

Animating Cell Biology for Research and Education

Janet H. Iwasa

Department of Cell Biology, Harvard Medical School

ABSTRACT

In recent years, there has been a rapid growth in the use of animation as a means to communicate complex biological processes to a wide range of audiences. Using 3D animation software from the entertainment industry, it is possible for animation experts to synthesize data from diverse sources to create a coherent and contextualized view of how molecular and cellular systems operate. These visualizations have served not only to make molecular concepts more accessible to students and the public at large, but have also proven to be extremely useful for researchers seeking to build and refine their hypotheses. New efforts are now underway to create molecular biology-centric 3D animation software for biologists to use in their research efforts.

KEYWORDS: Animation, cell biology, molecular visualization.

1 INTRODUCTION

Model building is an essential activity in all branches of scientific inquiry. In the biological sciences, visualizing conceptual models of molecular processes is critically important for the formulation and communication of hypotheses. Ideally, visual models should synthesize and represent preexisting knowledge of molecular structure, movement, interactions, and localization. Through the act of creating and manipulating elements of the model, the researcher can gain great insight into a specific molecular mechanism.

Historically, physical models have played key roles in major discoveries in chemistry and biology. Famous examples include the use of ball-and-stick chemistry models in the discovery of molecular stereoisomerism, and the use of paper models in the discovery of the DNA double helix and the protein alpha helix [1].

In cell biology, researchers have long relied on 2-dimensional illustrations to convey hypotheses of how cellular processes proceed. These illustrations often appear as the first or last figure of scientific publications, and are referred to as the “model figure.” In many cases, model figures are often roughly drawn, and depict proteins and other molecules in a highly exaggerated, simplified form. These oversimplified illustrations fail to accurately convey protein shape, size and dynamics – all crucial elements needed to better understand a molecular process.

In the last decade researchers have increasingly turned to animation for the visualization of complex molecular events. Typically, molecular animators create animations using software designed for the entertainment industry, such as Autodesk Maya or Blender, in conjunction with molecular modeling software, such as UCSF Chimera or Pymol. Although the resulting animations can be used for a wide variety of audiences, my specific focus has been to better understand the creation and use of animation within the research community.

2 USING ANIMATION IN RESEARCH

I have worked extensively with researchers to create spatially and temporally accurate animations of molecular and cellular processes. From these experiences, I have found that animation can serve as a powerful means to synthesize data from diverse experimental sources. In essence, these animations act as a visual scientific hypothesis, and can often capture fine details of a complex and dynamic biological event.

The process of building an animation itself can be enlightening, as many researchers rarely have the opportunity to visualize and manipulate molecules in four dimensions in the manner afforded by animation software. We have found that the process of creating an animated model can be accompanied with sudden epiphanies, as researchers are presented with a visual model of a process that they had previously only envisioned internally. Creating visual models also requires the researcher to formalize and criticize their hypotheses, as nothing is “hidden” in the animated model. This visualization work can have a direct impact on scientific research. Some of our collaborators have, for example, started a new line of experiments in the laboratory based on questions that have directly arisen from animation projects.

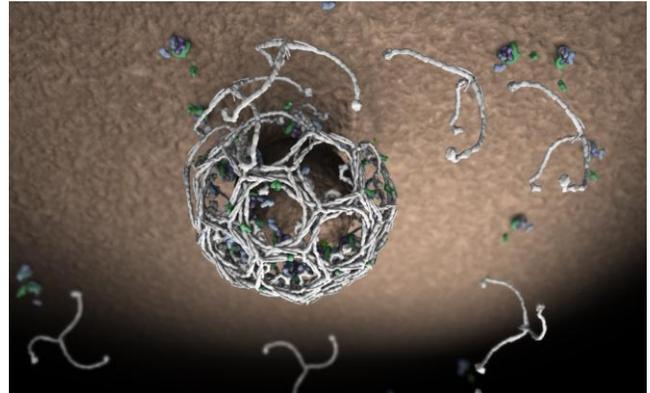


Figure 1. Still image from an animation depicting clathrin-mediated endocytosis.

