7 October 2008

Life science imaging applications at future XFEL sources

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Principle idea of coherent diffractive imaging

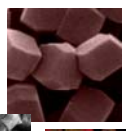
Principle:

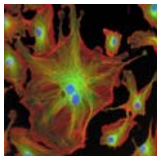
- Record coherent diffraction pattern & solve structure by iterative phase retri

Samples:

- single biomolecules (ideally membrane proteins, viruses)
- inorganic and organic nano-crystals (structure & strain)
- cells (fully hydrated and living)
- nano-structures (semiconductor devices)

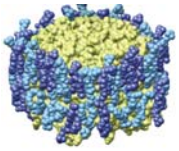
Why XFEL ?

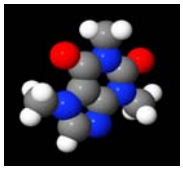




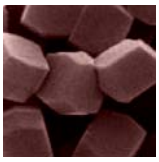
What is feasible at a future PSI-XFEL ?

Biomolecules

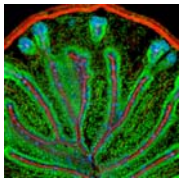


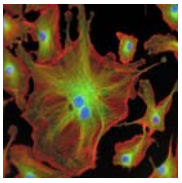


Nano-Crystals



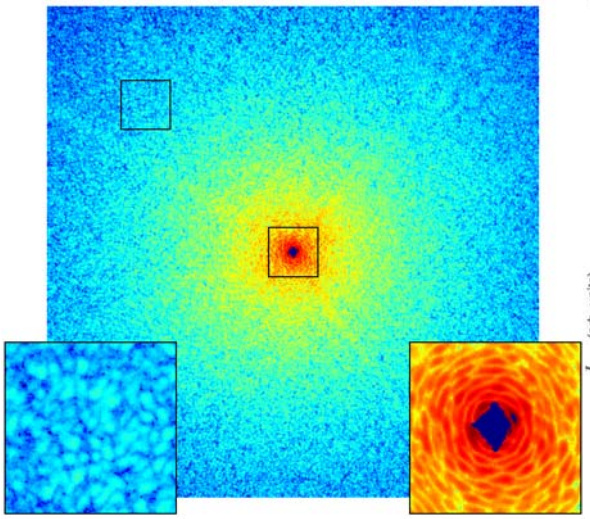
Cells



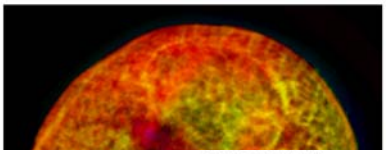


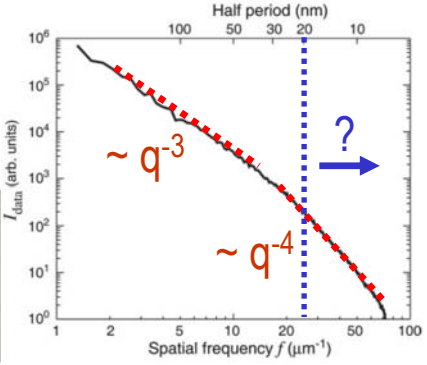
Today, we can image freeze-dried and unstained cells at 25 nm resolution

diffraction pattern with soft x-rays (750 eV, ALS), 65 sec



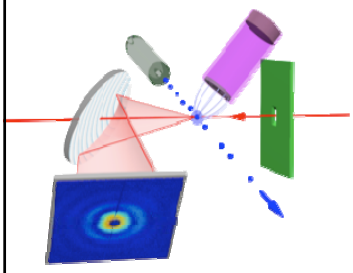
reconstruction

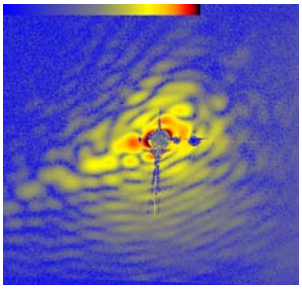


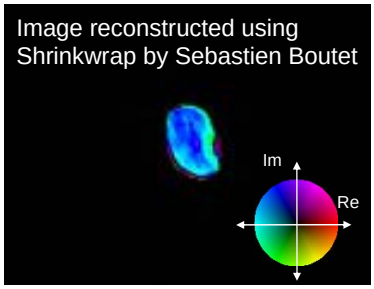


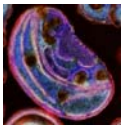
Shapiro et al., PNAS 102, 15343 (2006); Thibault et al. Acta. Cryst. 62, 248 (2007)

