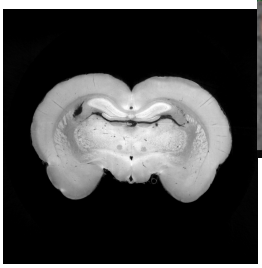

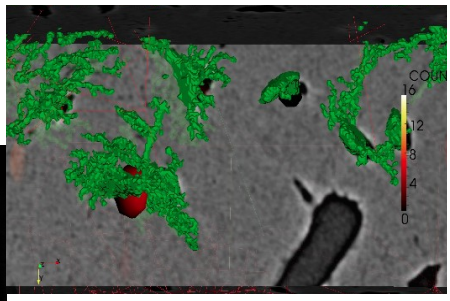

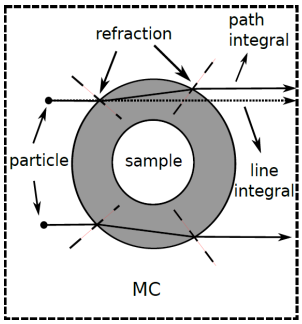

SLS Symposium on

X-rays for Biology

Tuesday, June 4, 2013

10:00 to 12:15, WBGB/019

10:00 Unraveling biological processes with 3D imaging and quantification
K. Mader, F. Bach-Gansmo, H. Birkedal, M. Stampanoni

10:30 On the General Use of Phosphor-SAD Phasing for Solving Nucleic Acid Structure
Peng G., Olieric V., Waltersperger S., Ennifar E., Dumas P., Wang M.

11:00 Coffee

11:15 Simulation of phase-sensitive X-ray imaging by combining wave-optics and Monte Carlo methods
Silvia Peter, Peter Modregger, Michael K. Fix, Werner Volken, Peter Manser and Marco Stampanoni

11:45 Fast Iterative Reconstruction of Differential Phase Contrast X-ray Tomograms
M. Nilchian, C. Vonesch, P. Modregger, M. Stampanoni and M. Unser

Unraveling biological processes with 3D imaging and quantification

K. Mader(1,2), F. Bach-Gansmo(3), H. Birkedal(3), M. Stampanoni (1,2)
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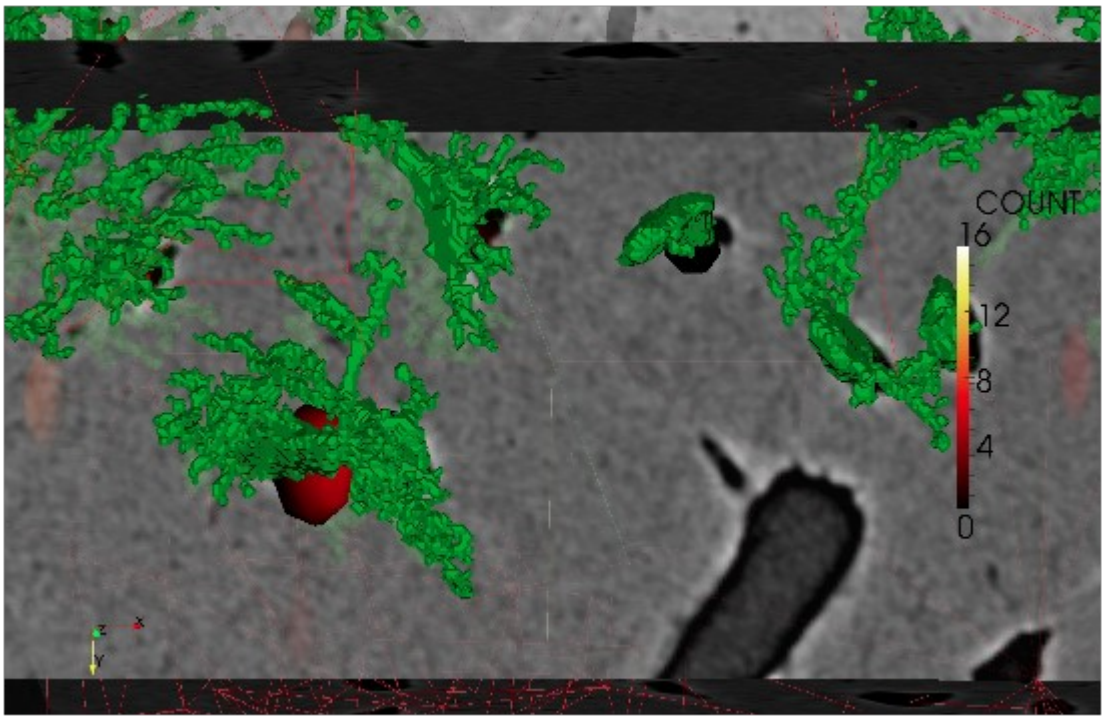
(2) Institute for Biomedical Engineering, University and ETH Zurich, Zurich, Switzerland
(3) iNano and Department of Chemistry, Aarhus University, Aarhus, Denmark

