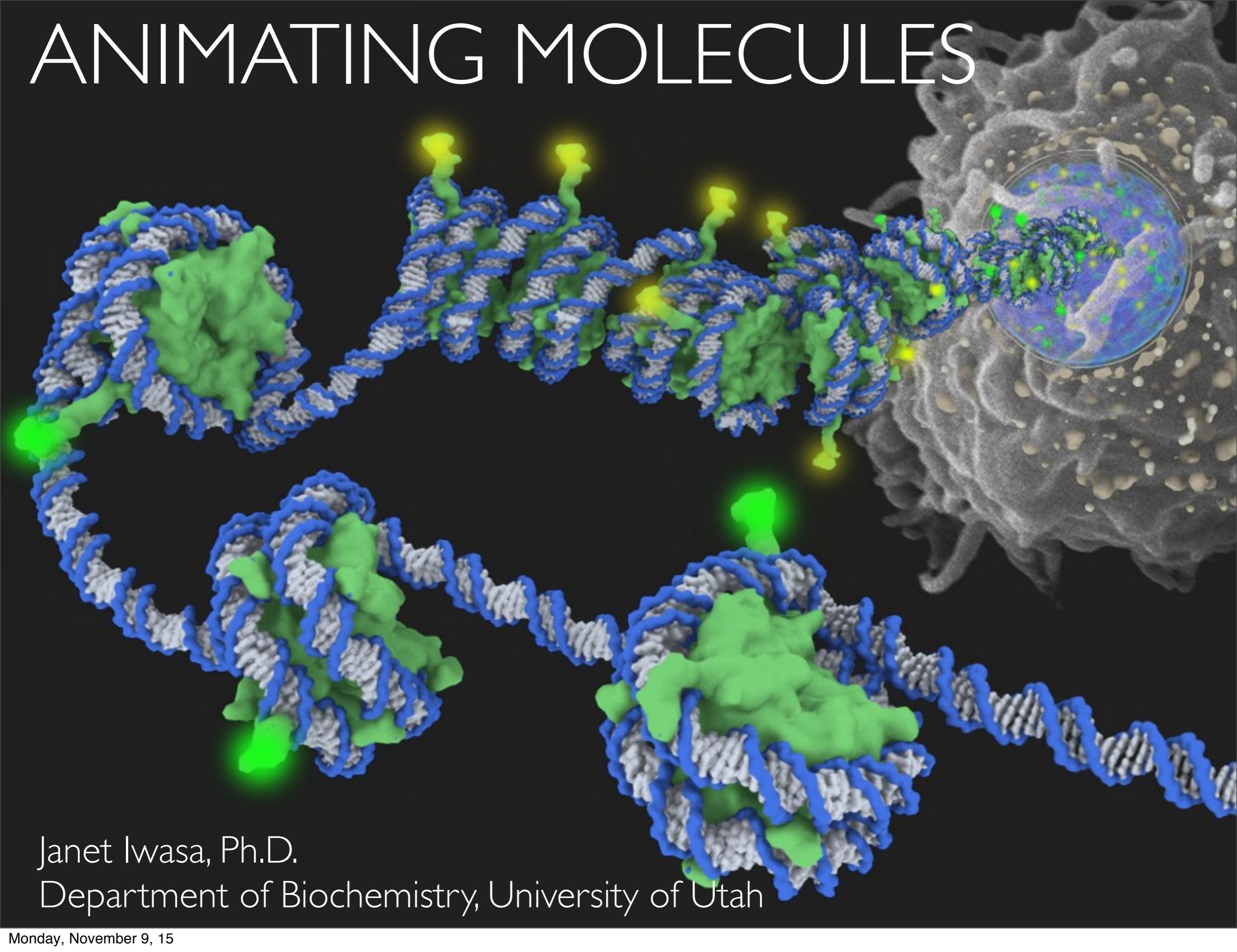


ANIMATING MOLECULES

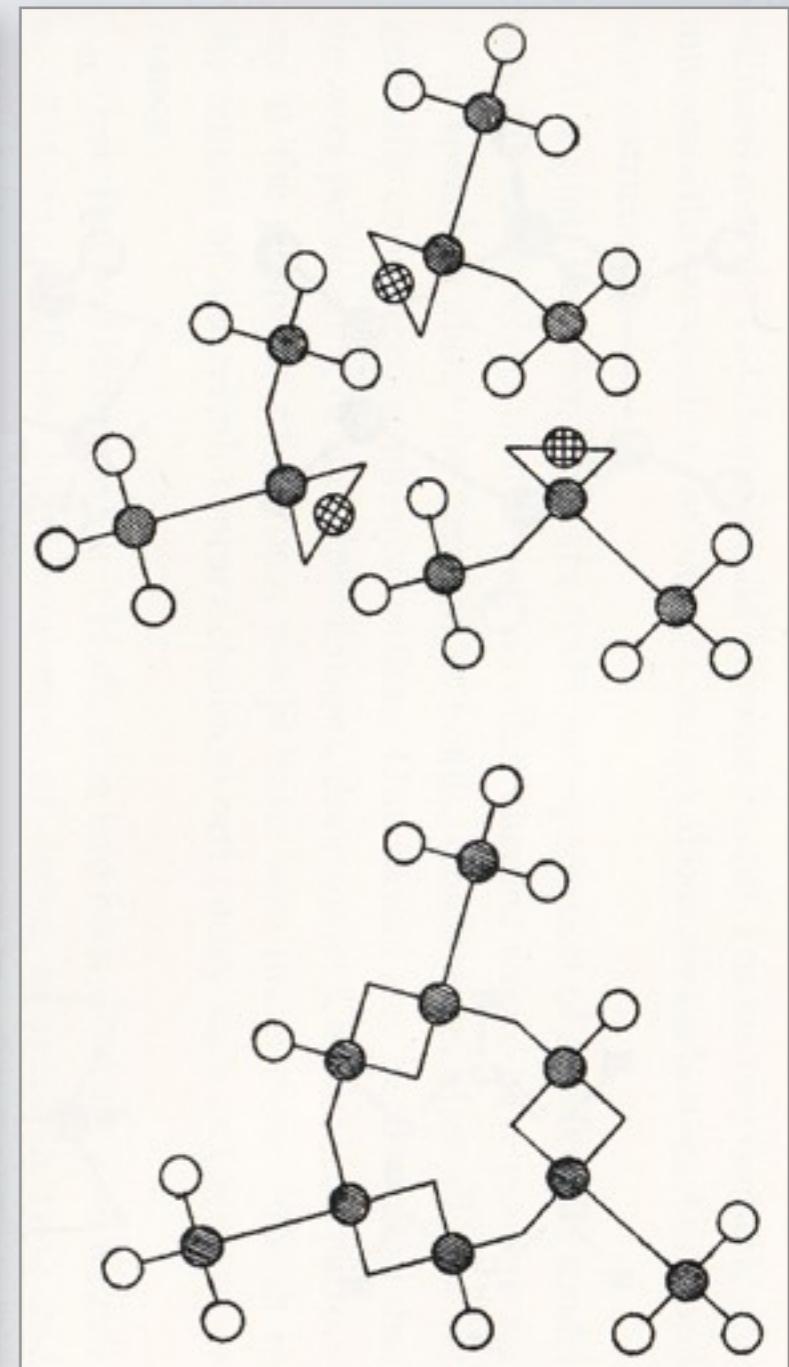
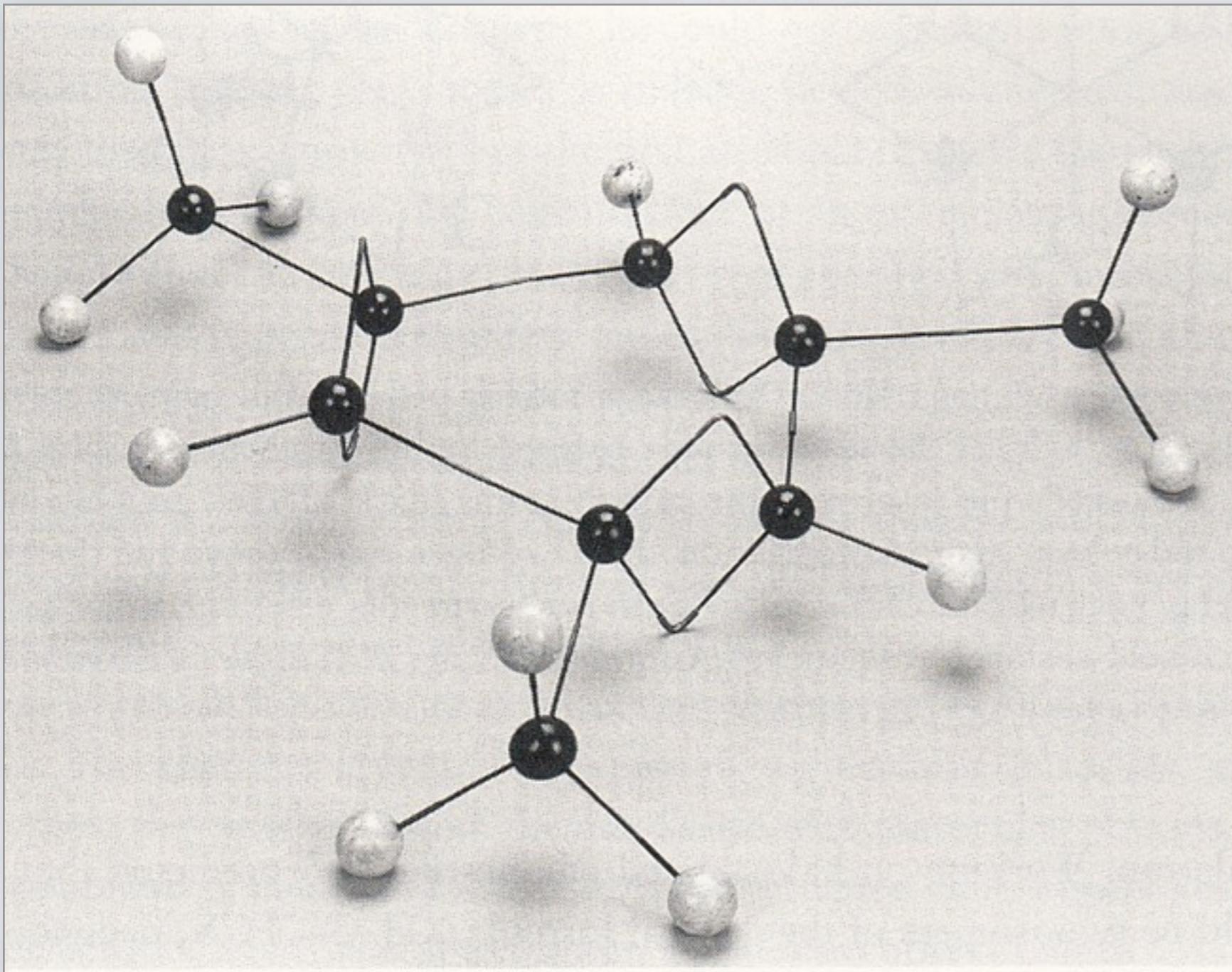


Janet Iwasa, Ph.D.

Department of Biochemistry, University of Utah

3D MODELS IN SCIENCE

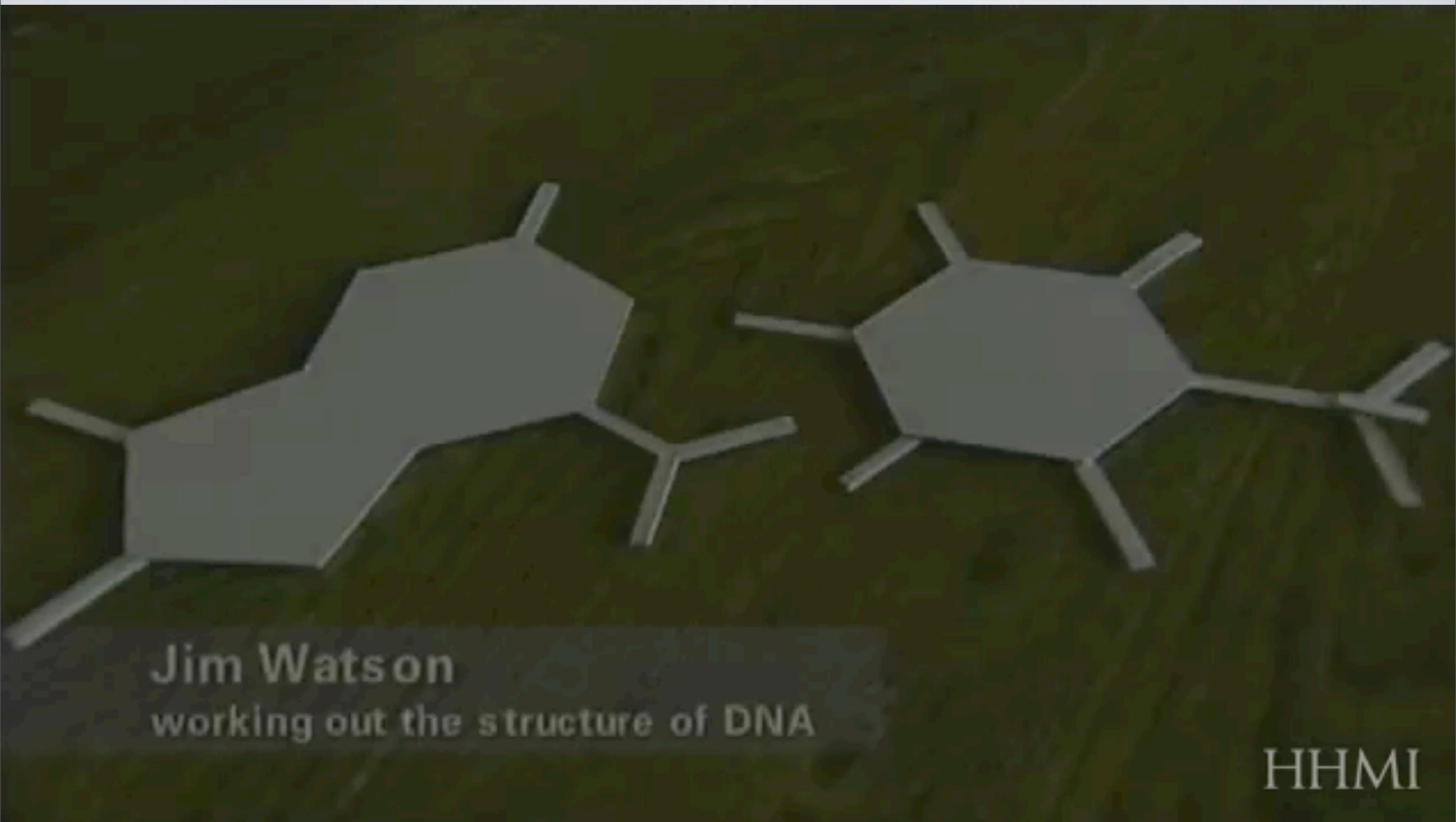
Early chemical models: August Kekulé



from Models: The Third Dimension of Science, edited by Soraya de Chadarevian and Nick Hopwood

3D MODELS IN SCIENCE

James Watson with paper base pair models

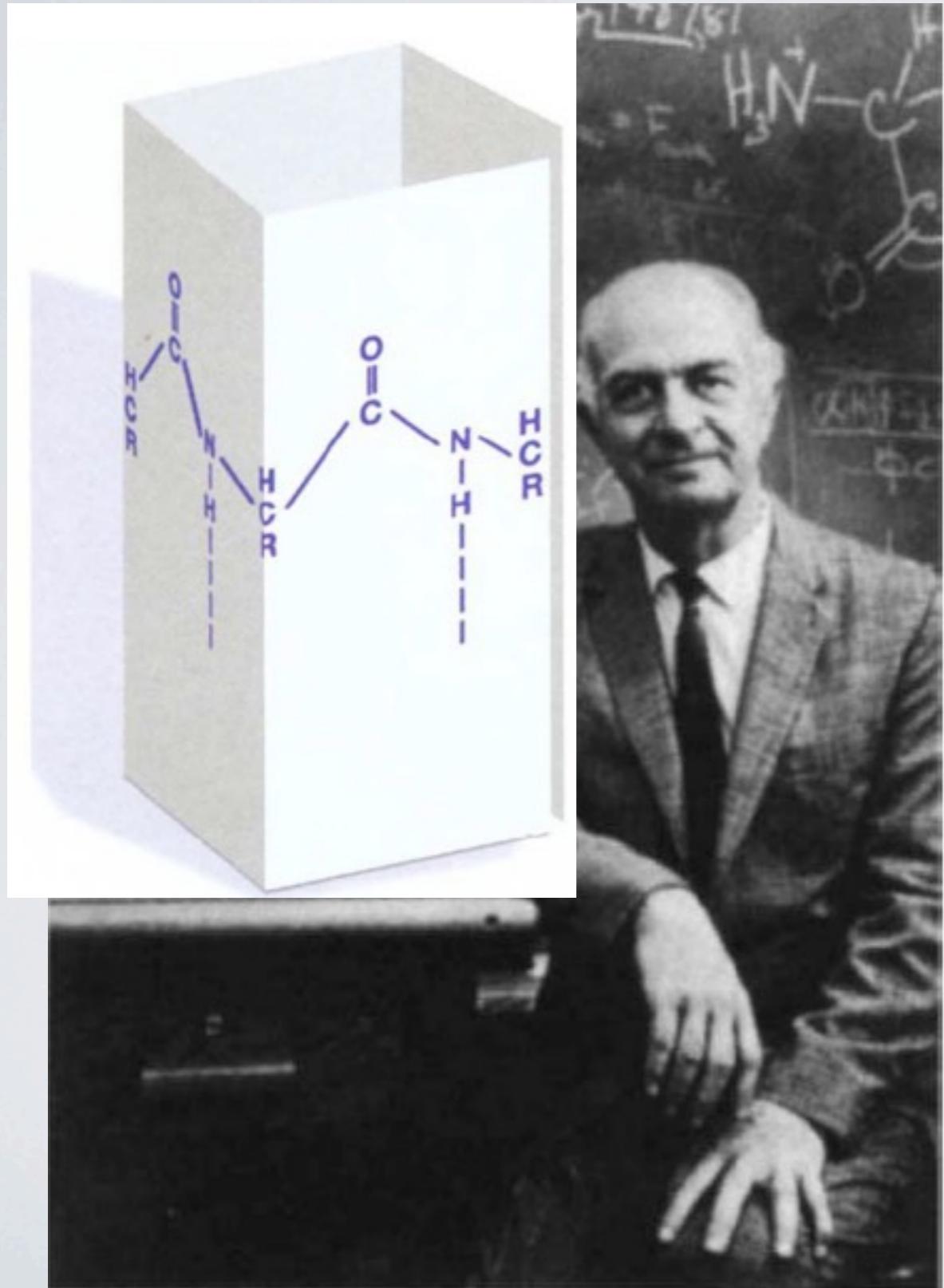


Jim Watson
working out the structure of DNA

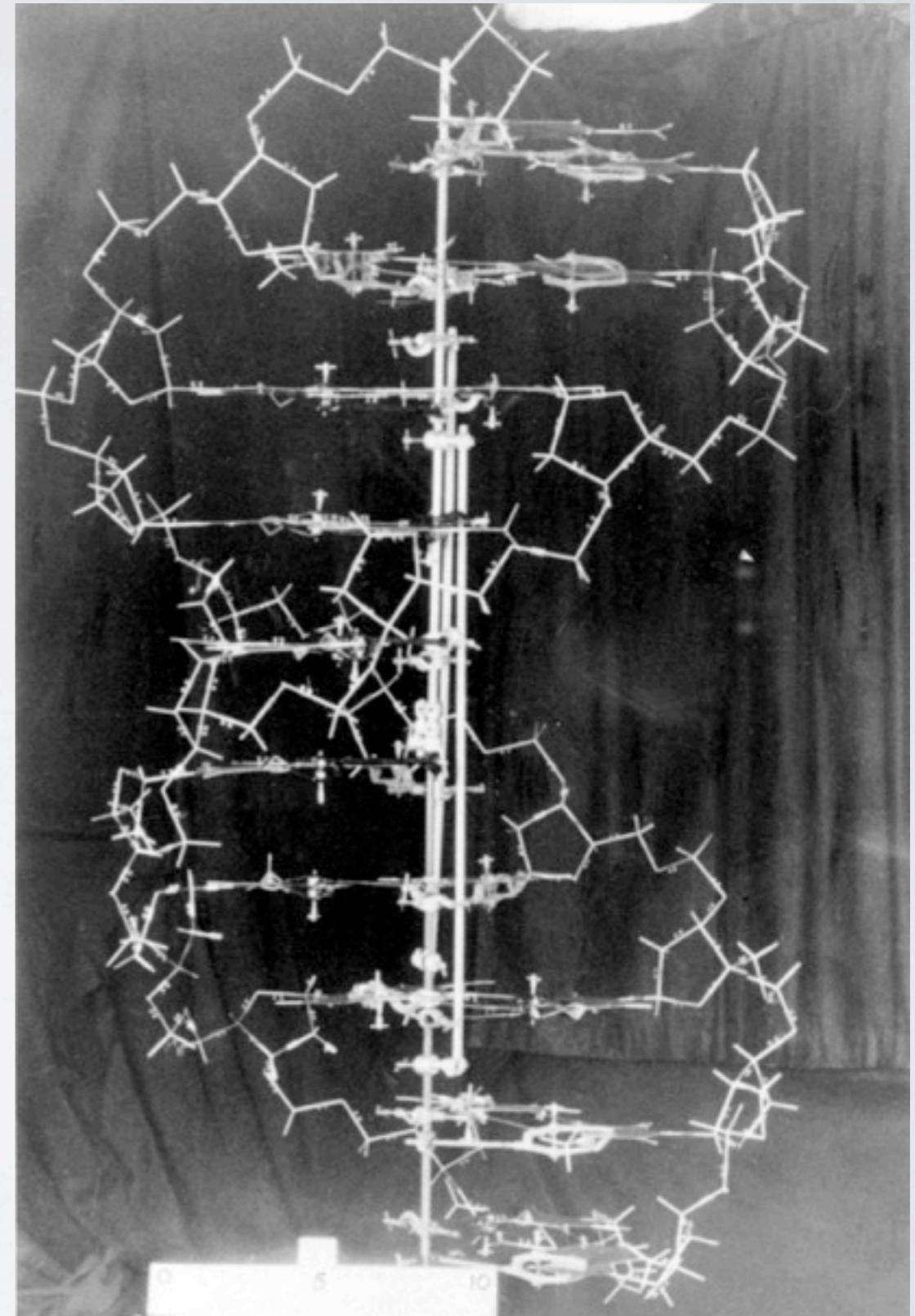
HHMI

from HHMI's "BioInteractive" (<http://hhmi.org/biointeractive>)

ALPHA & DOUBLE HELIX



from "String and Sealing Wax" Nat Struct Biol 1997



from Cold Spring Harbor Labs

3D MODELS IN SCIENCE

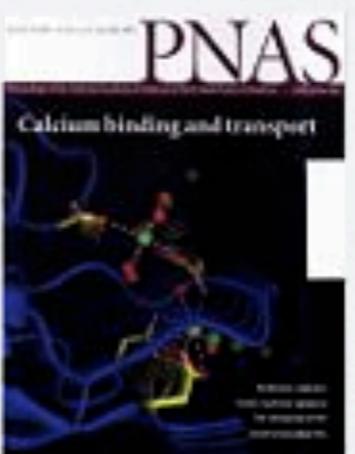
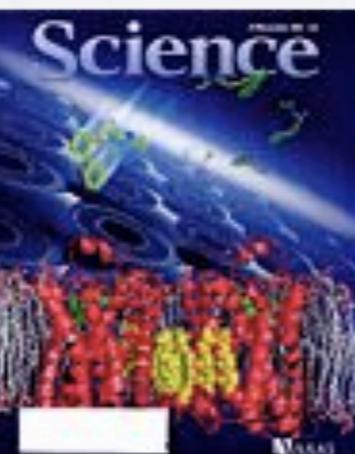
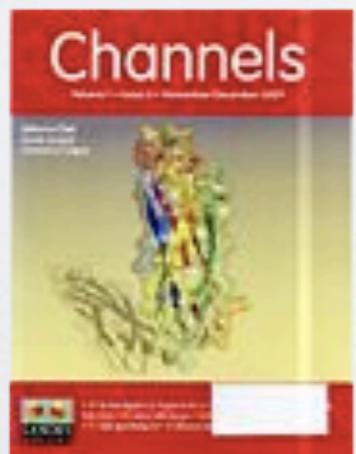
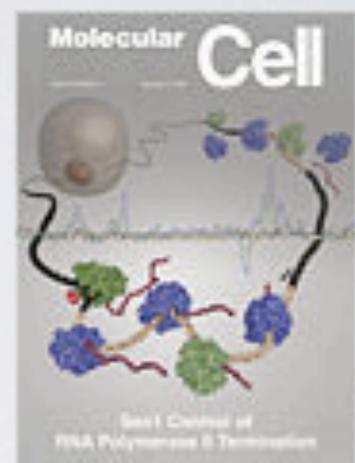
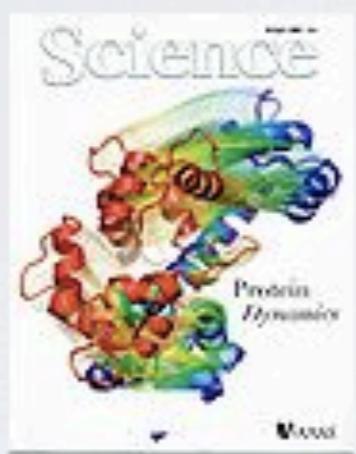
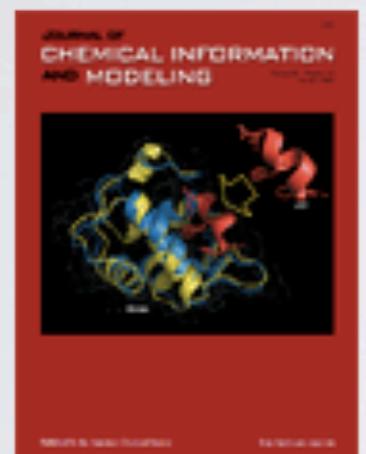
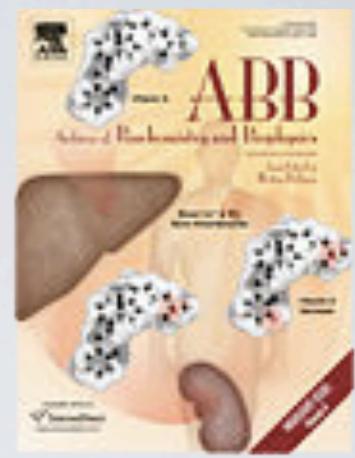
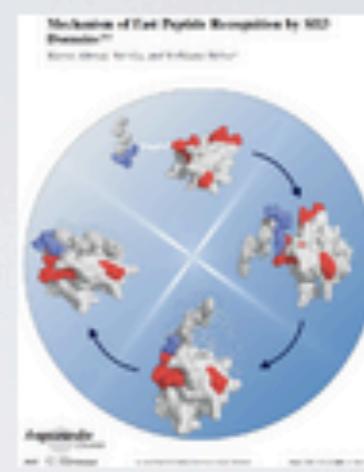
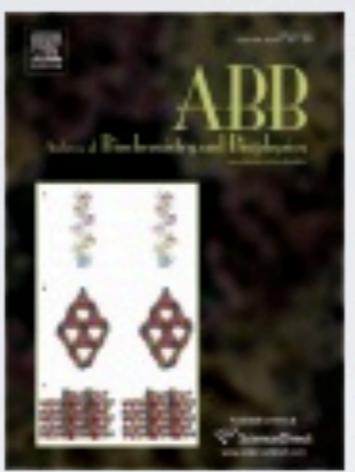
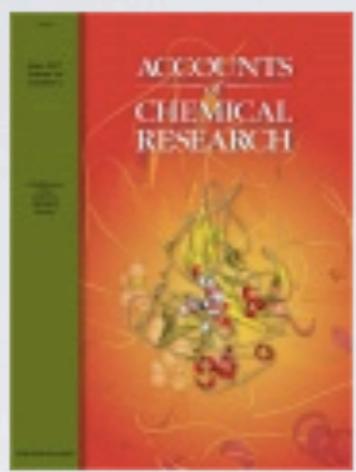
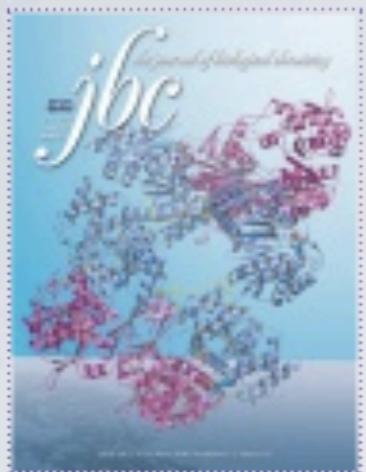
1958 - Myoglobin in a “forest of rods”



Image from: Dickerson RE. Chapter 2: myoglobin: a whale of a structure! J Mol Biol. 2009 Sep 11;392(1):10-23.

