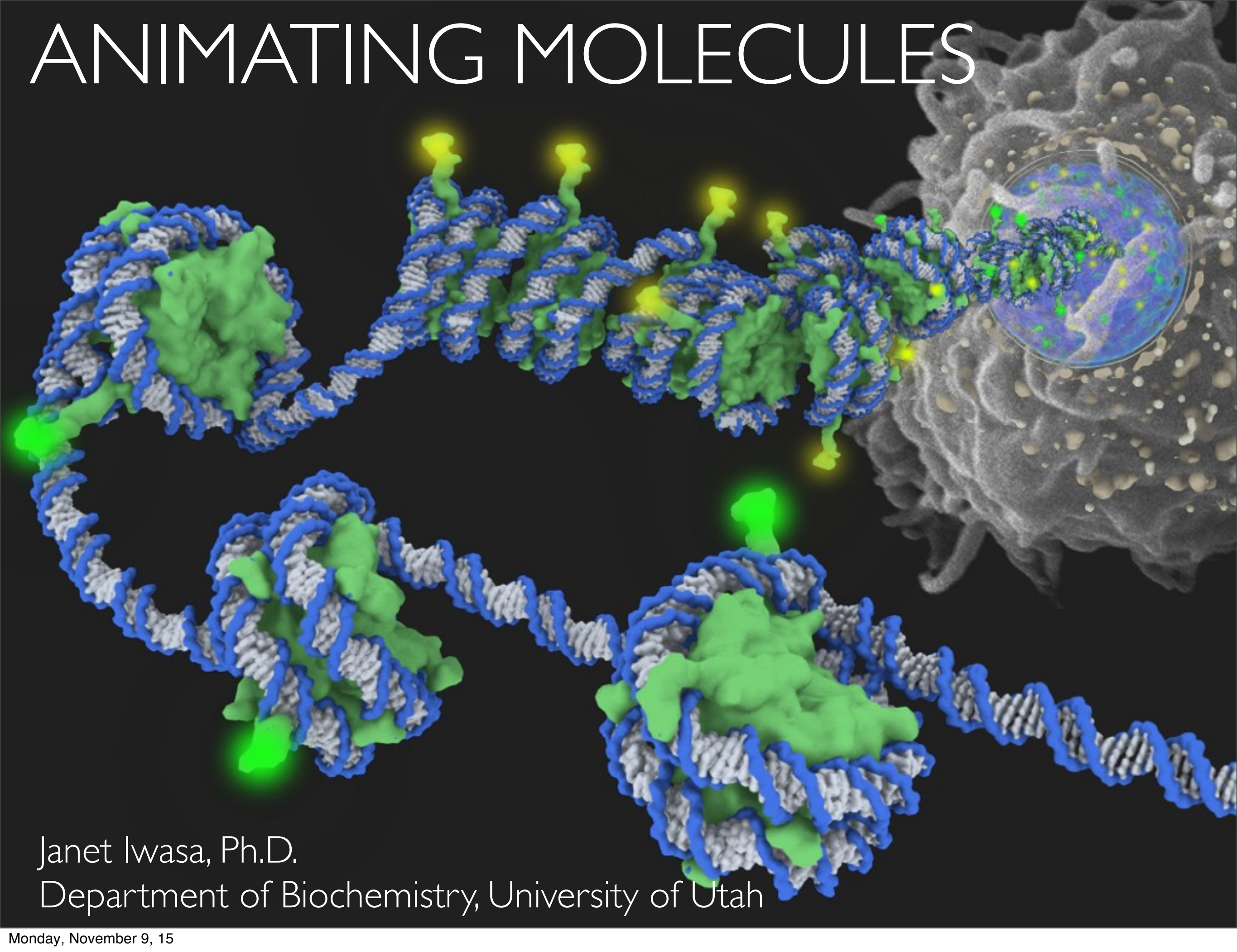


ANIMATING MOLECULES

