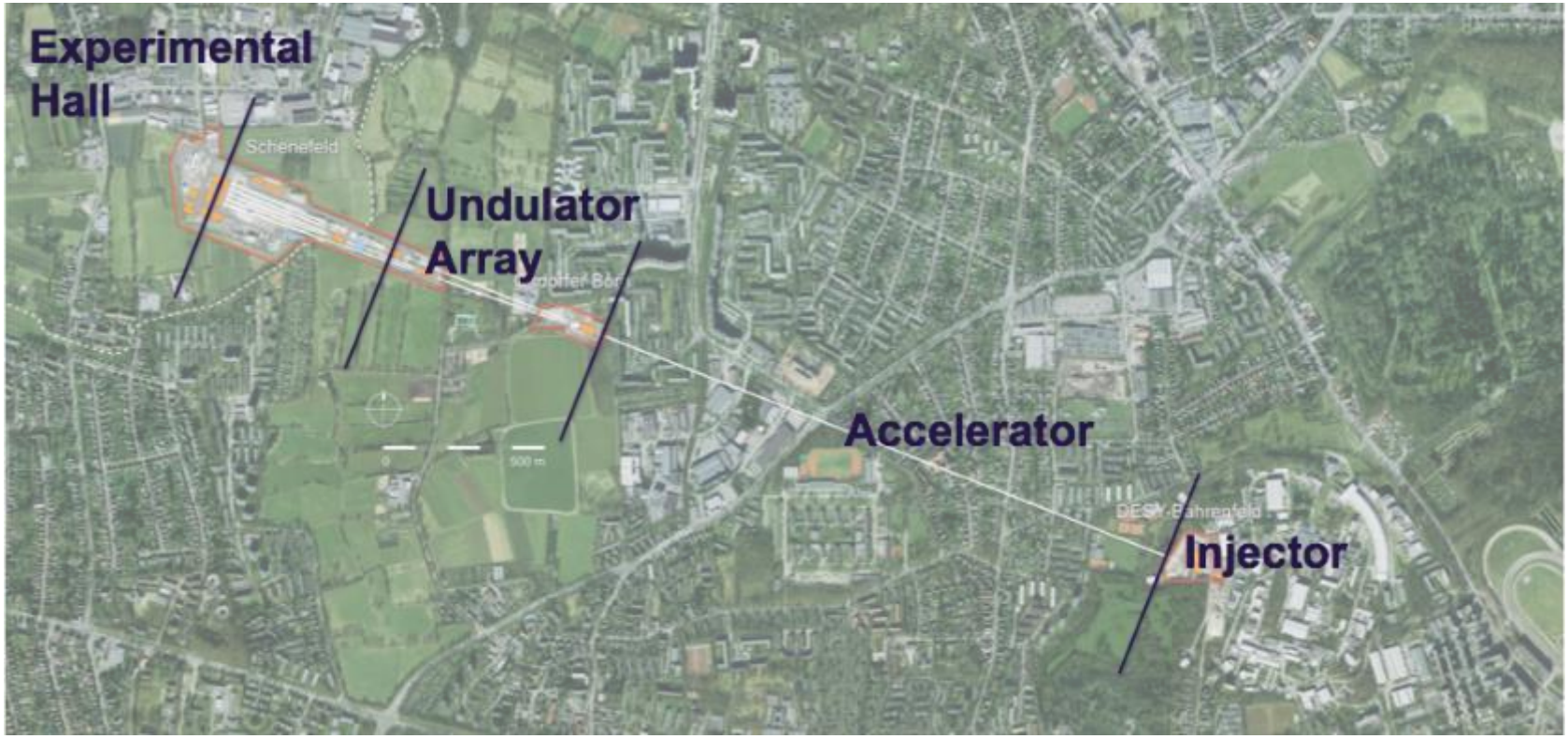
Seeing elusive protein structures at high resolution: Instrumentation for XFEL crystallography and imaging

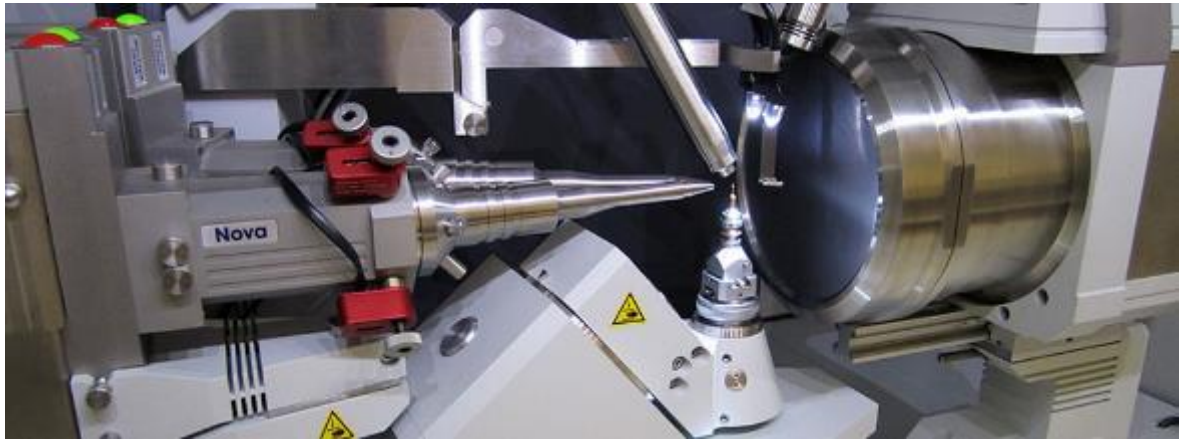
Grant Mills
SPB/SFX
Postdoctoral Scientist

Hamburg DESY, 09 June 2017

The European XFEL

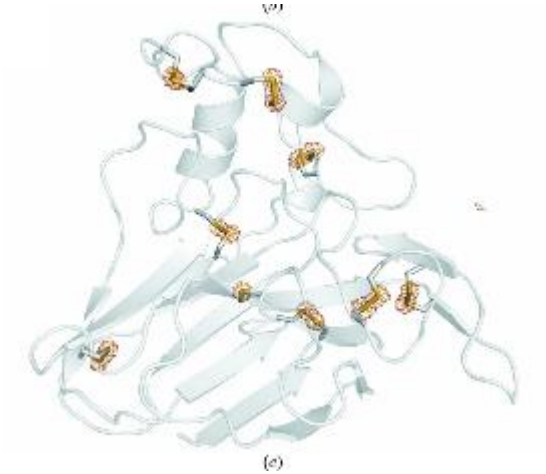


Traditional X-ray sources

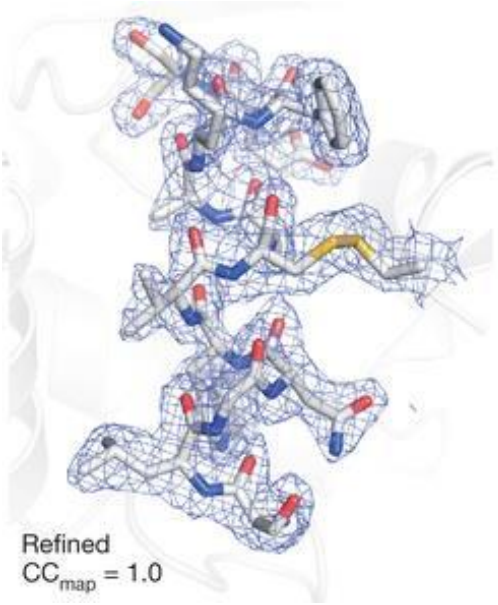


Images:
https://industry.gov.au
http://www.xstruct.ugent.be

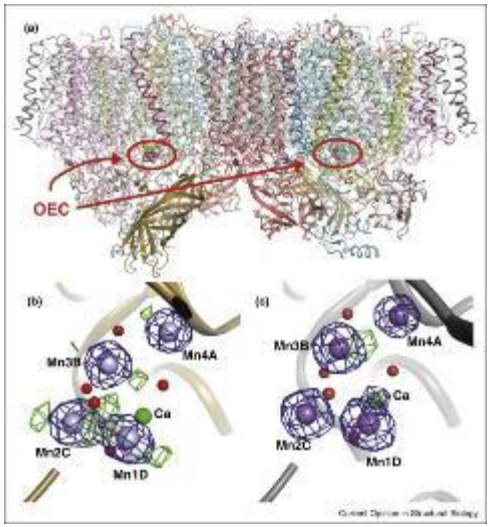
Protein structure



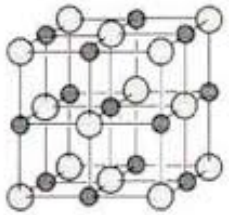
Nass et al. (2016)



TRM Barends et al. (2014)



R Neutze (2015)



Scattered x-rays is proportional to N^2
(~ 100 x 100 x 100 elements)

- If N=1, then scattering is proportional to 1
  (~ a million times less than above)

