Hybrid X-ray Area Detectors for High-Flux Applications

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Basic Hybrid Pixel Array Detector (PAD)

Diode Detection Layer

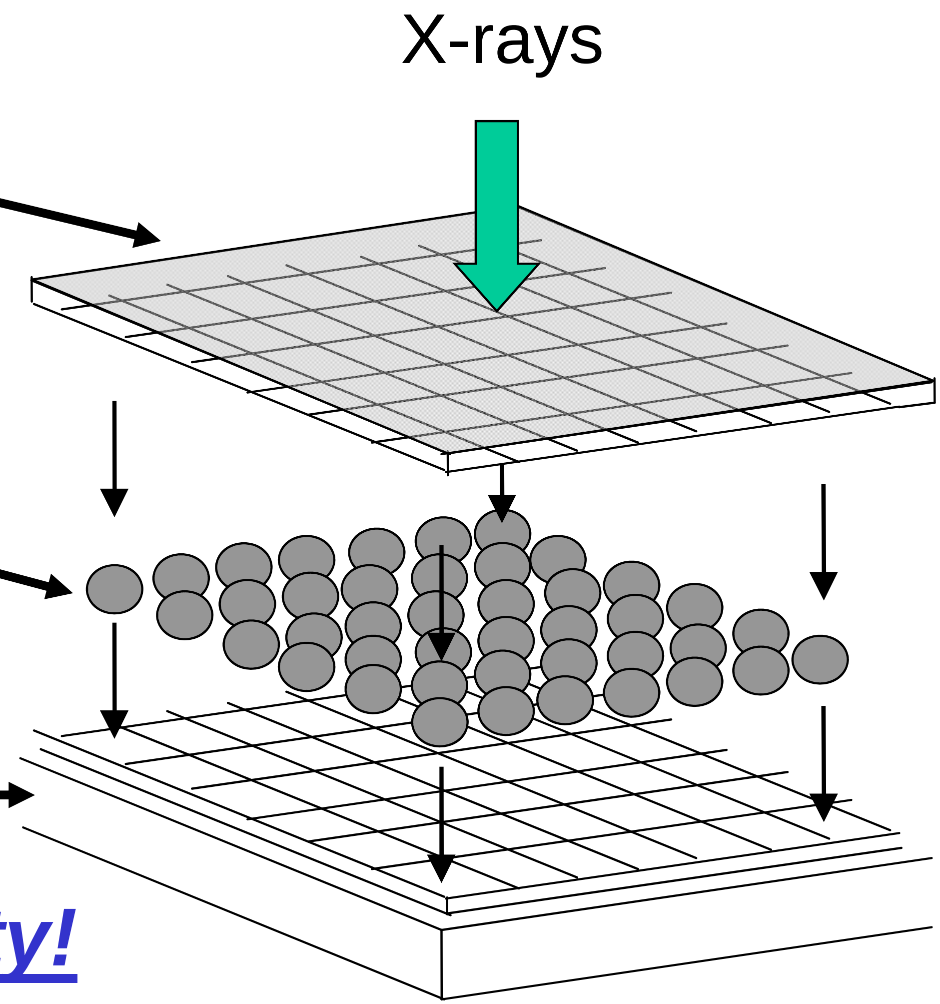
- **Fully depleted, high resistivity**
- **Direct x-ray conversion in Si**

Hybridized with Connecting Bumps

- **Solder, 1 per pixel**

CMOS Layer

- **Signal processing**
- **Signal storage & output**



Gives enormous flexibility!

PADs come in two varieties

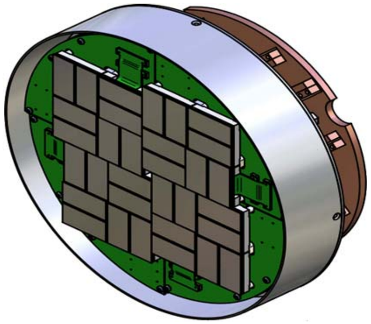
Photon counting PADs

- Front ends count each x-ray individually. (PILATUS, Medipix, Timepix, XPAD, etc.)
- Count-rate limited to ~10^6 -10^7 x-rays/pix/sec.

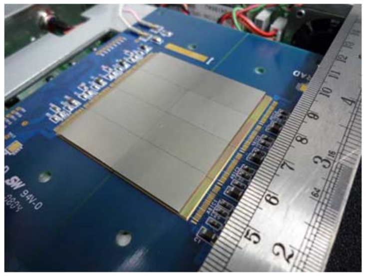
SLS PILATUS

Integrating PADs

- Use an integrating front-end to avoid the count-rate bottleneck.
- Capable of handling enormous count-rate.
- Existing variants include CSPAD, MMPAD, Acrorad, AGIPD, LPD, etc.



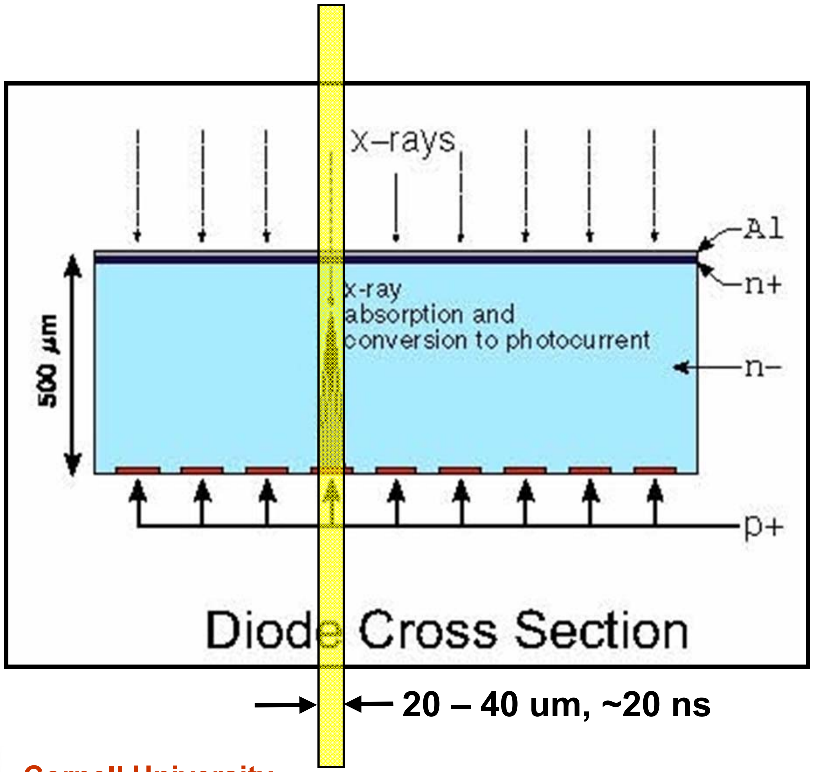
Cornell-SLAC LCLS



Acrorad CdTe

Basic Physics: Direct Detection in Silicon

- **Si is a superb x-ray to electrical signal converter.**
- **@ 10 keV, in < 1 ns, radius of e-h cloud ~ 1 micron.**
- **Number e-h pairs, N_{eh}: $E_{x\text{-}ray}$ / 3.65 eV**
- $\sigma(N_{eh})/N_{eh} = \sqrt{F/N_{eh}}$, where $F \equiv$ Fano Factor = 0.1.
- **10 keV yields N_{eh} = 2740 ± 20. (ΔE = ±3.65 x 20 eV = 146 eV width)**



Charge collection time sets limit on photon counting.

Example 1: High Speed Imaging

Requirements: Rapid Framing Imager

In pix storage for 8 frames

Selectable integration time (μs to seconds)

Dead time < few μs

Well-depth > 10^4 x-rays/pixel/frame (for 1% statistics)

Count rate >10^{10} x-rays/pixel/s ➡ Analog integration needed

Examples:

- Liquid jets
- Shock waves
- Crack propagation & materials failure
- Phase transitions in alloys, polymers & Liq. Crystals
- Cavitation
- Etc.

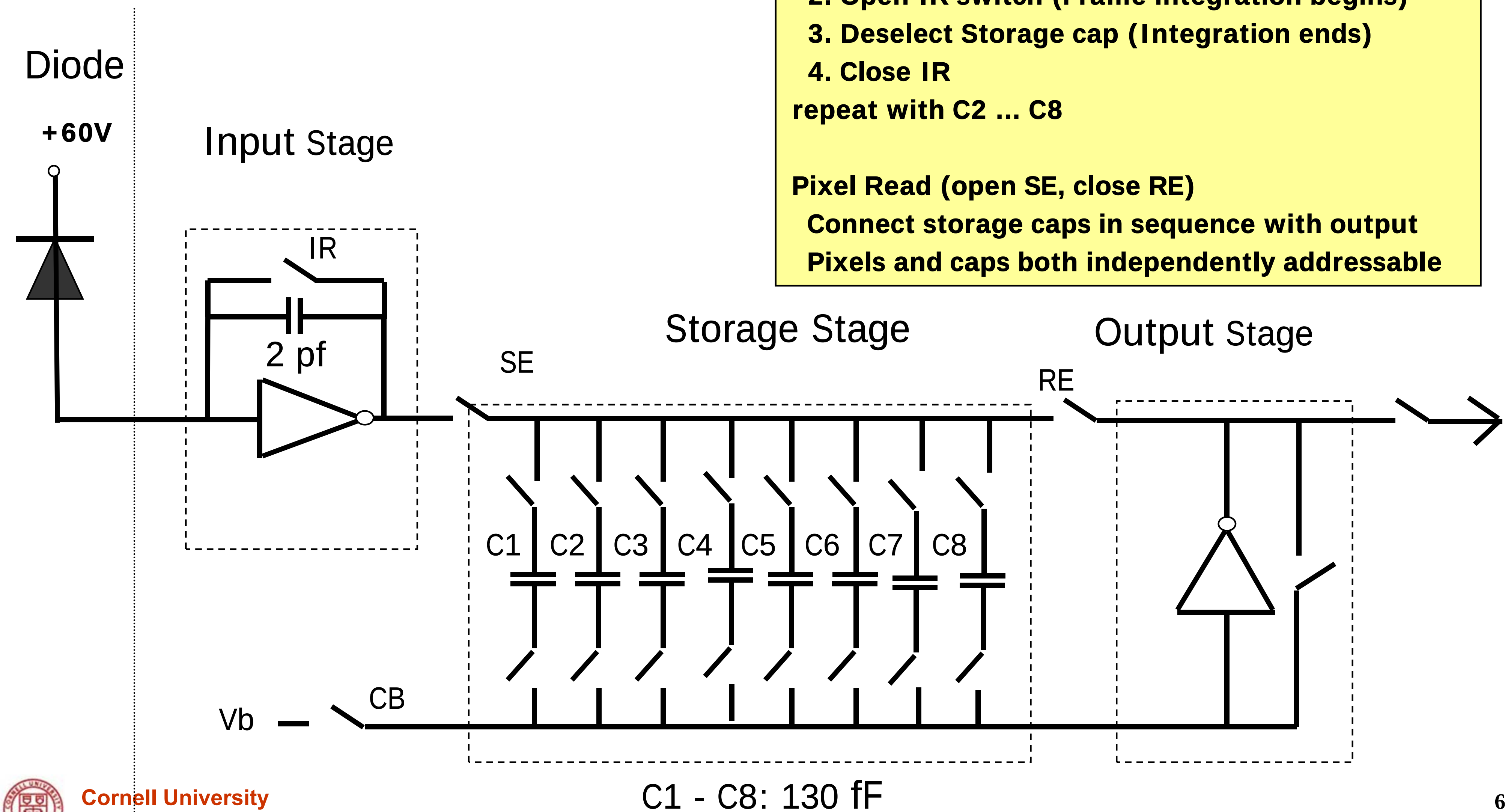
Cornell Prototype Integrating PAD

G. Rossi, M. Renzi, E.F. Eikenberry, M.W. Tate, D. Bilderback, E. Fontes, R. Wixted, S. Barna, S.M. Gruner , *J. Synchr Rad*, 6 (1999) 1096.