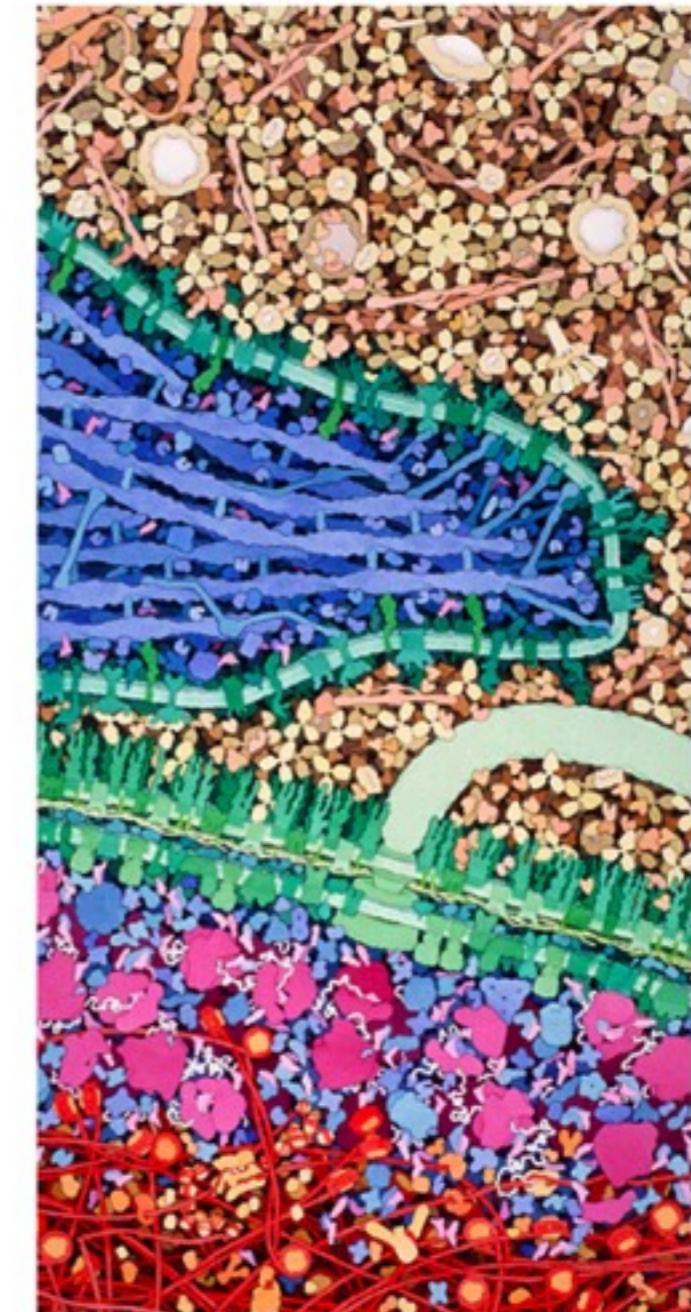
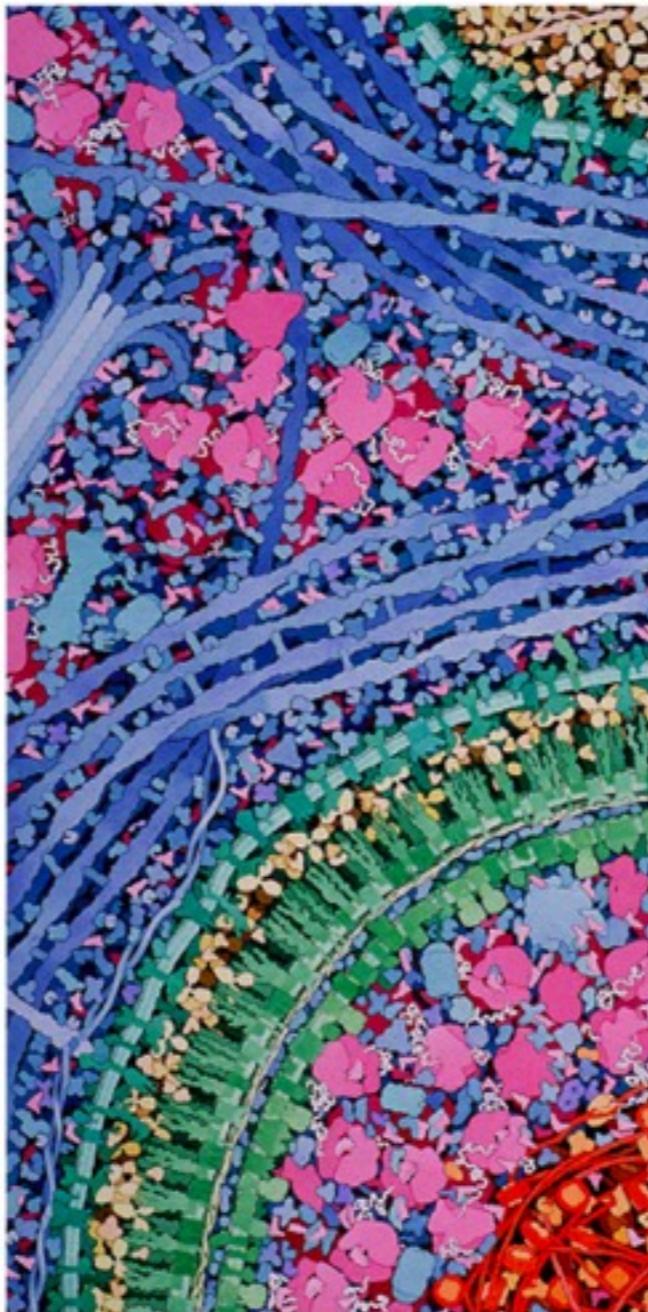
3D MODELS IN SCIENCE

Virtual models



Covers Made with Pymol - from the Pymol Wiki

VISUALIZING THE MESOSCALE



“Macrophage & Bacterium”
David Goodsell (Scripps Institute)

THE NEED FOR NEW MODELS IN BIOLOGY

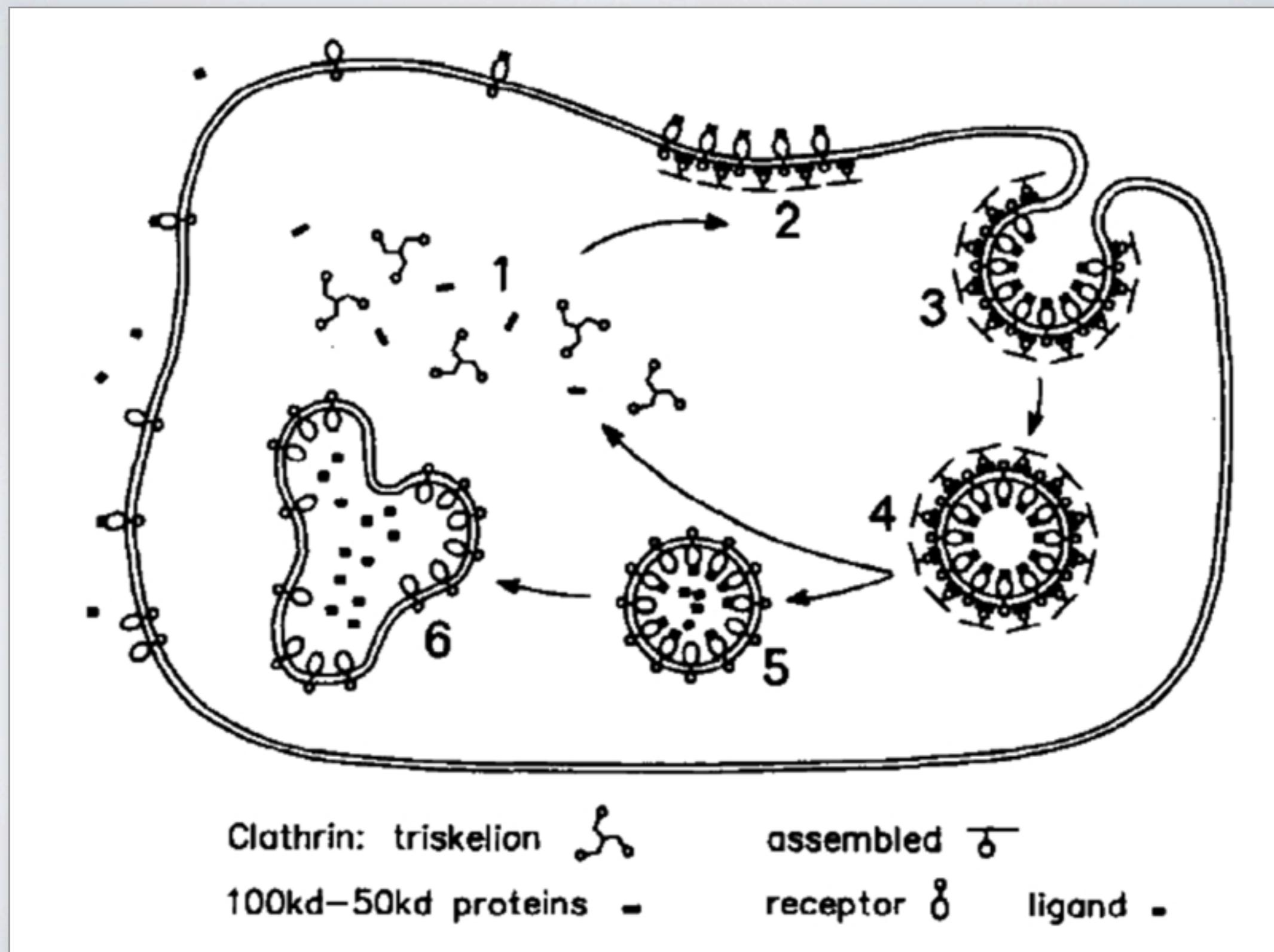
3D animation can synthesize diverse biological data ...

- protein structure
- protein activity
- dynamics
- localization
- simulation
- stoichiometry
- abundance

... allowing us to create a comprehensive visual hypothesis
of a cellular event

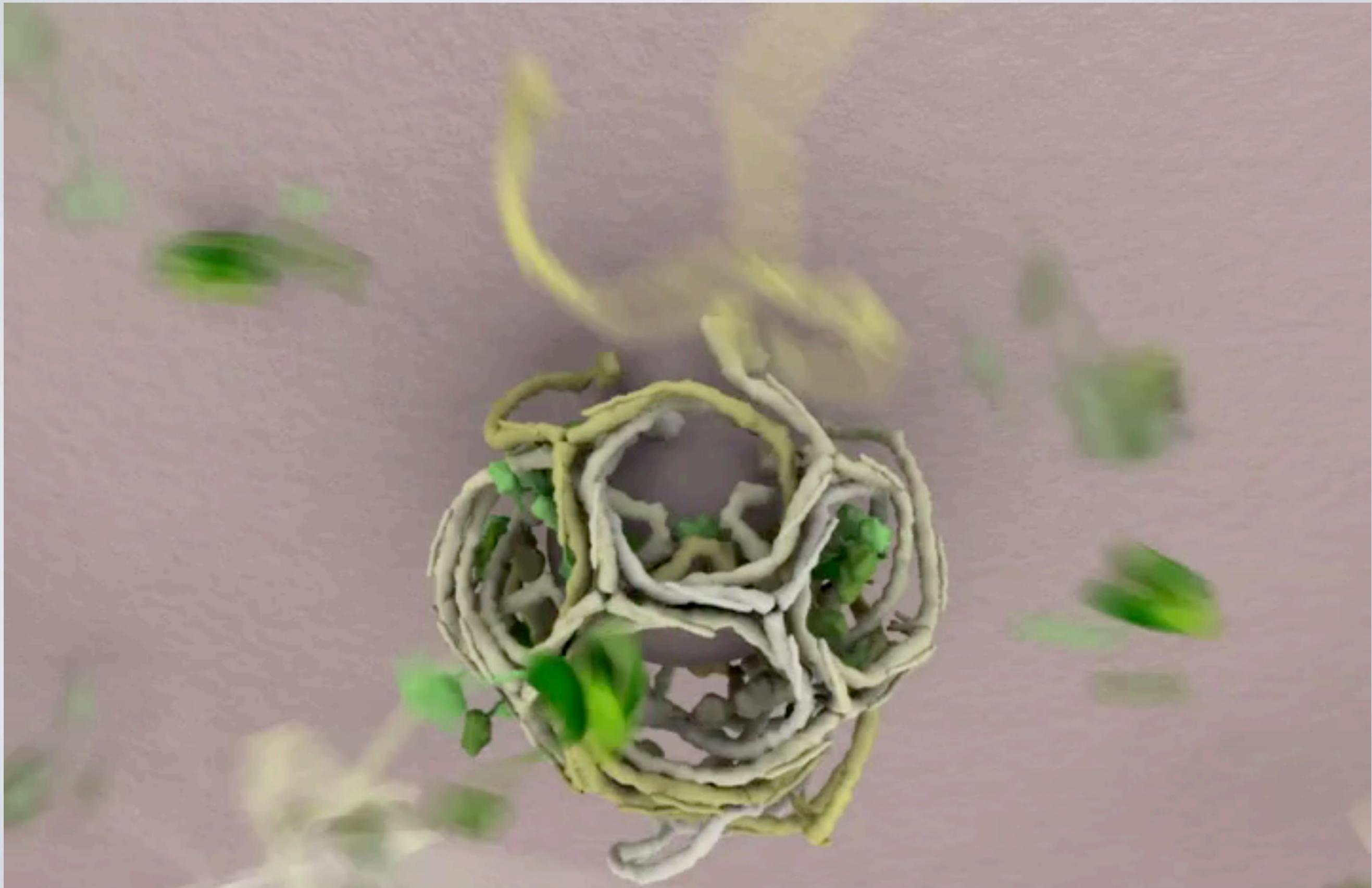
CLATHRIN MEDIATED ENDOCYTOSIS

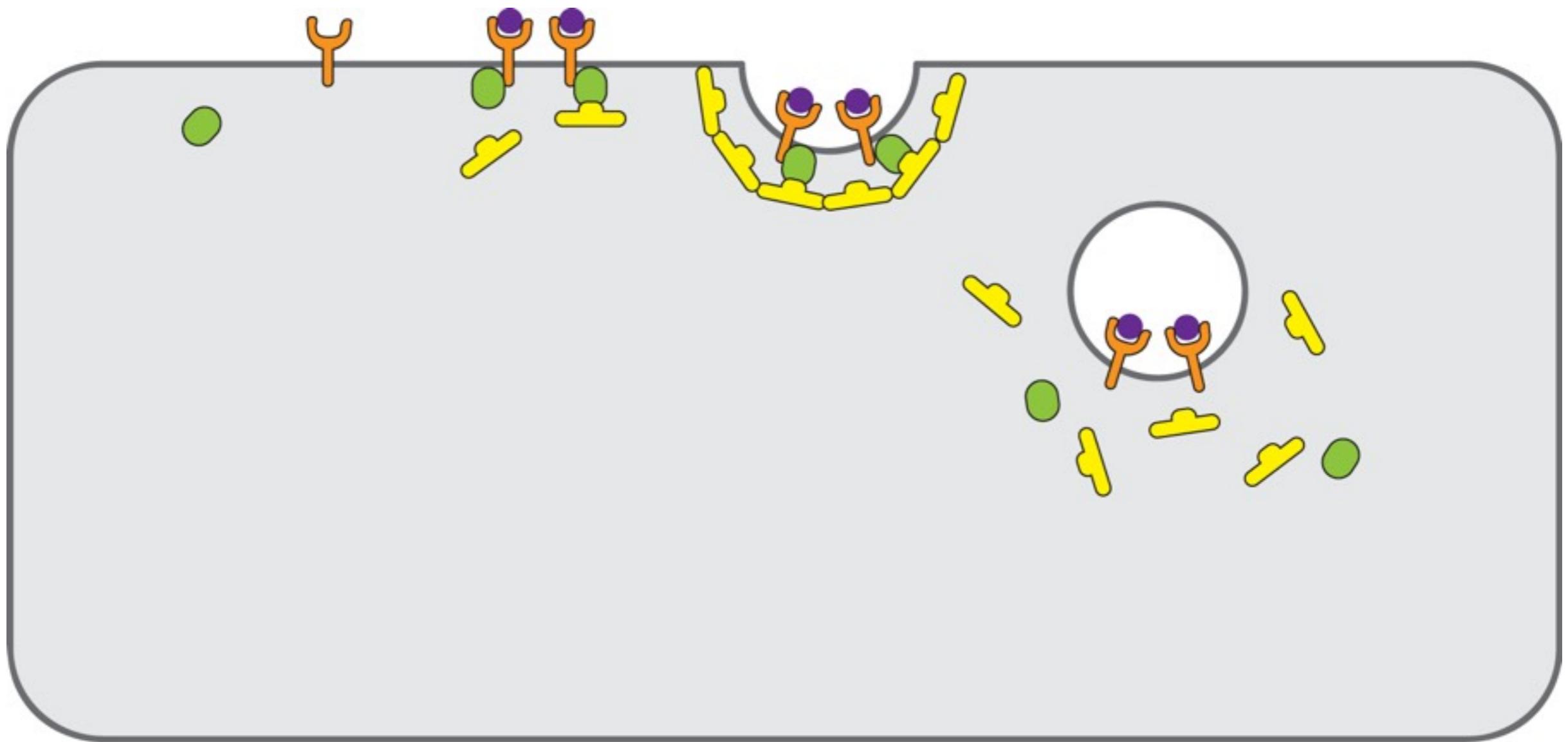
illustration by Pearse & Crowther, 1987



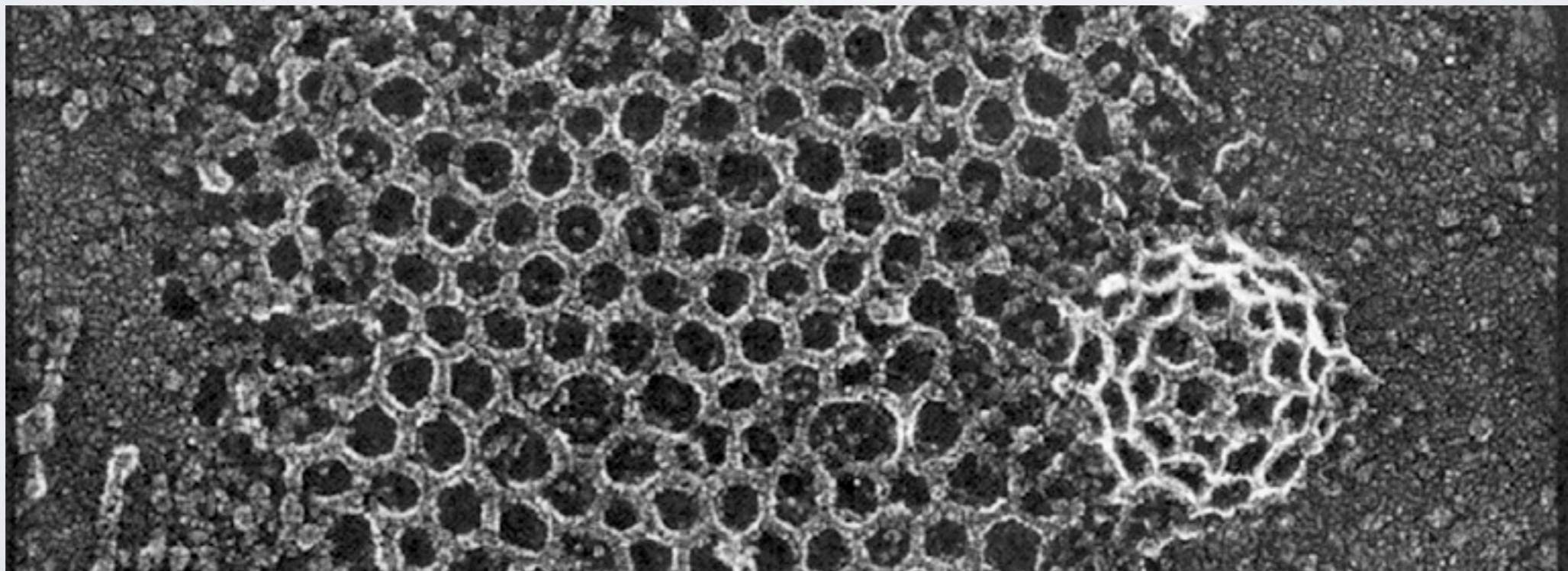
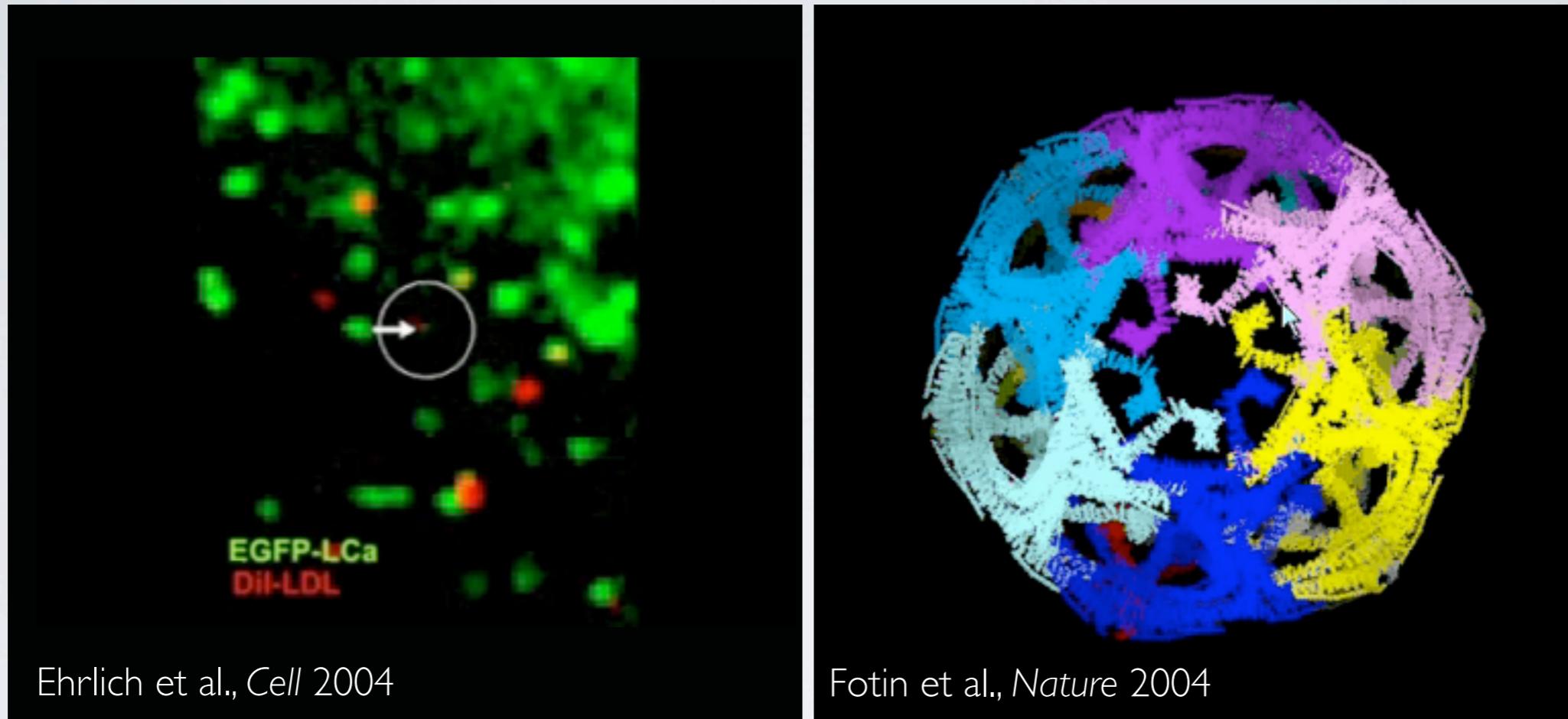
CLATHRIN MEDIATED ENDOCYTOSIS

an animation in collaboration with Tom Kirchhausen (2012)



