Ankylography: Three-Dimensional Structure Determination from a Single View

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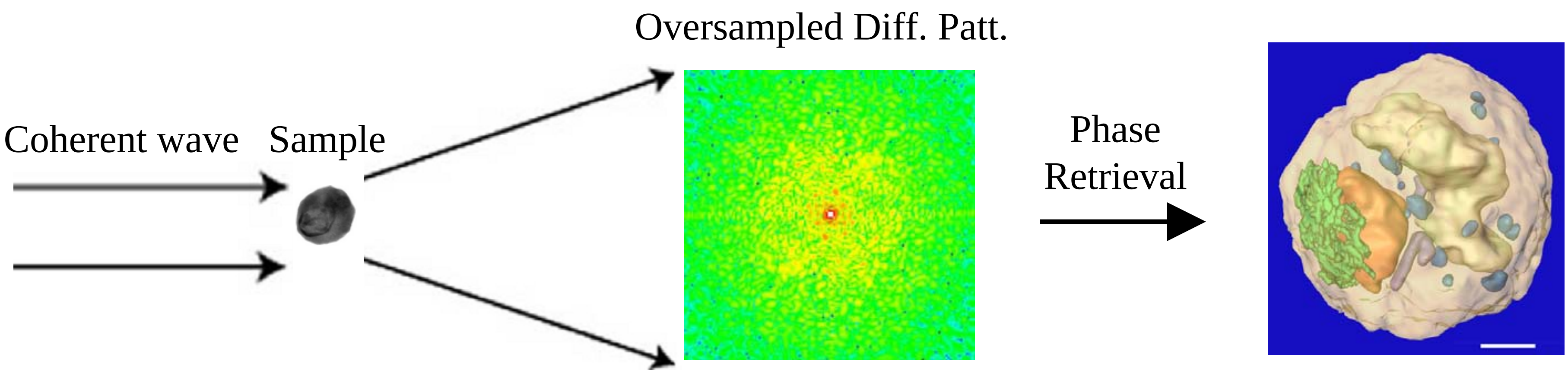
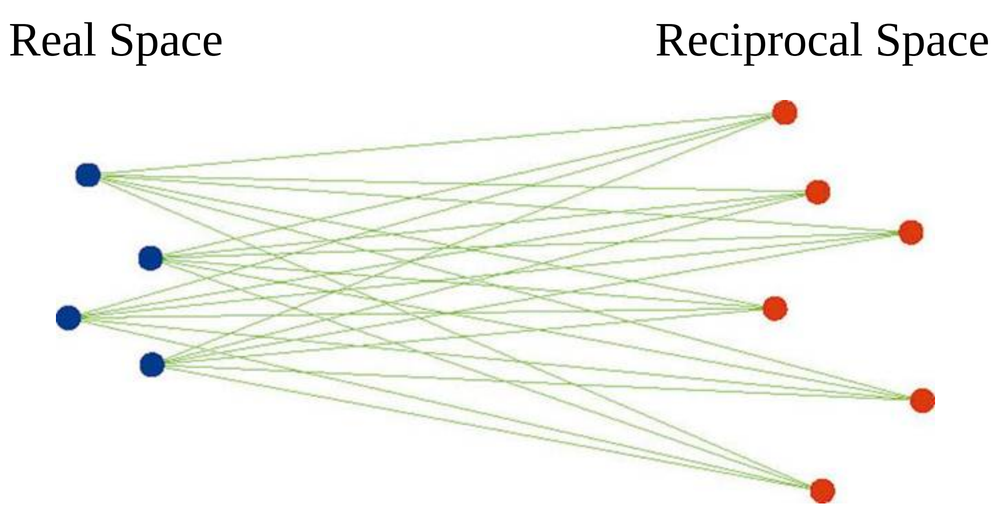
Foundation of Coherent Diffractive (Lensless) Imaging

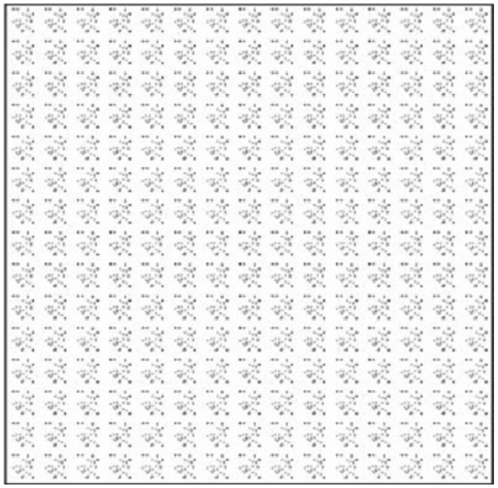




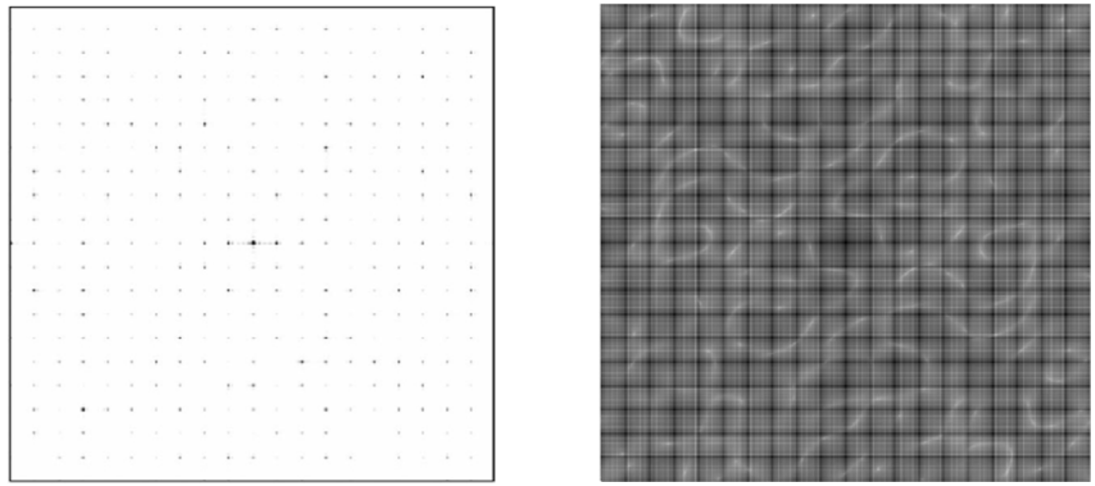
Coherence ⇒ Oversampled intensity points that are correlated ⇒ Iterative algorithm ⇒ Phases

Miao, Ishikawa, Johnson, Anderson, Lai & Hodgson, *PRL* **89**, 088303 (2002).

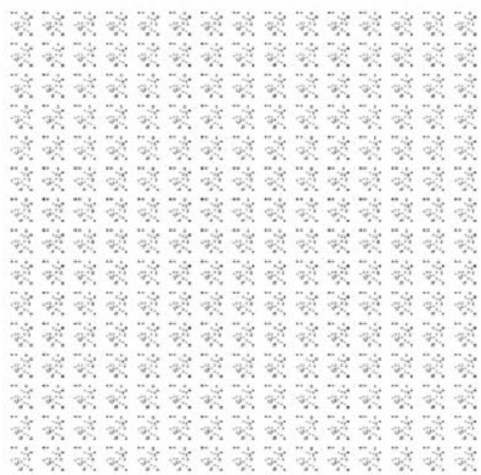
Coherence Length > the Size of a Nanocrystal



