High-Accuracy Prediction of Protein-Carbohydrate Interactions

Andreas Kerzmann[1], Dirk Neumann[2], Oliver Kohlbacher[1]

[1]University of Tübingen, Tübingen, Germany
[2] Center for Bioinformatics, Saarland University, Saarbrücken, Germany

Abstract

Modeling lectin-sugar interactions computationally became possible very recently with the increase in the number of lectin-sugar complexes from X-ray crystallography available through protein databases. Although the number of structures is still very limited, it is now possible to venture into the field of analyzing the interactions on an atomistic level and use the insights gained for creating an energy scoring scheme for this special kind of protein interaction. Until now energy functions used for calculating binding free energies of lectin sugar complexes were standard molecular mechanics force fields which were parameterized for that purpose or time consuming free energy perturbation calculations which gained high accuracy at the prize of week-long calculations. Additionally, these force fields do often neglect important contributions to the binding of sugars to lectins, like hydrogen bonding, solvation effects and electrostatics.

The goal of our work is the development of an energy scoring function tailored to the somewhat special case of sugar lectin binding keeping accuracy and computational efficiency in mind. We use an extensive set of thoroughly researched lectin sugar complexes from crystallography data and their binding free energies obtained from microcalorimetric studies. We analyzed the data, removed structural problems and used it for the calibration and validation of our newly created SLICK energy function. This function is derived from empirical scoring functions for the protein-peptide case and modified for lectin-sugar interactions by incorporating lectin-sugar specific contributions and improving those parts of the model that we deem important for the binding process. The prediction quality of our function on the validation set is encouraging, yet there is still work to be done for improving the robustness and the accuracy of our predictions.