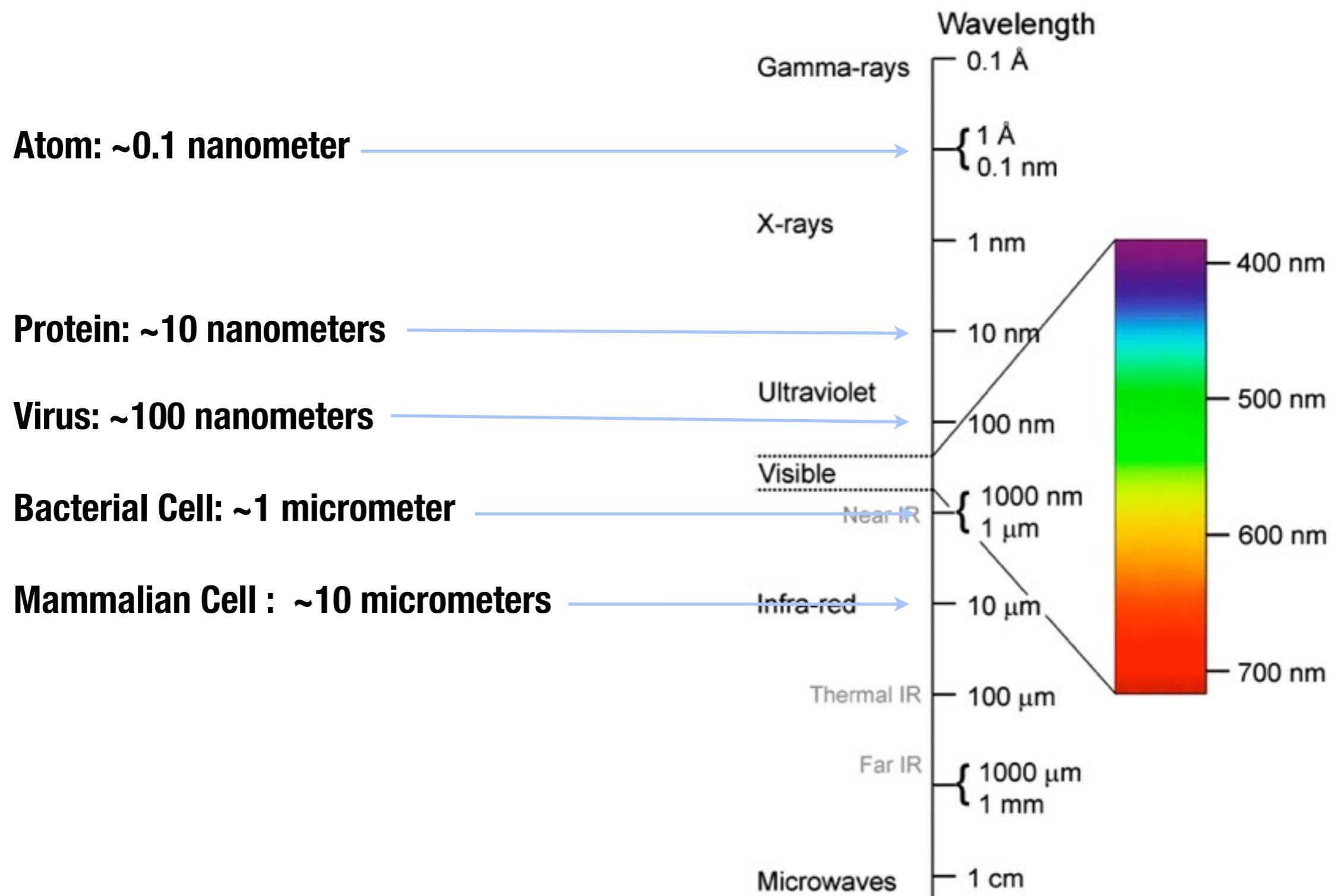


SYNTHESIS OF DIVERSE DATA



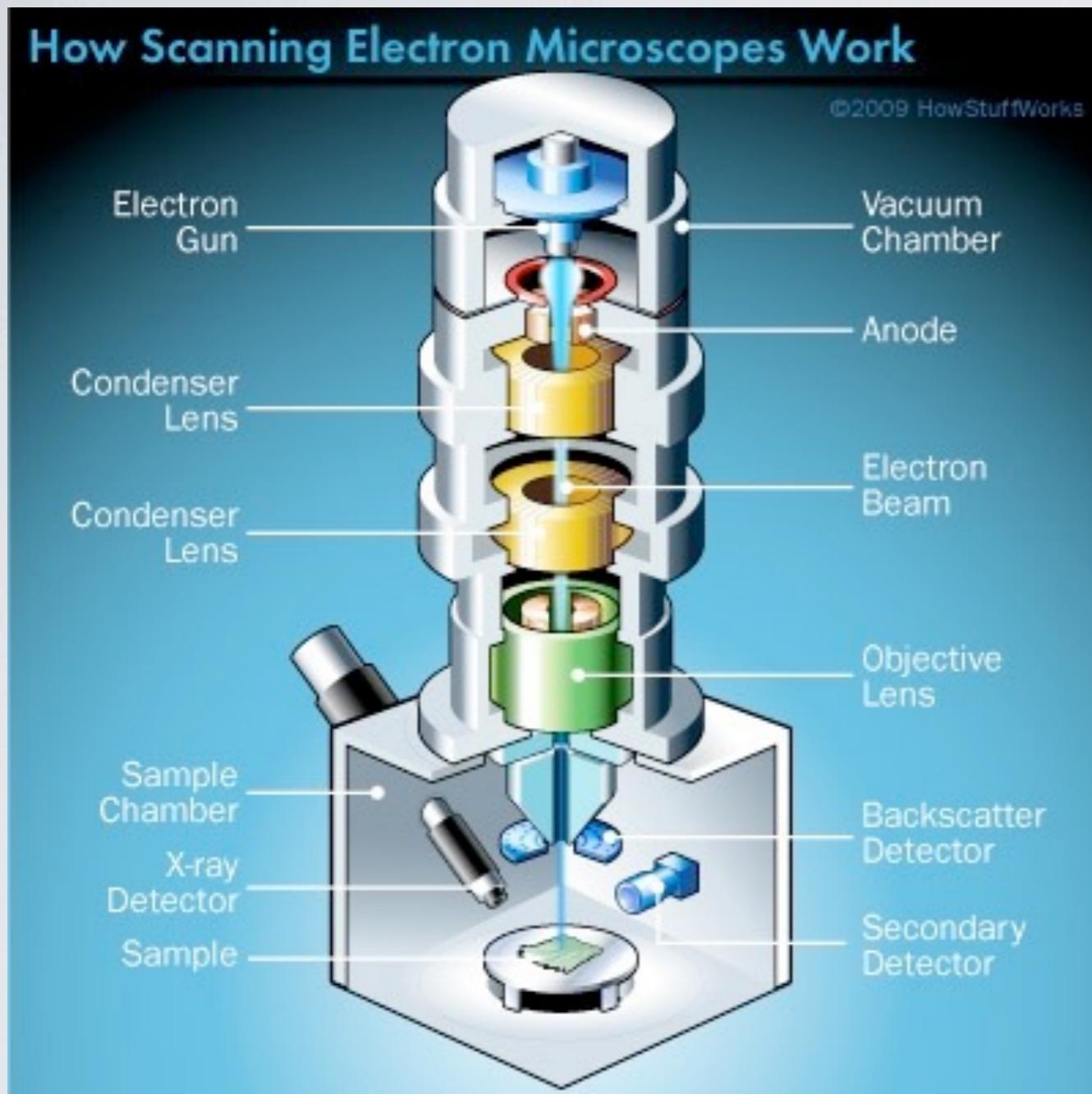
Heuser & Keen, 1998 clathrin structures on cell plasma membrane by “deep etch” electron microscopy

LIMITATIONS OF LIGHT MICROSCOPY



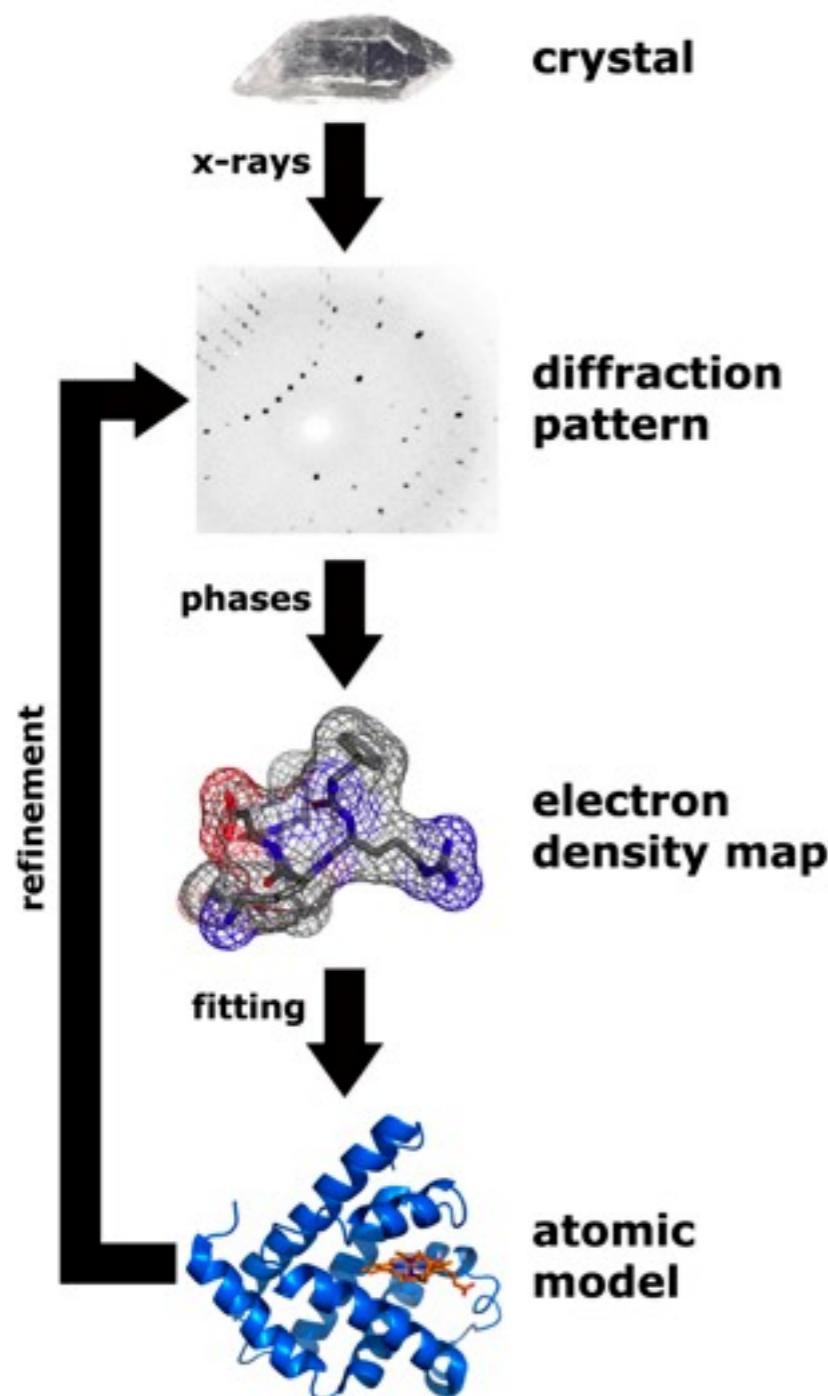
Louis E. Keiner - Coastal Carolina University

ELECTRON MICROSCOPY

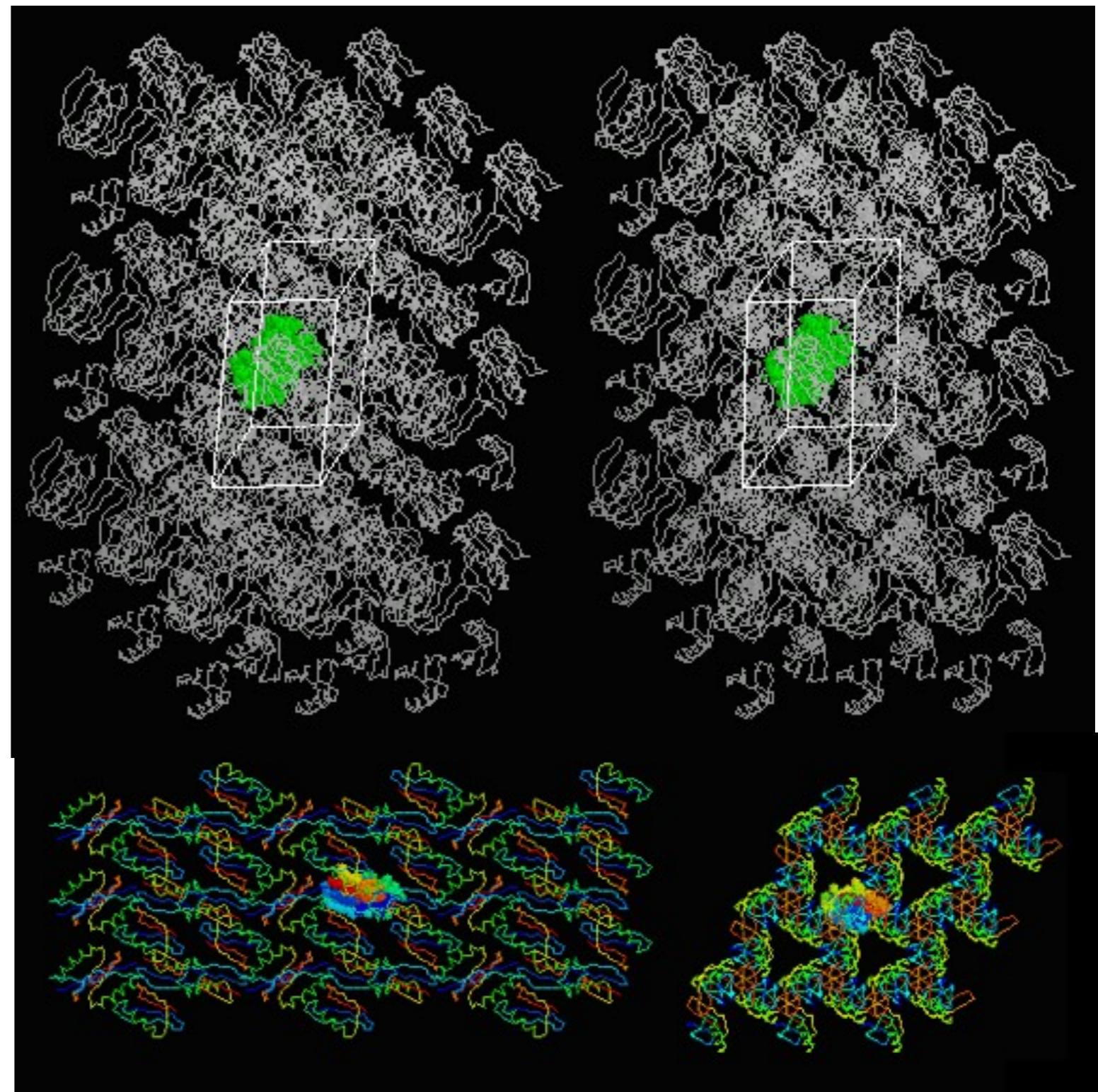


Insect coated in gold
Peter Halasz

X-RAY CRYSTALLOGRAPHY



Thomas Splettstoesser / wikipedia



Eric Martz / U. Massachusetts

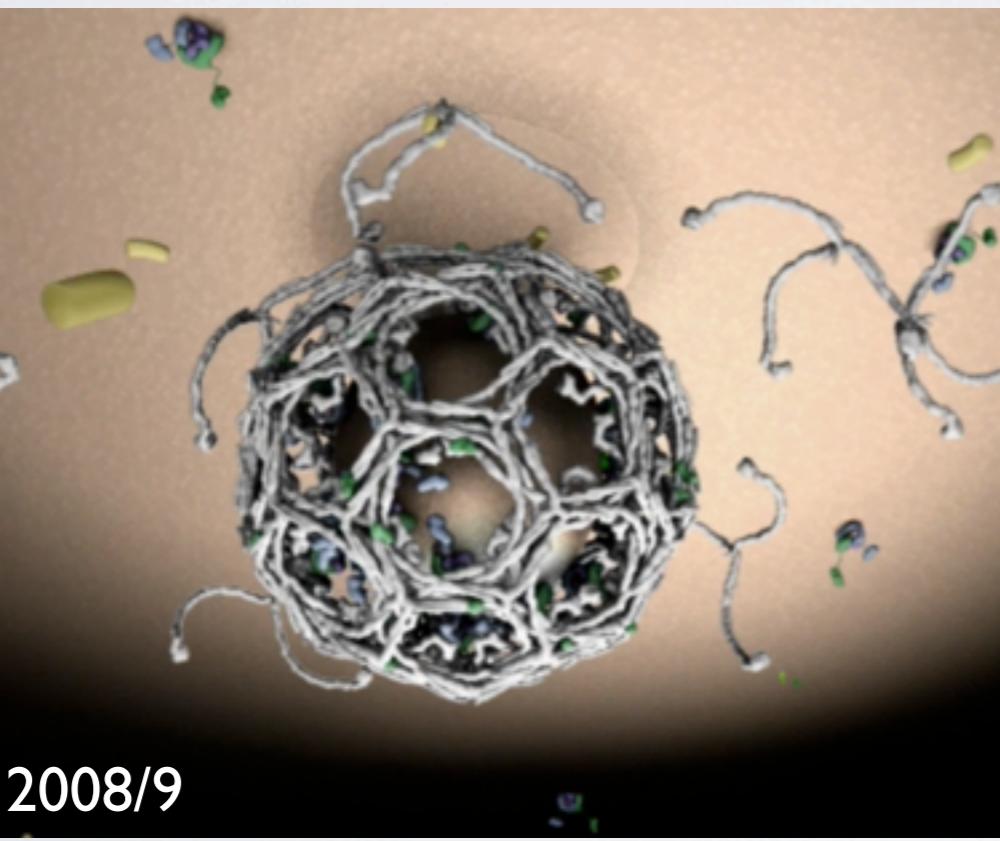
DRAFTS & REVISIONS



2007a



2007b

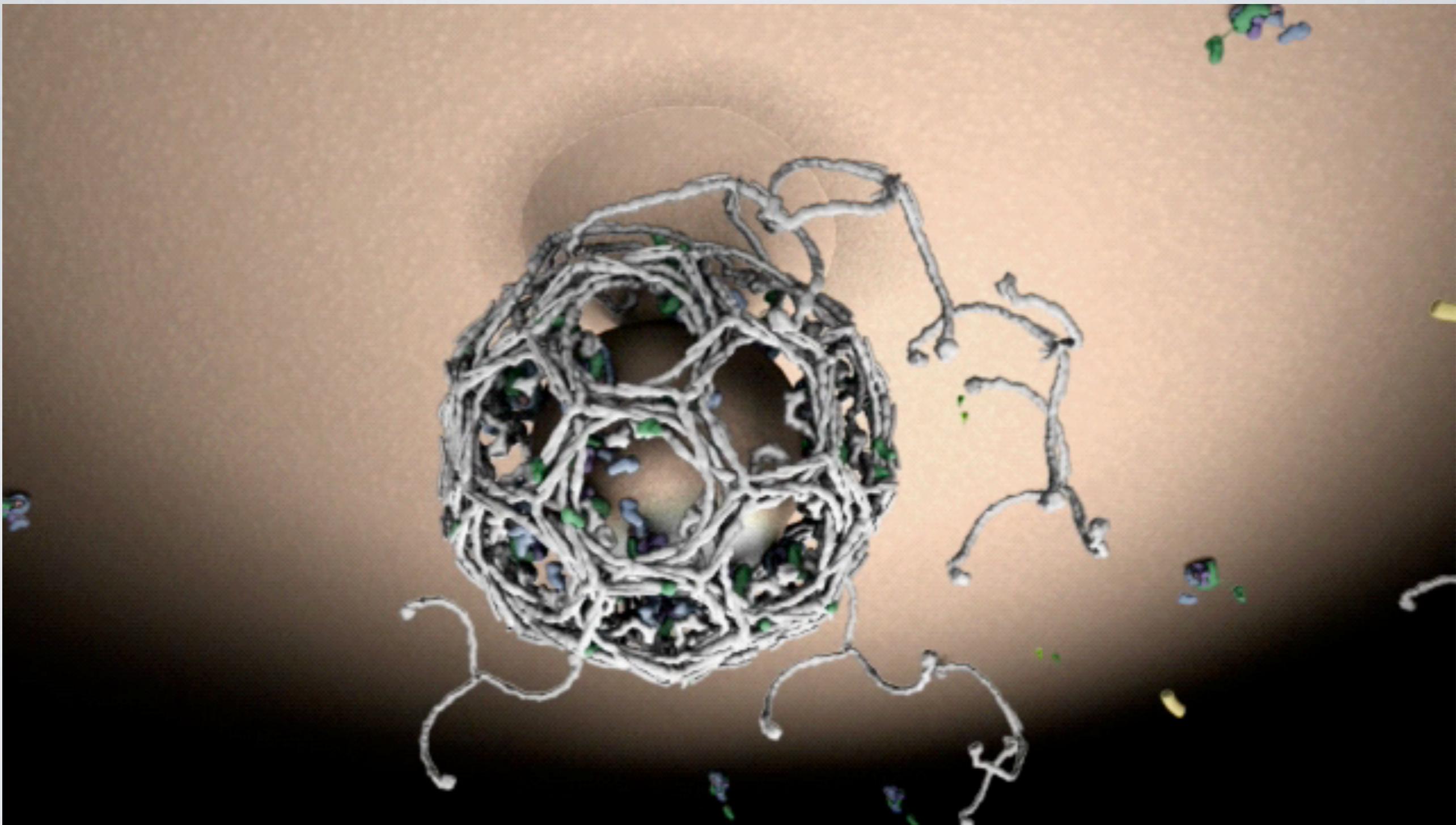


2008/9



2011/12

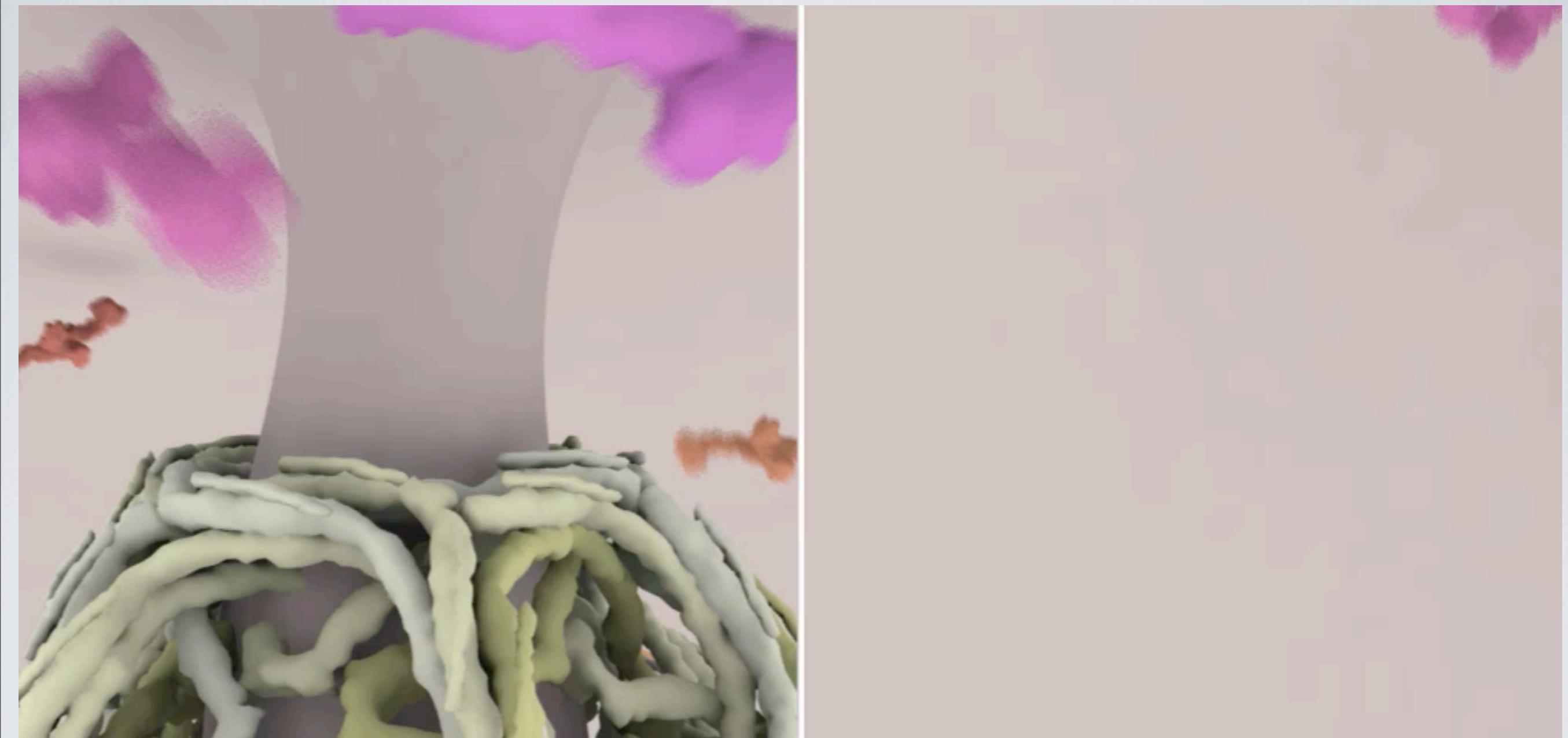
DYNAMIN - 2008

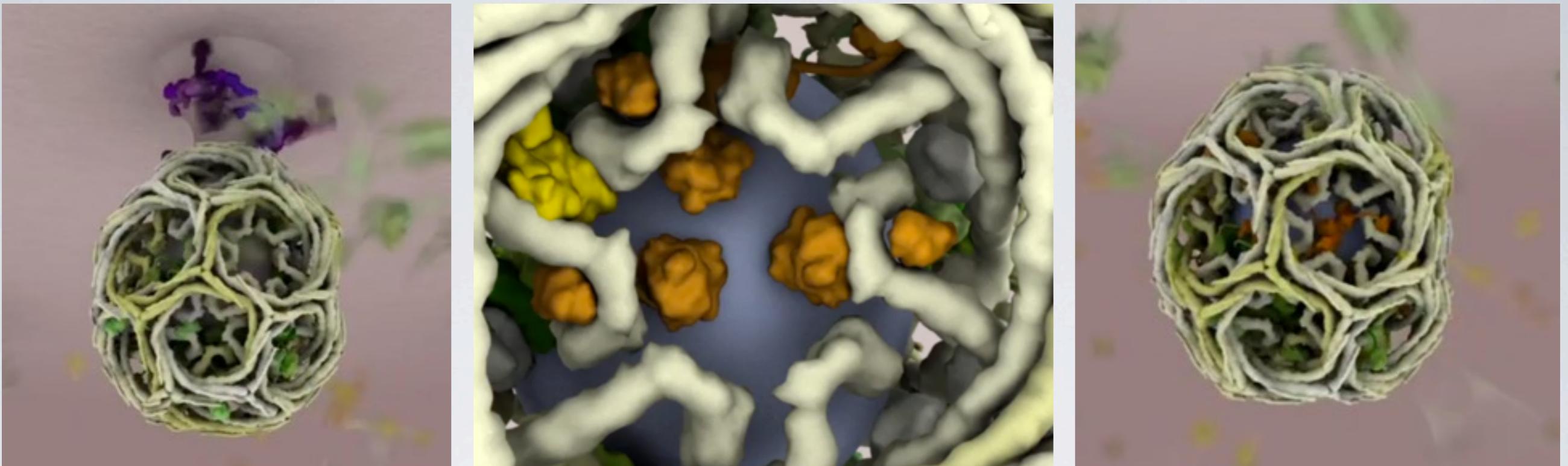


DYNAMIN - 2012



DYNAMIN - 2014



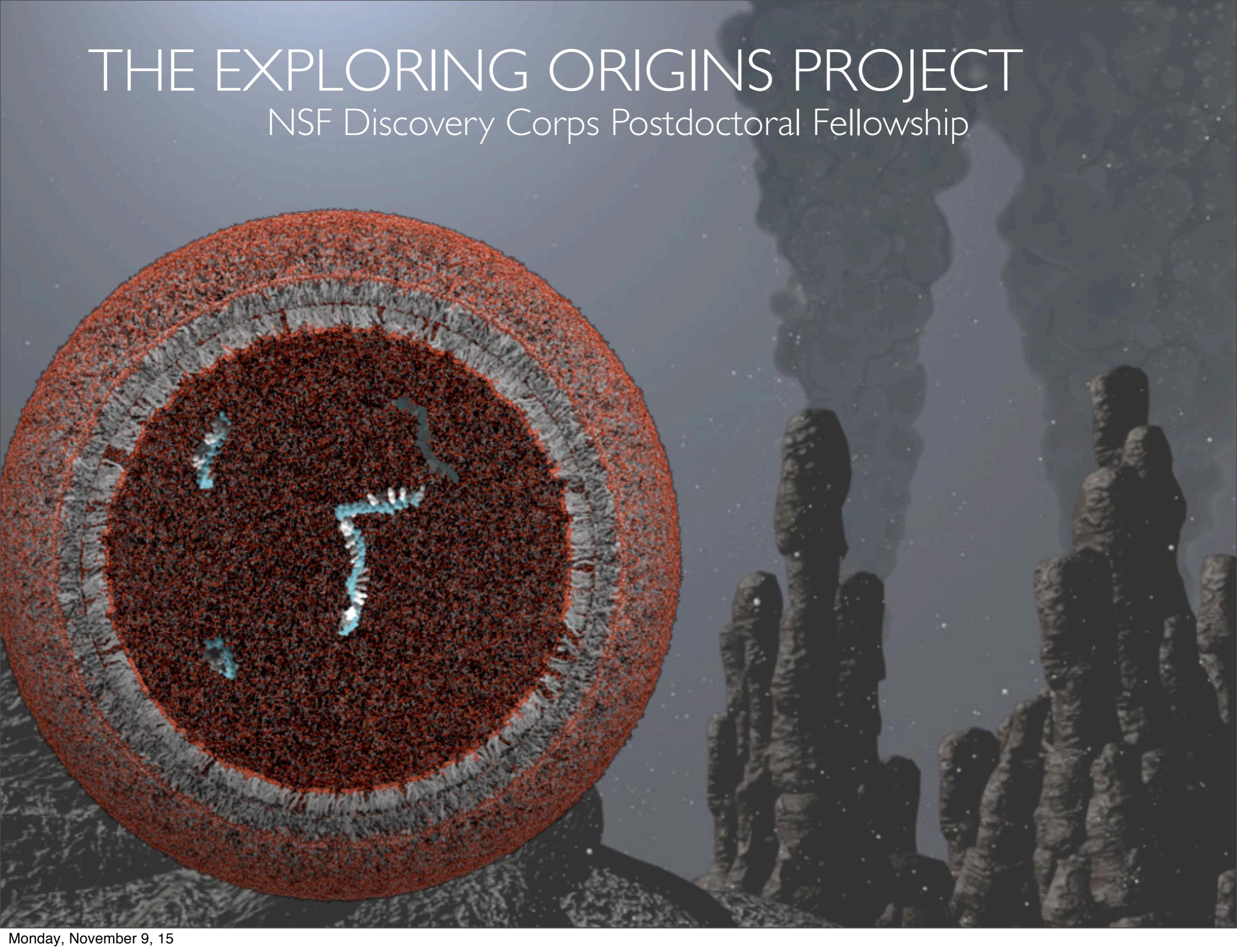


“Molecular 3D animations inform both the scientist who creates them and the audience that views them, through an active process leading to further inquiry and discovery.”

