Overview thesis Gydo van Zundert

**On explorative and integrative modeling of biomolecular complexes**

*Chapter 1: Introduction*

Overview of the integrative modeling field, with an emphasis on cryo-electron microscopy and cross-links from mass spectrometry.

*Chapter 2: Fast and sensitive rigid body fitting into cryo-EM density maps with PowerFit.*

Here I introduce software called PowerFit for automatic fitting of high-resolution subunits in cryo-EM densities, using a new more-sensitive scoring functions, and other algorithmic tweaks to accelerate the docking.

*Chapter 3: Exploring and leveraging the limits of rigid body fitting in cryo-EM densities with multi-scale image pyramids.*

The limits of rigid body fitting of high-resolution subunits into cryo-EM density maps is systematically tested using the concept of the image-pyramid; the results are subsequently leveraged to reduce the time required for an automatic fit with PowerFit up to two orders of magnitude.

*Chapter 4: Integrative modeling of biomolecular complexes: HADDOCKing with cryo-EM data.*

Our inhouse data-driven docking program HADDOCK is extended such that cryo-EM data can be used actively during all stages of the docking and is still fully compatible with all other available sources of information.

*Chapter 5: DisVis: Quantifying and visualizing the accessible interaction space of distance-restrained biomolecular complexes.*

I introduce a second piece of software called DisVis to quantify and visualize the information content of distance restraints, e.g. from cross-links with mass spectrometry. In addition, it gives insight into the presence of false-positive restraints and can identify the culprit.

*Chapter 6: Extracting interface residues from distance-restraints for high-resolution HADDOCKing.*

Using an extension of DisVis, residues likely to be at the interface can be extracted from distance-restraints with high recall and sensitivity. The resulting residues can be used as input for HADDOCK to increase the performance for the docking.

*Chapter 7: Perspectives*

The last chapter shows perspectives on integrative modeling and showcases a few uses.