Fitting High-Resolution Electron Density Maps from Atomic Models to Solution Scattering Data

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Solution scattering provides information of protein conformation and dynamics in solution that complements high resolution structure techniques such as crystallography and cryo- electron microscopy (cryo-EM). Our algorithm DENSS performs ab-initio 3D electron density reconstruction from the 1D scattering profile. The primary limitation in the resolution of these reconstructions is the lack of information in the 1D scattering profile. Hybrid modeling approaches combining high-resolution structural information with solution scattering improves the resolution from solution scattering data.

In order to integrate a hybrid model approach with DENSS, we developed a method to calculate accurate high resolution electron density maps from atomic models that accurately fit solution scattering data.

Real space form factors were calculated to generate an electron density map, then converted to reciprocal space to calculate a scattering curve to compare with experimental data. The form factors of atoms in solution include components from the in-vacuo form factor, the excluded bulk solvent (excluded volume), and the hydration shell. Real space Cromer-Mann form factors were calculated using an analytical radial Fourier transform.

Gaussian dummy atoms centered at protein coordinates were used to directly calculate the excluded volume in real space. The hydration shell was represented as a shell of water molecules at the surface of the protein. Fitting parameters were assigned to bulk solvent density, excluded volume, and the hydration shell contrast. A minimization technique was used to fit these parameters such that the high-resolution electron density map had a scattering profile that best matched experimental data.

This algorithm successfully fit electron density maps for several wide-angle x-ray scattering (WAXS) benchmark datasets obtained from the Small Angle Scattering Biological Data Bank (SASBDB). This algorithm will allow for future development of tools of hybrid density-based modeling.