2.1 Animation as a communication tool

Molecular animation is widely appreciated for its ability to communicate difficult and complex concepts to broad audiences. Many of the researchers I work with utilize animations during lectures as a means to summarize their own research findings, or the findings accumulated over years or decades of research by the scientific community.

One example of an animation that has been used for communication purposes is that of clathrin-mediated endocytosis (Figure 1), which I completed in collaboration with Tomas Kirchhausen at Harvard Medical School. The animation was based on several structures that were previously determined by X-ray crystallography and electron microscopy techniques [2-3], and hypothesized how individual steps leading up to clathrin coat

disassembly might occur. We modeled the steps of the animation to show the endocytosis process as accurately as possible in real time. The resulting model gives insight into the dynamics of clathrin cage assembly and disassembly.

These types of animations function as a means to view an individual's hypothesis of how a molecular process occurs. By no means does it represent a consensus view, or even necessarily a hypothesis shared by more than one or a small group of researchers.

One common and valid criticism of molecular animation is the lack of annotation showing which elements of an animation are supported by experimental data and which are not. This is a particular problem when animations are taken out of the context of a research talk, and presented simply as "fact."

2.2 Animation as a modeling tool for molecular hypotheses

Animation software provides a means for researchers to model and visualize molecular processes in space and time. These dynamic molecular models can be particularly useful for researchers studying proteins that undergo significant conformational changes and movements.

Over the past couple of years, I have worked with the Reck-Peterson lab at Harvard Medical School, a group that is interested in understanding the dynamics of the microtubule motor protein dynein. Motor proteins are a class of proteins that are able to move across substrates in the cell, often by means of dramatic swinging or stepping motions. The Reck-Peterson lab is striving to understand the mechanism by which dynein is able to "walk" on microtubules. We built an articulated model of dynein that accurately reflects its known physical dimensions and expected conformational changes based on published data. Structural data give us information on how flexible different regions of the protein are, and where "hinge" type regions may exist. The goal of the dynein project was not to create a finished and polished animation, but to give researchers a visual model that they can manipulate and animate to see and visually test their hypotheses. From the articulated model of dynein, we were able to create short animations that depict possible walk cycles of the protein along a microtubule (Figure 2). These animations can then be used to design experiments that can further refine or eliminate possible models.

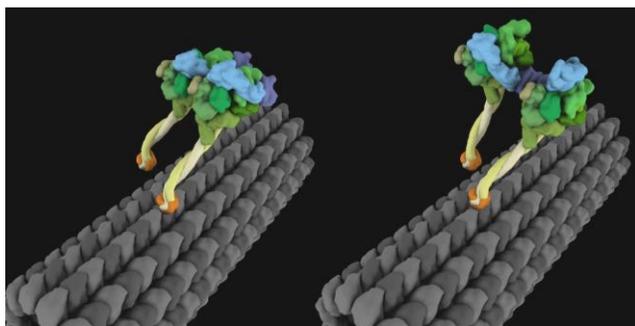


Figure 2. Still image from an animation depicting clathrin-mediated endocytosis.

3 FUTURE DIRECTIONS

There have been several significant issues that have kept animation from becoming a more widespread tool within the biological research community. One major issue is the steep learning curve presented to researchers trying to become

proficient at animation. Learning animation typically requires weeks or months of training, a span of time few graduate students or postdoctoral fellows feel they can afford. In addition, simply importing molecular geometry into an animation package can be a several-step process. Several groups have recently created molecular "toolkits" for researchers to more easily import and manipulate molecules within several popular animation platforms including Maya, Blender and Cinema4D [4-6]. Although these toolkits are mainly designed for current users of animation software, they may also act to encourage new users to explore animation as a research tool.

At Harvard Medical School, courses for biology researchers to learn animation have been consistently oversubscribed, revealing a growing interest amongst researchers in animation. Widespread adoption of animation software within the research community, however, is unlikely without the development of biology-specific application that significantly decreases the learning curve. Towards that end, we have just begun working towards rebuilding the open source software Blender to create a molecular biology-centric animation application, with biology researchers as our target audience. We are excited about the prospect of providing researchers with a means to communicate molecular concepts to broad audiences, as well as a powerful new tool for modeling and hypothesis visualization.

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