A nanocrystal consisting of 15 x 15 unit cells



Oversampled diffraction pattern in a linear and logarithmic scales



The reconstructed nanocrystal

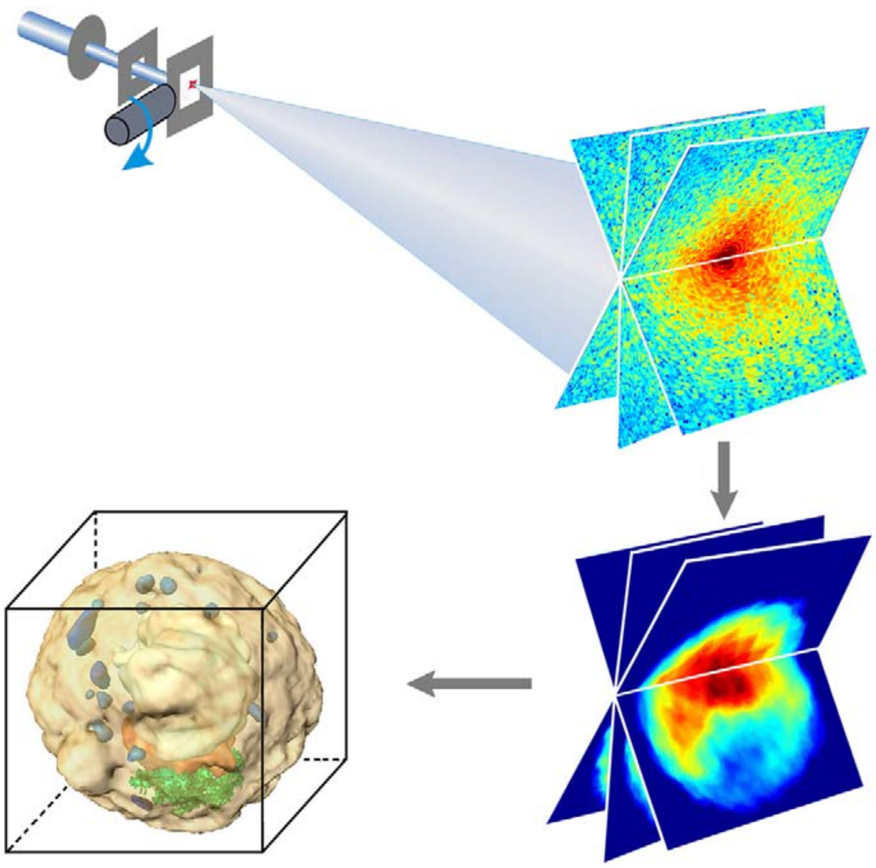
"…, the phase information could be recovered from computer-generated oversampled diffraction patterns of small specimens that are (a) perfect or imperfect crystals, or (b) have a repeated motif without orientational regularity, or (c) are an unrepeated motif, such as an amorphous glass, a single molecule or a single biological cell."

Miao & Sayre, *Acta Cryst*. A **56**, 596-605 (2000).

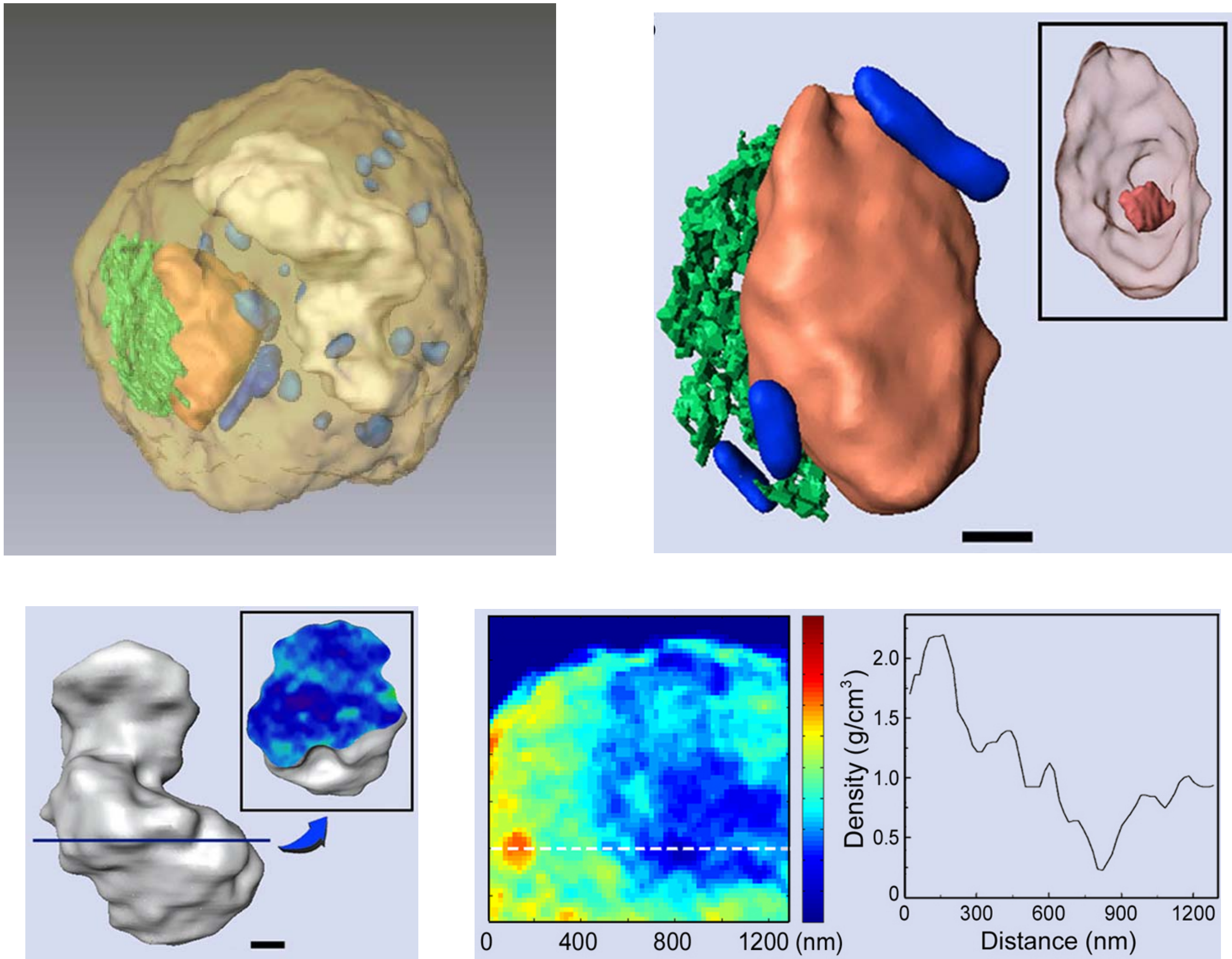
Current 3D Structure Determination Techniques

Crystallography, Tomography, 3D Coherent Diffractive Imaging:
Acquiring multiple measurements at various sample orientations.

Confocal microscopy: Scanning a series of thin sections through a sample.



Quantitative 3D Imaging of a Yeast Spore Cell



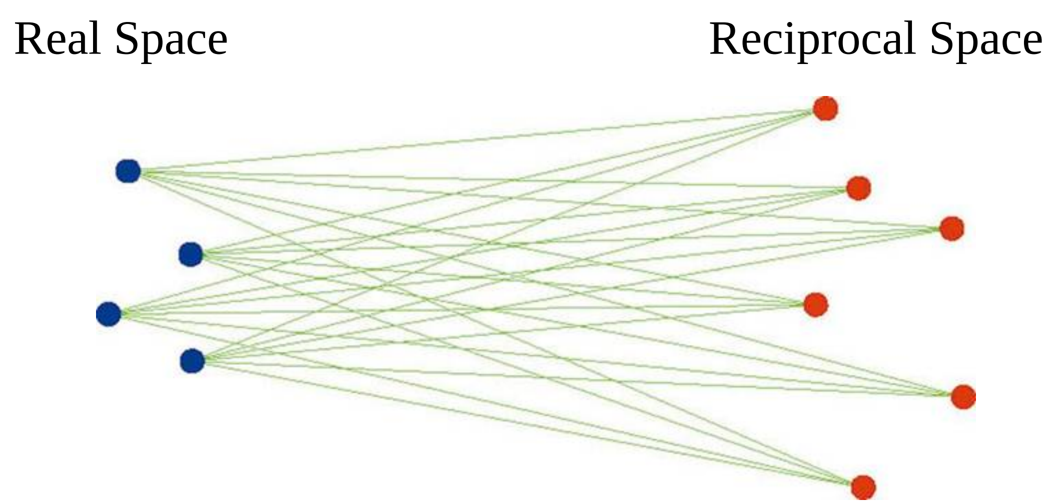
Jiang, Song, Chen, Xu, Raines, Fahimian, Lu, Lee, Nakashima, Urano, Ishikawa, Tamanoi & Miao, *PNAS* **107**, 11234 (2010).