- Tomas Kirchhausen, Harvard Medical School

THE EXPLORING ORIGINS PROJECT

NSF Discovery Corps Postdoctoral Fellowship



THE IMPORTANCE OF COMMUNICATION

getting the public excited about your science

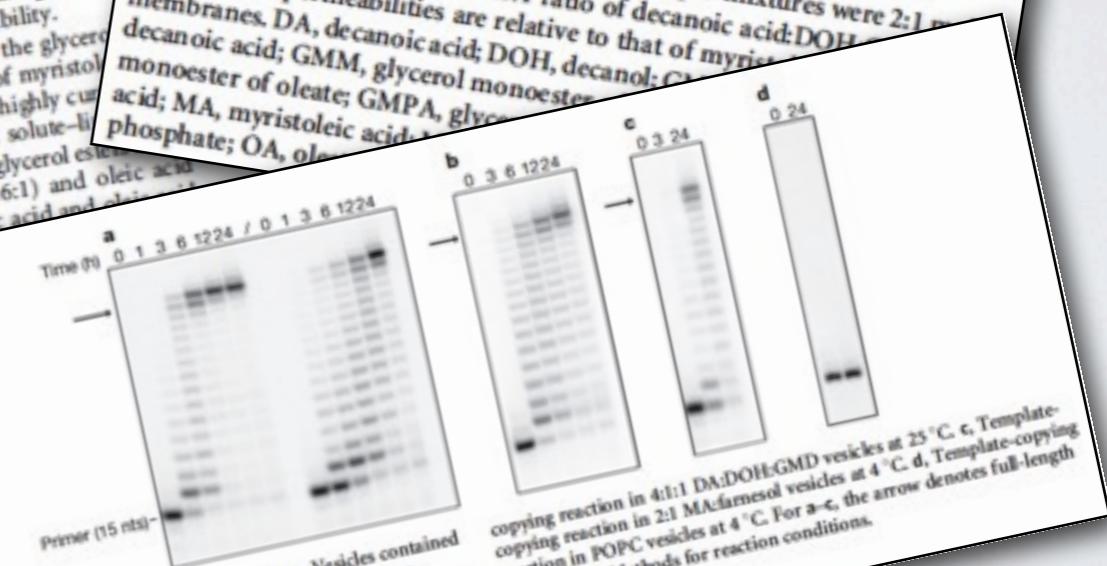
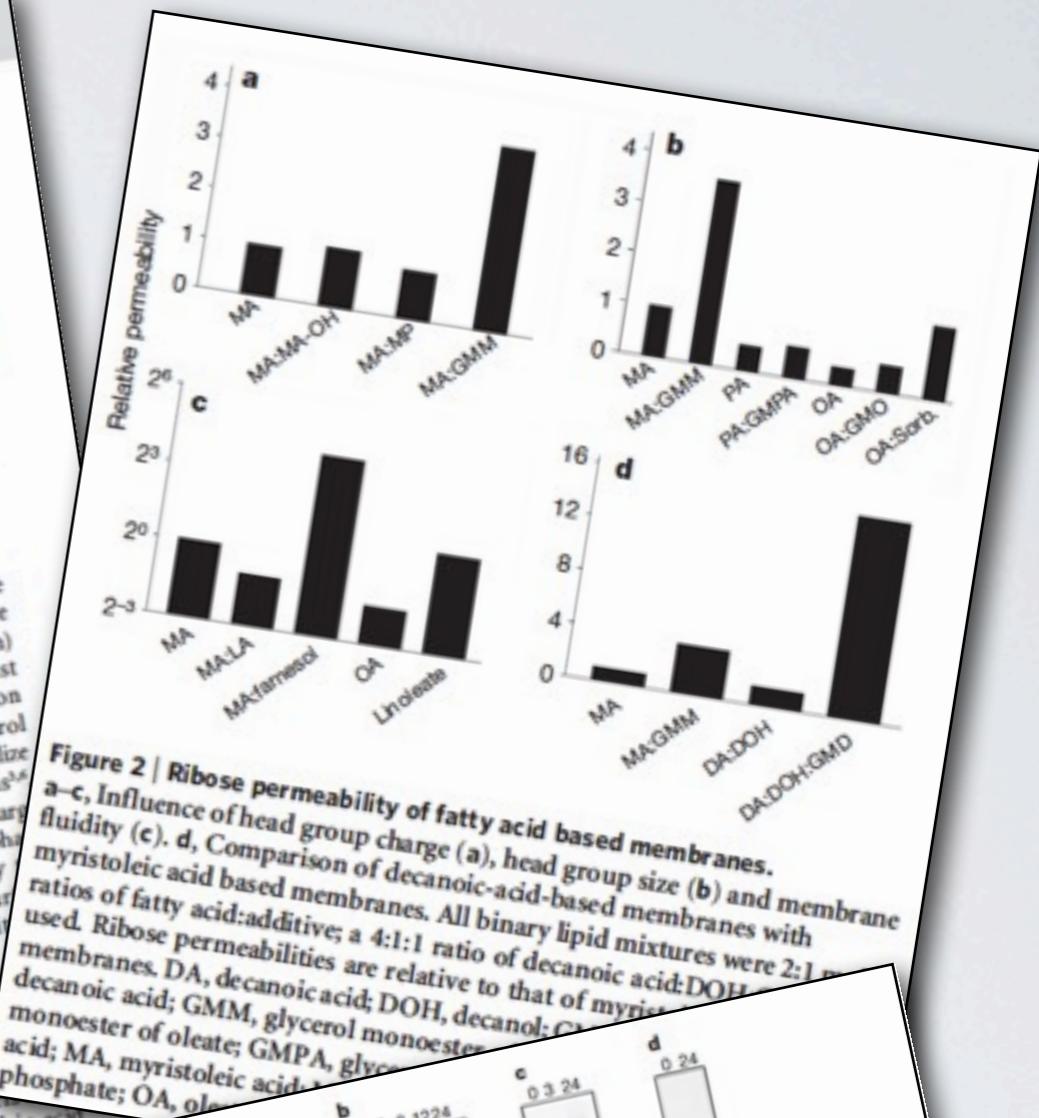
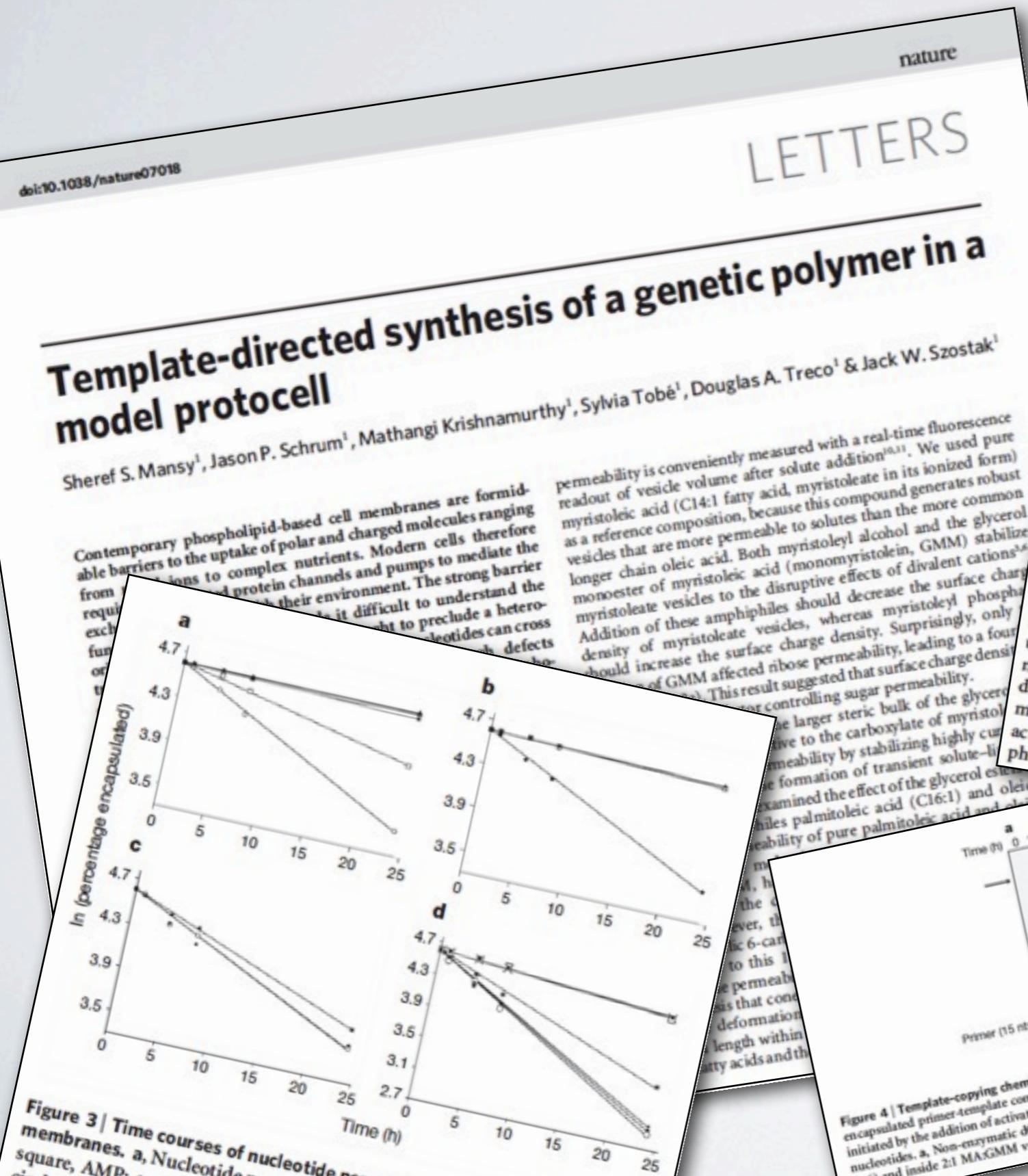
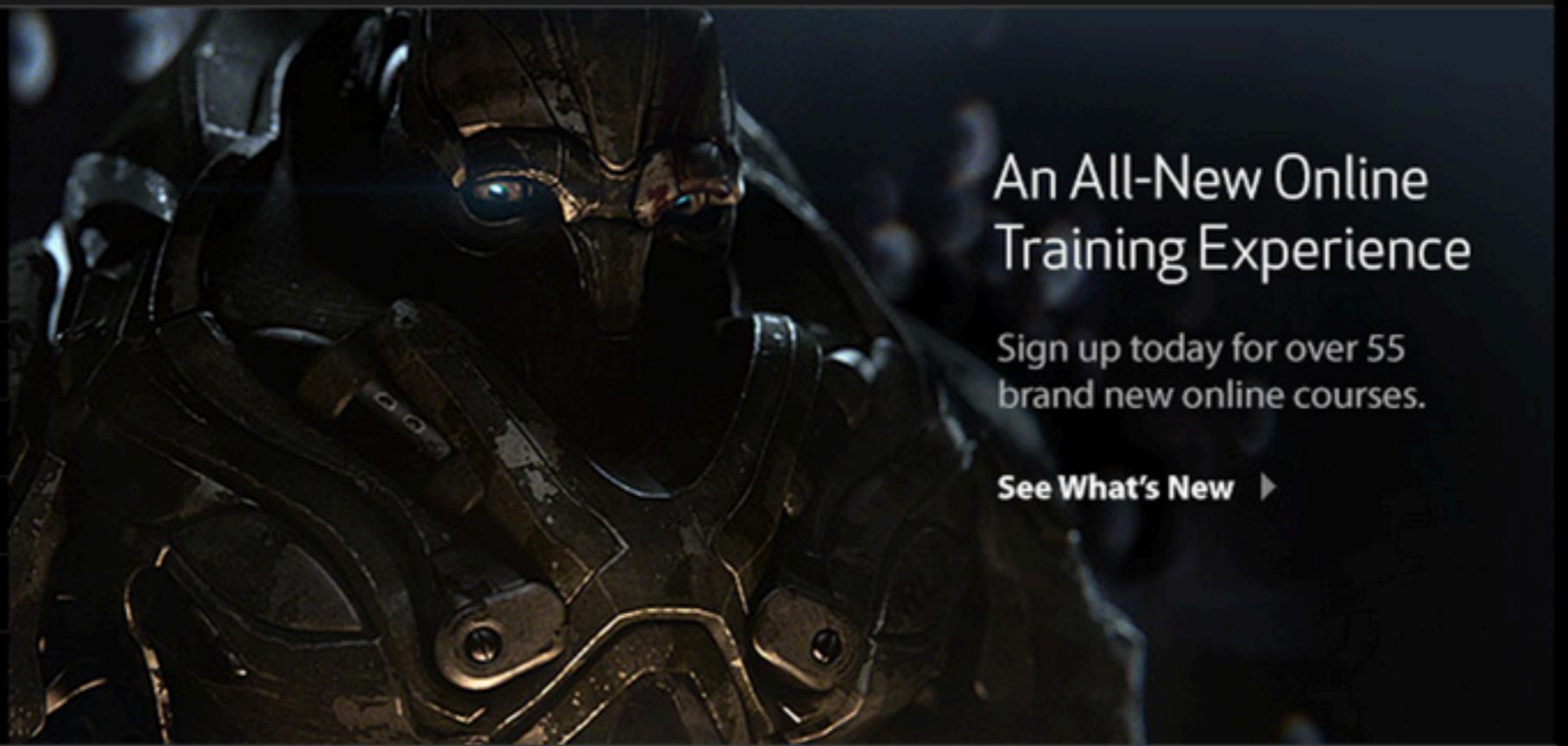


Figure 4 | Template-copying chemistry inside vesicles. Vesicles contained encapsulated primer-template complexes, and template-copying was initiated by the addition of activated monomer to the external solution. nts, nucleotides. a, Non-enzymatic dC₁₅-template copying in solution (lanes 1–6) and inside 2:1 MAGMM vesicles (lanes 8–13) at 4 °C. b, Template-copying reaction in 4:1:1 DA:DOH:GMD vesicles at 25 °C. c, Template-copying reaction in 2:1 MA:famesol vesicles at 4 °C. d, Template-copying reaction in POPC vesicles at 4 °C. For a–c, the arrow denotes full-length product. See Methods for reaction conditions.

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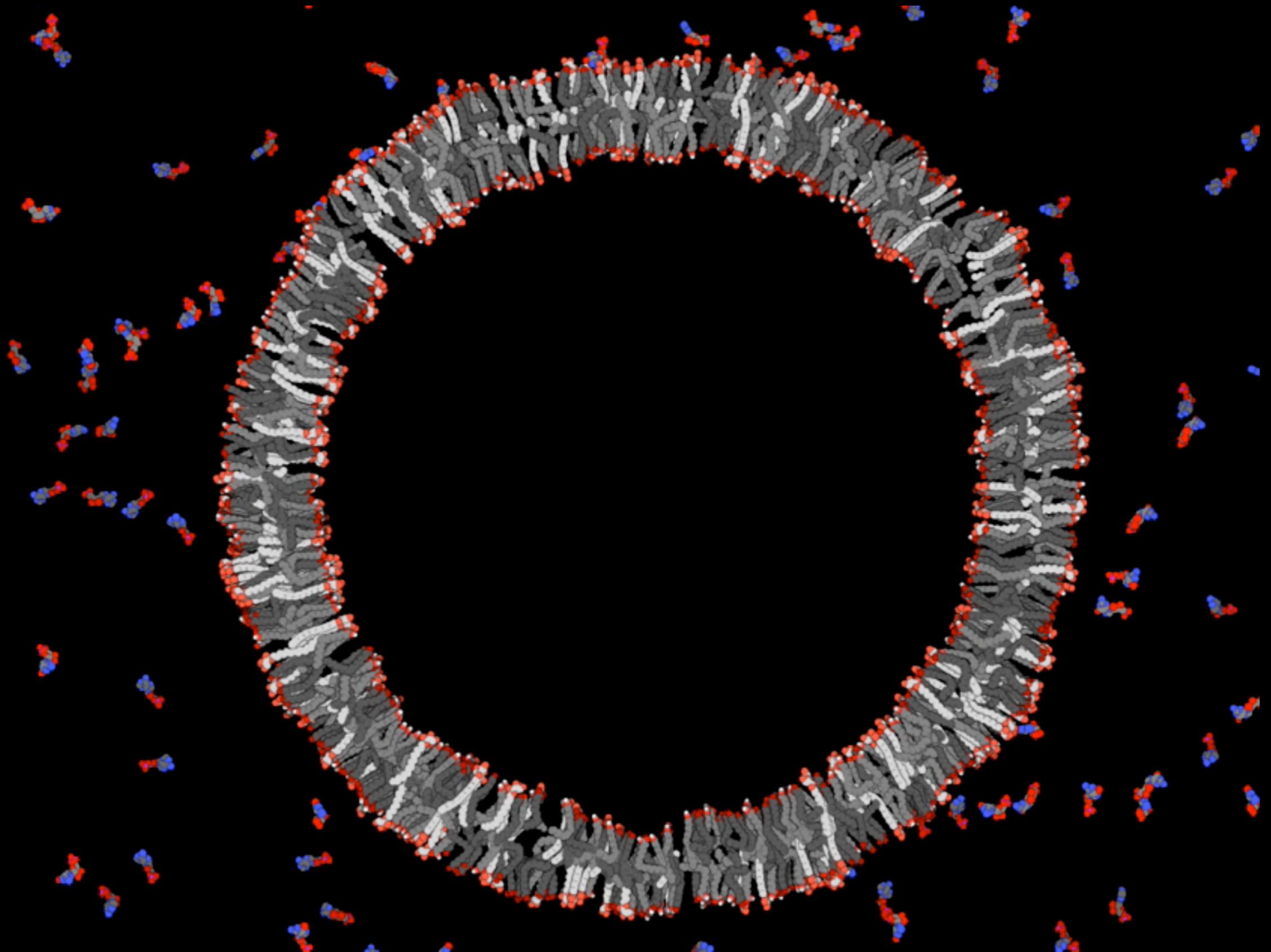
Jorik Dozy
Pacific Rim
Digital Matte Painter, ILM

[View More »](#)

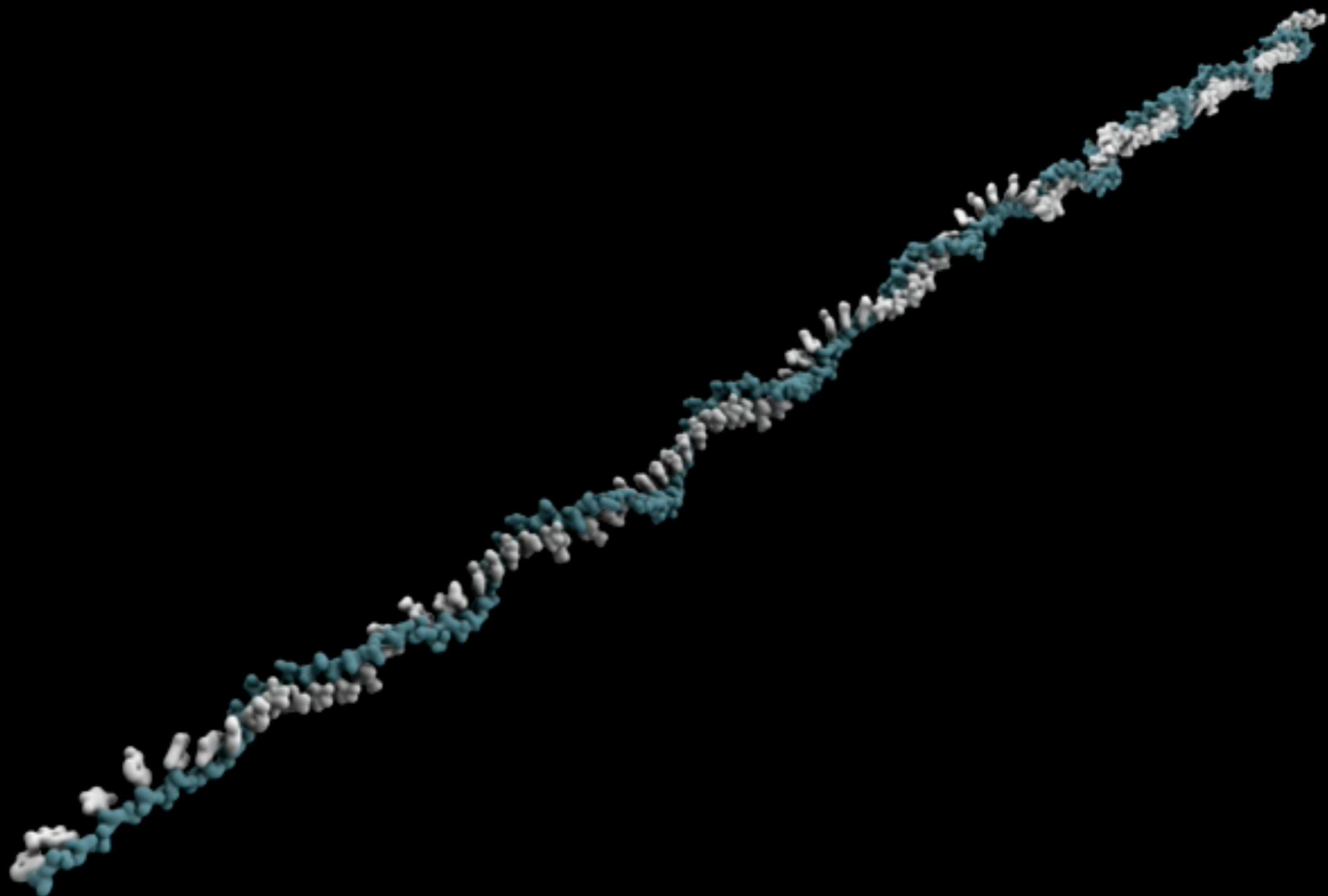
News and Events



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Entry of Small Molecules into Vesicles
with Jack Szostak | Harvard Medical School



A simplified depiction of RNA folding
with Jack Szostak | Harvard Medical School



Exploring Origins: Exhibit
Museum of Science, Boston 2008-2013



<http://exploringorigins.org/>



Google



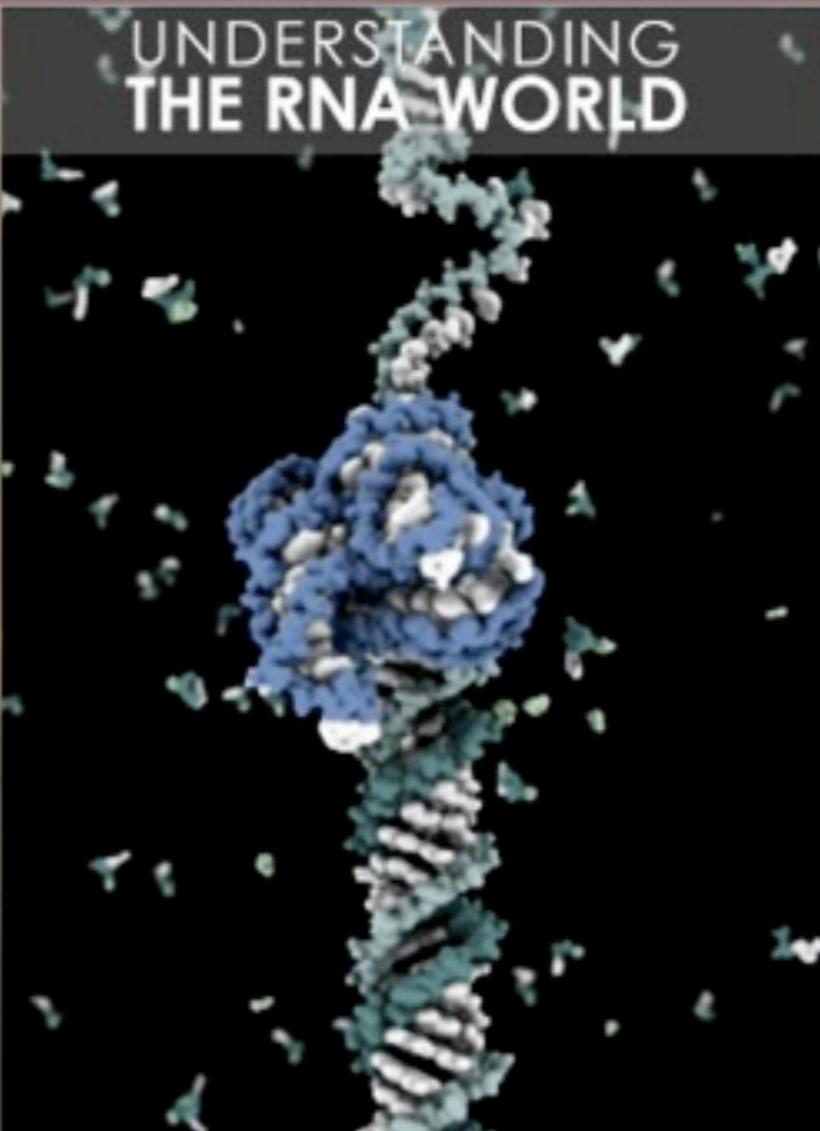
Gmail weather Google Scholar Szostak Lab Highend3d Wikipedia downloads calendar

EXPLORING LIFE'S ORIGINS

A TIMELINE OF
LIFE'S EVOLUTION

UNDERSTANDING
THE RNA WORLD

BUILDING
A PROTOCELL



Exploring Origins: A Virtual Exhibit
with Jack Szostak | Harvard Medical School

THE IMPORTANCE OF VISUALIZATION

getting the public excited about your science

WIRED GEAR SCIENCE ENTERTAINMENT BUSINESS SECURITY DESIGN

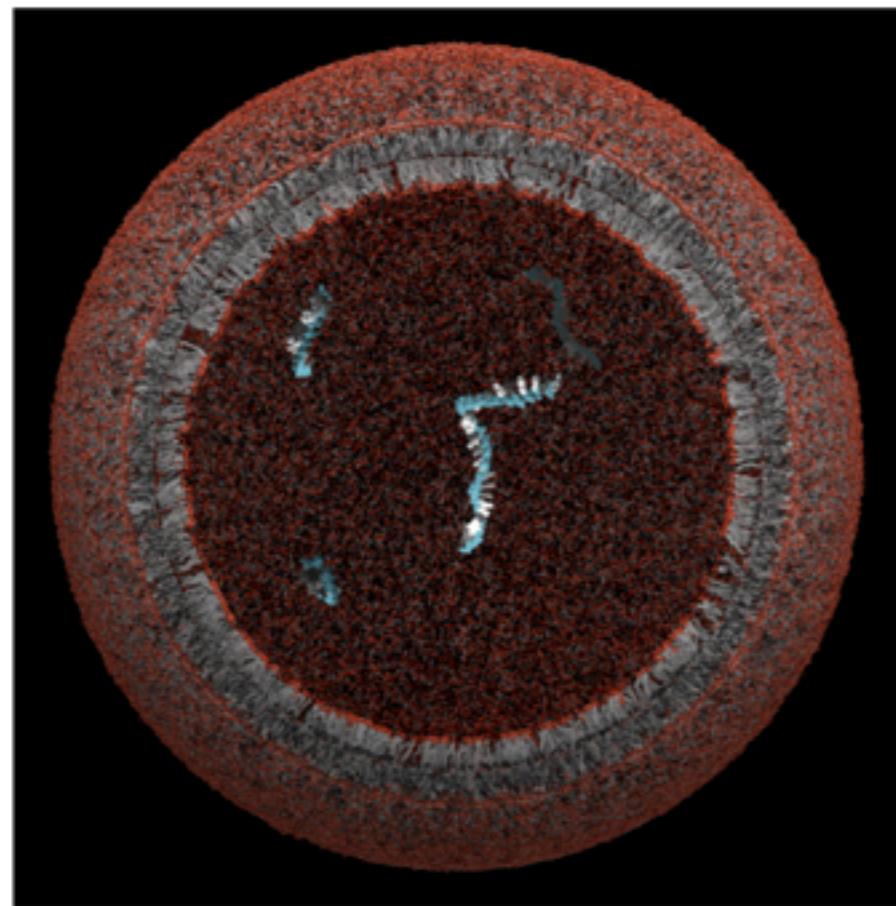
Wired Science's 13 Most Popular Stories of 2008

BY BETSY MASON 12.30.08 | 5:14 PM | PERMALINK

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It was a good year for Wired Science, and we have our readers to thank for that. So, for the dual purposes of thanking you and patting ourselves on the back, here is a list of our most read stories of 2008 (and a couple we think should have been).

