Workshop

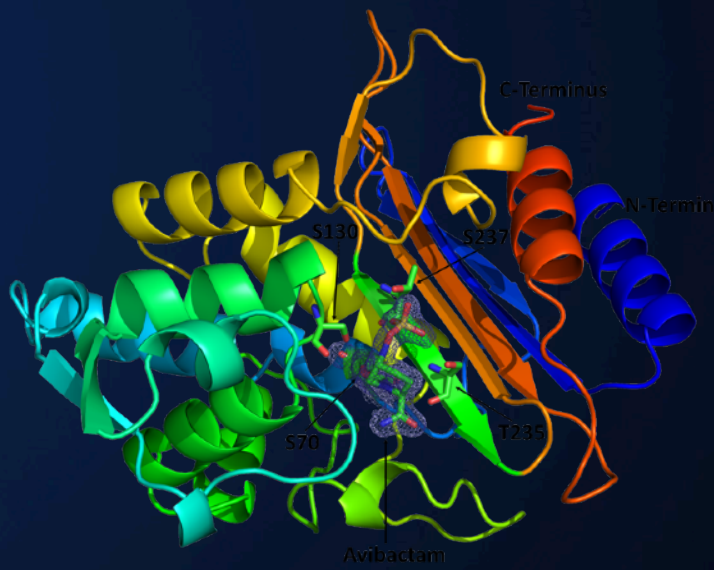
“New Scientific Capabilities at European XFEL”

25 March – 27 March 2019

Session VIII: “Structural biology applications”

08:30 – 08:55	Anton Barty (CFEL / DESY) “Structural biology possibilities for tunnels 4 and 5”
08:55 – 09:20	Poul Nissen (Uni Aarhus) “Structure and dynamics of biomembranes and membrane proteins”
09:20 – 09:45	Jim Naismith (Uni Oxford) “SPB/SFX lessons for the future”
09:45 – 10:25	Discussion
10:25 – 10:40	**Coffee Break**

Structural biology possibilities for tunnels 4 and 5



Anton Barty
Center for Free Electron Laser Science
(overview talk presenting results on behalf of many, many people)

What can not be done anywhere else in the world

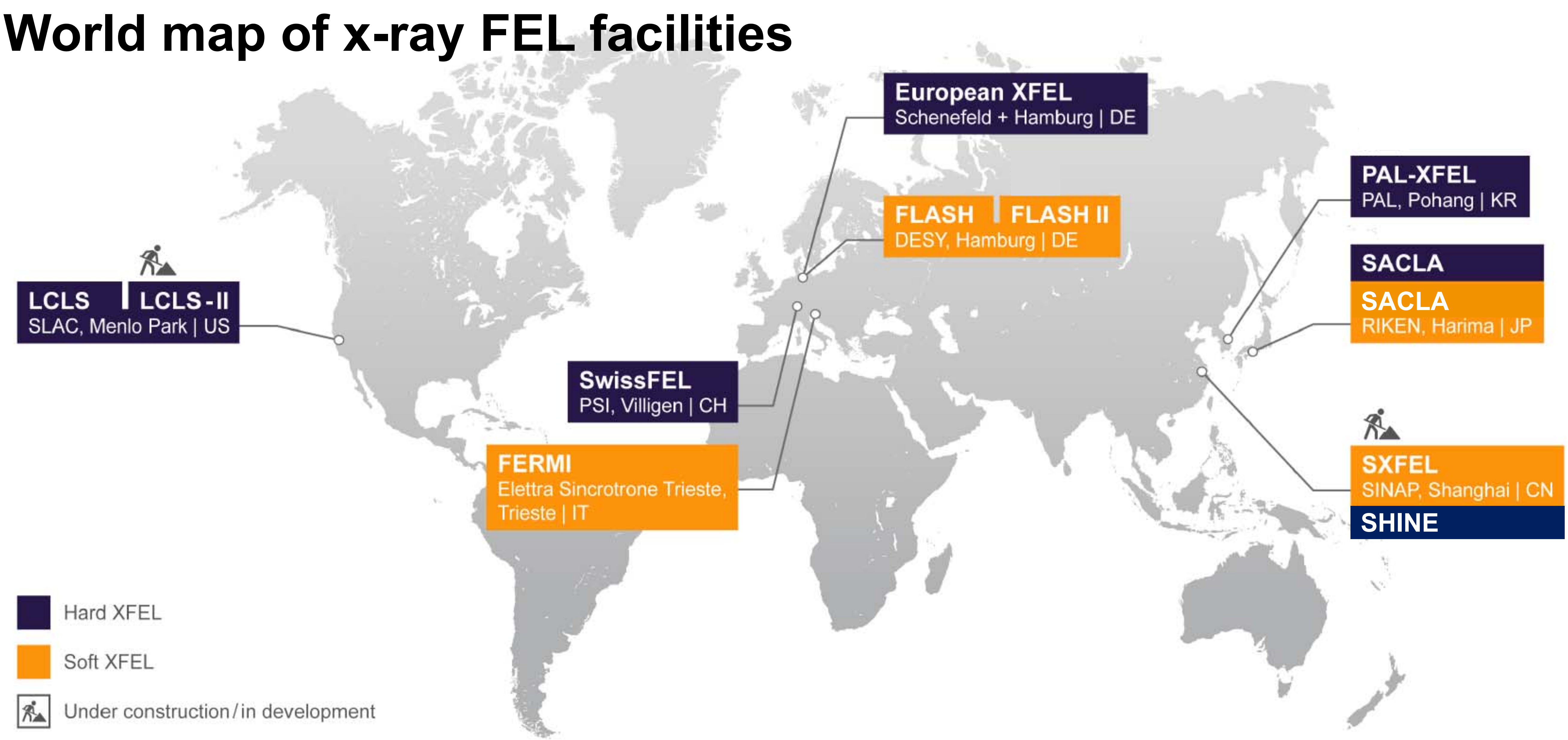
Users travel! A lot.
They will go wherever is best for their experiment. Worldwide.

Need to think about the competition - what is already possible elsewhere?

What can not possibly be done anywhere other than EuXFEL?

- 17.5 GeV linac is unique
- MHz pulse trains are unique
- 27,000 pulses per second is unique
- Capability for mJ peak power is world class

A range of X-ray free electron lasers are available worldwide

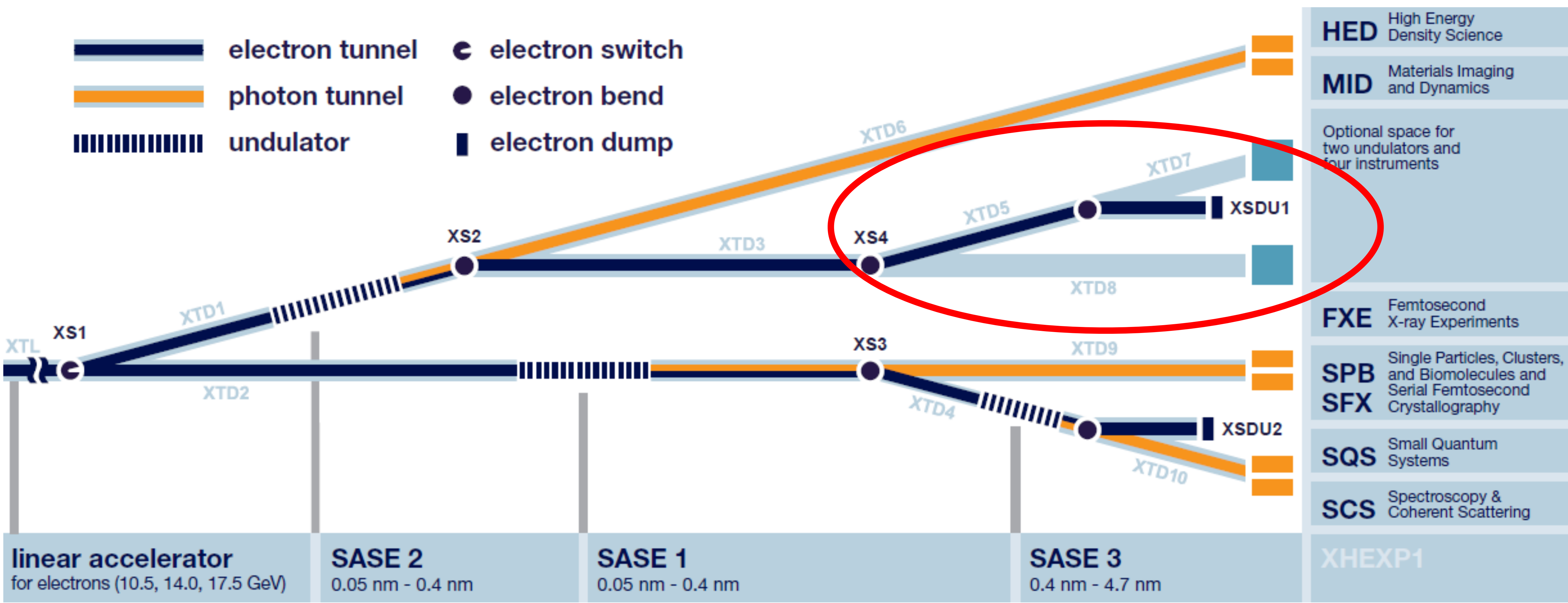


Source: Thomas Tschentscher

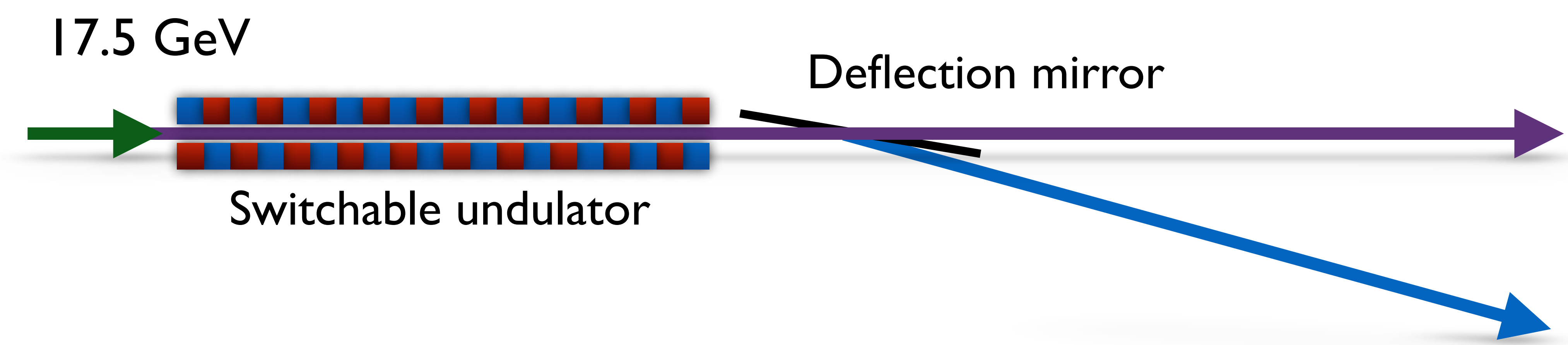
Where is the real gap in capability, or capacity?

What options for tunnels 4 and 5 can not be done elsewhere?

Future potential in the experiment hall



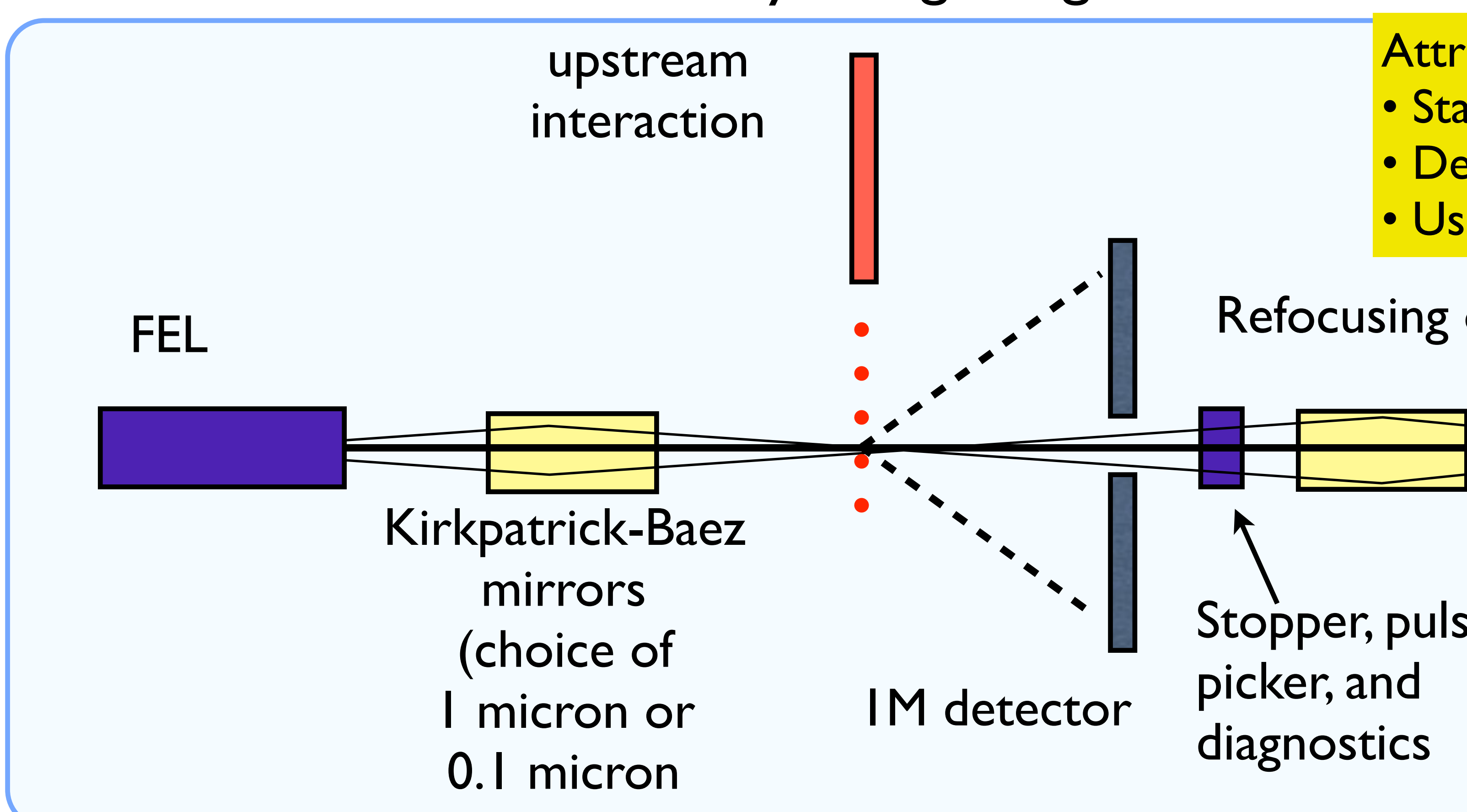
Tunnel 4 could host both a super-hard X-ray branch and dedicated SFX instrument for routine structure determination



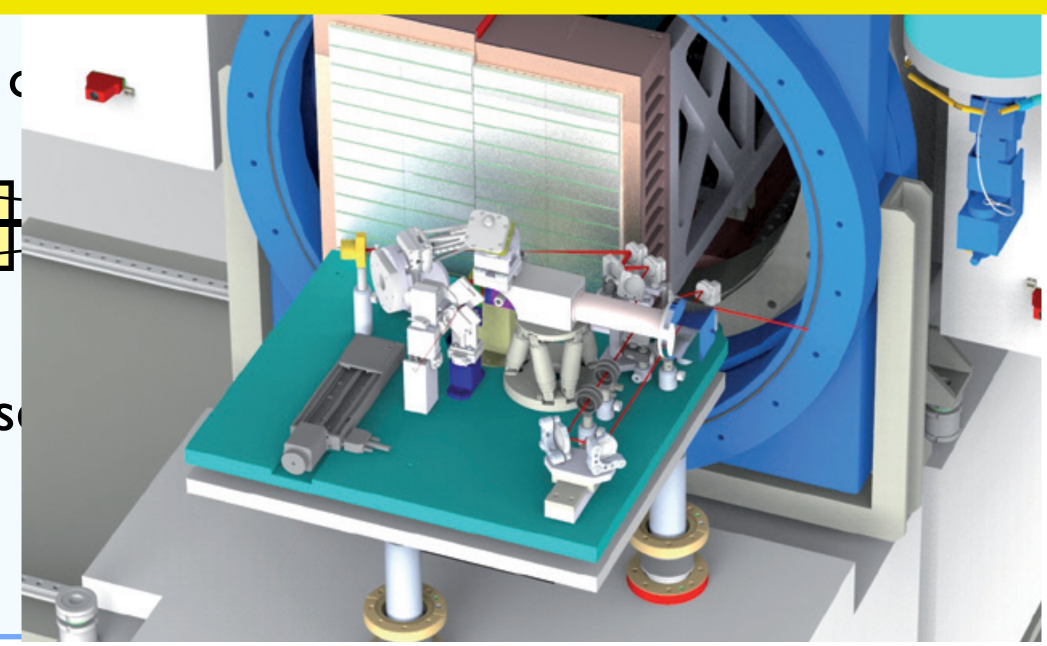
Super-hard X-ray branch
(25-100 keV)
for new experiments