Ankylography and Super-Resolution Crystallography

Ankylography: Derived from Greek words *ankylos* - 'curved' and *graphein* - 'writing'.

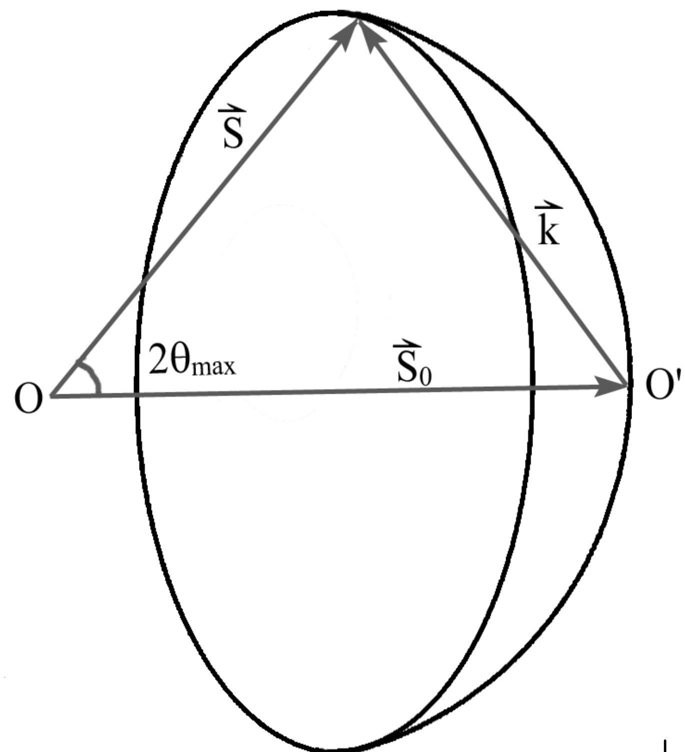
Raines, Salha, Sandberg, Jiang, Rodríguez, Fahimian, Kapteyn, Du, Miao, *Nature* **463**, 214-217 (2010).

Super-resolution crystallography: Schroder, Levitt, Brunger, Super-resolution biomolecular crystallography with low-resolution data, *Nature* **464**, 1218-1222 (2010).



Personnel view: the way of our thinking should not be confined with the Fourier transform.

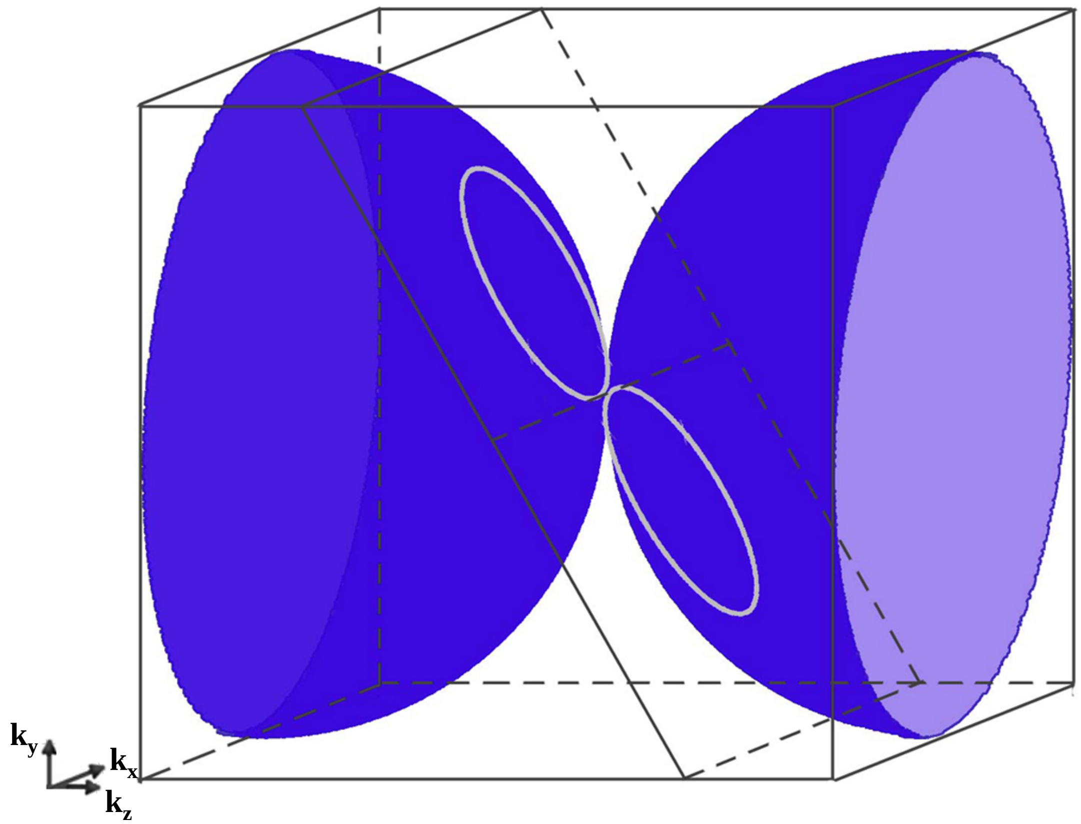
Oversampling of the Diffraction pattern on an Ewald Sphere Shell



$$\left|F(\theta,\varphi)\right| = \left|\int_V \rho(\vec{r}) e^{-\frac{2\pi i}{\lambda}\left[x\sin\theta\cos\varphi + y\sin\theta\sin\varphi + z(\cos\theta - 1)\right]} d^3\vec{r}\right|$$

O_d: The ratio of the number of non-centro-symmetrical intensity points on the Ewald sphere to the number of voxels sampling an object.

Oversampled Spherical Diffraction Pattern ⇒ All Possible Sample Orientations



The oversampled diffraction intensities on an Ewald sphere shell form a set of the intersected arcs, circles and point in *all possible* orientations of a 3D sample.

Considering a 3D Object and Phases as Unknown Variables

$$F(k_x,k_y,k_z) = A_{k_x,k_y,k_z}\exp(i\phi_{k_x,k_y,k_z})$$
$$= \sum_{x,y,z=-M}^{M} \rho(x,y,z)\exp\left[\frac{-2\pi i(k_x x + k_y y + k_z z)}{2N+1}\right]$$

$$A_{k_x,k_y,k_z}\cos(\phi_{k_x,k_y,k_z}) = \sum_{x,y,z=-M}^{M} \rho(x,y,z)\cos\left[\frac{2\pi i(k_x x + k_y y + k_z z)}{2N+1}\right]$$
$$A_{k_x,k_y,k_z}\sin(\phi_{k_x,k_y,k_z}) = -\sum_{x,y,z=-M}^{M} \rho(x,y,z)\sin\left[\frac{2\pi i(k_x x + k_y y + k_z z)}{2N+1}\right]$$

$$\forall\ k_x,k_y,k_z: \quad k_x^2 + k_y^2 + (k_z + N)^2 = N^2$$

Matrix Representation of the Oversampled Intensities on an Ewald Sphere Shell

$$A = BX$$

$$A = \begin{pmatrix} A_1 \cos(\phi_1) \\ \vdots \\ A_L \cos(\phi_L) \\ A_0 \\ A_1 \sin(\phi_1) \\ \vdots \\ A_L \sin(\phi_L) \end{pmatrix}$$

