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

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Cryo Electron Tomography (cryoET) plays an essential role in Structural Biology, as it is the only technique that allows us to study structure of macromolecular complexes in their close to native environment *in-situ*. The reconstruction process faces many challenges as the input projections suffer from very low signal-to-noise ratio and limited tilt angle. Moreover, the scanned specimen is larger than the detector, which introduces the interior problem into the reconstruction process. High-resolution protocols such as Subtomogram Averaging (SA) can alleviate some of these limitations; however, in order to be fully automatic they require reconstructions of high quality. Current state-of-the-art methods, such as Weighted Back Projection (WBP) or Simultaneous Iterative Reconstruction Technique (SIRT), deliver reconstructions that often require manual intervention during SA. We present a novel iterative approach to the tomographic reconstruction problem called Progressive Stochastic Reconstruction Technique (PSRT). The method is based on Monte Carlo random walks guided by a sampling strategy similar to the Metropolis-Hastings strategy. PSRT is designed to suit the specific conditions in cryoET - it delivers high-contrast reconstructions without any loss of high-resolution structural information and it 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.