1) Biologists on the Verge of Creating New Form of Life



Working with simple membranes and proteins, Harvard Medical School researcher Jack Szostak is closing in on creating a new form of life that might resemble the earliest life on earth. It was probably a combination of the frightening idea of scientists creating new life forms, and a fascination with how life evolved on Earth that landed this story at the top of the list.

Science Times

The New York Times

New Glimpses of Life's Puzzling Origins

By NICHOLAS WADE

Some 3.8 billion years ago, a shell in the orbit of the Sun's inner planets underwent a series of large comets and asteroids crashing into the inner solar system. These violent impacts stripped out the large comets and asteroids in the inner Solar System, heated Earth's surface into molten rock and boiled off its oceans into an incandescent vapor.

The rocks that formed on Earth 3.8 billion years ago almost as soon as the heavier bodies had stopped, contain possible evidence of biological processes. If life can arise from inorganic matter in space and easily移居 to a new abode in the outer system and beyond? If biology is an inherent property of matter, why have scientists so far been unable to reconstruct life, or anything close to it, in the laboratory?

The origins of life on Earth begin with peace and quietude. Which came

Researchers find new ways for biochemicals to self-assemble.

first, the process of living cells or the genetic information that makes them? How could the precursors of living things get started without an enclosing membrane to keep all the necessary chemicals together? But if life started inside a cell membrane, how did the necessary nutrients get in?

The questions may seem odd, since life did start somehow. But for the usual group of cosmobiologists who insist on knowing exactly how it started, frustration has mounted. Many once promising leads have led only to paths of dead ends. Scientists as eminent as Francis Crick, the chief theorist of molecular biology, have quietly suggested that life may have formed elsewhere before reaching the planet, let alone does it seem to find a plausible explanation for its emergence on Earth.

In the last few years, however, four surprising advances have renewed confidence that a terrestrial explanation for life's origins will eventually emerge.

One is a series of discoveries about the cell-like structures that could have formed naturally from fatty chemicals likely to have been present on the primitive Earth. This lead emerged from a long argument between these cell biologists as to whether a genetic system or a cell membrane came first in the development of life. They ultimately agreed that genetics and membranes had to have evolved together.

The three researchers, Jack W. Szostak, David P. Bartel and P. Luigio Lui, published a somewhat佐证的 article in *Nature* in 2003, declaring that the way to make a synthetic cell was to get a protein and a genetic molecule to grow and divide in parallel.

Continued on Page A



A START In one view of the beginnings of life, depicted in an animation, carbon monoxide molecules condense on hot mineral surfaces underground to form fatty acids, above, which are then expelled from geysers. The acids are drawn together in spherical clumps as water evaporates, above and below left, which then assemble in a sheet that becomes the precursor of a cell membrane, below right. To see the full animation, go to nytimes.com/science.



MAKING RESEARCH ACCESSIBLE

Google protocell

Web Images Maps Shopping More Search tools Janet Iwasa + Share

Definition Architecture Endosymbiont Theory Protopoints

functionalities

resource conversion, self-maintenance, growth, reproduction

selection & evolvability

metabolism (energy transformation)

information (inheritance)

components

container (localization)

identity, co-localization of genes & metabolism, & multiphase chemistry

Protocellular Organization

Monday, November 9, 15

The image shows a Google search results page for the query "protocell". The top navigation bar includes "Web", "Images" (which is selected), "Maps", "Shopping", "More", and "Search tools". On the right side, there are user profile icons, "SafeSearch" settings, and a "Share" button. Below the search bar, there are four main categories with sub-diagrams: "Definition" (a diagram of a protocell with internal components), "Architecture" (microscopic images of protocells), "Endosymbiont Theory" (a diagram illustrating the stages of cellular evolution), and "Protopoints" (a diagram of a protocell with various functional components labeled). The main search results area contains several more images, including a detailed diagram of a functional protocell with various molecules like antibodies, peptides, and lipids, and another diagram of a mesoporous silica nanoparticle. There are also microscopic images of protocells and a diagram of protocellular organization.

MAKING RESEARCH ACCESSIBLE

Google protocell

Web Images Maps Shopping More Search tools Janet Iwasa + Share

Definition Architecture Endosymbiont Theory Probiotics

functionabilities

resource conversion, self-maintenance, growth, reproduction

selection & evolvability

metabolism (energy transformation)

information (inheritance)

components

container (localization)

identity, co-localization of genes & metabolism, & multiphase chemistry

Functional protocell

Antibodies

Transmembrane proteins, ion channels

Water or lipid soluble drugs

DNARNA

Lipid soluble drugs

Cholesterol

Mesoporous silica core

Phospholipid bilayer

PEG

Aptamers

amphiphilic template (gene molecule)

light sensitizer (metabolic molecule)

Eplids (container molecules)

Mesoporous Silica Nanoparticle

Endosomolytic Peptide

Targeting Peptide

Supported Lipid Bilayer

Ricin Toxin A-Chain

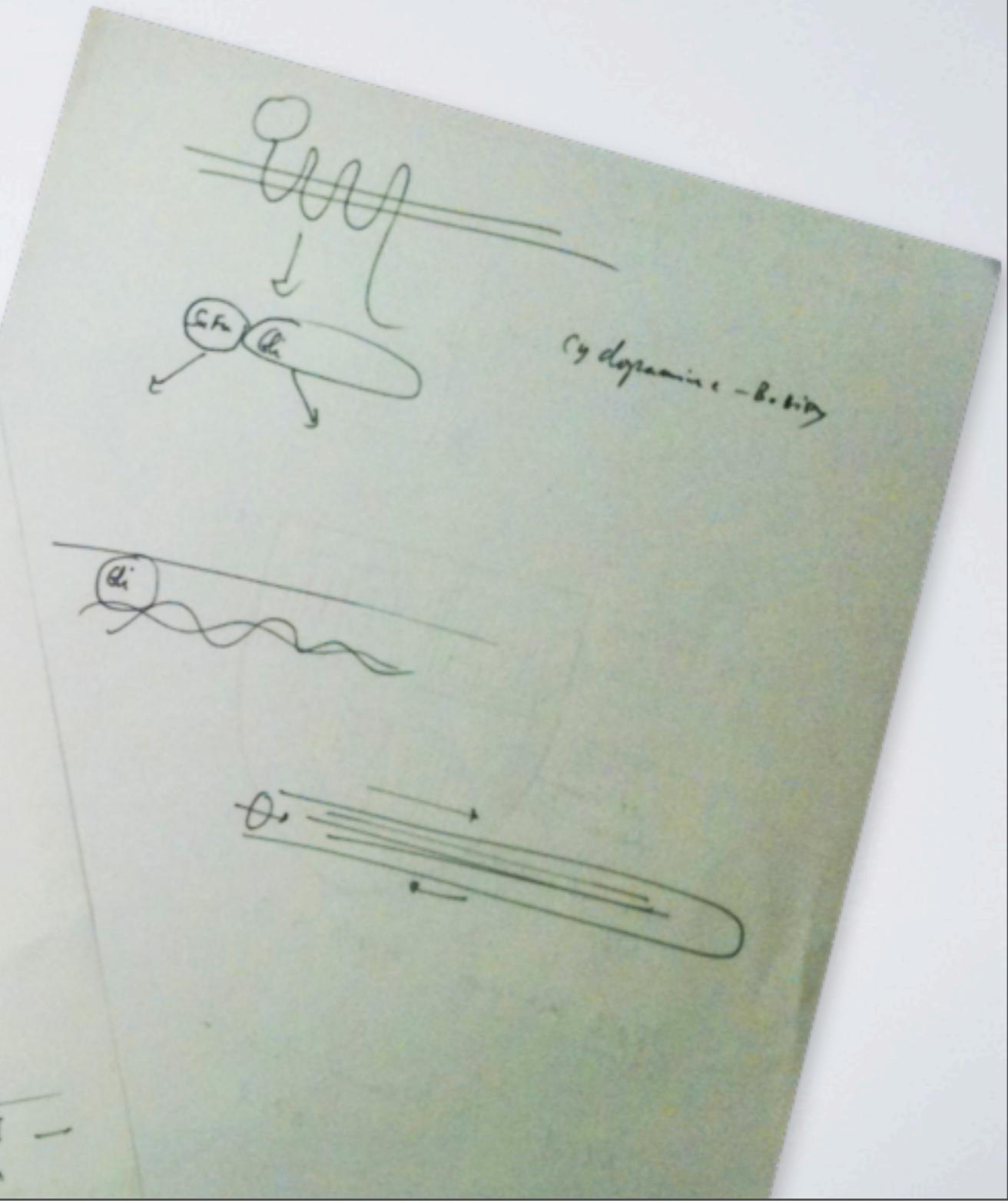
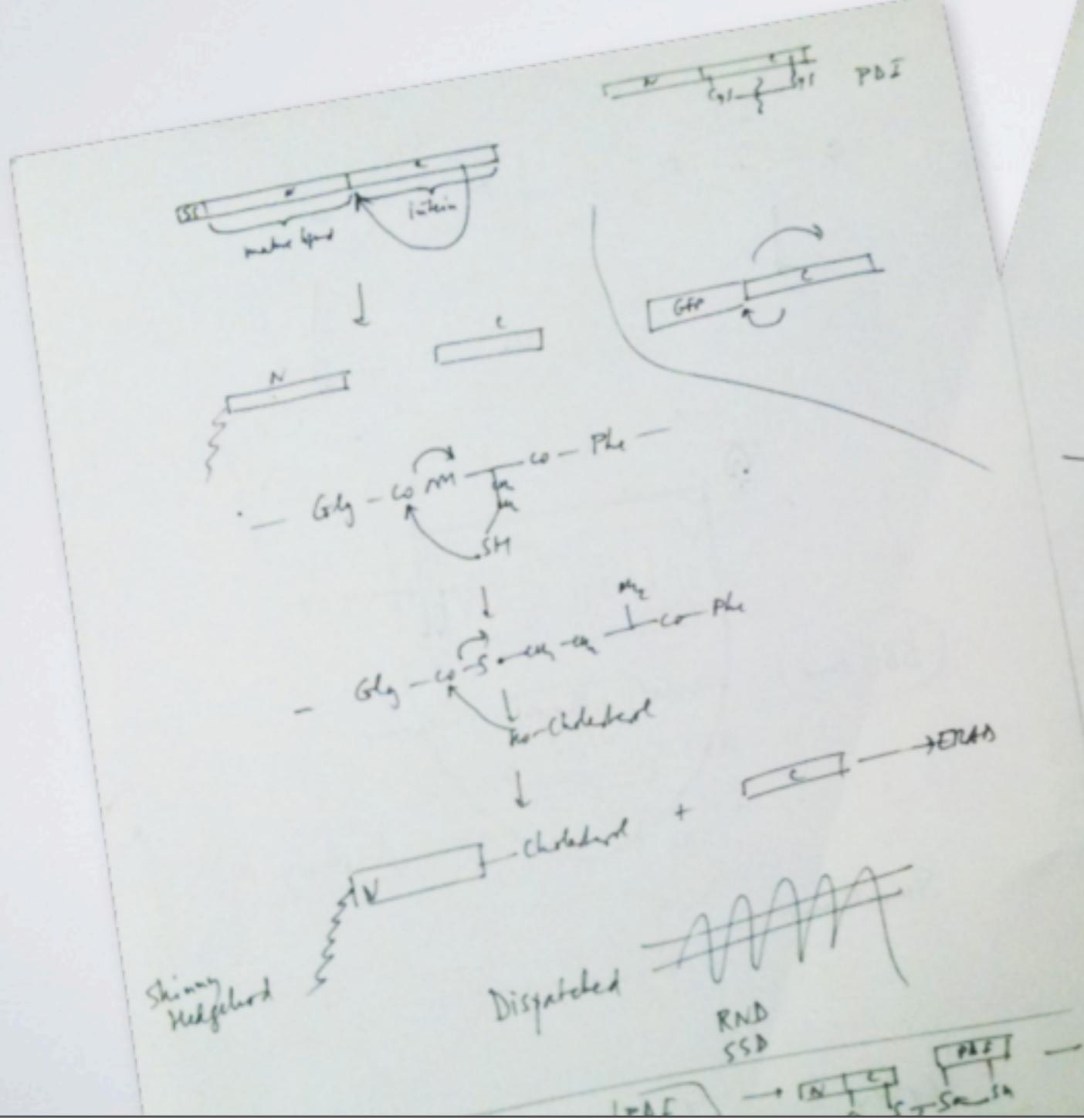
Protocellular Organization

Monday, November 9, 15

The image shows a Google search results page for the query "protocell". The "Images" tab is selected. The results are organized into four main categories: "Definition", "Architecture", "Endosymbiont Theory", and "Probiotics". Each category contains several images. A pink box highlights the first image under "Definition", which is a diagram of a protocell with a red outer layer and a dark interior. Another pink box highlights the third image under "Architecture", which is a circular diagram showing the relationships between "functionabilities", "components", and "container (localization)". A third pink box highlights the first image under "Probiotics", which is a diagram of a protocell with a complex internal structure. A fourth pink box highlights the bottom right image under "Probiotics", which is a diagram of a protocell containing various organelles and molecules. Other images include micrographs of protocells and detailed diagrams of their internal components like membranes, proteins, and nucleic acids.

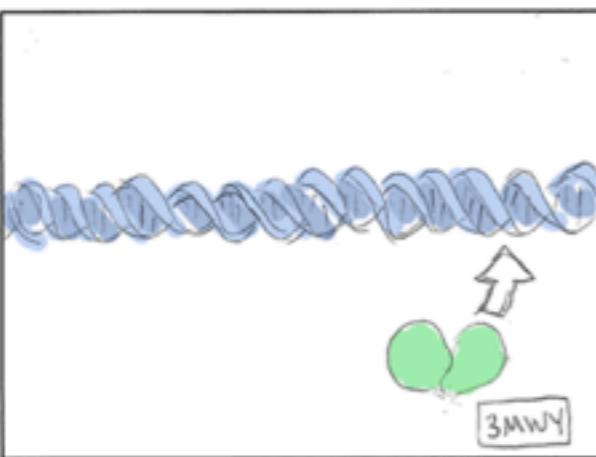
THE MAKING OF AN ANIMATION

I. What is the story?

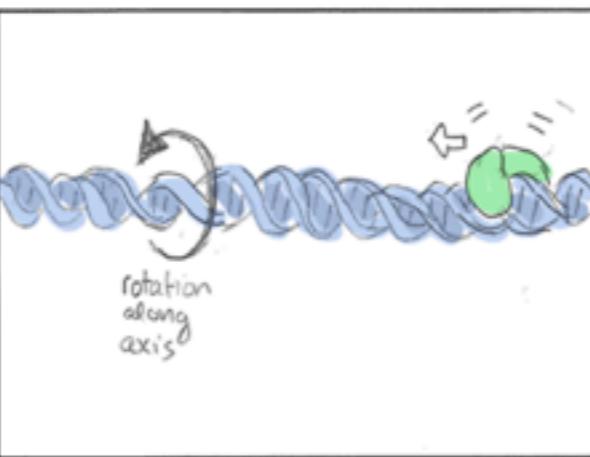


THE MAKING OF AN ANIMATION

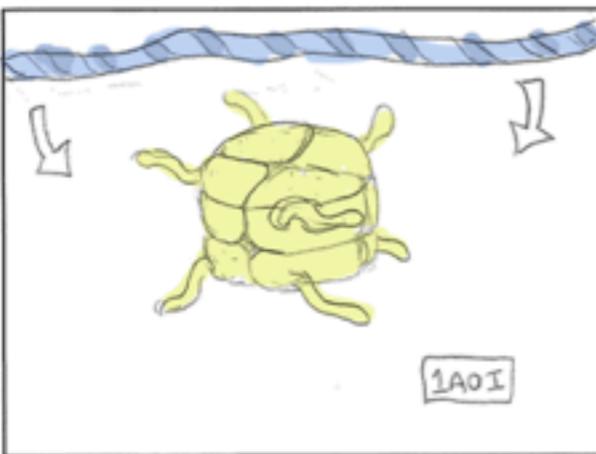
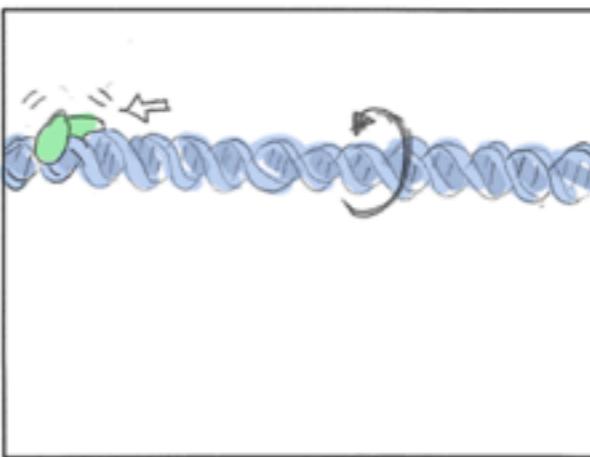
2. Drawing a storyboard



use 3MWY (see file from (adrie))

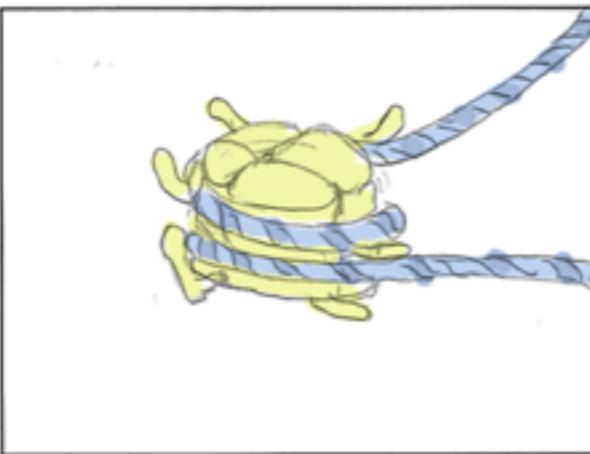


inchworm mechanism - where does
DNA bind? Speed? Step size?
Show flashes of light to indicate
ATP hydrolysis

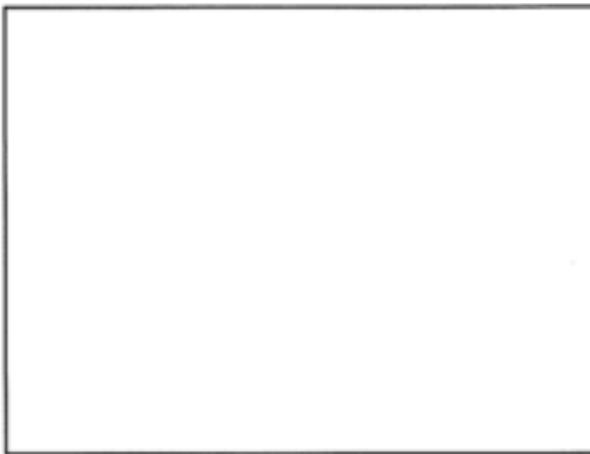


Rotation, labelling of octamer,
use 1AOI

Highlight regions that bind DNA
Highlight H4 base patch

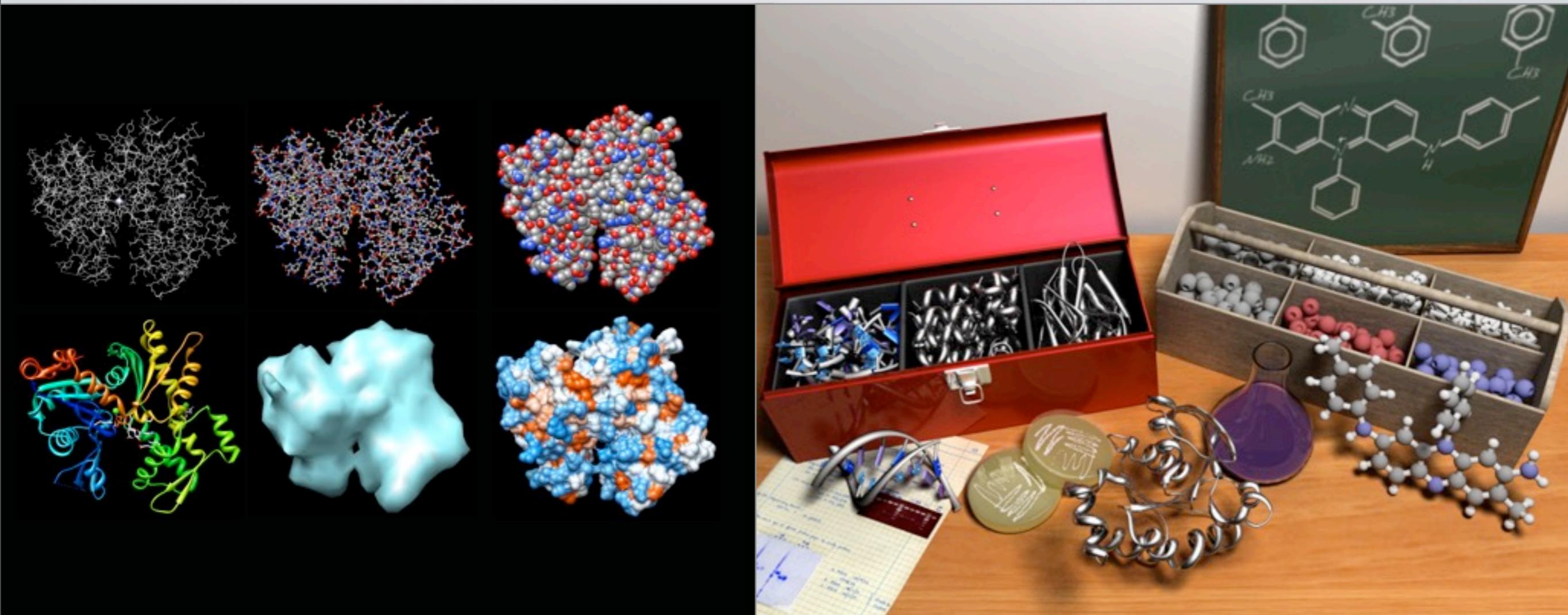


Show interaction b/w histone tails + DNA?



THE MAKING OF AN ANIMATION

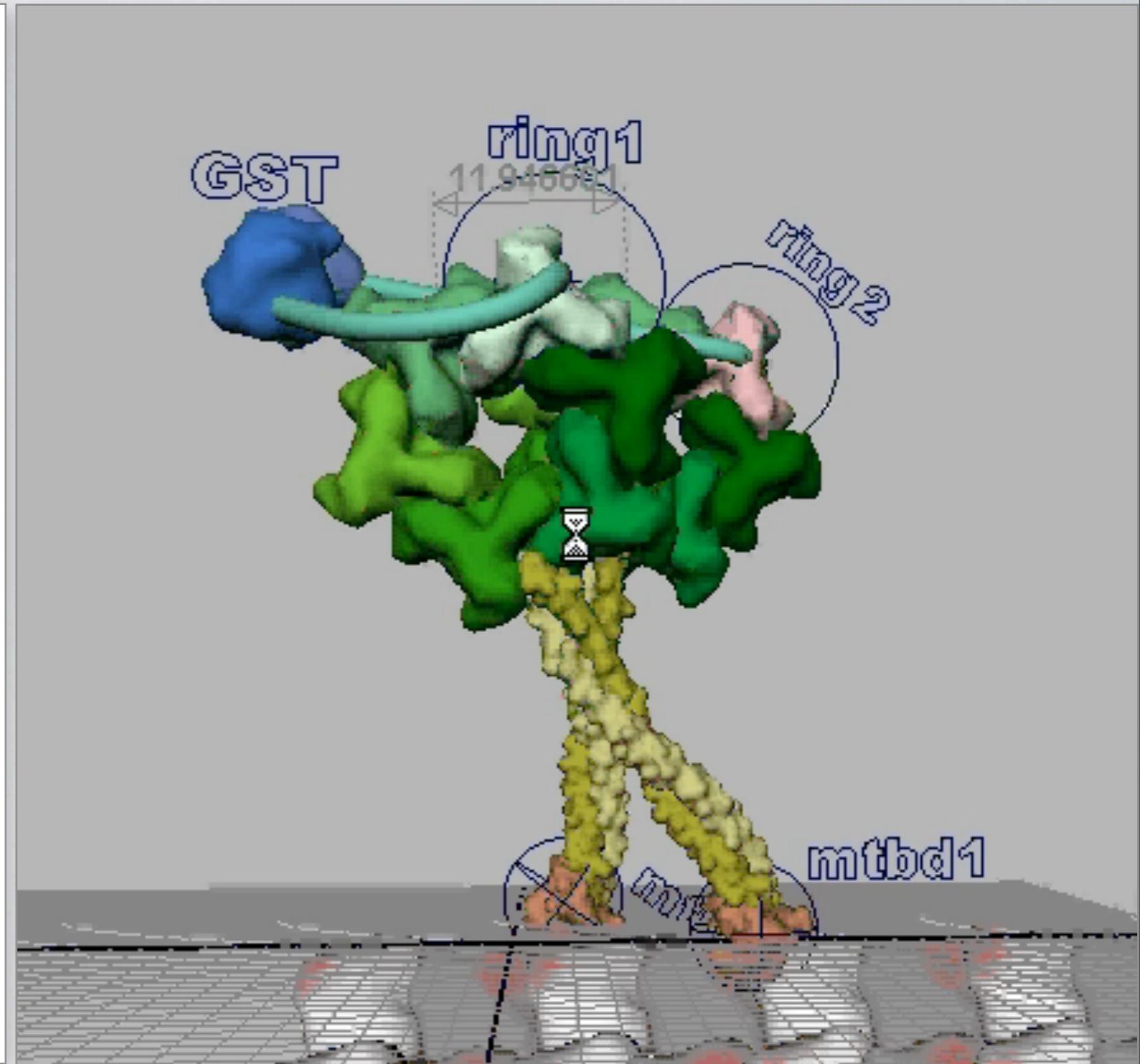
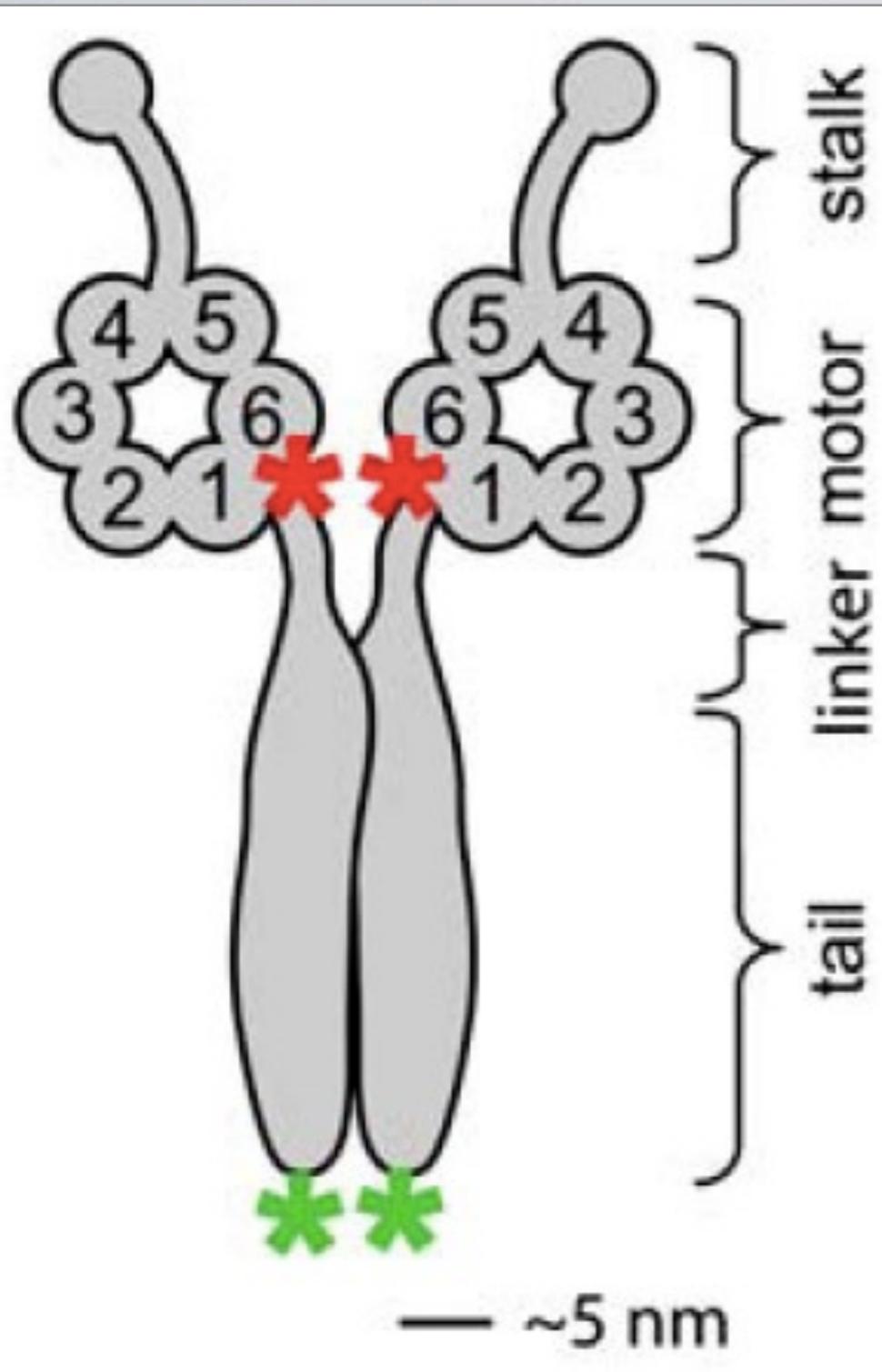
3. Modeling proteins and other structures



with Wendell Lim and Brian Yeh, *Nature Chemical Biology* 3 (2007)