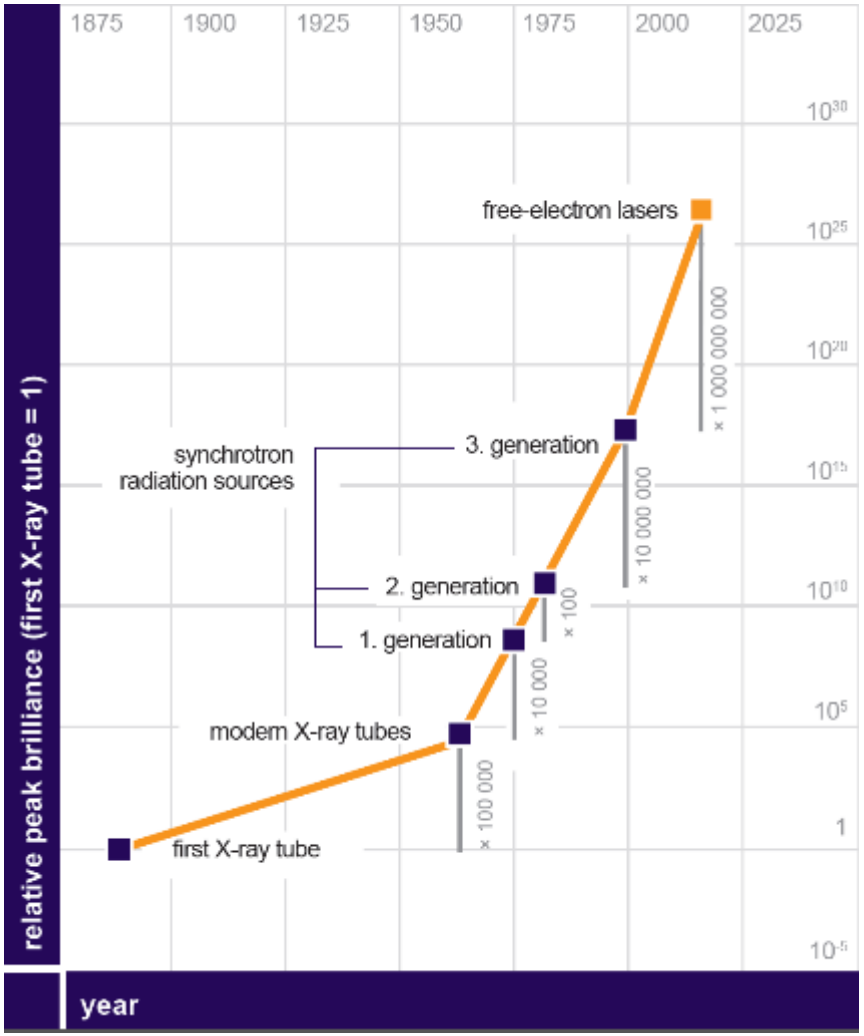
Conclusion: Need a lot more x-rays

Slide modified: A. P. Mancuso

SASE radiation

FELs offer improvements over 3rd generation synchrotrons

- Orders of magnitude brighter
- Extremely short pulse duration
- Both µm and nm focus



Diffraction before destruction

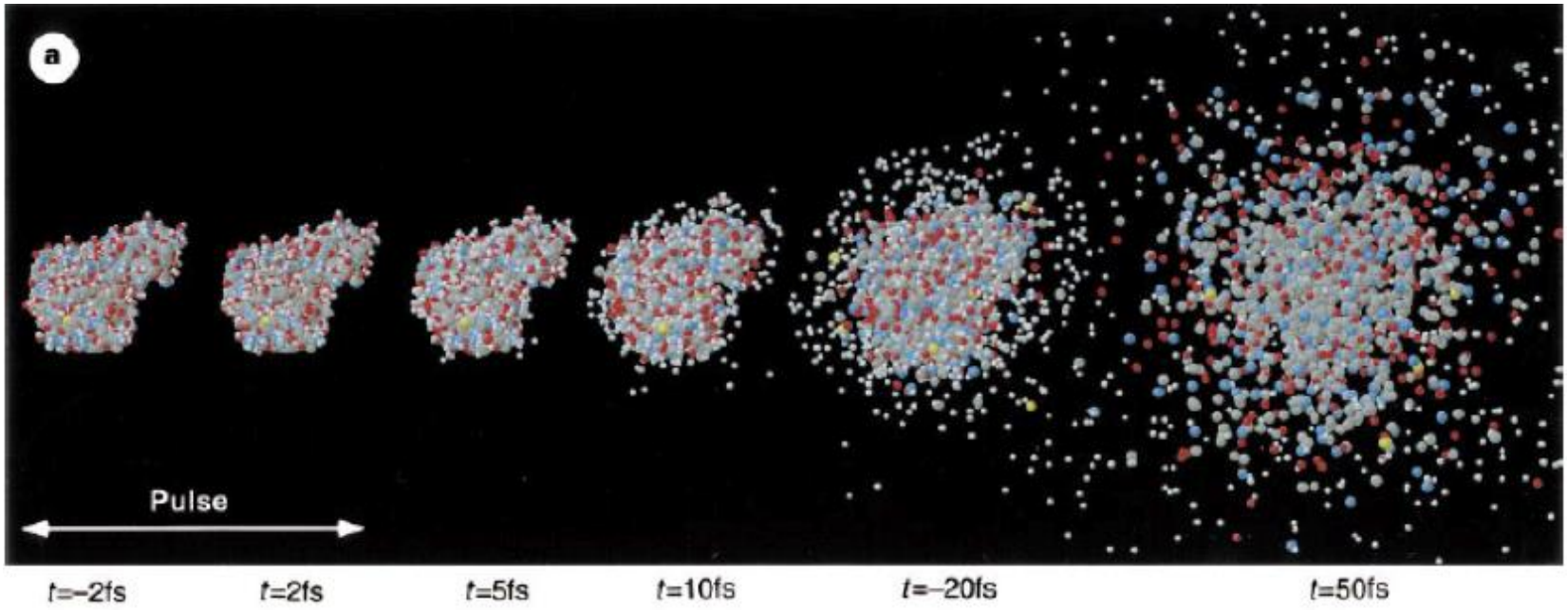
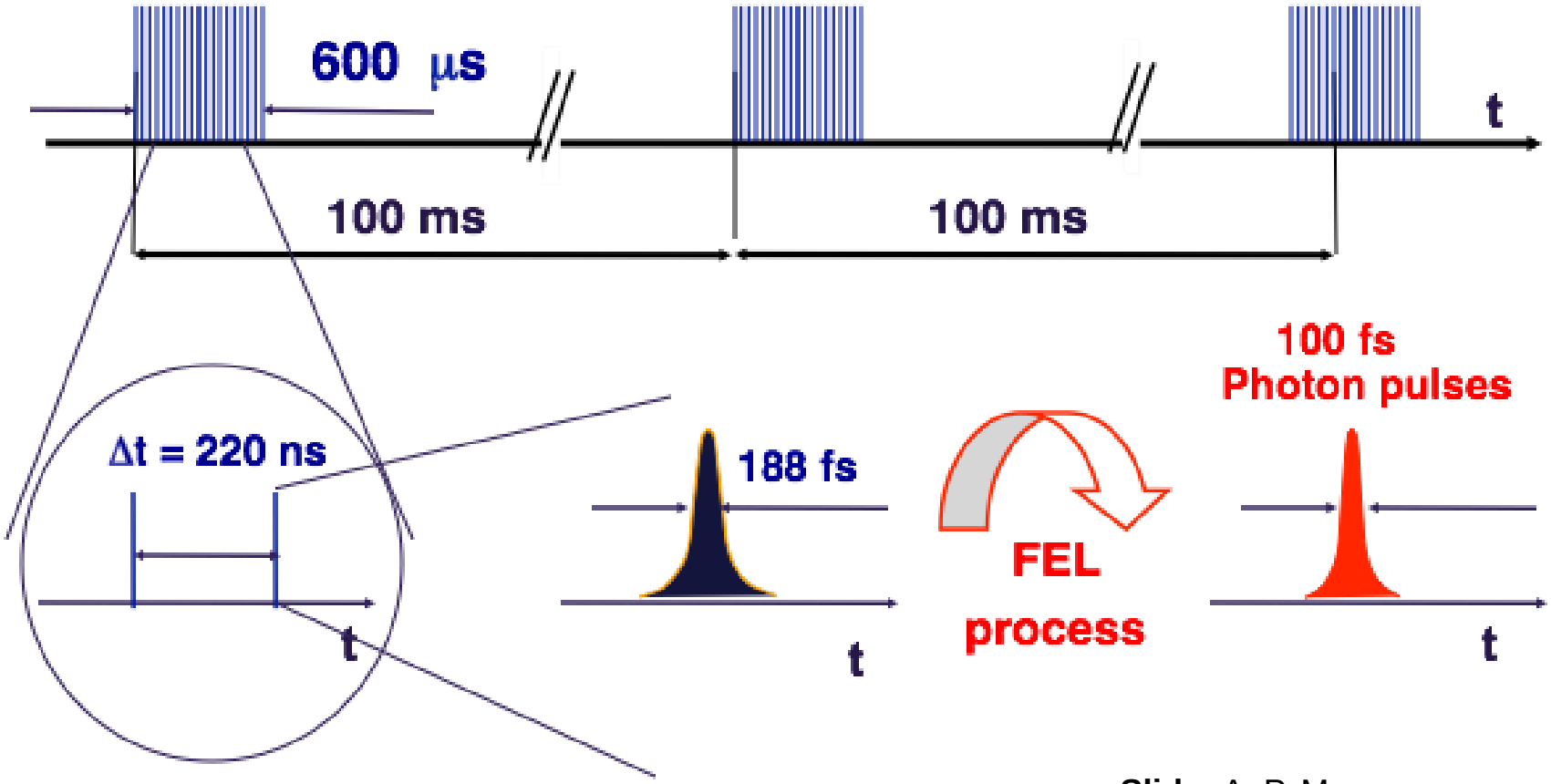