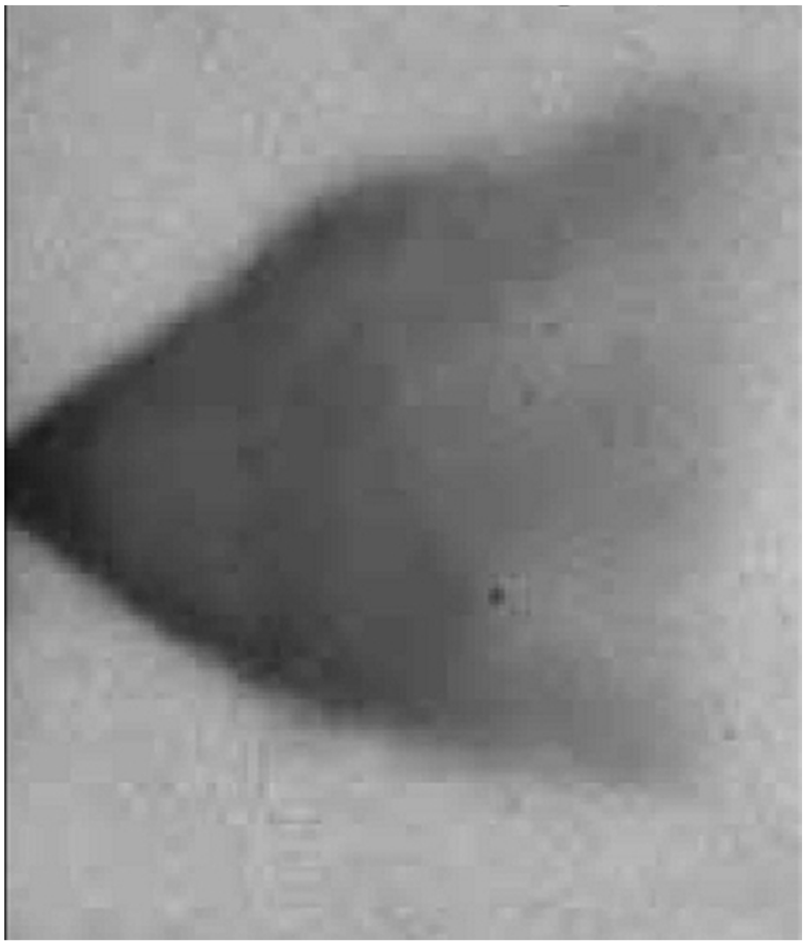
Rapid framing (SE, IR closed)
1. select storage cap C1
2. Open IR switch (Frame integration begins)
3. Deselect Storage cap (Integration ends)
4. Close IR

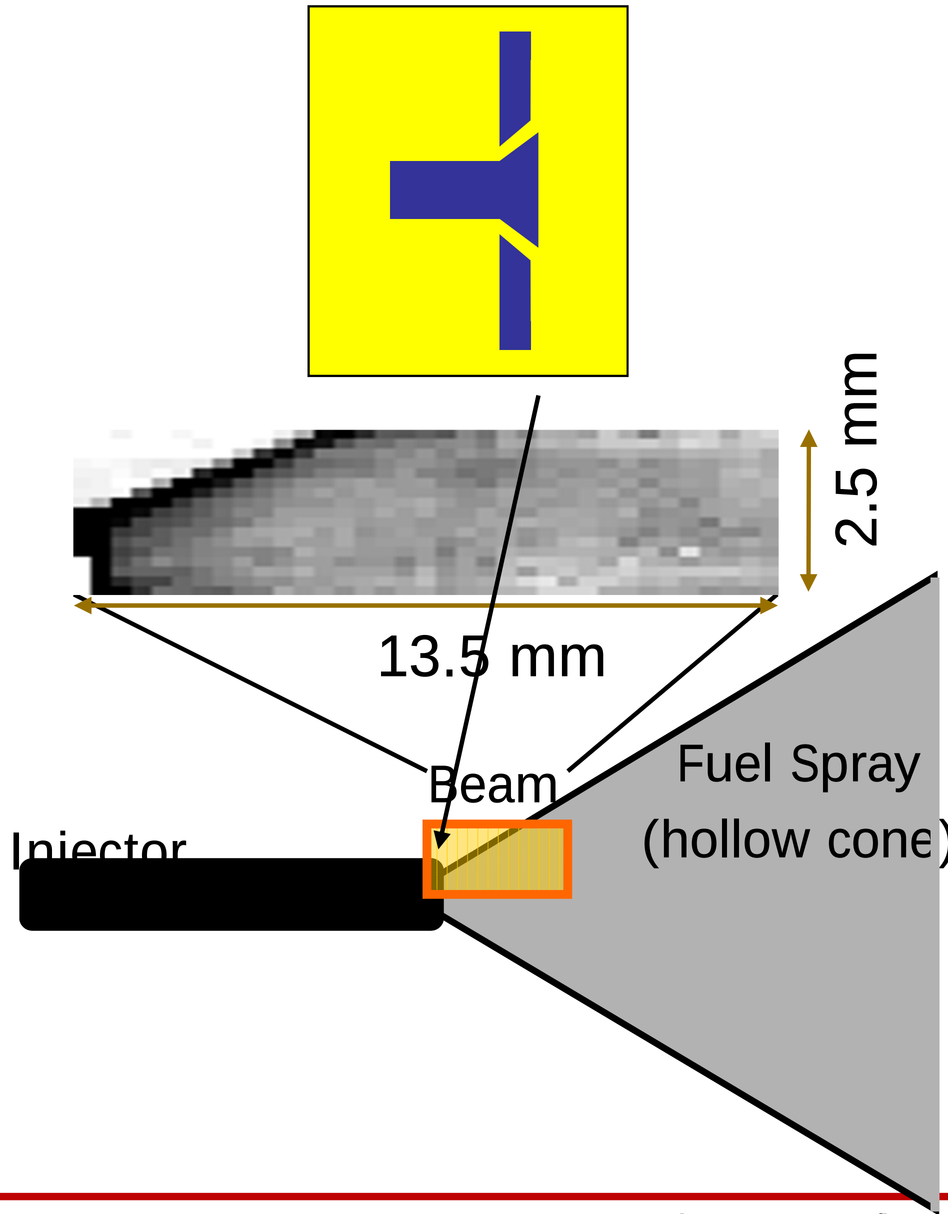
repeat with C2 ... C8

Pixel Read (open SE, close RE)
Connect storage caps in sequence with output
Pixels and caps both independently addressable



Gasoline fuel injector spray

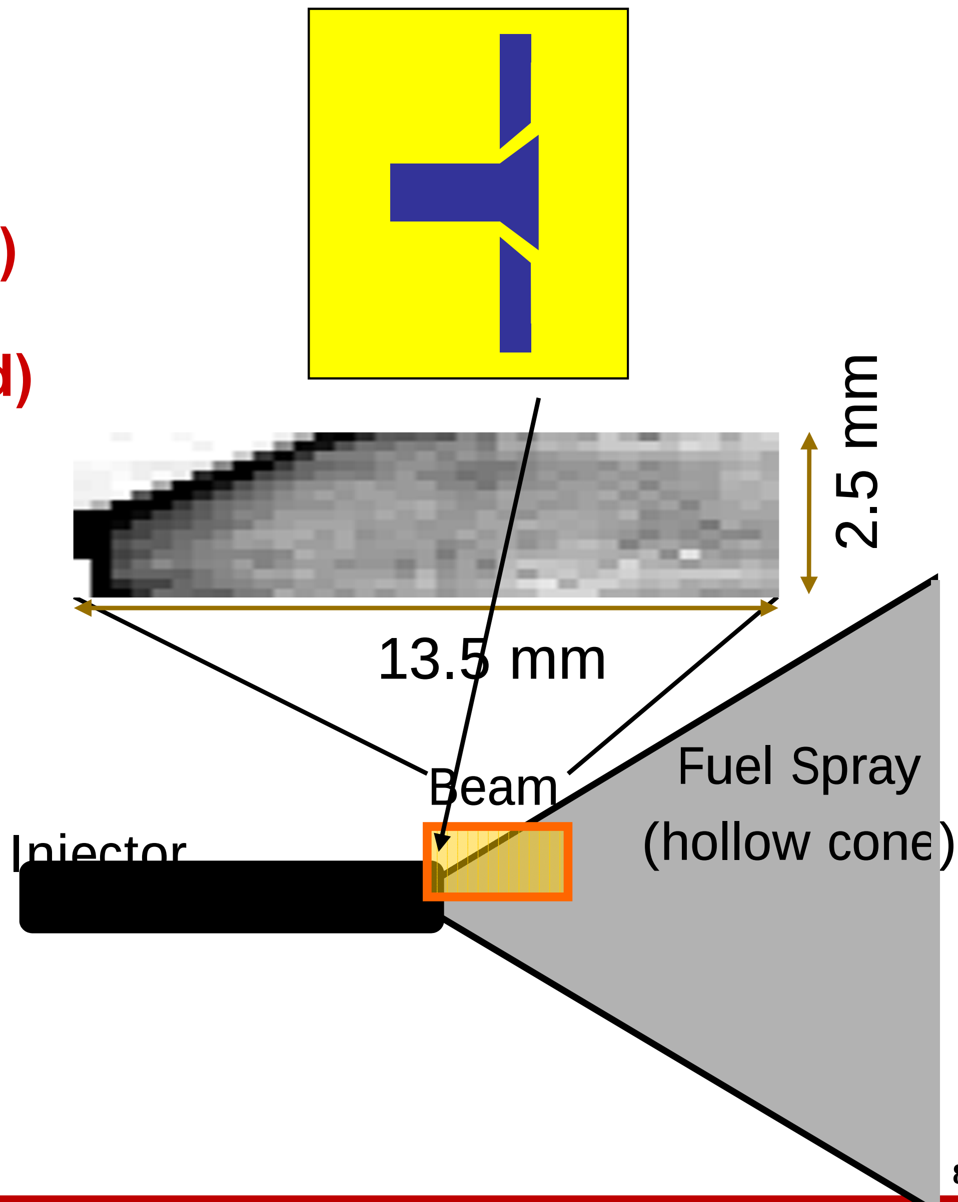




Gasoline fuel injector spray

X-ray beam
- CHESS Beamline D-1
- 6 keV (1% bandpass)
- 2.5 mm x 13.5 mm
- (step sample to tile large area)
- 10^9 x-rays/pix/s
- 5.13 μs integration (2x ring period)

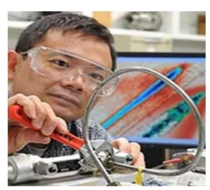
Fuel injection system
- Cerium added for x-ray contrast
- 1000 PSI gas driven
- 1 ms pulse
- 1 ATM Nitrogen



Collaboration: Jin Wang (APS) & S.M. Gruner (Cornell)

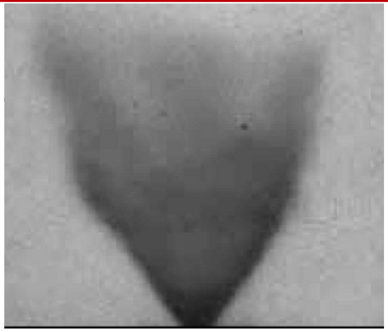
See: Cai, Powell, Yue, Narayanan, Wang, Tate, Renzi, Ercan, Fontes & Gruner

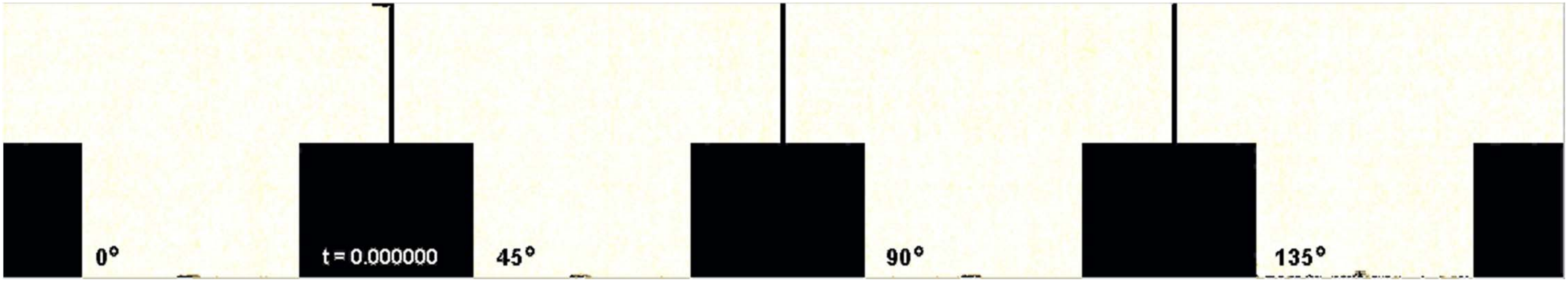
Appl. Phys. Lett. 83 (2003) 1671.



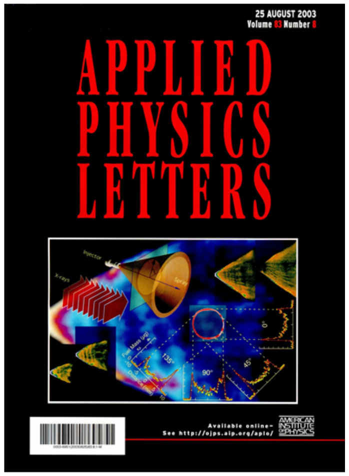
Jin Wang

Gasoline fuel injector spray





- 1.8 ms time sequence (composite). 10^5 images
- 5.13 μs exposure time. (15.4 μs between frames)
- 88 frames (11 groups of 8 frames), Avg. 20x for noise.
- 1000 x-rays/pixel/μs
- Data taken with 4 projections.



