

**P023** pH-dependent conformational change of a flavivirus fusion protein

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Important viral pathogens such as influenza or flaviviruses (e.g. dengue fever, yellow fever and TBE) enter their host cells via low pH-dependent membrane fusion. After endocytosis of the virus the host cell lowers the endosomal pH. Acidification in turn triggers a conformational change of the viral envelope proteins, which then are thought to fuse the envelope with the host membrane. Through sequence alignment and structural analysis several highly conserved histidines were identified in dengue virus type 2 envelope protein. Some are located at domain and subunit interfaces and have been proposed to play a critical role in triggering refolding into the post-fusion form. To shed light on this process, Molecular Dynamics (MD) simulations were performed under different effective pH conditions. The simulations rapidly exhibit initial stages of dimer disassembly and considerable conformational change, suggesting that specific histidine interactions act as switches in the refolding from pre-fusion to fusion state.