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Short Talk 7, Ryan Oliver - Integrative structural biology with complementary experimental methods to describe viral capsid protein self-assembly

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The genetic code of viruses, RNA or DNA, are typically protected in an icosahedral capsid, which is primarily assembled from over a hundred subunits of the same protein in a spontaneous self-assembly process. Similar highly efficient assembly processes are ubiquitous in biological systems; viral capsids 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 additionally the effect and organization of nucleic acid present during assembly. Here, we present results from small-angle neutron scattering experiments using
contrast variation to reveal the final assembled structural organization of both the protein and nucleic acid components from recombinant Hepatitis B virus (HBV) capsid protein and a synthetically prepared RNA containing the capsid protein binding domain. These data revealed that RNA was localized along the inner capsid
surface. Time-resolved small-angle x-ray scattering (SAXS) experiments were also used to determine the structure during HBV capsid assembly 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. Additional single-particle cryoEM reconstructions are
provided to assess the effect of RNA on the resulting assembled capsid structure. The combination of timeresolved
scattering data, Bayesian statistics, and cryoEM structural analysis, provides a framework which not only describes the viral self-assembly process, but can be extended to other hierarchical assemblies in biology.

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