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SeeingScience

BY KATHARINE MILLER

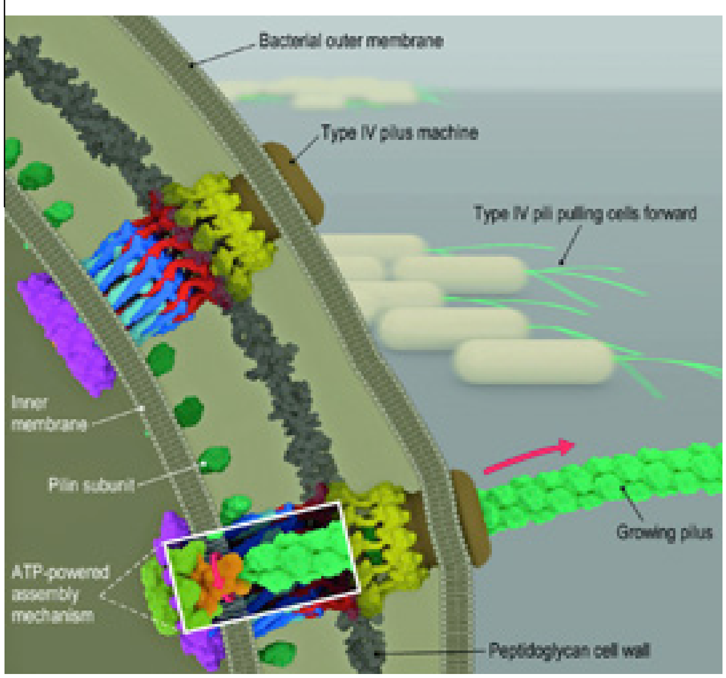
ANIMATING HYPOTHESES

In addition to illustrating complex biological molecules, animations can sometimes offer insight into how those molecules function.

That's what happened when **Grant Jensen, PhD**, professor of biophysics and biology at Caltech, and **Yi-Wei Chang, PhD**, a research scientist at Caltech, decided to animate their model of the strongest known molecular motor—the bacterial type IVa pilus machine. This motor resides in the cell membranes of many bacteria, including several that cause human diseases such as meningitis and gonorrhea. It extends and retracts a filament (the pilus) that pulls the bacteria forward. Jensen and Chang knew the components of the machine, but not the details of how it worked. So they used cryotomography to image the machine and assemble a pseudoatomic model.

When they enlisted **Janet Iwasa, PhD**, research assistant professor of biochemistry at the University of Utah, to animate the structure, Jensen and Chang had a pretty good idea of how the machine worked and even storyboarded most of it. But the animation took them further. "It made us think about the details more carefully than we had," Jensen says. In fact, the animation revealed that the cage at the base of the machine was too tight for pilin monomers to enter. "That led us to hypothesize that there must be a conformational change that occurs there when pilus assembly starts," Jensen says.

"Molecular animations are not just entertaining visual candy," Jensen says. "They are by far the fastest and clearest way to communicate complex hypotheses to a broad audience, and they force us all to think in even greater depth about what might be happening inside cells. Beyond pictures, animations are worth even more than a thousand words." □



In Iwasa's animation of the type IVa pilus machine, the ATP-powered assembly mechanism in the inner membrane causes the blue birdcage area to open up, allowing the entry of pilin subunits. The hypothesis is that the protein shown in yellow here binds the subunits and rotates, adding them to the growing pilus as it extends. During retraction, a different ATP-ase steps in and the process reverses itself. The animation is posted at http://jensenlab.caltech.edu/movies/. Reprinted from YW Chang, LA Rettberg, A Treuner-Lange, J Iwasa, L Søgaard-Andersen, GJ Jensen, Architecture of the type IVa pilus machine, Science *351:6278 (2016) with permission from AAAS.*