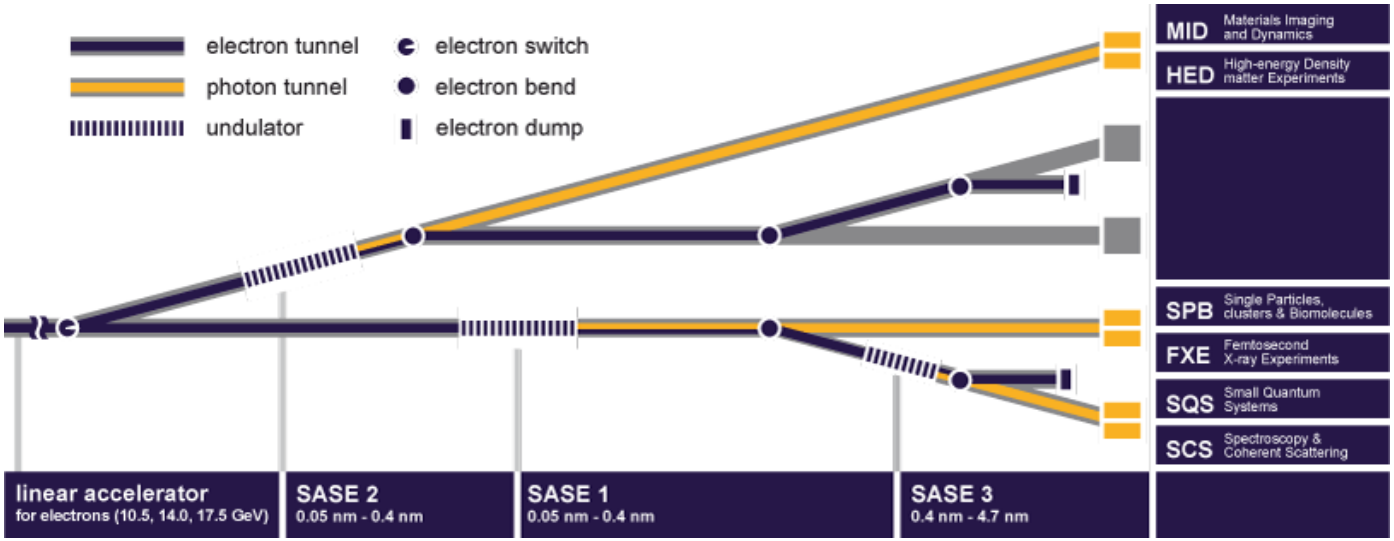
Image: R. Neutze et al. Nature (2000)

SASE pulse train

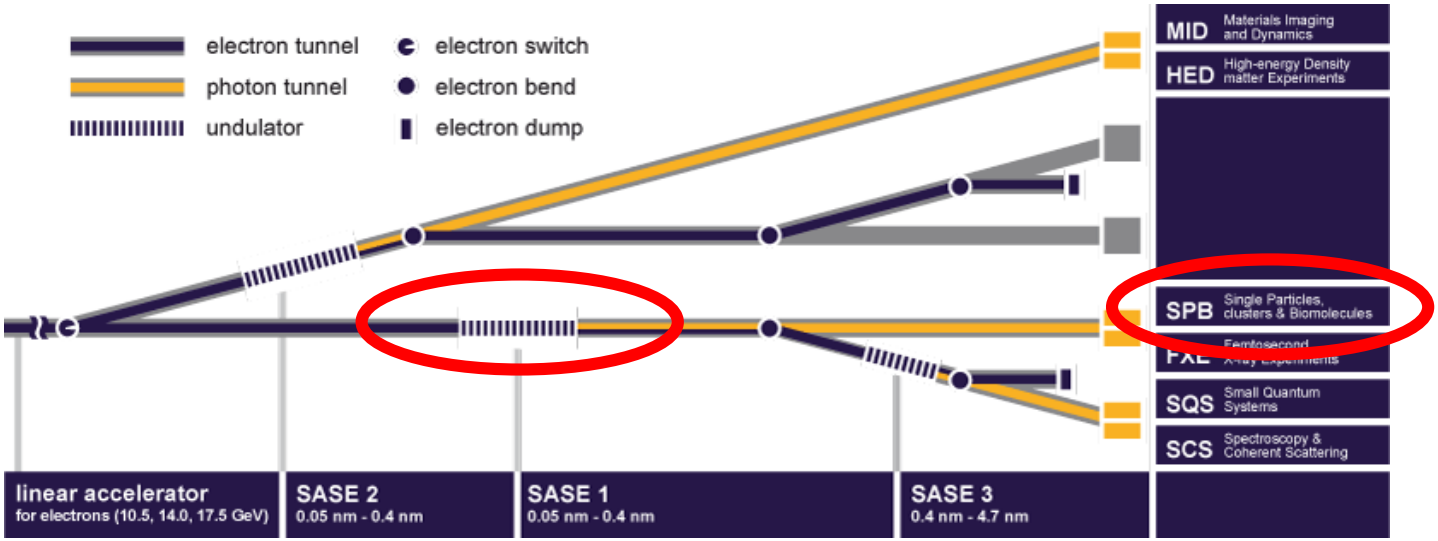


Slide: A. P. Mancuso

Undulator


electron tunnel
photon tunnel
undulator
electron switch
electron bend
electron dump
MID
Materials Imaging and Dynamics
HED
High-energy Density matter Experiments
SPB
Single Particles, clusters & Biomolecules
FXE
Femtosecond X-ray Experiments
SQS
Small Quantum Systems
SCS
Spectroscopy & Coherent Scattering
linear accelerator
for electrons (10.5, 14.0, 17.5 GeV)
SASE 2
0.05 nm - 0.4 nm
SASE 1
0.05 nm - 0.4 nm
SASE 3
0.4 nm - 4.7 nm

Undulator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0.05 nm - 0.4 nm
SASE 1
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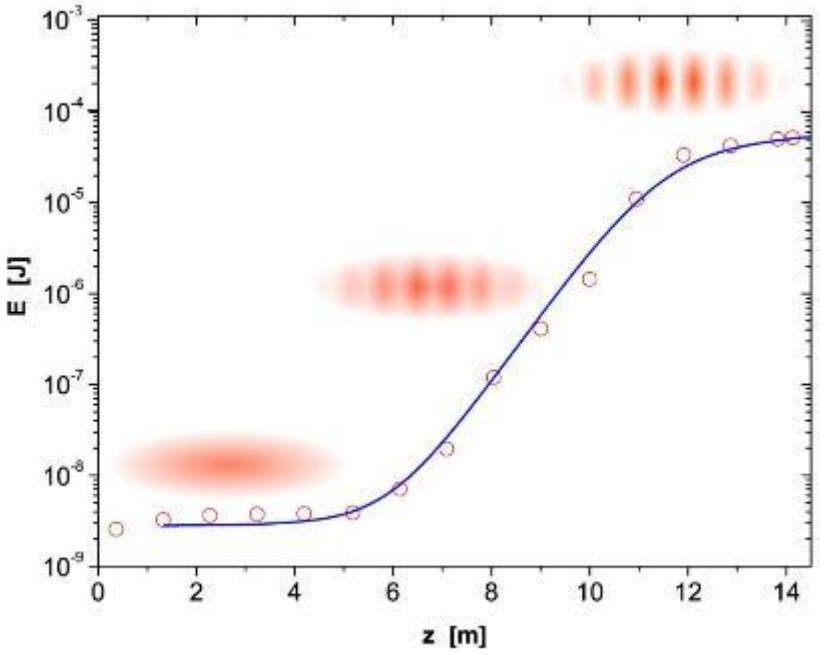
SASE 3
0.4 nm - 4.7 nm

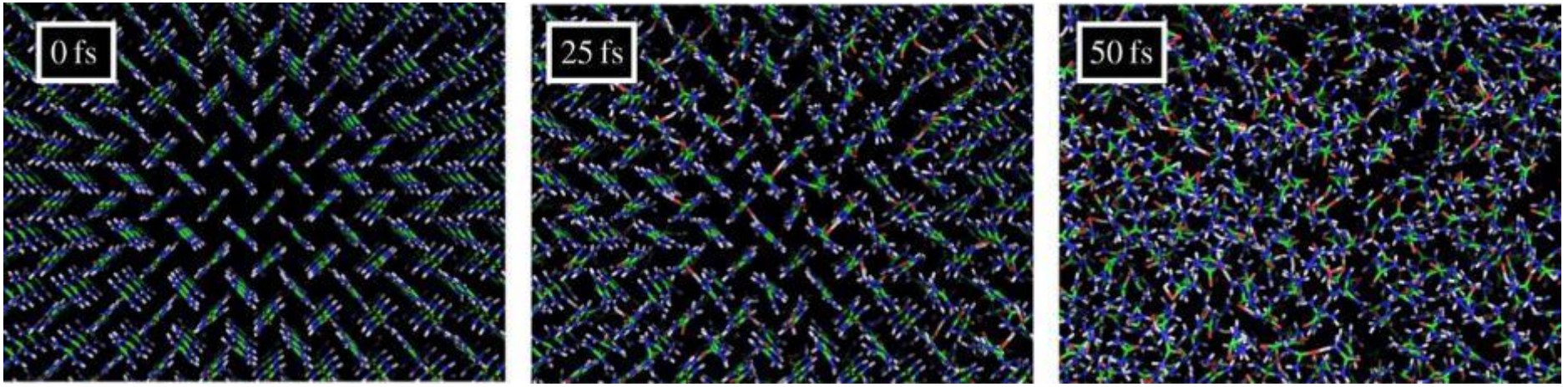
Undulator

Coherent radiation is emitted from 175 m of SASE undulator

- Initial section of undulator produces radiation
- The radiation couples with the electron's to bunch the electrons
- Saturation occurs when the electrons are completely microbunched
- This process greatly amplifies the radiation emitted