...and we know how to get them into the beam (slide by H. Chapman)





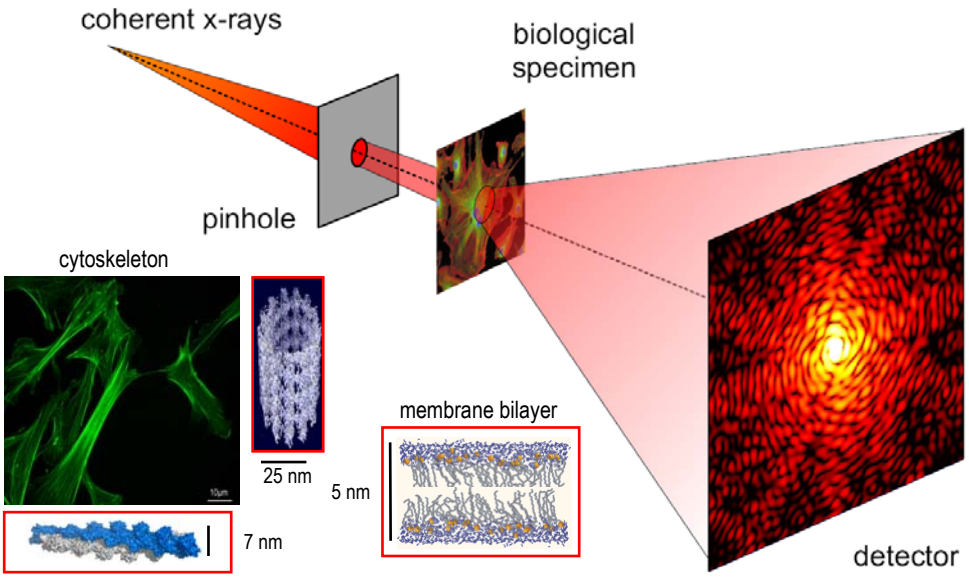




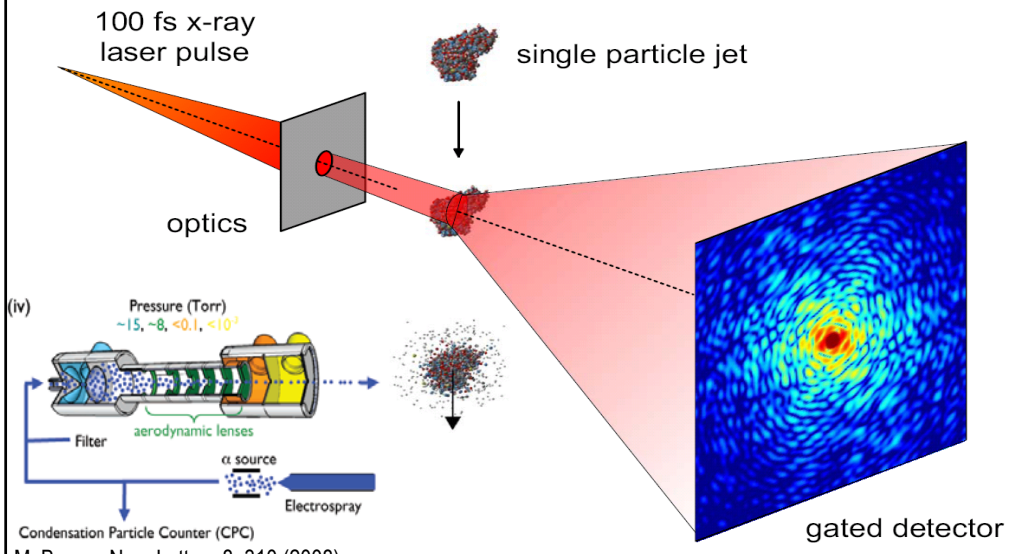
- Single shot ~10 fs diffraction pattern recorded at FLASH (DESY) at a wavelength of 13.5 nm of a picoplankton organism.
- Injected into vacuum from solution, and shot through the beam at 100 m/s

J. Hajdu, I. Andersson, M. Svenda, M. Seibert (Uppsala)
S. Boutet (SLAC); M. Bogan, H. Benner, U. Rohner, H. Chapman (LLNL)

At the XFEL, we will be able to obtain snapshots (projections) of frozen-hydrated cells at a few nanometer resolution !