$$B = \begin{pmatrix} \cos\left[\frac{2\pi(k_{x1}x_{-M} + k_{y1}y_{-M} + k_{z1}z_{-M})}{2N+1}\right] & \cdots & \cos\left[\frac{2\pi(k_{x1}x_{M} + k_{y1}y_{M} + k_{z1}z_{M})}{2N+1}\right] \\ \vdots & \vdots & \vdots \\ \cos\left[\frac{2\pi(k_{xL}x_{-M} + k_{yL}y_{-M} + k_{zL}z_{-M})}{2N+1}\right] & \cdots & \cos\left[\frac{2\pi(k_{xL}x_{M} + k_{yL}y_{M} + k_{zL}z_{M})}{2N+1}\right] \\ 1 & \cdots \quad \cdots & 1 \\ -\sin\left[\frac{2\pi(k_{x1}x_{-M} + k_{y1}y_{-M} + k_{z1}z_{-M})}{2N+1}\right] & \cdots & -\sin\left[\frac{2\pi(k_{x1}x_{M} + k_{y1}y_{M} + k_{z1}z_{M})}{2N+1}\right] \\ \vdots & \vdots & \vdots \\ -\sin\left[\frac{2\pi(k_{xL}x_{-M} + k_{yL}y_{-M} + k_{zL}z_{-M})}{2N+1}\right] & \cdots & -\sin\left[\frac{2\pi(k_{xL}x_{M} + k_{yL}y_{M} + k_{zL}z_{M})}{2N+1}\right] \end{pmatrix}$$

$$X = \begin{pmatrix} \rho(x_{-M}, y_{-M}, z_{-M}) \\ \vdots \\ \rho(x_M, y_M, z_M) \end{pmatrix} \qquad \forall\, k_{xi}, k_{yj}, k_{zk} : \quad \left(N - \frac{1}{2}\right)^2 \le k_{xi}^2 + k_{yj}^2 + (k_{zk} + N)^2 < \left(N + \frac{1}{2}\right)^2$$

Making *B* a Square Matrix by Padding Zeros around the Object

$$B' = \begin{pmatrix} \cos\left[\frac{2\pi(k_{x1}x_{-L} + k_{y1}y_{-L} + k_{z1}z_{-L})}{2N+1}\right] & \cdots & & \cdots\cos\left[\frac{2\pi(k_{x1}x_{L} + k_{y1}y_{L} + k_{z1}z_{L})}{2N+1}\right] \\ \vdots & & B & \vdots \\ -\sin\left[\frac{2\pi(k_{xL}x_{-L} + k_{yL}y_{-L} + k_{zL}z_{-L})}{2N+1}\right] & \cdots & & \cdots -\sin\left[\frac{2\pi(k_{xL}x_{L} + k_{yL}y_{L} + k_{zL}z_{L})}{2N+1}\right] \end{pmatrix}$$

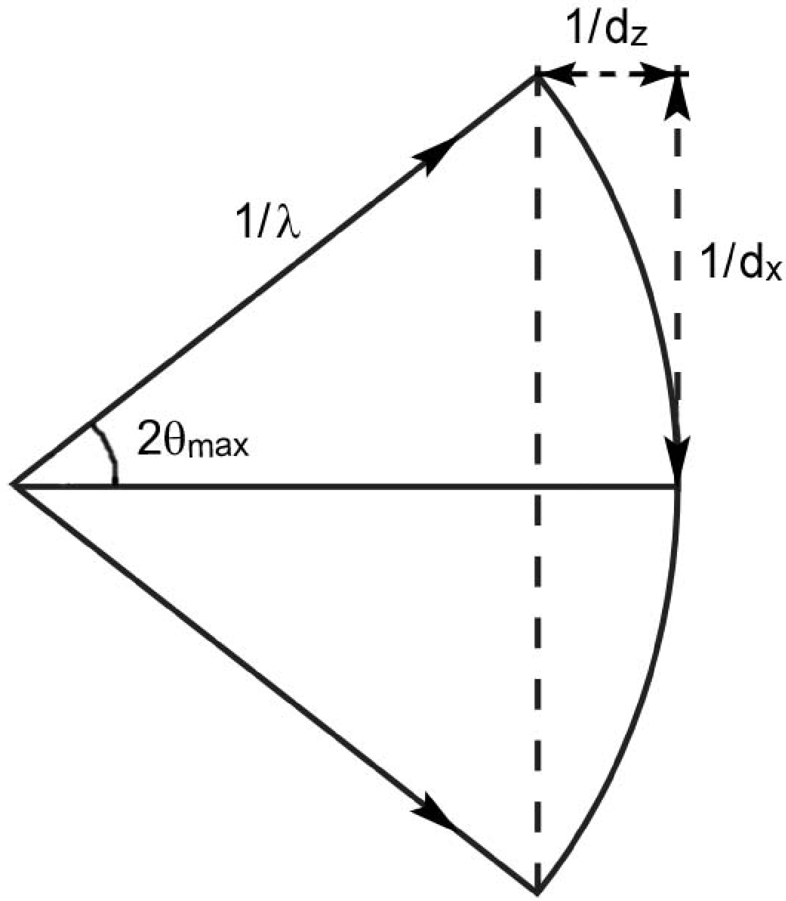
$$X' = \begin{pmatrix} 0 \\ \vdots \\ 0 \\ X \\ 0 \\ \vdots \\ 0 \end{pmatrix}$$

$$B'X' = A$$

For small objects, the rank of B' > the number of unknown variables.

For larger objects, extra real-space constraints are needed to reduce the # of unknown variables.

3D Spatial Resolution in Ankylography

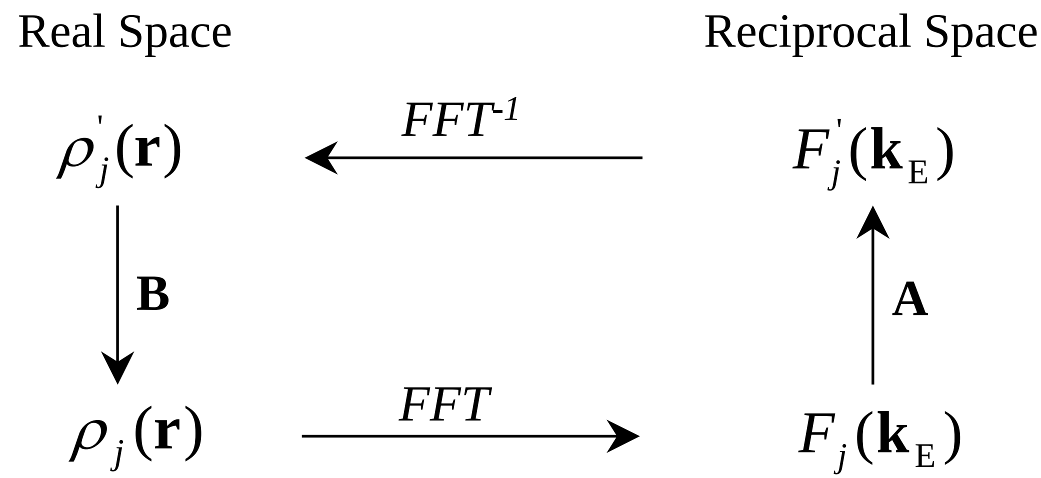


$$d_x = d_y = \frac{\lambda}{\sin(2\theta_{max})}$$

$$d_z = \frac{\lambda}{2\sin^2\theta_{max}}$$

Paraxial approximation ($\sin\theta \approx \theta$) is assumed in Fresnel and Fraunhofer diffraction, but not in Ankylography.

