Recovering structure from many low-information 2-D images of randomly-oriented samples

H T Philipp[1], K Ayyer[1], M W Tate[1], V Elser[1], S M Gruner[1,2,3]

1 Laboratory of Atomic and Solid State Physics, Cornell University, Ithaca, NY 14853 USA
2 Cornell High Energy Synchrotron Source, Cornell University, Ithaca, NY 14853 USA
3 Laboratory for Elementary Particle Physics, Cornell University, Ithaca, NY 14853 USA

E-mail: htp2@cornell.edu

Abstract. New sources and detectors are allowing scientists to look at matter with finer spatial and temporal resolutions. These experiments can produce data that are a series of severely Poisson limited snap-shots of randomly oriented samples. An extreme case of this is destructive imaging of single particles with an x-ray free-electron laser – many frames are needed for a reconstruction, but there is no a priori information associated with the frames about particle orientation. We use Cornell's Pixel Array Detectors (PADs) to examine the practical limits of an expectation maximization (EM) algorithm designed to deal with extremely low-fluence data, having just a few photons per frame. We demonstrate image reconstruction of a high-contrast sample using hundreds of thousands of randomly oriented frames with an average x-ray photon occupancy as low as 2.5 photons per frame. Practical aspects of reducing low-fluence data, such as thresholding and noise limits, will be discussed for high- and low-contrast samples; and data collected in the presence of significant background signal.

1. Introduction

New light sources like x-ray free electron lasers (XFELs) that have fast, focused x-rays, make probing of matter on extremely short time scales (femtoseconds) with extremely small samples (single macromolecules) possible. The extreme of this is single molecule imaging. [1] When the scientific potential of these sources is maximized, the nature of the data collected can be categorically different than data collected with macroscopic samples on long time scales. There are many reasons for this, but two stand out: 1) The cross-sections of small samples is small. This means that even with intense, focused x-rays, the number of photons per snap-shot is limited. 2) The time scales important for small samples are extremely short. This means, generally, that fast snap-shots are used for gathering orientation specific information and that successive snapshots are uncorrelated. In the case of single molecules, the sample is destroyed, but one could imagine other situations involving a non-destructive measurement of a sample in a random, unknown orientation.

When using imaging detectors, like pixel array detectors (PADs), the type of information generated is a collection of low-information images. Dealing with this data requires careful treatment. Since the frames of data are "low-information", an enormous number of frames (hundreds of thousands or millions) are necessary to perform a successful measurement. The measurement-significant signal must be extracted from each of these frames and with many frames, measurements become more sensitive to characteristics of the detector like the signal-to-noise ratio, gain variation, and small offsets in the zero level of charge integrating detectors.

After the per-frame data are reduced, it must be used to reconstruct orientation specific information. Different methods have been proposed for doing this in cases where many identical samples are examined, but each in an unknown orientation. [2, 3] When dealing with data from frames that have cross-correlations of approximately zero, it has been demonstrated that the recovery of orientation specific information is possible using an expectation maximization algorithm. [4]

2. Collecting and reducing data

Charge integrating detectors are well-suited for high-speed experiments when the instantaneous arrival rate of photons per pixel exceeds the count rates achievable with photon counting detectors. Areas of the detector where the average fluence is low benefit from signal discrimination after charge integration to distinguish photon detection events from non-events (i.e. offsets from the average zero-level that are the result of noise in the signal measurement or errors in the zero-level). To do this, the signal-to-noise ratio of the detector must be sufficiently high so as to let the average fluence of data frames be distinguished with high fidelity. [5] The threshold level used must take into account the detector gain, the signal-to-noise ratio, systematic offsets in detector dark levels, and the signal level (photons per pixel per frame).

Integration detectors that have low photon-equivalent noise for the x-ray energy of interest can be used to discriminate single photon events simply by applying a threshold level to the detector output at the appropriate level. If the anticipated fluence is low, so that double photon events are exceedingly rare, then the detector output over many frames (i.e. a functional histogram) can be represented as two Gaussians of equal width, one about the zero-level and one about the single photon level. Integrating the the curves from the threshold value to infinity gives the relative contributions of non-events and photon events to the detector output. Increasing the threshold monotonically increases the certainty that a photon was detected, but decreases efficiency. In the context retrieving of spatial orientation, loss of pixel detection efficiency means a reduction in the number of photons per frame. Lowering the threshold increases effective pixel efficiency, but also effectively lowers contrast – making recovery of structural information more difficult. Optimization of data reduction before the application of algorithms to the many frames of data collected is not straight forward. It depends on the detector characteristics, the sample being measured and the nature of the tools used downstream to recover the desired information – for example, the convergence of the of iterative algorithms.

