Electron diffraction project WP4

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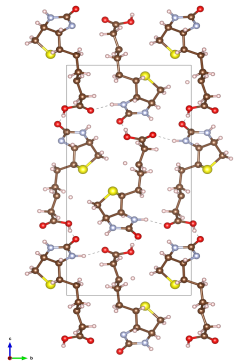
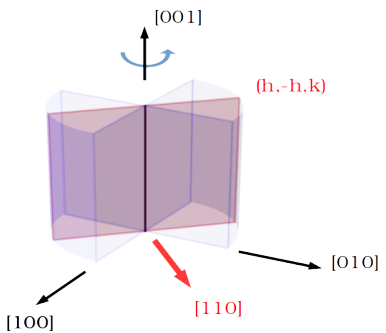
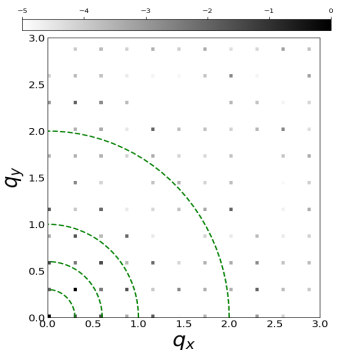
Simulating electron diffraction patterns of macromolecular crystals
Identifying correction opportunities at the scaling stage in DIALS







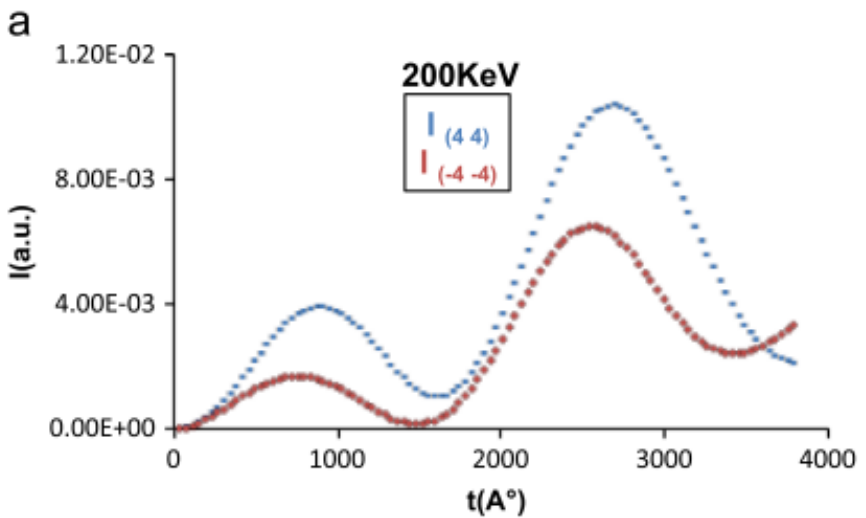
Discrepancy between theory and experiments

Macromolecules solved from experimental Electron Diffraction (ED) data

Sample	Year	Resolution
Lysozyme (14.4 kDa)	2013	2.9 Å
Sup35 prion protein core (905 Da)	2016	1.0 Å
$Au_{146}(p\text{-}MBA)_{57}$ nanoparticle (37.5 kDa)	2017	0.85 Å

B. L. Nannenga and T. Gonen, "The cryo-EM method microcrystal electron diffraction (MicroED)," Nat. Methods, vol. 16, no. May, pp. 369–379, 2019

Multiple scattering should prevent use of standard X-ray kinematic technique



G. Subramanian, S. Basu, H. Liu, J. Zuo, and J. C. H. Spence, "Solving protein nanocrystals by cryo-EM diffraction : Multiple scattering artifacts," Ultramicroscopy, vol. 148, pp. 87–93, 2015

Electron diffraction and dynamical scattering

Atomic scattering factors and cross section

$$\left\{ \frac{\hbar^2}{2m_0} \nabla^2 + V(\mathbf{r}) \right\} \Psi(\mathbf{r}) = E\Psi(\mathbf{r})$$

