Final Report

Image Reconstruction Algorithms

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Summary

Our group develops image reconstruction algorithms and applies them to data collected with x-ray sources (synchrotron, XFEL) and electron microscopes. Some of the challenges we face are (1) extremely low signal levels and noise, (2) missing information (phase, sample orientation), and (3) large, very sparse datasets. We have made significant progress in all three of these areas in our DOE project. This final report highlights two results produced during the extension of the project that proved to be spectacular successes. Publications and software products generated over the entire project period are listed at the end of the report.

This project has no unexpended funds.

Electron ptychography

Over the past several years we have been working with the group of David Mueller (Cornell, Applied Physics) to improve and automate tomographic (3D) reconstructions of solid state materials. Motivated by the acquisition of a high dynamic range, fast read-out detector, we recently implemented a ptychographic imaging system. Ptychography is an enhanced mode of scanning-probe transmission microscopy, where contrast is recorded not just by the total number of electrons scattered into the detector for each scan position, but by the 2D diffraction patterns that are produced. High spatial frequency information is captured in these images and can be accurately interpreted because consistency among the diffraction patterns allows for the precise reconstruction of the electron focus, the "probe function".

One of the two graduate students supported by this project, Yi Jiang, was first author on a Nature publication [PTYCHO] that reported the first applications of our ptychographic imaging system. This paper has attracted much attention in the popular media, including recognition by the Guinness Book of World Records[1], because we were able to achieve a new resolution record for electron microscopes: 0.39Å. In Figure 1, reproduced from the Nature paper, we can see how our ptychographic reconstruction of a MoS_2 monolayer is able to resolve individual sulfur atom vacancies.

Sparse data crystallography

We have completed a full structure determination from microcrystals delivered by lipid-gel column for "serial crystallography" at a synchrotron source (APS beamline 23-ID-D). Though still a proof-of-concept demonstration, the data are now taken in the same experimental conditions as a proposed structural biology pipeline. Because of the large background from the lipid-gel, and the small crystal sizes, about 120,000 data frames — about 40% of the total collected — did not have discernible Bragg peaks that could be indexed

[1] http://www.guinnessworldrecords.com/world-records/highest-resolution-microscope

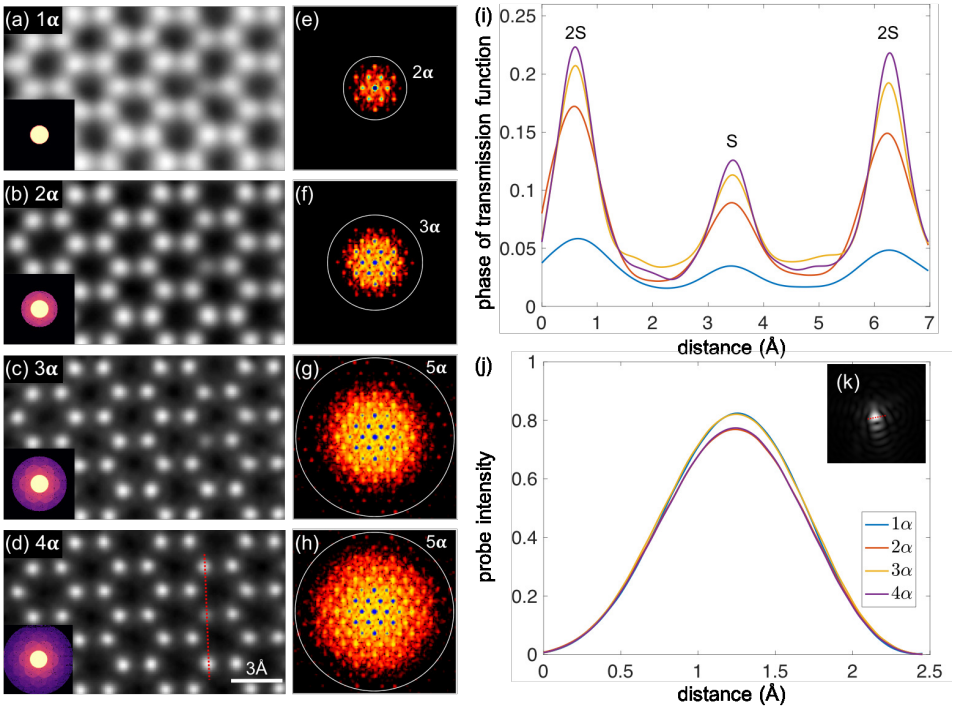

Figure 1: Ptychography reconstructions [PTYCHO] using data with different cutoff angles. (a-d) Reconstructions using electrons collected with cutoffs at multiples 1-4 of the aperture size (α). The averaged diffraction patterns are shown in the lower-left corners and false-color diffractograms (on a log-scale) of the reconstructions are shown in (e-h). (i) Line profiles across three sulfur columns, as indicated by the red dashed line in (d). (j) Line profiles across the reconstructed probe function at different cutoffs. (k) Probe intensity reconstructed by ptychography using the data set with the 4α cutoff.

and used to orient the data in 3D. In an earlier analysis of the data [5UVJ] these very sparse frames — originating from very small crystals — were simply discarded. Our analysis, led by the second student on the project, Ti-Yen Lan, used *only* the discarded frames and had to rely on the Expand-Maximize-Compress [EMC] algorithm to recover the crystal orientations. The resolution of our reconstruction, at 2.1Å, matches that of the study that used only the high quality/ large crystal data. An example of a reconstructed plane of Bragg peaks and a plot showing the agreement between all Bragg intensities and those obtained from the larger crystal data set [5UVJ] is shown in Figure 2 (reproduced from [SPARSE]).