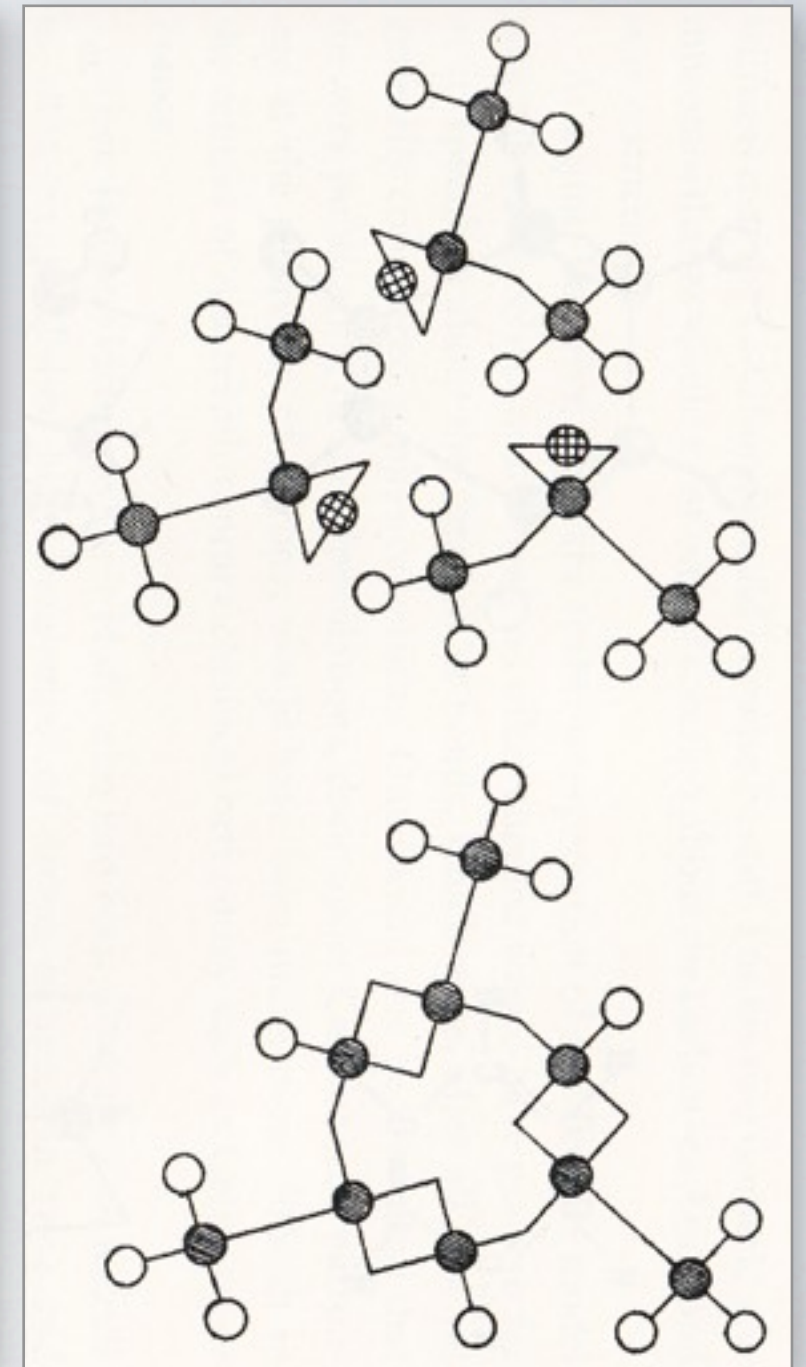
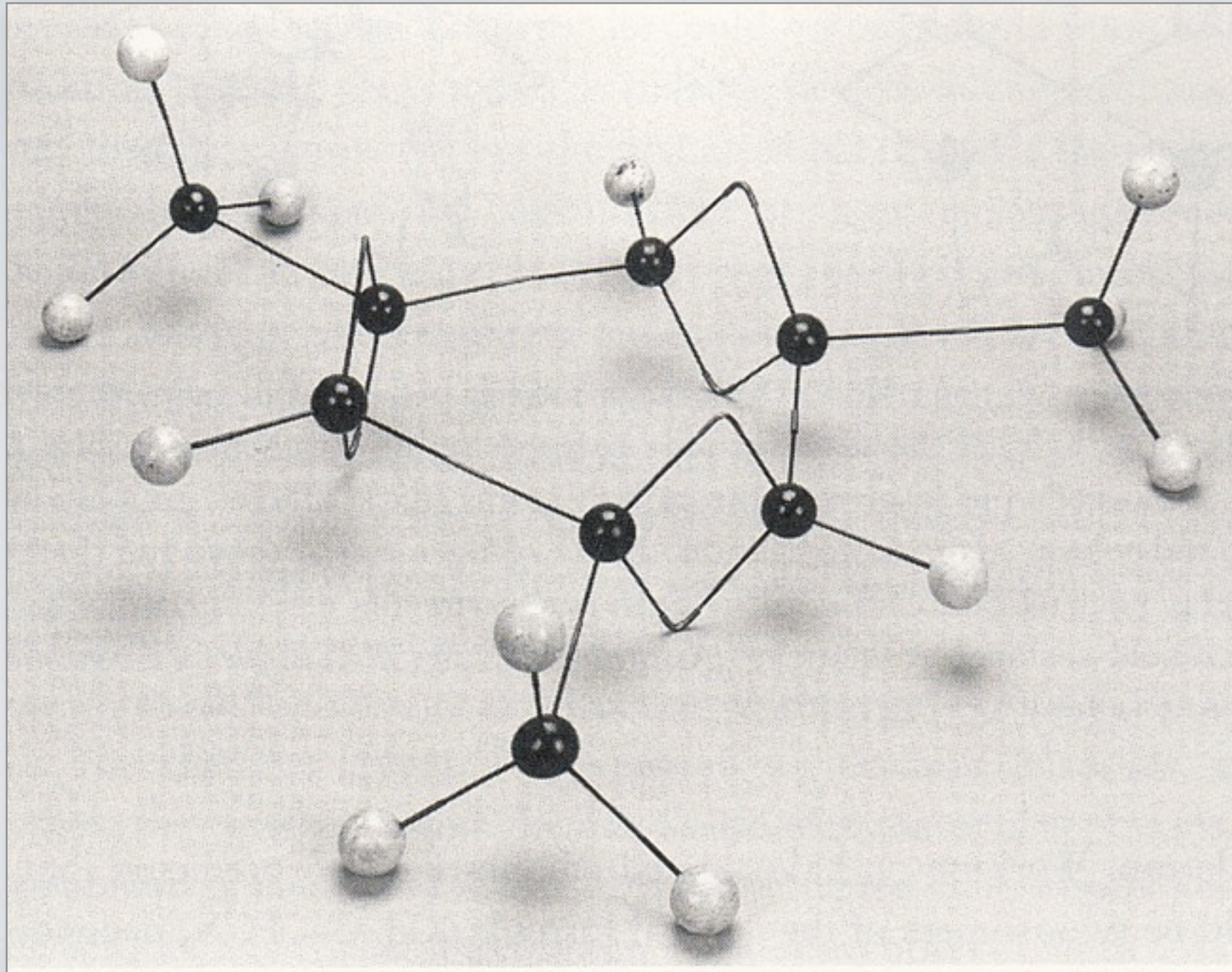


Janet Iwasa, Ph.D.