THE MAKING OF AN ANIMATION

an articulated model of dynein



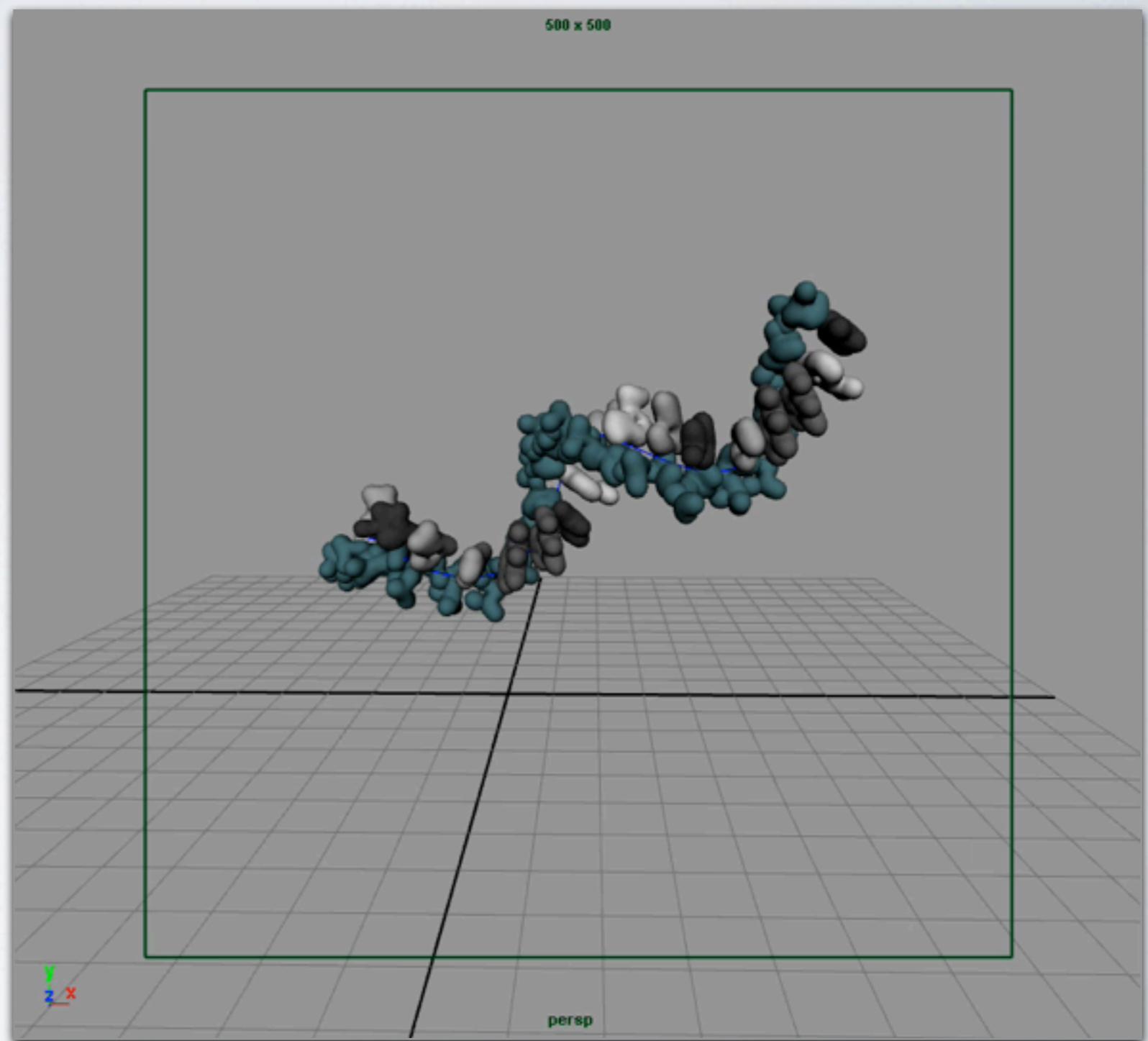
with Sam Reck-Peterson, Harvard Medical School

THE MAKING OF AN ANIMATION

4. Animation

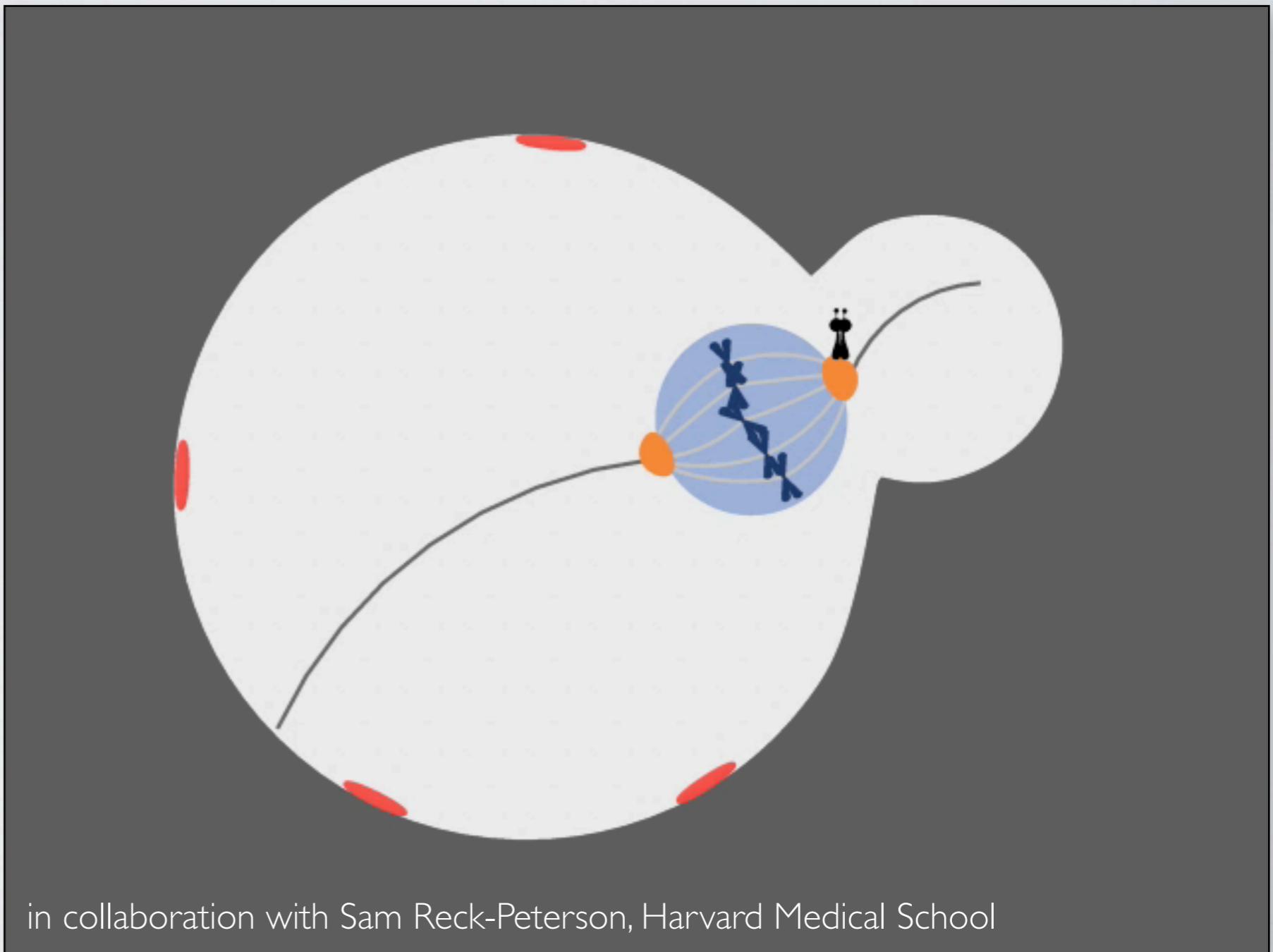
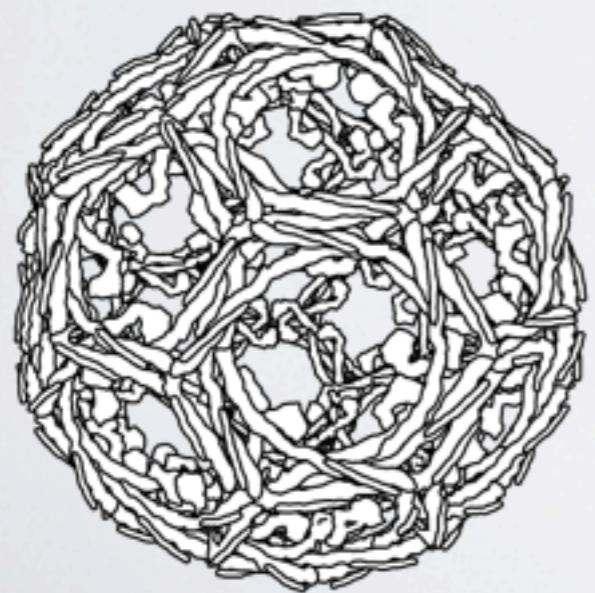
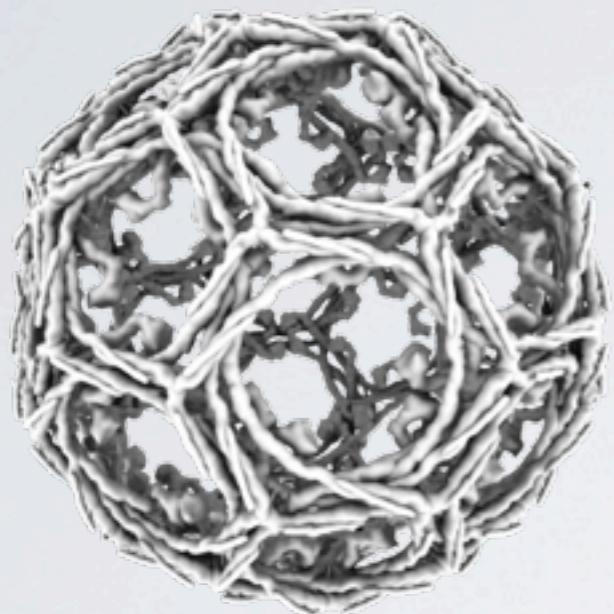
What tools are available?

How to create animations
that can depict expected
molecular motions?

