Orientation Determination Algorithm in Single Particle Coherent Imaging

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One of the most exciting proposal for ultrabright X-ray Free Electron Laser (XFEL) is to determine the 3D structure of single biological molecules to sub-nanometer resolution [1], which is beyond the conventional damage limit. This idea is based on imaging many copies of reproducible biological samples, which are injected into the femto-seconds pulses of the FEL beam in a random orientation [2] (see Fig.1,a). For short (less then 50 fs) and very intense (10^{12} photons) x-ray pulses diffraction pattern can be measured before the sample is destroyed. By determining the orientation of each 2D diffraction pattern, a single three-dimensional (3D) diffraction pattern may be composed and reconstructed to give electron density inside the sample.

![Figure 1: The experiment schematics (a) in real space and (b) in reciprocal. Inset in (a) – the sample used.](image)

We used two samples in our simulations. The first one was human adenovirus 2C6S [3] (icosahedral symmetry, 27 nm in diameter, about 200 000 non-hydrogen atoms) – see inset in Fig.1a. And the second one was an asymmetrical structure made artificially from 2BTV and 8RUC macromolecular structures [3] (size 13x19x28 nm3, about 124 000 non-hydrogen atoms) – Fig.3.e. The maximum scattering angle 2\theta = 45° and 3Å wavelength give the resolution of about 4Å. Sampling rate for both structures was in the range 2–3.5. The incoming flux was focused into the 100x100 nm^2 spot. Diffraction patterns were simulated using the program MOLTRANS and Poisson noise was added to all patterns. For the first structure we calculated 12 000 randomly oriented patterns and for the second - 23 328 patterns with 10° step for each of three Euler angles.

Each measurement with XFEL (Fig.1,a) represents a cut by the Ewald sphere in reciprocal space (Fig.1,b). As soon as samples are identical all measurements correspond to the same reciprocal space. Each measurement represents a cut of the reciprocal space at different angle – Fig.2,a. These cuts usually intersect each other along some common arcs (yellow in Fig.2,a), so intensities along an arc on two patterns are equal. If the maximum scattering angle is big, 2\theta > 10°, this arc uniquely fixes positions of both patterns with respect to each other (Fig.2,b). [4]

For a single FEL pulse the first sample scatters about 0.15 photons per pixel at the edge of the detector and the second one – about 0.05 photons (Fig.3,a). After arranging all diffraction patterns in 3D, a section of the reciprocal space was extracted (Fig.3,b). In Fig.3,c such section for infinite number of photons is shown. The orientation determination was performed with 5° and 3° angular step. The angular dispersion from the ideal orientation is presented in Fig.3,d.
Using XFEL radiation 3D imaging of single reproducible particle can be obtained [5]. Resolution of 4Å at 3Å incident radiation and more than 10000 measured diffraction patterns can be achieved. The task of orienting individual patterns in 3D can be solved by analysis of correlation along common arcs simultaneously for many patterns. Contrary to other techniques [6,7], proposed approach can be applied to a big number of resolution elements (computational time scales linearly) and doesn't require preliminary classification of the measured patterns. It also allows to use parallel computations to increase the speed of calculations.

References