Ankylographic Reconstruction



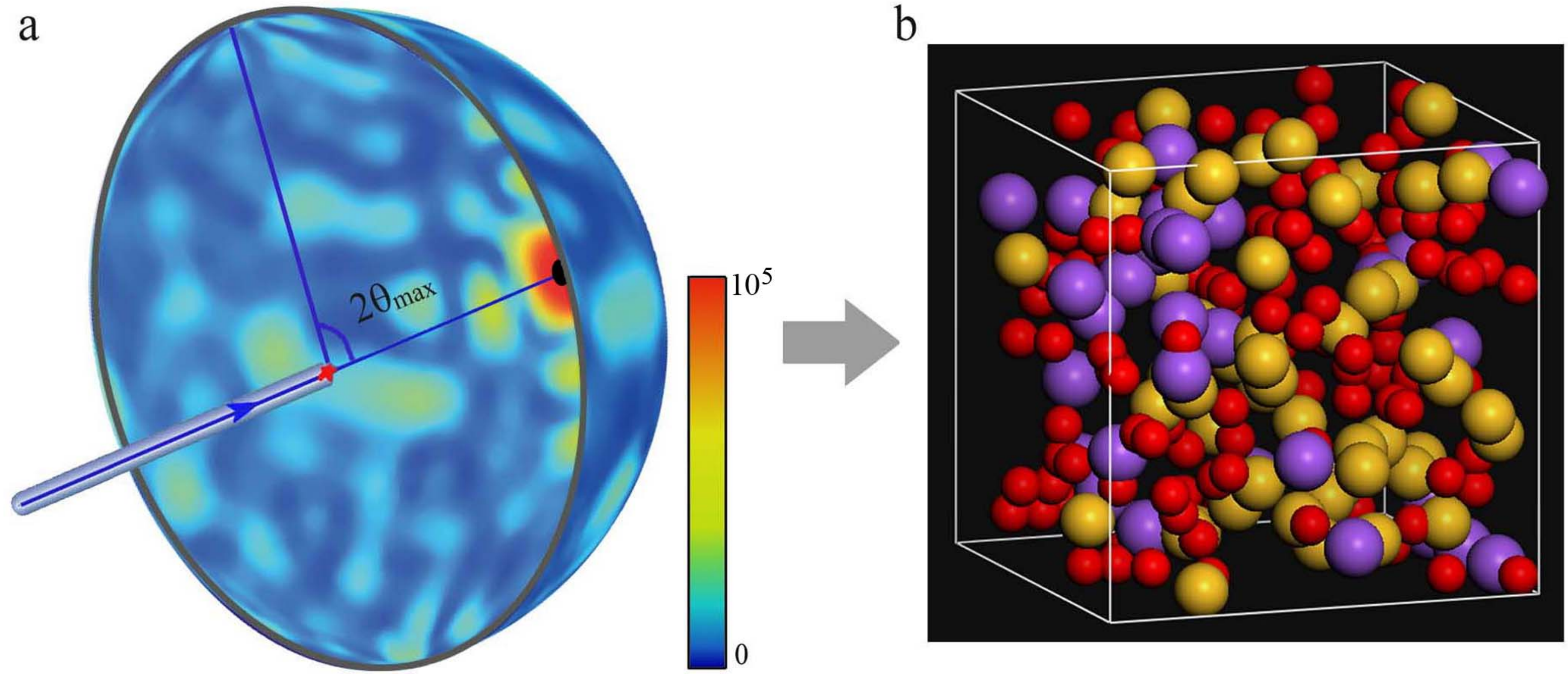
Real-Space Constraints:

(i) Optimization of the random initial phase set.
(ii) Uniformity outside the support.
(iii) Positivity and continuity inside the support.
(iv) Amplitude extension[1,2].
(v) More possible constraints: atomicity, histogram matching, bond distance and angles, molecular replacement, noncrystallographic symmetry

[1] Raines, Salha, Sandberg, Jiang, Rodríguez, Fahimian, Kapteyn, Du, Miao, *Nature* **463**, 214-217 (2010).

[2] Schroder, Levitt, Brunger, Super-resolution biomolecular crystallography with low-resolution data, *Nature* **464**, 1218-1222 (2010).

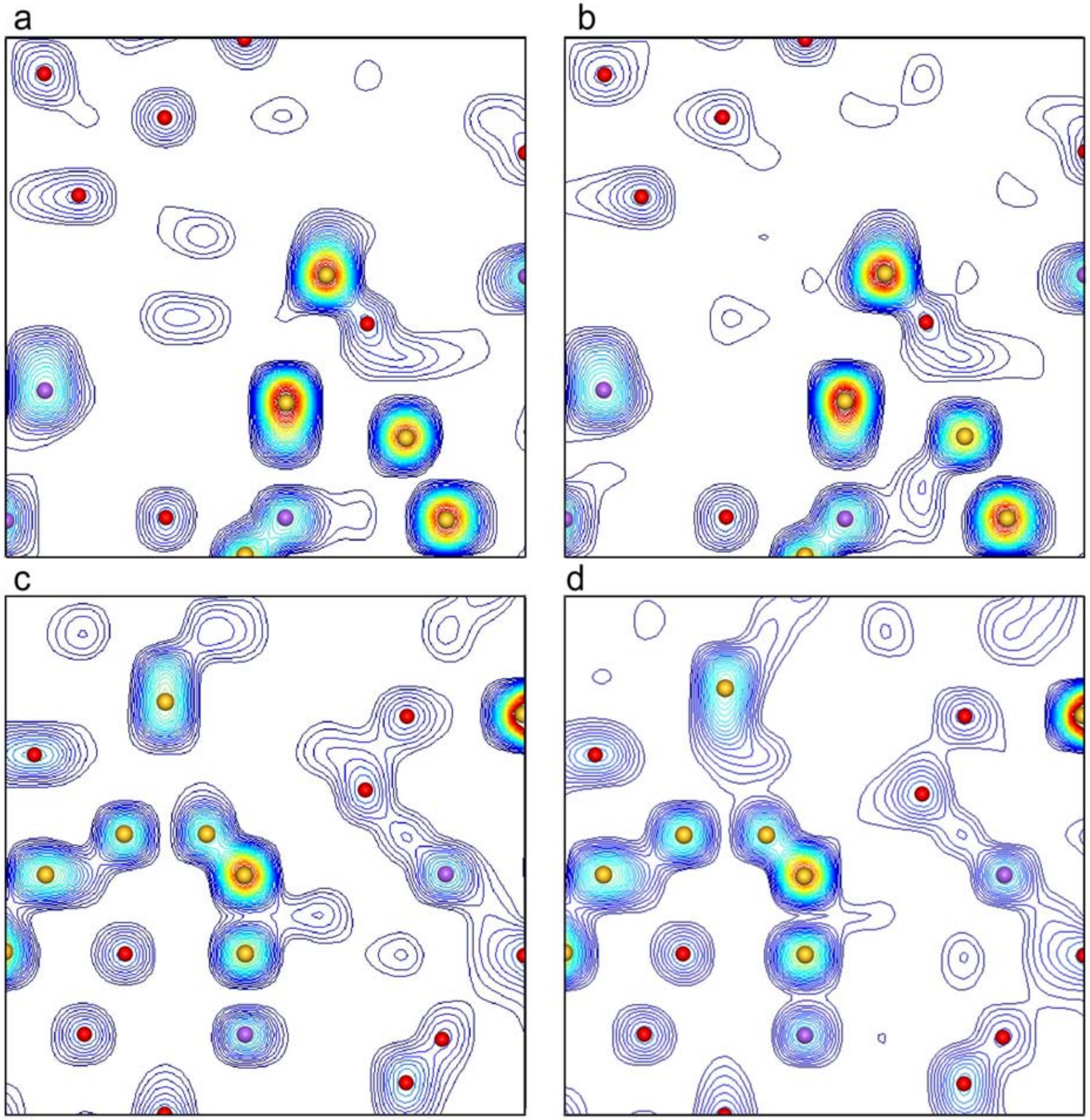
3D Structure Determination of a Sodium Silicate Glass Particle from a Simulated and Noisy 2D Spherical Diffraction Pattern Alone