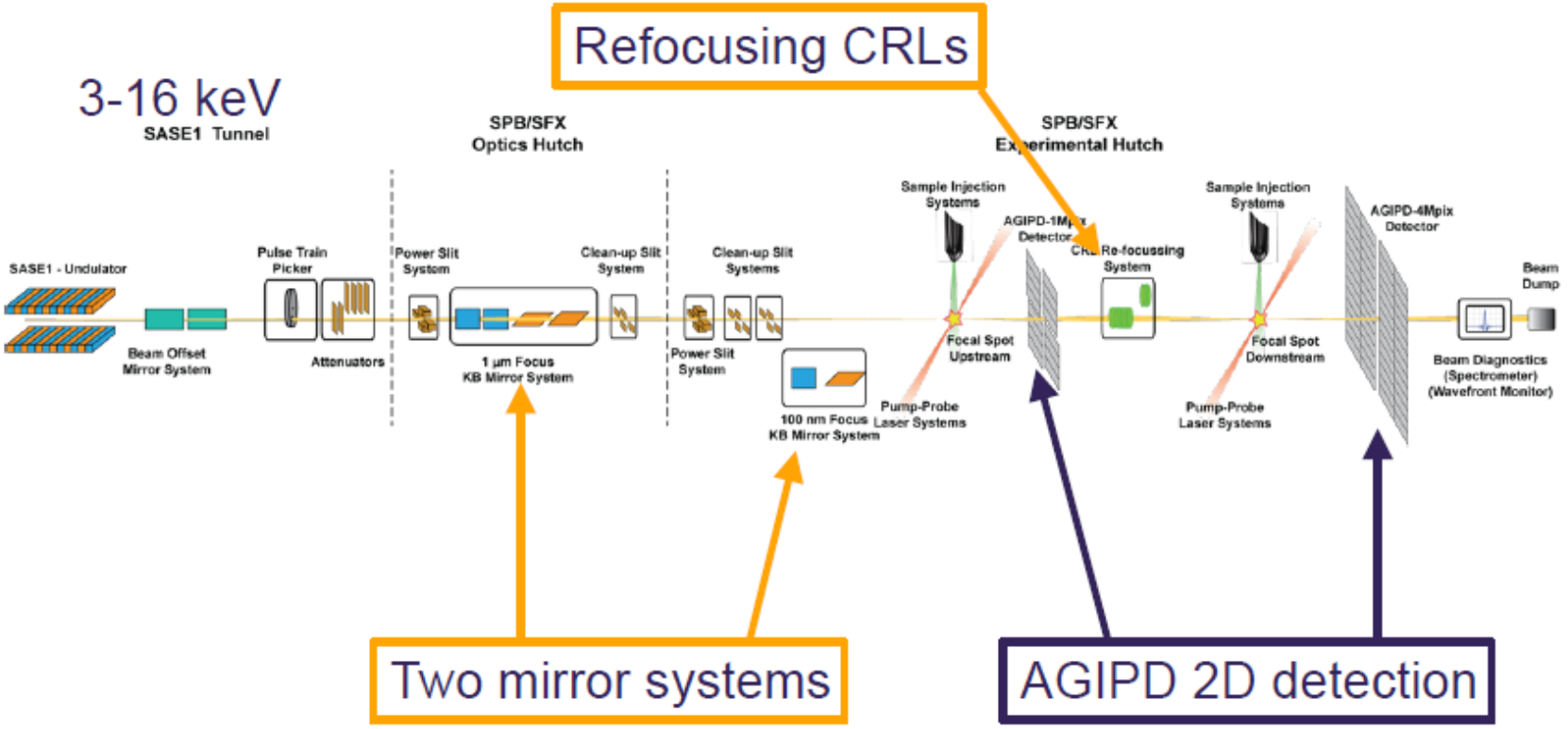


Radiation damage



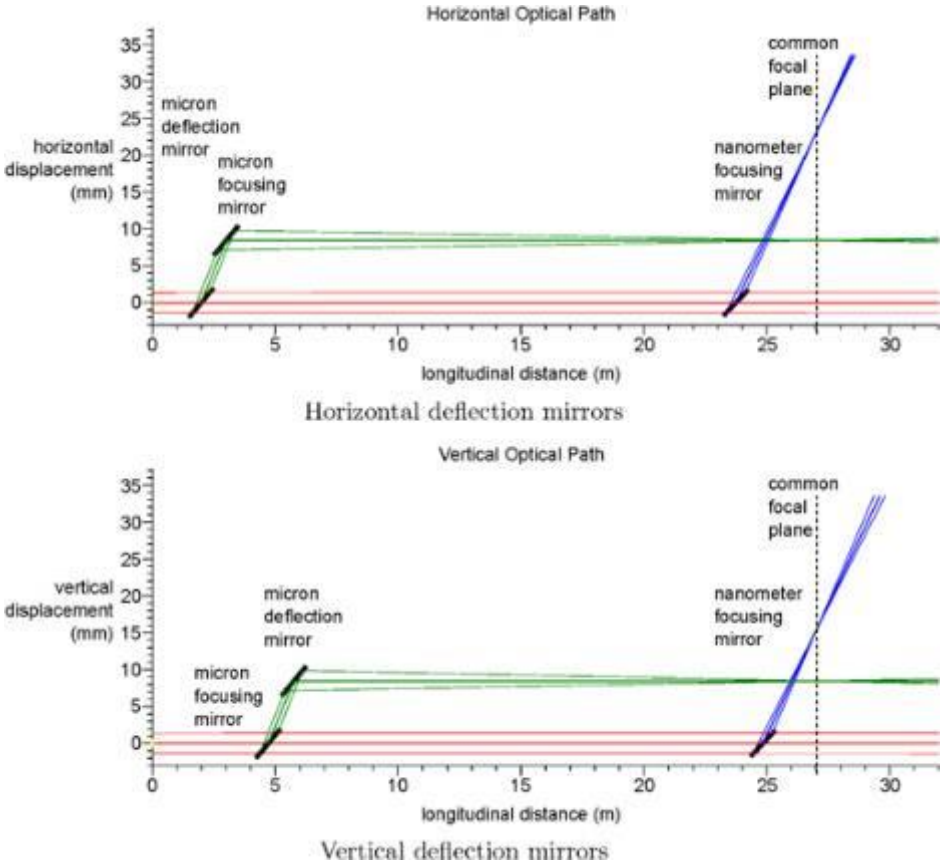
Diffraction before destruction (2014)
Henry N. Chapman, Carl Caleman, Nicusor Timneanu

Imaging biomolecules and X-ray radiation



Technical Design Report: Scientific Instrument SPB, (2013)
A. P. Mancuso, et al.

KB mirror systems

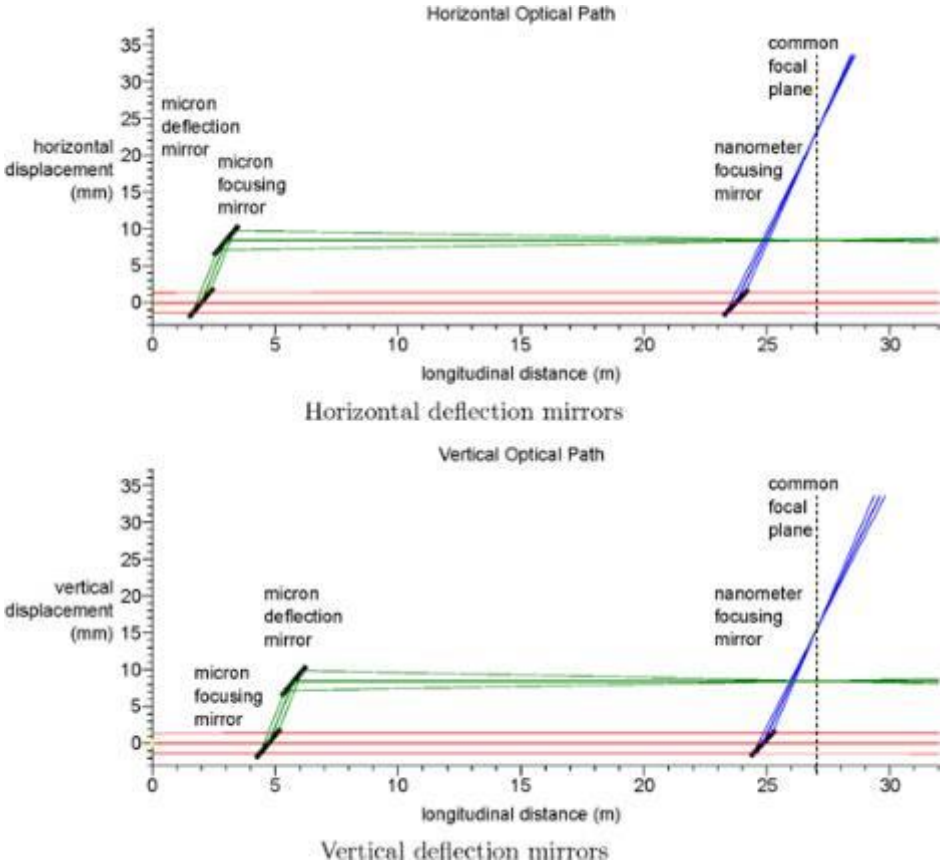


Kirkpatrick-Baez mirrors will produce a 1 micron and 100 nanometer focused beam

- 4 bounce system (1 µm) in green
- 2 bounce system (100 nm) in blue
- B_4C and Ru coatings

Design of the mirror optical systems for coherent diffractive imaging at the SPB/SFX instrument of the European XFEL, (2016) Richard J Bean, et al.