Recent work: Liu *et al.*, Appl. Phys. Lett. **94** (2009) 184101

High speed radiography

Supersonic spray from diesel fuel injector

X-ray beam
- **CHESS Beamline D-1**
- **6 keV (1% bandpass)**
- **2.5 mm x 13.5 mm (step sample to tile large area)**
- **10^8 - 10^9 x-rays/pix/s**
- **5.13 μs integration (2x ring period)**

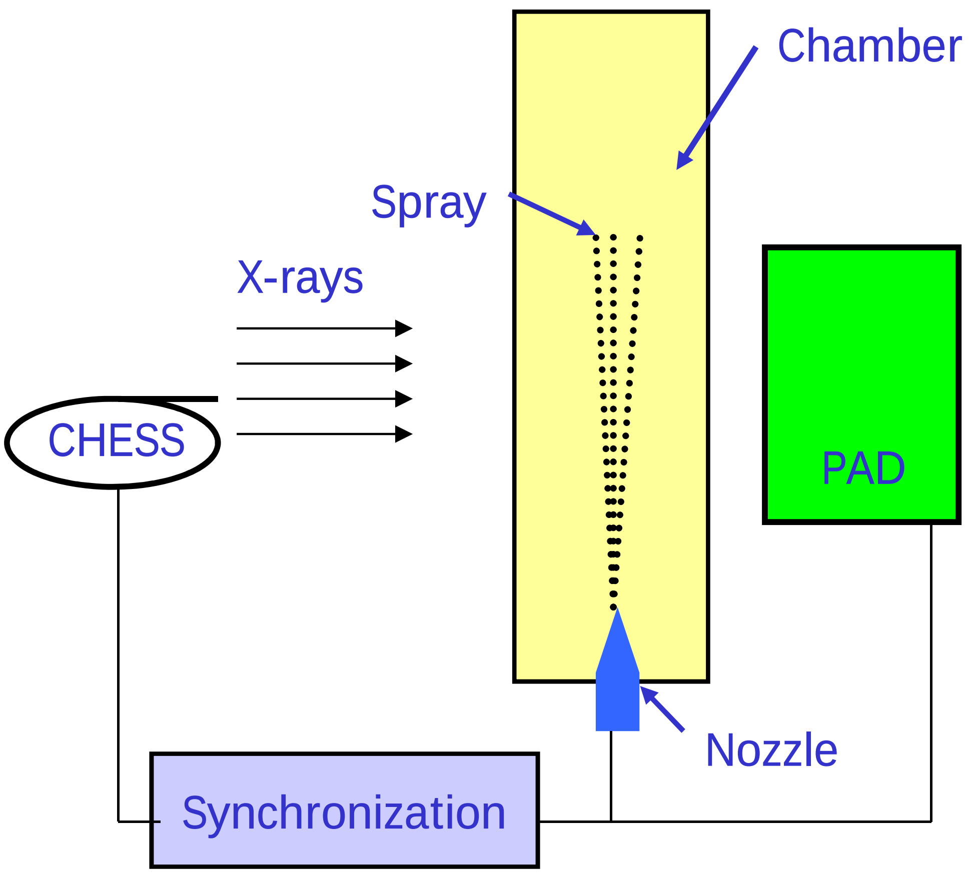
Diesel Fuel Injection System
- **Cerium added for x-ray contrast**
- **1350 PSI gas driven**
- **1.1 ms pulse**
- **1 ATM SF_6 in chamber**

Collaboration: Jin Wang (APS) & S.M. Gruner (Cornell)

See: McPhee, Tate, Powell, Yue, Renzi, Ercan, Narayanan, Fontes, Walther, Schaller, Gruner & Wang

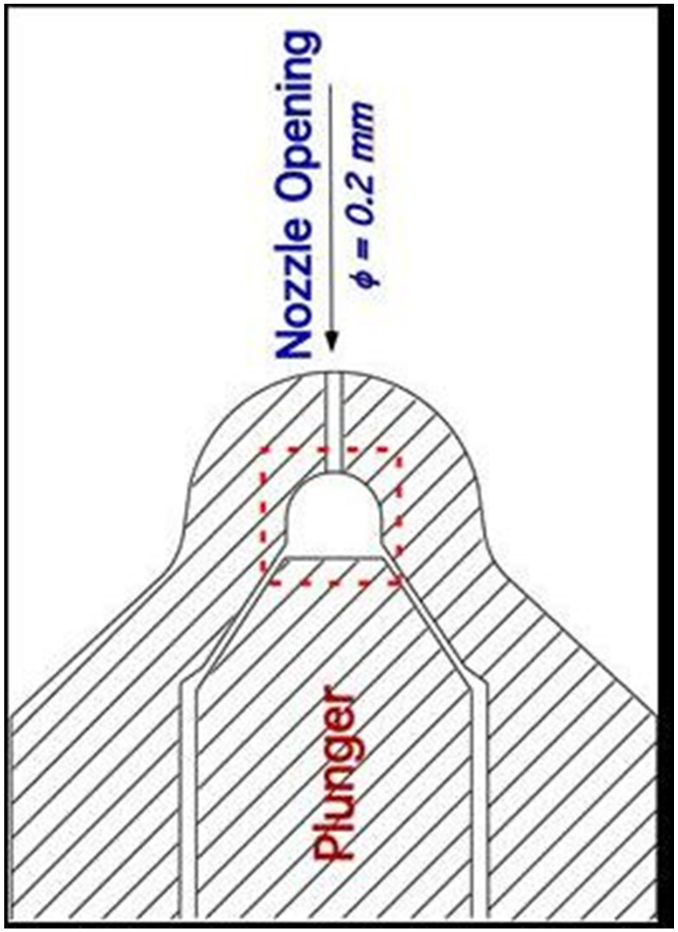
***Science* 295 (2002) 1261-1263.**

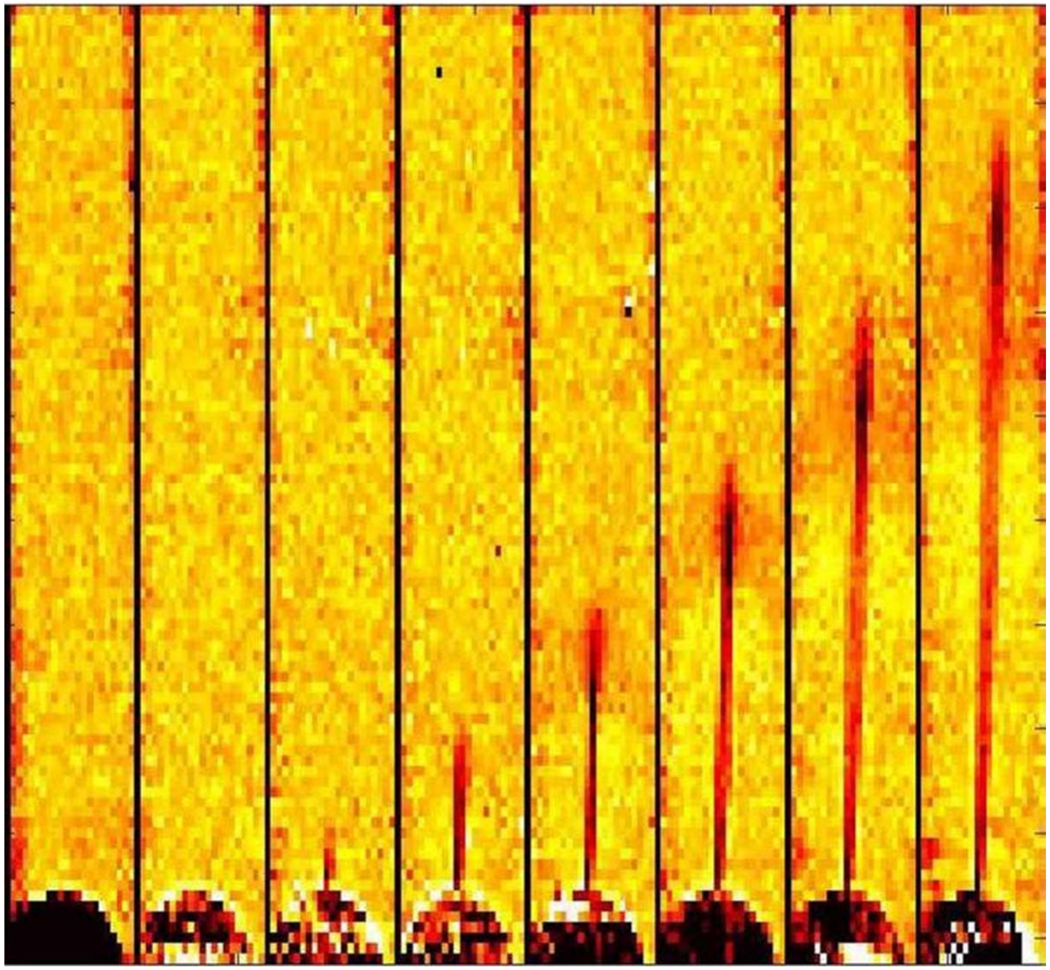
Recent work: Im *et al*.., Phys. Rev Lett. **102** (2009) 074501