3D tomography has enabled the probing and imaging of biological processes at previously unachievable temporal and spatial resolutions[1]. At these scales, many types of samples have tens of thousands of substructures with complicated patterns of spatial positioning, orientation, and shape. An examination of these structures provides insight into the underlying processes which drive growth, development, and mechanical behavior. In bone tissues the network of small cells called osteocytes, reflect the development course of the bone with more and less organized regions corresponding to newer and older bone respectively [2]. Furthermore as the primary mechanosensors of the bone their spatial positioning and distribution is a proxy for the mechanical sensitivity of the bone tissue. On a finer scale, small processes running in tunnels called canaliculi connect the osteocytes together and enable communication, nutrition, and waste removal. The connectivity of the network, while studied on the scale of dozens of cells, is crucial for understanding pathologies in bone which are known to occur when the intercellular signaling is suppressed.

Recent improvements in flux and image quality have allowed even these nanometer scale structures to be visualized in the context of the entire bone. At the TOMCAT beamline, we have developed a scalable framework [3] for characterizing these complicated structures and reliably condensing millions of voxels into useful quantitative results. Utilizing the cluster computing resources at PSI, the tools developed, while not yet real-time, enable rapid data exploration and preliminary analysis within the timeframe of a beamtime. The framework is easily adaptable to a wide variety of sample types and analyses ranging from egg-shells to ice-cream and even rheological characterizations of foam and volcanic rock.

[1] Mokso R, Marone F, Stampanoni M. Real-Time Tomography at the Swiss Light Source. AIP Conf. Proc. SRI2009, 2009.
[2] Mader K., Schneider P., Müller R., Stampanoni M. 2013. A Quantitative Framework for the 3D Characterization of the Osteocyte Lacunar System, Bone (Submitted)
[3] Mader K, Mokso R, Raufaste C. Quantitative 3D Characterization of Cellular Materials: Segmentation and Morphology of Foam. Colloids and Surfaces A: … 2012;415:230–238. doi:10.1016/j.colsurfa.2012.09.007



A segmentation of the lacunae (red) and canalicular network (green) inside rat bone (calcification density shown in gray-scale) showing the interconnectedness.

On the General Use of Phosphor-SAD Phasing for Solving Nucleic Acid Structure

Peng G. [1], Olieric V. [1], Waltersperger S. [1], Ennifar E. [2], Dumas P. [2], Wang M. [1]

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Attempts to use weak anomalous diffraction signal from Sulfur atoms to solve protein structure are now common practice at both home and synchrotron sources. Successful S-SAD phasing is limited by good diffracting crystal and care taken during data collection (for redundancy and radiation damage especially). Similar to S-SAD for protein, weak anomalous single-photon from Phosphorus atoms may be used to solving nucleic acids structure[1]. Since the Phosphorus are naturally composed in nucleic acid, Phosphorus SAD may have potential to be generalized as a method for various nucleic acid structure.

