What went wrong and right in trying to improve models for CASP-SAXS targets?

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Small-angle X-ray scattering (SAXS) provides information about the native states of proteins in solution. Such information is regarded as invaluable to elucidate protein function(s). Using SAXS data, we strove to improve prediction models of target proteins in the "data-assisted" category of the 13th Community-Wide Experiment on the Critical Assessment of Techniques for Protein Structure Prediction (CASP13).

For this category, we combined our prediction protocol based on template-based modeling and the selection procedure of protein models using SAXS data. Our prediction protocol to construct models for a target protein comprises the following steps: 1) prediction of intrinsically disordered region (IDR) of the target protein, 2) profile construction for the target sequence except IDR, 3) profile–profile alignment and scoring against profile libraries of template sequences performed by FORTE series, that are our own profile–profile comparison methods, and 4) model construction based on the alignments using MODELLER. Subsequently, we selected models with better values in terms of two metrics, i.e., volatility of ratio and χ^2. For this selection procedure, we measured these two values using FoXS between the calculated SAXS scattering profile from a model and the experimental SAXS scattering profile.

Results show that, by considering SAXS data and also occasionally considering models from server predictions, we improved prediction models of protein complexes for some CASP-SAXS targets. However, contrary to our expectations, we worsened models of monomers. In some cases, the SAXS scattering profiles calculated from crystal structures differ from experimentally obtained profiles in terms of the two metrics. We will present examples of these problems and discuss issues that should be addressed to avoid them.