Department of Biochemistry, University of Utah

3D MODELS IN SCIENCE

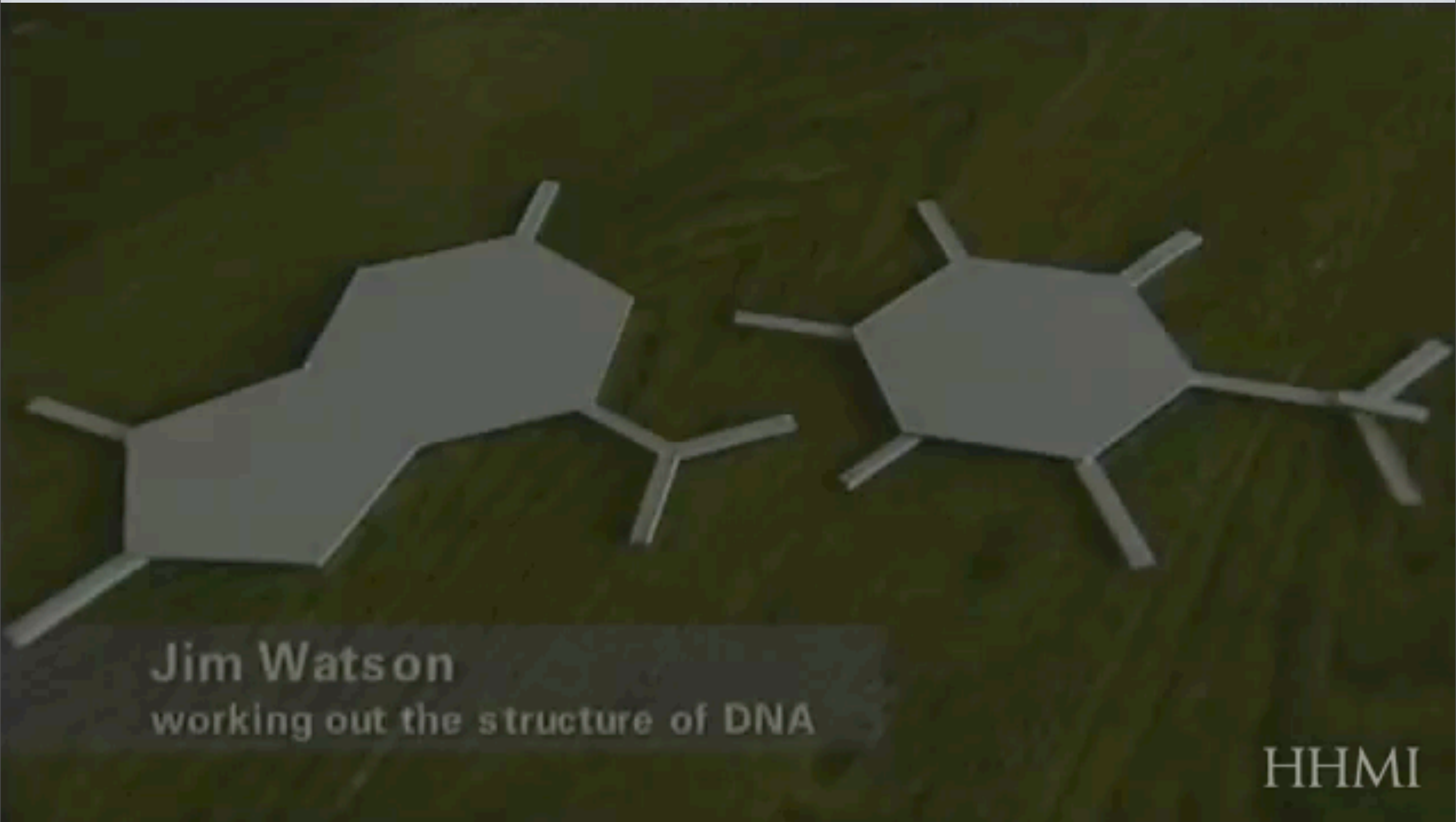
Early chemical models: August Kekulé



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

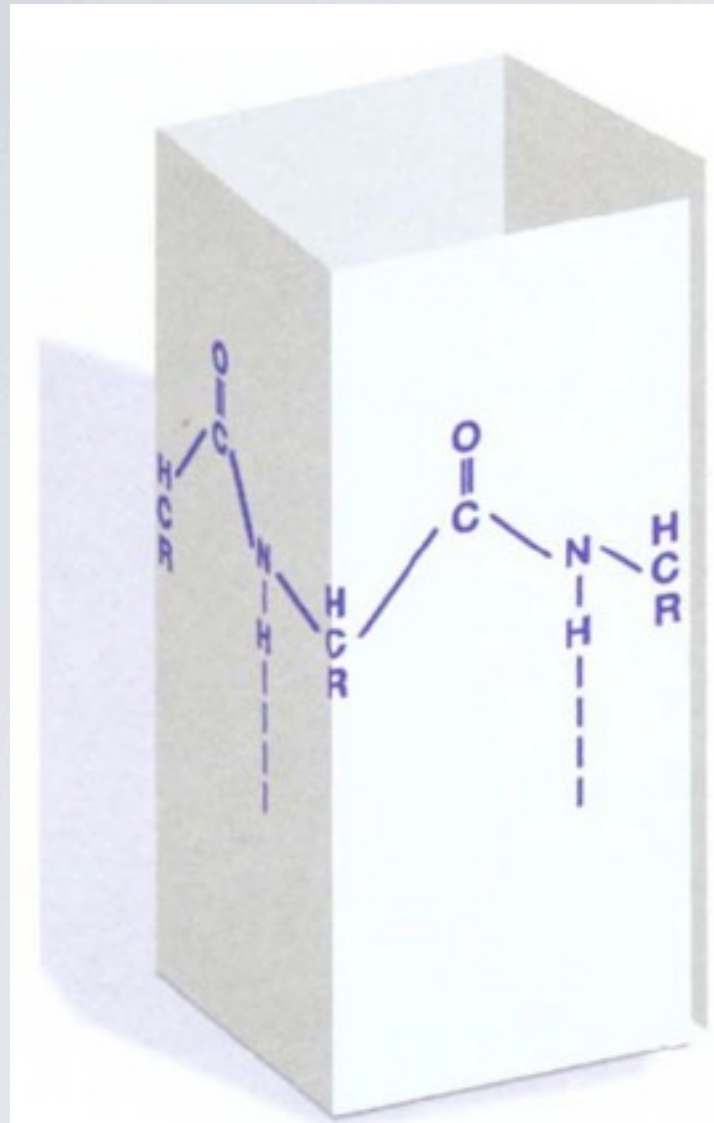


Jim Watson
working out the structure of DNA

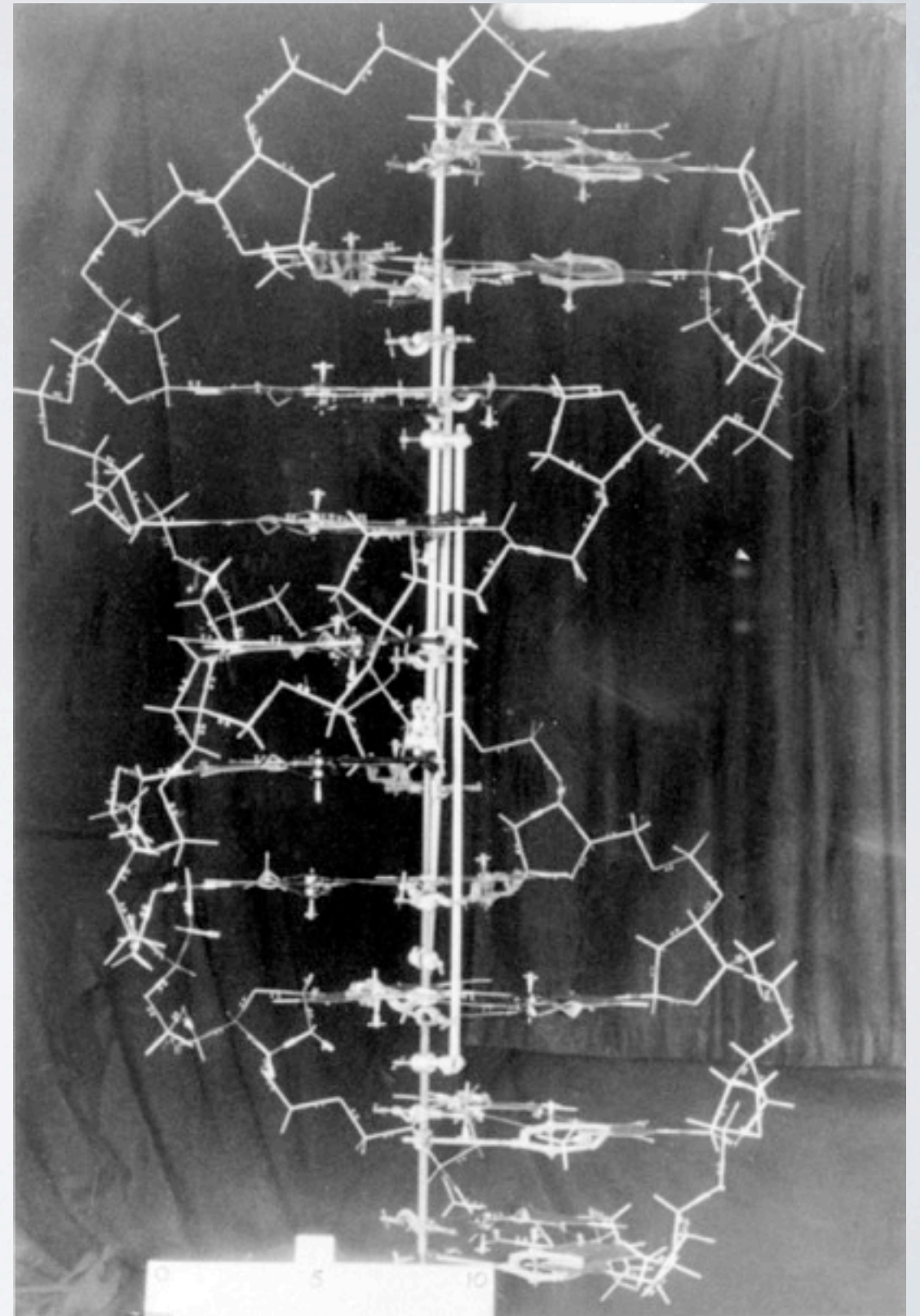
HHMI

