Picture This: Molecular Maya Puts Life in Life Science Animations

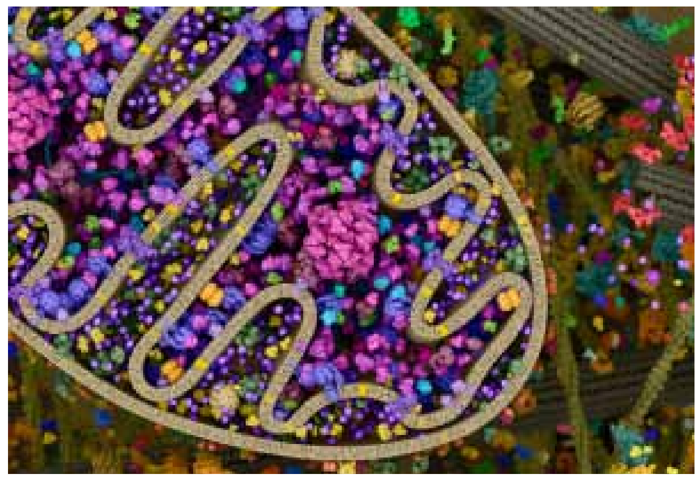
[Data Visualization] Based on the Autodesk platform, Digizyme plug-in proves aesthetic and educational effectiveness.

BY KEVIN DAVIES

In 2010, a reporter sat in a Life Technologies hotel suite admiring a promotional video illustrating one of the company's latest research projects—a single-molecule sequencing system featuring enzymes tethered to fluorescing quantum dots. The video was impressive not merely for pushing the boundaries of sequencing technology, but equally for showcasing some powerful production qualities in 3D animation and rendering that, until recently, would have seemed the provenance of a Pixar movie.

That video was produced by a Boston company called Digizyme (www.digizyme.com), founded in 1999 by Gaël McGill as a side business while he worked on his Ph.D. at Harvard Medical School. Since then, Digizyme has become a respected source for educational and promotional animations, simulations and videos for many diverse life science applications.

"The visual communication of science—that's where my passion is," says McGill. He recognized early on that graphic design, animation and visualization tools were needed by several industries, not least his fellow scientists. Clients include academics as well as biotech, pharma, medical device companies, along with science museums, and public television stations.

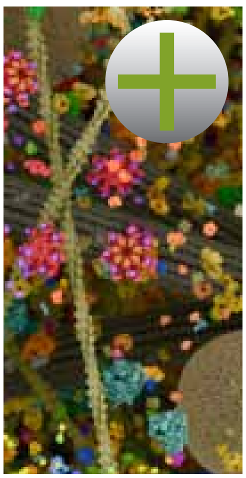


A mitochondrial molecular landscape depicting signaling proteins in apoptosis (created by Digizyme for Cell Signaling Technology)."

After a hiatus to run the company full time after his postdoctoral fellowship, McGill joined the Harvard Medical School faculty five years ago in the Center for Molecular and Cellular Dynamics, where his research focuses on how visualization impacts research and education. He is also creating a new graduate program to train students in biovisualization approaches.

Most companies offering animation tools are staffed by visual specialists or animators with a strong artistic background collaborating with scientists. "There are some great companies in this space, but what sets us apart is that we're scientists," says McGill. "Everyone at Digizyme is dually-trained as a scientist-animator, scientist-artist, or scientist-programmer. As a result, our visualizations are directly informed by the primary literature and based on raw data."

At Digizyme, McGill recruits twin-threat staff with a science graduate degree as well as strong artistic talent. The company has created stereoscopic movies for science museums, custom projects for pharma clients including Amgen, J&J, Novartis, Life Technologies, and Genentech, as well as completed work for several major hospitals, research institutes, and universities. McGill is also the Digital Media Director and a collaborating author for E.O. Wilson's 'Life on Earth' digital biology textbook.



Going Hollywood

The software that powers the Digizyme platform is Maya, a suite developed by Autodesk, which is a modeling, animation, simulation, and rendering application widely used in media and entertainment circles to create video game characters and environments and special effects for feature films. Of course, such software was never intended to display life sciences data.

"What are we doing with Hollywood software?" says McGill. "There's been billions of dollars invested in films to create powerful software suites, such as Maya."

McGill says that current bioscience research features "an incredible richness of datasets that is just overwhelming. We see visualization as the key to knowledge integration—it offers a powerful and flexible platform to import and synthesize data from various fields—data that would not otherwise interact."

One example would be to create an intracellular landscape using cryoEM tomography data to map the location of proteins in a cell. This map could be populated with atomic resolution protein structures, and then set in motion and simulated using various algorithms including Brownian dynamics. "This begs the question: What software do I use for this sort of thing? It doesn't currently exist, but it's something that interests many scientists. Our approach is to modify and adapt existing animation tools from Hollywood—platforms like Autodesk Maya—to advance toward that goal."

