameter	Unit	Requirement	Motivation / Remarks
Beam parameters			
Energy	keV	> 8	Diffraction at biomolecules
	stability	0.1 %	
Bandwidth	%	0.1	
	stability	< ±10 % bw	
Beam position	stability	< 1 μm	
Beam size	μm	5 - 10	
Photons per pulse	#ph	> 10 <sup>11</sup>	Maximal flux wished
	stability	< ±10 %	
Pulse length	fs	< 50	Diffract and destroy regime required
	stability	20%	
Pulse arrival time	stability	fs	Not an issue
Beam parameter changes during experiment			Not an issue

### Sketch of Experimental Setup for Nanocrystals Analysis



Strüder et al. Nuclear Instr.Meth.Phys.Res.A 2010

### Other Special Requirements

- special sample delivery to the beam (Spence gun or grid scanning)
- sample to detector distance ~ 1m
- strong computer capacity for direct data processing