On a novel approach to 3D reconstruction in Cryo Electron Tomography: Progressive Stochastic Reconstruction Technique (PSRT)

Beata Turoňová[1,2,*], Lukas Marsalek[1,3,4], Tomáš Davidovič[1] and Philipp Slusallek[1,3,5]
[1] *Saarland University, Campus E 1.1, 66123 Saarbrücken, Germany*
[2] *IMPRS-CS, Max-Planck Institute for Informatics, Campus E 1.4, 66123 Saarbrücken, Germany*
[3] *Agents and Simulated Reality Group, DFKI GmbH, Campus E 3.4, 66123 Saarbrücken, Germany*
[4] *Eyen SE, Na Nivách 1043/16, 14100 Prague, Czech Republic*
[5] *Intel VCI, Campus E 1.1, 66123 Saarbrücken, Germany*

[*]turonova@cs.uni-saarland.de; Phone : +49 681 302 3836, Fax : +49 681 302 3843

1. INTRODUCTION

Cryo Electron Tomography (cryoET) plays an essential role in Structural Biology, as it allows us to study structure of large macromolecular complexes in their close to native environment in-situ. It is often combined with high-resolution protocols such as Subtomogram Averaging (SA) to obtain structures of individual complexes from the tomograms. For successful and fully automatic application of these protocols, high-quality reconstructions are necessary. However, the current state-of-the-arts methods, such as Weighted Back Projection (WBP) and Simultaneous Iterative Reconstruction Technique (SIRT), deliver low-contrast and noisy reconstructions which often require manual intervention during SA.

2. RECONSTRUCTION METHOD

The reconstruction in cryoET faces many challenges as the input projections suffer from very low signal-to-noise ratio (SNR) and limited tilt angle. Moreover, the scanned specimen is larger than the detector, which introduces the interior problem into the reconstruction process. We present a novel iterative approach to the tomographic reconstruction problem called Progressive Stochastic Reconstruction Technique (PSRT) [1].

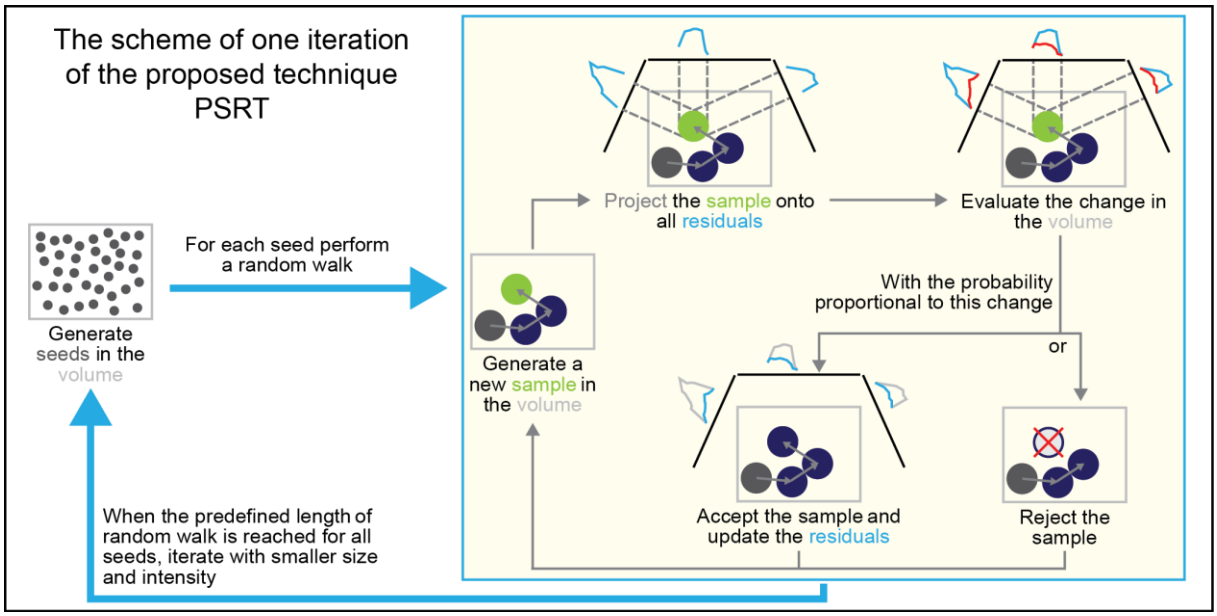

Figure 1. One iteration of PSRT algorithm.