Born approximation

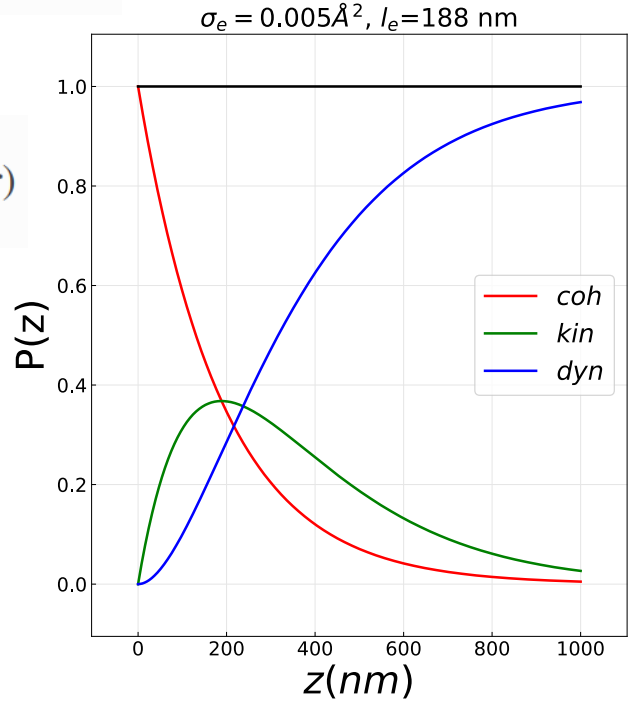
$$f(\theta) = -\frac{2me}{h^2} \int d^3 r e^{i\mathbf{q}\cdot\mathbf{r}} V(r)$$

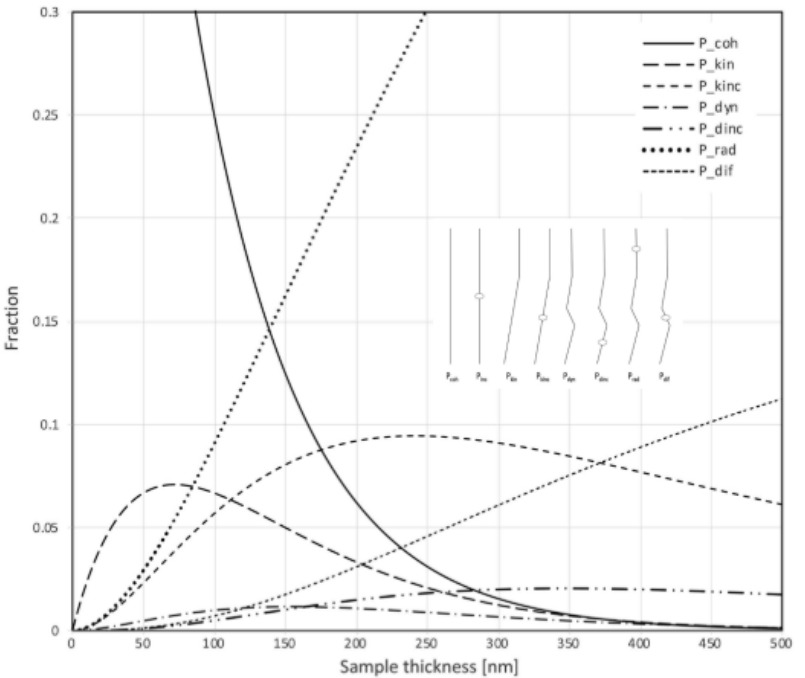
Atomic cross section

$$\frac{d\sigma}{d\Omega} = |f(\theta)|^2$$

Mean free path

$$l_e = 1/\sigma_e \rho$$





T. Latychevskaia and J. P. Abrahams, "Inelastic scattering and solvent scattering reduce dynamical diffraction in biological crystals," Acta Crystallogr. Sect. B Struct. Sci. Cryst. Eng. Mater., vol. 75, pp. 523–531, 2019

Numerical simulation tools of ED patterns

$$\left\{\frac{\hbar^2}{2m_0}\nabla^2 + V(\mathbf{r})\right\}\Psi(\mathbf{r}) = E\Psi(\mathbf{r})$$

$$\partial_z^2 \ll 2ik_0\partial_z$$

Fast electron wave equation

$$\frac{\partial\Psi(x,y,z)}{\partial_z} = \left\{\frac{i\lambda}{4\pi}\nabla_{xy}^2 + i\sigma V(x,y,z)\right\}\Psi(x,y,z)$$

Method	Exact/ consistent	Speed	Memory (per atoms)	Periodic structure	Grid based	Package
Multislice (MS)	no	fast	10 points	yes	yes	**TEMSIM** PRISM
Bloch wave (diagonalization in reciprocal space)	yes	slow	10 points	yes	no	EDM muSTEM PyQt
Near bragg (real space path difference integral)	no	??	1 point	no	no	NearBragg (James Holton)

Multislice (MS) algorithm

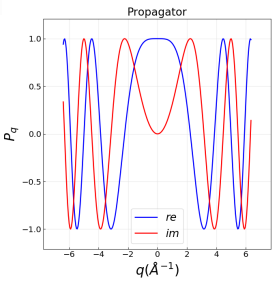
$$\frac{\partial \Psi(x,y,z)}{\partial_z} = \left\{ \frac{i\lambda}{4\pi} \nabla^2_{xy} + i\sigma V(x,y,z) \right\} \Psi(x,y,z)$$