Hard X-ray branch
(8-20 keV)
dedicated to routine SFX

The SFX instrument is already being integrated at SPB

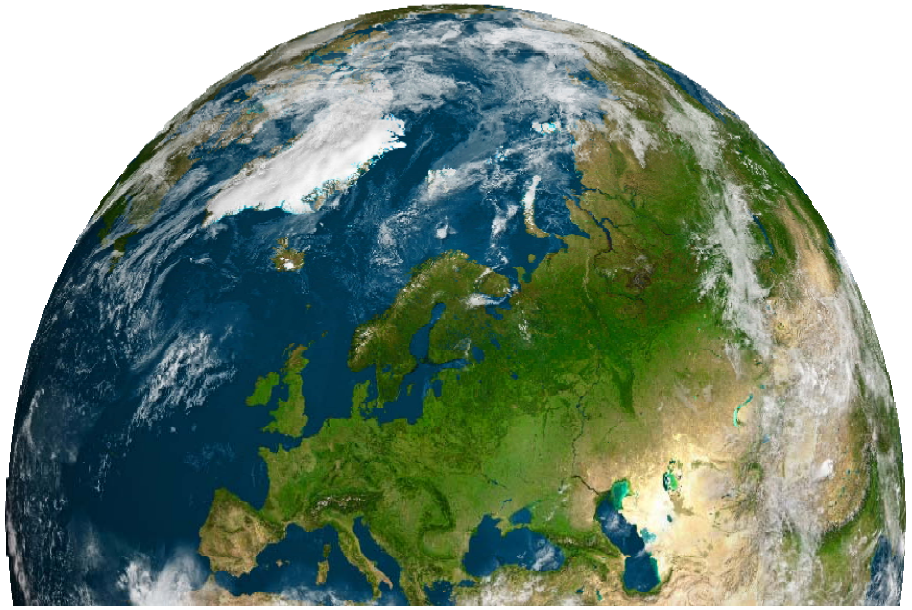


Attraction:
- Stable configuration
- Demonstrated and unmet user demand
- Useable whenever the other branch is not used

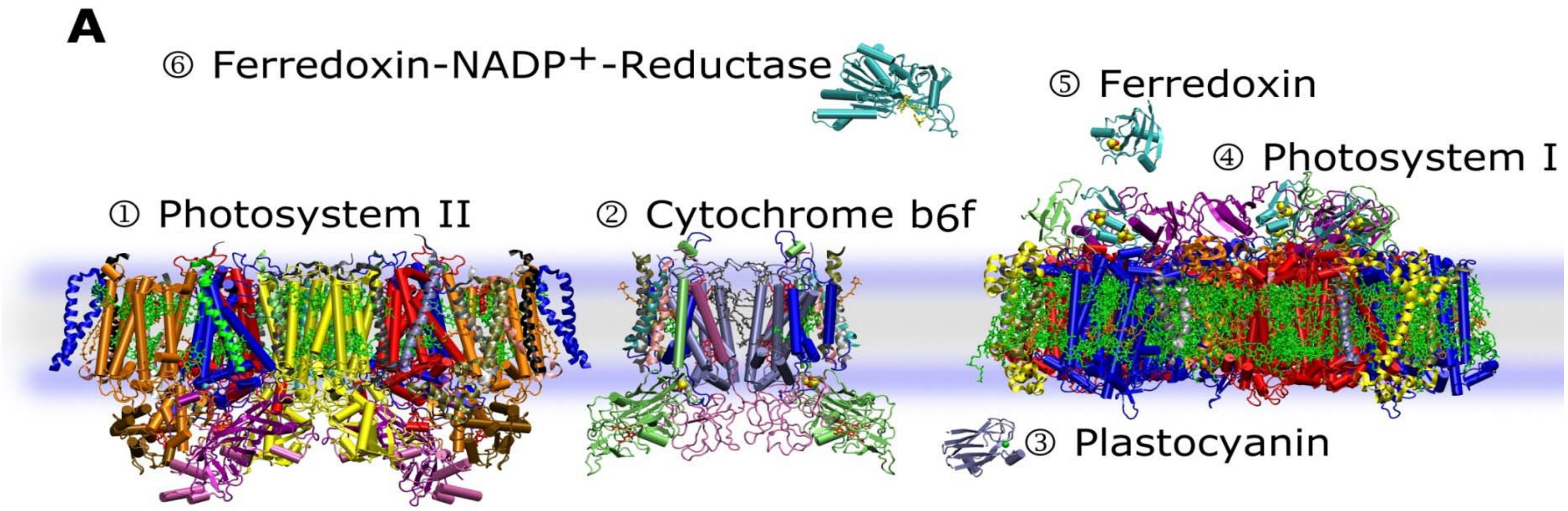


Why?

Scientific Background

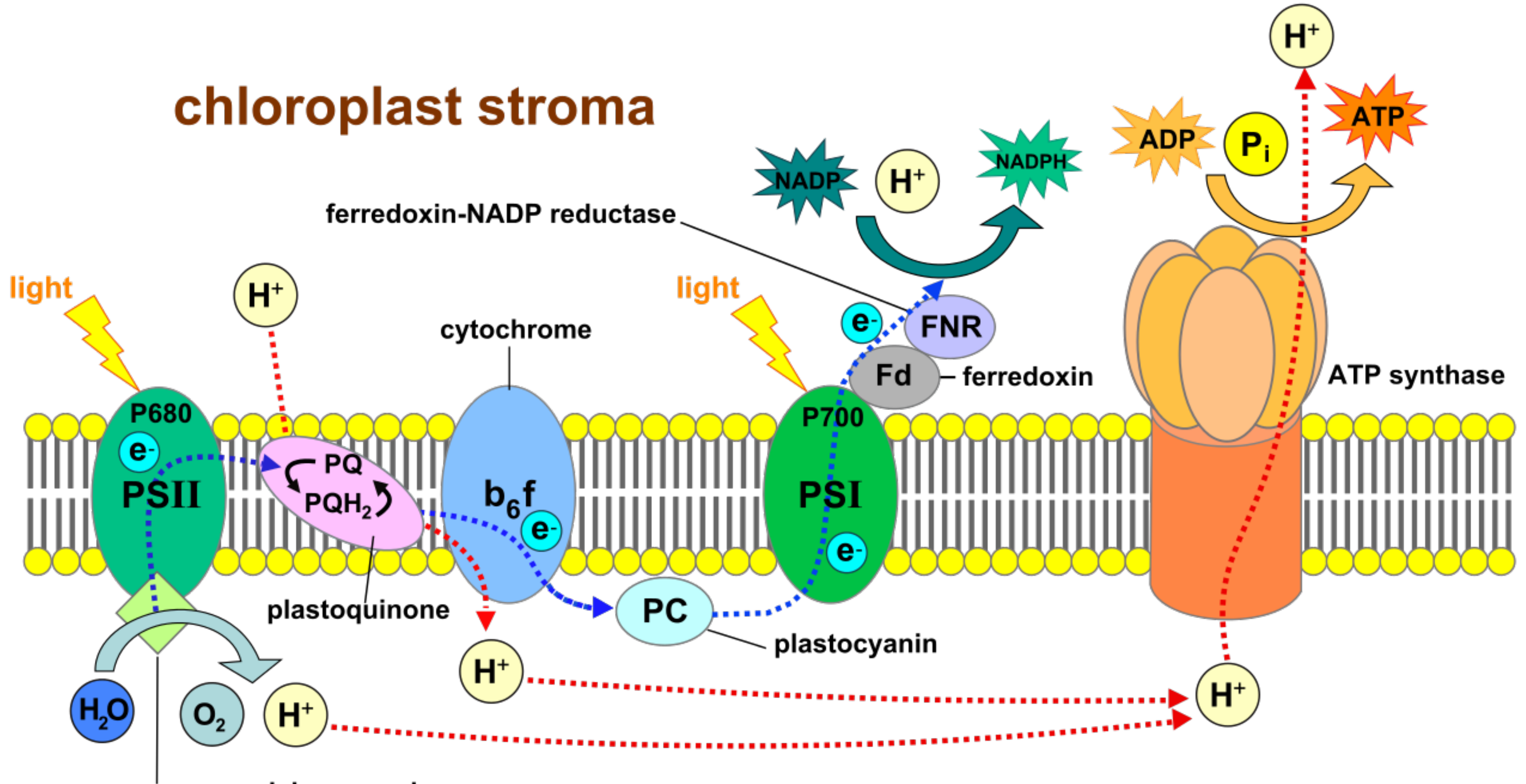


Photosynthesis transformed our planet 2.5B years ago producing oxygen, capturing solar energy and CO_2, that slowly converted to fossil fuels.

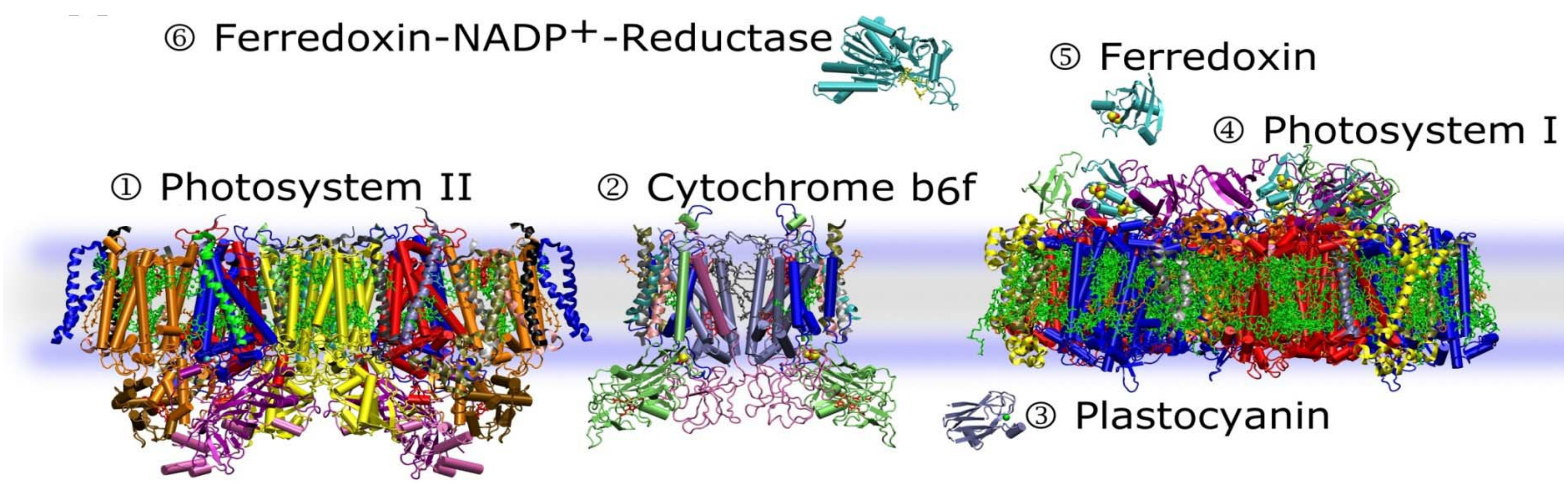


Source: Petra Fromme, ASU

Why?

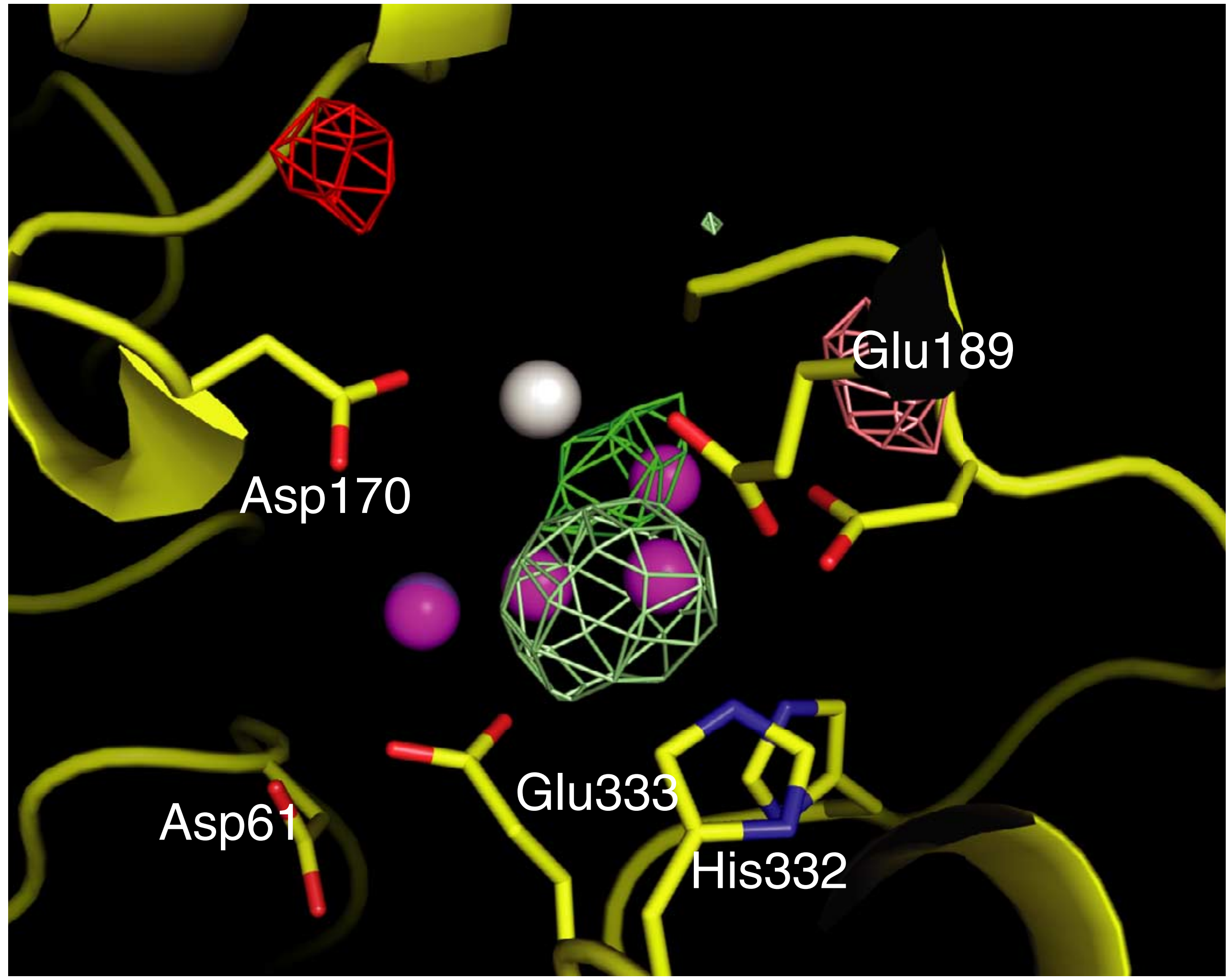


https://en.wikipedia.org/wiki/Photosystem#/media/File:Thylakoid_membrane_3.svg

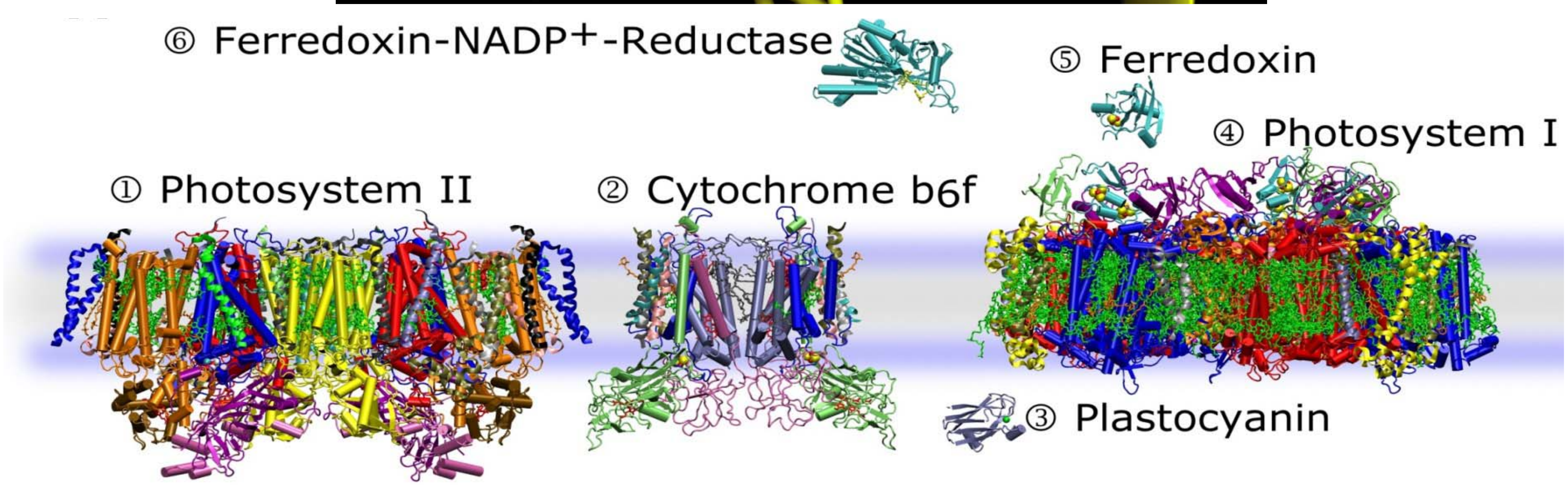


Source: Petra Fromme, ASU

Why?

