AI-enabled multiscale modeling of SARS-CoV-2 replication transcription complex

Arvind Ramanathan

Data Science and Learning Division, Argonne National Laboratory

The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) replication transcription complex (RTC) is a multi-domain protein responsible for replicating and transcribing the viral mRNA inside a human cell. Attacking RTC function with pharmaceutical compounds is a pathway to treating COVID-19. Conventional tools, e.g., cryo-electron microscopy and all-atom molecular dynamics (AAMD), do not provide sufficiently high resolution or timescale to capture important dynamics of this molecular machine. Consequently, we develop an innovative workflow that bridges the gap between these resolutions, using mesoscale fluctuating finite element analysis (FFEA) continuum simulations and a hierarchy of AI-methods that continually learn and infer features for maintaining consistency between AAMD and FFEA simulations. We leverage a multi-site distributed workflow manager to orchestrate AI, FFEA, and AAMD jobs, providing optimal resource utilization across HPC centers. Our study provides unprecedented access to study the SARS-CoV-2 RTC machinery, while providing general capability for AI-enabled multi-resolution simulations at scale.