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POSTER ABSTRACT PRESENTATIONS

SESSION TITLE: ADVANCES IN EM TECHNOLOGY AND PROCESSING

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Abstract P-4: Robust Method for Background Subtraction in Serial X-ray Diffraction Data

Egor Marin[2], Daniil Vakhrameev[1], Anastasiia Gusach[1], Aleksandra Luginina[1], Kirill Kovalev[1,3], Wei Liu[4], Uwe Weierstall[4], Jaehun Park[2], Ki Hyun Nam[2], Cho Yunje[2], Alexey Mishin[1], Vadim Cherezov[1,5], Valentin Borshchevskiy[1]

[1]*Research Center for Molecular Mechanisms of Aging and Age-related Diseases, Moscow Institute of Physics and Technology, Dolgoprudny, Russia*
[2]*Pohang Accelerator Laboratory, POSTECH, Pohang, Republic of Korea*
[3]*Forschungszentrum Julich, Julich, Germany*
[4]*School of Molecular Sciences and Biodesign Center for Applied Structural Discovery, Biodesign Institute, Arizona State University, Tempe, Arizona, USA*
[5]*Bridge Institute, Department of Chemistry, University of Southern California, Los Angeles, California, USA*

Background: Membrane receptors play an important role in signal transduction across the cell membrane in all living organisms. Their structural studies have been enabled by multiple technological breakthroughs in their heterologous expression, stabilization, crystallization, and crystallographic data collection as well as in cryogenic electron microscopy (cryoEM). During the last decade, serial femtosecond crystallography (SFX) using X-ray free electron lasers (XFELs) has enabled structure determination of previously inaccessible proteins, including several G-protein-coupled receptors (GPCR), that produce only micrometer-sized crystals, thus paving the way towards understanding their activation mechanism and rational drug discovery. In addition to experimental difficulties, membrane protein structure determination is also often accompanied by data processing challenges. In particular, the lipidic cubic phase that serves as a carrier for membrane protein microcrystals, as well as various XFEL beam-shaping devices may generate substantial background scattering that could complicate the structure factor extraction from the diffraction images.

Methods: In this work, we tested an adaptation of the denoising algorithm via matrix decomposition to XFEL-SFX data. We benchmarked its performance using high-background data from PAL-XFEL and established its applicability to serial crystallography image denoising, as well as compared it to the CrystFEL-based image denoising algorithm.
Results: We find that, although the decomposition-based image denoising does not outperform CrystFEL median subtraction, it performs better than the integration without any additional subtraction. We find the non-negative matrix factorization performing better than more traditional singular-value decomposition methods, both in terms of visual interpretability and final data quality.
Conclusion: We hope that this work will draw attention to background subtraction methods in structural biology, and will pave the way towards processing of most challenging datasets in structural biology, in particularly, those collected from membrane proteins.

Key Words: serial crystallography • background subtraction • membrane proteins

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****Corresponding author**: Egor Marin. E-mail:marin@phystech.edu*

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