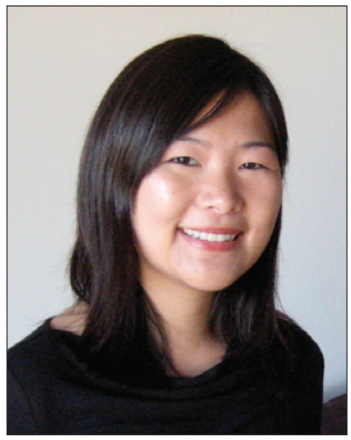
# Janet Iwasa


Janet Iwasa

Janet Iwasa has an unusual résumé—but then she has had an unusual career. Iwasa's résumé doesn't list only her bachelor's degree from Williams College; her doctorate from the University of California, San Francisco (UCSF); and a National Science Foundation (NSF)–funded postdoctoral fellowship in Jack Szostak's Harvard lab at Massachusetts General Hospital. It also lists her studies at the Gnomon School for Visual Effects in Hollywood, CA. Iwasa recalls that, at 29, "I was the oldest one in my class and the only female. There were all these 20-year-old guys hoping to get into the entertainment or video game industries." Iwasa was hoping to get into something entirely different—a research career using animation as an investigative methodology that can transform cell biology, much as electron microscopy turned structural biology on its ear.

Last fall, Iwasa took another step along that path, becoming a lecturer in molecular visualization in the Department of Cell Biology at Harvard Medical School (HMS). The position was created around her research interests and her usefulness to HMS researchers in making their cell biology dance before the eyes of the world. Iwasa has her own small animation "render farm" right on the HMS quad, as well as a growing list of scientific collaborators who are eager for her help in unveiling the secrets of cellular life.

**At the Gnomon School for Visual Effects in Hollywood, Iwasa recalls, "I was the oldest one in my class and the only female. There were all these 20-year-old guys hoping to get into the entertainment or video game industries."**

Life was different at her visual alma mater back in Hollywood, Iwasa remembers. "I had to couch my questions in ways that the [Gnomon] instructors would understand. I would ask, 'Say you have a soccer ball. Could you take all the faces apart and then put them back together in a specific order?' And they'd look at me and say, 'Sure you could do that. But why would you want to?'" Iwasa thought the ability to peel apart spherical polyhedrons might come in handy for animating protein or viral coats.

Iwasa still goes back and forth between the two worlds. She regularly attends Gordon conferences and ASCB Annual Meetings, but she also wouldn't miss the yearly Siggraph, a special-interest group for devotees of computational graphics and interactive techniques. At Siggraph, Iwasa first saw Massive, a cutting-edge, crowd simulation software package. Massive creates the illusion of massed individuals by treating tens of thousands of figures as independent agents operating under a defined parameter set. "I thought, 'Hey, this is something that can allow you to animate tens of thousands of things.' The demonstration examples they showed us were arena scenes or huge crowds walking across a field or large-scale battles, but I was sitting there thinking, 'My gosh, proteins.'"

## Beating Swords into Signaling Cascades

In her Harvard lab, Iwasa is tweaking Massive to see whether she can model complex biological systems such as the nucleation elongation process. Adapting a software program designed to depict 10,000 sword-waving warriors to show an extended cell signaling cascade instead can sharpen both the model and the modeler, she believes. No matter how quantitative their research, most scientists have a mental model of how their work fits into the larger scale. When a researcher sits down with a scientific animator to draw out something the researcher knows so well, the animator's questions can reveal the contours of what is not known.

Such has been Joan Brugge's experience. Brugge is the chair of cell biology at HMS and was a strong advocate for Iwasa's molecular visualization position. Brugge reports that animation has unexpected effects on researchers. Recently, Brugge and postdoc Michael Overholtzer have been exploring a new cellular process that they call endosis. This process has

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been seen in parasites invading host cells. But Brugge and Overholtzer have documented endosis for the first time in cultured human cells. They watched one human cell ratchet itself into the interior of another. The invading cell remains independent, living and even dividing inside the host before either forcing its way out again or being digested. Their photomicrograph videos of labeled cells clearly showed endosis, but Brugge found that the geometry was so complex that, at presentations, "We'd always end up using our fingers to show what is going on."

For an upcoming iBioSeminar, Brugge wondered whether animation could improve on fingers. Working with Iwasa, Brugge was struck by how the animation process affected her own thinking. "It's so hard to think in three dimensions," says Brugge. "Developing an animation forced us to think of the [endosis mechanism] in much greater depth than we had before in order for Janet to model it. I'm probably most excited about that because the whole process forces you to ask questions in a way that you may not have considered before and to go into such details."

**To the question of whether a scientist can pursue a serious research career using animation as a methodology, Covert says that Iwasa is "an existence proof"—she exists; therefore, it is possible.**

## Career in Progress

Her career in research animation is a work in progress for Iwasa. She was born in Bloomington, IN, where her father was finishing a postdoc in biophysics, but she grew up in suburban Maryland after her father joined the National Institutes of Health. The youngest of three children and the only girl, Iwasa was determined to stay off the beaten family paths. Her brothers did well in Spanish and French; she chose German. Her father was a whiz in physics; she avoided the subject. Her mother and brother excelled at painting and drawing; Iwasa took her last formal art lesson in grade school.

Yet Iwasa was always interested in biology, even if she lacked the stomach for anatomy or medicine. She had a high school internship one summer at the Institute for Genomic Research, Craig Venter's private, genome-sequencing startup. Her internship gave her a glimpse of the excitement sweeping biology in the early 1990s. At Williams, a small liberal arts college in western Massachusetts, Iwasa pursued a double major in biology and Asian Studies but found a home in Rob Savage's lab, cloning out segmentation genes from *Helobdella* leeches.