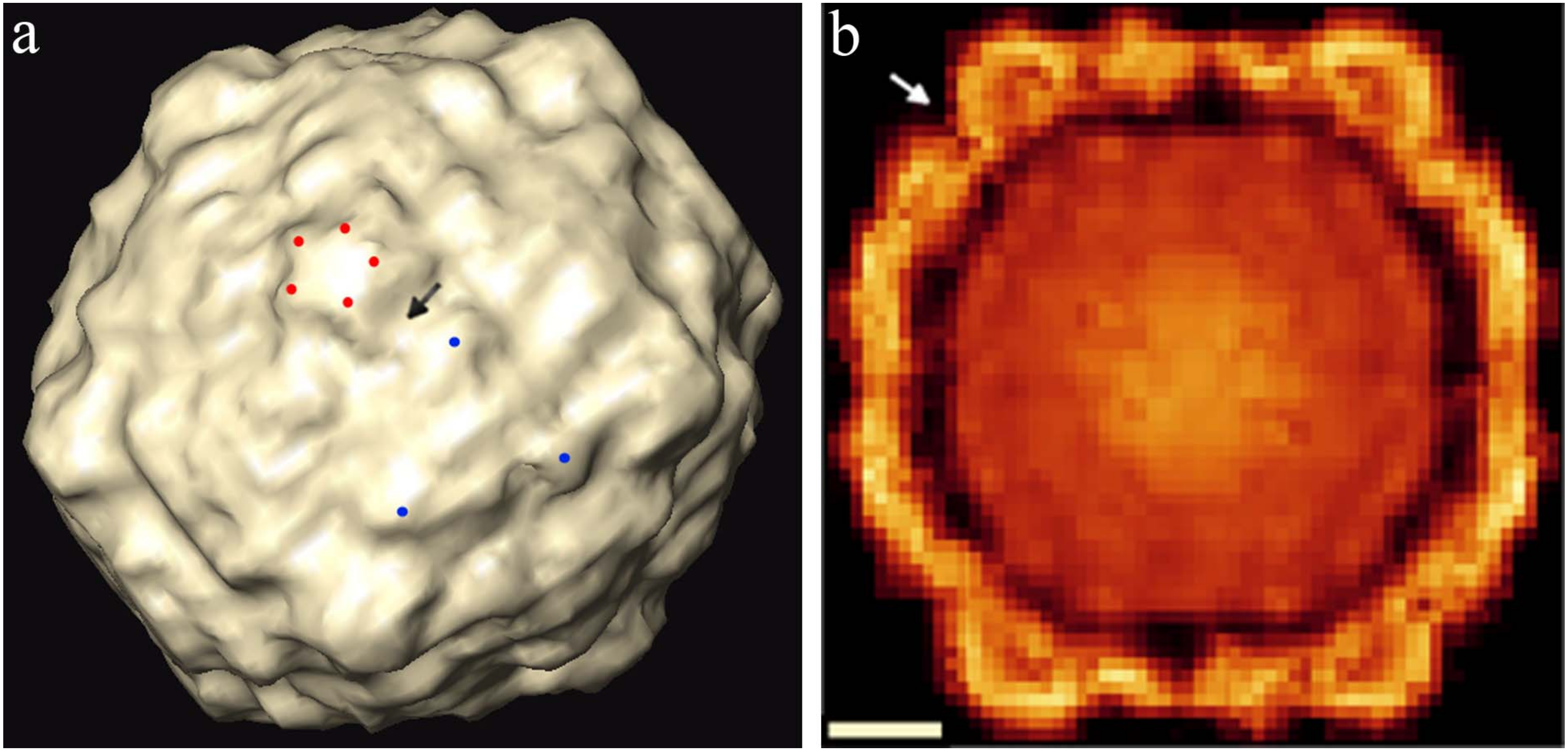
Red, purple and yellow: O, Na and Si atoms

Particle Size: 14×14×14 Å^3	λ = 2 Å	Incident flux = 10^{13} photons
$2\theta_{max}$ = 90°	$d_x = d_y = d_z$ = 2 Å	Poisson noise added
Sample array: 14^3 voxels		Fourier-space array: 64^3 voxels

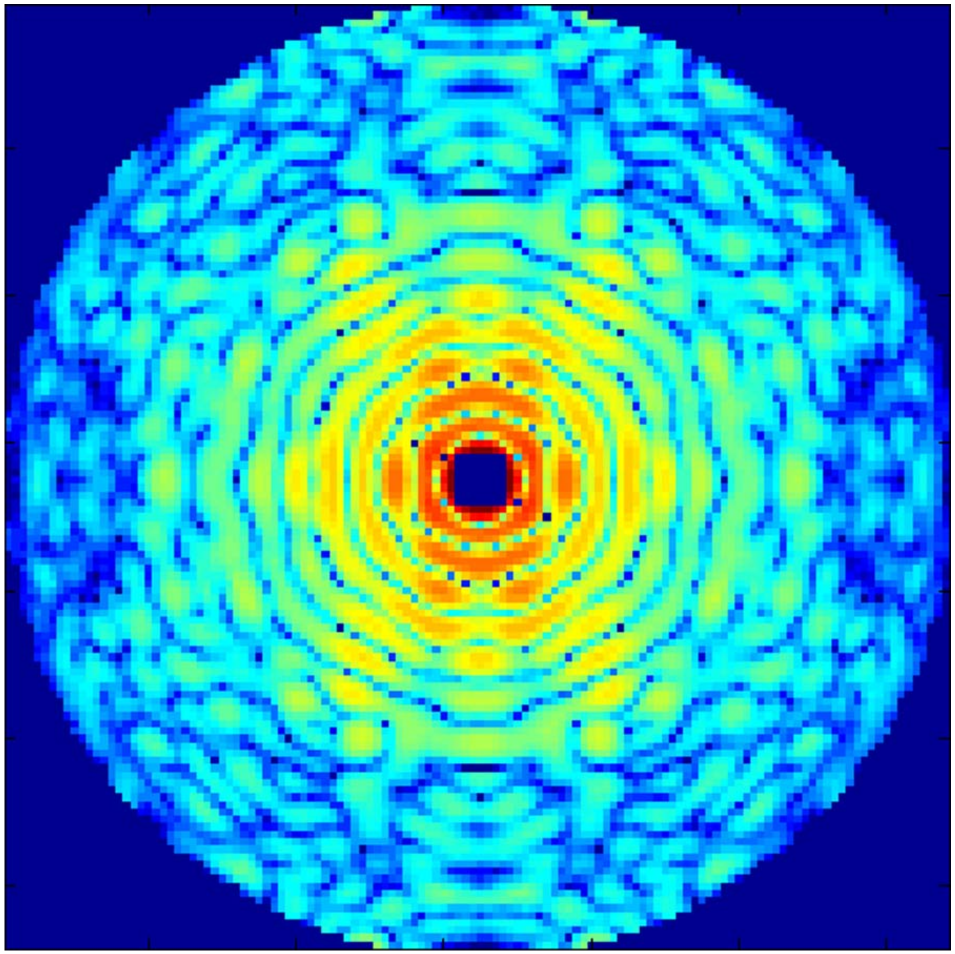
Two Perpendicular Slices of the Reconstructed Sodium Silicate Glass Particle



3D Structure of a Poliovirus Displayed at 2 – 3 nm Resolution



Simulated 2D Spherical Diff. Pattern of an Individual Poliovirus from a Single X-FEL Pulse

