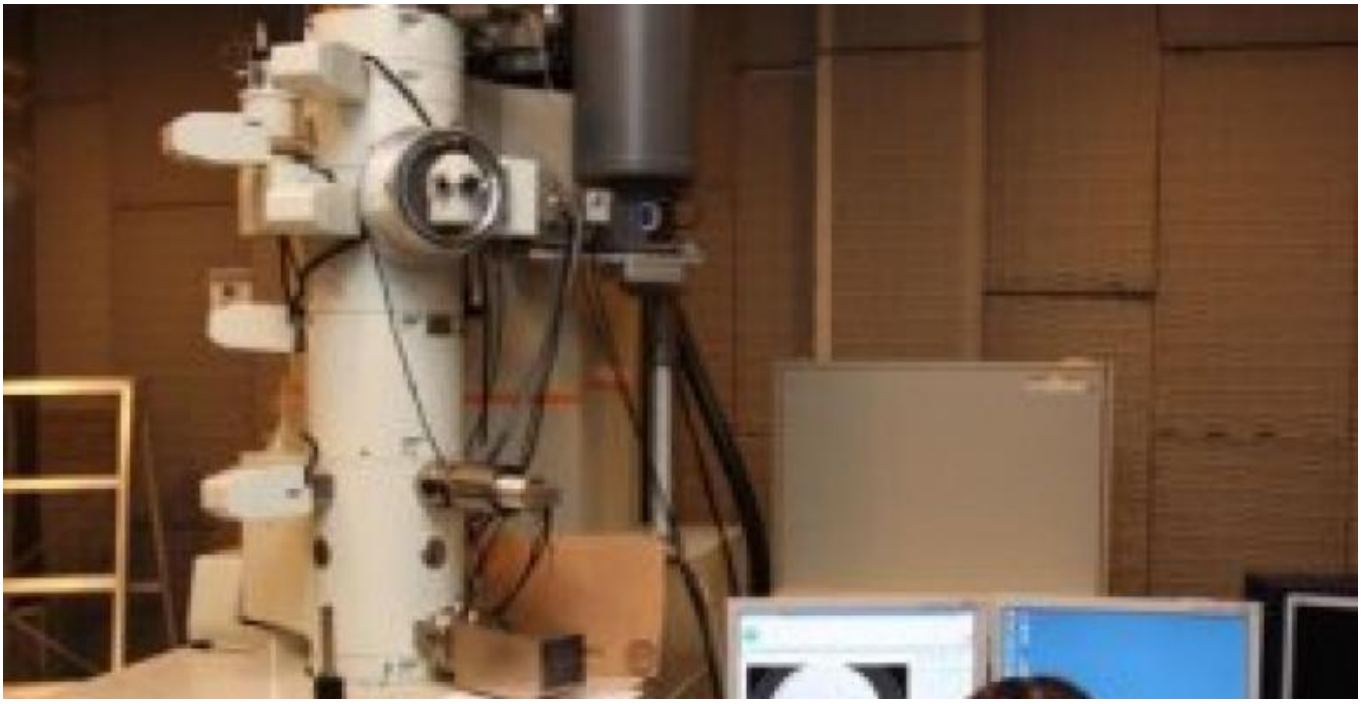
Scientist pioneers new technology, maps giant virus

28/03/2017



In a laboratory at Michigan State University, scientists took a DIY approach to build a retrofitted cryo-electron microscope that allowed them to map a giant Samba virus -- one of the world's largest viruses.

"If the common cold virus is scaled to the size of a ladder, then the giant Samba virus is bigger than the Washington Monument," said Kristin Parent, assistant professor of biochemistry and molecular biology and co-author of the paper featured on the cover of the journal *Viruses*. "Cryo-EM allowed us to map this virus' structure and observe the proteins it uses to enter, or attack, cells."

It seems counterintuitive that bigger organisms are harder to see, but they are when using cryo-electron microscopy. That's because these microscopes usually are used to look at thin specimens and can't decipher larger organisms to reveal their biological mechanisms. For thick samples, scientists see only dark gray or black blobs instead of seeing the molecular framework.

Cryo-EM allowed Parent's team to image the giant Samba virus and understand the structures that allow it to enter an amoeba. Once inside, Samba opens one of its capsid layers and releases its nucleocapsid -- which carries the genetic cargo that sparks an infection. While Samba isn't known to cause any diseases in humans, its cousin, the mimivirus, may be a culprit for causing some respiratory ailments in humans.

"If you scoop up a handful of water from Lake Michigan, you are literally holding more viruses than there are people on the planet," said Parent, who published the paper with Jason Schrad and Eric Young, MSU biochemistry and molecular biology graduate students. "While scientists can't study every virus on Earth, the insights we glean from viruses like the giant Samba can help us understand the mechanisms of other viruses in its family, how they thrive and how we can attack them."

As bacteria become more resistant to antibiotics, looking for new ways to fight diseases will continue to grow in importance. Parent's lab also studies how bacteria-infecting viruses enter cells using this method, which could potentially lead to new antibacterial treatments. Yet the world's best cryo-EM microscope costs more than $5 million. Limited by funds but not drive, Parent was able to upgrade an existing microscope at MSU to do cryo-EM -- one that is a tinkerer's dream.

This traditional transmission electron microscope was retrofitted with a cryostage, which keeps viruses frozen in liquid nitrogen while they're being studied. Parent and her team then added a Direct Electron DE-20 detector, a powerful camera -- the mighty microscope's piece de resistance.

Parent didn't invent cryo-EM, but establishing it on campus serves as a viable proof-of-concept for MSU, opening the door for many interdisciplinary partnerships. This cutting-edge microscopy has applications across many fields, from those addressing a single protein to others studying entire cells. Virtually anyone studying complex molecular machines can advance their work with this tool, Parent added.

Parent has earned an AAAS Marion Milligan Mason Award for Women in the Chemical Sciences. This award, her paper in *Viruses* and being the co-author who performed cryo-EM work in a recent Nature Communications paper, lays the groundwork to some day have a more advanced cryo-EM microscope housed at MSU to be able to perform high-resolution structural studies.

"We've done quite a bit with our limited resources, but we're primed to do more," Parent said. "I think MSU could serve as a cryo-EM center and to increase the prevalence of this technology in the Midwest and beyond."

As one example, scientists from Universidade Federal de Minas Gerais (Brazil) and Universidade Federal do Rio de Janeiro (Brazil) also contributed to this study and benefitted from the technology MSU has to offer.