KB mirror systems



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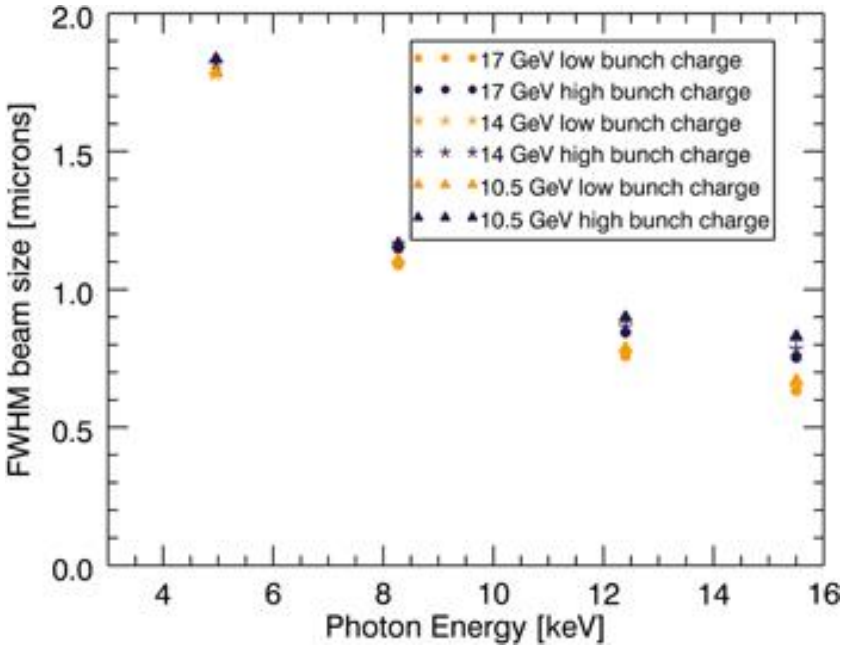
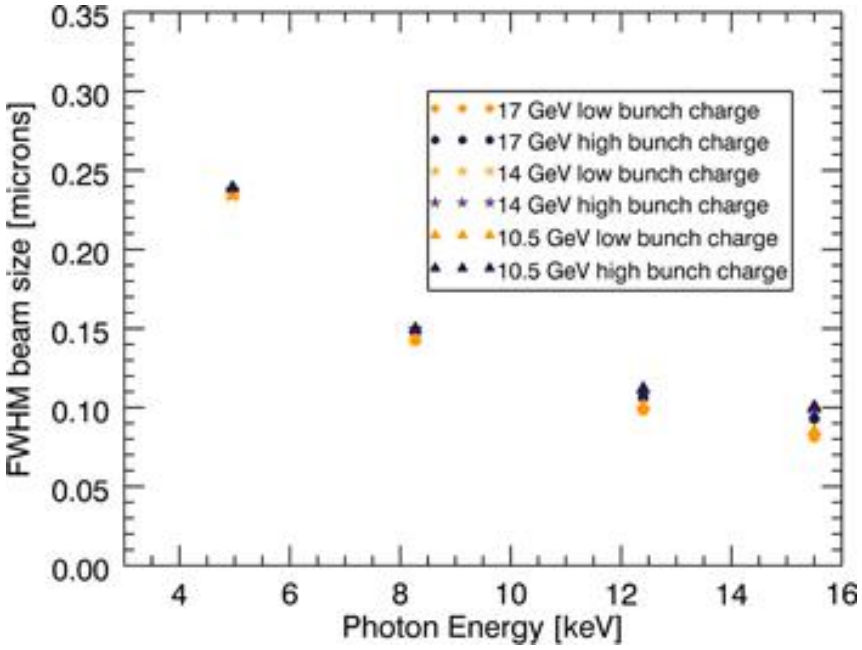
KB mirror systems

micron focus



nano focus



Design of the mirror optical systems for coherent diffractive imaging at the SPB/SFX instrument of the European XFEL, (2016) Richard J Bean, et al.

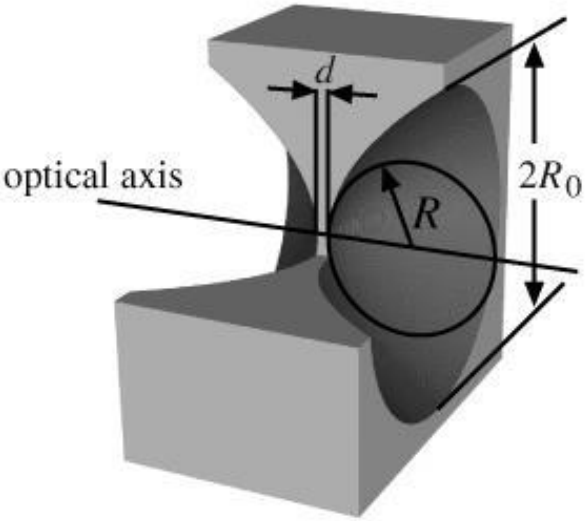
Manufacturing achievements

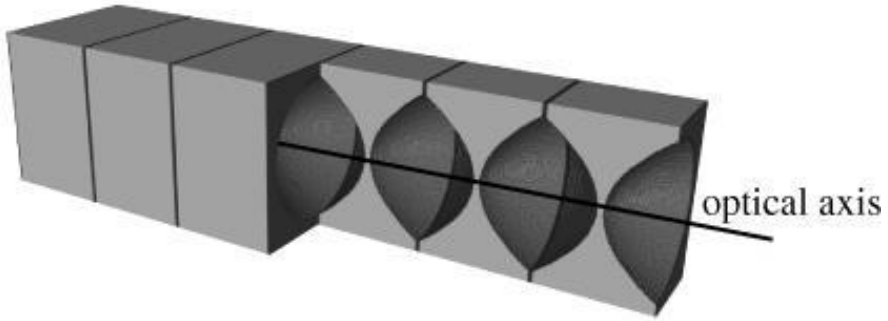
- 970 x 25 mm clear aperture
- 1.8 nm peak to valley variation
- 2x 50 nm thick polished coatings
  - B_4C and Ru
  - 950 x 10 mm

Compound refractive lenses

Initial operation will use the CRL in the tunnel

- CRL is a repeating structure of parabolic surfaces
- 12 mm diameter
- 2 mm thickness
- Focus to 2.5 µm diameter



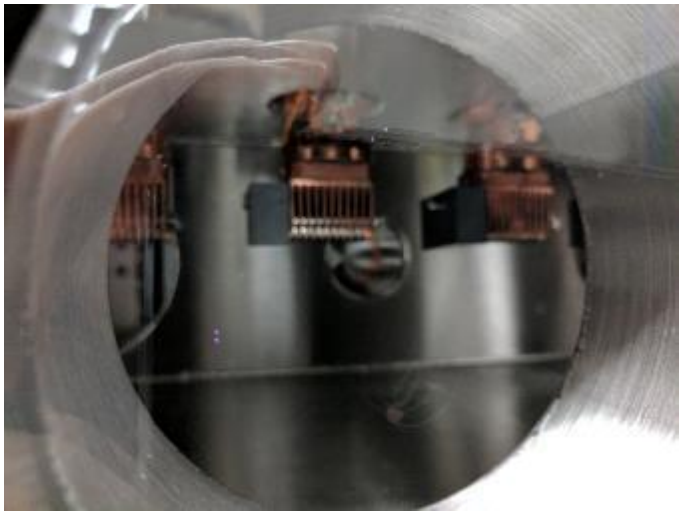


Refractive x-ray lenses (2005) B. Lengeler, et al

Cassette ordering

Initial operation will use the CRL in the tunnel

- 1, 2, 4, 8, 10, 10 …..
- Allows the change of X-ray energy while still maintaining focal location



Interaction region

There are two inline interaction regions, thes 1st upstream region is available day 1

- Day 1 will provide 60 pulses per trai
  10 Hz
- Photons at 8.4 keV
- Pulse energy at 2 mJ
- Pulse duration 43 fs
- 120° open scattering cone

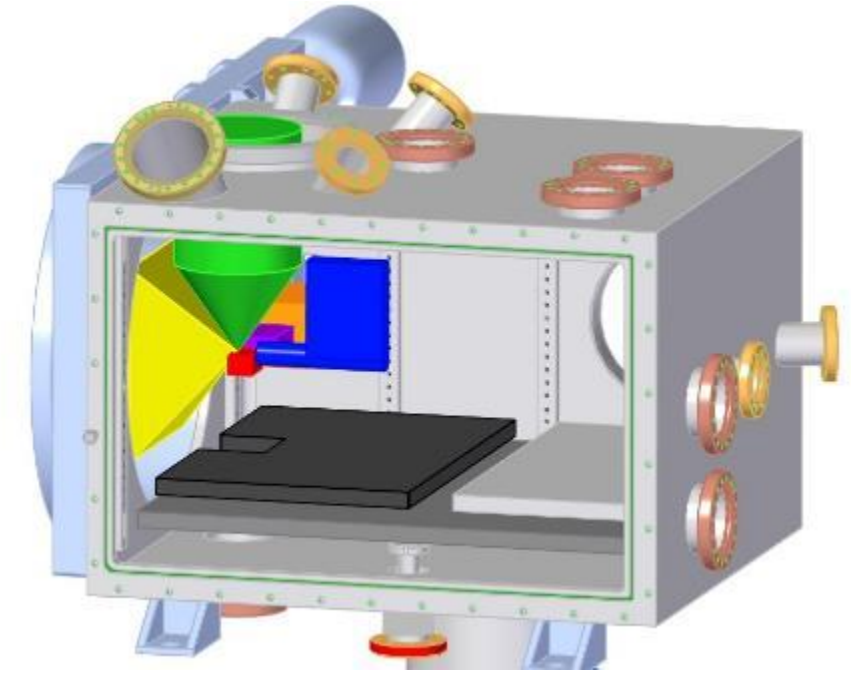
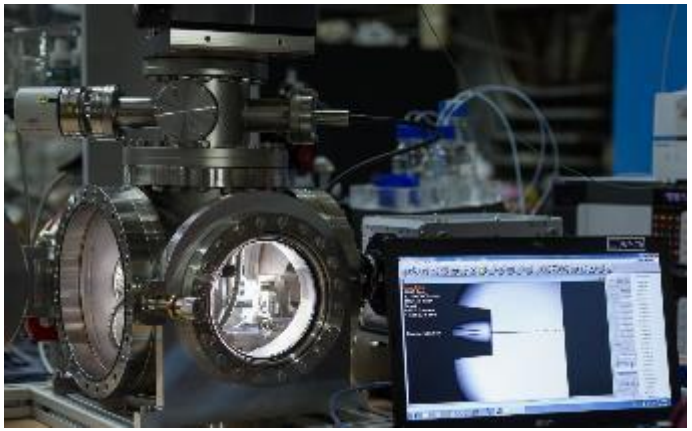


Image: Joachim Schulz

Sample injection

Many methods have been adopted to deliver sample into the interaction region

- GDVN
- Aerosol
- Fixed targets



Images: J. Schulz and R. Graceffa

Gas Dynamic Virtual Nozzle

- Capillary guides the sample into the interaction region
- Inert gas focuses the jet into a thin stream
- A µm thin jet can be maintained over more than 100 µm distance
- A modified system can also handle viscous solutions

