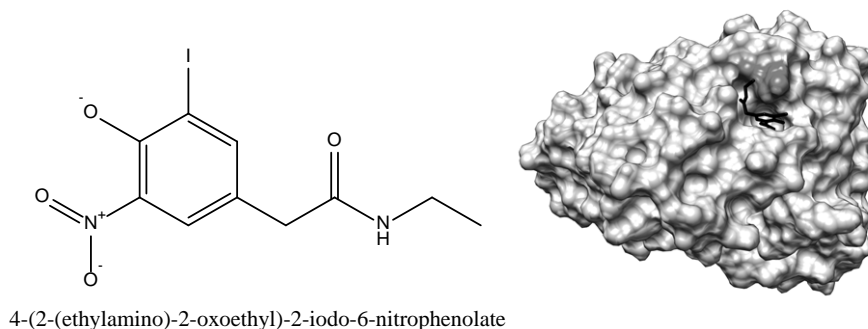


Study of the Hapten-Binding Properties of Antibody B1-8 Using Steered Molecular Dynamics

Benedikt Diewald, Heinrich Sticht

*Bioinformatik, Institut für Biochemie, Friedrich-Alexander-Universität Erlangen-Nürnberg
Fahrstr. 17, 91054 Erlangen*



Left: Structure of NIP. Right: B1-8 FV-Fragment (light grey) with NIP (black) and Y101_H highlighted in dark grey.

Antibodies are vital to humoral immunity. With recurring exposures to the same antigen, the affinity of serum antibodies for this specific antigen will increase. This process is referred to as affinity maturation and can yield antibodies in a secondary response that have an affinity several orders of magnitude higher than in the primary response. The hapten-binding antibody B1-8 represents a model system to investigate affinity maturation. The mutation W33L in the heavy chain (W33_HL) is especially interesting since it always occurs in the secondary response and increases affinity approximately by one order of magnitude. This study uses MD-simulations of wildtype B1-8 and W33_HL B1-8 in an unliganded state and bound to 4-(2-(ethylamino)-2-oxoethyl)-2-iodo-6-nitrophenolate (NIP) to assess the molecular basis for this increase in affinity. In addition steered MD-simulations are used to pull NIP out of the binding pocket and determine the effect of the mutation on the exit path and the off-rate.