What about biomolecules, proteins or viruses ?



M. Bogan, NanoLetters 8, 310 (2008)

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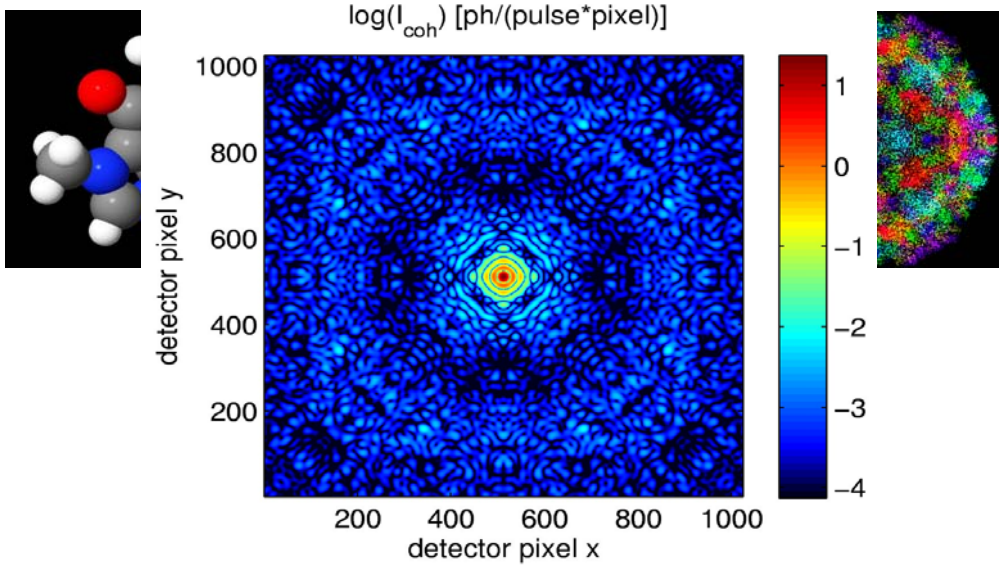
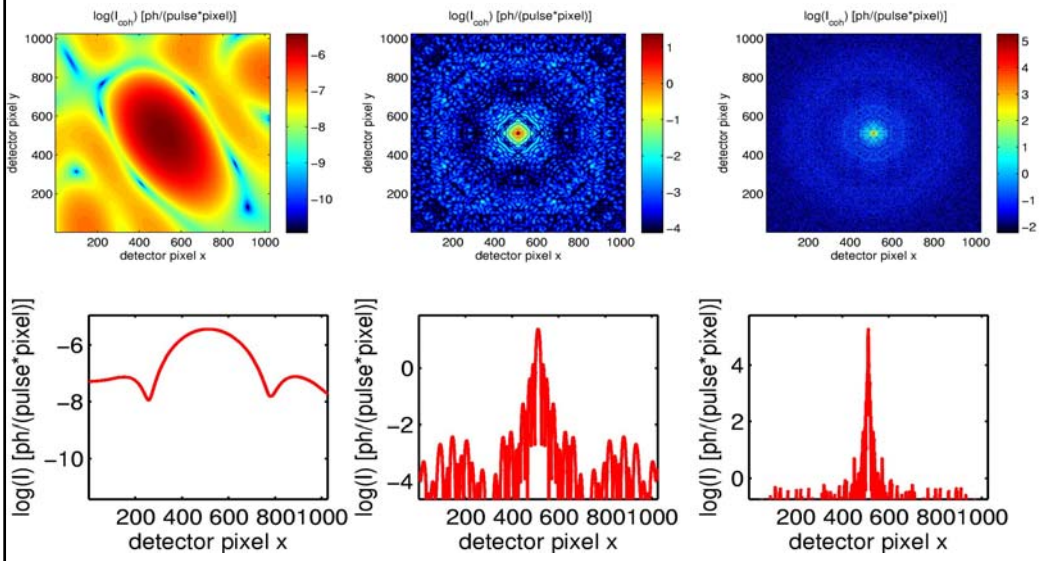
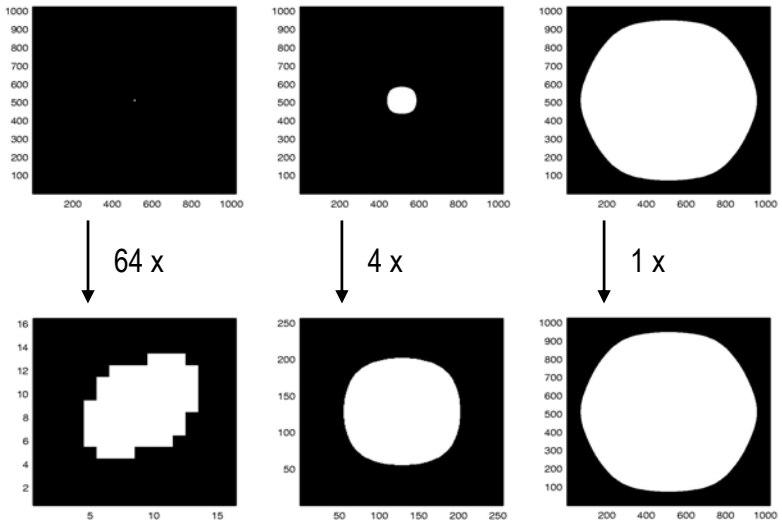