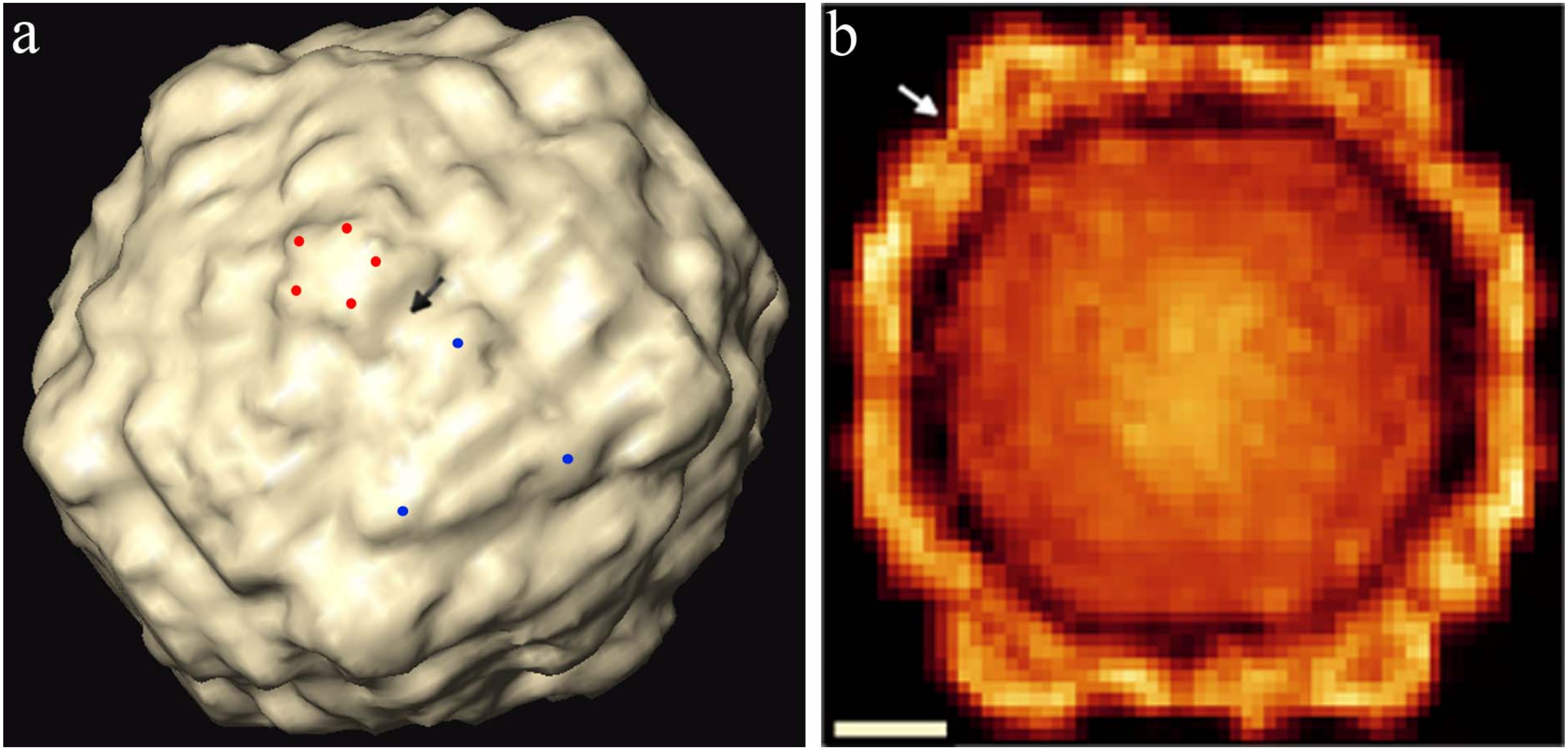


$\lambda = 1.77$ nm Flux = 10^{13} photons Focal spot: 100 nm

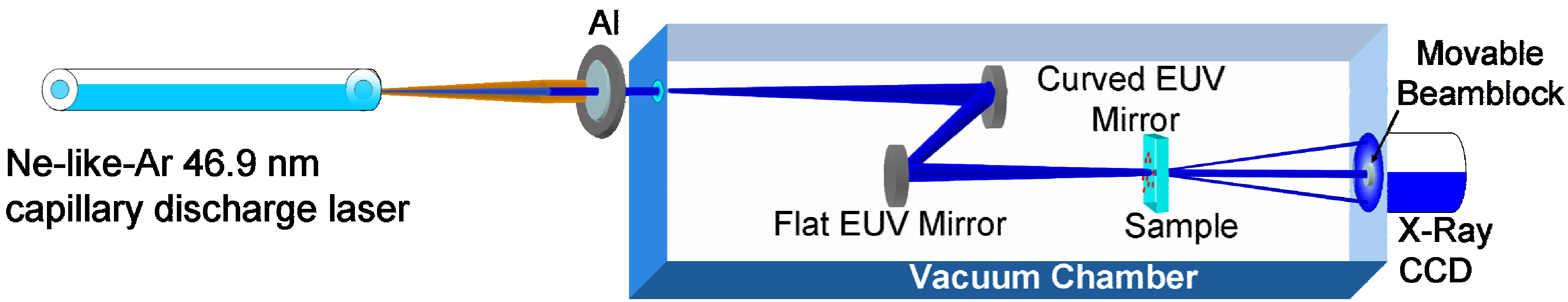
Poisson noise added $2\theta_{max} = 62.7°$ $d_x = d_y = 2$ nm and $d_z = 3.3$ nm

Sample array: 32×32×20 voxels Fourier-space array:128×128×78 voxels

3D Structure Determination of the Poliovirus from a Single Simulated X-FEL Pulse



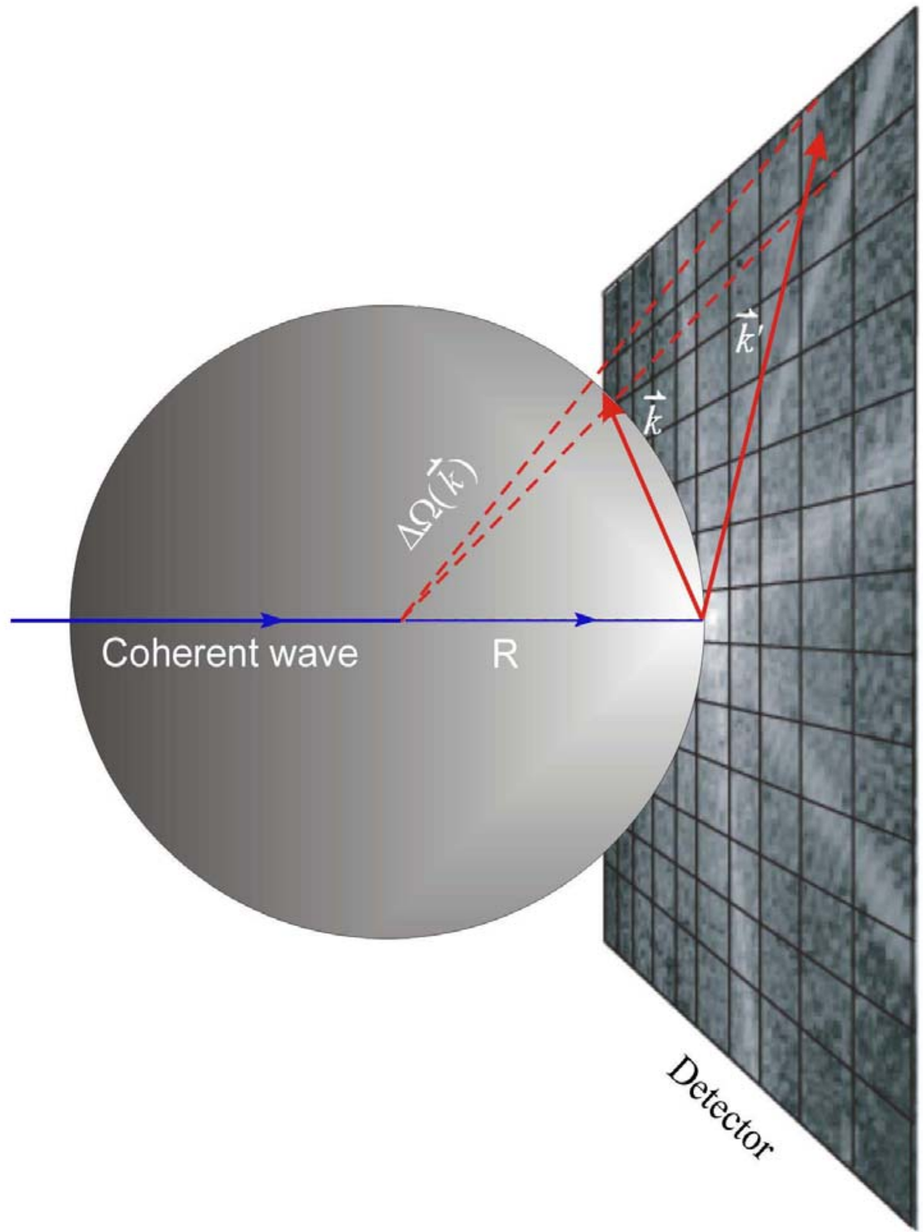
Soft X-ray Laser Used for Experimental Demonstration of Ankylography



