(i.e. base pairing). Of particular interest, our results demonstrate that the amount and pattern of base pairing significantly alter the amount of polymer packaged within the capsid, providing a biologically relevant example of the relationship between cargo structure and capsid assembly.

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Simulation Studies on the Role of the M2 Protein in Viral Budding

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The budding of enveloped viruses is a complex multi-step process requiring alterations in membrane curvature and scission at the neck of the budding virion. M2 is a pH-dependent matrix protein from influenza virus widely known for its role in viral uncoating and the target of the amantadine flu drug that prevents proton transport. An additional role played by M2 relies on collective effects where M2 clusters have been hypothesized to induce local membrane curvature, resulting in a reduced energetic cost associated with the bending of the membrane and where the budding of virus particles takes place in a cholesterol dependent manner (Rossman et al., Cell 142, pp. 902-913, 2010).

We use computer simulations to study the effect of M2 tetramers on lipid mixtures consisting of sphingomyelin, DOPC and cholesterol in different ratios and temperatures in a range where lipid mixing and segregation take place. We are working on estimating entropic and free energy contributions to membrane curving and other energetic and structural effects through large-scale simulations with the coarse-grained MARTINI model. These models will form the basis for understanding in detail how M2 induces curvature in membranes as part of the viral budding mechanism in influenza.

2126-Pos Board B145

Atomic Model of Rabbit Hemorrhagic Disease Virus by Cryo-Electron Microscopy and Crystallography

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Rabbit hemorrhagic disease, first described in China in 1984, causes hemorrhagic necrosis of liver after infection. Its etiological agent, rabbit hemorrhagic disease virus (RHDV), belongs to the *Lagovirus* genus in the *Caliciviridae* family. The molecular structure of member of *Lagovirus* is still unknown in detail. Here, we reported a cryo-electron microscopic reconstruction of wild RHDV at 6.5 Å, the crystal structures of the S and P domain of its major capsid protein VP60 at 2.0 Å, and the building of a complete atomic model of the RHDV capsid. RHDV VP60 has a conserved S domain and a specific P2 sub-domain that differ from those found in other caliciviruses. Comparison between our high-resolution model and previously reported model of RHDV capsid reveals distinct structures of the P2 sub-domains and different conformations of the NTA domains. Sequence alignments of VP60 from six groups of RHDV strains reveal seven varied regions that can be mapped onto the surface of P2 sub-domain and suggest three putative binding pockets that might be responsible for histo-blood group antigen binding. A flexible loop (a.a.300-318) selected from these regions is found to interact with rabbit tissue cells and to contain an important epitope for anti-RHDV antibody production. Our study provides the first authentic atomic structure of a *Lagovirus* and suggests a new candidate for an efficient vaccine to protect rabbits from RHDV infection.

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The Role of RNA Secondary Structure in Viral Assembly

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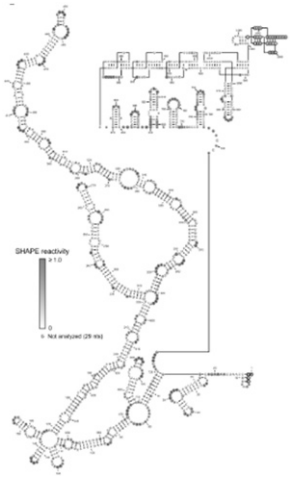
Some small icosahedral RNA viruses (e.g., MS2) require a specific packaging signal for the formation of virus particles. Others (e.g., cowpea chlorotic mottle virus (CCMV); Pariacoto virus (PaV)) are able to encapsidate a wide variety of RNAs, forming virus-like particles (VLPs) whose structure are only slightly different from that of the wild-type virus. We have determined the structure of the genomic RNA of satellite tobacco mosaic virus (STMV) in an in vitro transcript (see image below). This structure is very different from the structure of STMV RNA probed inside the virus by Schroeder et al. (BJ 101:167 (2011)), which consists of a string of stem-loops connected by single-stranded regions. We have also developed all-atom models for three viruses: PaV (using a hypothetical secondary structure and a non-viral sequence); STMV (using the true sequence and the Schroeder secondary structure); and MS2 (using the true sequence and a hypothetical secondary structure). In this talk, we discuss the implications of these secondary structures and three-dimensional models for the pathways of viral assembly.



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The cryo-EM Reconstruction of Drosophila C Virus (DCV) at 5.4 Å

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The Dicistroviridae family, which is currently classified under the Picornavirales order, groups a pool of arthropod-infecting viruses with bicistronic genomes. The interest in this family of viruses has been fueled due to the economical implications of their hosts, which range from beneficial arthropods (bees and shrimps) to insect pests (crickets, ants and triatomines). Two crystallographic structures of dicistroviruses have been reported to date: Cricket Paralysis Virus (CrPV, type species of the Cripavirus genus) and Triatoma Virus (TrV). their structures revealed that dicistroviruses share a core archetypal organization, which is complemented by external and internal capsid-wide differences that likely have arisen from unique host adaptation. In this work we report the cryoEM reconstruction at 5.4 Å resolution, and C-alpha trace of Drosophila C Virus (DCV), a viral pathogen that infects Drosophila melanogaster, among other Drosophila species. This virus holds a 65.8% sequence identity with CrPV and, given the ability of the latter to replicate in Drosophila hosts, a detailed comparison can give insight into the infective cycle of dicistroviruses.

Keywords: cryoEM, reconstruction, dicistroviridae, DCV

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Molecular Structures of Native HA Trimers on 2009 H1N1 Pandemic Influenza Virus Complexed with Neutralizing Antibodies

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Antigenic variation of influenza virus hemagglutinin (HA) remains the principal challenge in developing more effective vaccines. Here, we report determination of the 3D structures of HA trimers on intact 2009 H1N1 pandemic virus particles in the absence and presence of neutralizing antibodies. We studied HA trimer structures bound to H17-L10, an antibody that recognizes a quaternary epitope near the head region of the trimer, and to C179, a broadly neutralizing antibody that is reactive to the conserved stem region of HA and neutralizes viruses expressing a broad range of HA subtypes (H1, H2, H5, and H9). We deduce the locations of the molecular surfaces of HA involved in interaction with each of these antibodies. Despite the dense packing of HA trimers on the viral surface, and the location of the stem region close to the viral membrane, we show that ~75% of HA trimers have C179 bound to the stem domain. Thus, the majority of HA trimers on intact virions are available to bind anti-stem antibodies that target conserved HA epitopes, suggesting that universal influenza vaccines that elicit such antibodies could be effective.