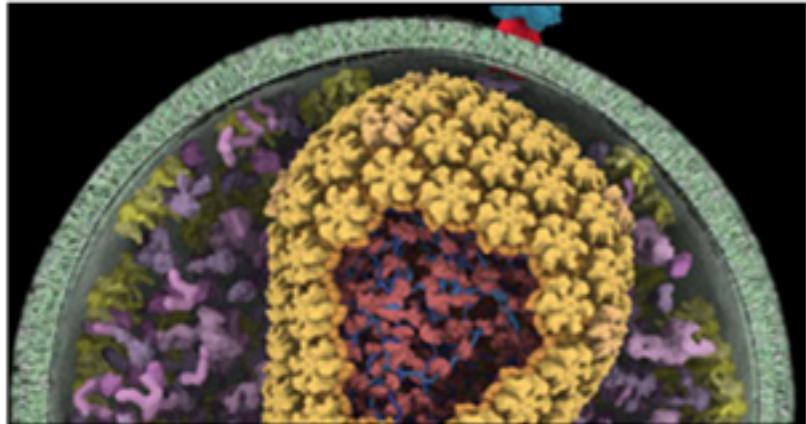


THE MAKING OF AN ANIMATION

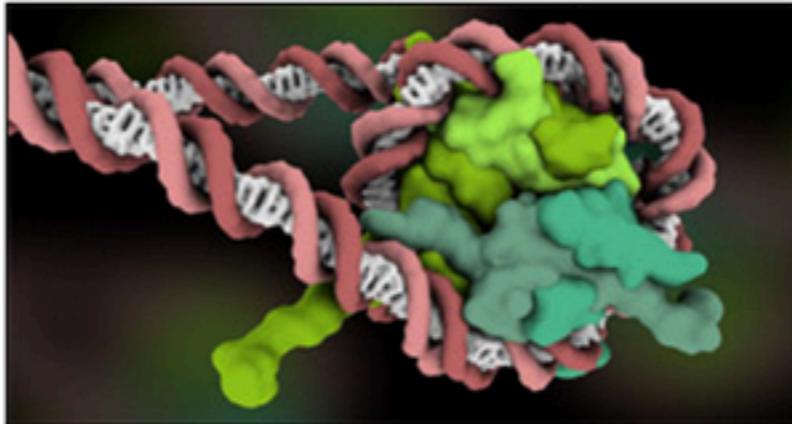
5. Rendering



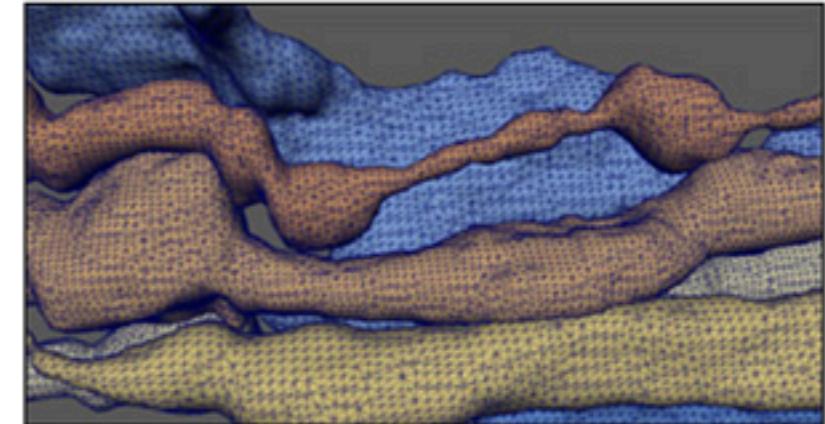
CURRENT PROJECTS



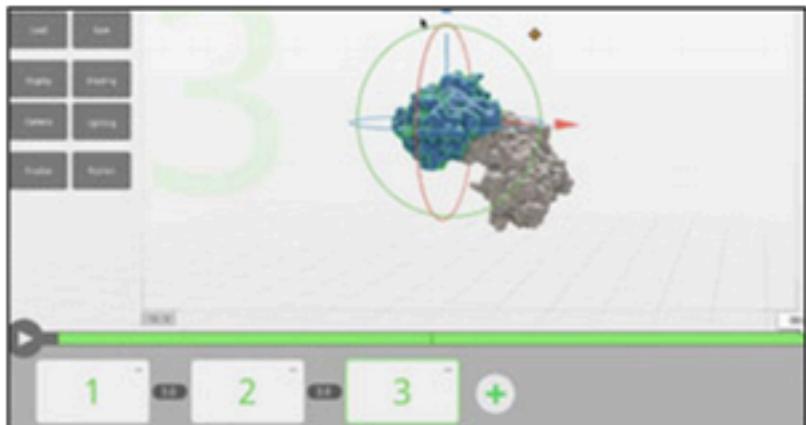
HIV entry and egress



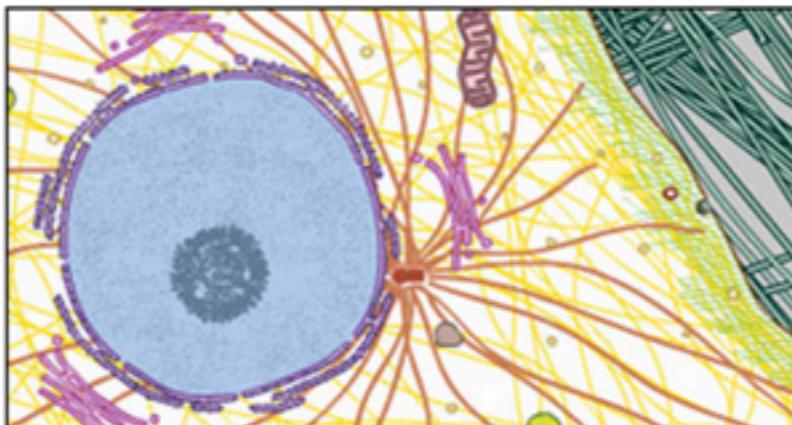
Chromatin remodeling



Visualizing neurons



Molecular flipbook

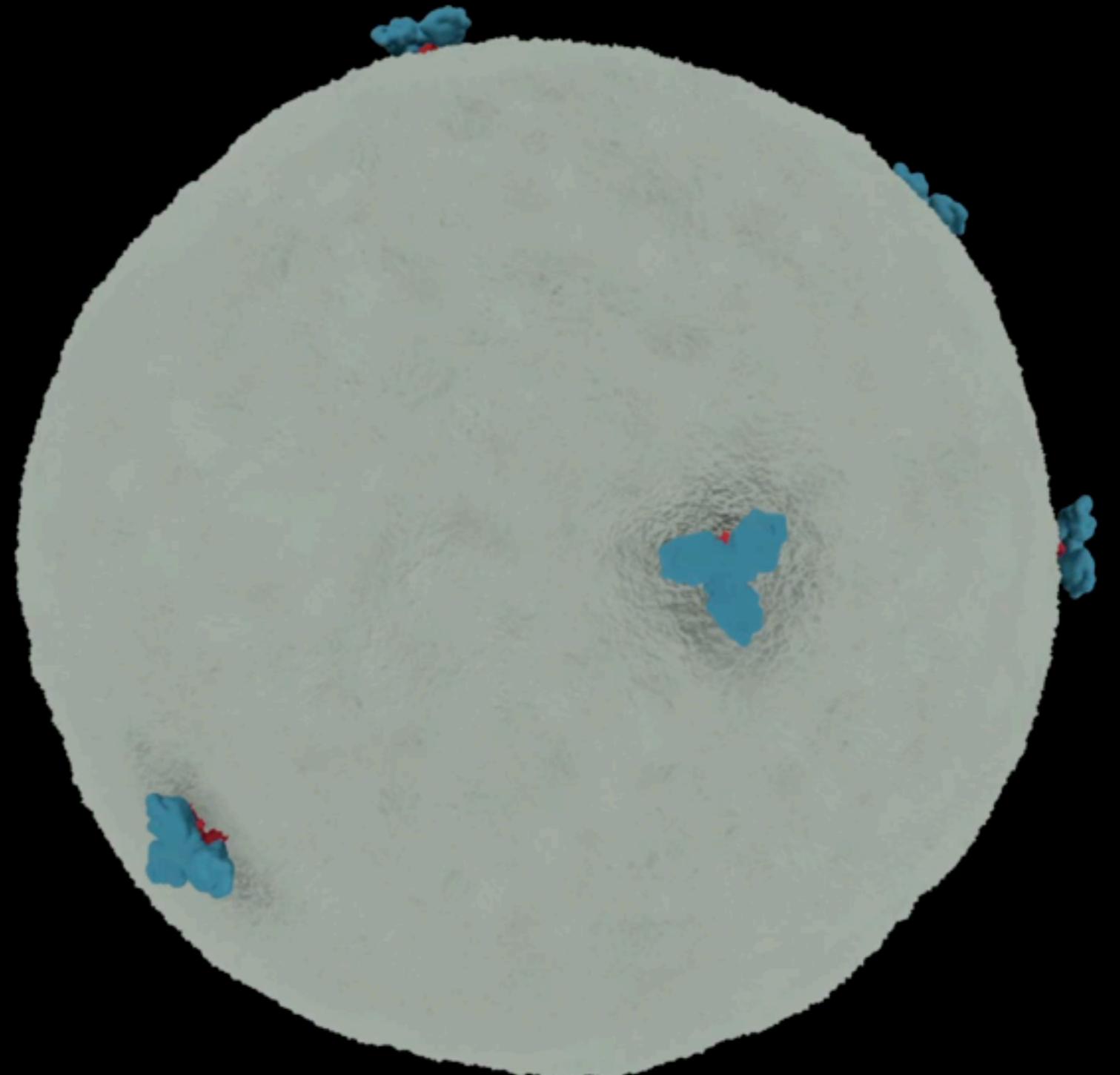


Cell image library

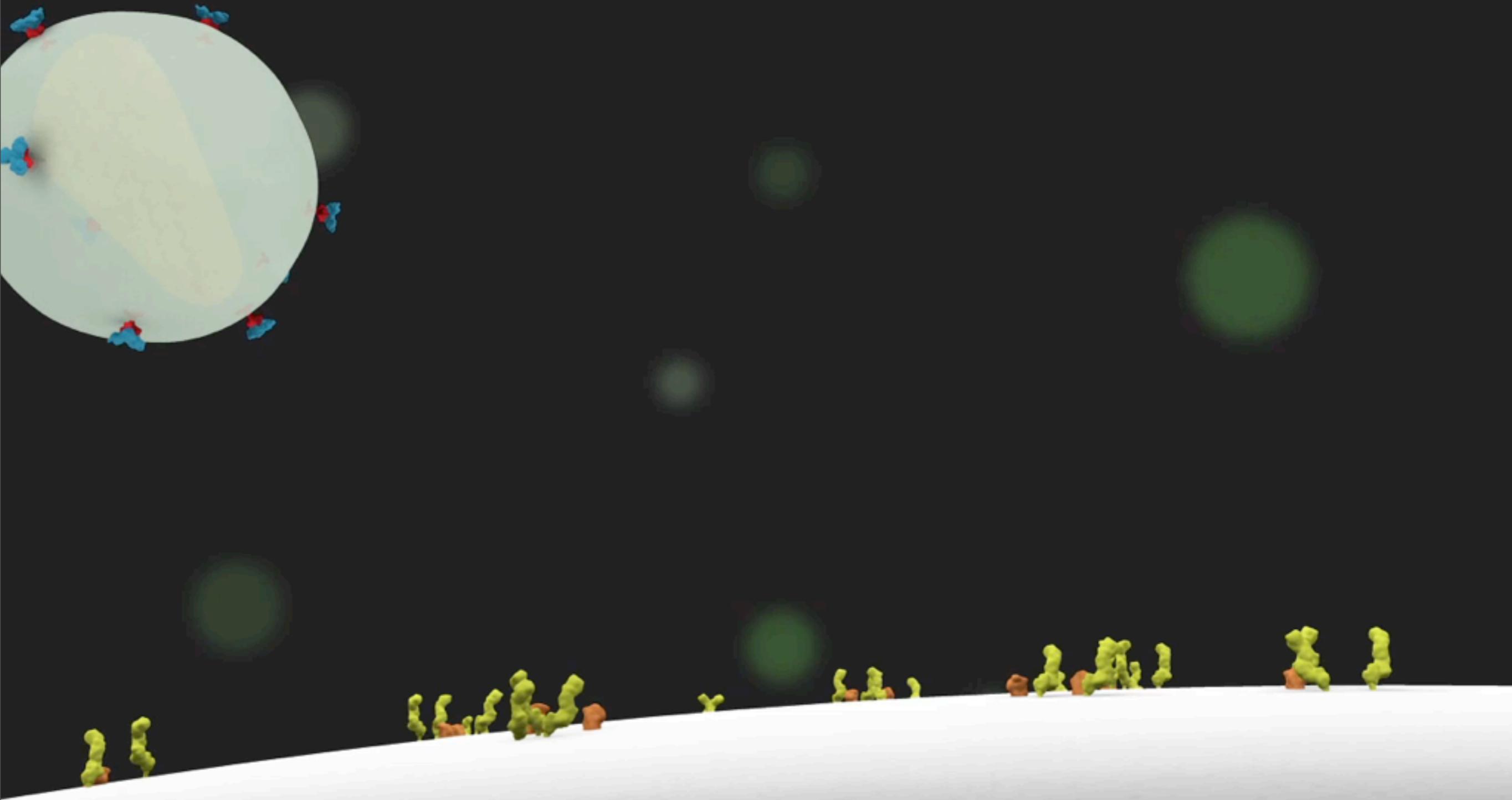
ANIMATING THE HIV LIFE CYCLE

with NIGMS (P50) Centers for HIV/AIDS Related Structural Biology

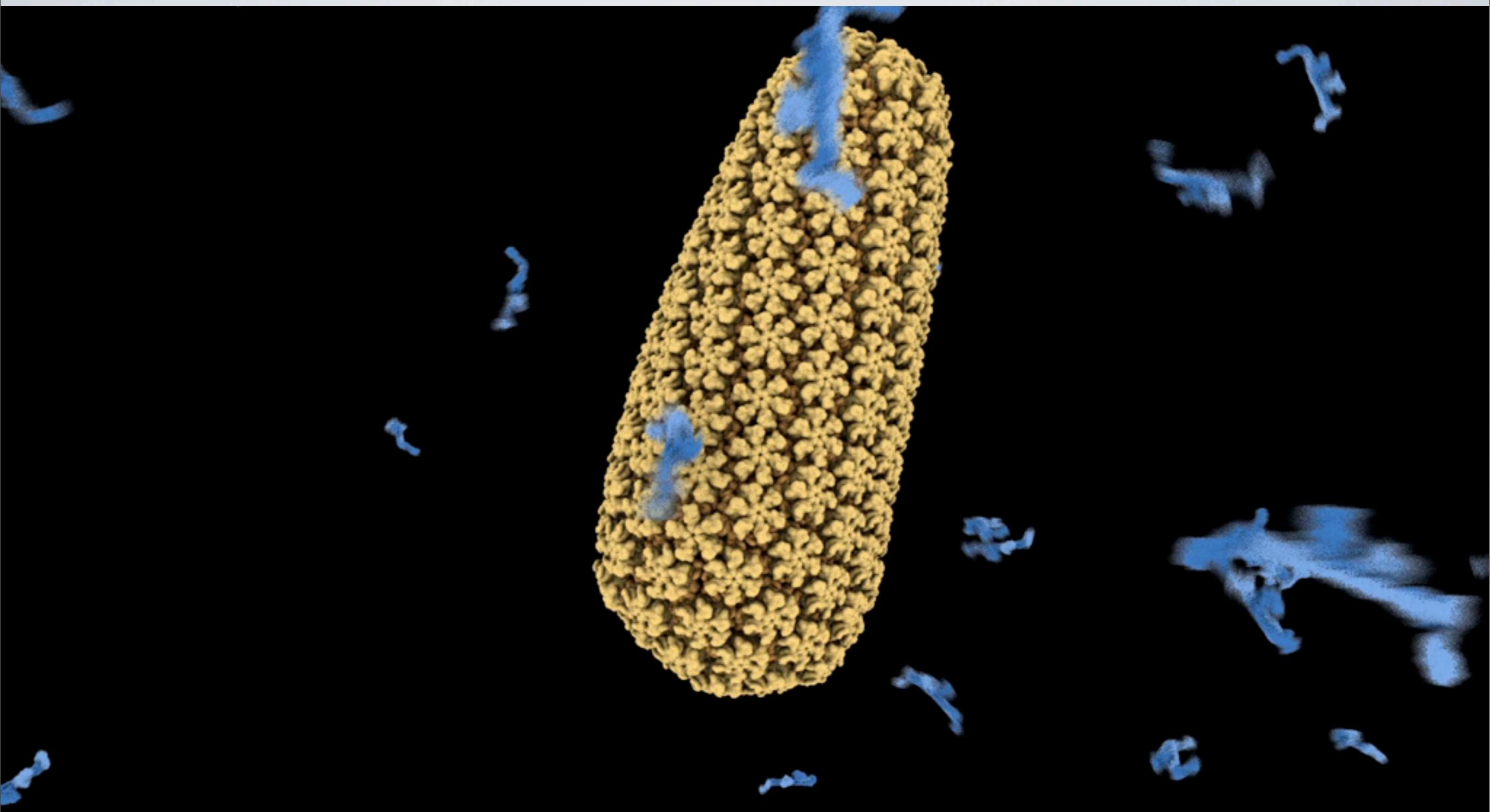
**Human
Immunodeficiency
Virus
(HIV)**



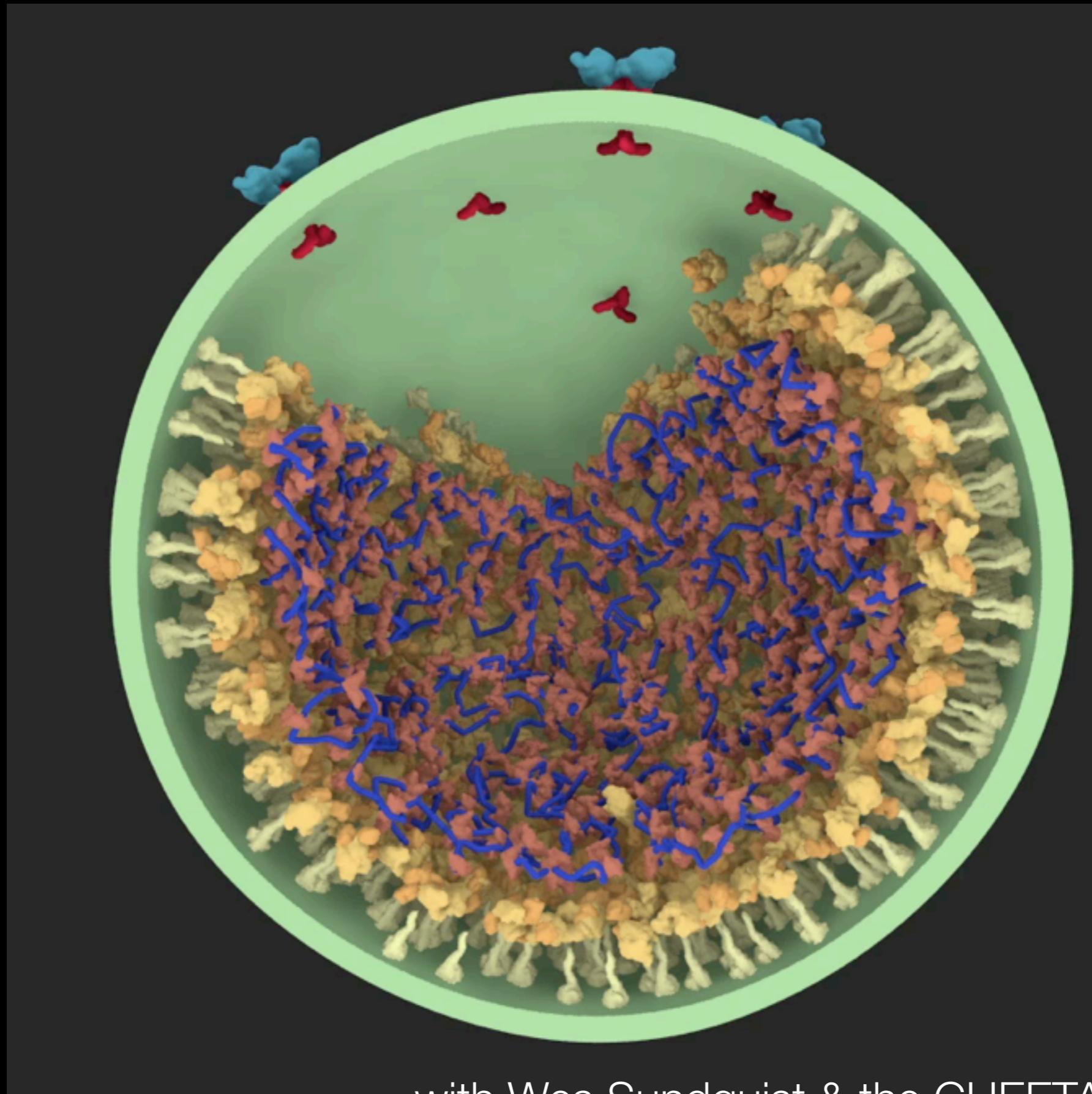
HIV ENTRY



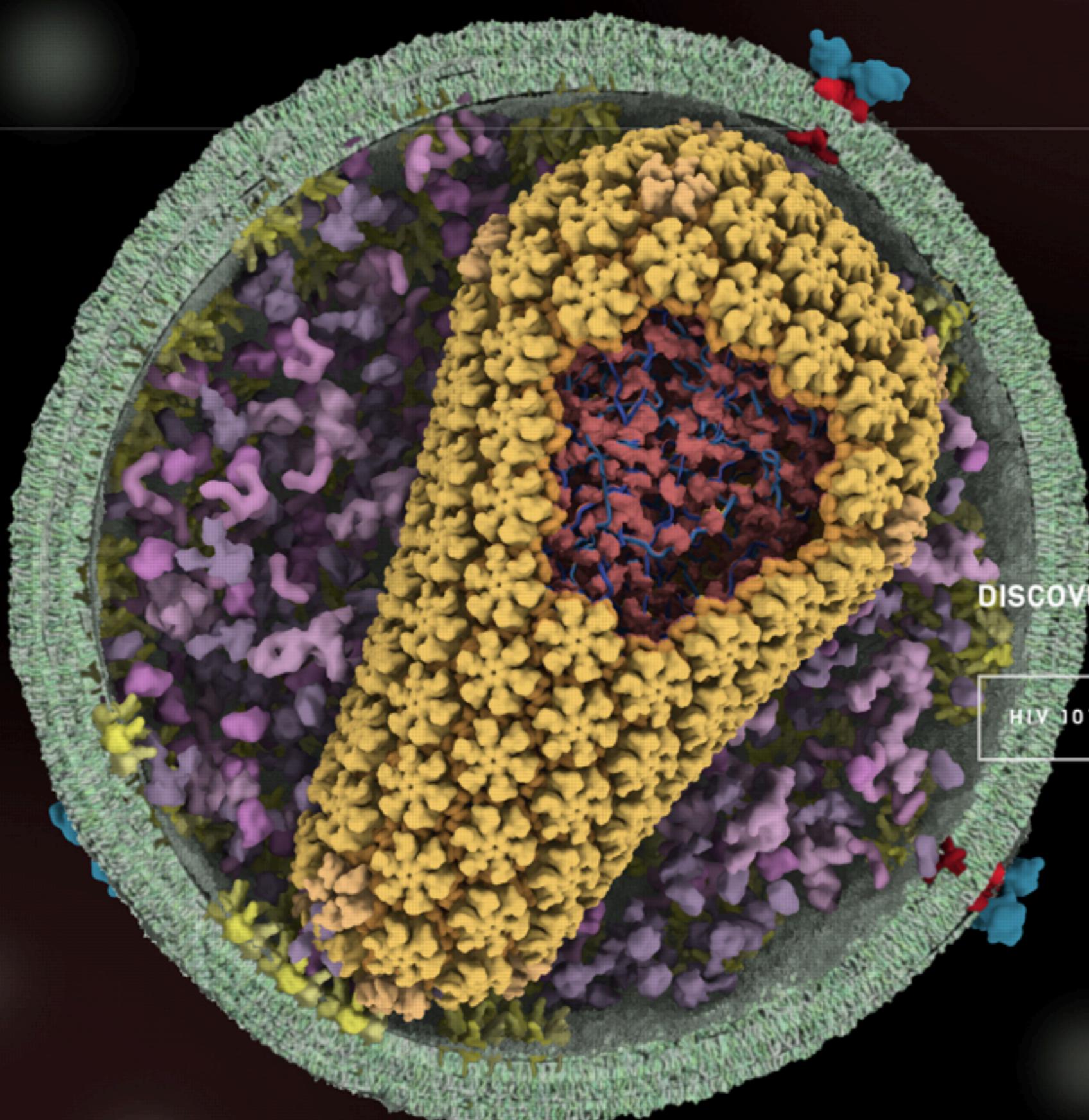
TRIM5 α LATTICE FORMATION



HIV MATURATION



with Wes Sundquist & the CHEETAH consortium

[HOME](#) [HIV 101](#) [VISUALIZING HIV](#) [ABOUT](#)

DISCOVER THE SCIENCE OF HIV

HIV 101

VIEW ANIMATIONS OF HIV

Build a lesson around any TED-Ed Original, TED Talk or YouTube video

Create a Lesson +

Why it's so hard to cure HIV/AIDS - Janet Iwasa



52,903
Views

458
Questions
Answered

Let's Begin...

In 2008, something incredible happened: a man was cured of HIV. In over 70 million HIV cases, this was a first, and, so far, a last, and we don't yet understand exactly how he was cured. But if we can cure people of various diseases, like malaria and hepatitis C, why can't we cure HIV? Janet Iwasa examines the specific traits of the HIV virus that make it so difficult to cure.

A thumbnail for a video titled "Why it's so hard to cure HIV/AIDS". The thumbnail features a grid of 40 colorful, stylized human faces in circles. Overlaid on the grid are three dark bars with text: "WHY IT'S SO HARD" in green, "TO CURE" in light blue, and "HIV/AIDS" in orange. A large black play button is positioned in the center of the grid. At the bottom left is a video control bar showing a play button, volume icon, and the time "0:00 / 4:31".

Watch

Think

Dig Deeper

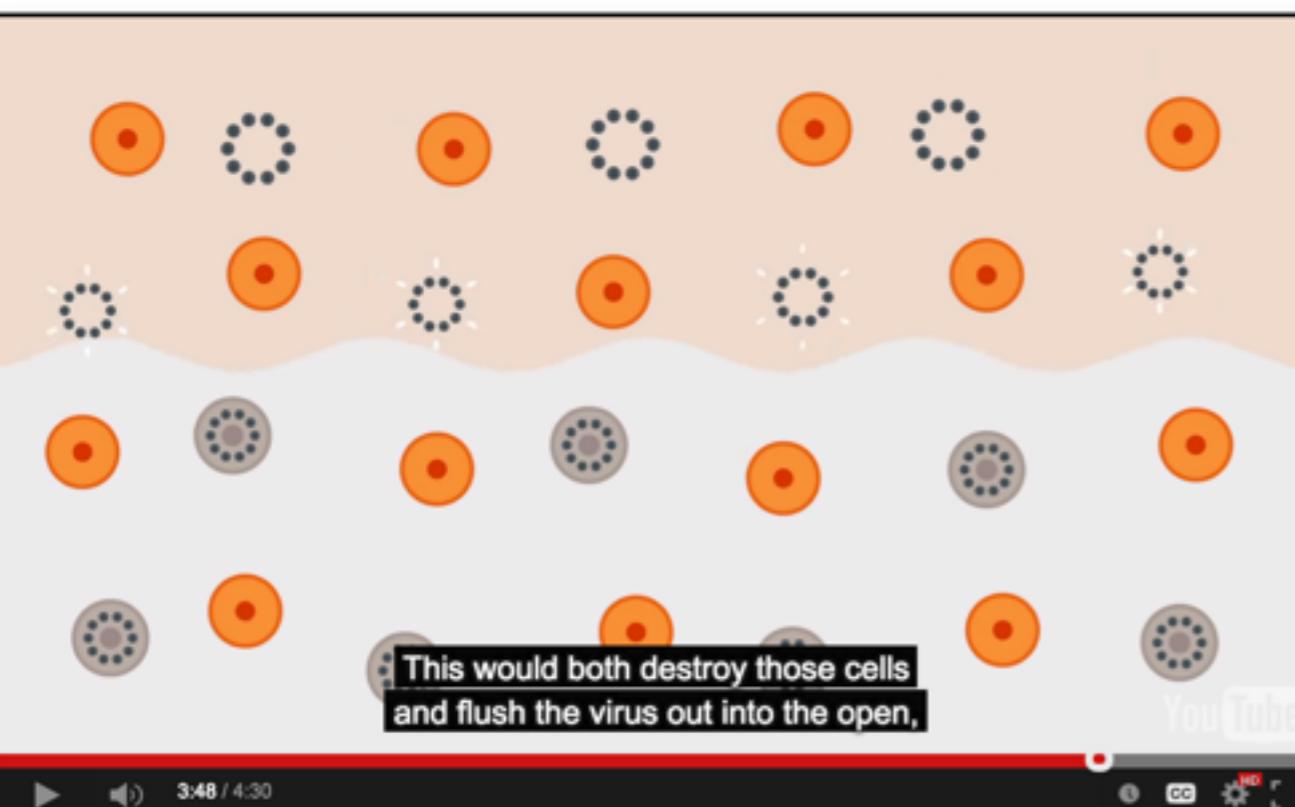
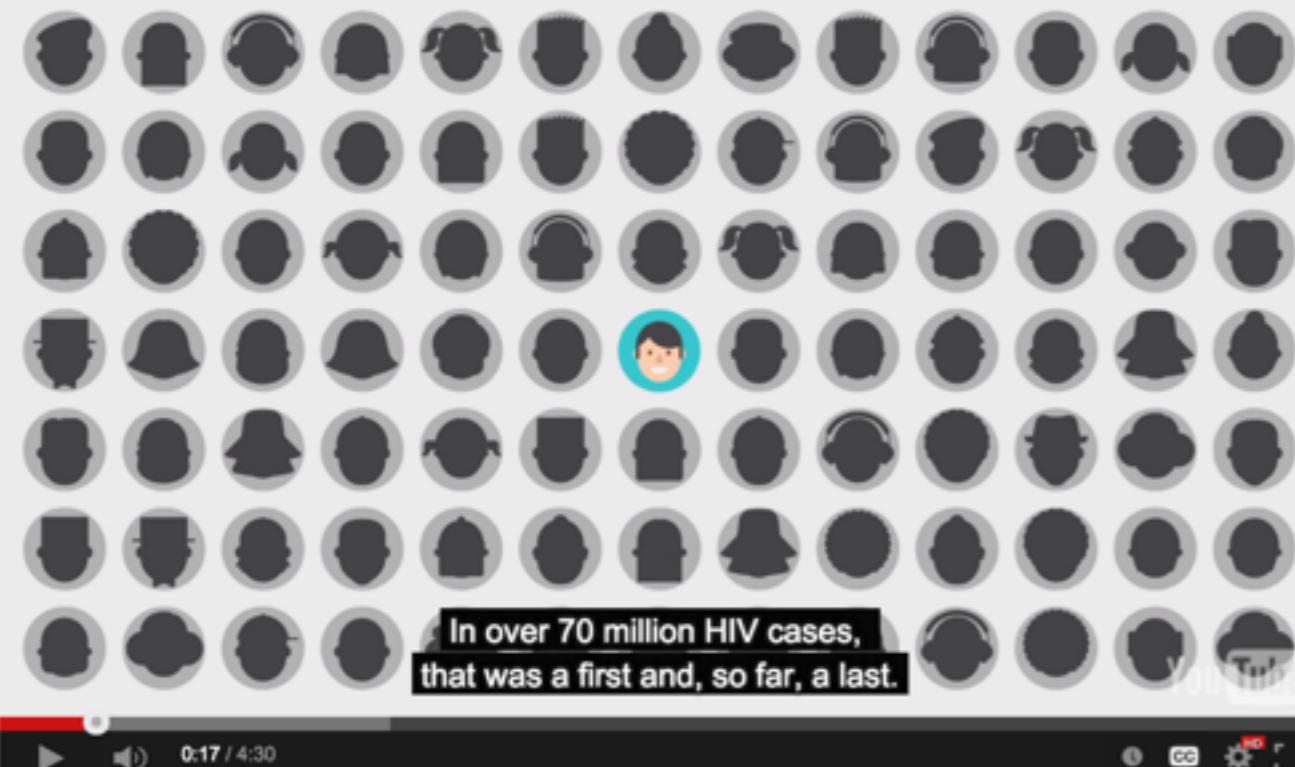
Discuss

Customize This Lesson

21

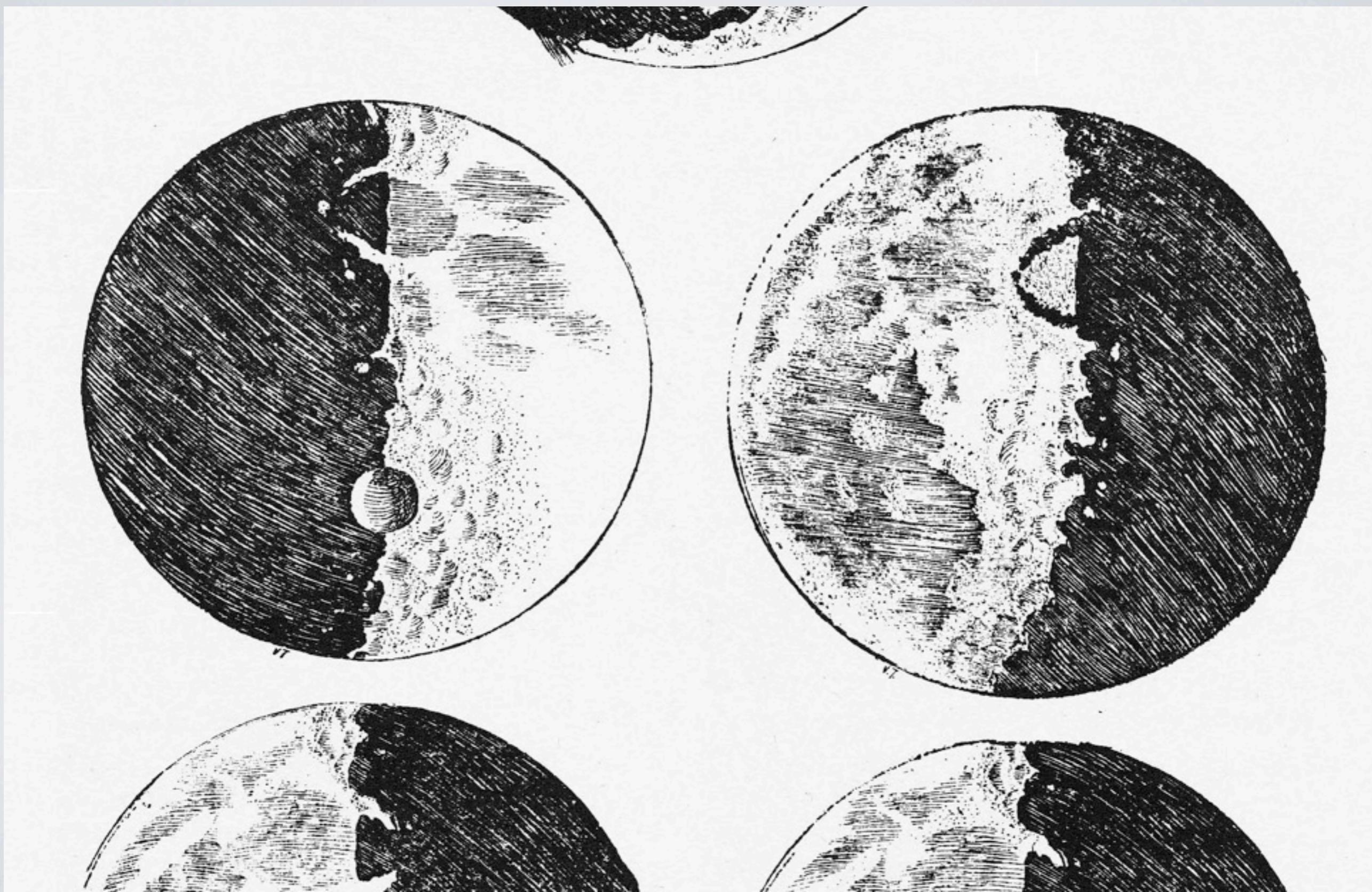
Create and share a new lesson based on this one.

ANIMATION SCREENSHOTS



with TED Ed & Javier Saldeña

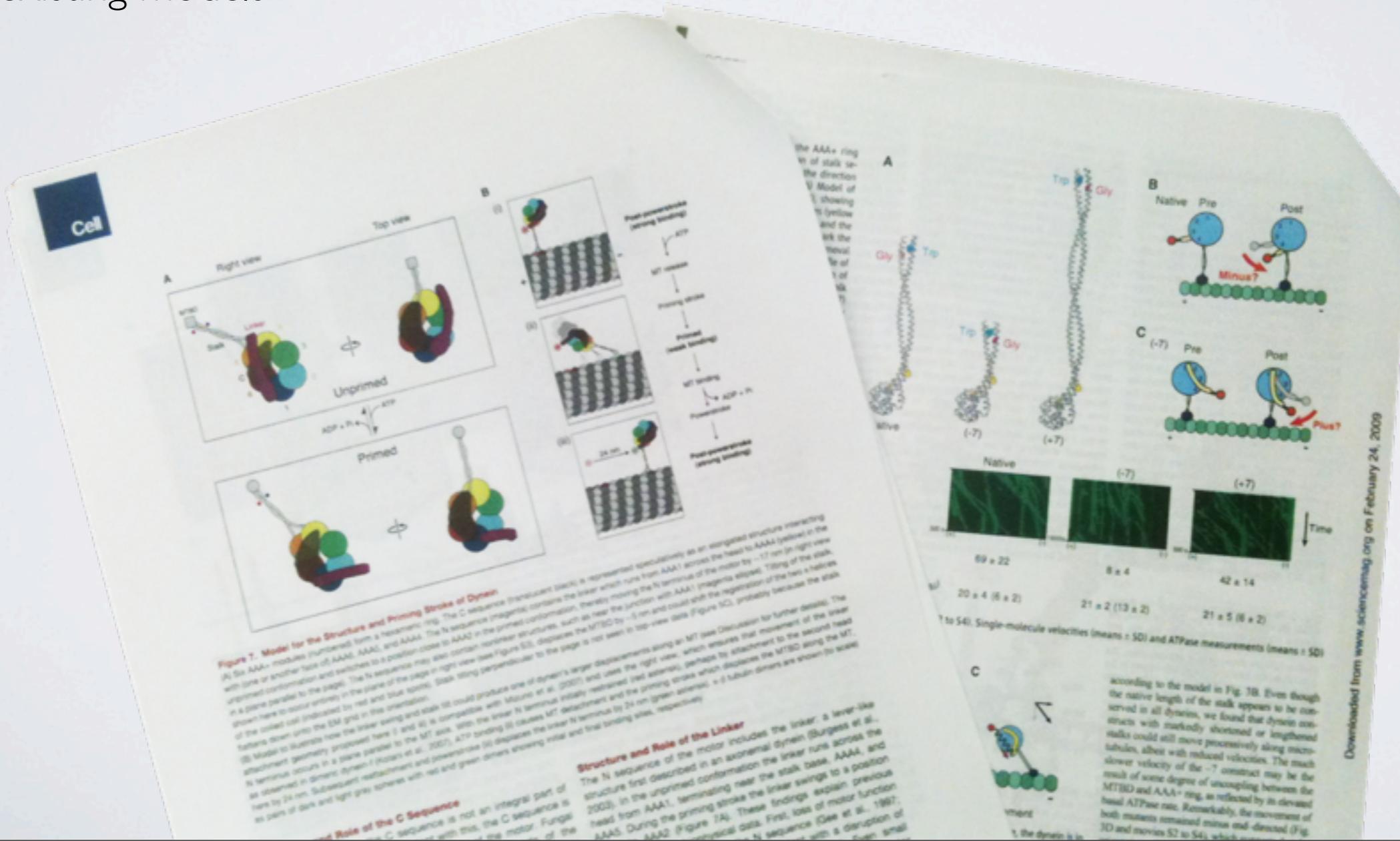
THE SCIENTIST AS ARTIST



THE ROLE OF THE MODEL FIGURE

Benefits for the audience

- a description of the current understanding of a process
- background and context
- an understanding of the authors' specific hypothesis, and how it adds to or alters existing models

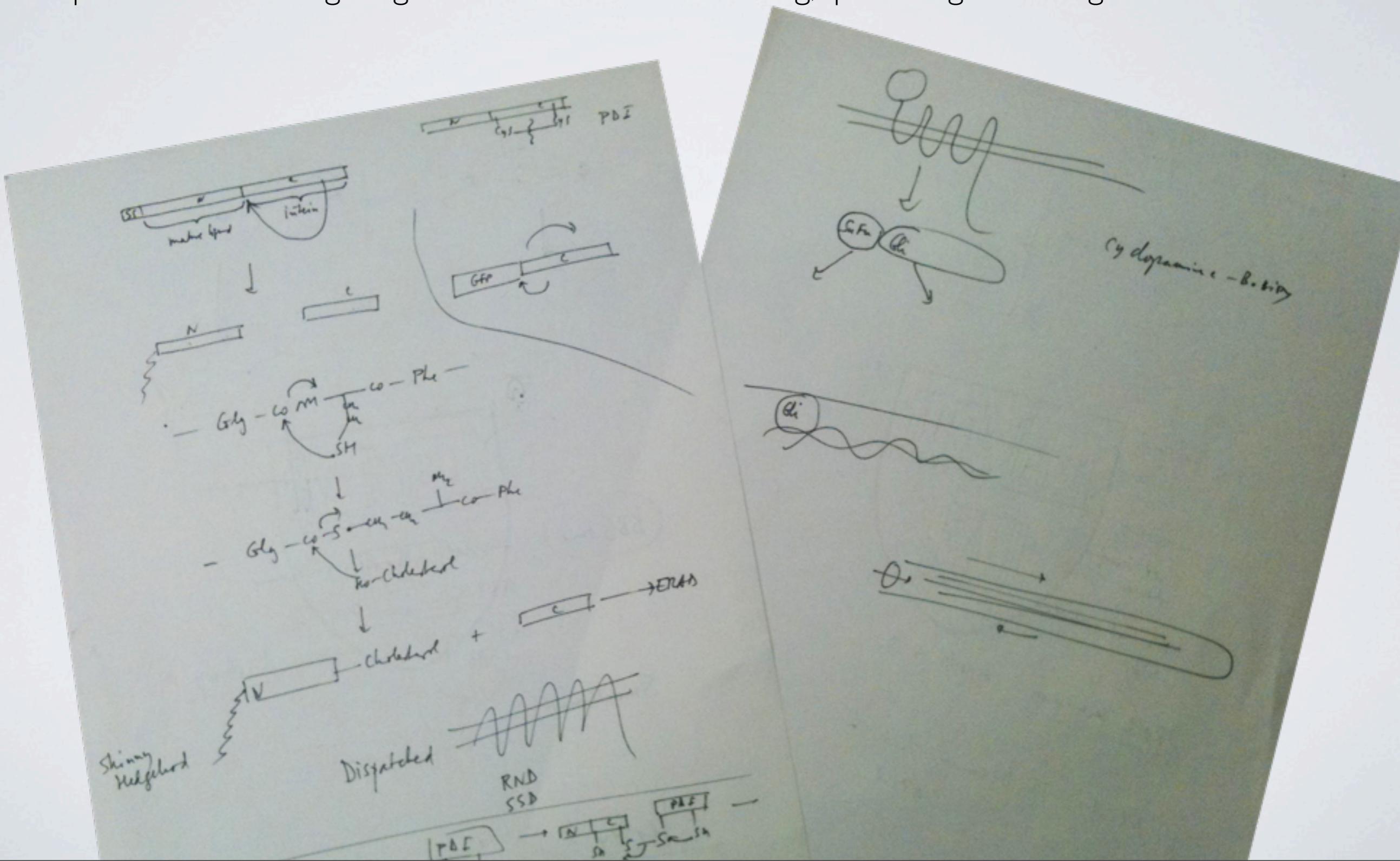


Downloaded from www.sciencemag.org on February 24, 2009

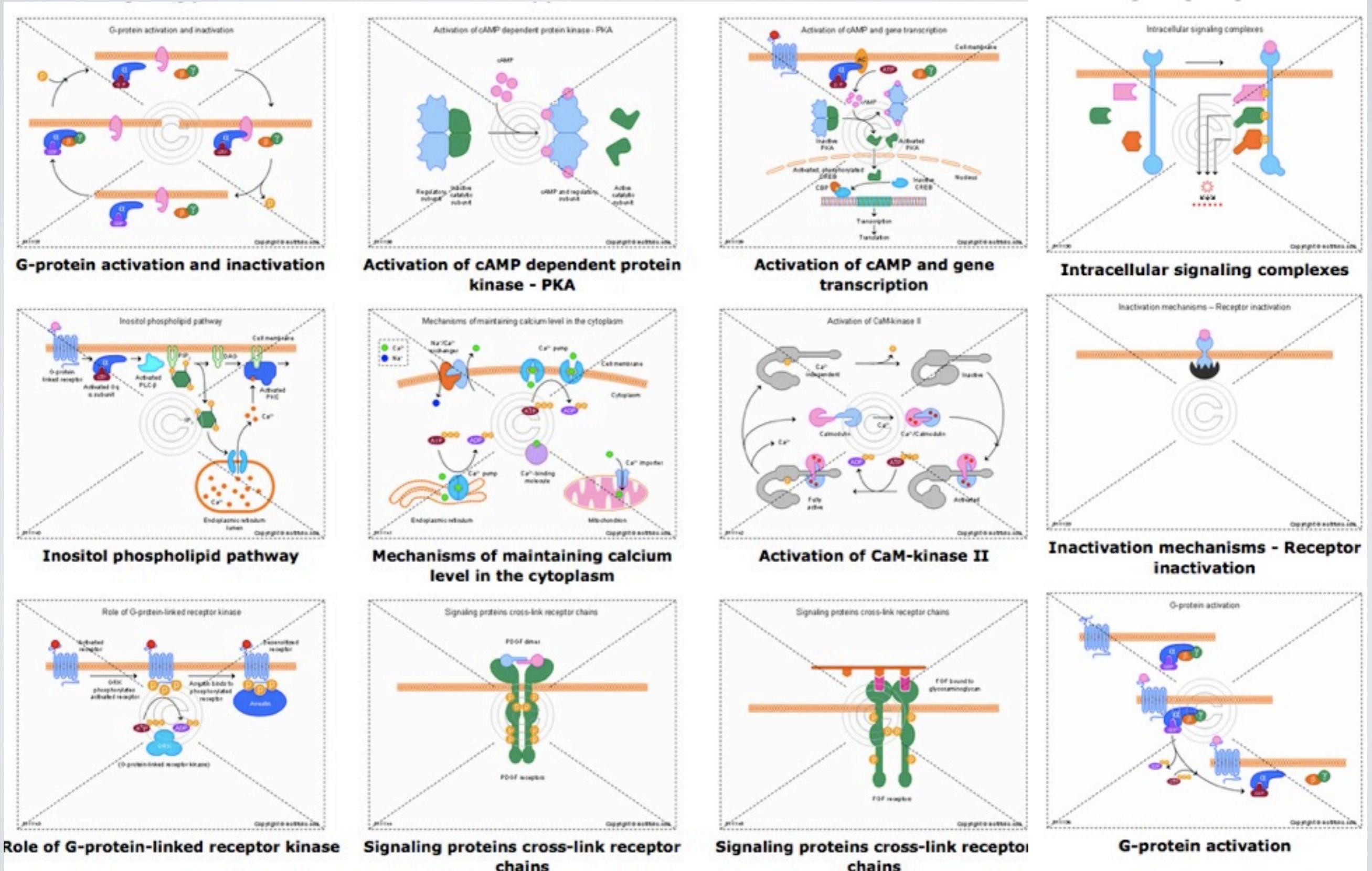
THE ROLE OF THE MODEL FIGURE

Benefits for the author

- process of drawing a figure can often be illuminating, providing new insights



INSTANT MODEL FIGURES?