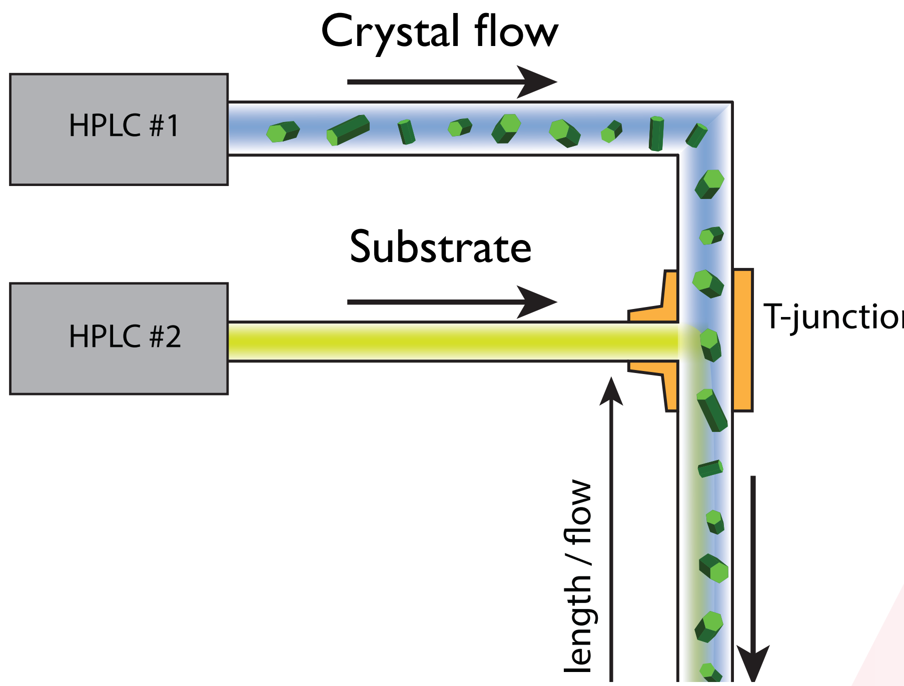


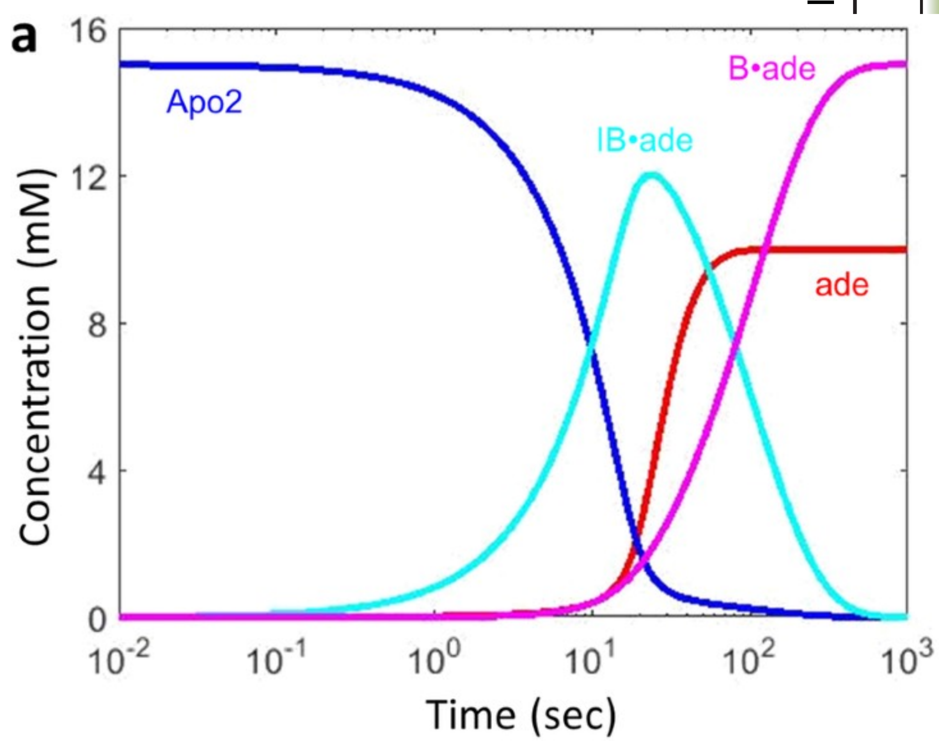
Kern et.al.
Nature Communications, 2014

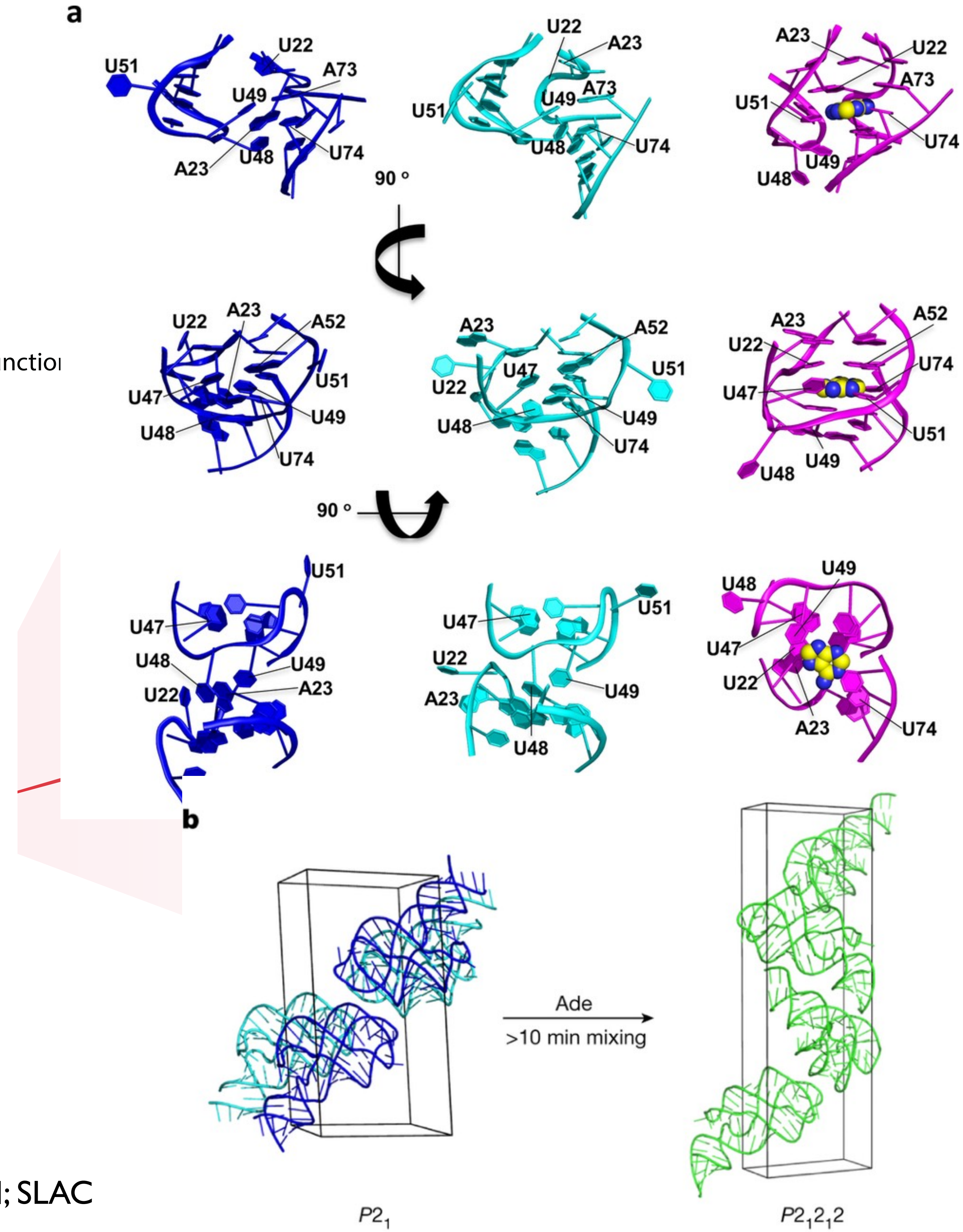


Source: Petra Fromme, ASU

The majority of biochemical dynamics are initiated by chemical triggers, such as the RNA riboswitch measured at LCLS

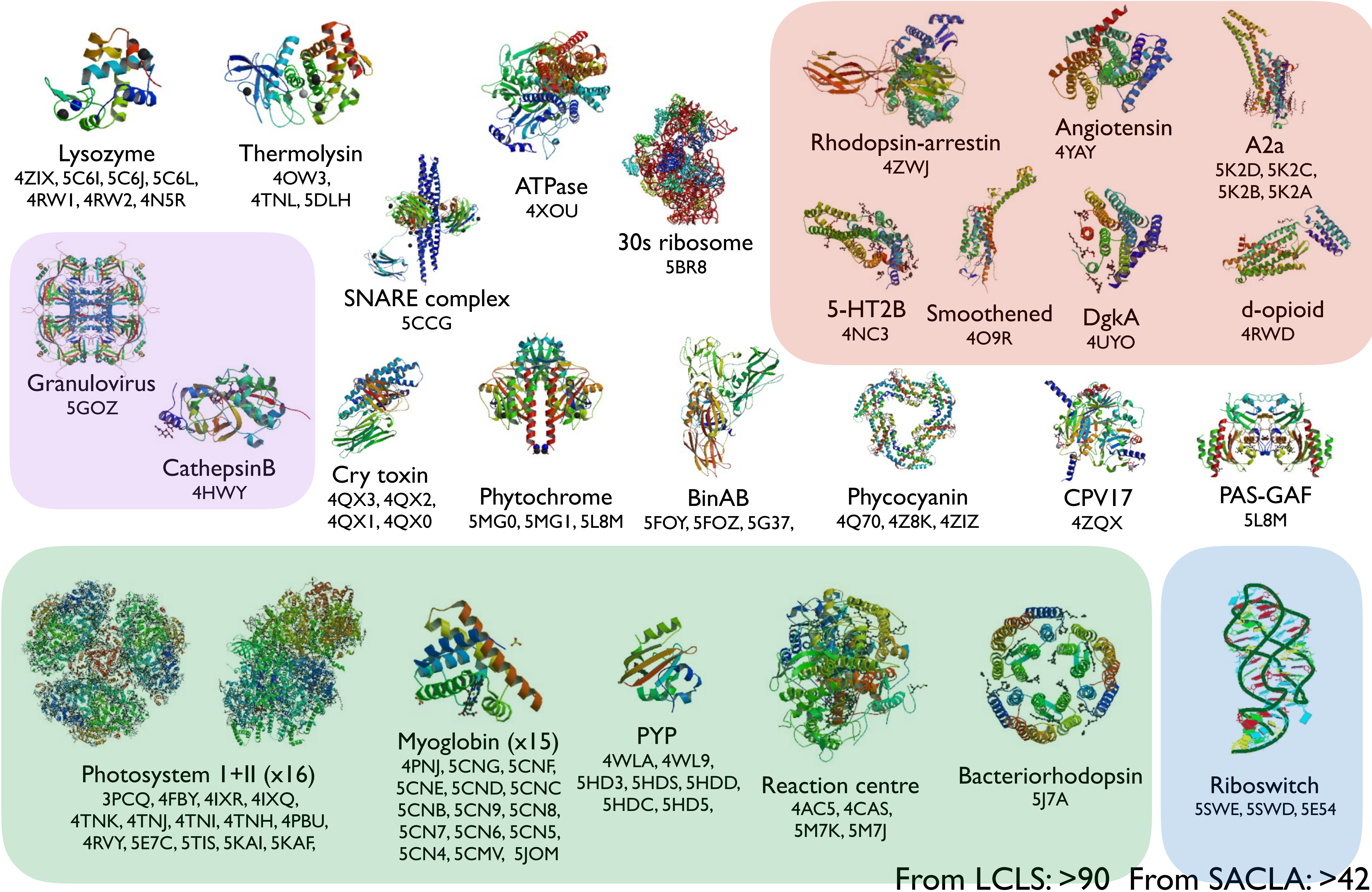




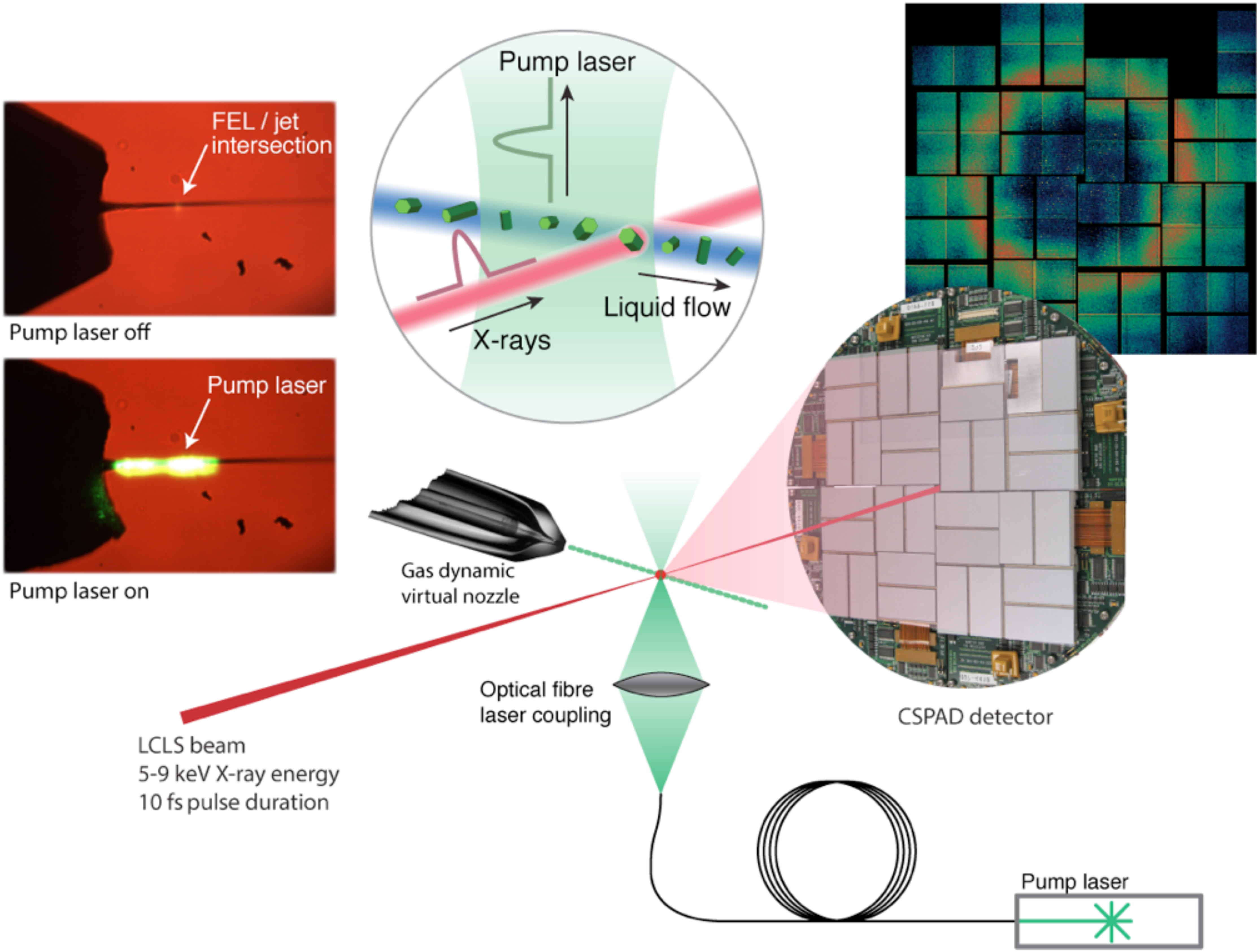


J. Stagno et al Nature 541, 242 (2017).
Y. Wang, NIH-NCI; ASU; Johns Hopkins U.; CFEL DESY; HHWI; SLAC

XFELs are used to solve difficult to crystallise and radiation sensitive proteins, and for time resolved structural dynamics

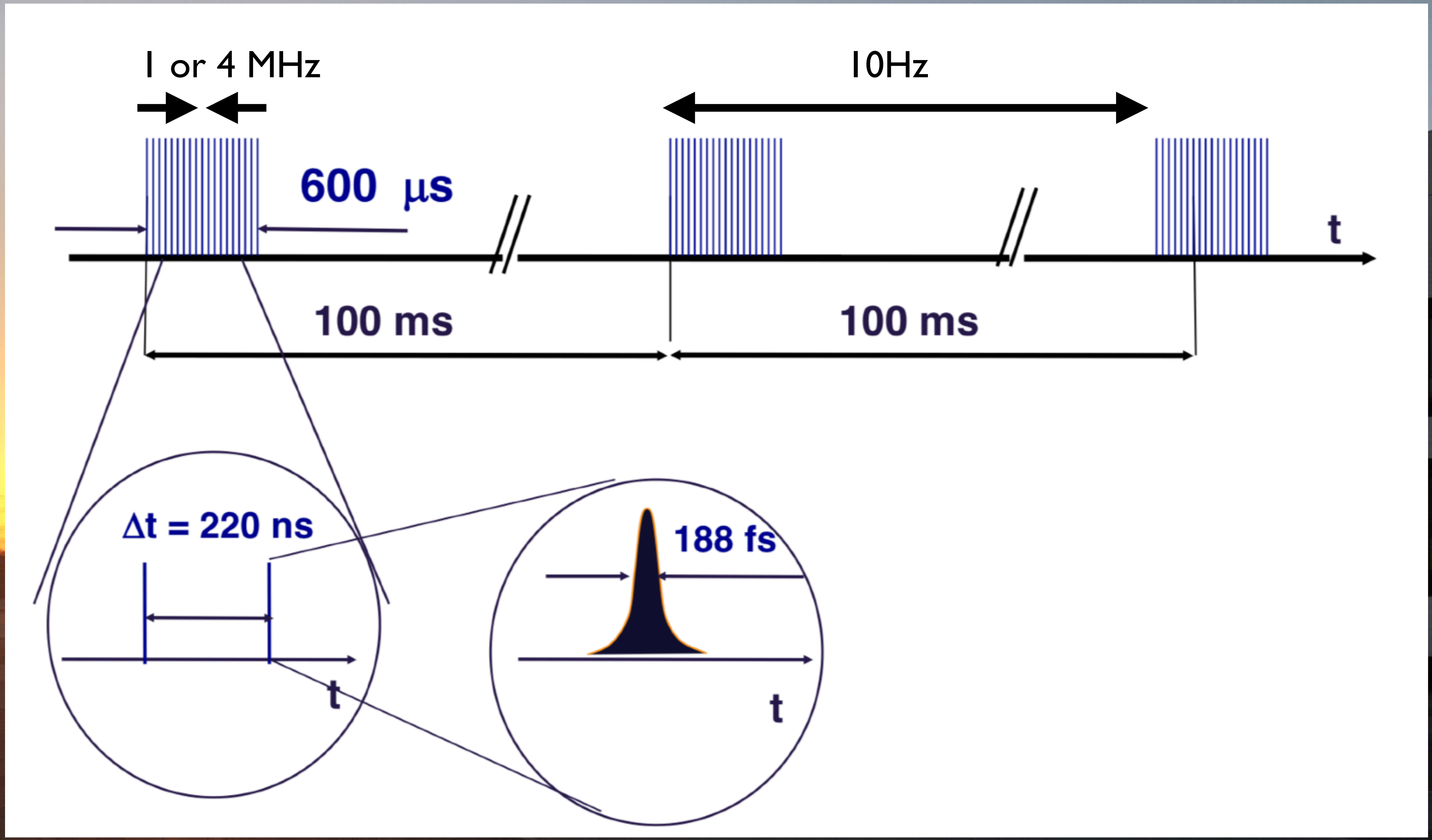


Serial crystallography data is merged from thousands of separate crystals each exposed only once



First user experiments at the European XFEL started on 14 September 2017

High data rate needs pulse trains
10Hz not competitive with other FELs



The first EuXFEL experiment at SFX/SPB was an open collaboration with over 100 participants