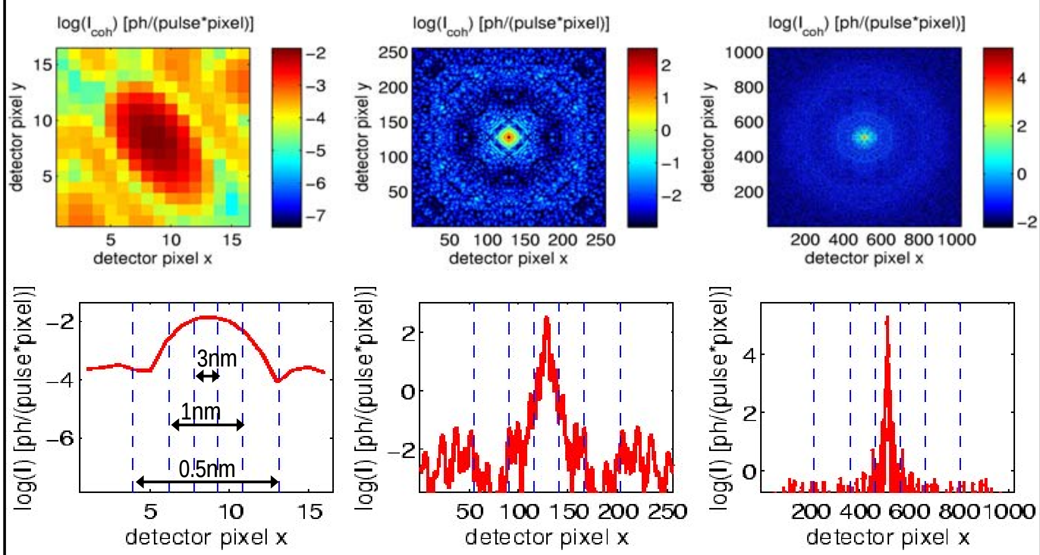
Expected diffraction patterns for single biomolecules



Determining binning factors from the auto-correlation



Single molecule data rebinned



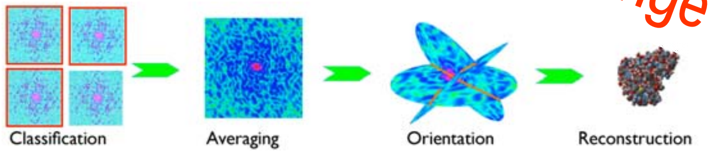
Statistics - repeating identical experiments

…provided, we learn how to orient molecules (strong electric fields, lasers)

	3 nm	1 nm	0.5 nm	0.3 nm
caffeine	299	767	8832	25424
ferritin (bio unit)	6	379	788	929
rice dwarf virus (bio unit)	4	34	72	164