The outcome of this project that we expect to have the most lasting impact is the software package that was developed and has been made public: EMC-for-SMX[2]. The programs in this package run in a cluster environment, such as AWS, and reconstruct the Bragg intensities from serial microcrystallography (SMX) data collected at storage ring synchrotron sources. Our software is fully documented and comes with a how-to guide for non-experts.

[2] `https://github.com/tl578/EMC-for-SMX`

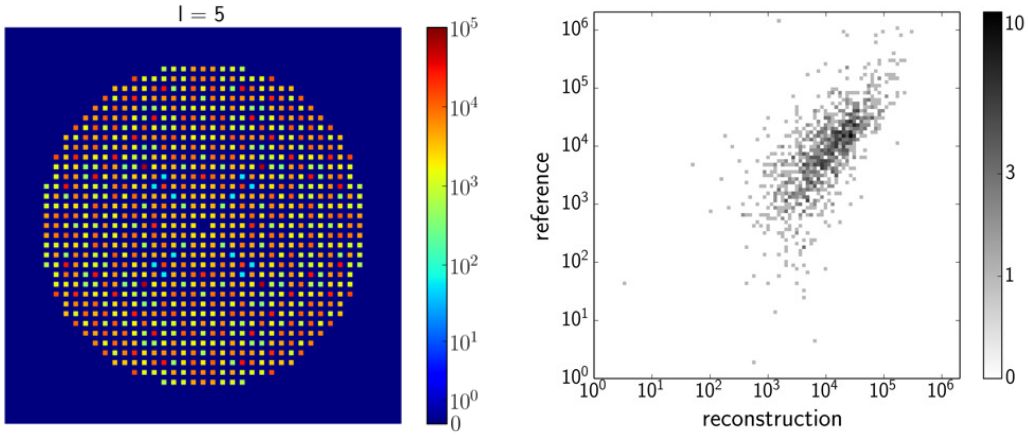

Figure 2: *Left:* Plane of Bragg intensities reconstructed by the EMC algorithm from very small crystals [SPARSE]. *Right:* Agreement between the reconstructed intensities (horizontal) and reference intensities obtained from large crystal data (vertical).

Theoretical phase retrieval

In that the conclusion of this project marks the PI's farewell to image reconstruction research, and phase retrieval in particular, it is fitting that one of the final publications [BENCH] is a review of phase retrieval algorithms, highlighted by a set of carefully designed benchmark problems to challenge future generations. The primary aim of this work was to build a bridge between phase retrieval as practiced by physicists and crystallographers on the one hand, and applied mathematicians on the other. While there has been an explosive growth in phase retrieval research by the latter, with many novel ideas and methods, this community has yet to produce any practical algorithms. The benchmark problems try to be more accessible to applied mathematicians by avoiding some of the complications of real data sets (e.g. space groups). On the other hand, these synthetic data are sufficiently realistic that solutions for the harder instances would represent true progress.

References

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[5UVJ] J. M. Martin-Garcia, et al., *Serial millisecond crystallography of membrane and soluble protein microcrystals using synchrotron radiation*, IUCRJ **4**, 439-454 (2017).

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[SPARSE] T.-Y. Lan *et al.*, *Solving protein structure from sparse serial microcrystal diffraction data at a storage-ring synchrotron source*, IUCrJ **5**, 548-558 (2018).

[BENCH] V. Elser, T.-Y. Lan & T. Bendory, *Benchmark problems for phase retrieval*, SIAM Journal on Imaging Sciences **11**, 2429-2455 (2018).

BES-Supported Publications (2014-2018)

[1] Y. Jiang *et al.*, *Electron ptychography of 2D materials to deep sub-ångström resolution*, Nature **559**, 343-349 (2018).

[2] T.-Y. Lan *et al.*, *Solving protein structure from sparse serial microcrystal diffraction data at a storage-ring synchrotron source*, IUCrJ **5**, 548-558 (2018).

[3] V. Elser, T.-Y. Lan & T. Bendory, *Benchmark problems for phase retrieval*, SIAM Journal on Imaging Sciences **11**, 2429-2455 (2018).

[4] T.-Y. Lan *et al.*, *Reconstructing three-dimensional protein crystal intensities from sparse unoriented two-axis X-ray diffraction patterns*, Journal of applied crystallography **50**, 985-993 (2017).

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