SPB/SFX Instrument Scientists
Adrian Mancuso
Richard Bean
Klaus Giewekemeyer
Marjan Hadian
Yoonhee Kim
Romain Letrun
Marc Messerschmidt
Grant Mills
Adam Round
Tokushi Sato
Marcin Sikorski
Stephan Stern
Patrik Vagovic
Britta Weinhausen

XFEL Detector
Steffen Hauf
Alexander Kaukher
Astrid Münnich
Jolanta Sztuk-Dambietz

AGIPD
Heinz Graafsma
Aschkan Allahgholi
Dominic Greiffenberg
Alexander Klyuev
Manuela Kuhn
Torsten Laurus
Davide Mezza
Jennifer Poehlsen
Ulrich Trunk

Samples
Dominik Oberthuer
Carolin Seuring
Imrich Barak
Sadia Bari
Christian Betzel
Matthew Coleman
Chelsie Conrad
Connie Darmanin
XY Fang
Petra Fromme
Raimund Fromme
S. Holmes
Inari Kursula
김경현
Kerstin Mühlig
Anna Munke
Allen Orville
Arwen Pearson
Markus Perbandt
Lars Redecke
Mia Rudolph
Iosifina Sarrou
Marius Schmidt
Robin Schubert
Jonas Sellberg
Megan Shelby
Jason Stagno
Yun-Xing Wang

Jets & Diagnostics
Max Wiedorn
Saša Bajt
Jakob Andreasson
Salah Awel
Miriam Barthelmess
Anja Burkhardt
Francisco Cruz-Mazo
Bruce Doak
Yang Du
Holger Fleckenstein
Matthias Frank
Alfonso Gañán Calvo
Lars Gumprecht
Janos Hajdu
Michael Heymann
Daniel Horke
Mark Hunter
Siegfried Imlau
Juraj Knoska
Jochen Küpper
Julia Maracke
Alke Meents
Diana Monteiro
Xavier Lourdu
Tatiana Safenreiter
Ilme Schlichting
Robert Shoeman
Ray Sierra
John Spence
Claudiu Stan
Martin Trebbin
Uwe Weierstall

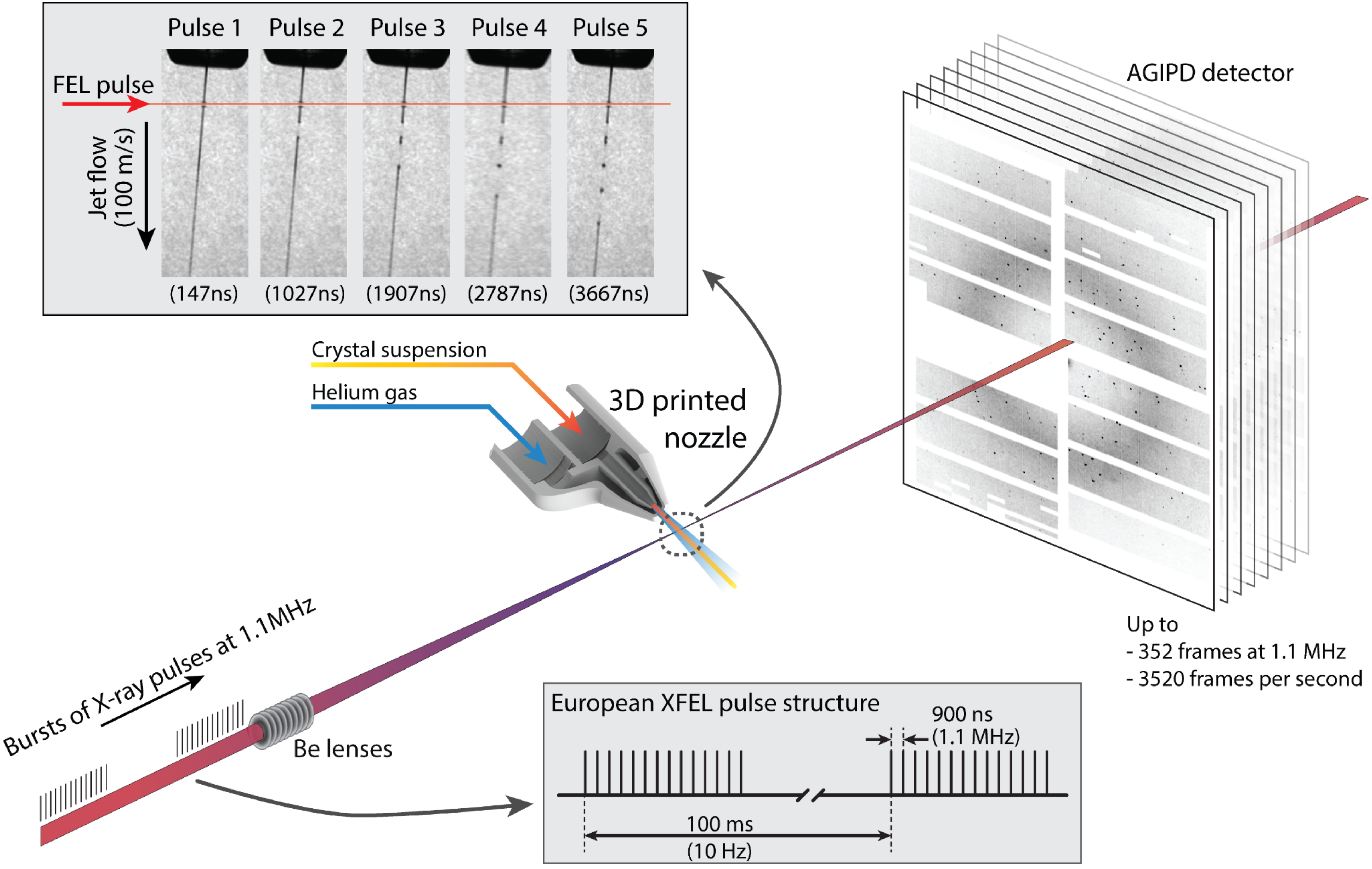
Analysis
Anton Barty
Steve Aplin
Andrew Aquila
Kartik Ayyer
Wolfgang Brehm
Aaron Brewster
Henry Chapman
Florian Flachsenberg
Yaroslav Gevorkov
Helen Ginn
Rick Kirian
Filipe Maia
Valerio Mariani
Andrew Morgan
Keith Nugent
Peter Schwander
Marvin Seibert
Natasha Stander
Pablo Villanueva-Perez
Thomas White
Oleksandr Yefanov
Nadia Zatsepin

XFEL Sample Environment
Johan Bielecki
Katerina Dörner
Rita Graceffa
Joachim Schulz

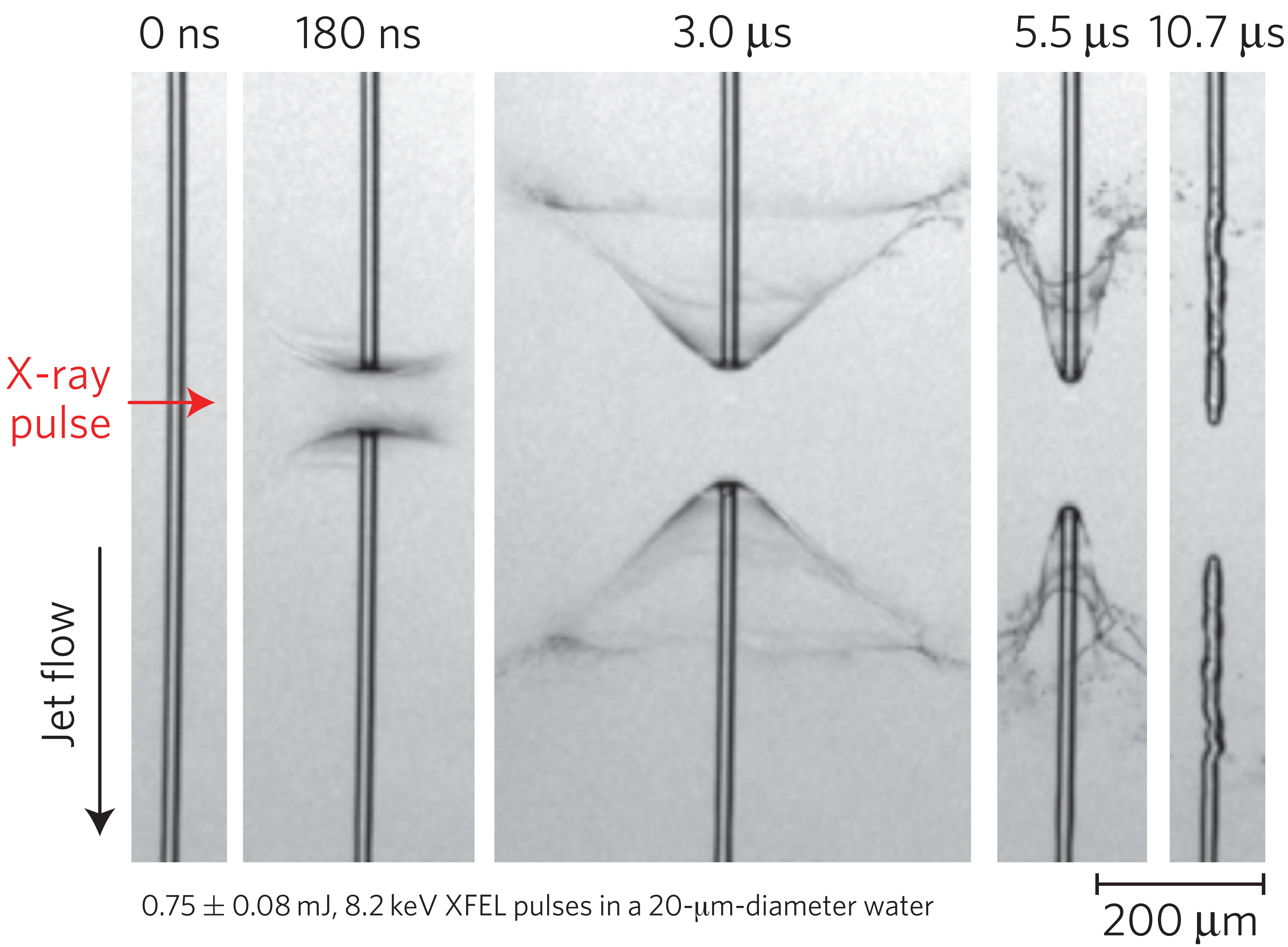
XFEL Information Technology and Data
Krzysztof Wrona
Djelloul Boukhelef
Illia Derevianko
Jorge Elizondo
Kimon Filippakopoulos
Manfred Knaack
Siriyala Kujala
Luis Maia
Maurizio Manetti
Bartosz Poljancewicz
Gianpietro Previtali
Nasser Al-Qudami
Eduard Stoica
Janusz Szuba

XFEL Controls and Software
Sandor Brockhauser
Andreas Beckmann
Valerii Bondar
Cyril Danilevski
Wajid Ehsan
Sergey Esenov
Hans Fangohr
Gero Flucke
Gabriele Giovanetti
Dennis Goeries
Burkhard Heisen
David Hickin
Anna Klimovskaia
Leonce Mekinda

SFX at the European XFEL



Liquid jets explode in the X-ray beam and need to recover before the next pulse

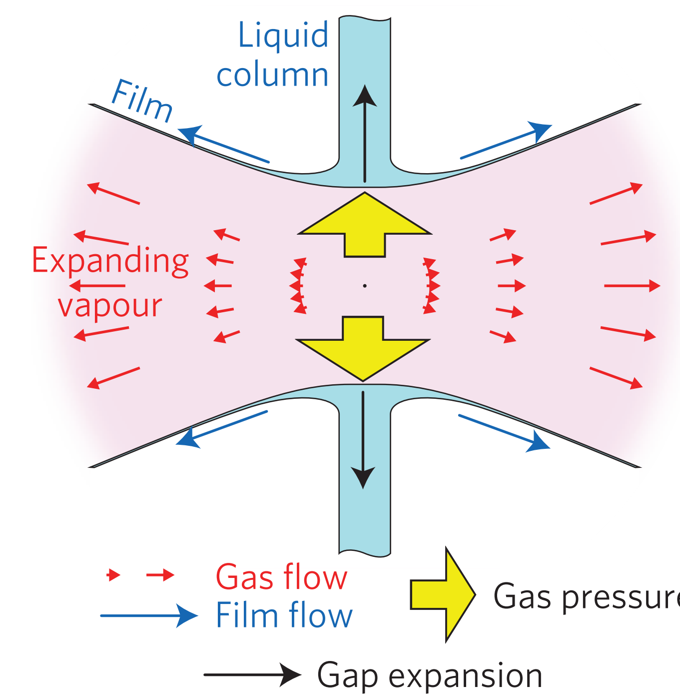


0.75 ± 0.08 mJ, 8.2 keV XFEL pulses in a 20-µm-diameter water

nature physics
ARTICLES
PUBLISHED ONLINE: 23 MAY 2016 | DOI: 10.1038/NPHYS3779

Liquid explosions induced by X-ray laser pulses

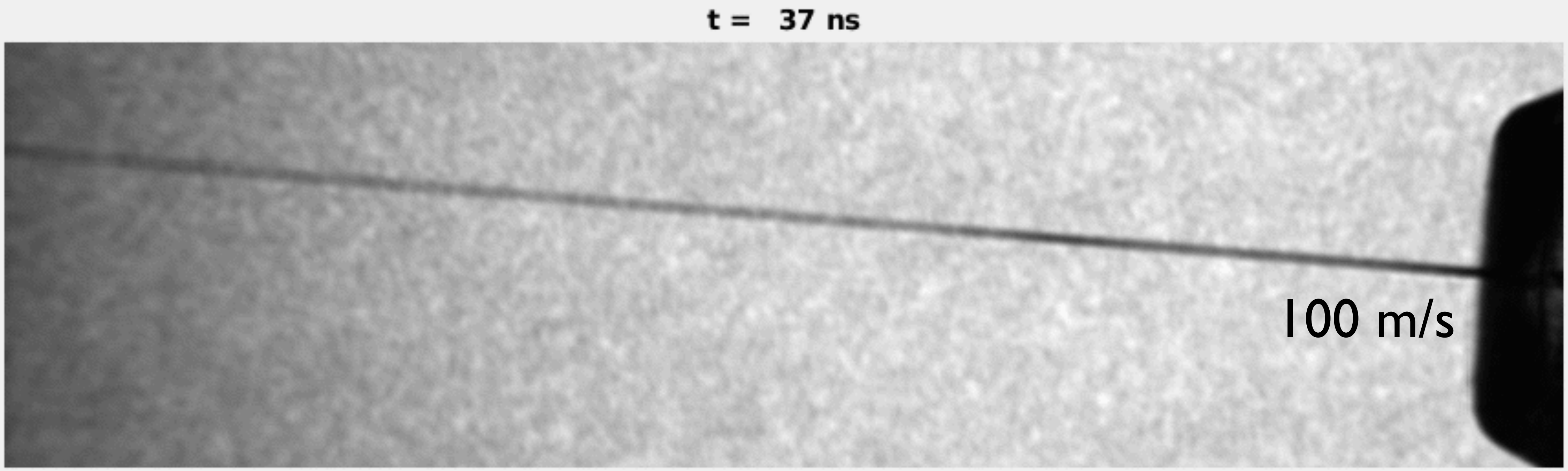
Claudiu A. Stan[1]*, Despina Milathianaki[2], Hartawan Laksmono[1], Raymond G. Sierra[1], Trevor A. McQueen[3], Marc Messerschmidt[2†], Garth J. Williams[2†], Jason E. Koglin[2], Thomas J. Lane[2], Matt J. Hayes[2], Serge A. H. Guillet[2], Mengning Liang[2], Andrew L. Aquila[2], Philip R. Willmott[2,4], Joseph S. Robinson[2], Karl L. Gumerlock[2], Sabine Botha[5†], Karol Nass[5], Ilme Schlichting[5], Robert L. Shoeman[5], Howard A. Stone[6] and Sébastien Boutet[2]



Shock waves propagate even faster

Claudiu Stan, SLAC, Nature Physics, 2016

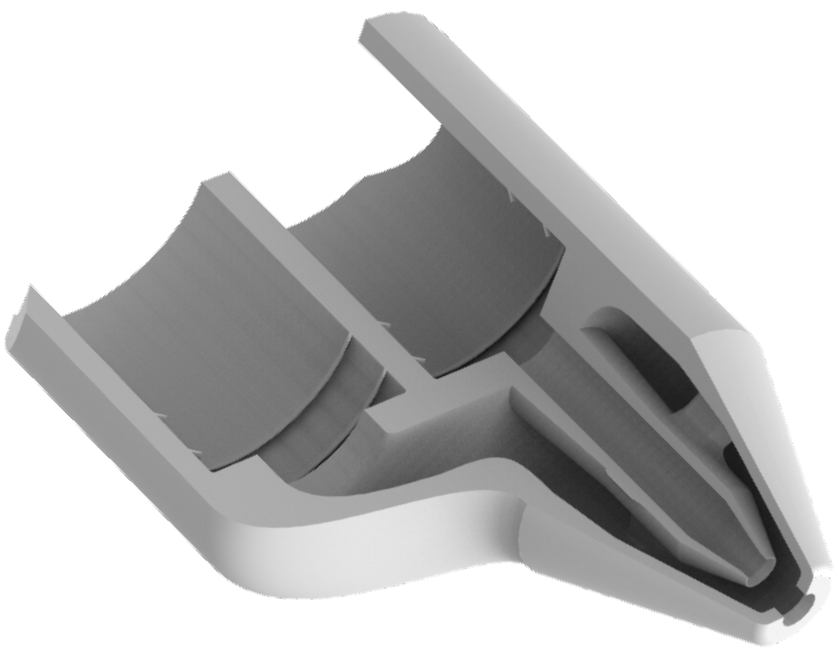
Fast jets recover in time for the next pulse at 1.1 MHz repetition rate