Highly redundant data were collected on crystals of Sarcin Ricin Loop RNA (27 nucleotides)[2] at a wavelength of 1.6 Å at beamline X06DA of the Swiss Light Source. Successful phasing of this macromolecule, to our knowledge the largest nucleic acid structure solved by P-SAD, showed the validity of the method for medium size RNA. The strategies for sub-structure determination and subsequent phasing procedure will be presented as well as the effects of redundancy and energy of data collection. The potential and limitation of P-SAD phasing for even larger nucleic acid structures and nucleic acid/protein complexes will be discussed in the context of multi-axis goniometry and single-photon counting detector (PILATUS) usage.

References

[1] Z. Dauter and D. Adamiak, Acta. Cryst. D **57,** 990-995, (2001).
[2] C. Correll, I. Wool and A. Munishkin, JMB, **292**, 275-287, (1999).

Simulation of phase-sensitive X-ray imaging by combining wave-optics and Monte Carlo methods

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Due to its high sensitivity towards electron density variations, phase-sensitive X-ray imaging is well suited for the imaging of soft tissue matter. A recently established method is grating interferometry (GI) which produces three complementary types of contrast: absorption, phase and dark-field [1]. However there are still open questions about the image formation process, for example details of the dark-field contrast formation process are not yet fully understood.
A convenient method for developing a deeper understanding of the contrast formation process are numerical simulations. We developed a framework that combines Monte Carlo (MC) methods with wave-optics since for a realistic simulation of phase-sensitive X-ray imaging both particle- and wave-like properties of X-rays have to be taken into account. The simulation framework was split into two parts. The first part containing source and sample was implemented using MC, the second part containing the gratings was implemented using wave-optics. To account for the phase-shift of X-rays passing through the sample the refraction process and the optical path length were included in the MC part. In order to transfer the signal from the MC to the wave-optics the phase-space of particles is transformed into a complex amplitude by regarding each particle as a plane wave which are coherently summed up. In the wave-optics part the amplitude is propagated through the gratings. To validate the framework, comparisons between simulations and measurements obtained at TOMCAT beamline [2] were performed. The results show that the combination of MC with wave-optics was successful and the comparisons showed good agreement between simulations and experimental results, establishing the framework as a reliable technique to model GI. Thus the developed simulation framework, taking refraction and scattering such as Compton and Rayleigh into account, can now be used for detailed investigations of the phase contrast imaging formation process and is particularly suited to study the scattering/dark-field contribution of such processes.

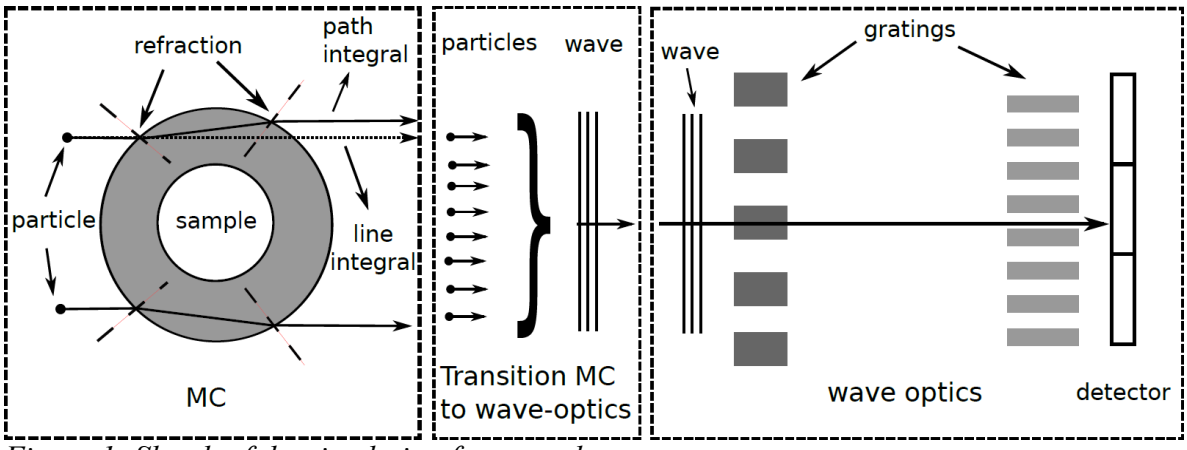

Figure 1: Sketch of the simulation framework.