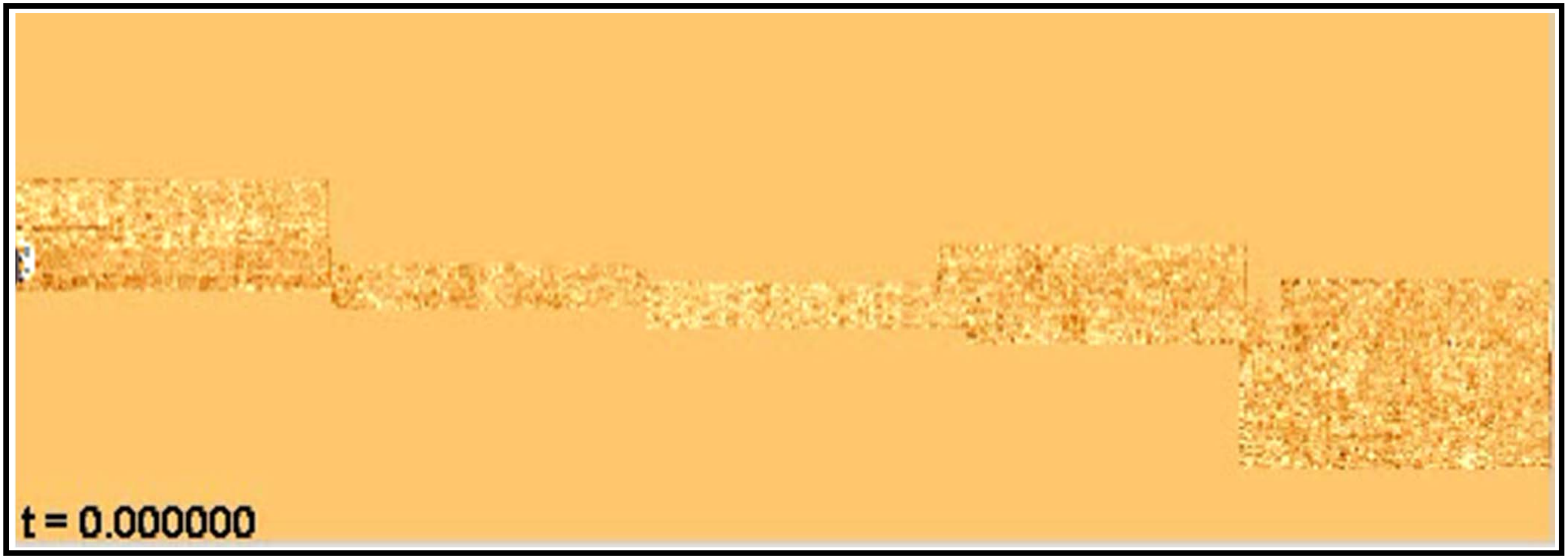
High speed radiography

Supersonic spray from diesel fuel injector





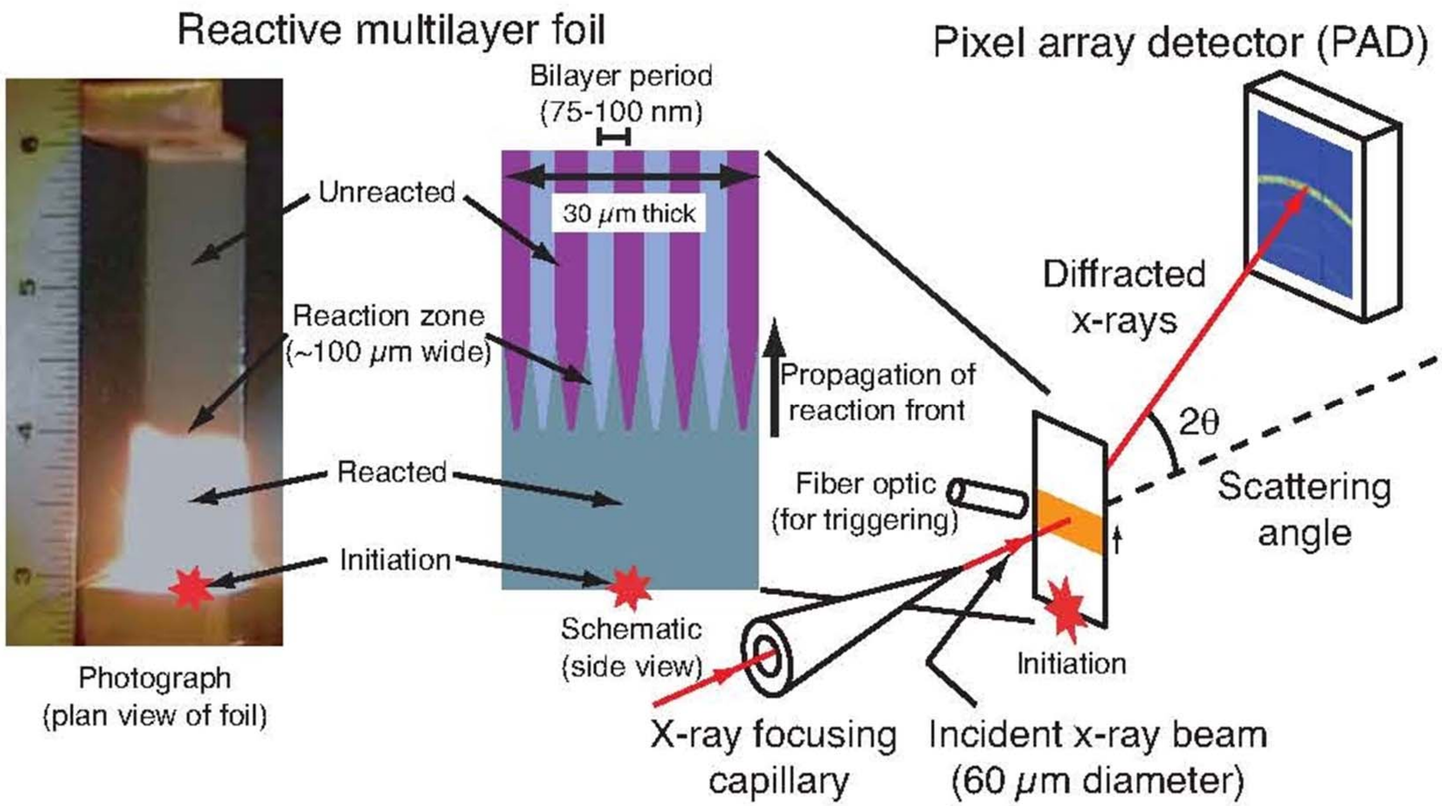
Diesel fuel injector spray

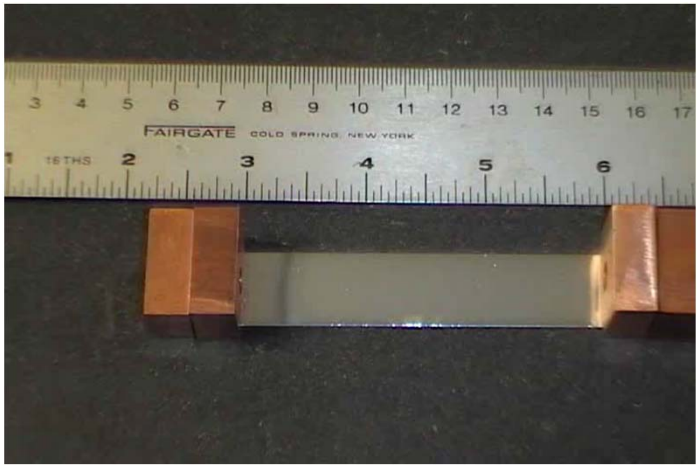


- 1.3 ms time sequence (composite of 34 sample positions)
- 5.13 μs exposure time (2.56 μs between frames)
- 168 frames in time (21 groups of 8 frames) Average 20x for S/N
- Sequence comprised of 5 x 10^4 images

A. MacPhee, *et al*, Science (2002). **295**, 1261-1263.

Time-Resolved Phases of Reactive Metal Foils

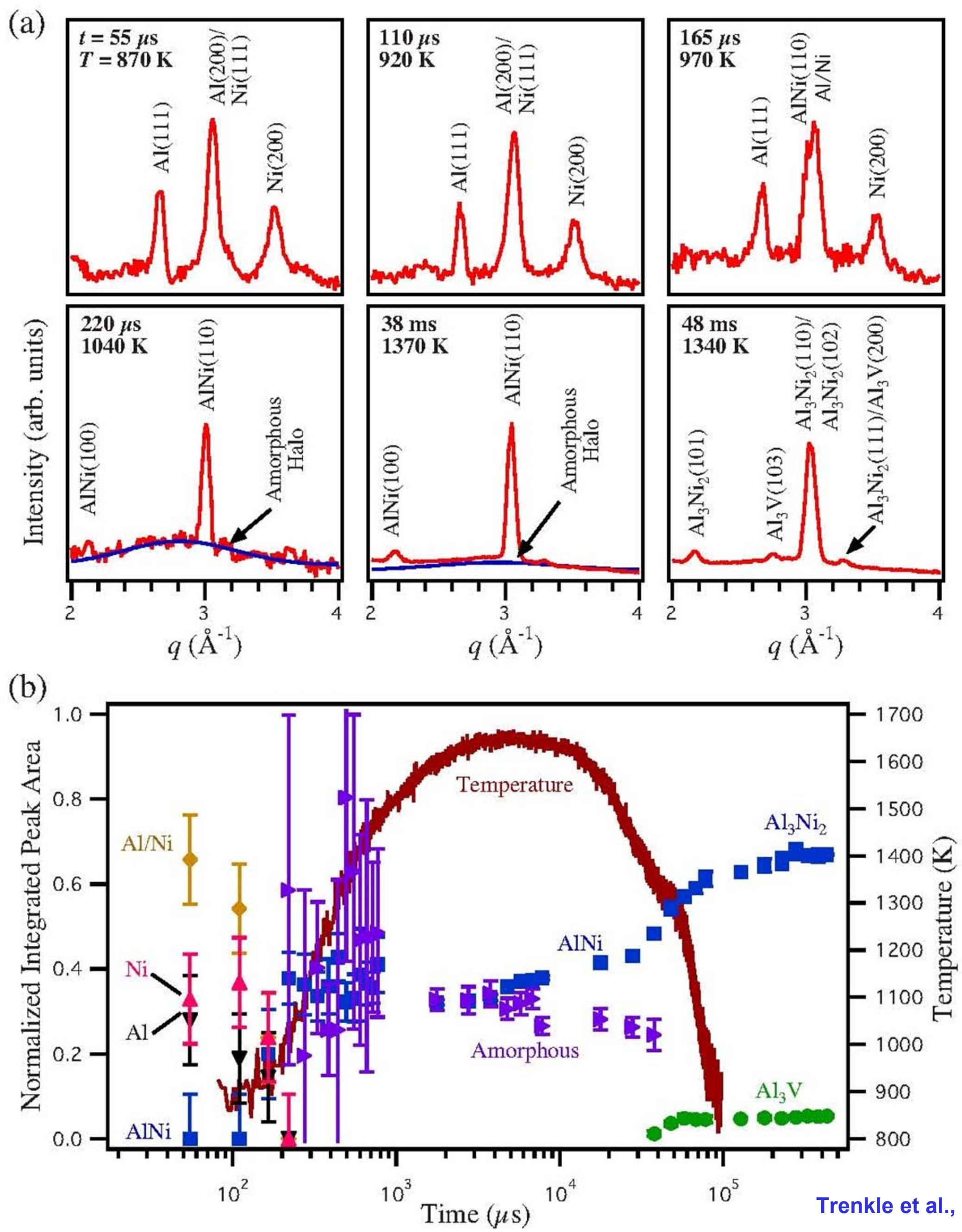




Trenkle et al., J. Appl. Phys, 107 (2010) 113511

Collaboration with Hufnagel & Weihs at Johns Hopkins University.

Time-Resolved Phases of Reactive Metal Foils



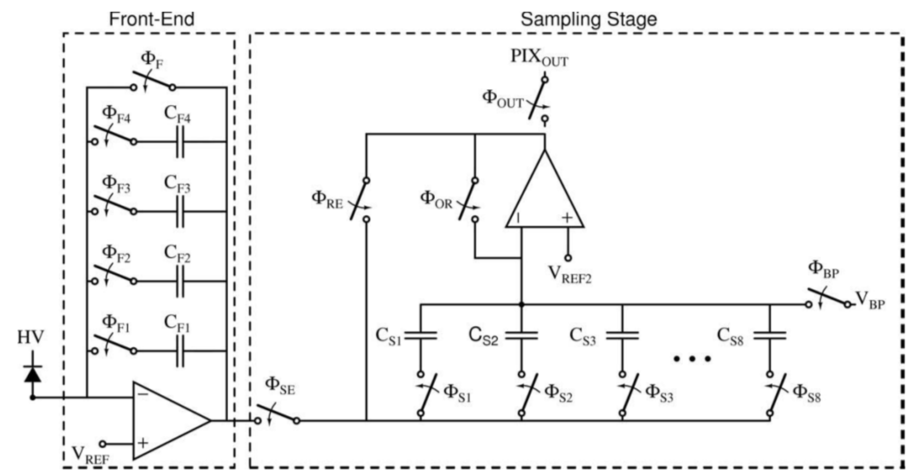
Trenkle et al., J. Appl. Phys, 107 (2010) 113511

Keck PAD

Considerations:

- **Front-end amplifier settling time.**
- **Time to transfer data to off-ASIC digital memory. Parallelize!**

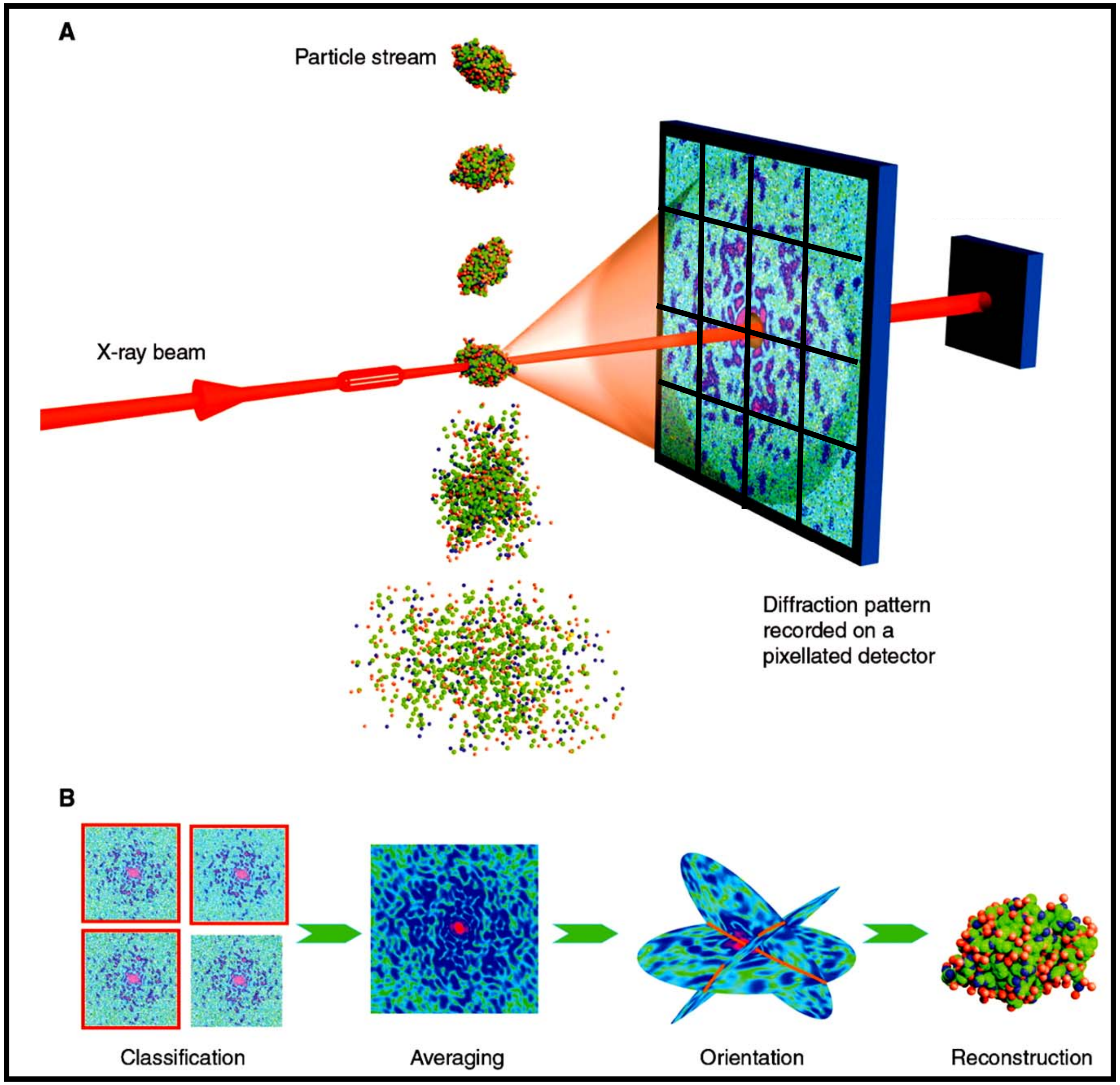
KECK PAD	
Parameter	**Target Value**
Noise	< 0.5 x-ray/pixel/accumulation
Minimum exposure time	<150 ns for 12-bit imaging
Capacitor well depth	2000 – 4000 x-rays
Nonlinearity (% full well)	< 0.2%
Diode conversion layer	500 µm thick Si
Number of capacitor wells/pix	8
Full chip frame time	1 msec/frame, e.g., 8 msec for 8 capacitors
Radiation lifetime	> 50 Mrad at detector face @ 8 keV
Pixel size	150 µm on a side, or 128 x 128 pixels per IC
Detector chip format	2 x 4 chips = 256 x 512 pixels
Dark current	2 x-rays/pix/sec