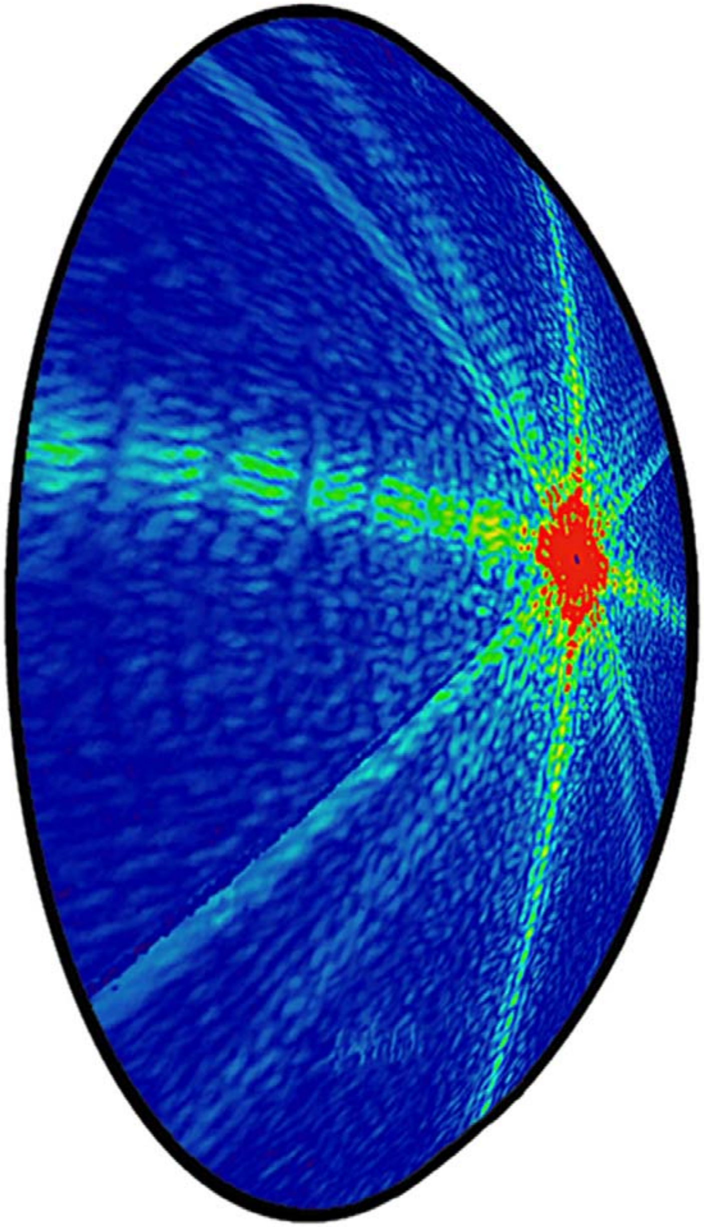
$$\lambda = 46.9\, nm \qquad \lambda / \Delta\lambda = 10^4$$

Andor CCD detector (2048×2048 pixels, 13.5 μm×13.5 μm pixel size).

Projection of an Oversampled 2D Diff. Pattern from a Planar Detector onto the Ewald Sphere



Oversampled Diffraction Pattern of a Test Specimen on the Ewald Sphere



420×420×240 voxels

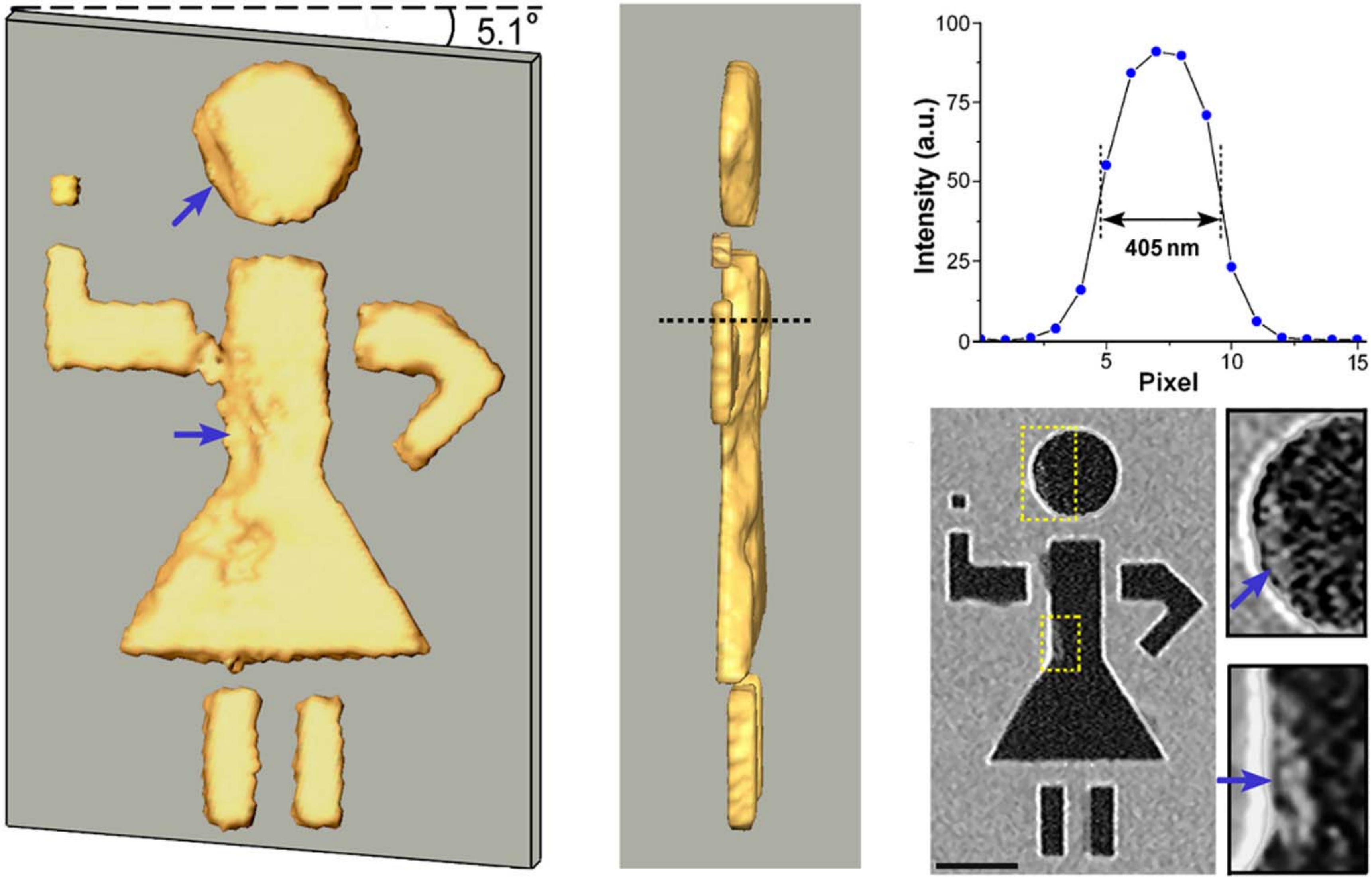
$O_d = 2.6$

Diffraction angle at the corner: 48.3°

Diffraction angle at the edge: 35.9°

Reconstruction error R-factor : 8%

Demonstration of Ankylography Using Experimental Data Obtained with the Soft X-ray Laser



Summary

- Oversampled diff. pattern on an Ewald sphere shell $\Rightarrow$ 3D structure information.
- 3D structure determination of a sodium silicate glass particle at 2 Å resolution from a simulated 2D spherical diffraction pattern alone.
- 3D structure determination of an individual poliovirus from a single simulated X-FEL pulse.
- Demonstration of ankylography using experimental data obtained with a soft X-ray laser.
- Ankylography – Science of Cubism?

Collaborators

JILA & U. Colorado, Boulder	*Richard Sandberg, Henry Kapteyn, Margaret Murnane*
RIKEN/SPring-8	*Changyong Song, Tetsuya Ishikawa*
University of North Texas	*Jincheng Du*
LBNL	*Anne Sakdinawat*
Colorado State University	*Jorge Rocca's group*
UCLA Medical School	*Fuyu Tamanoi*
Academia Sinica, Taiwan	*T.-K. Lee*