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

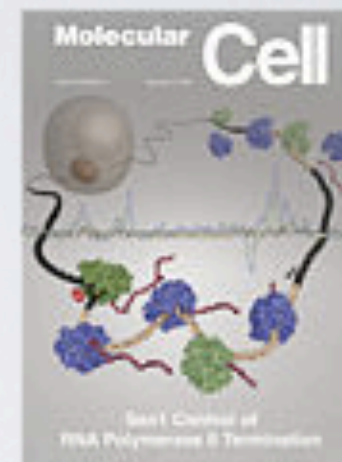
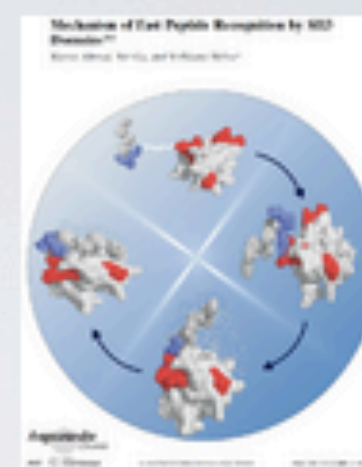
1958 - Myoglobin in a “forest of rods”



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

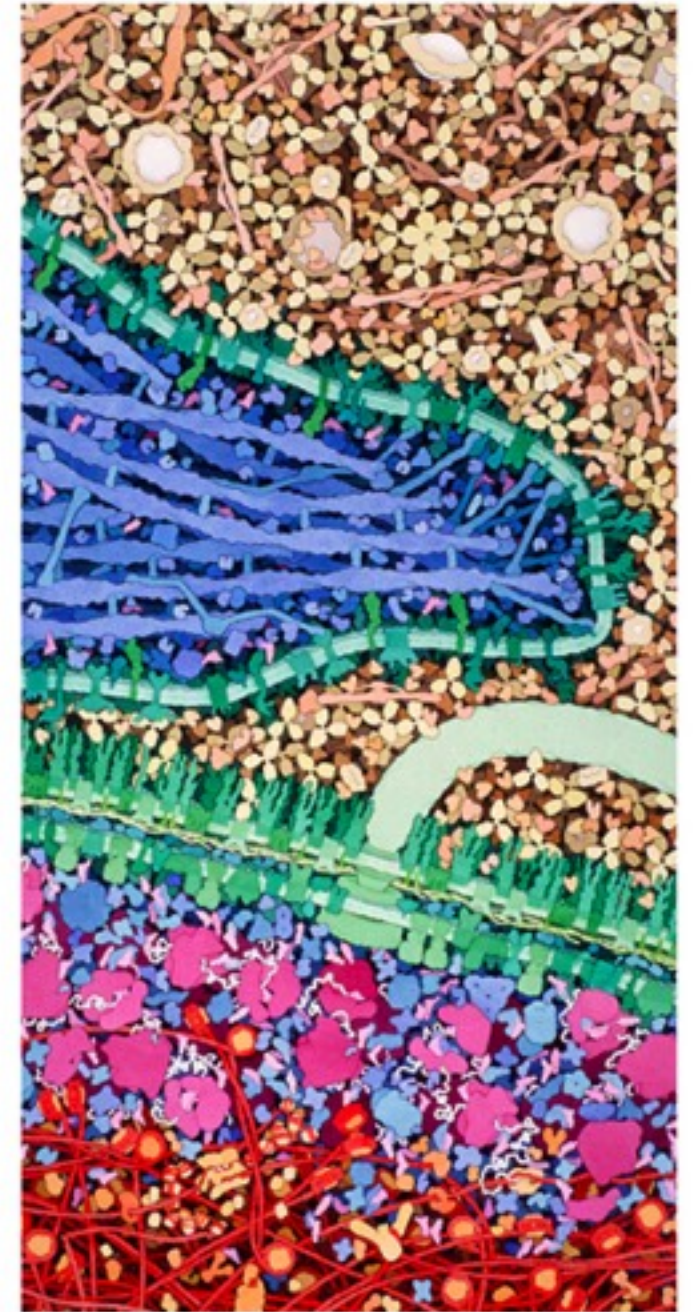
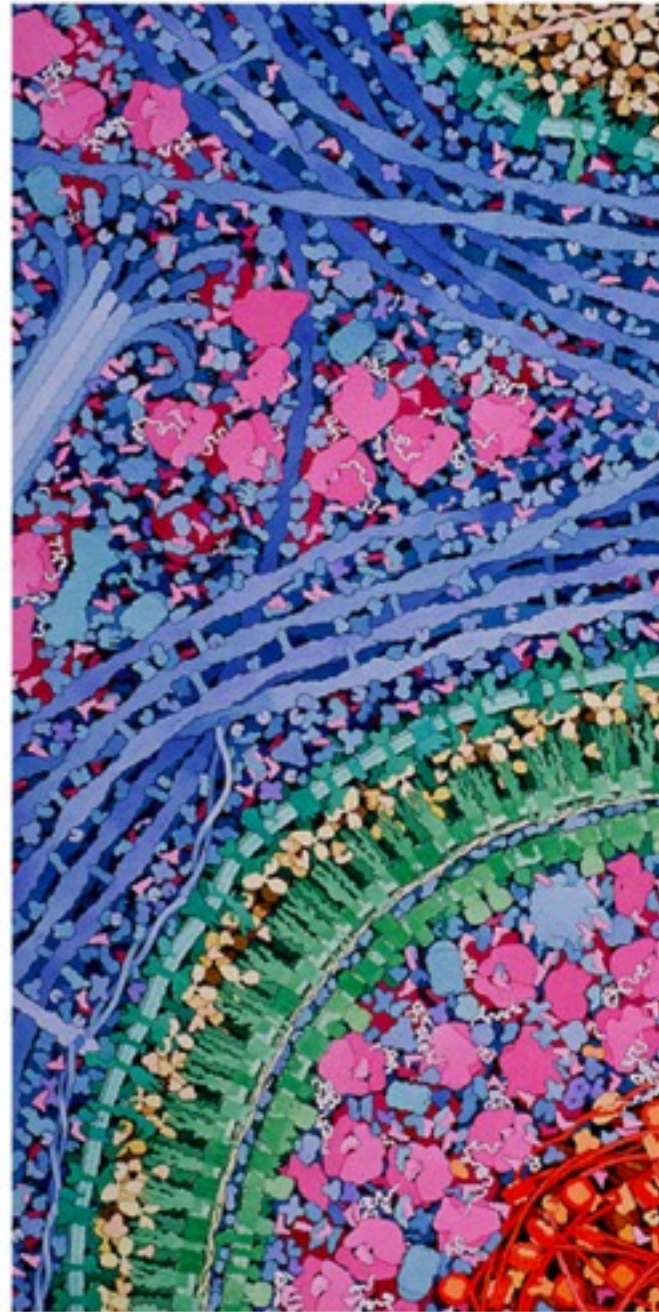
3D MODELS IN SCIENCE