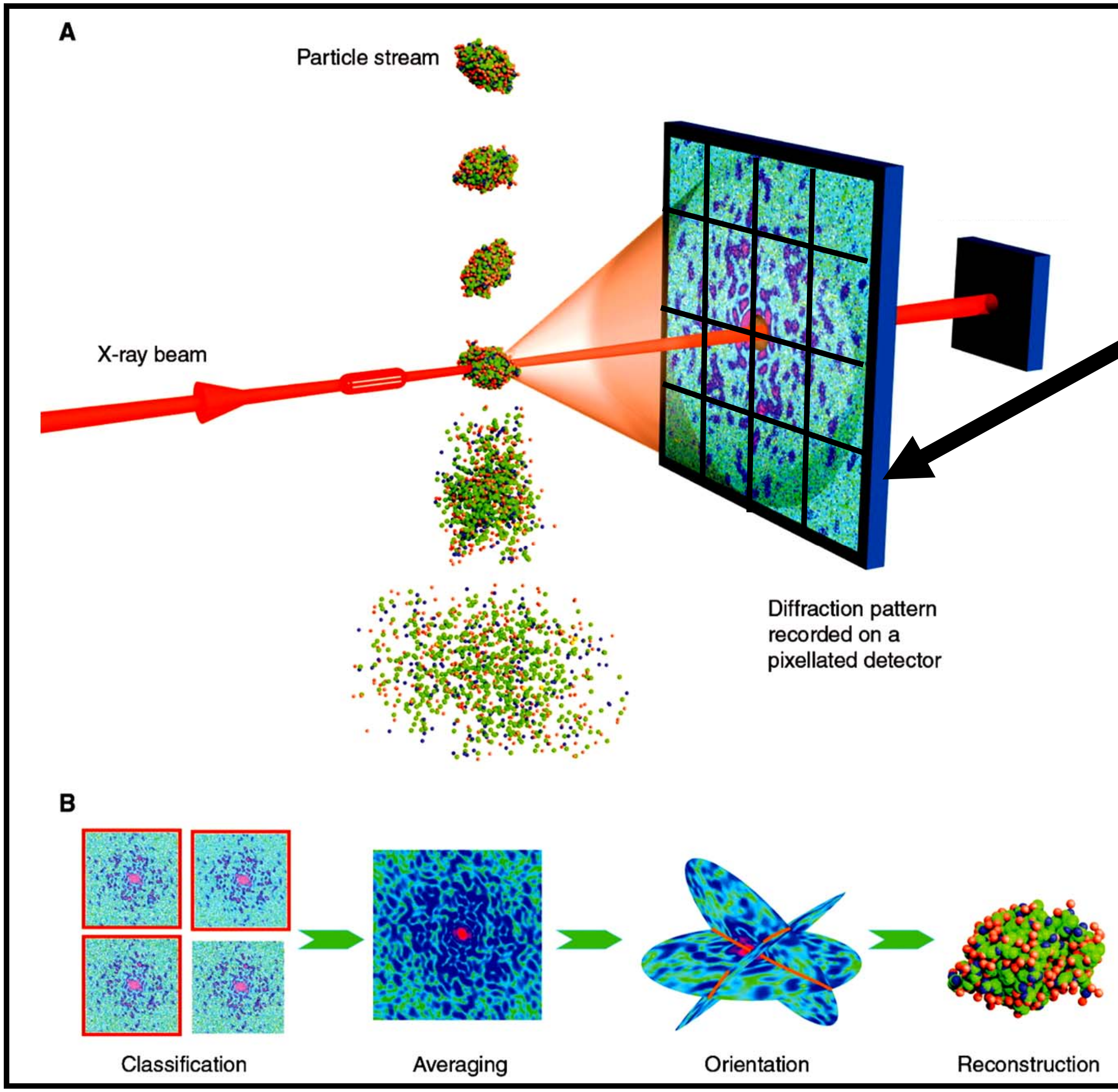
Koerner & Gruner, J. Synchro. Rad. 18 (2011) 157.

< 150 ns for 12 bit settling shown. Equivalent to ~4000 8 keV x-rays. Faster for fewer bits. A few bits in 10's of ns should be feasible.

Example 2: LCLS Coherent Imaging Experiment

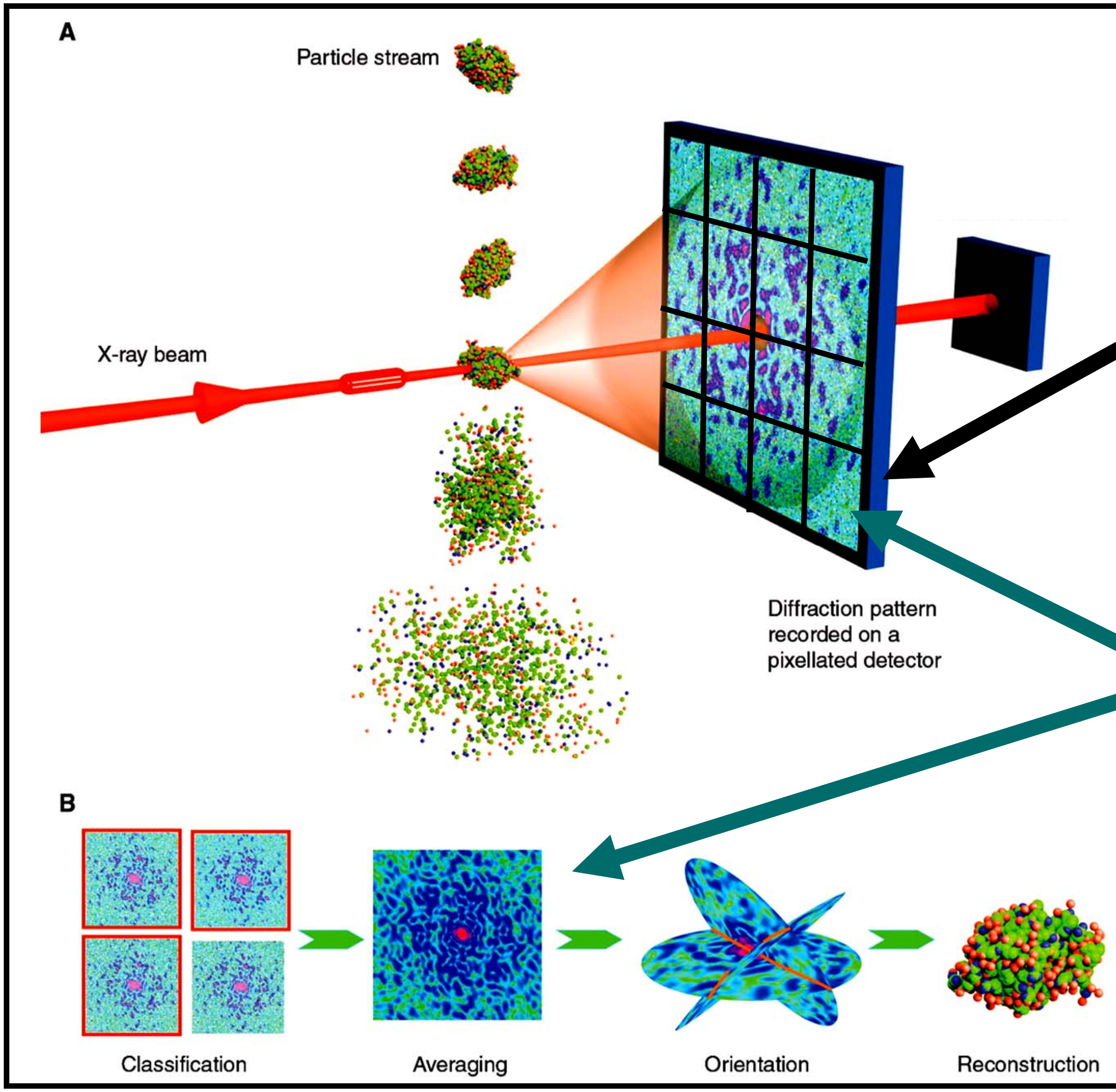


Example 2: LCLS Coherent Imaging Experiment



- Tiled PAD.
- 120 Hz frame.

Example 2: LCLS Coherent Imaging Experiment



- Tiled PAD.
- 120 Hz frame.

- Diffuse Scattering
- Variable envelope
- << 1 X-ray/pix/frm
- SAXS: Lots of x-rays

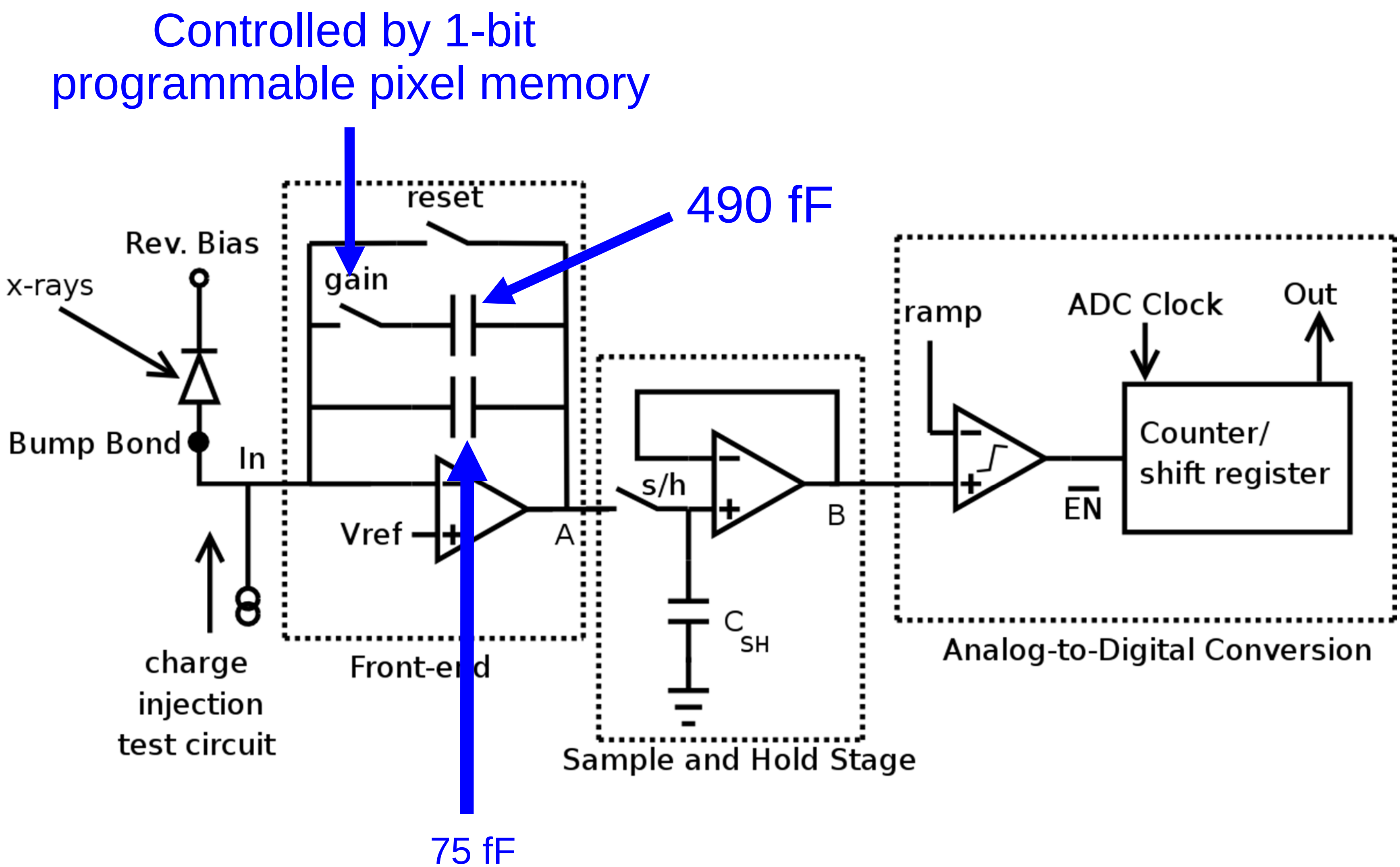
Requirements

Parameter	Minimum Requirement
Energy Range	4-8 keV
Well-depth/pixel	10^3
Readout Frame rate	120Hz
Signal/Noise	>3 for single 8 keV photon
DQE	> 90% at 8 keV
Pixel size	100-200µm
Detector Area	500x500 pixels

