COMPUTATIONAL CHALLENGES FOR WIDE-ANGLE X-RAY SOLUTION SCATTERING OF PROTEINS

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INTRODUCTION

The advent of high-brilliance third-generation synchrotrons like the Advanced Photon Source (APS) has enabled the development of high-resolution X-ray solution scattering studies called WAXS (wide-angle X-ray solution scattering) (1). Experiments on protein solutions demonstrate that significant structural information is encoded in the measured scattering patterns (2). The interpretation of measured scattering remains hindered by the lack of available software for estimating scattering given protein structure. Existing tools such as CRYSOL (3) exploit significant approximations for computational efficiency in small-angle X-ray scattering (SAXS) studies, but these approximations are of questionable accuracy for wide-angle investigations. We are developing methods to estimate WAXS patterns with high accuracy and efficiency.

METHODOLOGY

We estimate the scattering at a particular momentum q using the formula

$$I(q) = < |A_{prot}(\vec{q}) + A_{excl}(\vec{q}) + A_{hyd}(\vec{q})|^2 >_\Omega$$

where $I(q)$ represents the total scattering intensity (averaged over all protein orientations), the Fourier transform of the protein electron distribution is written as $A_{prot}(q,W)$, the transform of the solvent-excluded volume as $A_{excl}(q,W)$, and the transform of the hydration layer as $A_{hyd}(q,W)$. In the present implementation, the protein is assumed to be rigid; future work will develop methods for calculating time-averaged scattering from flexible molecules.

We calculate the average over orientation angles numerically. Other implementations such as CRYSOL (2) have avoided numerical averaging by modeling the excluded volume as a sum of atomic volumes or by representing the molecular geometries using spherical harmonics. Our more flexible treatment enables us to use more realistic representations of the excluded volume and hydration layer.

We have also analyzed different methods of defining the excluded-volume function $A_{excl}(\mathbf{r})$, whose transform is $A_{excl}(\mathbf{q})$. Most software for estimating scattering model this function as a sum of the excluded volumes for each of the protein atoms. Strictly speaking, however, the excluded volume is the *union* of atomic excluded volumes. Our program SoftWAXS allows the use of either model. We use pre-existing software to generate the surface that bounds the union of atomic volumes and calculate the Fourier transform hierarchically using oct-trees.

RESULTS

The Fourier-transform and spherical-averaging algorithms in SoftWAXS have been validated using analytical test cases (Figure 1). Comparison of scattering patterns calculated using SoftWAXS and CRYSOL is underway (Figure 2).

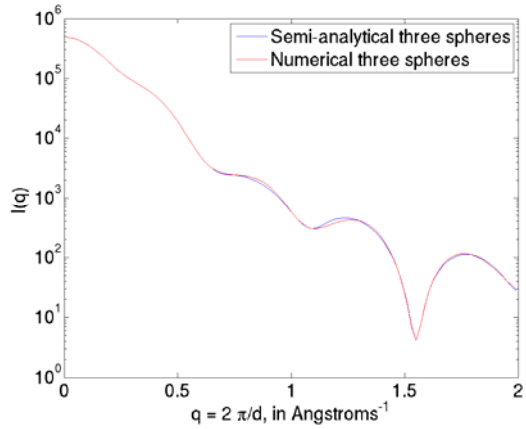

Figure 1. Validation of the hierarchical Fourier transform and spherical averaging procedures.

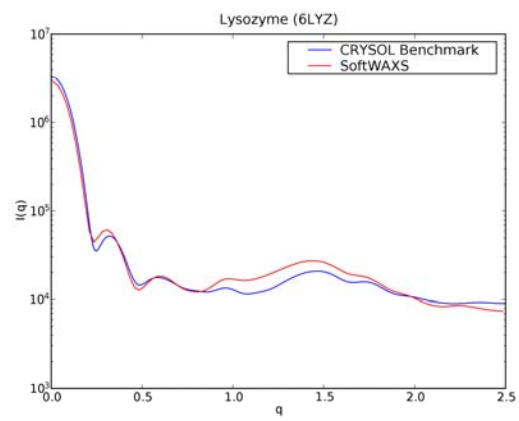

Figure 2. Comparison of lysozyme scattering estimated using SoftWAXS and CRYSOL.

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