

*Biomedical Computation Review*

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seeing science

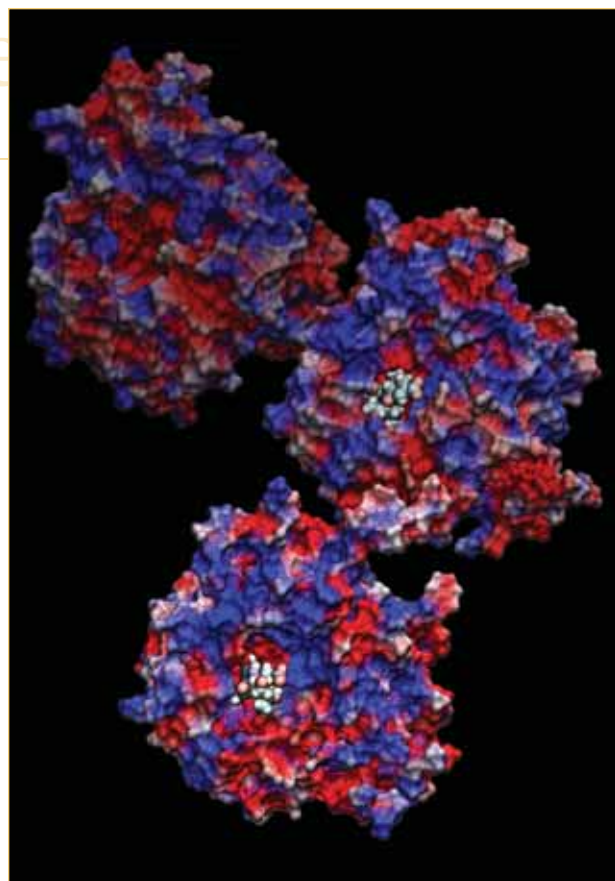
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BY KATHARINE MILLER

## Swine Dynamics

**T**he antiviral drugs Tamiflu and Relenza target a key flu protein—neuraminidase—preventing it from doing its job of releasing virus particles from infected cells into the body. The type of neuraminidase protein (N1) in the 1918 Spanish flu (H1N1), the 2003 avian flu (H5N1) and the 2009 swine flu (A/H1N1) is responsive to these drugs. But a few mutations in a key part of the N1 protein can render the drugs useless. To better understand why, a team of researchers at the University of Utah and the University of Illinois, Urbana-Champaign used molecular dynamics simulations to observe how Tamiflu and Relenza bind to the N1 protein of each of these three viruses. The work has not yet been published.

Because the swine flu virus is so new, the researchers had to first create a model of that flu's N1 protein. Next, they simulated the antiviral drugs binding to the neuraminidases from all three viruses. The stable binding observed (in the simulations) reflected the fact that these drugs are effective for the wild type strains. The researchers were also able to observe which specific atomic interactions within and near the binding pocket were most important—and hypothesized which mutations in some of these areas might cause drug resistance. Such hypotheses will form the basis for further simulations as well as for experimental work on antiviral drug resistance in flu. "Our observations help to establish a baseline set of drug-protein interactions that one can compare to the case of drug resistant mutants," says **Eric H. Lee, PhD**, a postdoctoral scientist at the University of Illinois, Urbana-Champaign. The group is already running new simulations involving such mutations. □



*These three neuraminidase protein structures show (from bottom to top): H1N1 swine flu with Relenza bound, H5N1 avian flu with Tamiflu bound, and H1N1 of the Spanish flu without a drug bound. The simulations compare the binding of FDA-approved drugs for the different flu strains and also characterize neuraminidase mutants of flu strains that developed Tamiflu resistance. Image courtesy of **Thanh Truong, PhD**, professor in the department of chemistry at the University of Utah, **Ly Le**, a graduate student in his lab, **Klaus Schulten, PhD**, professor of physics at the University of Illinois, Urbana-Champaign, and **Eric H. Lee, PhD**, a postdoctoral scientist in Schulten's lab.*