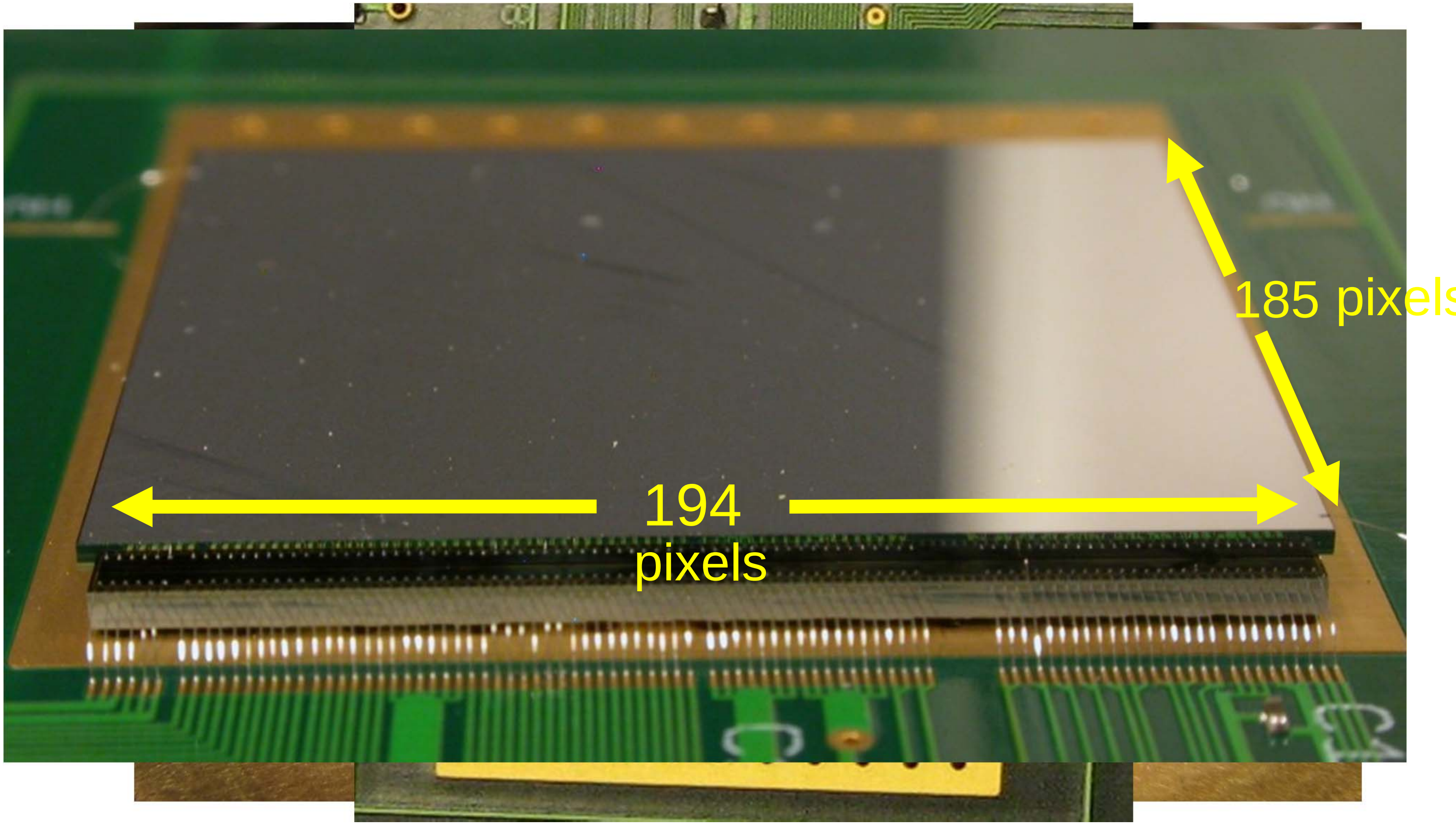
Requirements

Parameter	Minimum Requirement
Energy Range	4-8 keV
Well-depth/pixel	10^3 → > 2500 8 keV x-rays/pixels/image
Readout Frame rate	120Hz
Signal/Noise	>3 for single 8 keV photon → 8
DQE	> 90% at 8 keV
Pixel size	100-200µm → 110 x 110 microns
Detector Area	500x500 pixels → 1516 x 1516 pixels

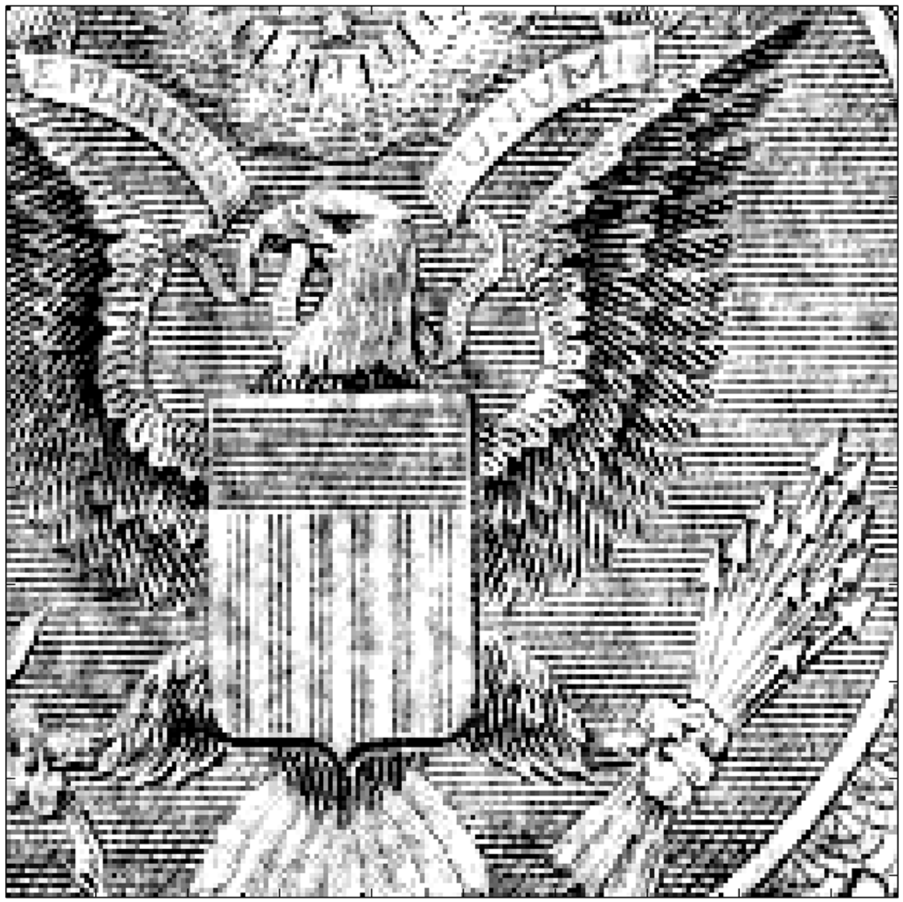
Pixel-Level Schematic



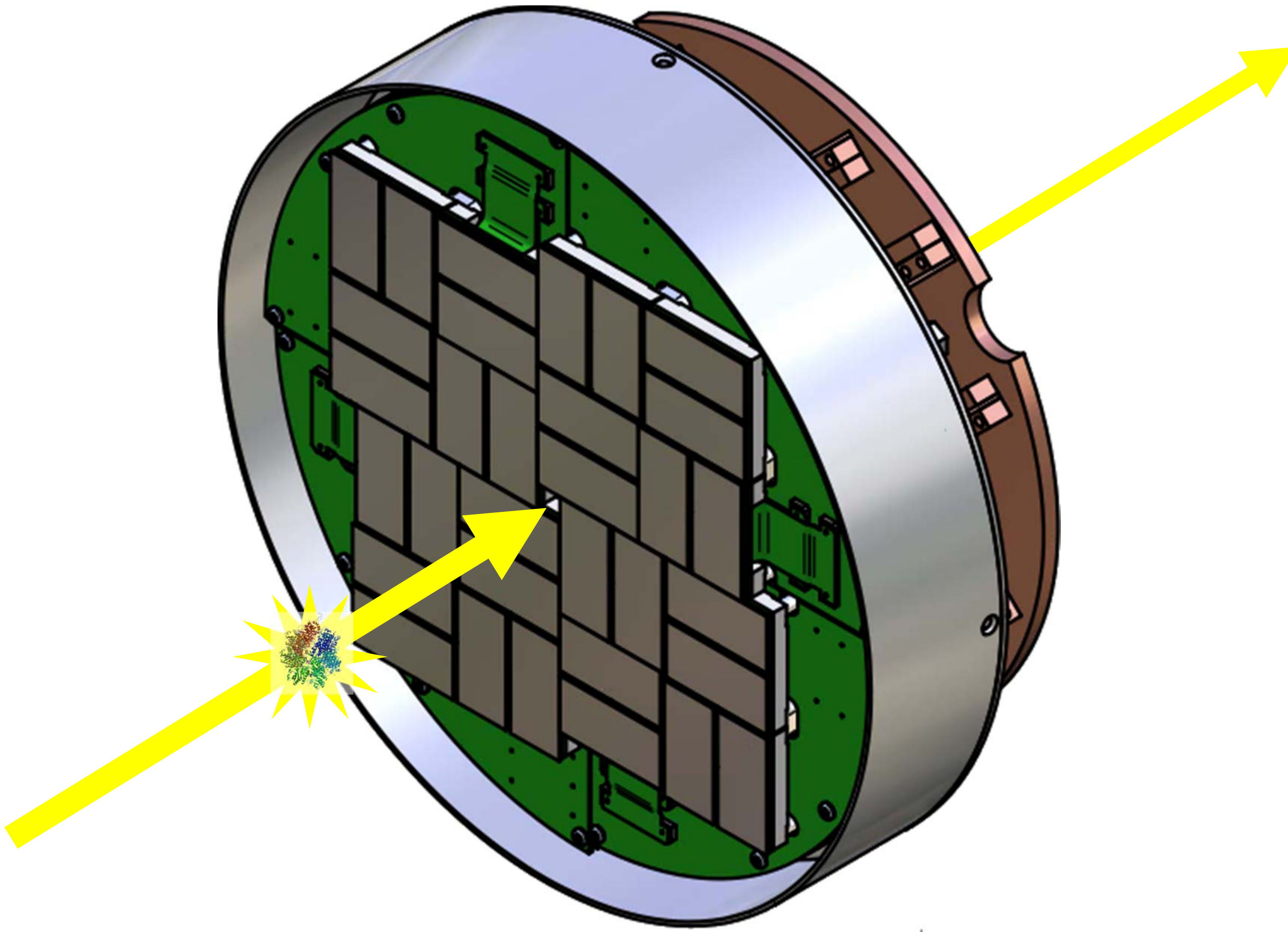
Detector



Example Radiograph of a Dollar Bill



So, what does the final detector look like?
Cornell-SLAC PAD (CSPAD)



1.9 Å Structure from microcrystal at LCLS

Sciencexpress
Reports

High-Resolution Protein Structure Determination by Serial Femtosecond Crystallography

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[1]Linac Coherent Light Source (LCLS), SLAC National Accelerator Laboratory, 2575 Sand Hill Road, Menlo Park, CA 94025, USA. [2]Max-Planck-Institut für Medizinische Forschung, Jahnstrasse 29, 69120 Heidelberg, Germany.[3]Max Planck Advanced Study Group, Center for Free-Electron Laser Science, Notkestrasse 85, 22607 Hamburg, Germany. [4]Center for Free-Electron Laser Science, DESY, Notkestrasse 85, 22607 Hamburg, Germany. [5]Department of Physics, Arizona State University, Tempe, AZ 85287, USA. [6]Particle Physics and Astrophysics, SLAC National Accelerator Laboratory, 2575 Sand Hill Road, Menlo Park, CA 94025, USA. [7]Department of Physics, Laboratory of Atomic and Solid State Physics, Cornell University, Ithaca, NY 14853, USA. [8]Wilson Laboratory, Cornell University, CHESS, Ithaca, NY 14853, USA. [9]Electrical and Computer Engineering, SUNY Oswego, Oswego, NY 13126, USA. [10]The Johns Hopkins University Applied Physics Laboratory, 11100 Johns Hopkins Road, Laurel, MD 20723, USA. [11]Nikhef, National Institute for Subatomic Physics, Science Park 105, 1098 XG, Amsterdam, Netherlands. [12]European Synchrotron Radiation Facility, 38043 Grenoble Cedex, France. [13]Department of Chemistry and Molecular Biology, University of Gothenburg, SE-405 30 Gothenburg, Sweden. [14]PULSE Institute, SLAC National Accelerator Laboratory, 2575 Sand Hill Road, Menlo Park, CA 94025, USA. [15]Department of Chemistry and Biochemistry, Arizona State University, Tempe, AZ 85287–1604, USA. [16]University of Hamburg, Luruper Chaussee 149, 22761 Hamburg, Germany. [17]Joint Laboratory for Structural Biology of Infection and Inflammation, Institute of Biochemistry and Molecular Biology, University of Hamburg, and Institute of Biochemistry, University of Lübeck, at DESY, Hamburg, Germany. [18]Laboratory of Molecular Biophysics, Department of Cell and Molecular Biology, Uppsala University, Husargatan 3 (Box 596), SE-751 24 Uppsala, Sweden. *To whom correspondence should be addressed. E-mail: sboutet@slac.stanford.edu

Structure determination of proteins and other macromolecules has historically required the growth of high-quality crystals sufficiently large to diffract x-rays efficiently while withstanding radiation damage. We applied serial femtosecond crystallography (SFX) using an x-ray free-electron laser (XFEL) to obtain high resolution structural information from microcrystals (<1×1×3 μm³) of the well-characterized model protein lysozyme. The agreement with synchrotron data demonstrates the immediate relevance of SFX for analyzing the structure of the large group of difficult-to-crystallize molecules.