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

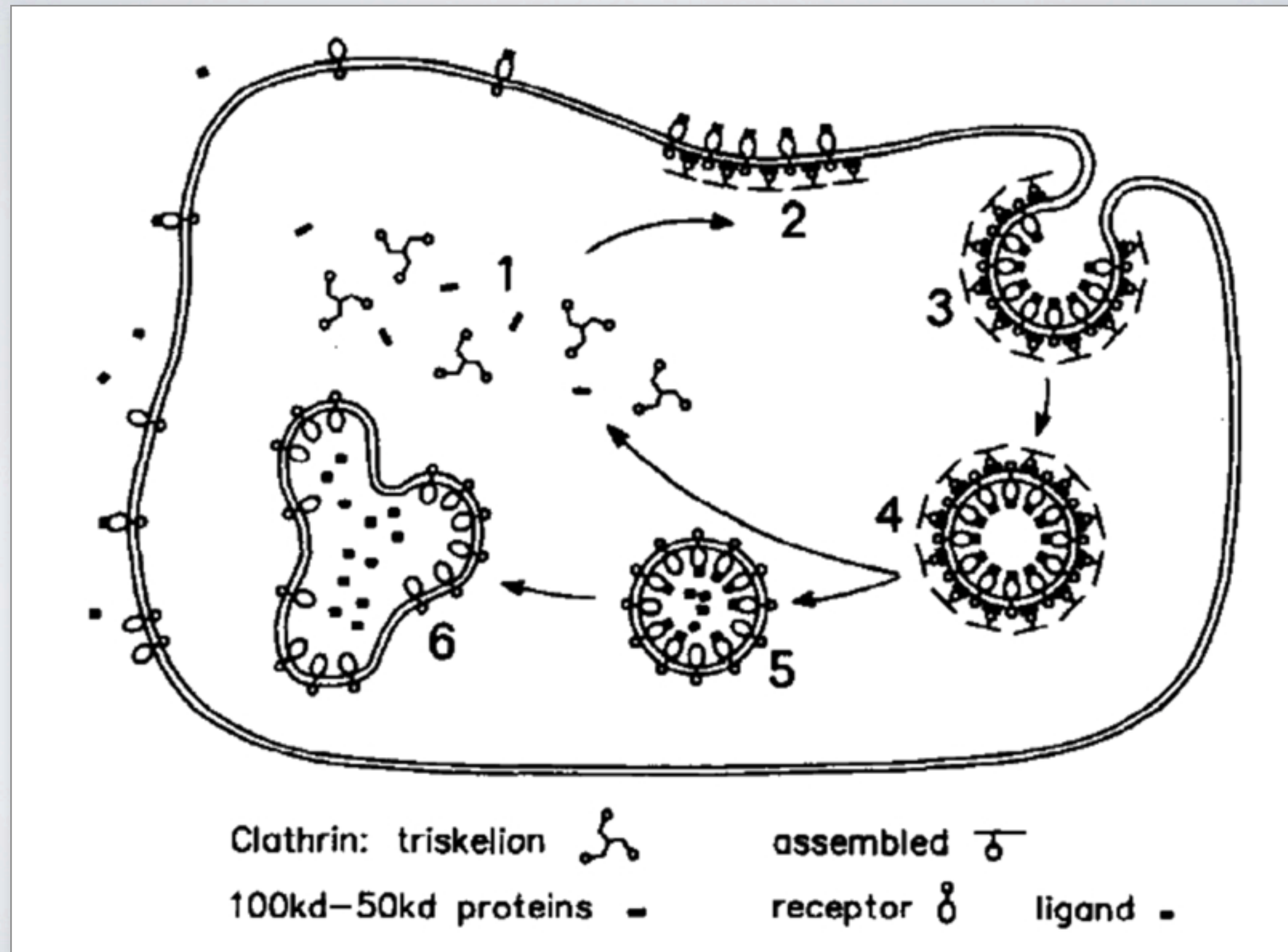
3D animation can synthesize diverse biological data ...