McGill's team built a new layer of code to make Autodesk's Maya more biologically relevant, resulting in a plug-in toolkit called Molecular Maya (mMaya). (see, "A Better World")

Molecular Maya focuses the modeling, animation, rendering, and simulation capabilities of Maya in the context of biological animations and structures. For example, instead of modeling DNA from scratch, it provides a direct link to a scientific database that downloads data directly into Maya and automatically creates the 3D model. McGill and his team are also developing tools in mMaya to rig macromolecules to facilitate biophysically-accurate animations as well as to build molecular environments.

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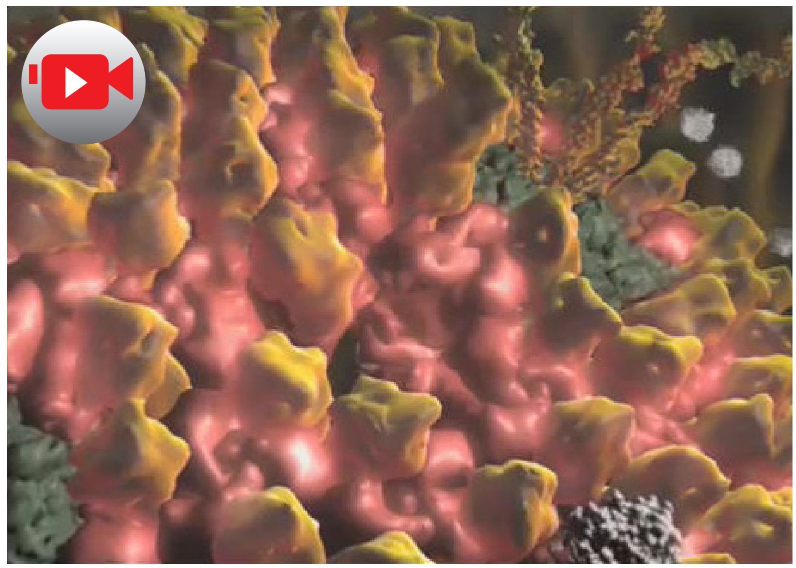
Molecular Maya is written in languages (including Python and MEL—Maya Embedded Language) that allow other researchers to extend its capabilities. "We've created a series of free, open-source scripts that lets anybody type in a protein ID, say, and with a click, have this directly connect to the Protein Data Bank so they can model, manipulate and animate a protein within seconds," says McGill.

This accessibility came to light in the recent IGEM (International Genetically Engineered Machine) world jamboree, where student teams from around the world used synthetic biology principles to design novel cellular circuits and hybrid proteins. "For a student team trying to design something in a forward engineering approach, the design piece is not just making a pretty picture, it can be an integral part of the conceptualization and experimental approach," says McGill. For the past few years, he has been involved with this competition by hosting seminars and offering workshops to help students use Maya and Molecular Maya. (Autodesk has also sponsored IGEM the past three years.)

Not Just Pretty Pictures

McGill underscores the critical role that visualizations can play in experimental research. "I've worked with colleagues at Harvard Medical School where the process of creating a visualization can change one's understanding of the protein," says McGill.

In one project carried out in collaboration with renowned structural biologist Stephen Harrison, who specializes in proteins on the surface of HIV, McGill created an animation that depicts how a viral surface protein—gp41—spears the target cell membrane and refolds on itself to drive membrane fusion and facilitate viral infection. Proteins aren't static, they're shape shifters," says McGill. "gp41's conformational change cannot be depicted with the typical linear interpolation morphing techniques. It undergoes a helical transition and refolds completely." And trying to communicate such a critical and unusual conformational change in a standard research paper was next to impossible.

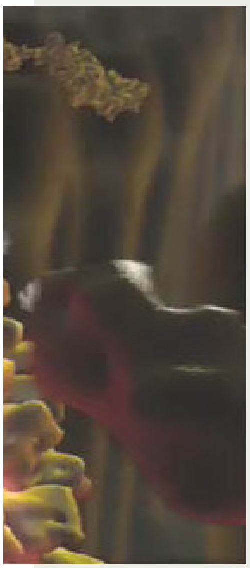


Digizyme models the cellular entry of a reovirus.

McGill's group helped Harrison visualize gp41's unique conformational change and, in the process, communicate the mechanism in a way that hopefully facilitates drug discovery. "Understanding the specific mechanism of how gp41 refolds may drive better approaches to drug

A Better World

The life sciences community might appear a little staid next to some of Autodesk's other marquee clients, including James Cameron, Frank Gehry, Disney, and Boeing. Not so, insists Patrick Byrne, director of business development for the Californian company that celebrates its 30th anniversary in 2012.