For graduate school, she chose the Tetrad program sponsored by the programs in biochemistry and molecular biology, cell biology, genetics, and developmental biology at UCSF because it was on the West Coast and because it was at the leading edge in cytoskeleton research. That front edge had been illustrated by Dyche Mullins, her UCSF mentor. While still a postdoc in Tom Pollard's lab at Johns Hopkins, Mullins had created a famous diagram of Arp2/3 (actin-capping protein regulation) that became a standard slide at actin cytoskeleton meetings. In the Mullins lab at UCSF, his students referred to it as "the *über* model." Iwasa got the idea of animating the *über* model; in retrospect, she believes that it was a terrible idea. "Animation is not always a way of making things clearer. The thing about Dyche's *über* model is that it was already very clear. It was already a great illustration." Learning what subjects not to animate is also an important skill, according to Iwasa.

## Animating Fridays

Learning to animate was difficult enough. Iwasa recalls, "I went to talk with Dyche and honestly I was a little afraid. I had the impression that no one would approve of going in this direction with a Ph.D." Mullins, though, was enthusiastic. Through an exchange agreement with San Francisco State University, Iwasa took an all-day Friday course in basic computer animation. After that, Mullins gave her Fridays off to continue her animation work. He didn't, however, excuse Iwasa from the rest of her thesis bench work on imaging Arp2/3 and tropomyosin through confocal light and speckle fluorescent microscopy.

Her early animation efforts drew encouragement but few concrete suggestions for a next step. Then a graduate school friend spotted an online announcement for the Discovery Corps, a small training program funded by NSF's Chemistry Division for early-career scientists interested in innovative public outreach and science education. Her Discovery Corps fellowship underwrote her Gnomon School course on a Hollywood animation

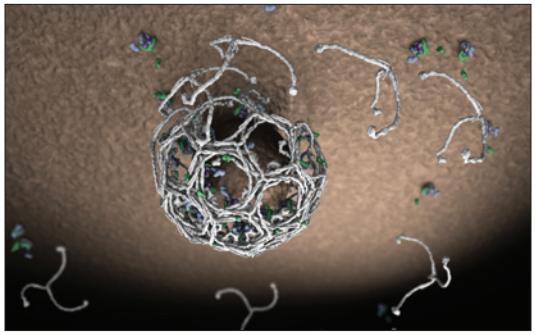
software called Maya and her postdoc in the Szostak lab. In Boston, Iwasa designed and animated an elaborate multimedia extravaganza called "Exploring the Origins of Life" for the Museum of Science. It had its own website, automated information kiosk, and stage presentations. With Szostak, she worked on a double track. They did simplified animations about early Earth protobiology for the museum and more scientifically complex work for Szostak's use in teaching and at scientific meetings.

As word got around Harvard of a postdoc who did scientifically sophisticated animations, more PIs dropped by. Thomas Kirchhausen was one of the first. Most scientific animators come to their work from an artistic background, says Kirchhausen. But Iwasa was different. "Janet is a scientist, and now that she's into these animations, her training as a scientist really shows," Kirchhausen says. "I was able to sit down with her and explain how things work, but she already has the basic feeling for how molecules should move and how they should rotate."

## Plotting Triskelions

Their animation project—clathrin triskelions assembling around an endocytic particle waiting to enter the cell membrane—required Kirchhausen to think carefully through his mental model. "What we were trying to do was to bring the complexity to our colleagues," Kirchhausen recalls. "There are some parts of the process that are extremely clear to us—how the parts of the [clathrin] skeleton come together and then how everything falls apart. But there are other parts, which we didn't understand in such detail—for example, how the vesicle pinches off the membrane. Janet and I agreed that we would only show clearly the things that we did understand." Their clathrin animation won first place in the ASCB's Celldance 2008 cell biology film contest last December at the Annual Meeting in San Francisco. (See p. 19.)

Her "Exploring Origins" work also attracted critical notice. Katharine Covert, who was Iwasa's program officer at the NSF Discovery Corps, points to the Honorable Mention for Interactive Media that Iwasa earned in the 2008 Science and Engineering Visualization Challenge run jointly by NSF and *Science* magazine. "Janet probably didn't tell you about that, but coming in as an honorable mention behind a big commercial outfit isn't too bad for a one-person operation," says Covert. To the question of whether a scientist can pursue



*A still image from Iwasa's winning Celldance entry of spinning triskelion clathrin proteins*

a serious research career using animation as a methodology, Covert says that Iwasa is "an existence proof"—she exists; therefore, it is possible.

Iwasa tries to remain realistic about her career path. "I get a lot of emails from people who are interested in following this path, but it's hard for me to give them advice. I don't think it's easy." She points out that NSF discontinued the Discovery Corps program after four years and 17 fellowships. Her HMS lectureship gives her independent status as a researcher but is not a tenure-track position. Her long-term goal is to remain in research academia, using animation to cut through difficult scientific problems.

"There are still a lot of scientists who think of animated models as eye candy," Iwasa concedes. "They don't think of an animation as a true model. A lot of people don't realize until they sit down with me that I am going to ask them a lot of questions and press them for a lot of quantitative information before I can flesh out their experiments. I make them show me exactly where something is in the process and where to find the evidence in the literature."

In the Iwasa lab, scientific animation is fundamentally an eye-opening experience. ■

*—John Fleischman*

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## Animations

Iwasa's NSF-funded "Exploring Origins" work with the Boston Museum of Science:
http://exploringorigins.org

Iwasa's freelance website:
www.onemicron.com

The Iwasa lab website:
http://iwasa.hms.harvard.edu

If there is a central gathering spot for bioscience animators, this is it:
www.molecularmovies.com/showcase