MOLECULAR FLIPBOOK



a community resource for creating & sharing molecular animations

(1) A 3D ANIMATION TOOLKIT

which will allow biologists to readily create molecular and animations using open-source animation software

(2) A WEBSITE AND DATABASE

where users can upload and share their animation scene files and completed animations

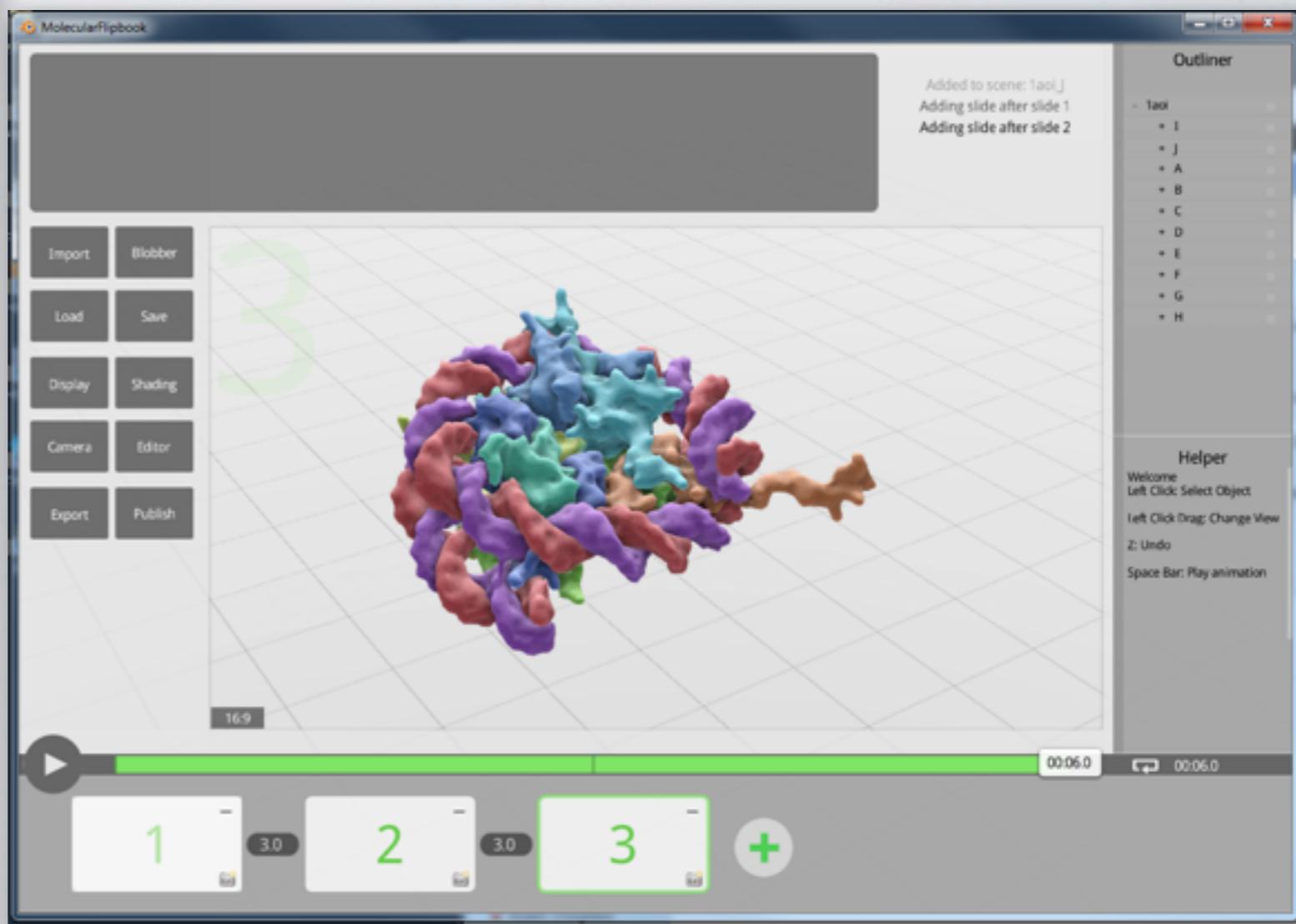
MOLECULAR FLIPBOOK TOOLKIT

a community resource for creating & sharing molecular animations

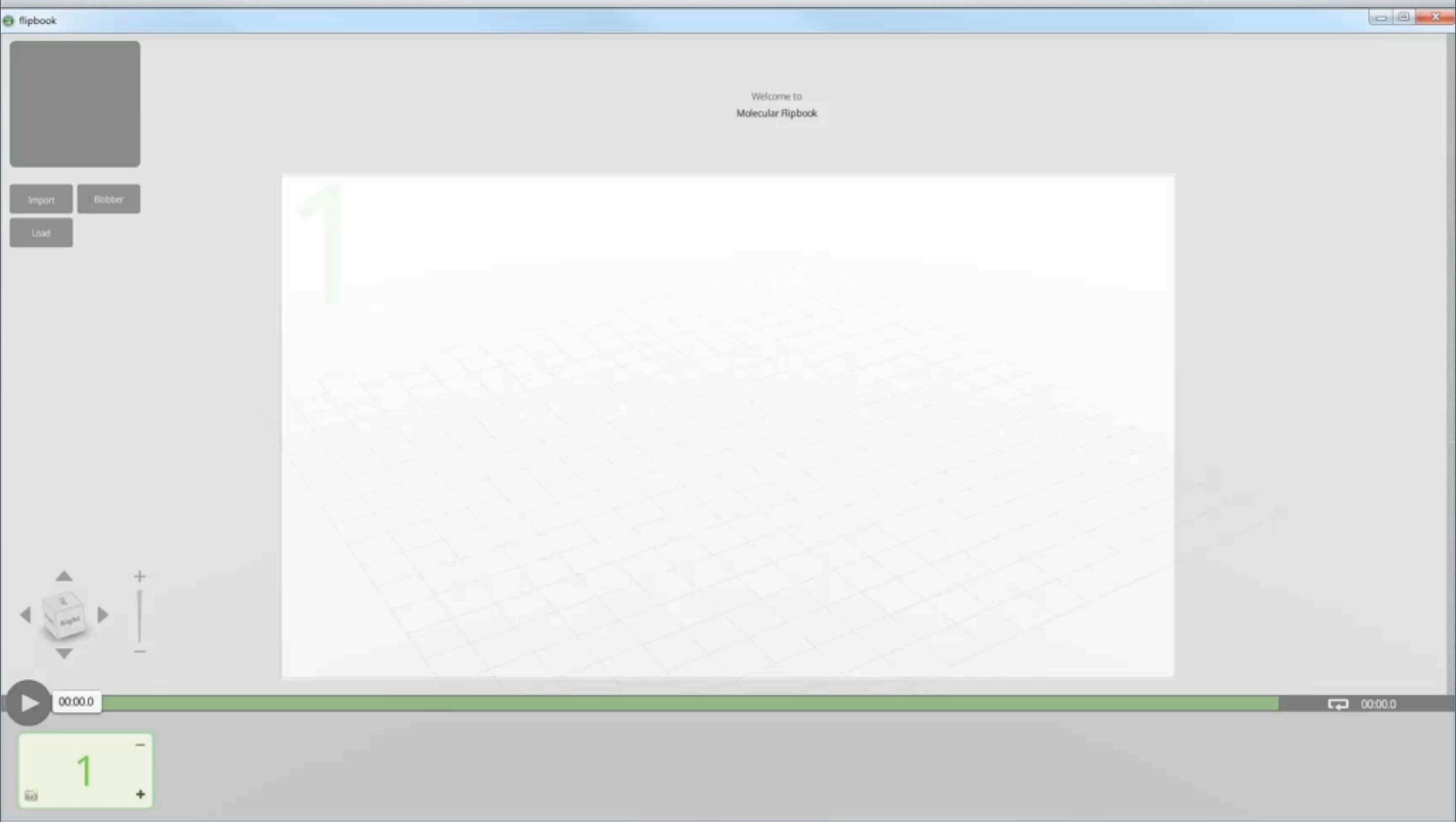
- suite of molecular animation tools built in Blender's game engine which will include import, modeling, animation and rendering modules.
- intuitive interface, simple controls
- ability to start creating animations after watching a short video tutorial.

Primary challenge:

How do we make 3D animation intuitive for users new to animation (and to those returning after a long break)?



MOLECULAR FLIPBOOK TOOLKIT



MOLECULAR FLIPBOOK TOOLKIT

a community resource for creating & sharing molecular animations

Molecular Flipbook Toolkit Features (Beta Version)



PDB import

Upload molecular structures as PDB files, either from your computer or from the Protein Data Bank database.



Blobber tool

Create a "blobby" as a stand-in for proteins that you don't have a structure file for. All you need to know is a molecular weight or approximate dimensions to create a blobby!



Animate colors and shaders

It's easy to animate your molecules changing color (to signify activation, for example) and to change its look using the Shader tool.



In-app tutorials

The in-application tutorials launch automatically and will walk you through how to use Flipbook.



Save your animation as a video

Once you create your animation, you can export it as a movie file that you can then embed in presentations and share with others!



Slide-based animation

If you've ever used Powerpoint or Keynote, you'll already be an expert in creating animations in Molecular Flipbook.



Create protein markers

Create and animate protein markers that can indicate, for example, where post-translational modifications are made.

Features that we're currently working on

To be notified when we release updated versions of Molecular Flipbook, please fill out our [Feedback form](#).



Linker tool

Create a dynamic and flexible linker that connects two domains of a protein.



Cut chains

Create two different surfaces from a single chain – this can be useful to animate



Create biological units

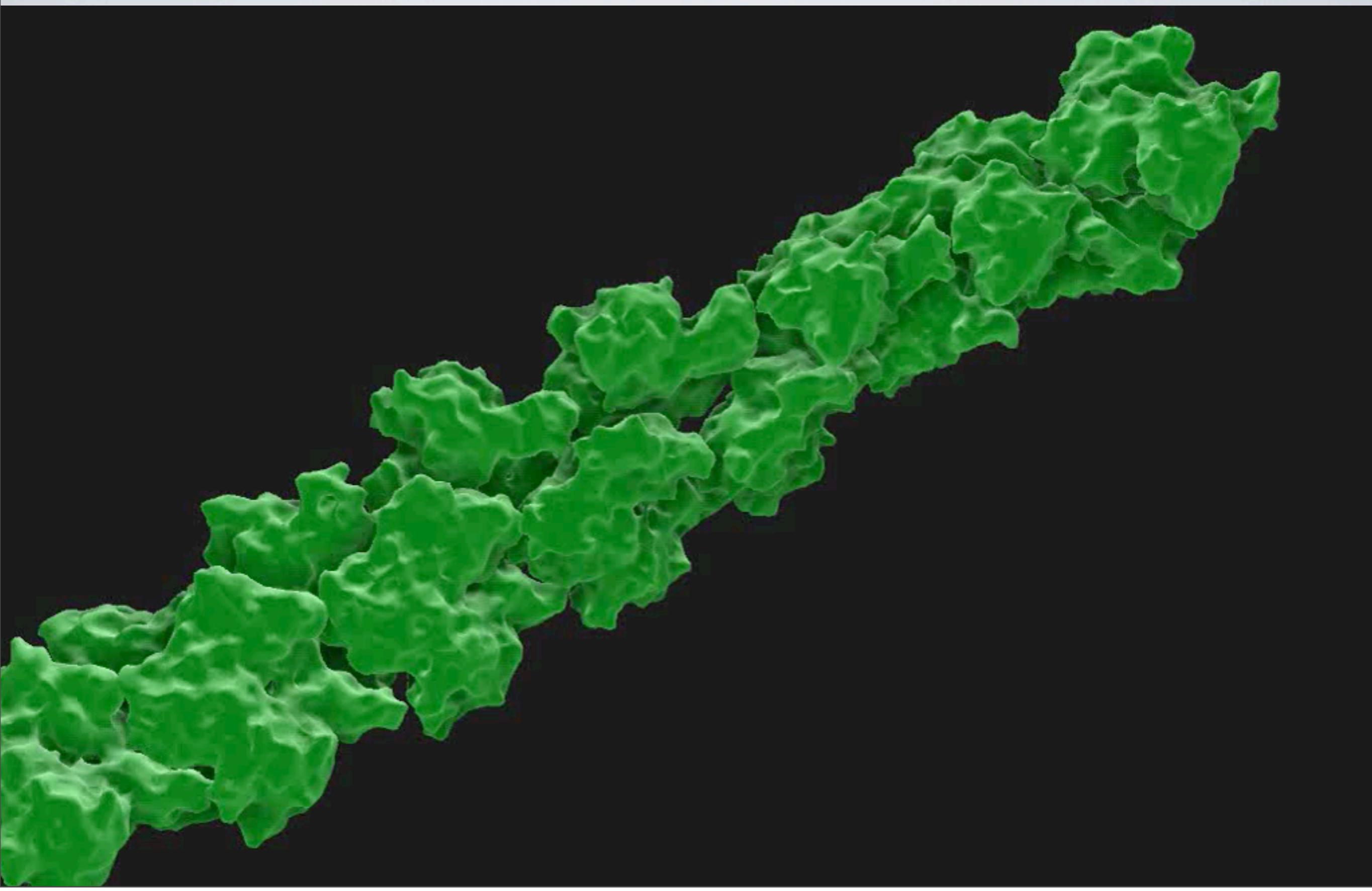
Create larger biological assemblies (of virus capsids, for instance) using the BIOMT coordinates inside a PDB.



Import additional filetypes

Import geometry files, such as reconstructions from the EMDB, or other files (such as .stl) that may have been generated in another program.

MOLECULAR FLIPBOOK EXAMPLE



MOLECULAR FLIPBOOK TOOLKIT

a community resource for creating & sharing molecular animations

<http://MolecularFlipbook.org>



Download a beta version of the Molecular Flipbook toolkit - it's free and open source.

Download Molecular Flipbook for Mac

Click to download the Mac version of the Molecular Flipbook Beta 0.1 Animation Toolkit!

[Download Flipbook for Mac](#)

Download Molecular Flipbook for PC

Click to download the Windows version (64bit only) of the Molecular Flipbook Beta 0.1 Animation Toolkit!

[Download Flipbook for PC](#)

Molecular Flipbook Toolkit Features (Beta Version)



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MOLECULAR FLIPBOOK WEBSITE

a community resource for creating & sharing molecular animations

- searchable, easy-to-use online database that also hosts community/social interactions/collaborations
- will allow users to share not only Blender-based animation, but also Illustrator, Photoshop files, etc.
- provides a visual way of following the evolution of a hypothesis over time

Primary challenge:

How do we get users to share their visualizations with others?

The screenshot shows the homepage of the Molecular Flipbook website. At the top, there is a navigation bar with links for Home, About, Download, Library, and Help. To the right of the navigation bar are buttons for Search, Login, Sign Up, and Upload. Below the navigation bar, there is a section titled "Featured Animation" with a sub-section titled "Crystal structure of the nucleosome core particle at 2.8 Å resolution." A large image of a nucleosome structure composed of various colored proteins and DNA is displayed. To the right of this image, there is a brief description of the software: "Molecular Flipbook is a free and open-source molecular animation software toolkit that has been specifically designed with the needs of biology researchers in mind." Below this, there is a button labeled "Download Now!" and a link to "Browse the Library".

The screenshot shows the "Browse Scene Files" page of the Molecular Flipbook website. At the top, there is a navigation bar with links for Home, About, Download, Library, and Help. To the right of the navigation bar are buttons for Search, Login, Sign Up, and Upload. Below the navigation bar, there is a section titled "Browse Scene Files" with sub-links for Most Viewed, Most Faved, Most Recent, and Staff Picks. Two thumbnail images are shown: one of a nucleosome structure and another of a yellow molecular model. To the right of these thumbnails, there is a brief description of the software: "Molecular Flipbook is a free and open-source molecular animation software toolkit that has been specifically designed with the needs of biology researchers in mind." Below this, there is a button labeled "Download Now!"

MOLECULAR FLIPBOOK WEBSITE



Search



Login

Sign Up

Upload

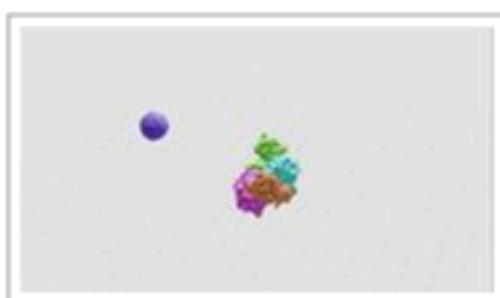
Home About Download Library Tutorials News Help

Browse the Library

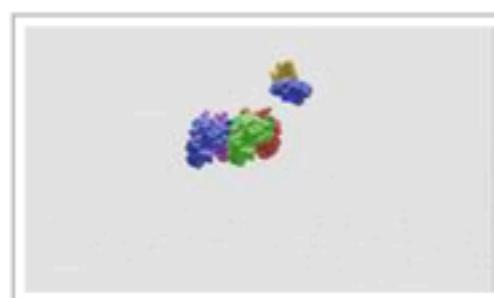
Most Viewed

Most Recent

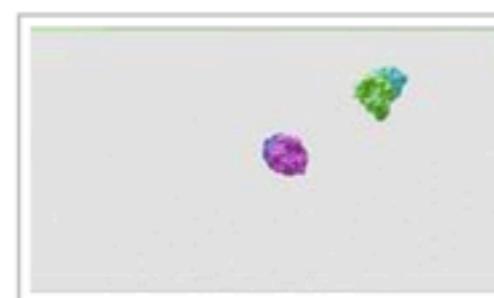
Staff Picks



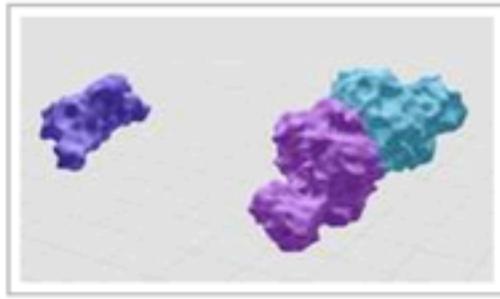
enzyme



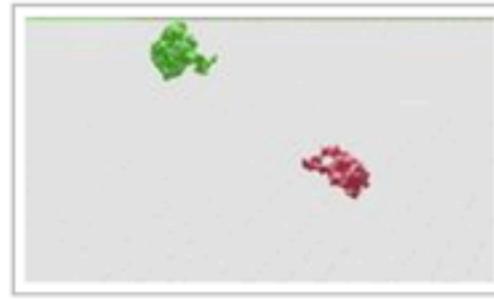
JiminLee. Acetyl-CoA



Enzyme Video



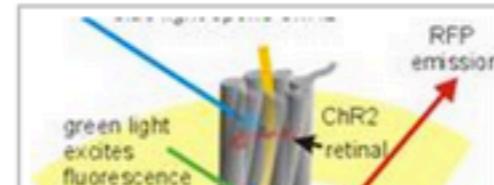
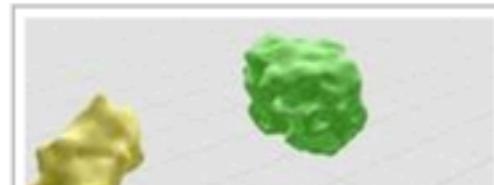
Seungjun Lee - Biotin and...



Jenny Kang co enzyme



Lipase & Colipase



Browse by tag

hannahchey aldehyde filament
actin seungjunlee
seoyeonkang samuel lee
molecular flip book for biology
block e
won joon justin lee carboxylase
biotin oxidoreductase
ferredoxin
ferredoxin oxireductase 3cat
8cat enzyme I virus hiv
treadmilling depolymerization

TOWARDS A DIGITAL CELL

TOOLS

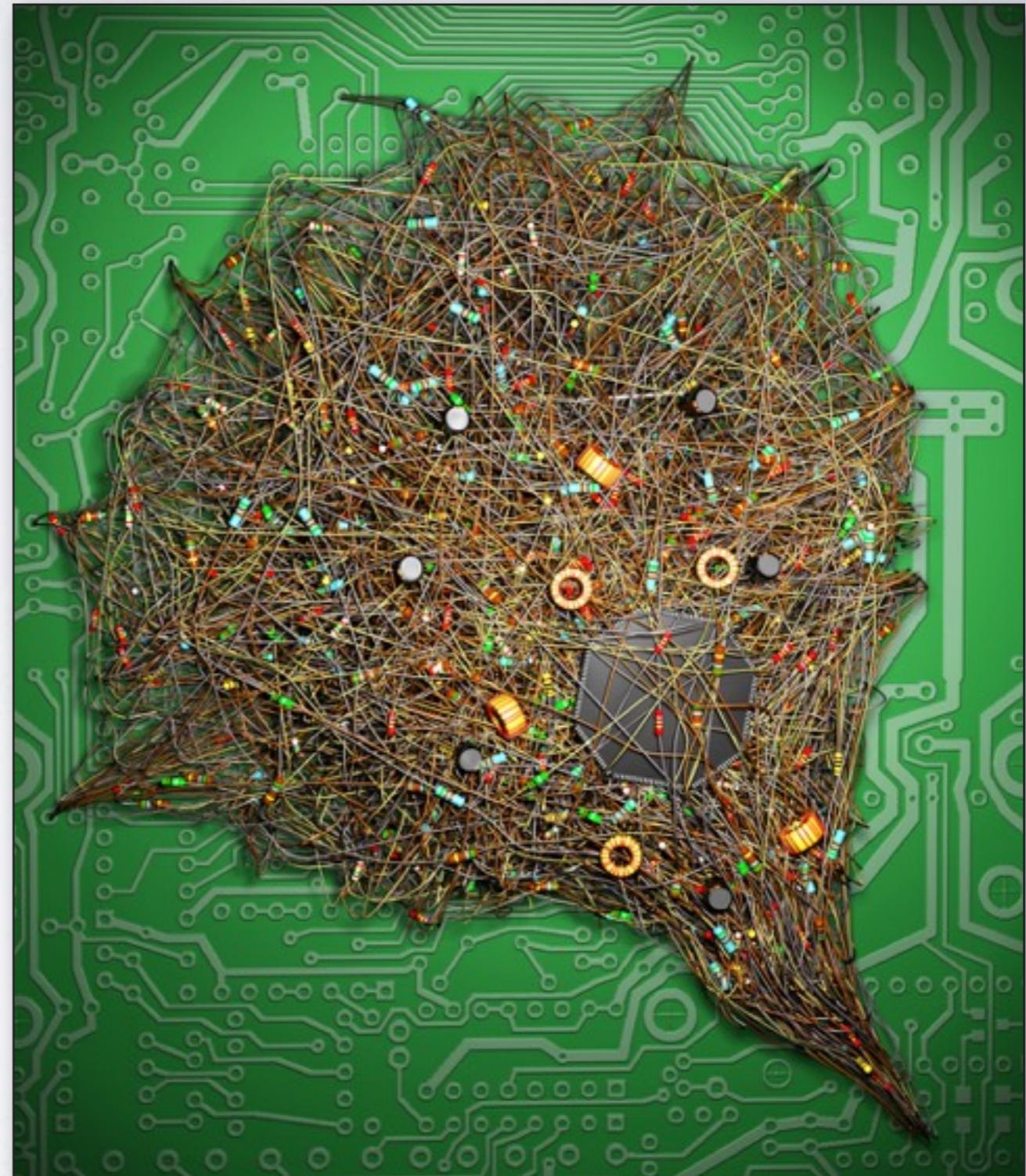
intuitive animation/visualization tools that could allow integration of multiscale data from different sources

TRANSPARENCY

standardized means of providing references and sources used in visualizations

ARCHIVES

centralized repository for cellular data, images and animations



MANY THANKS

Tom Kirchhausen Harvard Medical School

Wes Sundquist, Michael Kay and the CHEETAH Consortium University of Utah
Molecular Flipbook Team: Mike Pan, Rise Riyo, Gaël McGill (HMS), Piotr Sliz (HMS)

Sam Reck-Peterson Harvard Medical School

Jack Szostak Massachusetts General Hospital/Harvard Medical School



National Science Foundation
National Institutes of Health (NIGMS)
The TED Fellows Program

LINKS

University of Utah website: <http://biochem.web.utah.edu/iwasa>

The Science of HIV Project: <http://ScienceofHIV.org>

The Molecular ViewBook Project: <http://MolecularFlipbook.org>

The Exploring Origins Project: <http://ExploringOrigins.org>

Tutorials, Movies and Molecular Maya: <http://molecularmovies.org>