"Our mission is helping customers imagine, design and create a better world," says Byrne. The principal customers are in architecture/engineering, manufacturing and media/entertainment. Within the latter group, Autodesk has been building a product development group to extend Maya into life sciences. "It sits in our media and entertainment team, because Maya was developed for media professionals," says Byrne.

But why life sciences? "When we look at the range of industries we're in, the concept of design workflows is transparent across all industries. Whether you're in one of those industries, our tools enable you to be more efficient, more iterative and more creative. And when we look at academic research, we see an interesting place," says Byrne. "Without much ado from us, people like Gael have taken Maya and used it as a platform to develop visualization tools for their industries. We want to extend and enable that."

One of the keys to Maya's popularity is not just the modeling, texturing and rendering capability, but its extensible nature. Users can write their own plug in, which can be complex or very simple. For students and academic users, Autodesk offers free access to the software for three years in a termed-free license (http://students.autodesk.com/). "As you're perfecting your skill, let's make sure you have access to the tools to perfect your craft," says Byrne.

Byrne sees three prime opportunities for Maya in the life sciences: first, as a platform for innovative tools; second, use in science education curricula; and third, helping scientists in industry visualize and communicate research to a wider marketplace.

There is some strong competition in the marketplace, including an open-source product called Blender, and its derivative Bio-Blender, but Byrne sees the market expanding.

Support of the IGEM competition, for example, puts Maya in the hands of a global student body eager to harness the software in various synthetic biology applications. Byrne says he is proud of the MIT group, which won the 2011 IGEM prize in the health/medicine category, enabling cells to autonomously regenerate. ▪

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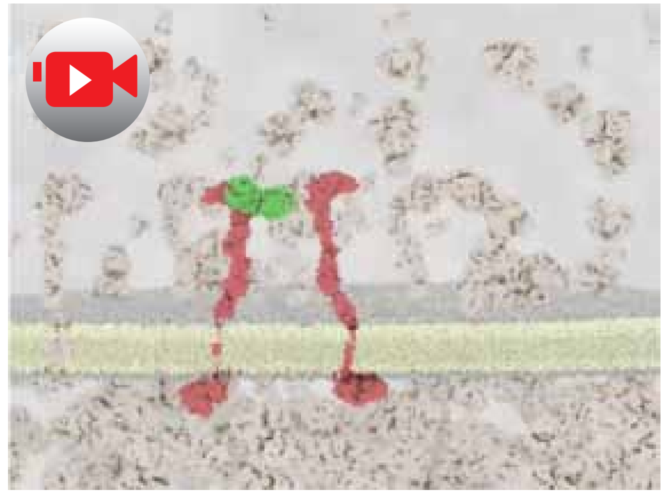
discovery or vaccine development," he says.

Another example is Shawn Douglas (Wyss Center, Harvard Medical School), a former visualization student of McGill's and now a leading figure in the field of DNA Origami—designing novel DNA molecules to fold in vitro to create biologically useful entities. Douglas' Maya plug-in, Cadnano (http://cadnano.org), greatly simplifies DNA origami projects and brings the power and ease of use of typical modeling tools in Maya to this rapidly growing field.

"We're now collaborating to have both plug-ins—mMaya and Cadnano—work together inside Maya," says McGill. "Cadnano figures out how to create the genetic sequences that, when mixed in a test tube, fold into the shape of an object modeled in Maya. It's magic—a great example of how a design tool can transform a process that previously took weeks or months to navigate."

Visualization research isn't just about making movies but also about understanding how to design the most effective movie to impact a target audience. Says McGill: "We're very interested in understanding how design choices—how we represent or animate a process—can have an impact on the effectiveness of a movie, especially in the context of educational animations. We strive to create animations and interactives that have a high pedagogical impact on students, not just animations that are engaging and aesthetically pleasing."

In one recent project, hundreds of students assessed four different styles of animating a simple molecular interaction: a hormone binding to a cell surface receptor. McGill and his collaborators tested students before and after viewing these animations as well as monitored their reactions using eye-tracking methods. "Typical medical animations often impart decision-making properties to molecular entities—as if molecules know where they are going. This couldn't be further from the truth!" says McGill. He acknowledges that creating animations that depict both the stochastic nature of the molecular world while keeping students' attention on the mechanism and specificity of an interaction is quite a design and technical challenge.



3D visualization techniques prove a valuable tool for teaching molecular biology.

McGill has created an educational web site called molecularmovies.com. It has three sections: one is a Showcase of some of the best online cell and molecular animations, organized by scientific topic. A Learning section contains McGill's teaching curriculum at Harvard Medical School, available free. And third is the Toolkit section, where researchers can download Molecular Maya.