17.7.2008

Research visit to the

Vrije Universiteit Amsterdam

7.4. – 30.6.2008

The research group Computational Medicinal Chemistry and Toxicology is located at the Department of Pharmaceutical Sciences at the Vrije Universiteit in Amsterdam. The research of the group focuses on molecular dynamics (MD) simulations of biomolecules, free energy calculations and docking and scoring of small compounds to protein structure. The group leader Dr. Chris Oostenbrink has long experience of using and developing Gromos simulation program.

The aim of my research visit was to create new tools for analyzing MD simulation trajectories. The effects of ligand binding into a nuclear receptor and signal transmission to the heterodimeric partner protein can be studied with MD simulations combined with fluctuation analysis. The main problem of this approach is that fitting of protein structures for the fluctuation calculation produces noise and smaller changes cannot be seen.

A new algorithm developed during my visit avoids this problem by using local fitting on stable atoms. The algorithm will be tested with the PPARα-RXRα heterodimer which is extensively studied earlier with other methods, and then applied on VDR-RXRα heterodimer, in which the changes are smaller and more sensitive methods are needed.

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