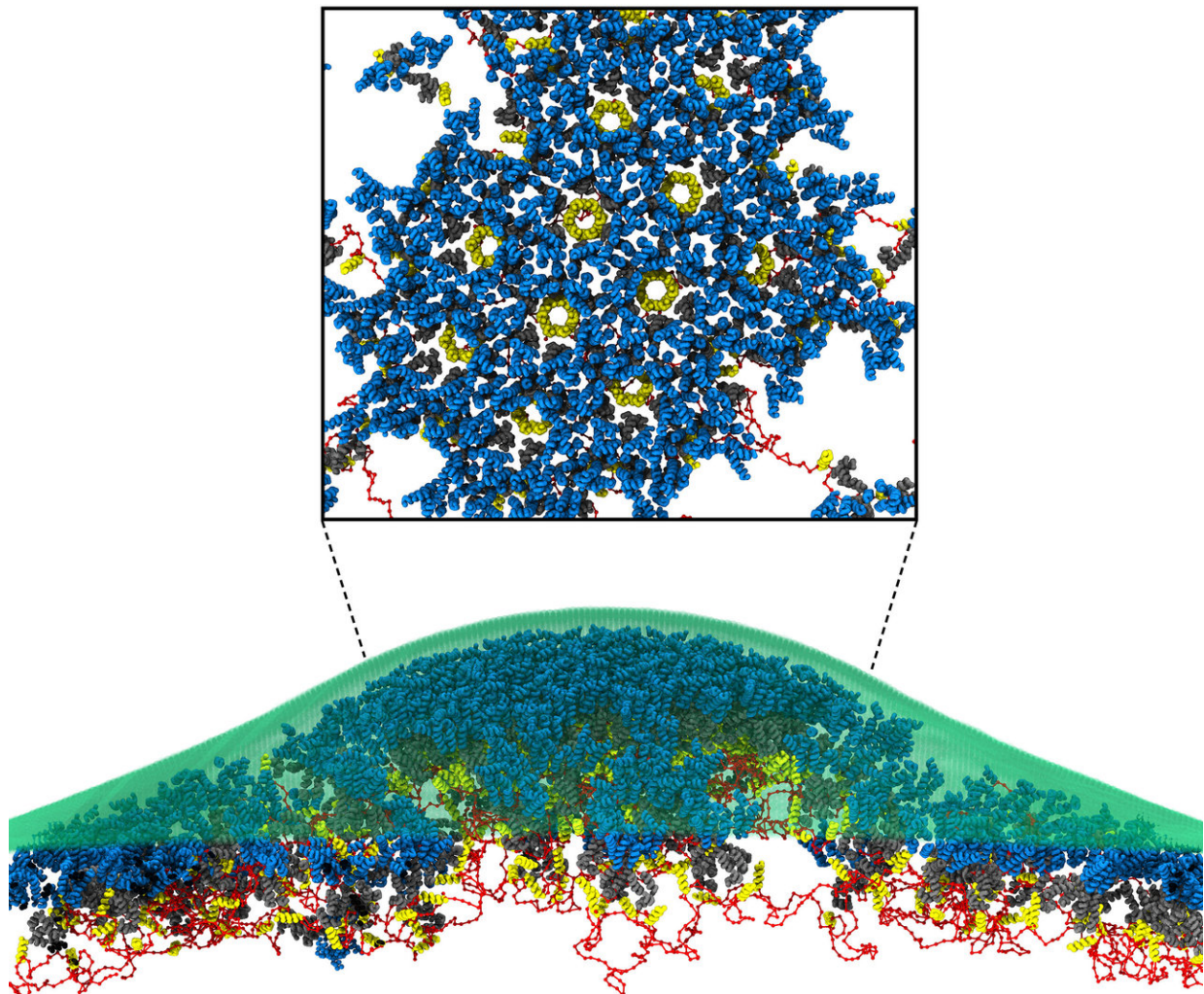


# Scientists find missing clue to how HIV hacks cells to propagate itself

November 8 2017, by Louise Lerner

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UChicago scientists modeled how the HIV protein Gag is involved in forcing a victim's cell to make a capsule of HIV to infect other cells, a process called

"budding." Credit: Voth et. al / University of Chicago

Computer modeling has helped a team of scientists, including several scholars from the University of Chicago, to decode previously unknown details about the process by which HIV forces cells to spread the virus to other cells. The findings, published Nov. 7 in *Proceedings of the National Academy of Sciences*, may offer a new avenue for drugs to combat the virus.

A key part of HIV's success is a nasty little trick to propagate itself inside the body. Once HIV has infected a cell, it forces the cell to make a little [capsule](#) out of its own membrane, filled with the [virus](#). The capsule pinches off—a process called "budding"—and floats away to infect more [cells](#). Once inside another unsuspecting cell, the capsule coating falls apart, and the HIV RNA gets to work.

Scientists knew that budding involves an HIV protein complex called Gag protein, but the details of the molecular process were murky. "For a while now we have had an idea of what the final assembled structure looks like, but all the details in between remained largely unknown," said Gregory Voth, the Haig P. Papazian Distinguished Service Professor of Chemistry and corresponding author on the paper.

Since it's been difficult to get a good molecular-level snapshot of the [protein](#) complex with imaging techniques, Voth and his team built a computer model to simulate Gag in action. Simulations allowed them to tweak the model until they arrived at the most likely configurations for the [molecular process](#), which was then validated by experiments in the laboratory of Jennifer Lippincott-Schwartz at the National Institutes of Health and the Howard Hughes Medical Institute Janelia Research Campus.

They built a model of missing parts of the Gag [protein complex](#), and tweaked it until they could see how the proteins assemble by taking advantage of cellular infrastructure in preparation for the budding process.

"It really demonstrates the power of modern computing for simulating viruses," Voth said.

"The hope is that once you have an Achilles' heel, you can make a drug to stop Gag accumulation and hopefully arrest the virus's progression."

The team plans next to study the structures of the Gag proteins in the HIV virus capsule after budding, he said.

**More information:** Alexander J. Pak et al, Immature HIV-1 lattice assembly dynamics are regulated by scaffolding from nucleic acid and the plasma membrane, *Proceedings of the National Academy of Sciences* (2017). [DOI: 10.1073/pnas.1706600114](https://doi.org/10.1073/pnas.1706600114)

Provided by University of Chicago

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