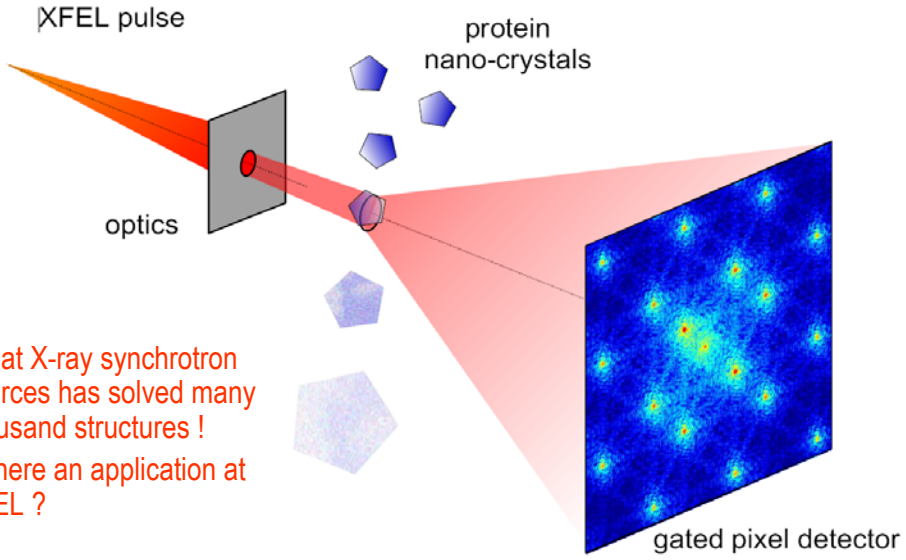
This will be a 'grand challange'

- or classify VERY noisy diffraction patterns using [illegible] algorithms



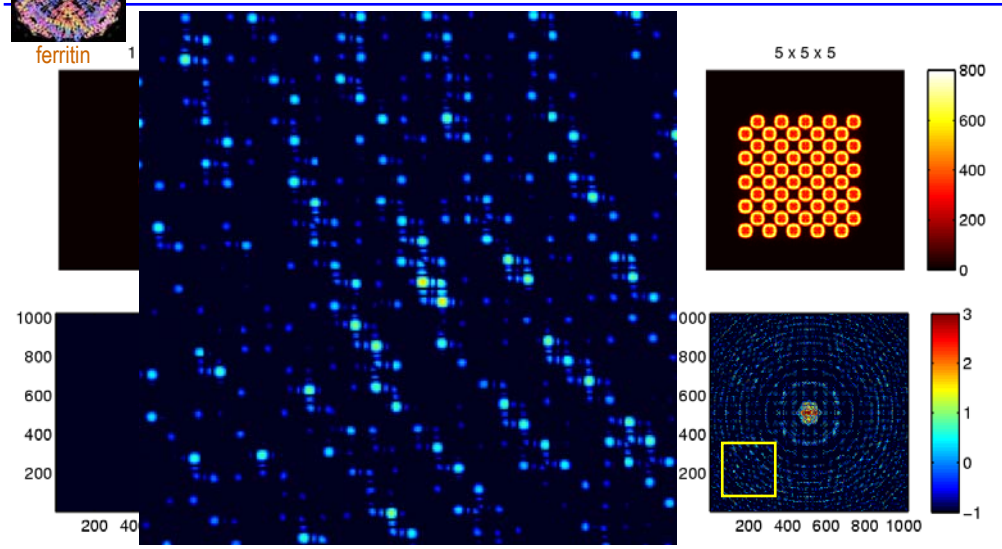
J. Hajdu et al., JSB 144, 219 (2003); G. Bortel et al. JSB 158,10 (2007)

A possible alternative: 'Flash' crystallography of protein nano-crystals ?



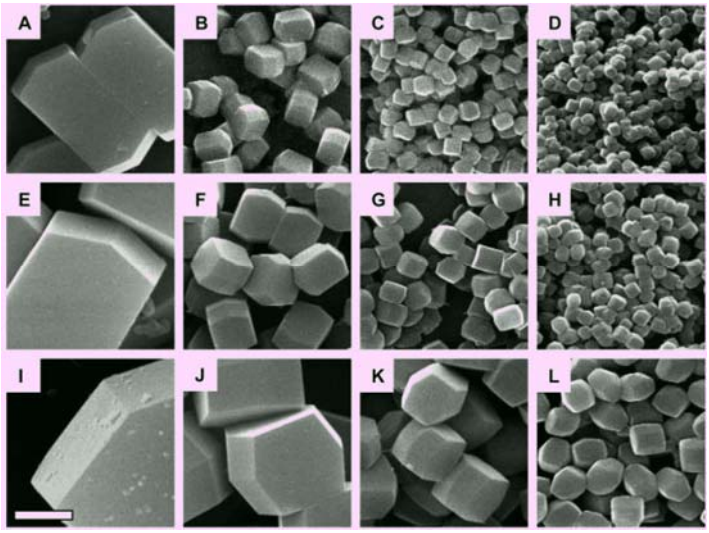
- PX at X-ray synchrotron sources has solved many thousand structures !
- Is there an application at XFEL ?