Elucidating macromolecular structures by x-ray crystallography is an important step in the quest to understand the chemical mechanisms underlying biological function. Although facilitated greatly by synchrotron x-ray sources, the method is limited by crystal quality and radiation damage (*1*). Crystal size and radiation damage are inherently linked, as reducing radiation damage requires lowering the incident fluence. This in turn calls for large crystals that yield sufficient diffraction intensities while reducing the dose to individual molecules in the crystal. Unfortunately, growing well-ordered large crystals can be difficult in many cases, particularly for large macromolecular assemblies and membrane proteins. In contrast, micron-sized crystals are frequently observed. Although diffraction data of small crystals can be collected using micro-focus synchrotron beamlines, this remains a challenging approach due to the rapid damage suffered by these small crystals (*1*).

Serial femtosecond crystallography (SFX) using x-ray free-electron laser (XFEL) radiation is an emerging method for 3D structure determination using crystals ranging from a few micrometers to a few hundred nanometers in size and potentially even smaller. This method relies upon x-ray pulses that are both sufficiently intense to produce high quality diffraction while of short enough duration to terminate before the onset of significant radiation damage (*2–4*). X-ray pulses of only 70 femtoseconds duration terminate before any chemical damage processes have time to occur, leaving primarily ionization and X-ray induced thermal motion as the main sources of radiation damage (*2–4*). SFX therefore promises to break the correlation between sample size, damage and resolution in structural biology. In SFX, a liquid microjet is used to introduce fully hydrated randomly oriented crystals into the single-pulse XFEL beam (*5–8*), as illustrated in Fig. 1. A recent low-resolution proof-of-principle demonstration of SFX performed at the Linac Coherent Light Source (LCLS) (*9*) using crystals of photosystem I ranging in size from 200 nm to 2 μm produced interpretable electron density maps (*6*). Other demonstration experiments using crystals grown in-vivo (*7*) as well as in the lipidic sponge phase for membrane proteins (*8*) were recently published. However, in all these cases, the x-ray energy of 1.8 keV (6.9 Å) limited the resolution of the collected data to approximately 8 Å. Data collection to a resolution better than 2 Å became possible with the recent commissioning of the LCLS Coherent X-ray Imaging (CXI) instrument (*10*). The CXI instrument provides hard x-ray pulses suitable for high-resolution crystallography and is equipped with Cornell-SLAC Pixel Array Detectors (CSPADs) consisting of 64 tiles of 192 × 185 pixels each, arranged as shown in Fig. 1 and figs. S1 and S2. The CSPAD supports the 120 Hz readout rate required to measure each x-ray pulse from LCLS (*11*).

Here we describe SFX experiments performed at CXI analyzing the structure of hen egg white lysozyme (HEWL) as a model system using microcrystals of approximately 1×1×3 μm³ (*4, 11*). HEWL is an extremely well-characterized protein that crystallizes easily. It was the first enzyme to have its structure determined by x-ray diffraction (*12*), and has since been thoroughly characterized to very high resolution (*13*). Lysozyme has served as a model system for many investigations, includ-

Sciencexpress/ http://www.sciencemag.org/content/early/recent / 31 May 2012 / Page 1/ 10.1126/science.1217737

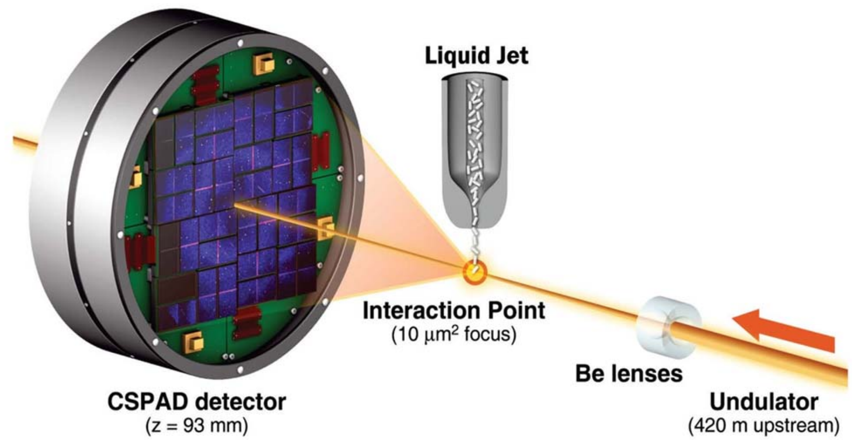


Fig. 1. Experimental geometry for serial femtosecond crystallography at the Coherent X-ray Imaging instrument. Single pulse diffraction patterns from single crystals flowing in a liquid jet are recorded on a CSPAD at the 120 Hz repetition rate of LCLS. Each pulse was focused at the interaction point using 9.4 keV x-rays. The sample-to-detector distance (z) was 93 mm.

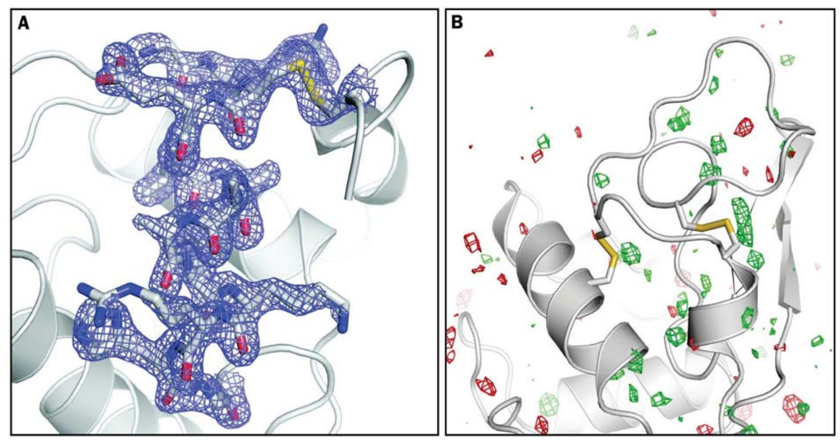


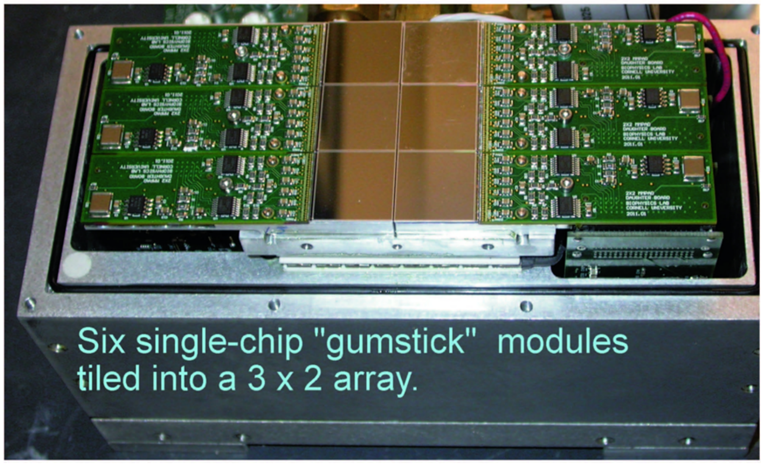
Fig. 2. (**A**) Final, refined $2mF_{obs}$-DF_{calc} (1.5σ) electron density map (*18*) of lysozyme at 1.9 Å resolution calculated from 40 fs pulse data. (**B**) F_{obs}[40 fs]-F_{obs}[synchrotron] difference Fourier map, contoured at +3 σ (green) and -3 σ (red). No interpretable features are apparent. The synchrotron dataset was collected with a radiation dose of 24 kGy.

Key point: Microxtals overcome the crystallization bottleneck.

Example 3: Mixed Mode PAD*

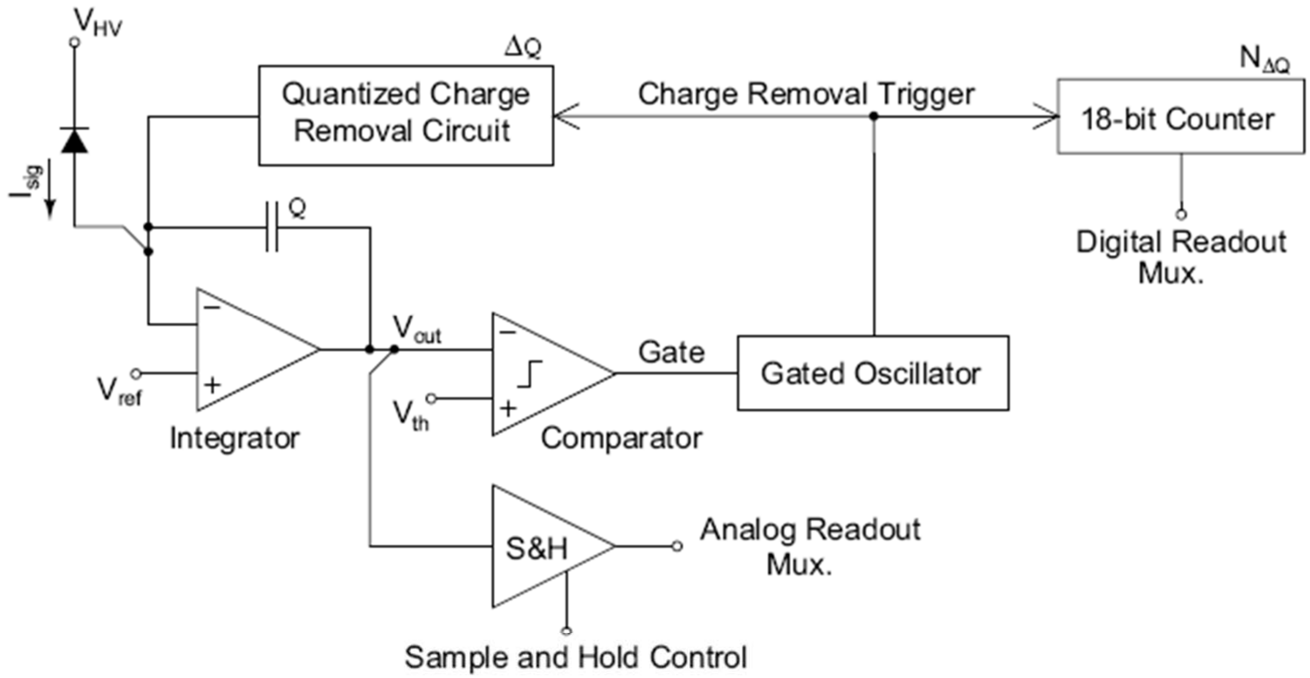
PAD Tile Format	6 modules, each 128 x 128 pixels
Pixel Size	150 μm x 150 μm
Max Frame Rate	1,000 Hz
Data Rate	400 MB/s
Read Noise (rms)	0.15 X-ray [8 keV] / pix
Sensor	300 um silicon, fully depleted
Well Capacity	> 3 x 10^7 X-rays/pix/frame

Reconfigurable Tiled Array



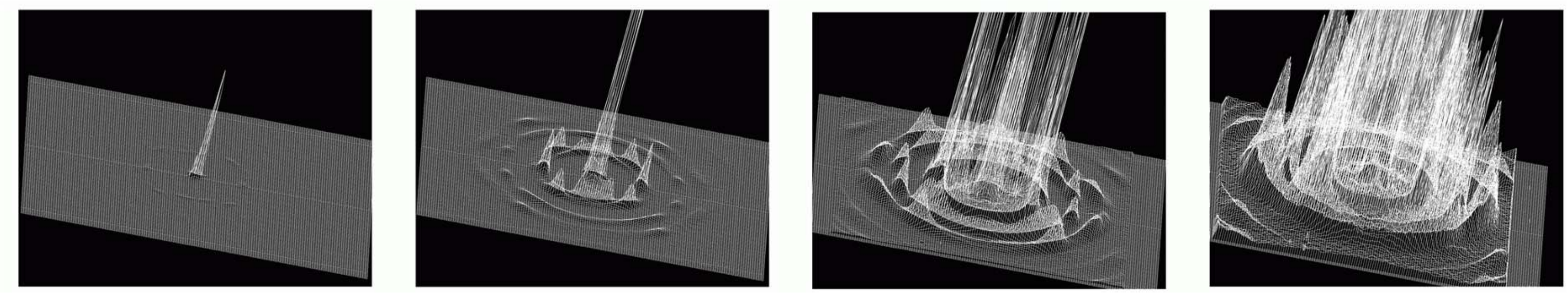
*Chip development: collaboration with Area Detector Systems Corp.

