# Molecular Dynamics Simulations of Neuraminidase - N1 Subtype

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Neuraminidase (NA) is a surface protein of the influenza virus and drug target for antiviral NA inhibitors. The avian influenza strain of 2005, the 2009 swine-origin influenza and the pandemic influenza of 1918 show the NA subtype N1. In crystal structures of avian N1 [1] and pandemic 1918 N1 [2] two different conformational states of the 150-loop occurred and an additional cavity next to the active site was revealed. Interestingly, in 2009 N1 only the closed state was observed [3].

We compare sequence and structure of the three N1 variants [1-3] and an oseltamivir-resistant variant [4]. Explicit solvent molecular dynamics (MD) simulations are performed for the 4 variants for 20ns applying the program Amber and the implemented forcefield ff99SB [5]. Dimer systems are investigated for the relevance of the protein-protein-interface. The simulations reveal the 150-loop as regions of higher flexibility for all variants. This observation is consistent with previous simulations of avian N1 [6]. The 2009 N1 shows reduced flexibility than the other N1 variants in the 150-loop.

The data indicate differences in flexibility for the neuraminidase subtype N1 variants. Sequence-dependent flexibility is applied to predict the susceptibility of established and new drugs towards emerging variants and mutants of NA.

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