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

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

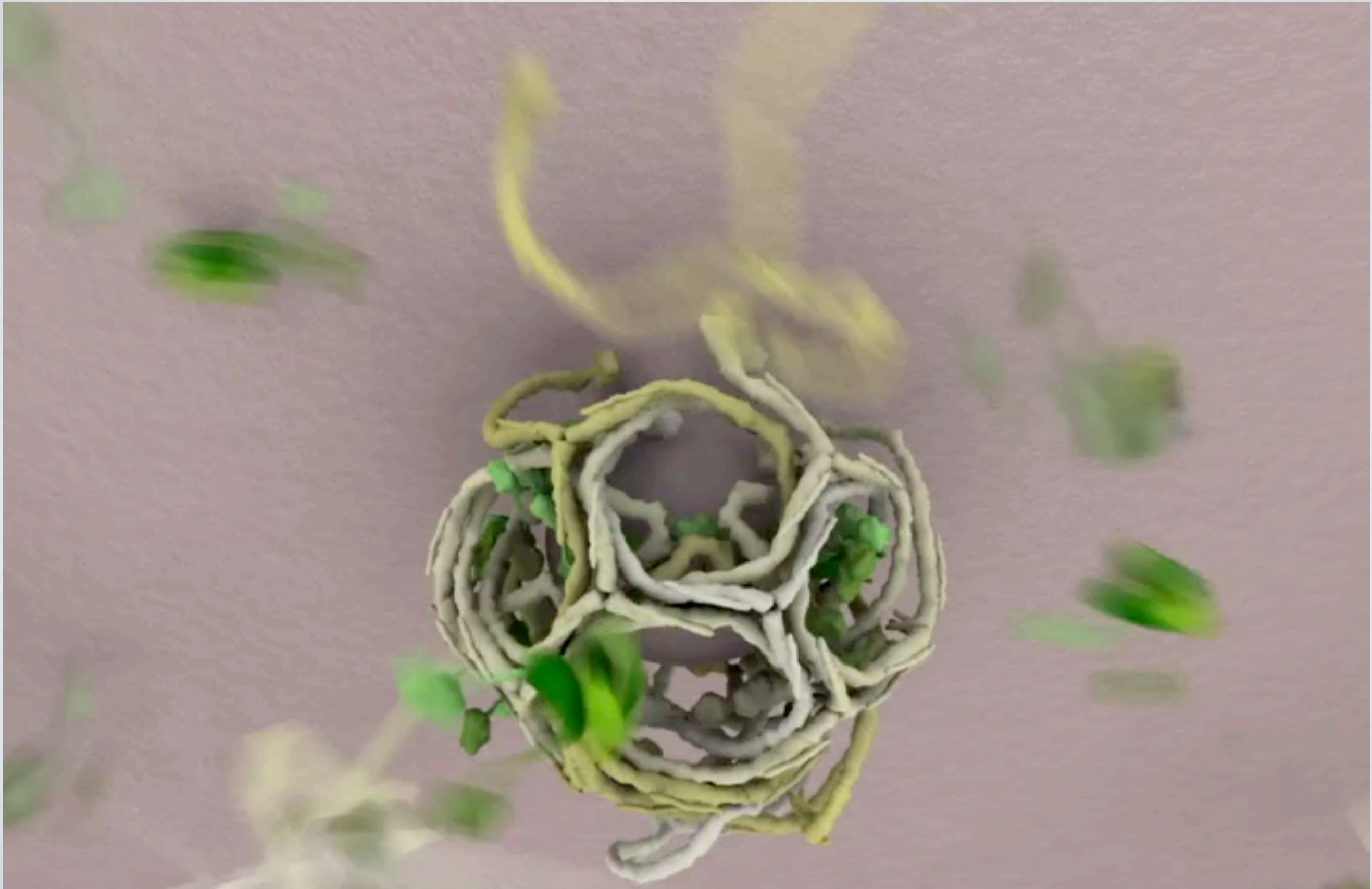
CLATHRIN MEDIATED ENDOCYTOSIS

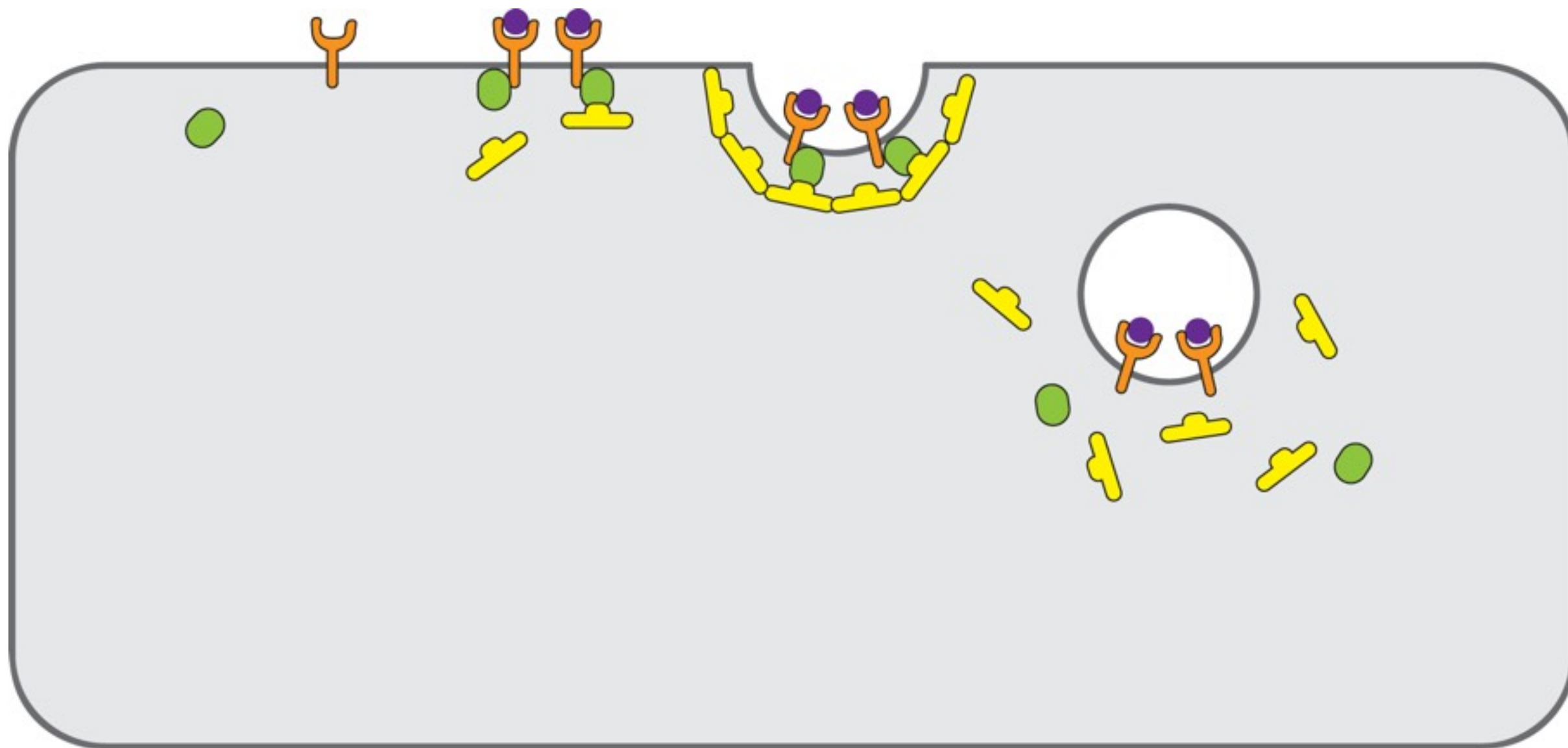