We have collected large numbers (millions) of low-fluence radiographs of randomly oriented objects using two charge integrating PADs developed at Cornell to test the signal conditioning, verify detector performance, and gain practical experience with reconstruction algorithms. The first of these is the LCLS-PAD [6], that has the same CMOS chips used to make the instrument installed at the Coherent X-ray Imaging (CXI) beamline at the Linac Coherent Light Source. Results of these measurements have recently been published. [4] The second PAD is the high dynamic range, kilohertz imaging, mixed-mode pixel array detector (MMPAD) that is the subject of another paper in these proceedings. [7]

For the LCLS-PAD, a copper anode x-ray tube (TruFocus 6050 Cu) was used to generate low-intensity Cu K_α x-rays. A 50 micron nickel filter was use to attenuate higher energy bremsstrahlung and K_β florescence. A pattern was cut out of x-ray opaque lead sheet to make a shadow mask. The sample was continuously rotated using a Newport URS100BPP rotation stage with an axis of rotation perpendicular to the face of the detector. The data framing and object rotation were not correlated. Hundreds of thousands of frames were collected with fluences as low as just 2.5 photons per frame. The images were thresholded and compressed into list of coordinates of photon hits. This compressed list of frames was scrambled and used as

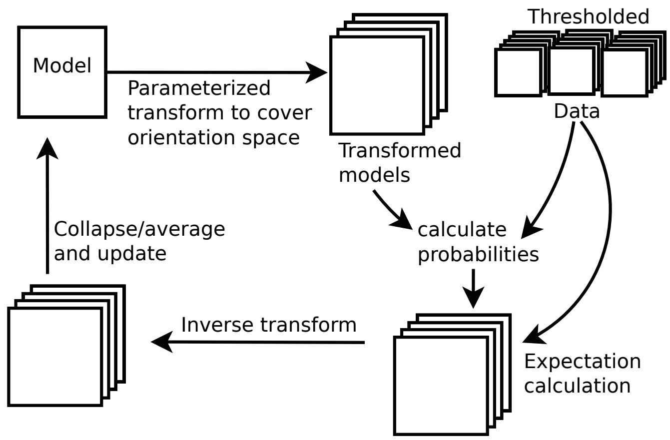

Figure 1. A graphical representation of the iterative expectation maximization algorithm used to recover structural information from a randomly rotated sample.

an input for an expectation maximization algorithm. [8] Details about the specific application of the expectation maximization algorithm applied to this data can be found in reference. [4] A simplified graphical representation of the iterative expectation maximization algorithm used is is shown in figure 1. The essence of the algorithm is this: An initial random model is generated without input from the data. The model is transformed (in our case, rotated) to with discrete values of a parameter so that the orientation space of the sample is covered to a desired resolution. For each of these transformed models, the probability that each of the data frames is associated with it is calculated. These probabilities are used, with the data frames to produce expectation updates to the transformed models. An inverse transform is then applied to each to put them in the same orientation. With the expectation updates in the same orientation, they are averaged and used as the input model for the next iteration.

Using thresholded data of a randomly oriented sample averaging 2.5 photon per frame as an input, this algorithm successfully recovered a high-contrast 2-D object – shown in figure 2.

Data collected with the MMPAD are meant to test the ability of similar recovery of a 3D structure with one axis of rotation and lower contrast. Millions of frames and well over a terabyte of data are still being analyzed. The silver anode x-ray source used was run at 20 keV and low current to produce a continuous x-ray spectrum below the florescence of the silver. A 1 mm aluminum filter was used to attenuate and harden the generated x-rays. Forty-five centimeters from the source, a sample was mounted in front of the detector, on a stage so that the axis of rotation was parallel to the plane of the detector. A static x-ray image of the sample taken with the detector is shown in Figure 2. A sample frame from a data set taken with about 100 photons above threshold is also shown, along with the comparison of summing 5000 frames with different thresholds. The 5000 frames is a small subset of data collected on the sample while continuously rotating. Without proper thresholding, Figure 2(c), detector systematics quickly dominated summed frames. Variations in pixel offsets, detector structure, and small temporal shifts in the detector become apparent.