Expected x-ray diffraction patterns @ XFEL



10^{12} ph/pulse focused into 100 nm, X-ray energy 12.4 keV, 200 micron pixel size, 300 mm detector distance

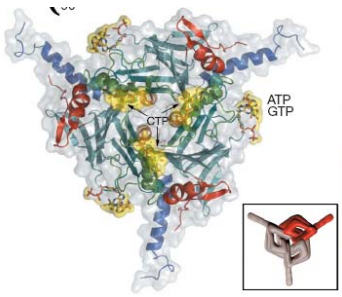
Protein nano-crystals exist !



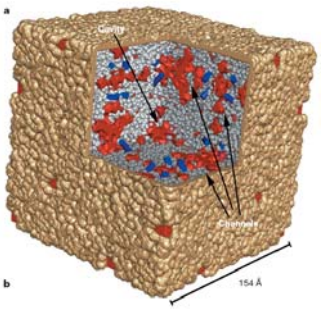
lysozyme
nano-crystals

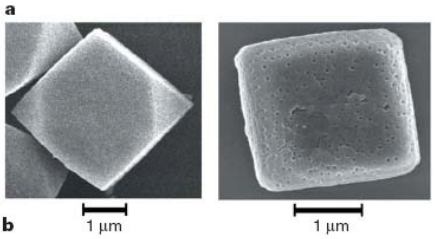
J.C. Falkner, et al, Chem. Mater. 17, 2679 (2005)

Organic nano-crystals are important in nature !