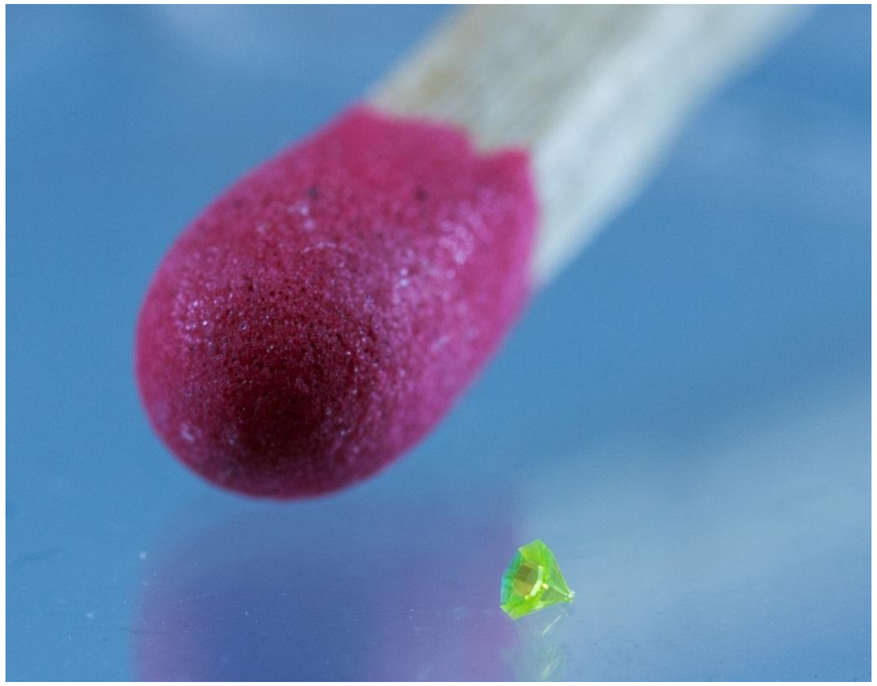


9.3 keV
580 mJ XFEL pulses
10 µm FWHM focus (or smaller)
1.1 MHz repetition rate

Max Wierdorn, Claudio Stan

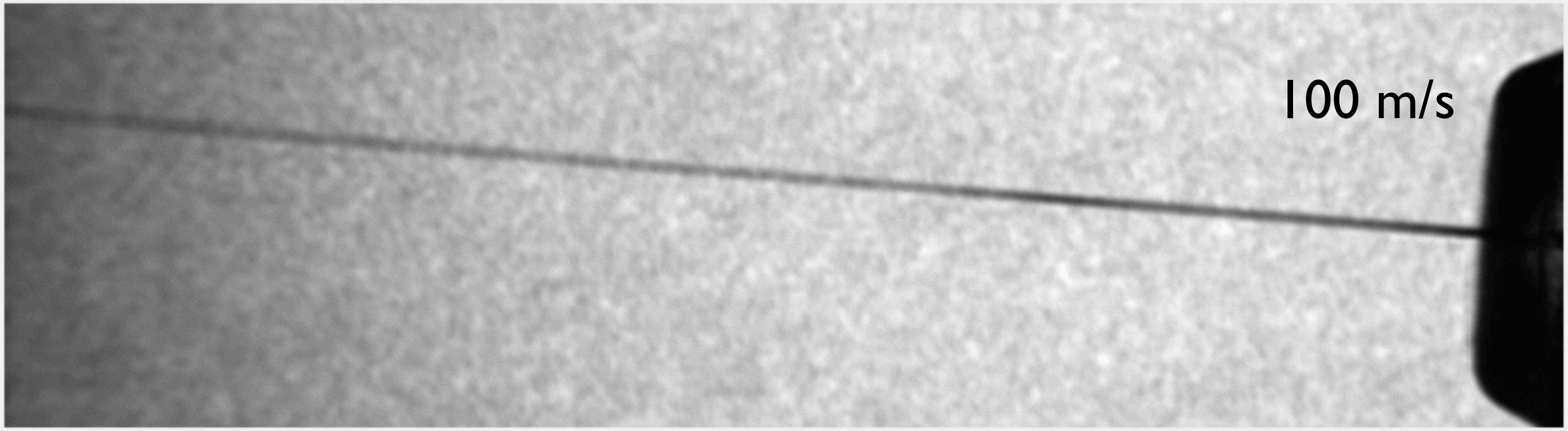
3D printed nozzle:
Juraj Knoska, Sasa Bajt, Michael Heymann





Fast jets recover in time for the next pulse at 1.1 MHz repetition rate

t = 37 ns



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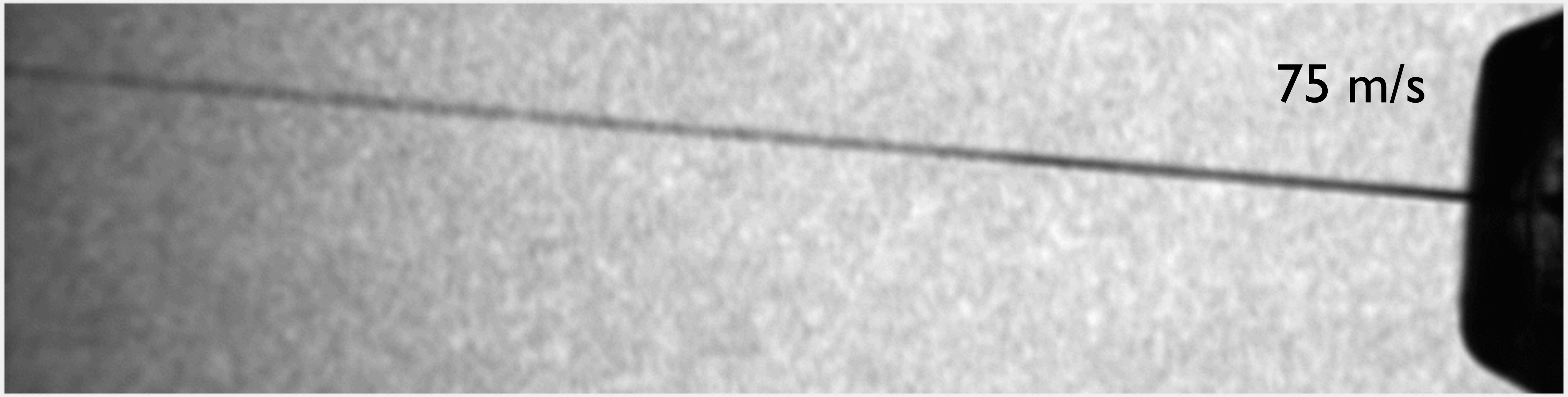
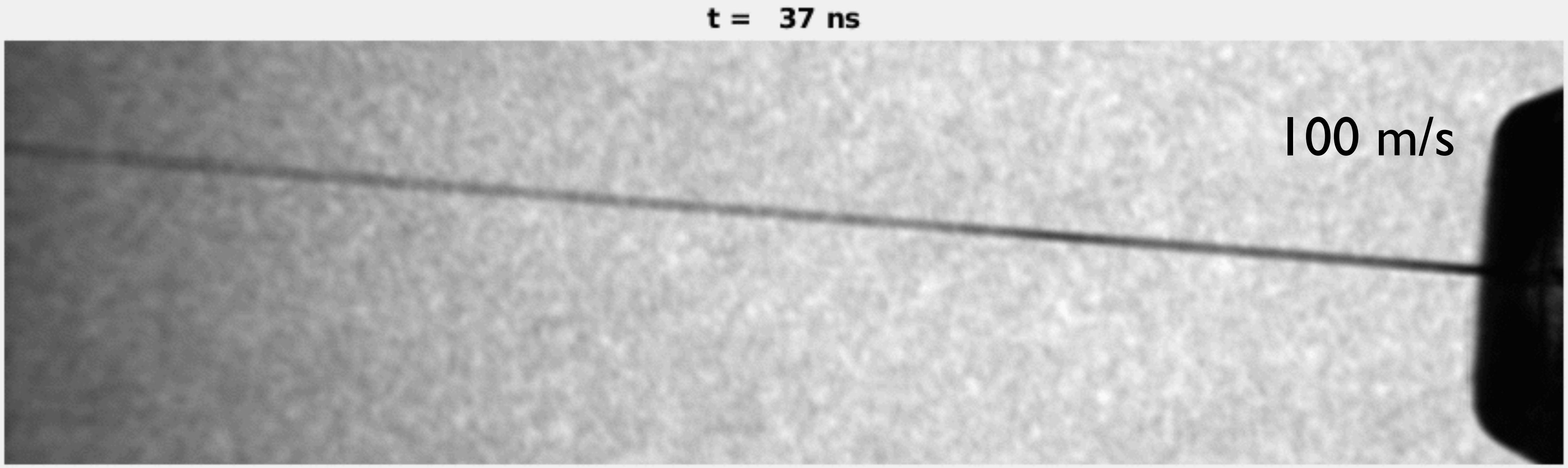
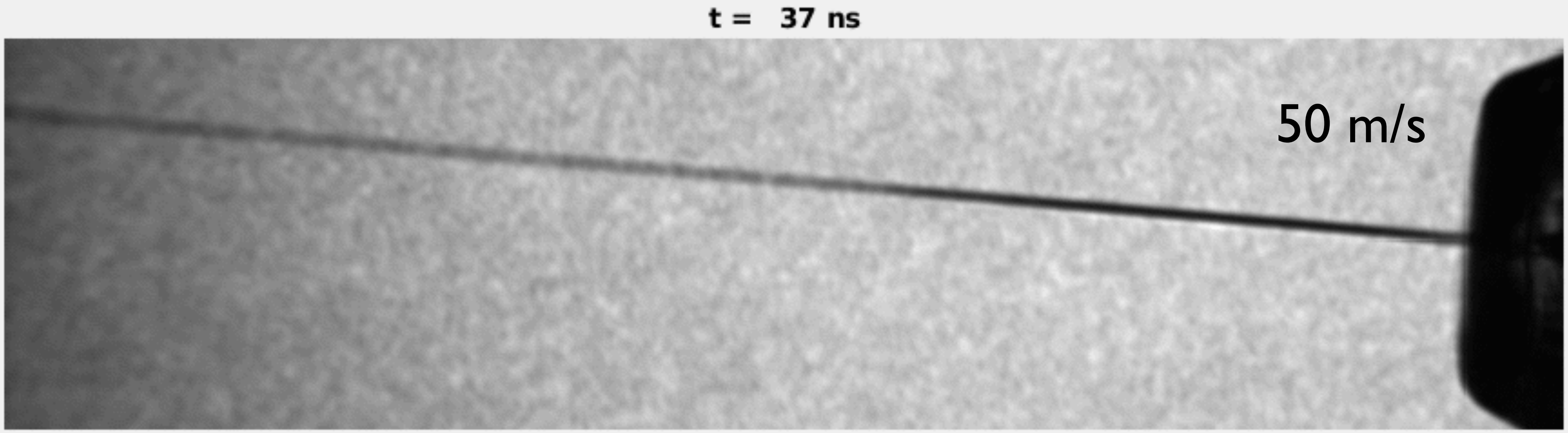


Max Wierdorn, Claudio Stan

Fast jets recover in time for the next pulse at 1.1 MHz repetition rate

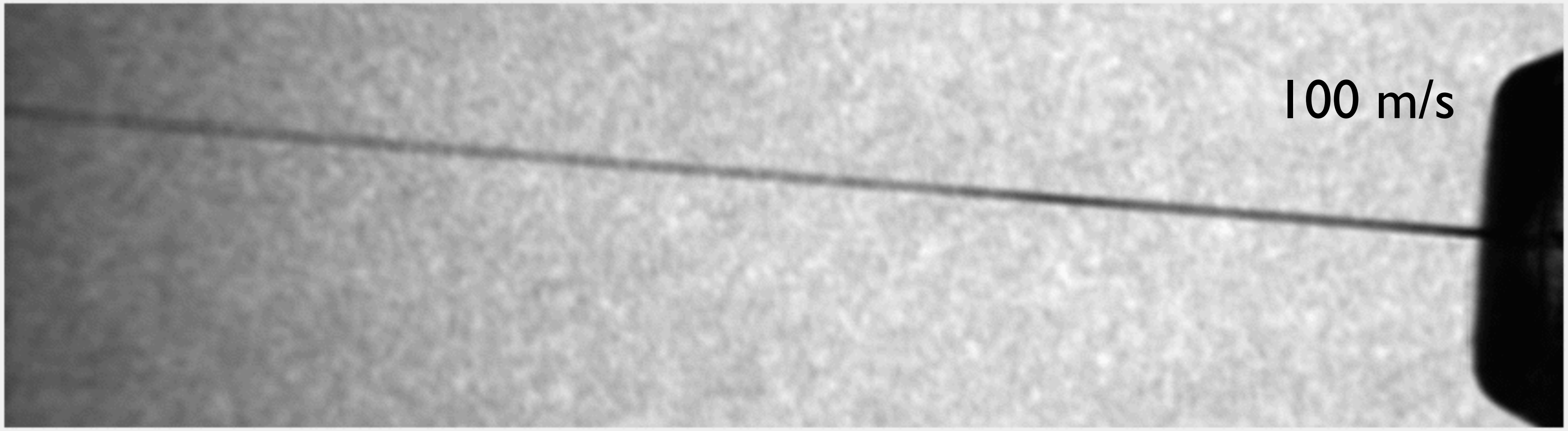




Max Wierdorn, Claudio Stan

CFEL-designed fast jets recover in time for the next pulse at 1.1 MHz repetition rate

t = 37 ns



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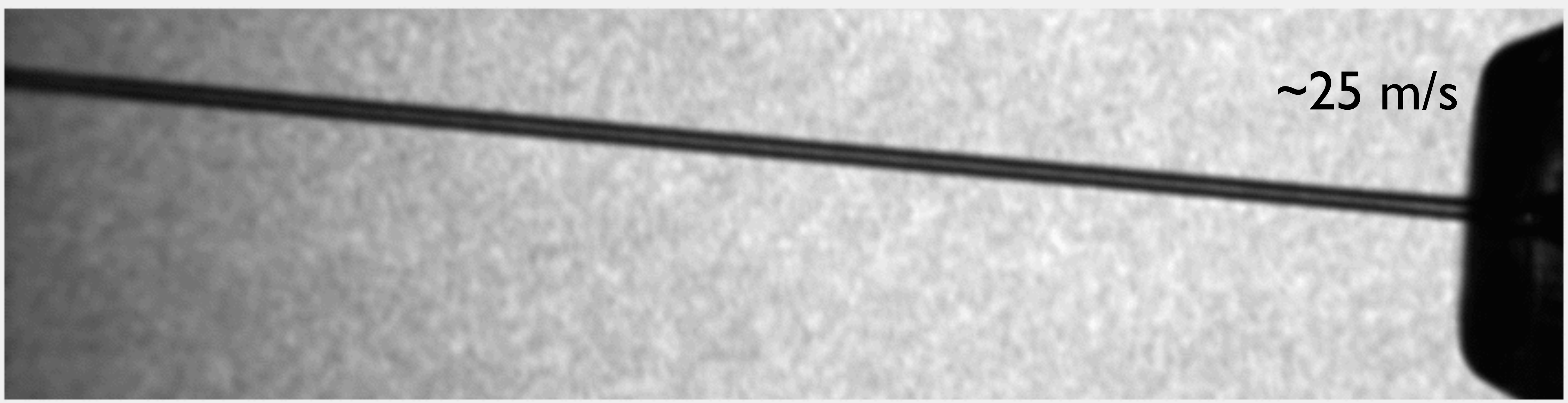
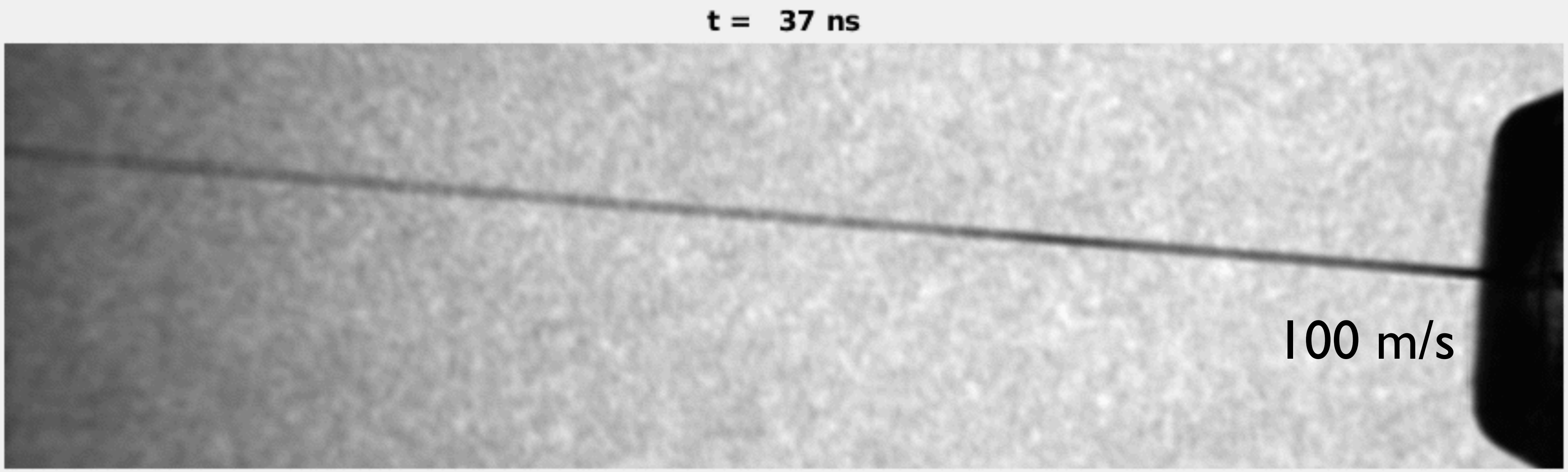
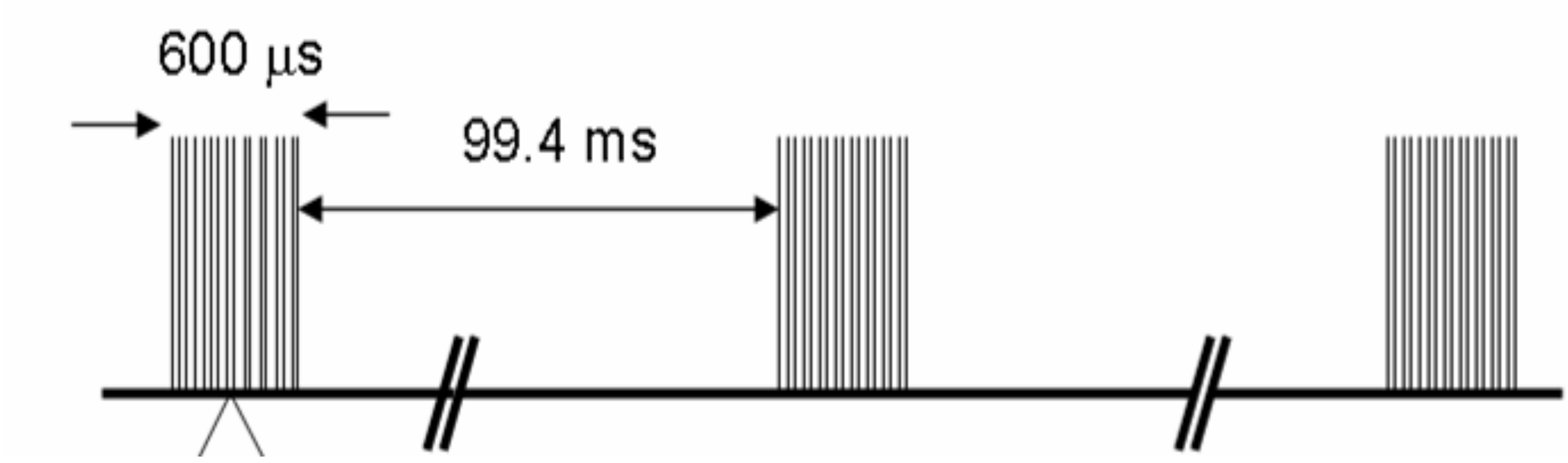