FFT

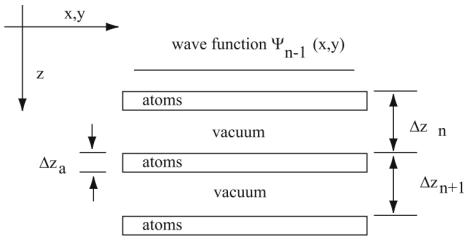
$$\Psi(z+\Delta z) = p(x,y,\Delta z) * \Big(t(x,y,z)\Psi(z) \Big)$$

Fresnel propagator

$$p(x,y,\Delta z) = \frac{1}{i\lambda\Delta z} e^{ik_0 \frac{x^2+y^2}{2\Delta z}}$$



Specimen is cut in slices
~ 1 Angstrom thick each

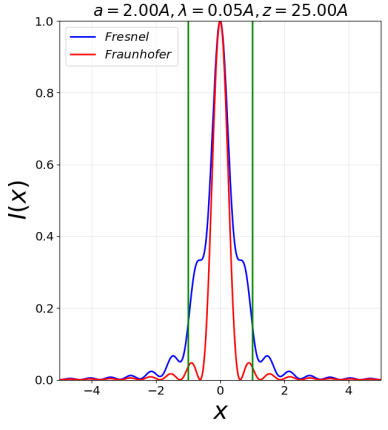


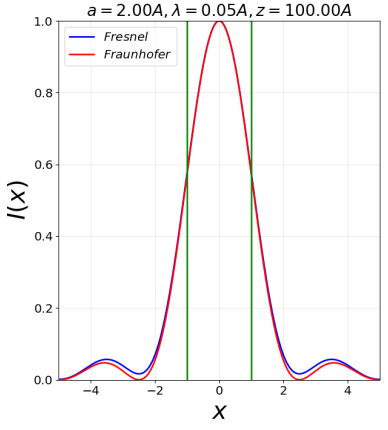
Transmission function

$$t(x,y,z) = e^{i\sigma\nu_{\Delta z}}$$

$$\approx 1 + i\sigma\nu_{\Delta z}$$

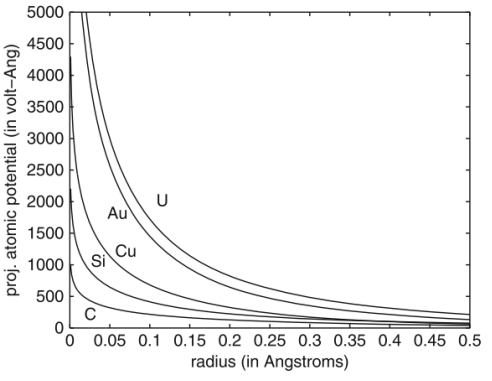
Weak potential





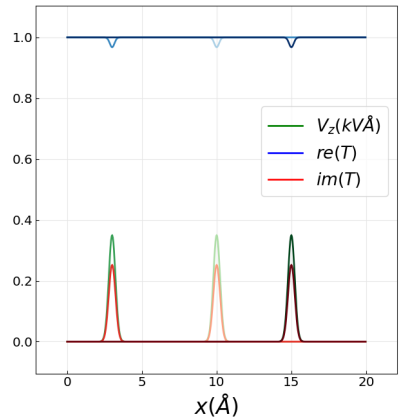
Projected potential

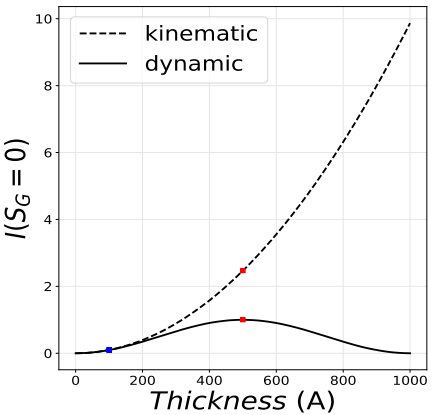
$$\nu_{\Delta_z} = \int_z^{z+\Delta z} V(x,y,z')dz'$$

