

SANS team finds structural differences in *Sindbis* virus particles from different host species

A research team using small-angle neutron scattering (SANS) at DOE's High Flux Isotope Reactor at ORNL has demonstrated for the first time that particles of the *Sindbis* virus from insect and mammalian hosts exhibit subtle structural differences. The *Sindbis* virus, discovered in 1952 in Cairo, Egypt, is transmitted from birds (vertebrate hosts) by mosquitos (invertebrate vectors) to humans (vertebrate mammalian hosts), causing sindbis fever, which is accompanied by joint pain, rash, and malaise.

The scattering data and modeling indicate that, although the radial position of the virus lipid bilayer is not significantly different between the two species, the *Sindbis* virus grown in mammalian cells has significantly more cholesterol in the lipid bilayer than the same virus grown in insect cells. Additionally, the outer protein coat of the mammalian *Sindbis* virus was found to be more extended, giving the virus a larger diameter. The SANS data also demonstrated that the mammalian-cell-grown virus has a different distribution of RNA in its core than does the virus from insect cells. The RNA and nucleocapsid protein in the mammalian virus were found to interact closely.

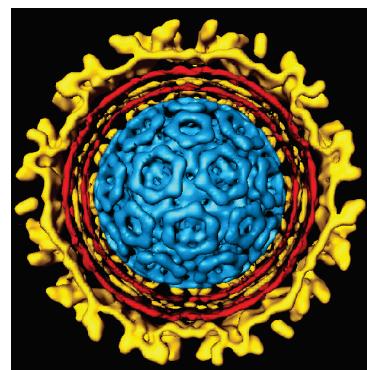
The complex natural cycle of vectored viruses that transition between host species, such as insects and mammals, makes understanding the full life cycle of the virus an

incredibly complex challenge. The *Sindbis* virus, an arbovirus and prototypic alphavirus that has an inner protein shell and an outer glycoprotein coat separated by a lipid membrane, is one example of a vectored virus that transitions between vertebrate (e.g., mammal and bird) and invertebrate (e.g., mosquito) hosts. Although evidence of host-specific differences in the *Sindbis* virus has been observed before, no research had been performed to characterize the impact of the host species on virus structure. This is the first study in which the structural differences between particles of *Sindbis* viruses grown in mammalian and insect cells were determined by SANS, a nondestructive technique that did not decrease the infectivity of the probed *Sindbis* virus particles. The study was published in the *Journal of Virology* and received the 2010 Best LDRD Project Award at ORNL.

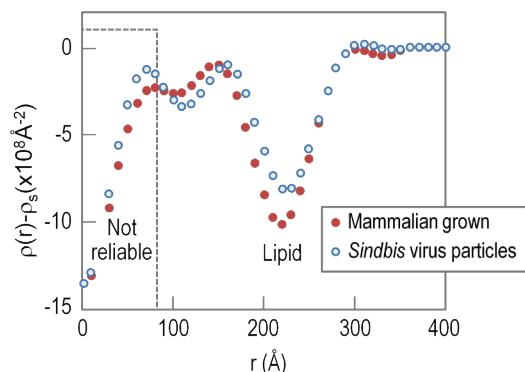
He, L. L., Piper, A., Meilleur, F., Myles, D. A. A., Hernandez, R., Brown, D. T. and Heller, W. T., "The Structure of *Sindbis* Virus Produced from Vertebrate and Invertebrate Hosts Determined by Small-Angle Neutron Scattering," *J. Virol.* **84**: 5270-5276 (2010).

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Sindbis virus: A mosquito-borne member of a class of viruses that includes those which cause Dengue fever and West Nile fever [A. M. Paredes et al., *Virology* **324**, 373 (2004)]



Radial-scattering-length-density distribution function of mammalian-grown and insect-grown *Sindbis* virus particles. The difference in the depths of the minima is indicative of a difference in composition.