Max Wierdorn, Claudio Stan

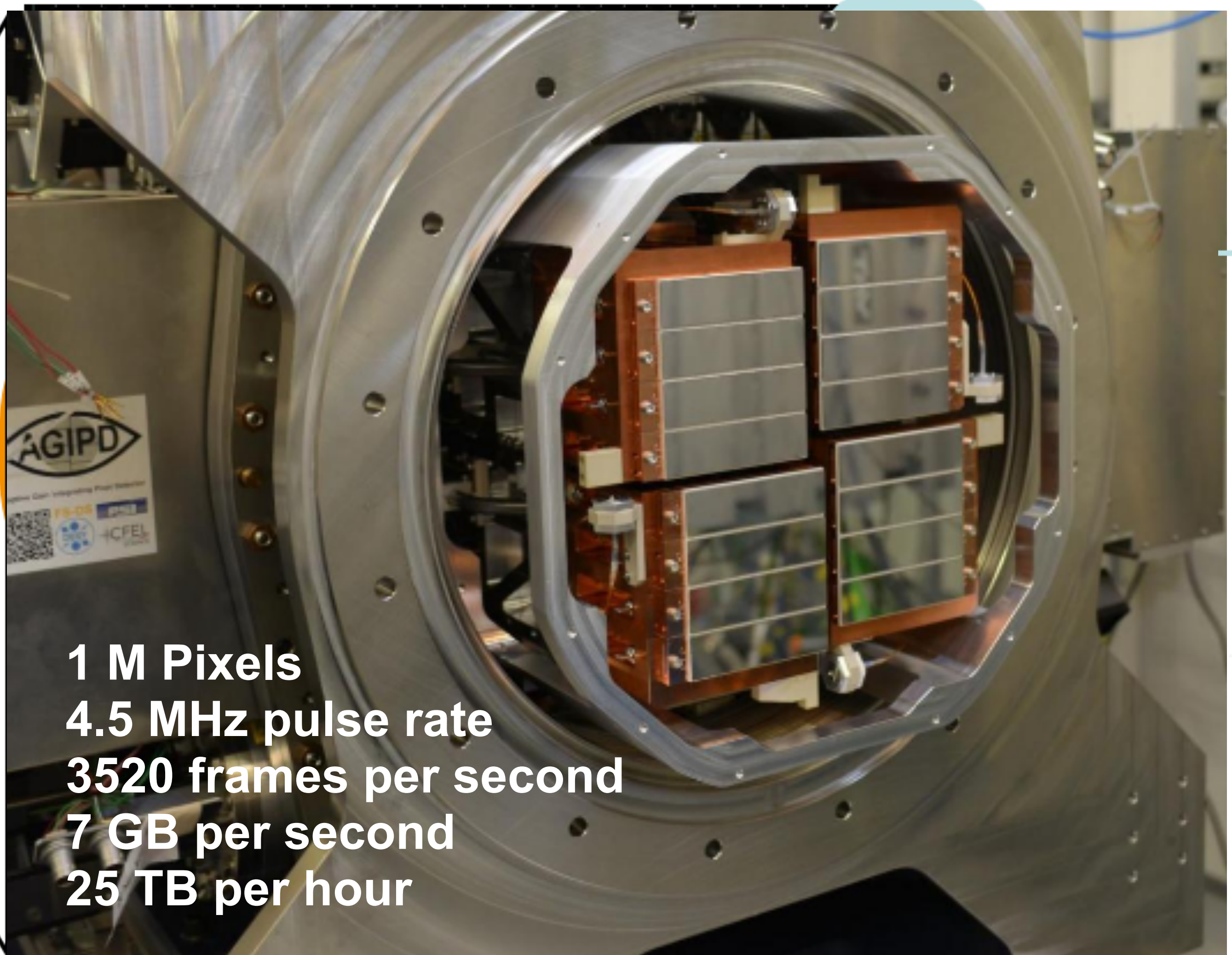
Burst mode means 99.4% of sample is wasted



99.4% of sample is wasted between bursts

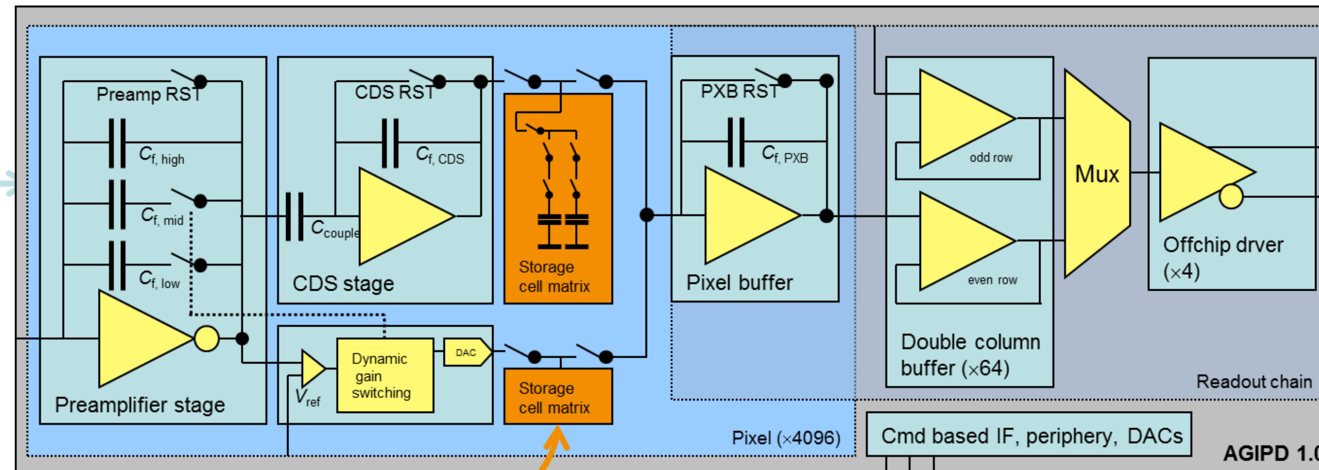


The Adaptive Gain Integrating Pixel Detector (AGIPD) can read out 3520 frames per second with MHz pulse spacing

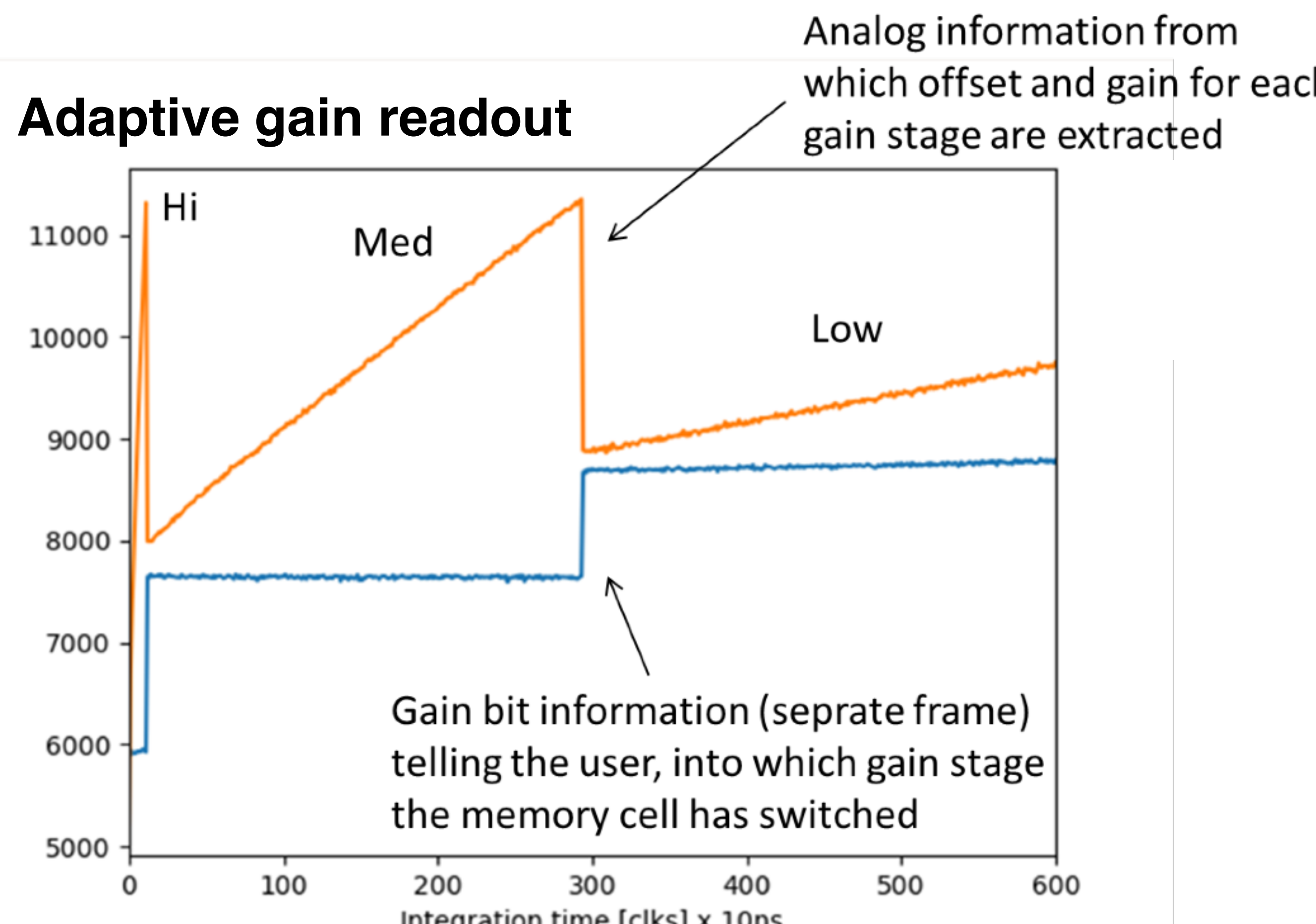


Energy range	**3keV-18keV**
Frame rate	**> 4.5MHz (burst)**
Memory depth	**352 frames**
Dynamic range	**1 to 10^4 photons/pixel/frame at 12.4 keV**
Pixel size	$(200\mu m)^2$
Operating principle	Charge integrating
Dynamic gain switching	Yes (3 gains)
Single Photon sensitivity	Yes

Pixel circuit overview

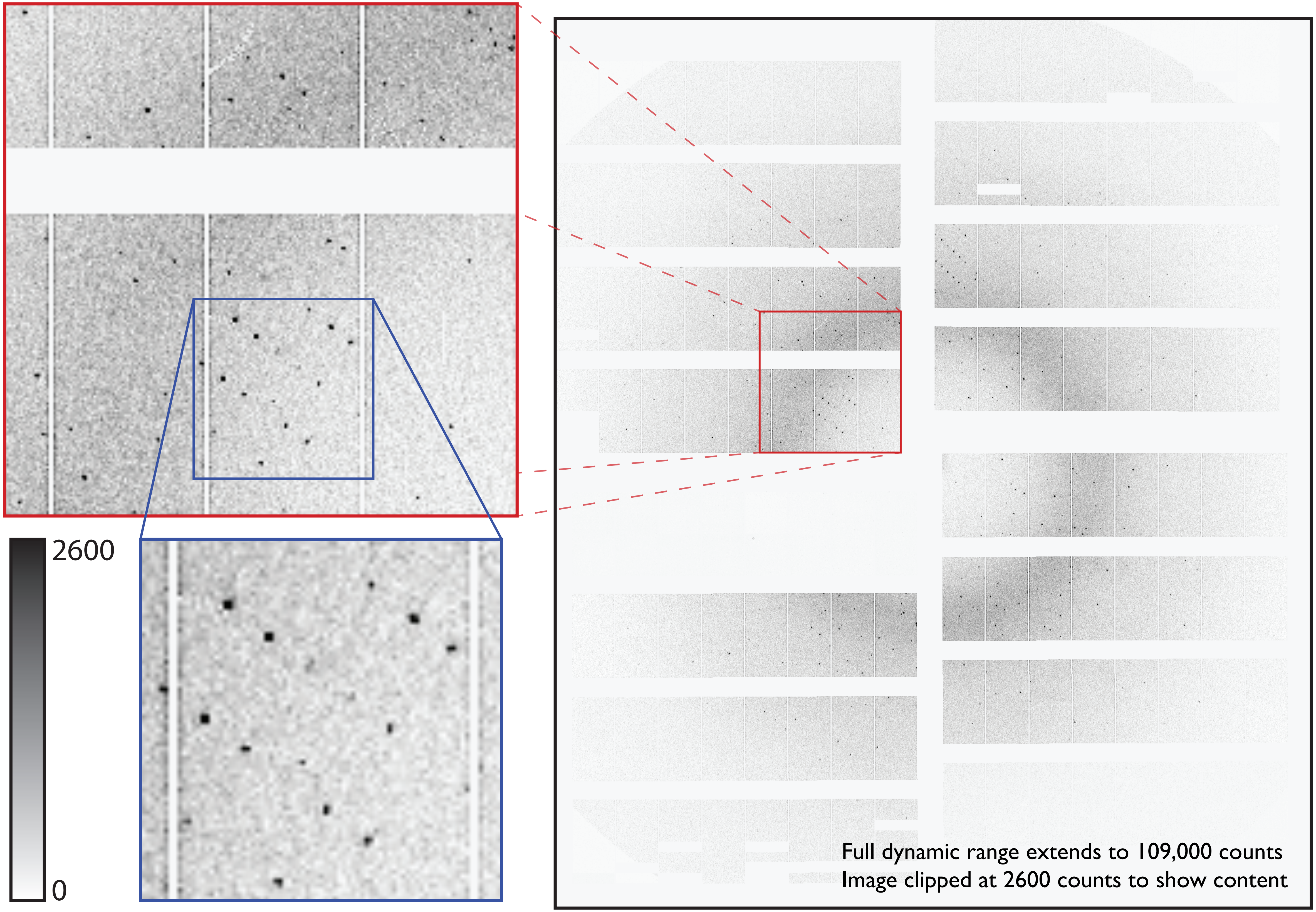


Adaptive gain readout



AGIPD consortium, Heinz Graafsma, DESY

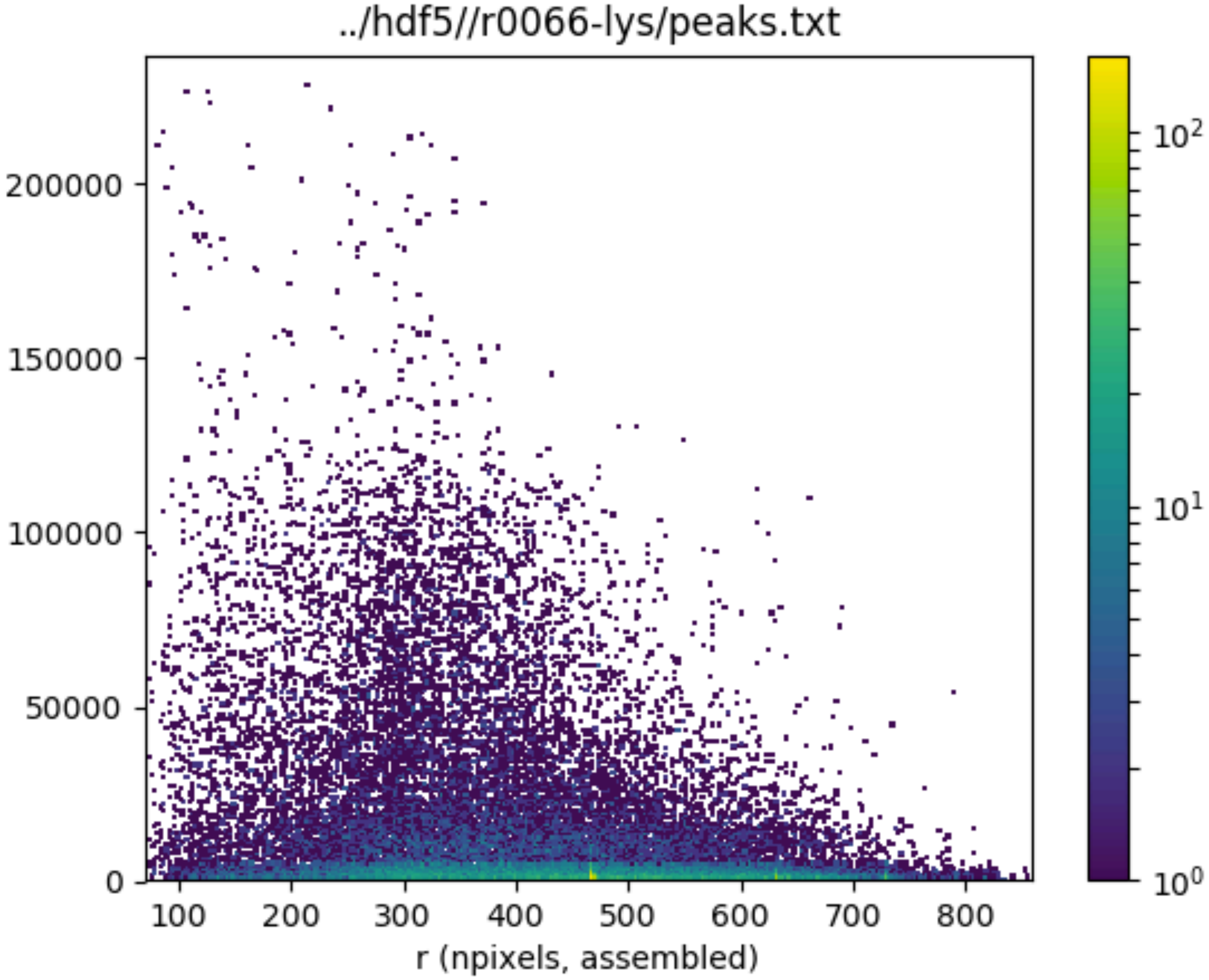
The AGIPD detector measures diffraction patterns with low noise and high dynamic range thanks to dynamic gain switching