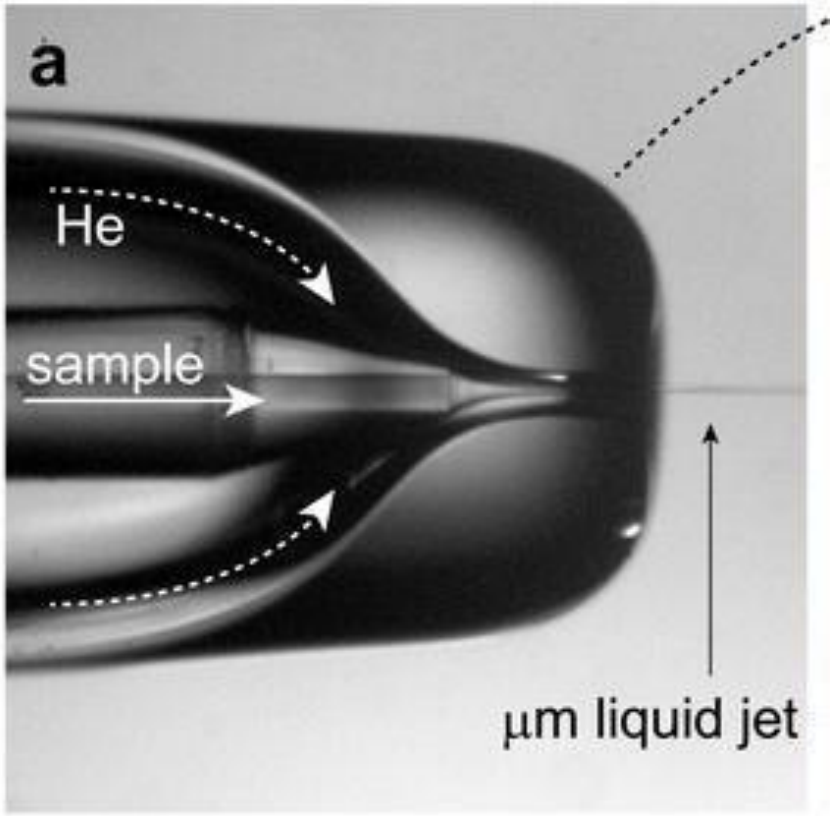


Image: http://www.sfx-consortium.org/e230143/e230213

Design study of a microfluidic mixing nozzle in 25 mm nozzle rod

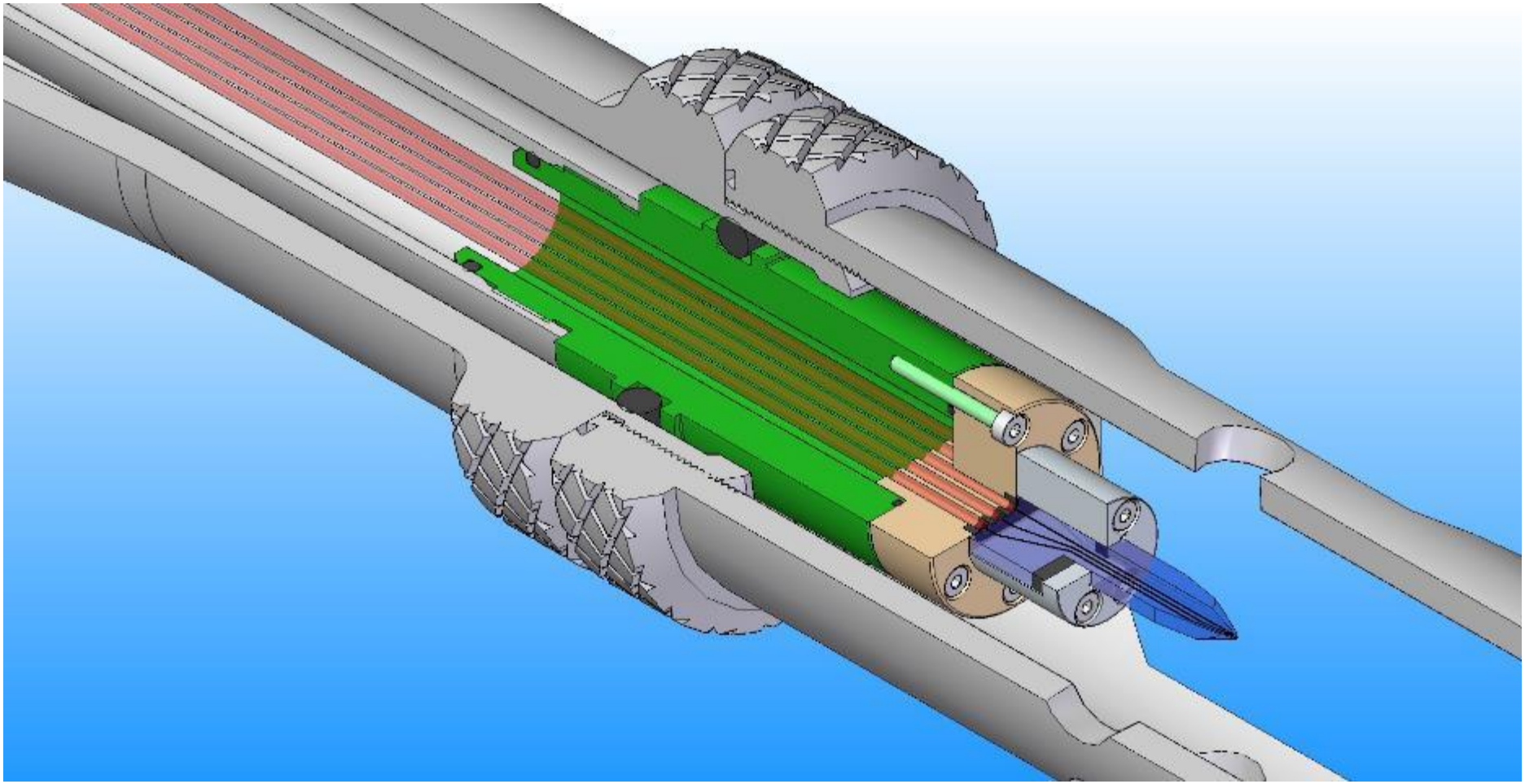


Image: Joachim Schulz, Rita Graceffa, Dennis Ropers

Aerosol injectors

- Injector creates particle beam
- Pressures decrease through the injector nozzle
- Rapid motion of sample

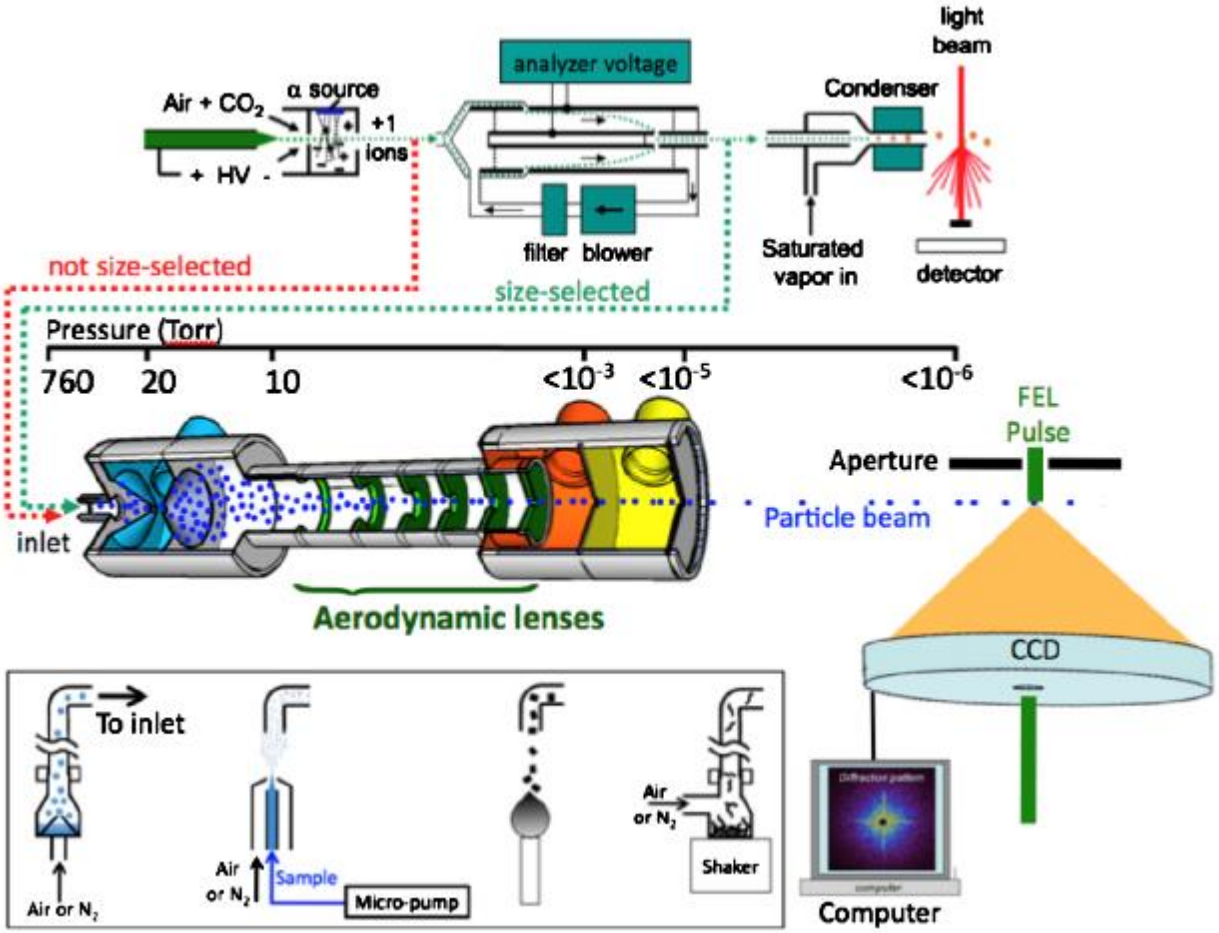
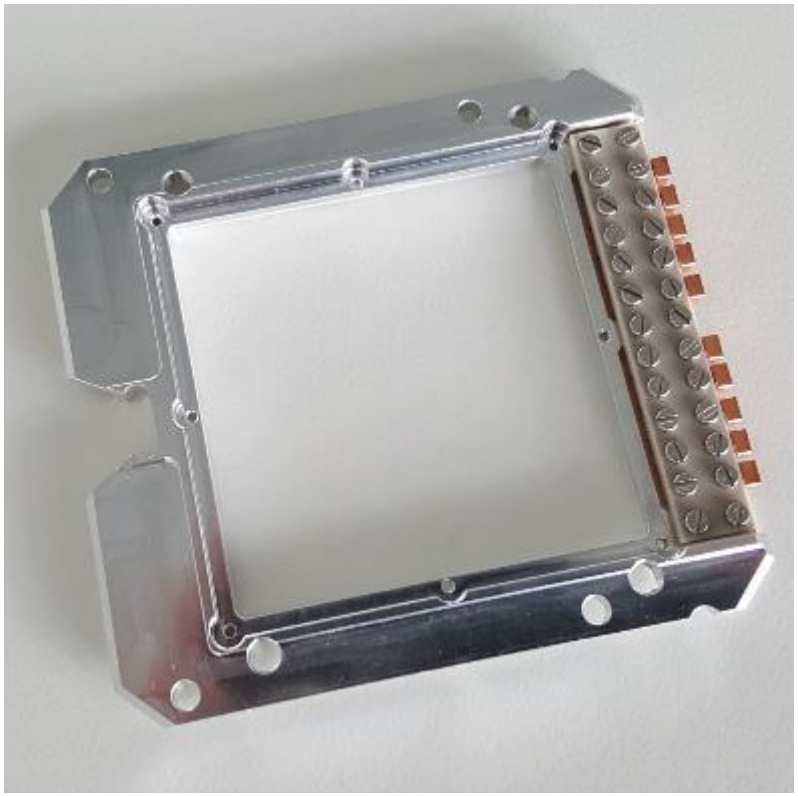