Cypovirus polyhedra



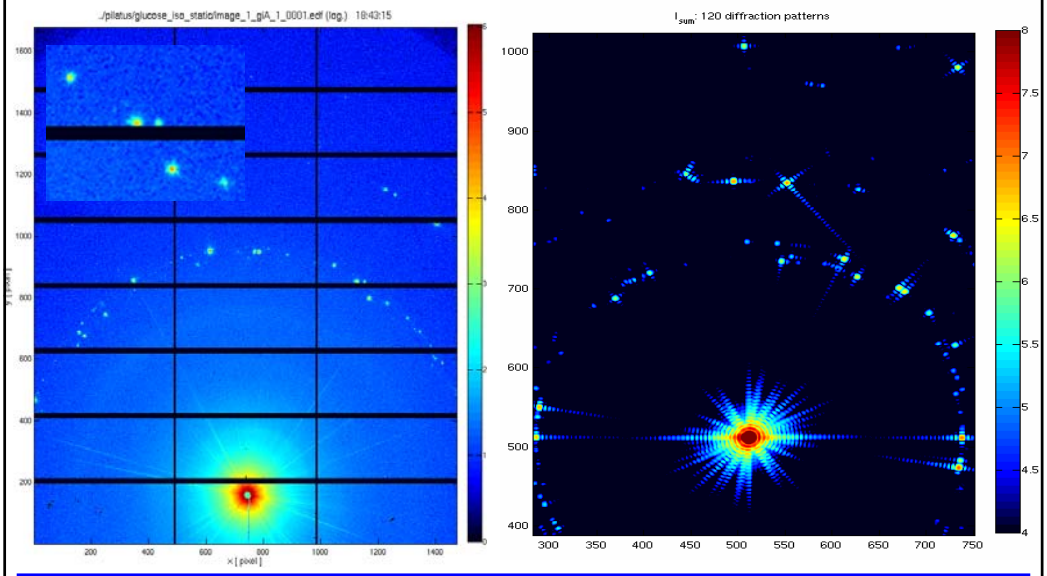


several hundred crystals screened,
final data set merged from ~ 10

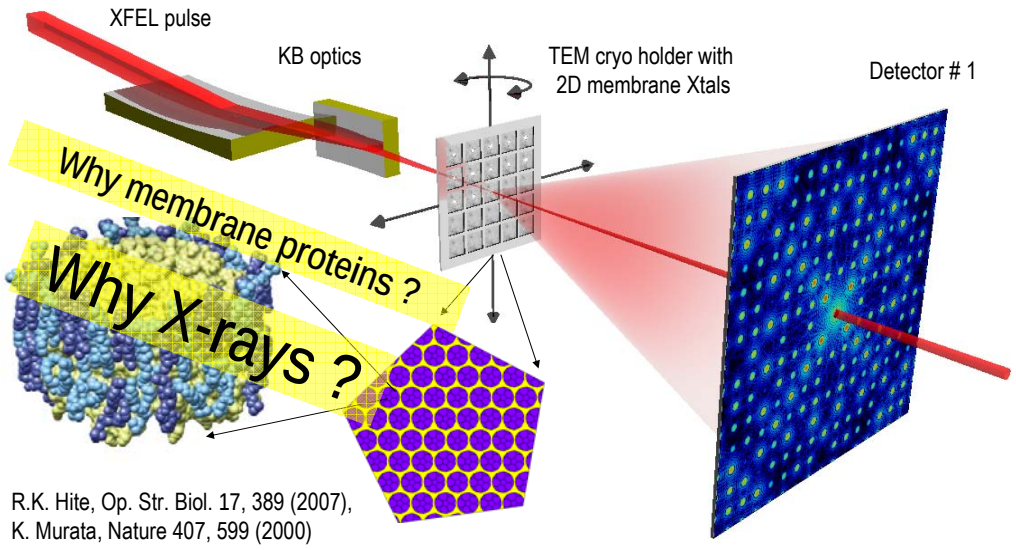
F. Coulibaly et al., Nature 446, 97 (2007)

Synchrotron results for D-Xylose Isomerase

(with M. Schiltz/ EPFL)