Example 3: Mixed Mode PAD

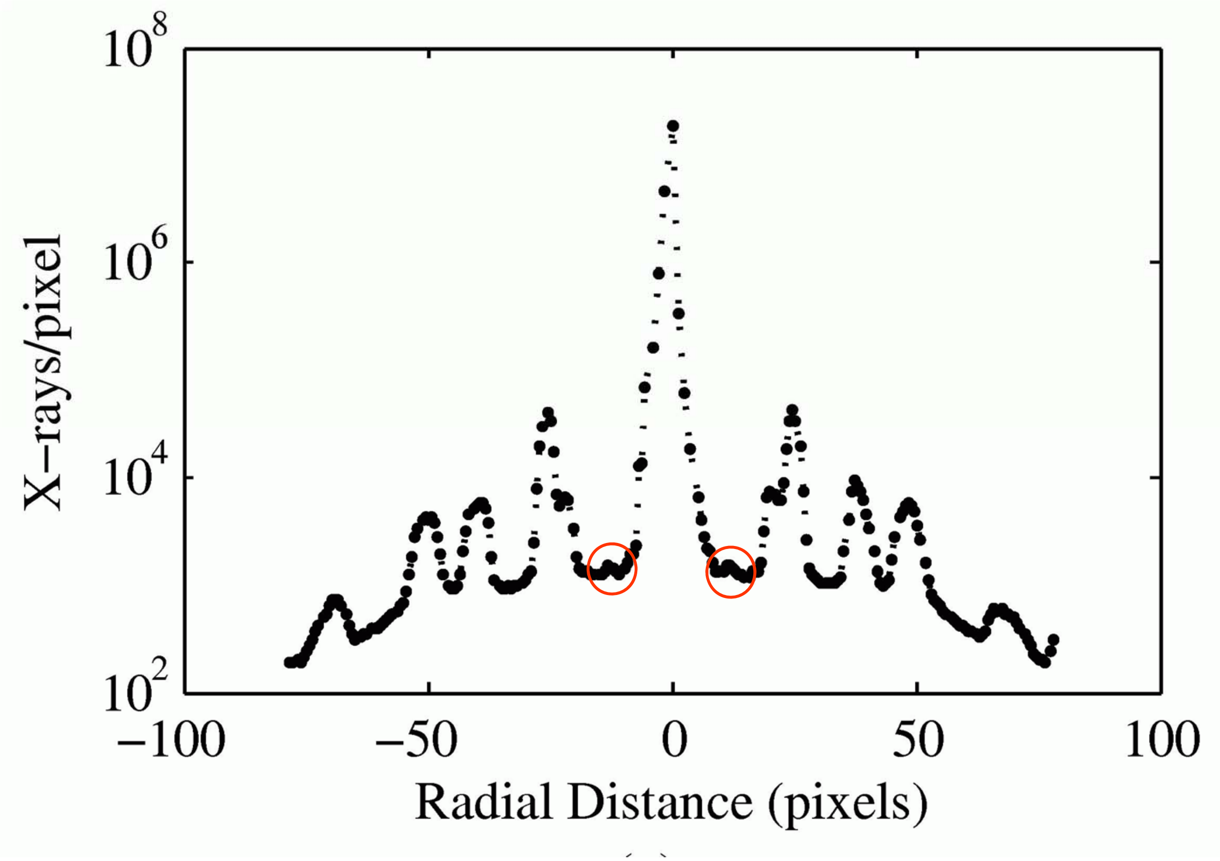


1. Photocurrent ($I_{\rm sig}$) collects in the integrator.
2. The integrator output ($V_{\rm out}$) slews towards ground.
3. When $V_{\rm out} < V_{\rm th}$, the comparator activates a gated oscillator.
4. Each oscillator cycle removes a fixed quantity of charge (ΔQ) from the integrator and increments an in-pixel counter ($N_{\Delta Q}$).

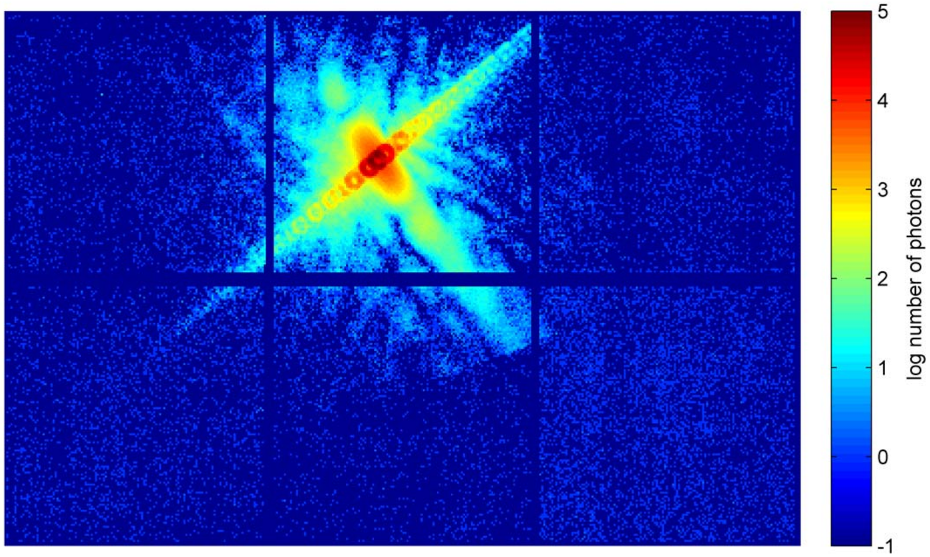
Direct Detection PSF is Superb!



MMPAD. At @ CHESS F2. 1 sec expos. No Beamstop!

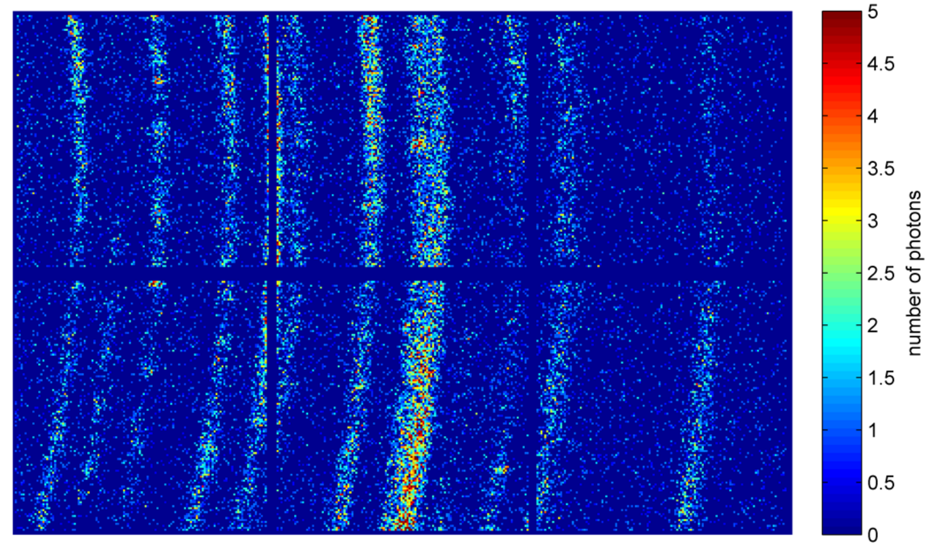


Wide dynamic range provides extraordinary experimental flexibility



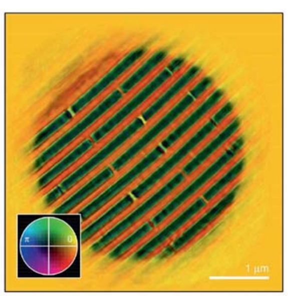
1 s diffraction from Pt zone plate. 10^5 photons full scale

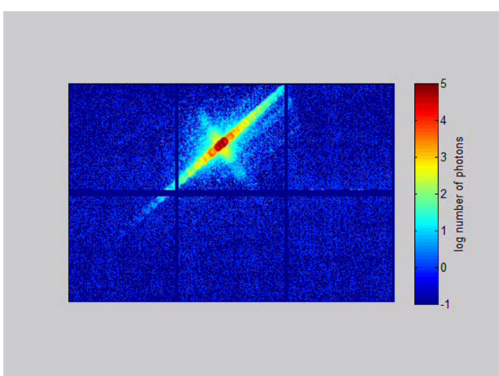
(APS: Vine, McNulty; XFEL: Mancuso Group; Cornell)

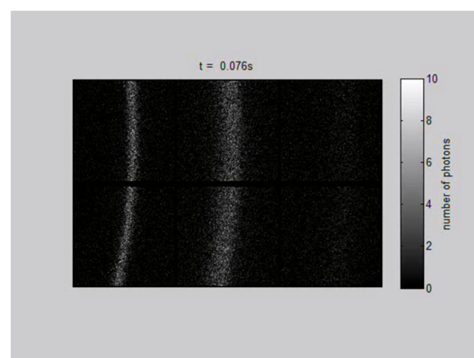


2 ms diffraction from Ni_3Al multilayer foil undergoing reaction. 5 photons per pixel full scale

(CHESS: Dale; Johns Hopkins: Hufnagel group; Cornell)

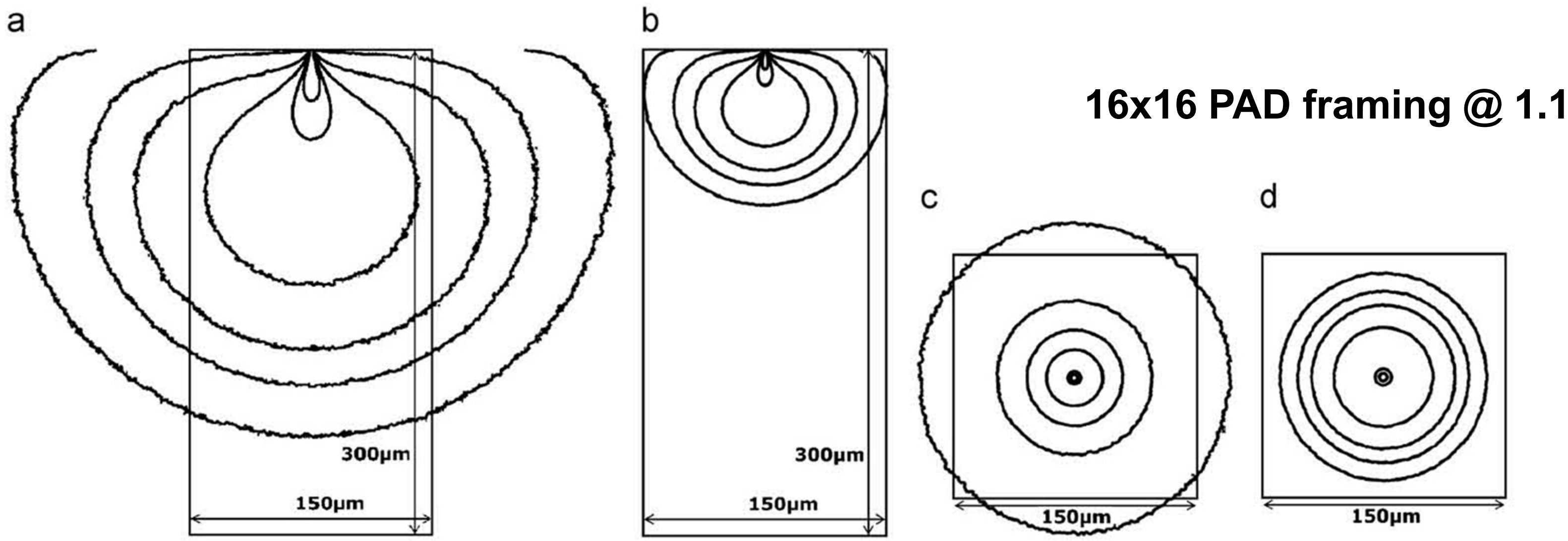






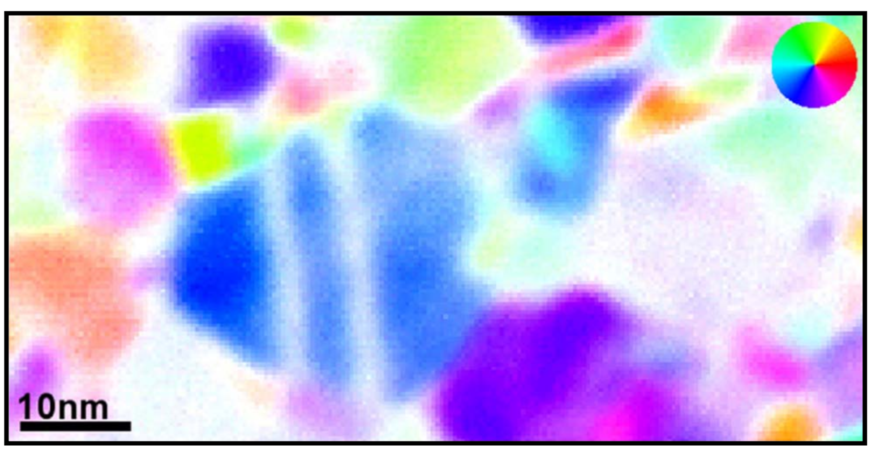
Example 4: Scanning Transmission EM (STEM)

Caswell, Ercius, Tate, Ercan, Gruner & Muller. *Ultramicros*. 109 (2009) 304.



16x16 PAD framing @ 1.1 kHz

200 keV | 120 keV | 200 keV | 120 keV



- Polycrystalline Cu sample.
- Define* $\vec{\mathbf{I}}_{i,j} = \sum I_p^{i,j} \vec{\mathbf{q}}_p / \sum I_p^{i,j}$
- Hue: Vector field direction of diffraction
- Saturation: Vector field magnitude

* *I* = intensity; *i,j*= pix; *p*=pixel subset; q=vector from beam center to center of region *p*

Cornell PAD Group

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- **Support:**
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  - U.S. National Science Found.
  - Keck Foundation

END