References

[1] T. Weitkamp et al, Opt. Express 2005; 13(16):6296.
[2] S. McDonald et al, J. Synchrotron Rad. 2009 16, 562

Fast Iterative Reconstruction of Differential Phase Contrast X-ray Tomograms

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Differential phase-contrast is a recent technique in the context of X-ray imaging. In order to reduce the specimen's exposure time, we propose two new iterative algorithms that can achieve the same quality as FBP-type methods, while using substantially fewer angular views. Our first approach is based on 1) a novel spline-based discretization of the forward model and 2) an iterative reconstruction algorithm using the alternating direction method of multipliers. Our second approach is rely on 1) a variational formulation with a weighted data term that leads to an iterative generalization of the filtered back-projection algorithm and 2) a variable-splitting scheme that allows for fast convergence while reducing reconstruction artifacts. Our experimental results on the real data suggest that the methods allows to reduce the number of the required views by at least a factor of four. This is a crucial step towards the diffusion of DPCI in medicine and biology.

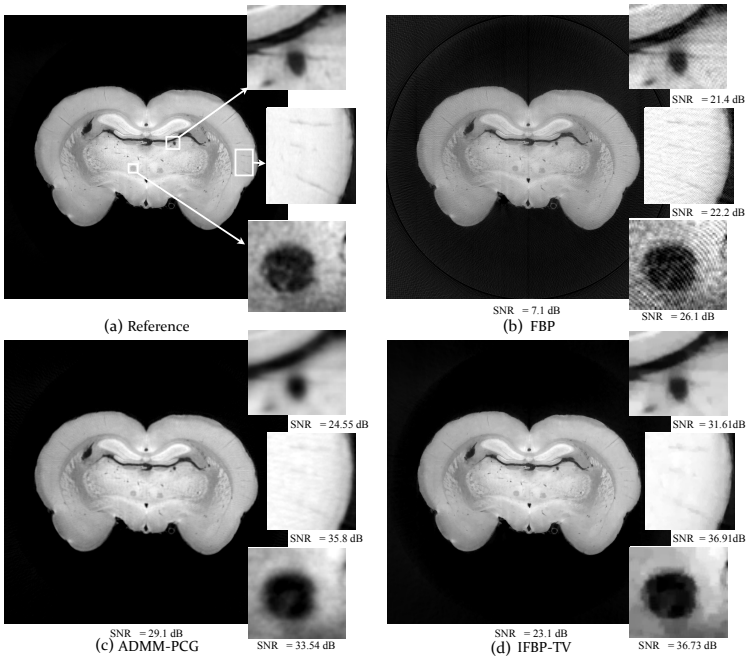

Fig 1 : Comparison of the results. (a) the iterative ADMM approach with 721 directions. (b) GFBP (c) First approach (d) Second approach. The sub-images correspond to the region between the thalamus and the hippocampus (top), a part of hippocampus (middle) and the Fornix (bottom).

References

[1] C. David, B. Nohammer, H. H Solak and E. Ziegler, "Differential x-ray phase contrast imaging using a shearing interferometer," Appl. Phys. Lett. (2002) **81**, 3287-3289 (2002).

[2] M.Nilchian and C.~Vonesch and P.~ Modregger and M.~Stampanoni and M.~Unser, "Fast iterative reconstruction of differential phase contrast X-ray tomograms," Opt. Exp. (2013) **21**, 5511--5528.