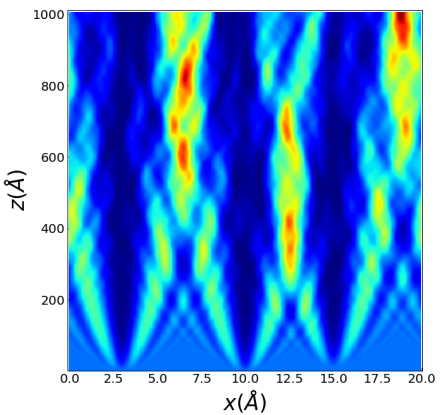


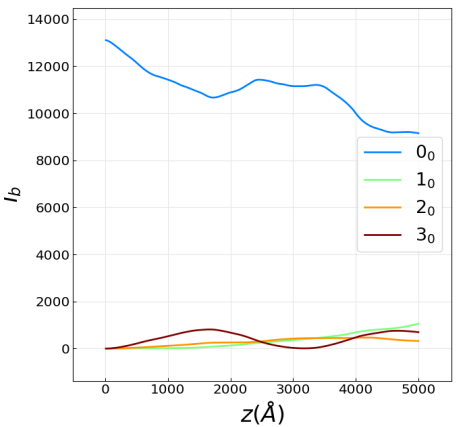
Multislice (MS)

Basic 2D example

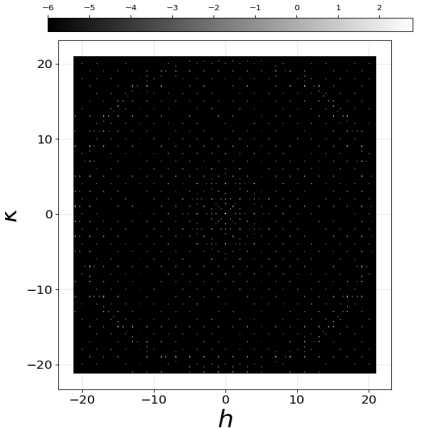


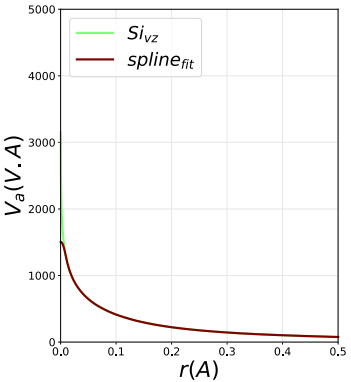






3D Silicon Diamond structure





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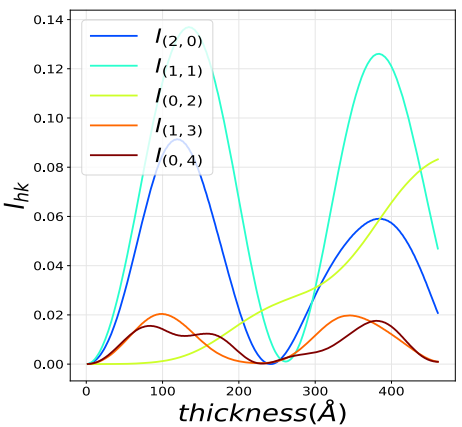

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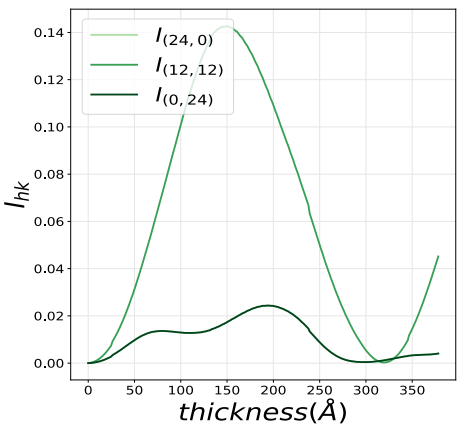
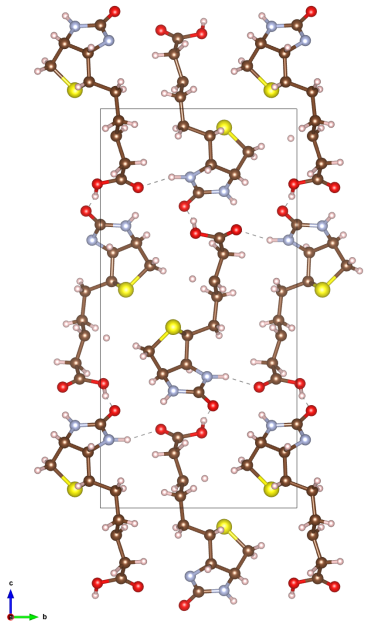


