Summary for non-experts

Viruses depend on a host for their continued existence: they invade a host cell and hijack its machinery to produce new virus particles. In this thesis we studied two virus species that infect humans. Influenza virus ("the flu") causes yearly epidemics due to its ability to extensively change appearance; this continuous shapeshifting makes the threat of a new, deadly influenza pandemic real. Chikungunya virus has recently spread across the globe and is transmitted by mosquitos whose range expands with global warming. Full protection or treatment against either virus remain unavailable. Both viruses have an envelope, a membrane wrapping the viral contents. A key step in entry is the merger of the viral envelope with the envelope that covers cells. Protein spikes on the outside of the virus mediate this fusion event. In the process, the proteins extend and grab the target membrane after which they fold back onto themselves. Thereby, they force both membranes to come together and merge, mixing the viral contents into the cell. This thesis focuses on determining the mechanisms that these proteins use to achieve entry. We use a microscopy technique that allows us to observe the behavior of individual virus particles. By controlling the experimental conditions and using agents that block fusion, new insight was obtained on the way these proteins function, and specifically, how multiple spike proteins need to work together to mediate fusion. Such knowledge of the exact mechanisms involved in viral fusion will help to guide the design of new antiviral therapeutics.