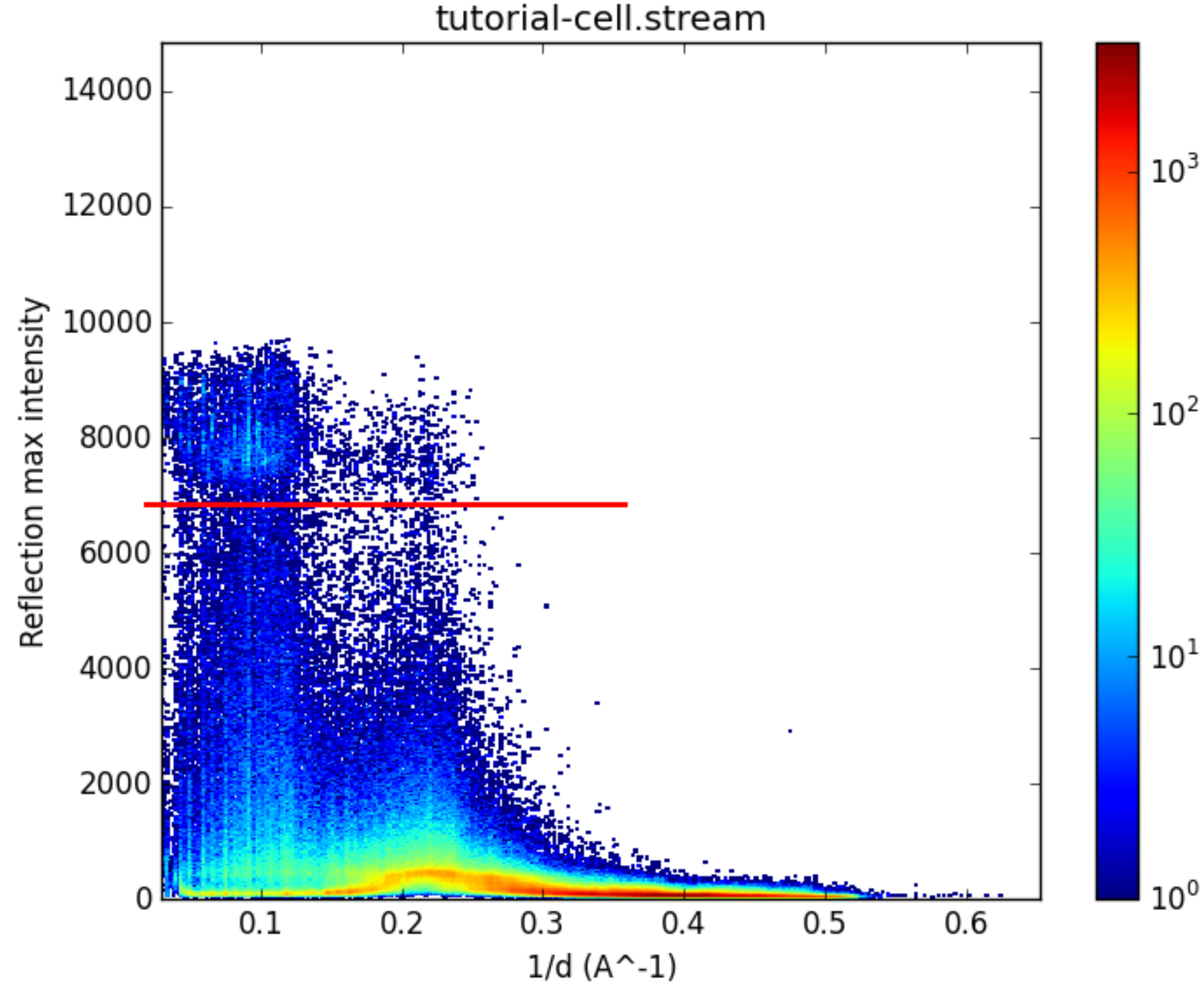
Wiedorn *et.al.* "Megahertz serial crystallography" Nat Commun. 9, 4025 (2018).

The distribution of peak intensities shows higher dynamic range than the CSPAD thanks to dynamic gain switching

AGIPD

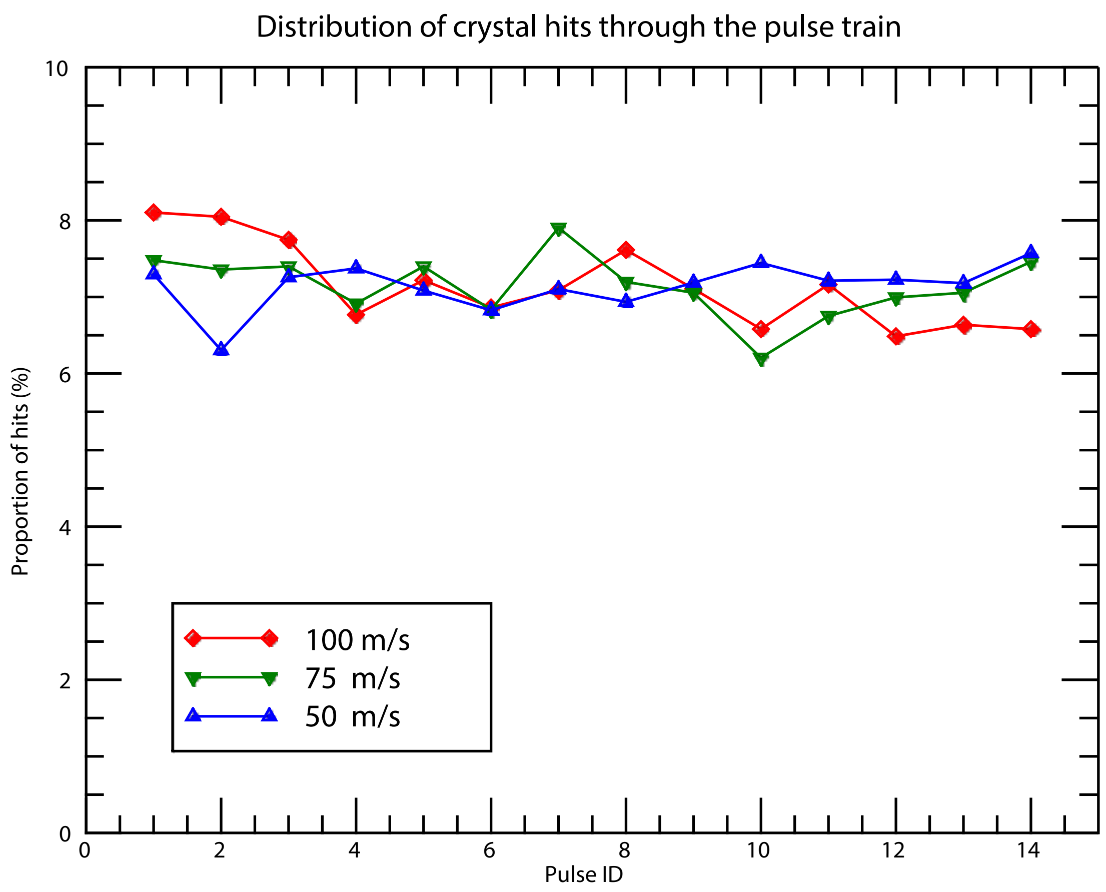


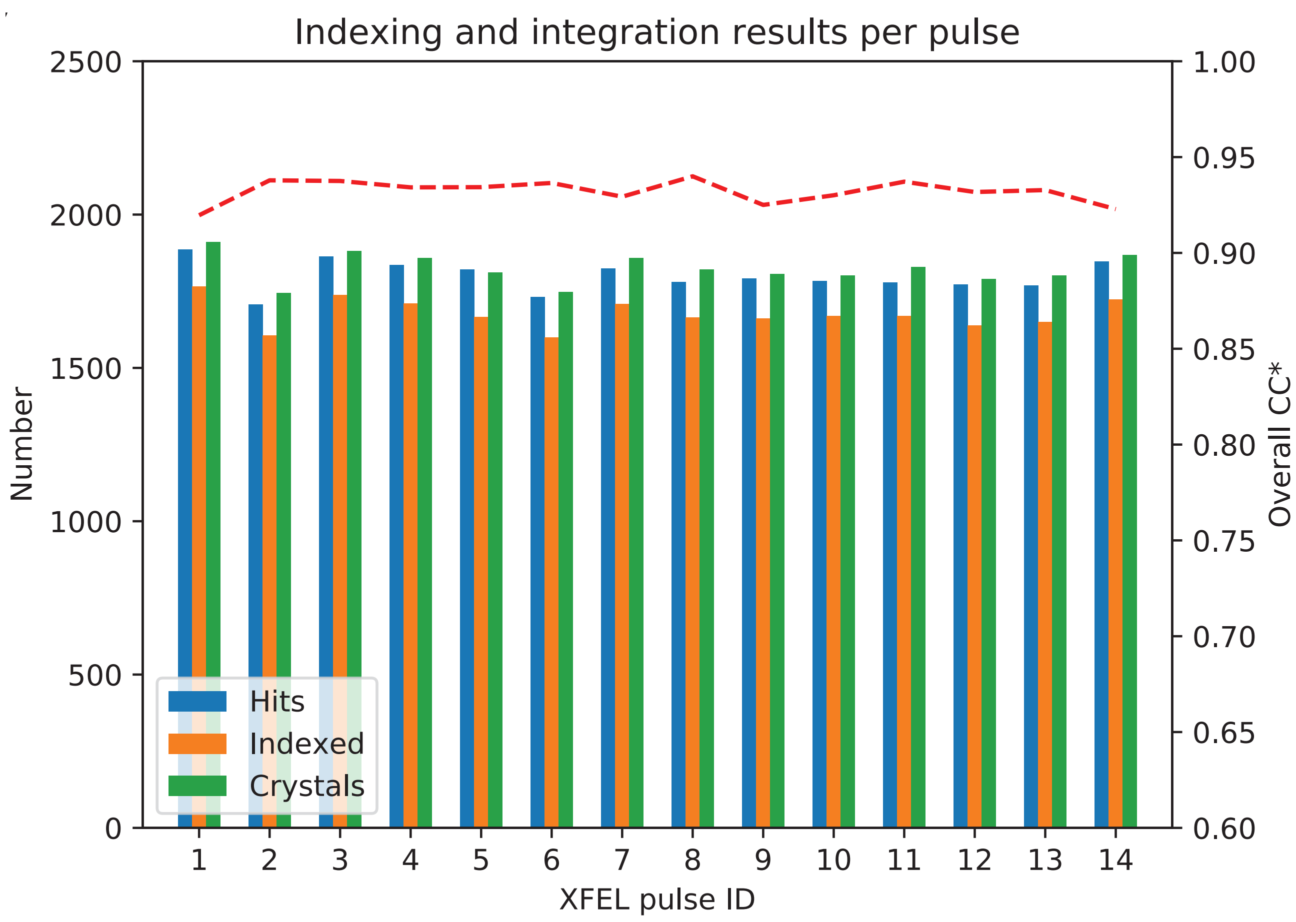
CSPAD



Anton Barty, Helen Ginn: AGIPD corrections + Cheetah integration
10 Nov 2017

Crystal hits are evenly distributed through the pulse train





September 2017:
15 pulses per train
150 pulses per second

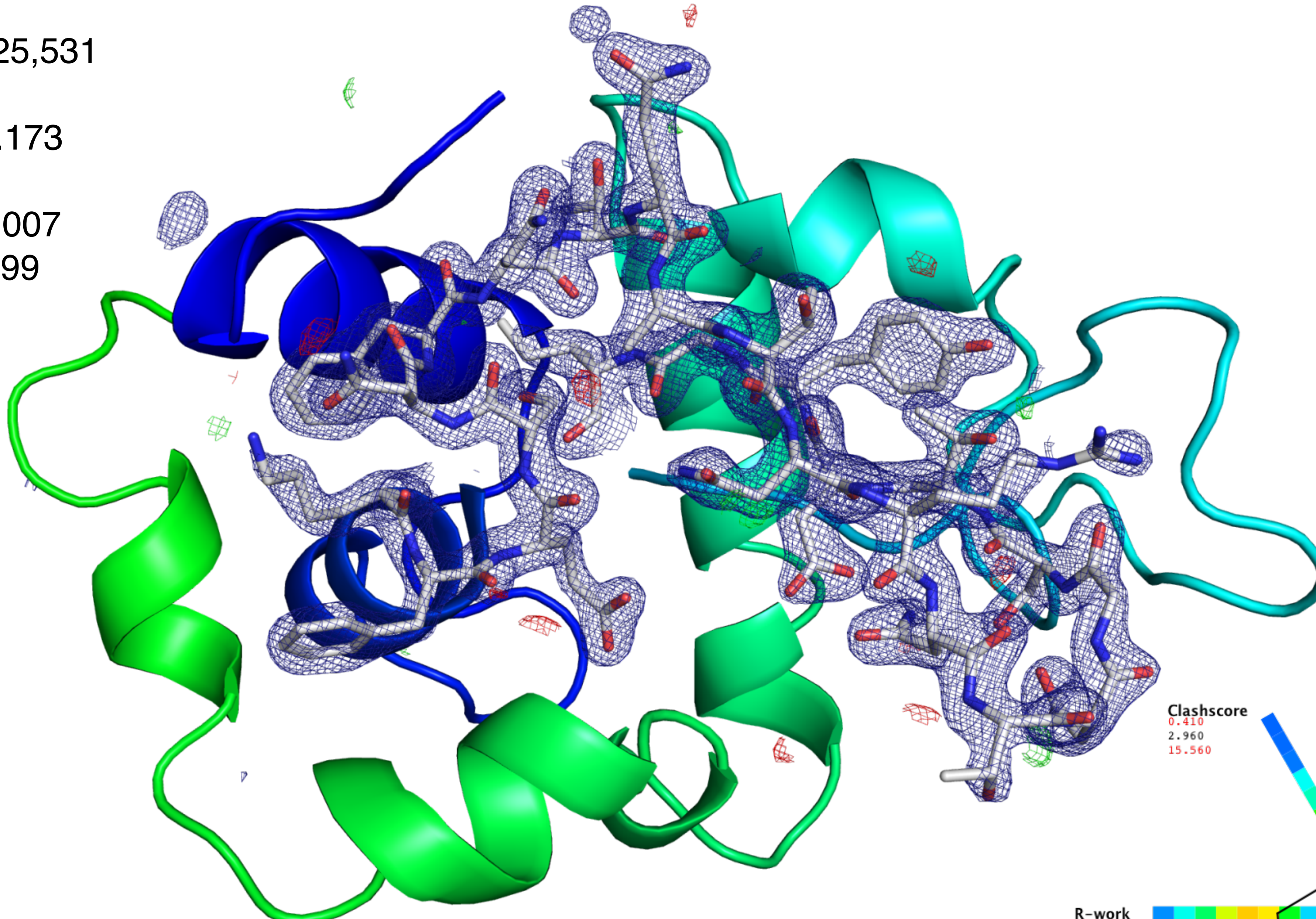
Wiedorn *et.al.* "Megahertz serial crystallography" Nat Commun. 9, 4025 (2018).