Simulation of biotin $C_{10}H_{16}N_2O_3S$

Structure $P2_12_12_1$

$a = 5.24A,$
$b = 10.35A,$
$c = 21.04A$



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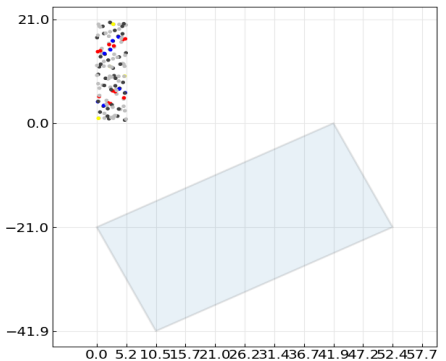

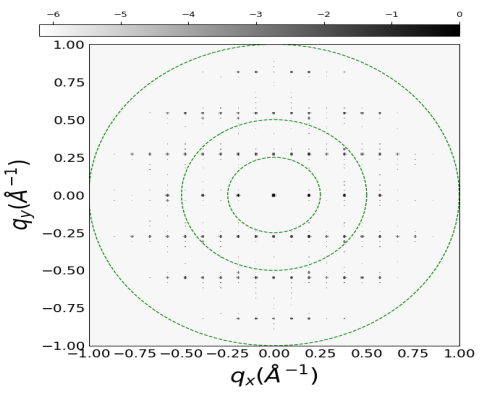

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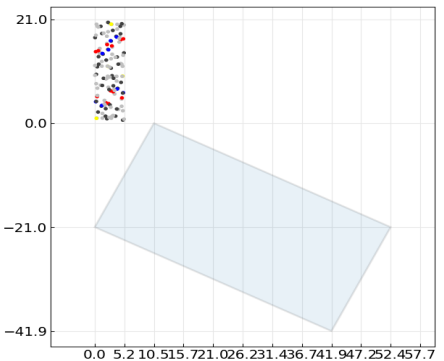

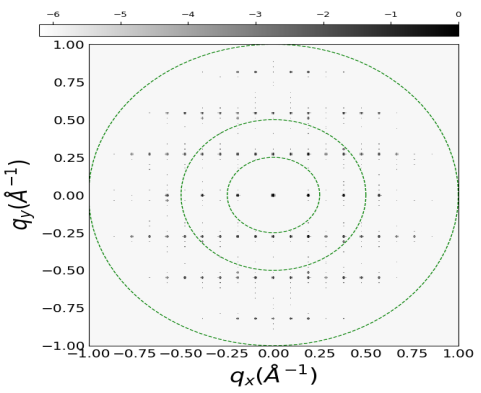

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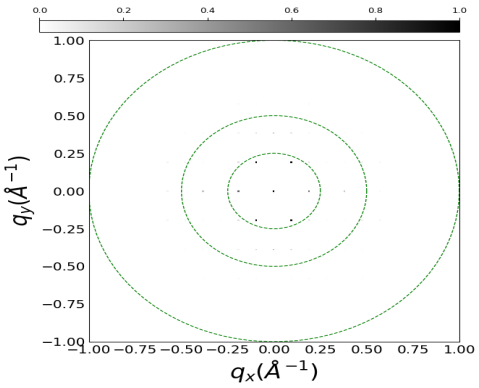
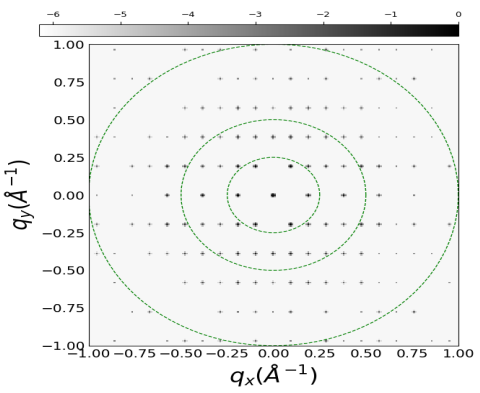




What's next?

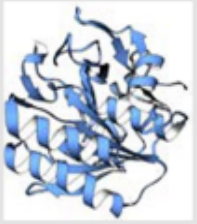
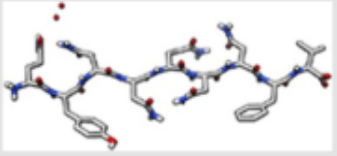
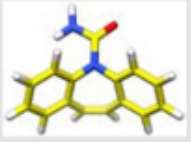
- *Explore opportunities with nearBragg simulator*

- *Perform simulations under continuous rotation*

- *Investigate the effect of defects and mosaicity*

- *Use CCP4 with the simulated data*

http://brno.rc-harwell.ac.uk:8000/

	Sample	Year	Resolution
Proteinase K (28.9 kDa)		2018	1.7 Å
Bank vole prion protein segment (1.1 kDa)		2018	0.75 Å
Carbamazepine (236 Da)		2018	0.85 Å