Image: Joachim Schulz

Fixed targets



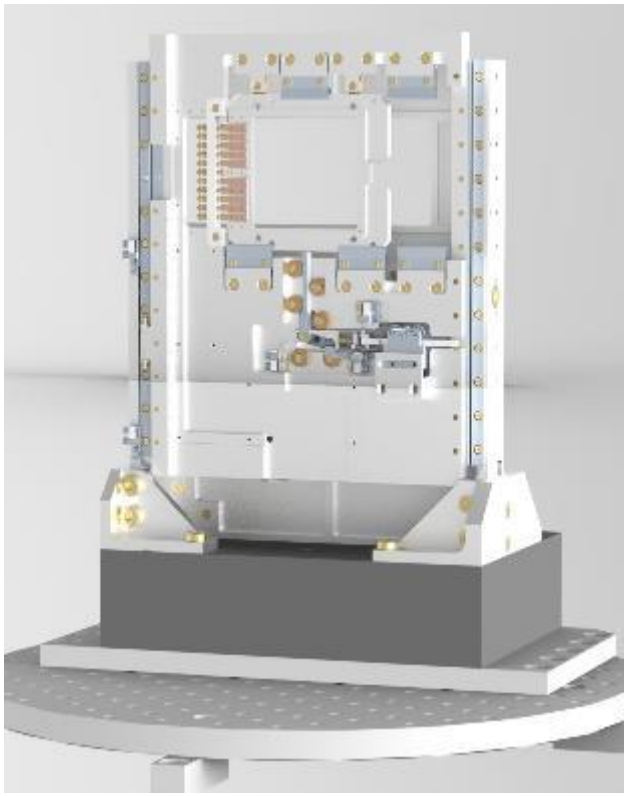


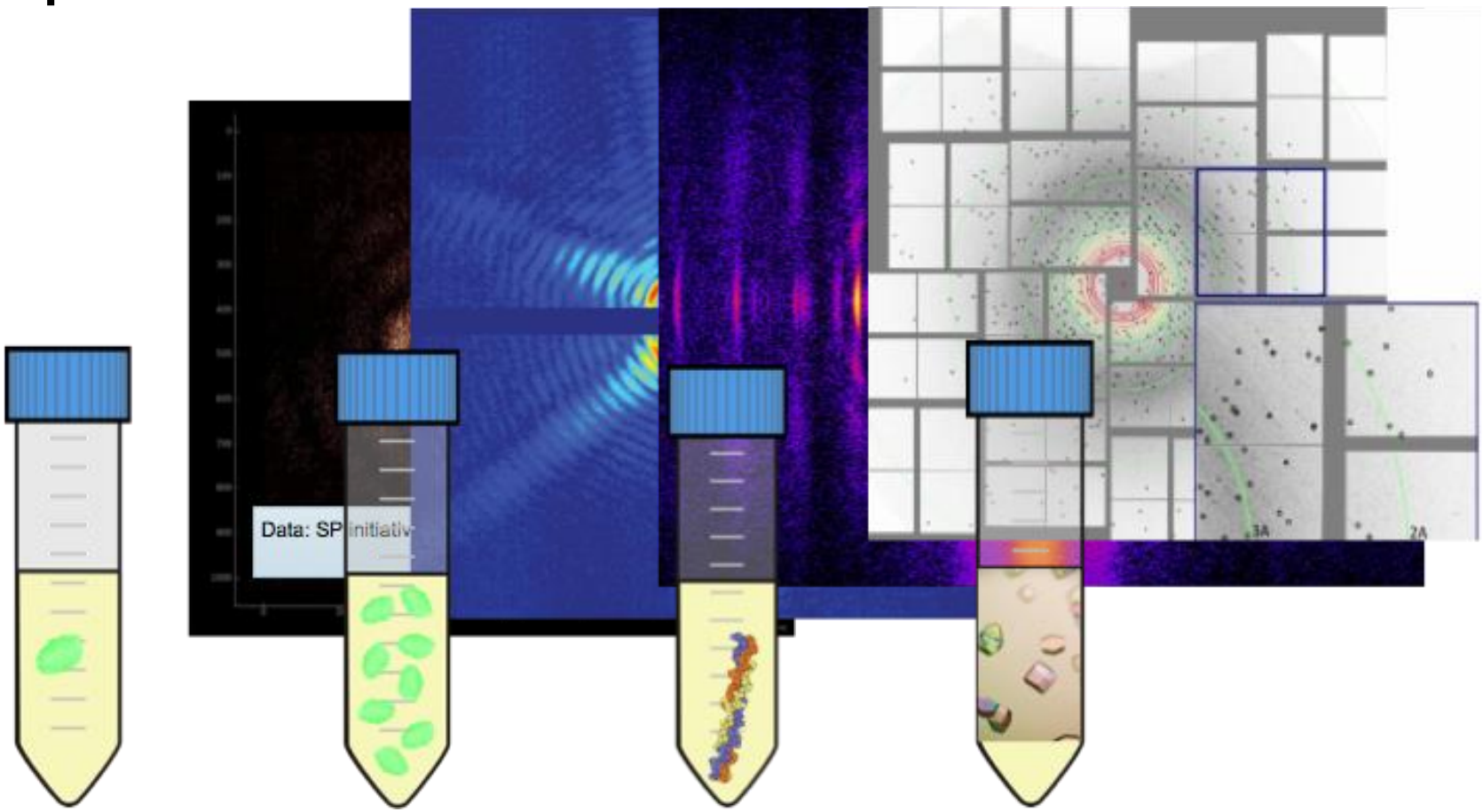
Image: Joachim Schulz

AGIPD Detectors

- 6 – 13 keV
- 1 x 10^4 at 12 keV dynamic range
- 5 σ at 12 keV sensitivity
- Number of storage cells 352
- Can store images at 4.5 MHz