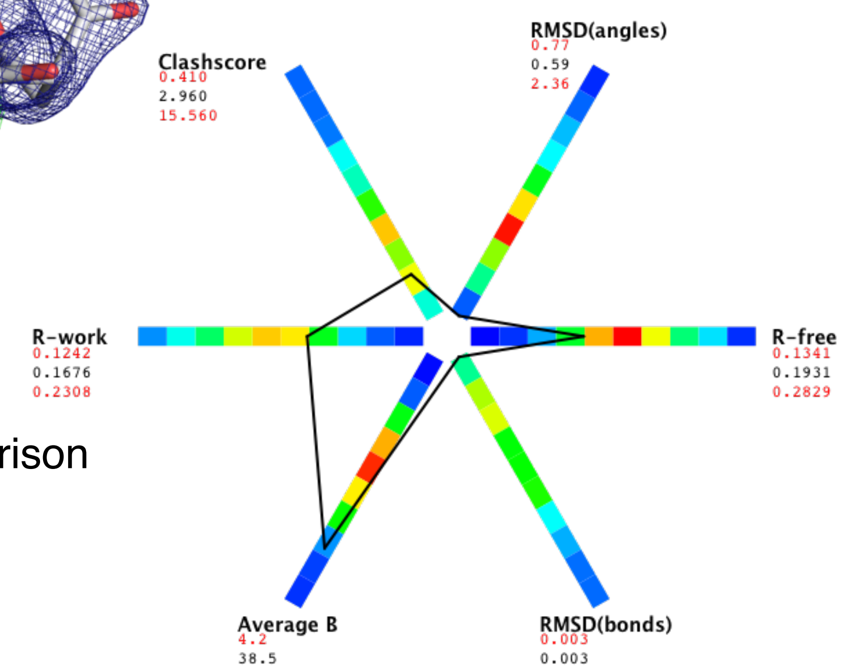
Lysozyme data confirms an accurate structure can be measured to 1.76Å resolution using MHz pulse trains

PDB: 6FTR

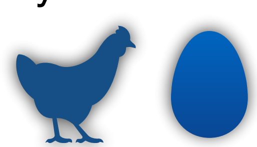
2mFo-DFc map (1.5σ)
and mFo-DFc map (3σ)
over residues 33-55

Number of lattices: 25,531
Resolution: 1.76Å
R_{work}/R_{free}: 0.157 / 0.173
Average B_{ISO}: 30 Å
RMSD bonds (Å): 0.007
RMSD angles (°): 0.99
CXIDB: ID-80





There are over 1800 Lysozyme PDB depositions for comparison

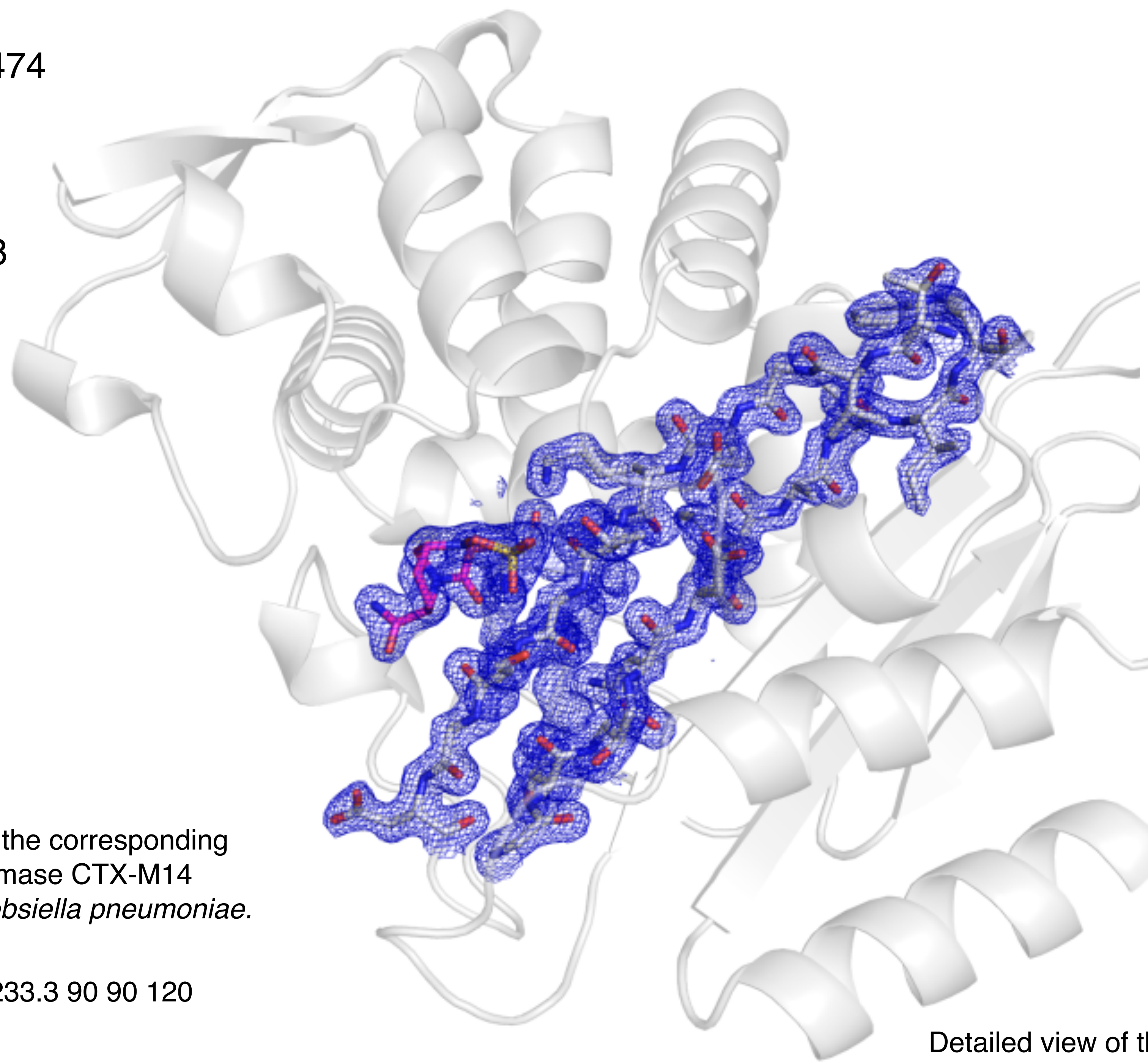


Wiedorn *et.al.* "Megahertz serial crystallography" Nat Commun. 9, 4025 (2018).

We solved the unknown structure of Beta-lactamase CTX-M-14 to 1.7 Å using data from 12,500 indexed lattices

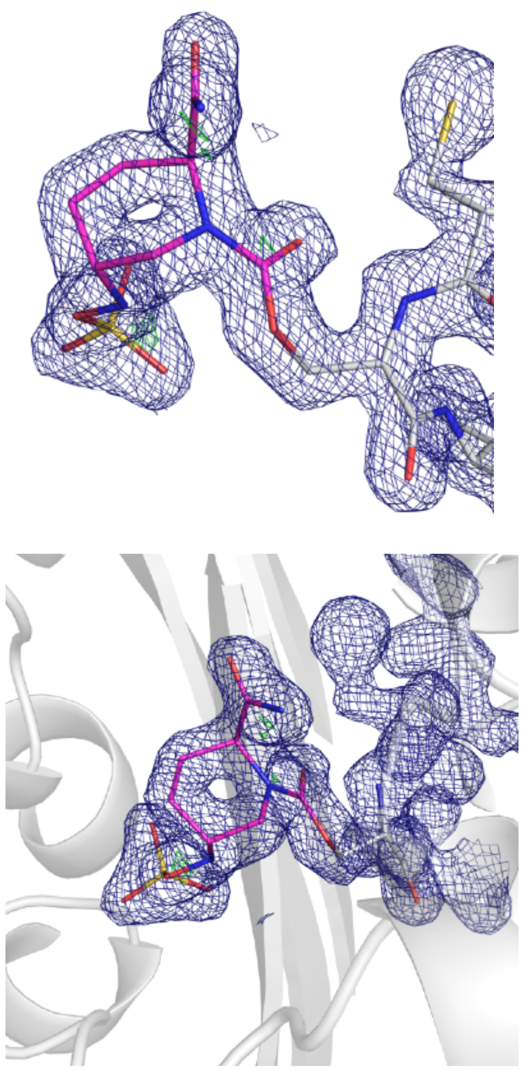
PDB: 6GTH

Number of lattices: 12,474
Resolution: 1.69Å
R_{work}/R_{free}: 0.176 / 0.21
Average B: 27.6
RMSD bonds (Å): 0.008
RMSD angles (°): 1.22
CXIDB: ID-83



2Fo-Fc map (at 1.5 σ) over the corresponding part of the model of ß-lactamase CTX-M14 from multidrug resistant *Klebsiella pneumoniae.*

$P3_221$ Unit Cell: 41.8 41.8 233.3 90 90 120

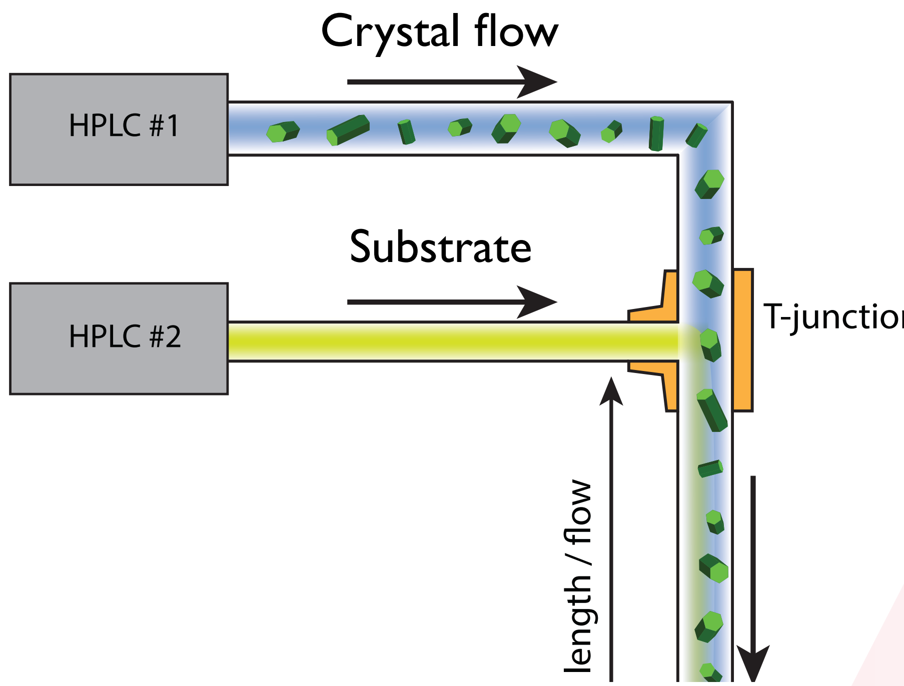


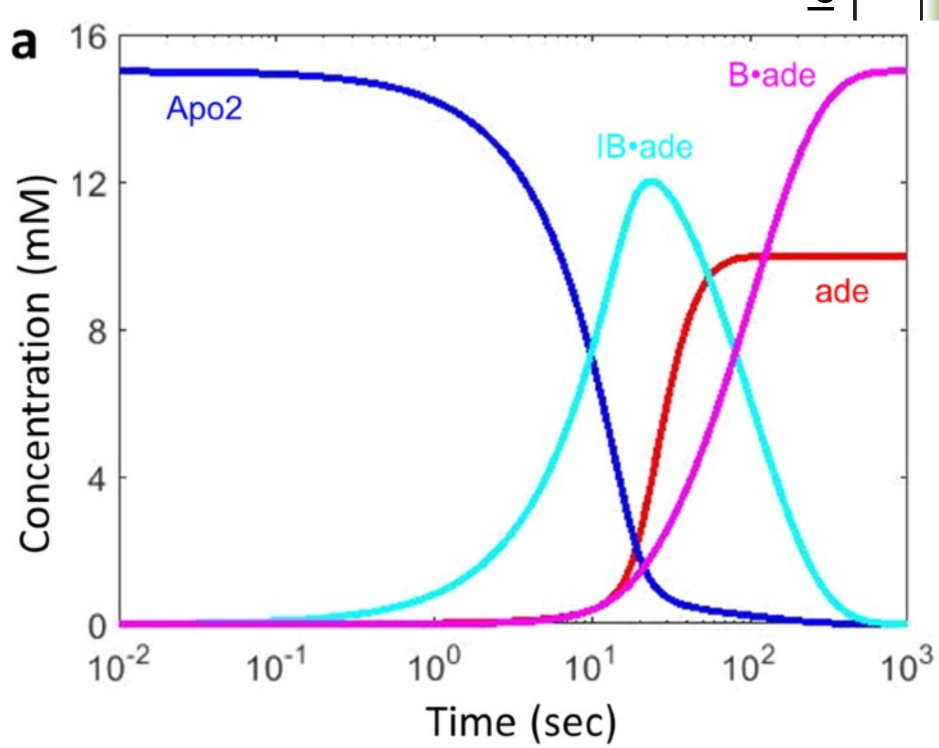
Detailed view of the binding of the ß-lactamase inhibitor avibactam to Ser70. The inhibitor is bound covalently to the protein (hemiacetal).

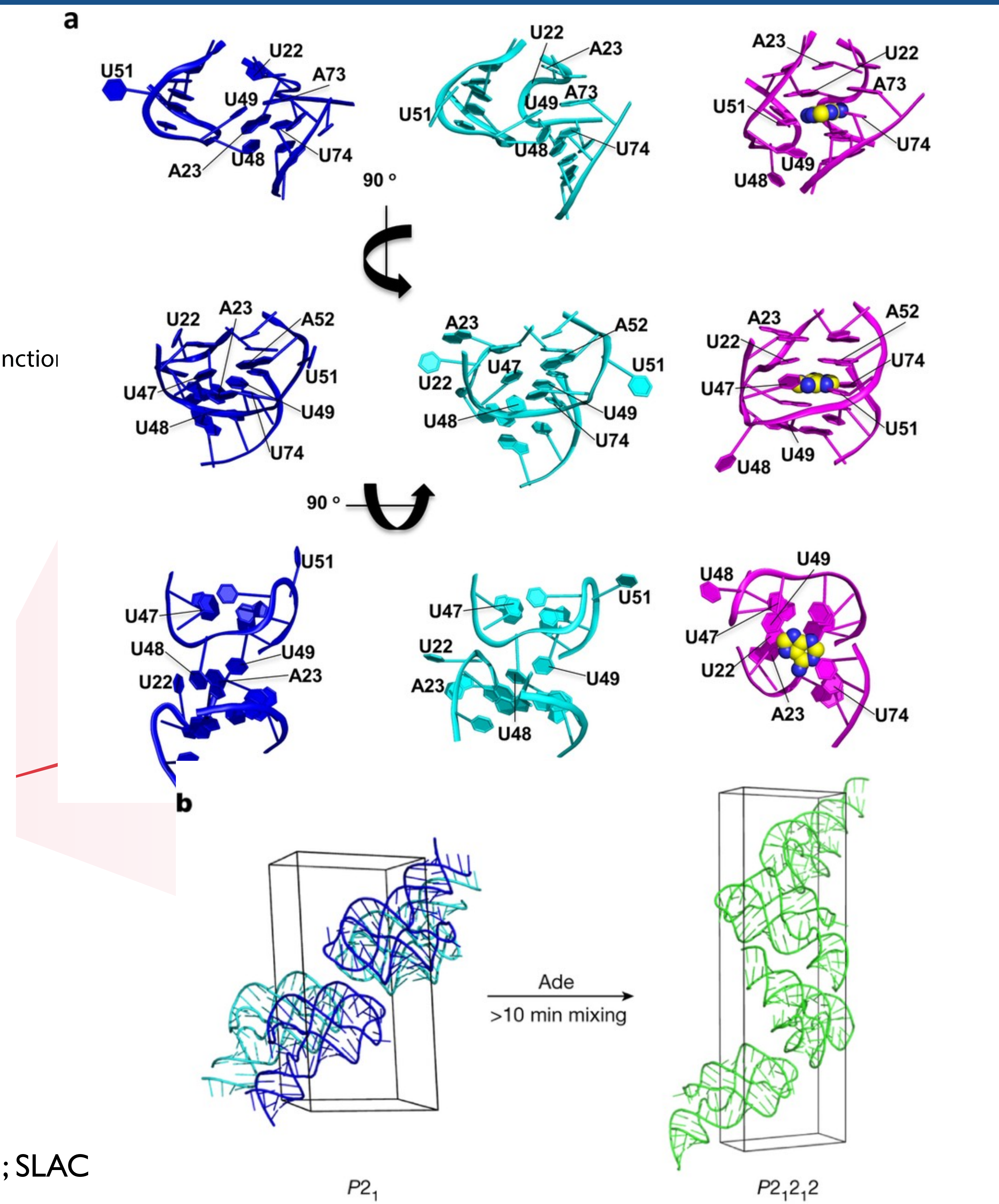
Wiedorn *et.al.* "Megahertz serial crystallography" Nat Commun. 9, 4025 (2018).

Sample: Christian Betzel, UHH

The majority of biochemical dynamics are initiated by chemical triggers, such as the RNA riboswitch measured at LCLS





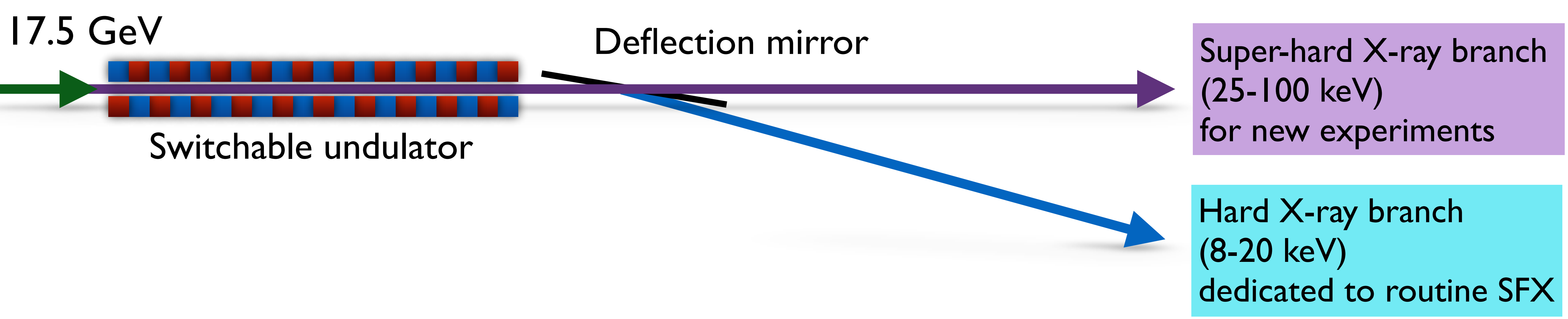


J. Stagno et al Nature 541, 242 (2017).

Y. Wang, NIH-NCI; ASU; Johns Hopkins U.; CFEL DESY; HHWI; SLAC

Tunnel 4 could host both a super-hard X-ray branch and dedicated SFX instrument for routine structure determination

<u>Super-hard</u>
New horizons not available anywhere else
- Penetrating single-shot imaging
- Phase contrast dynamic imaging
- Compton imaging
- Optimise elastic scattering to photoelectric absorption



<u>Routine SFX</u>
- Stable instrumentation for routine measurements
- Static structure screening
- Mixing experiments
- Mail in structure determination

Could relocate existing SFX instrument from SPB

The first EuXFEL experiment at SFX/SPB was an open collaboration with over 100 participants

Anton Barty	coordination
Richard Bean	XFEL contact
Max Weidorn	Jets
Dominik Oberthuer	Samples

Acknowledgement to the fantastic staff at European XFEL

Source: Robert Feidenhans'l

And to the fantastic Accelerator Staff

Source: Robert Feidenhans'l

And the FS-CFEL-1 group at DESY

A fly through the European XFEL tunnels

The end

Backup slides from here on