Acknowledgments
LCLS PAD development was supported by subcontract from SLAC under DOE Contract DE-AC02-76SF00515. Detector development at Cornell is also supported by DOE Grants FG02-

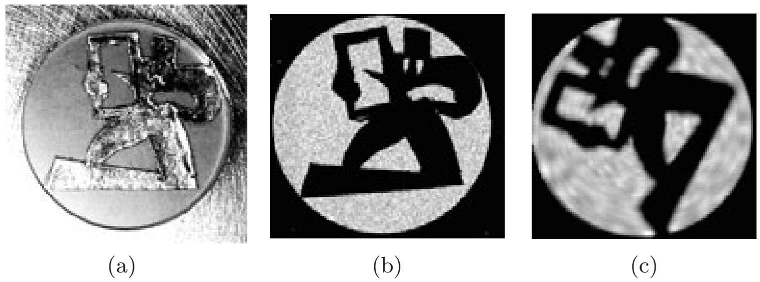

Figure 2. (a) A lead x-ray mask mounted in an aluminum aperture. (b) Static x-ray image of the pattern collected as 432 individual frames with approximately 1/5 photon per pixel per frame. The frames were thresholded and averaged. (c) A reconstruction using randomly-oriented data having an average 2.5 photons/frame and 1.2 million recorded photons. [4]

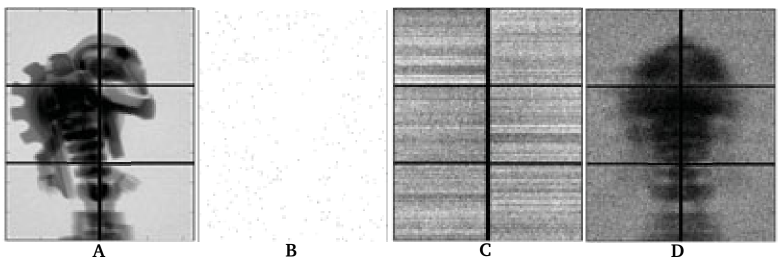

Figure 3. The effects of signal conditioning. A) a high flux static image of a test sample. B) a single low-flux frame. C) the addition of 5000 low-fluence frames with a threshold on the nominal zero level. D) the addition of the same 5000 frames with the threshold set at 15 ADU. The sample was continuously rotating.

97ER62443, DE-FG02-10ER46693 and the Keck Foundation. CHESS is supported by NSF and NIH-NIGMS under NSF Grant DMR-0936384. The data analysis dealing with the extraction from randomly-oriented, sparse data is supported by DOE Grant DE-FG02-11ER16210.

References

[1] Neutze R, Wouts R, van der Spoel D, Weckert E and Hajdu J 2000 *Nature* **406** 752–757 URL `http://dx.doi.org/10.1038/35021099`
[2] Coifman R R, Shkolnisky Y, Sigworth F J and Singer A 2008 *IEEE Trans Image Process* **17** 1891–9
[3] Loh N T D and Elser V 2009 *Physical Review E (Statistical, Nonlinear, and Soft Matter Physics)* **80** 026705 (pages 20) URL `http://link.aps.org/abstract/PRE/v80/e026705`
[4] Philipp H T, Ayyer K, Tate M W, Elser V and Gruner S M 2012 *Opt. Express* **406** 752–757
[5] Philipp H T, Tate M W and Gruner S M 2011 *Journal of Instrumentation*
[6] Philipp H T, Koerner L J, Hromalik M S, Tate M W and Gruner S M 2010 *IEEE Transactions On Nuclear Science* **57** 3795–3799
[7] Tate M W, Chamberlain D, Green K S, Philipp H T, Purohit P, Strohman C and Gruner S M 2012 *SRI2012*
[8] Baum L E, Petrie T, Soules G and Weiss N 1970 *The Annals of Mathematical Statistics* **41** 164–171 URL `http://www.jstor.org/stable/2239727`