illustration by Pearse & Crowther, 1987



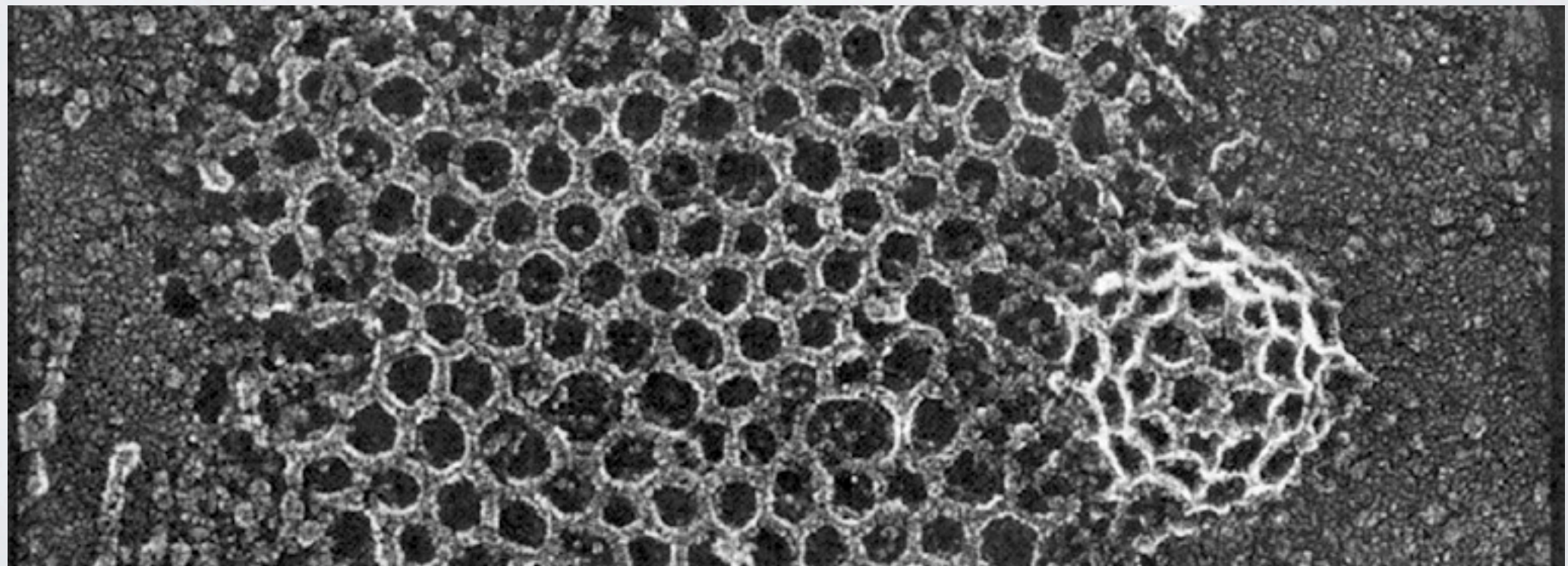
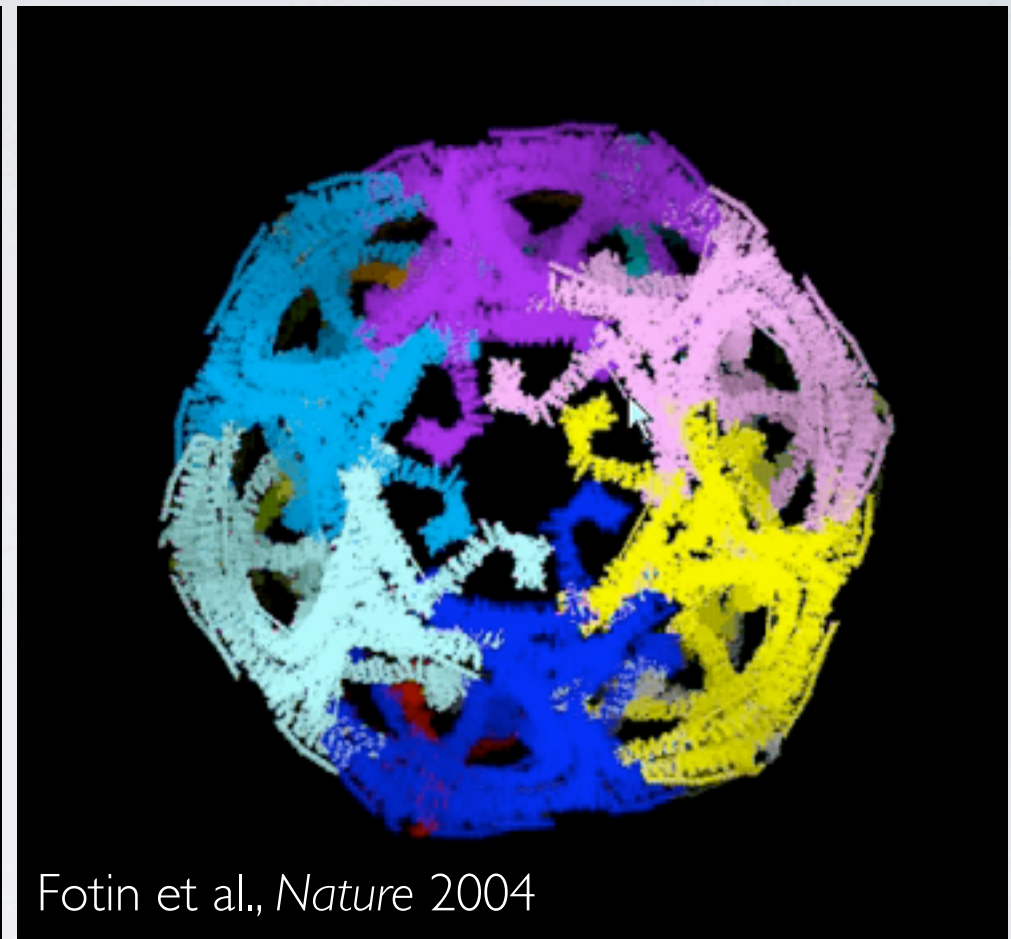
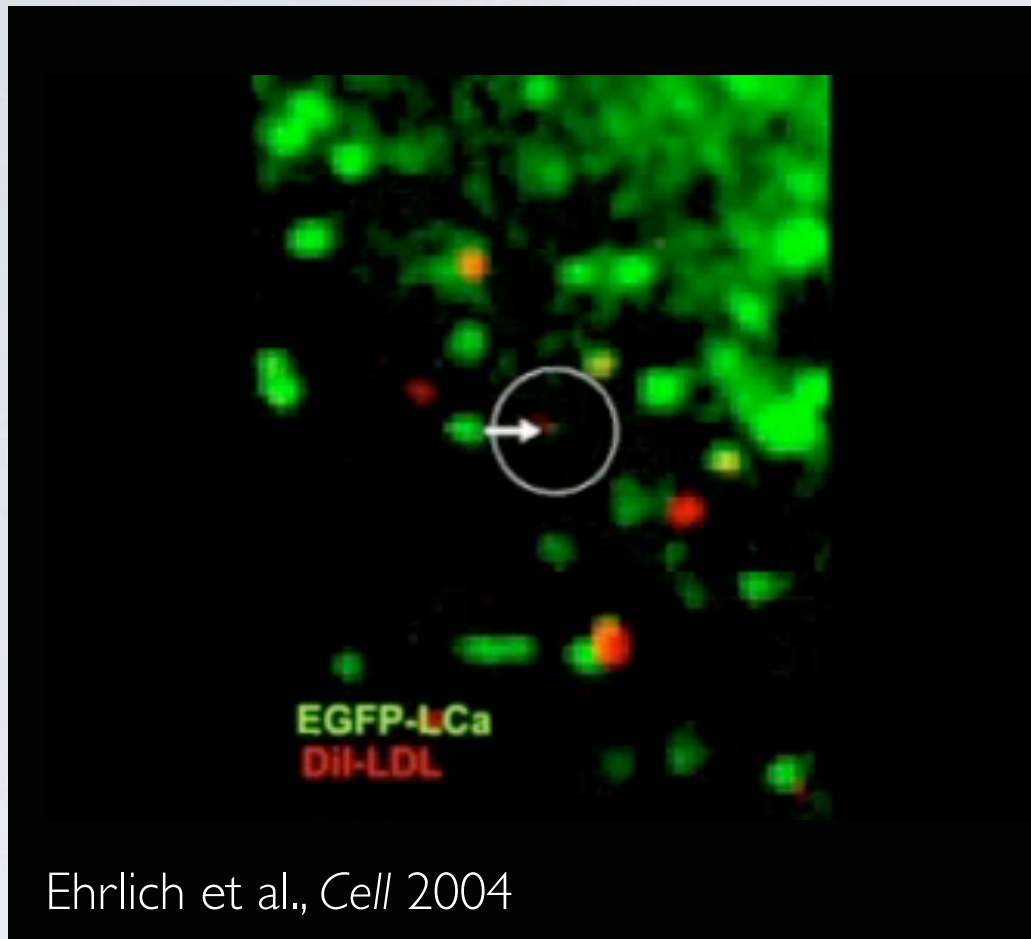
CLATHRIN MEDIATED ENDOCYTOSIS

