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COVID-19 Research at Neutron Sources

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The number of confirmed COVID-19 cases worldwide is marching towards one hundred million, while the number of deaths is approaching a grim milestone of two million. This deadly disease caused by the novel coronavirus SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) has become one of the leading causes of death in 2020, according to the World Health Organization. Although several vaccines have been developed to slow down the spread of SARS-CoV-2, there is a need for therapeutic agents, including small-molecule drugs that inhibit essential steps in the viral replication cycle. A large part of the genome of SARS-CoV-2 encodes for non-structural proteins (NSPs) that assemble in the endoplasmic reticulum of infected cells to support viral RNA synthesis and virus replication. These proteins display multiple functions and activities and were shown to form various complexes. Understanding the dynamic assembly and disassembly of NSPs and their interaction with RNA during virus replication is key to development of effective therapeutic agents against COVID-19. In this presentation, I will highlight how different neutron scattering techniques are being used for SARS-CoV-2 research. Neutron macromolecular crystallography is being used to pinpoint critical hydrogen positions in active sites of the main protease, a critical target for therapeutics development. Insights into how the NSPs of the SARS-CoV-2 replication machinery assemble to form complexes with each other and with viral RNA are being performed using small-angle neutron scattering. Interactions of SARS-CoV-2 surface proteins with host cell membranes are being studied using neutron reflectivity. Neutron spectroscopy techniques are providing information about the dynamical properties of drug molecules that can be used to inform computational drug design studies. These studies provide unique information about the SARS-CoV-2 replication machinery that is unattainable by other means.