The method is based on a different mathematical framework than the existing techniques - it uses Monte Carlo random walks to perform coarse-to-fine reconstruction: spherical elements, called samples, are placed into the volume at random positions until a stopping criterion is met (Fig. 1). Each sample has given size and

intensity, which are decreased during the reconstruction. A sample is accepted to the volume only if the improvement of the new volume estimate is sufficient with respect to an error metric. The placement of samples is guided by a sampling strategy that, similarly to the Metropolis-Hastings strategy, samples areas with higher acceptance potential more densely, thus speeding-up the convergence. Furthermore, by applying additional importance sampling we can focus only on specific parts of the tomogram, in fact performing a region-of-interest reconstruction. This can be very useful in SA, where one is often interested in individual complexes that are distributed within the whole volume but represent only small portion of it. Finally, PSRT implements a memory efficient solution to the interior problem, removing all associated artifacts.

We compare PSRT to the current state-of-the-art methods both on synthetic and experimental datasets and show that it delivers smoother reconstructions with enhanced contrast (Fig.2) and fewer artifacts. We successfully incorporate the method into a SA pipeline and obtain the correct high-resolution structure of a known biological system.

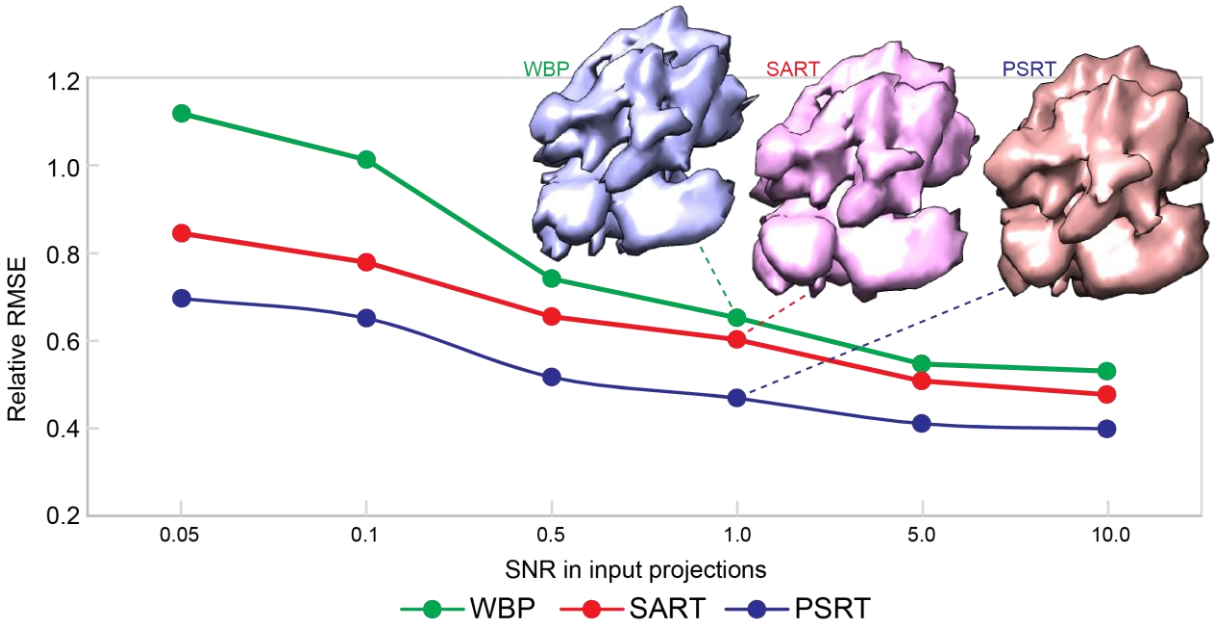

Figure 2. Comparison of relative Root Mean Square Error (RMSE) for reconstructions of a model of the E.Coli 70S ribosome (EMD-1921, filtered to slightly above 30Å) obtained by WBP, Simultaneous Algebraic Reconstruction Technique (SART), and PSRT in connection with different noise levels present in input projections (covering tilt angle from -59° to 63°).

3. CONCLUSION

PSRT is a novel approach to the tomographic reconstruction which is designed to suit the specific conditions in cryoET. It delivers high-contrast reconstructions without any loss of high-resolution structural information and implements memory efficient solution to the interior problem. Finally, it can be easily incorporated into a typical SA pipeline, where it significantly improves template-based localization and provides an elegant solution to the region-of-interest reconstruction.

ACKNOWLEDGEMENTS

The research leading to these results was mainly funded by an International Max Planck Research School for Computer Science (IMPRS-CS) scholarship. The research leading to these results has received additional funding from the European Union's Seventh Framework Programme under grant agreement n° FP7-267038 (NOTOX) and the DFG grant IMCL (AOBJ: 600875).

REFERENCES

[1] Turoňová, B., Marsalek, L., Davidovič, T. and Slusallek, P., *Journal of Structural Biology*, **189(3)**, 195-206 (2015)