Image: AGIPD Consortium

Experiments



Slide modified: Adam Round

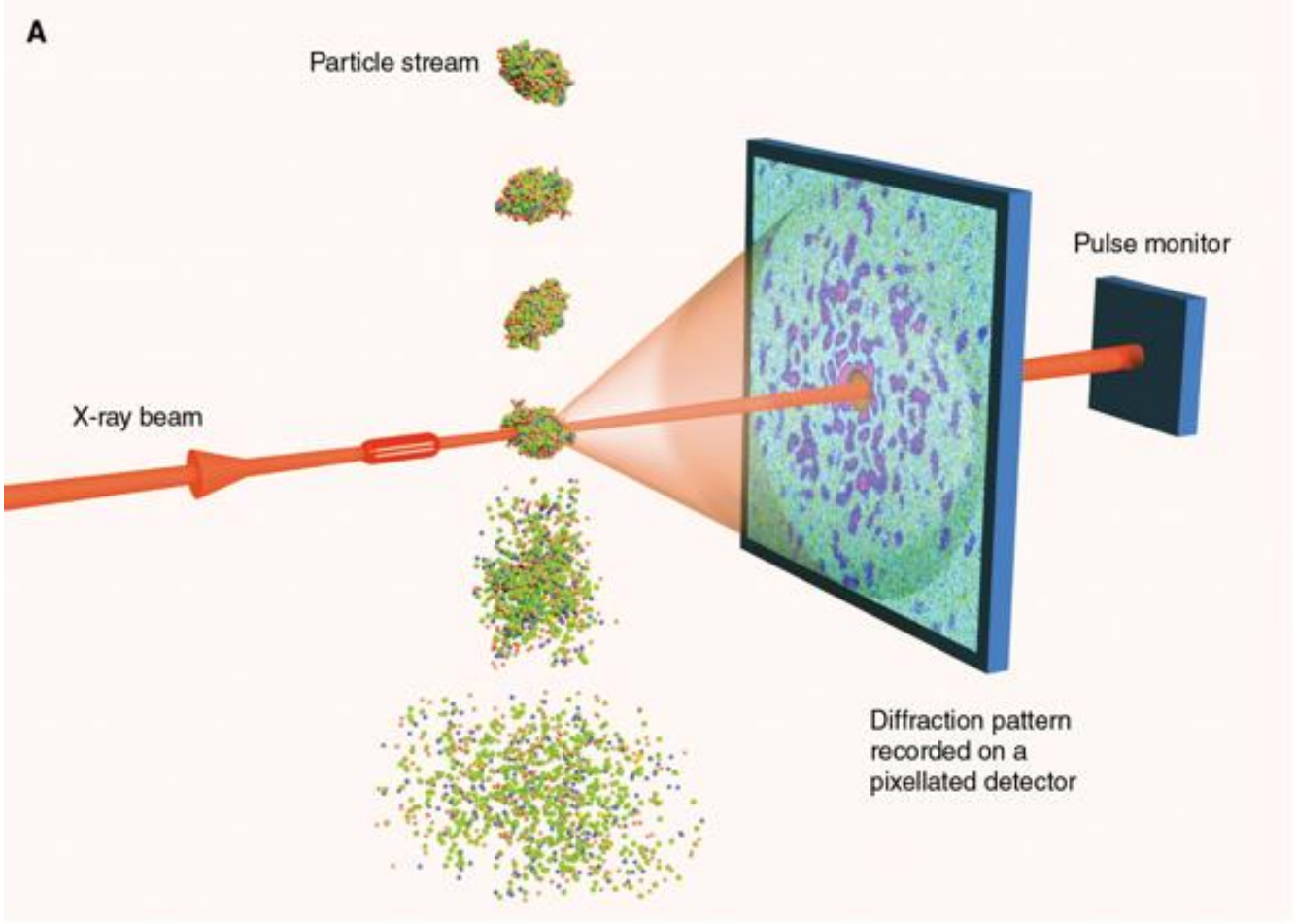


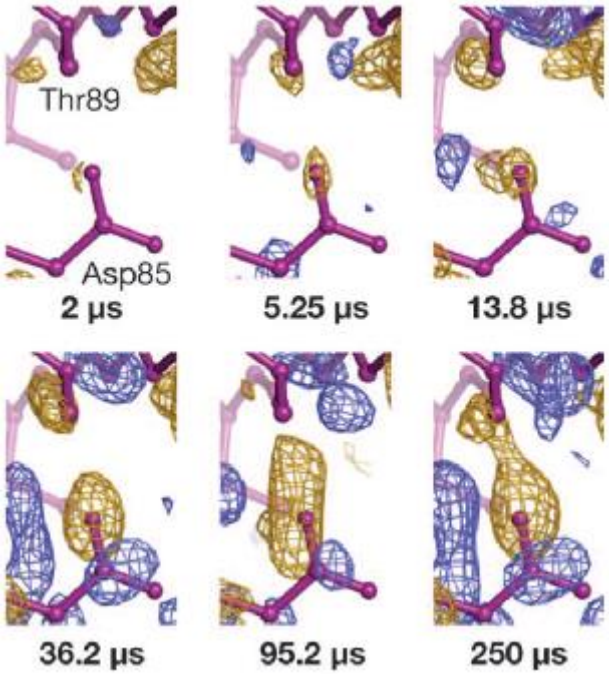
Image: Gaffney, Champman. Science (2007)

Experiments

STRUCTURAL BIOLOGY

A three-dimensional movie of structural changes in bacteriorhodopsin

- Time-resolved SFX
- Bacteriorhodopsin conformational changes
- 10 fs long pulses at SACLA

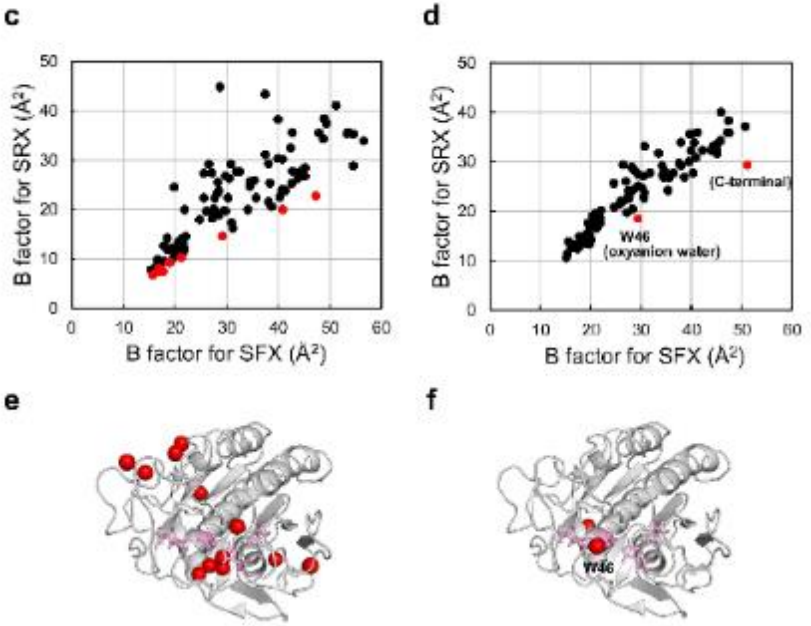


Eriko Nango, et al 2017, Science

Experiments

Atomic resolution structure of serine protease proteinase K at ambient temperature

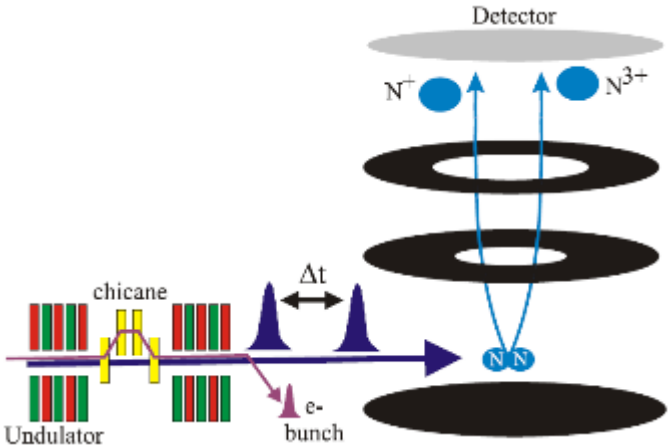
- High resolution SFX
- 1.2 Å res proteinase K
- Comparision of SFX and SRX B-factors

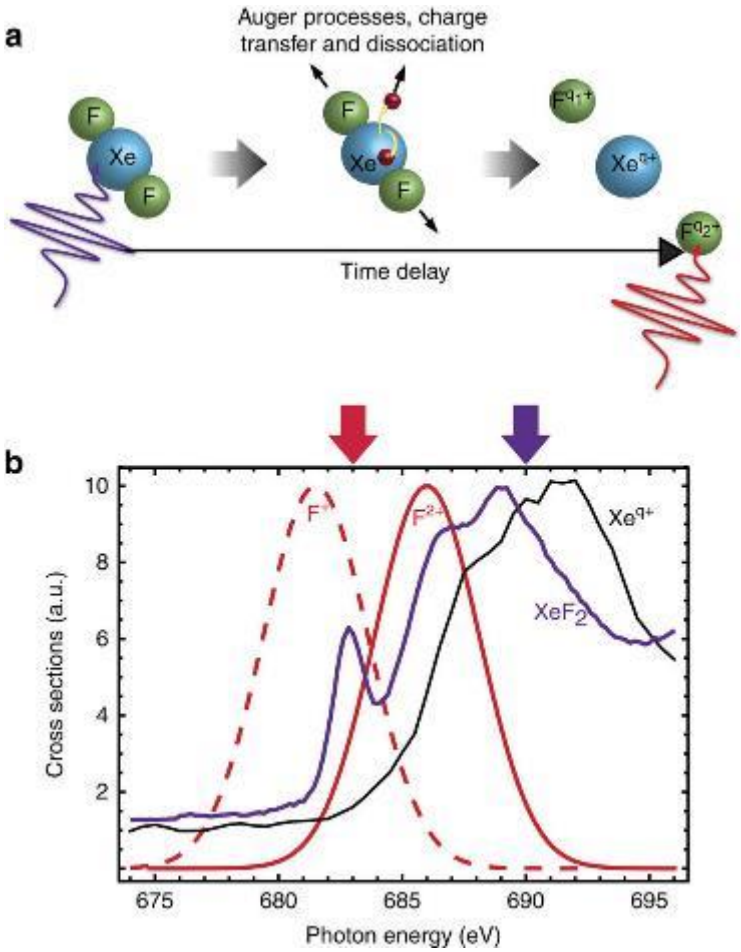


Tetsuya Masuda, et al 2017, Science Reports

Experiments

- Two-colour X-ray-pump/X-ray-probe scheme used for studying the molecular fragmentation of XeF_2
- These reactions occur on the fs timescale, perfect for the European XFEL





A Picón, et al 2016
CS Lehmann, et al 2016

Experiments

CXIDB
Coherent X-ray Imaging Data Bank

Home Mission CXI File Format Browse Data Resources Sponsors Contact Us

Browse Data

- ID 1 - Single mimivirus particles intercepted and imaged with an X-ray laser
- ID 2 - Single mimivirus particles intercepted and imaged with an X-ray laser
- ID 3 - Femtosecond diffractive imaging with a soft-X-ray free-electron laser
- ID 4 - High-resolution x-ray diffraction microscopy of specifically labeled yeast cells
- ID 5 - High-resolution x-ray diffraction microscopy of specifically labeled yeast cells
- ID 6 - High-resolution x-ray diffraction microscopy of specifically labeled yeast cells
- ID 7 - High-resolution x-ray diffraction microscopy of specifically labeled yeast cells
- ID 8 - High-resolution x-ray diffraction microscopy of specifically labeled yeast cells
- ID 9 - Cryptotomography: reconstructing 3D Fourier intensities from randomly oriented single-shot diffraction patterns
- ID 10 - Femtosecond free-electron laser x-ray diffraction datasets for algorithm development-

Deposit Data

If you are interested in depositing data please contact us.

In the future we hope to have a more automated way to deposit data.

Acknowledgments: People—the most important components

Sample Environment
AGIPD consortium
Adrian Mancuso
Zunaira Ansari
Richard Bean
Johan Bielecki
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Nadja Reimers
Adam Round
Tokushi Sato
Marcin Sikorski
Andrew Stawniczy
Stephan Stern
Britta Weinhausen
Patrik Vagovic
Prasad Thute

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Ministry of Education, Science, Research and Sport of the Slovak Republic
Universität Hamburg
DESY
wellcome trust

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