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Timescale of SARS-CoV2 spike protein mediated membrane fusion

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The fusion of viral and host cell membranes is a pivotal step in the infection and life cycle of any virus. Despite the massive global research interest in SARS-CoV-2 many aspects of the fusion process are still only rudimentarily understood. Biological fusion assays are widely applied to study different steps of viral-host membrane fusion, however, multidisciplinary approaches offer a broader range of parameters to study and the exact timescale of the fusion on a microscopical scale is still elusive. Here, we report the establishment of a new model system for viral fusion based on the neutron scattering behavior of tailored unilamellar lipid vesicles with specific membrane proteins, either SARS-Cov2 spike or ACE2 receptor proteins. Our target was to design individual vesicles from cellular material which only contain the membrane proteins included in the initial cellular plasma membrane and none of the organelle membranes within the cell. Thus, by protein expression on the cells, individual virion and target vesicles could be designed. The results of creating 100 nm unilamellar vesicles by extrusion were confirmed by several methods, among the dynamic light scattering as well as neutron scattering. A contrast matched fusion experiment with SANS allowed us to determine the timescale of the fusion between SARS-Cov2 virions and human host cells which speeds up by several orders of magnitude in the presence of the SARS-CoV2 spike protein.

[1] S. Jaksch et al., *Timescales of Cell Membrane Fusion Mediated by SARS-CoV2 Spike Protein and its Receptor ACE2*, in preparation.

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