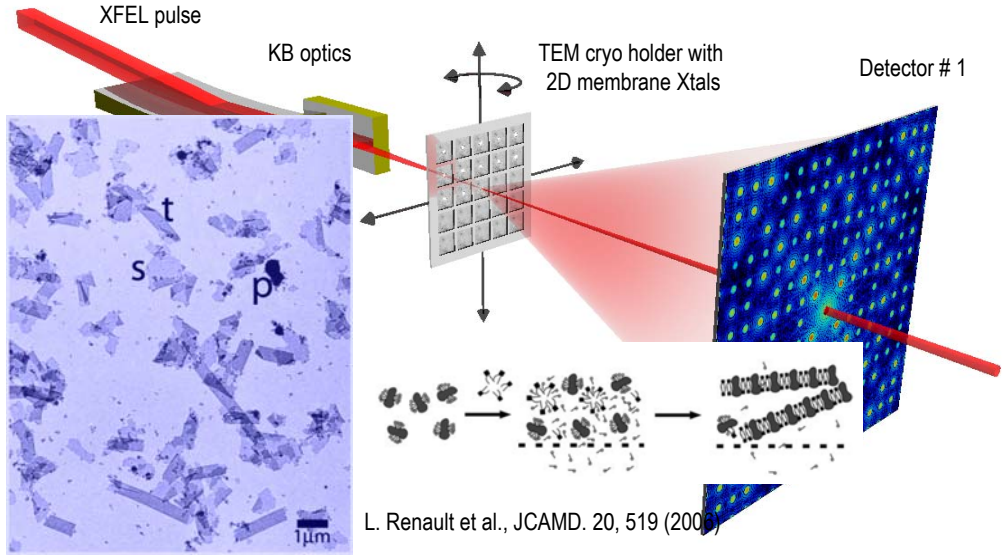


2D 'flash' crystallography of membrane proteins

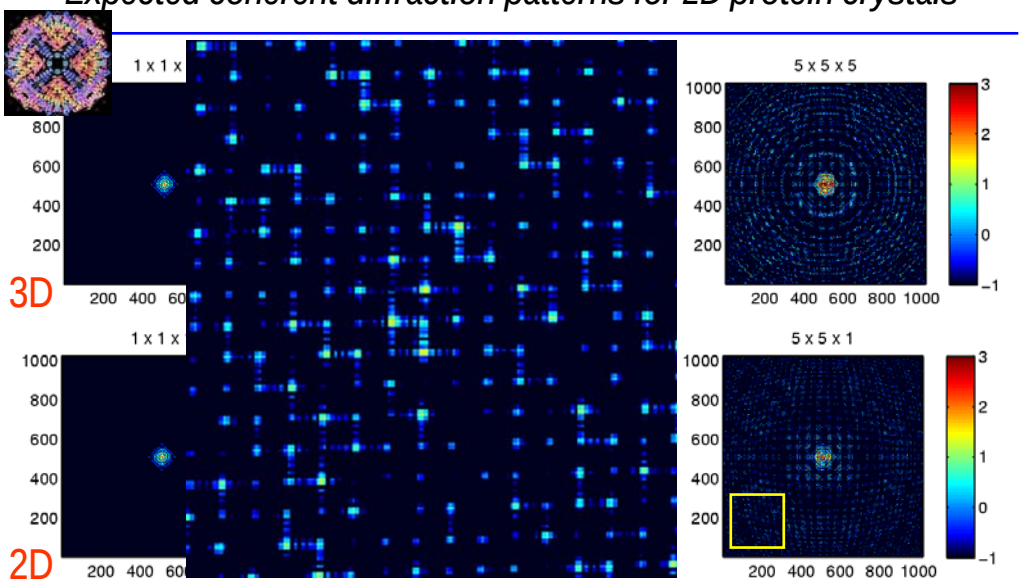


R.K. Hite, Op. Str. Biol. 17, 389 (2007),
K. Murata, Nature 407, 599 (2000)

2D 'flash' crystallography of membrane proteins

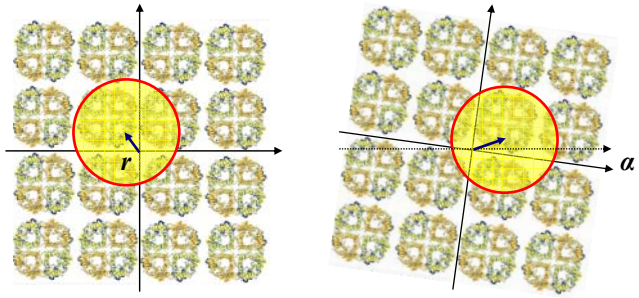


Expected coherent diffraction patterns for 2D protein crystals

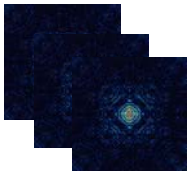


10^{12} ph/pulse focused into 100 nm, X-ray energy 12.4 keV, 200 micron pixel size, 300 mm detector distance

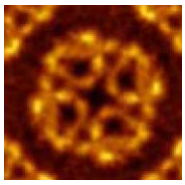
Reconstruction of 2D 'flash' crystallography data sets



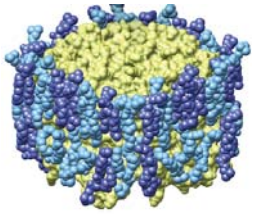
$I_m(r,\alpha,q)$



classified projections



tilt series & tomography



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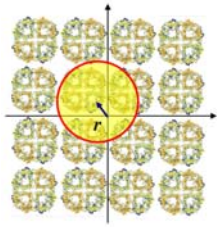
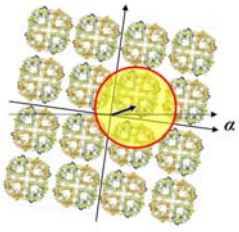
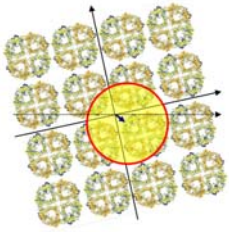


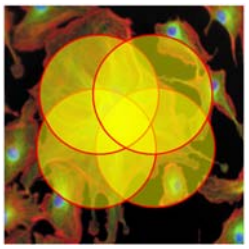


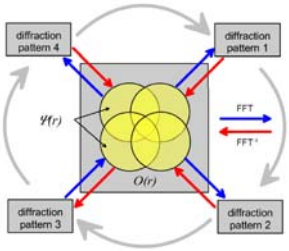


Reconstruction of periodic crystal data sets with finite illumination

Equivalent:

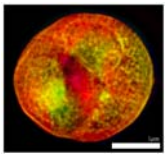
Ptychographic reconstruction of non-periodic objects



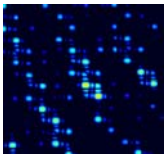


P. Thibault, F. Pfeiffer et al., Science 321, 379-382 (2008)

Conclusions & Messages



- Coherent Diffractive Imaging at the PSI-XFEL can yield snapshots of frozen-hydrated cells or cellular components with a resolution of a few nanometers



- 2D & 3D coherent 'flash' crystallography seems to be a very promising extension of macromolecular crystallography at a future XFEL source