A U S H A N G

FREIE UNIVERSITÄT BERLIN
Fachbereich Mathematik und Informatik

Promotionsbüro, Arnimallee 14, 14195 Berlin

D I S P U T A T I O N

Mittwoch, 19. Juni 2013, 14.00 Uhr

Ort: π-Gebäude, Arnimallee 6, 14195 Berlin, Raum 108/109

Disputation über die Doktorarbeit von

Herrn Alexander Bujotzek, M.Sc.

Thema der Dissertation:

Molecular Simulation of Multivalent Ligand-Receptor Systems

Thema der Disputation:

Modeling rebinding effects in multivalent chemical systems

Die Arbeit wurde unter der Betreuung von **PD Dr. M. Weber** durchgeführt.

Abstract: Multivalent ligand-receptor systems often show an enhancement in binding affinity compared to similar monovalent systems. This cooperative effect is also denoted as chelate cooperativity, as opposed to the more well-known type of allosteric cooperativity. Both effects play an important role in biological systems.

The cooperative effect in multivalent systems is often attributed to the favorable spatial preorganisation of the ligands with regard to the receptor, supposedly leading to a reduced entropy loss upon binding.

Another factor that has been shown to contribute to the cooperative effect in multivalent systems is "rebinding": As soon as a single ligand-receptor complex dissociates, the presence of one or more ligands still "anchored" to the receptor increases the probability of a rebinding event, which in turn will drive the system to a state where all ligands are bound. This leads to a significant deceleration of the dissociation rate and thus to very stable complexes – offering, for example, intriguing possibilities to improve the efficacy of drug molecules.

The talk will address the difficulties of modeling rebinding effects with current kinetic models while pointing out approaches to circumvent these problems. A predictive approach is presented that enables the researcher to estimate the rebinding propensity of a given system from both coarse and atomistic simulations.

Die Disputation besteht aus dem o. g. Vortrag, danach der Vorstellung der Dissertation einschließlich jeweils anschließenden Aussprachen.

Interessierte werden hiermit herzlich eingeladen

Der Vorsitzende der Promotionskommission
PD Dr. M. Weber