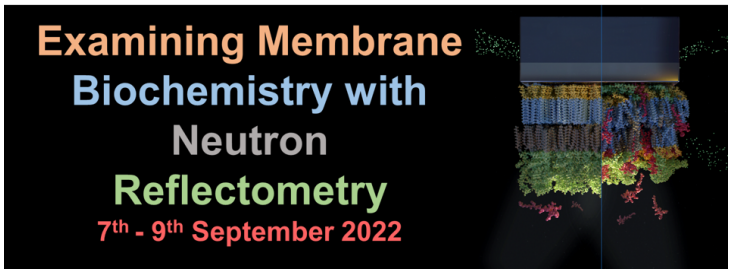

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Structural kinetics of Hepatitis B virus from small-angle scattering and computational modelling

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The genetic material of viruses is typically protected in an icosahedral capsid, which is primarily assembled from multiple subunits of the same protein in a spontaneous self-assembly process. Similar highly efficient assembly processes are ubiquitous in biological systems, and viral capsids in particular present a unique platform to exploit for therapeutic advances in the targeted cellular delivery of cargo packaged within the capsid. Our research aims to provide a more detailed understanding of how this precise viral capsid protein assembly process occurs from a pool of single building blocks, and specifically how the RNA is incorporated into the capsid. Here, we present results from small-angle neutron scattering (SANS) experiments using contrast variation to reveal the final assembled structural organization of both the protein and nucleic acid components from recombinant full-length Hepatitis B virus (HBV) capsid protein and a synthetically prepared RNA containing the capsid protein binding domain. Time-resolved small-angle x-ray scattering (SAXS) experiments were also used to determine the HBV assembly pathway in the presence and absence of RNA. We employed Bayesian statistics-based computational methods to extract kinetic parameters of assembly and the overall size and shape of the dominant structural intermediates from the SAXS data. The developed framework can be extended to other hierarchical assemblies in biology.

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