an animation in collaboration with Tom Kirchhausen (2012)



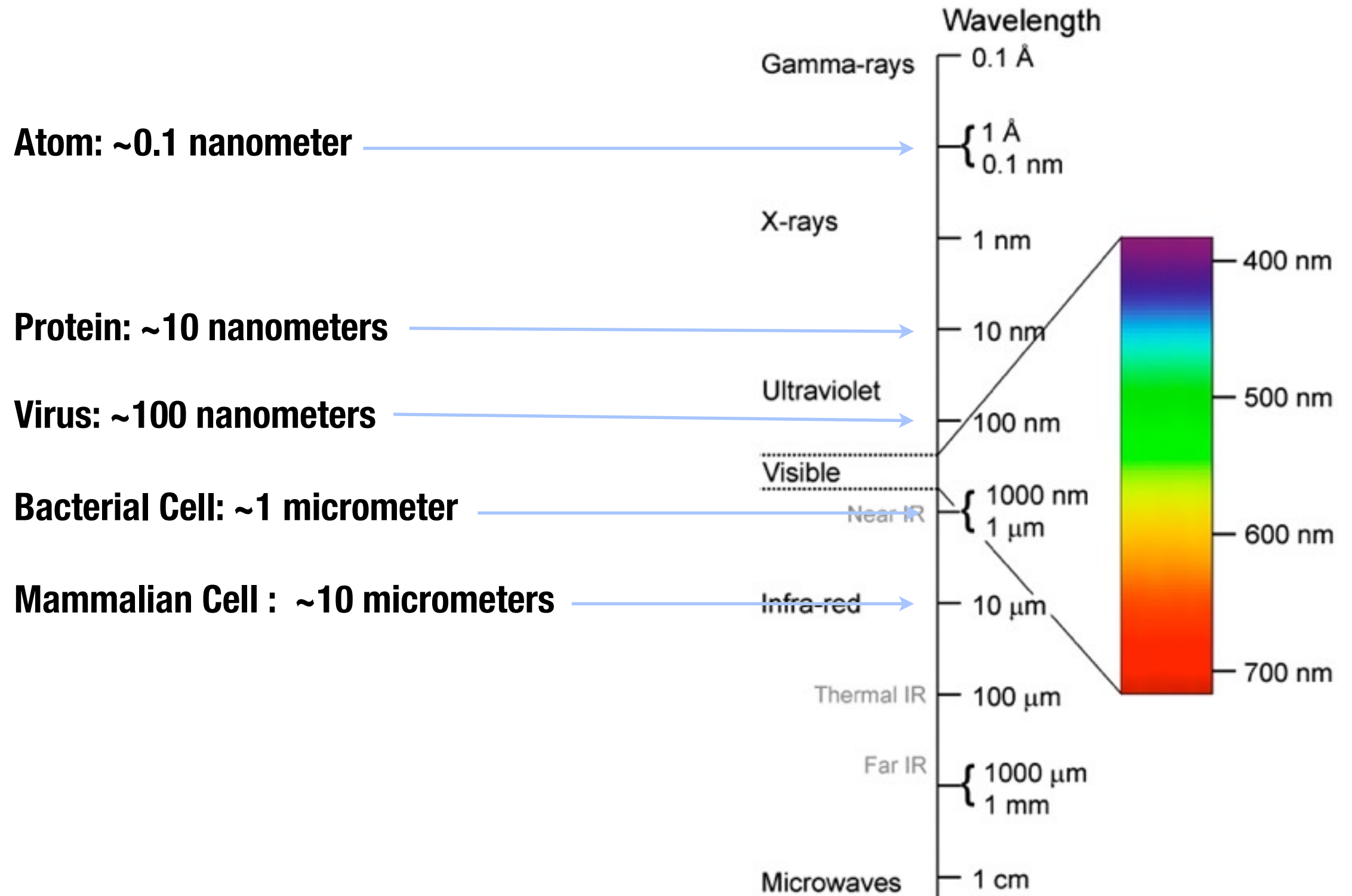


SYNTHESIS OF DIVERSE DATA



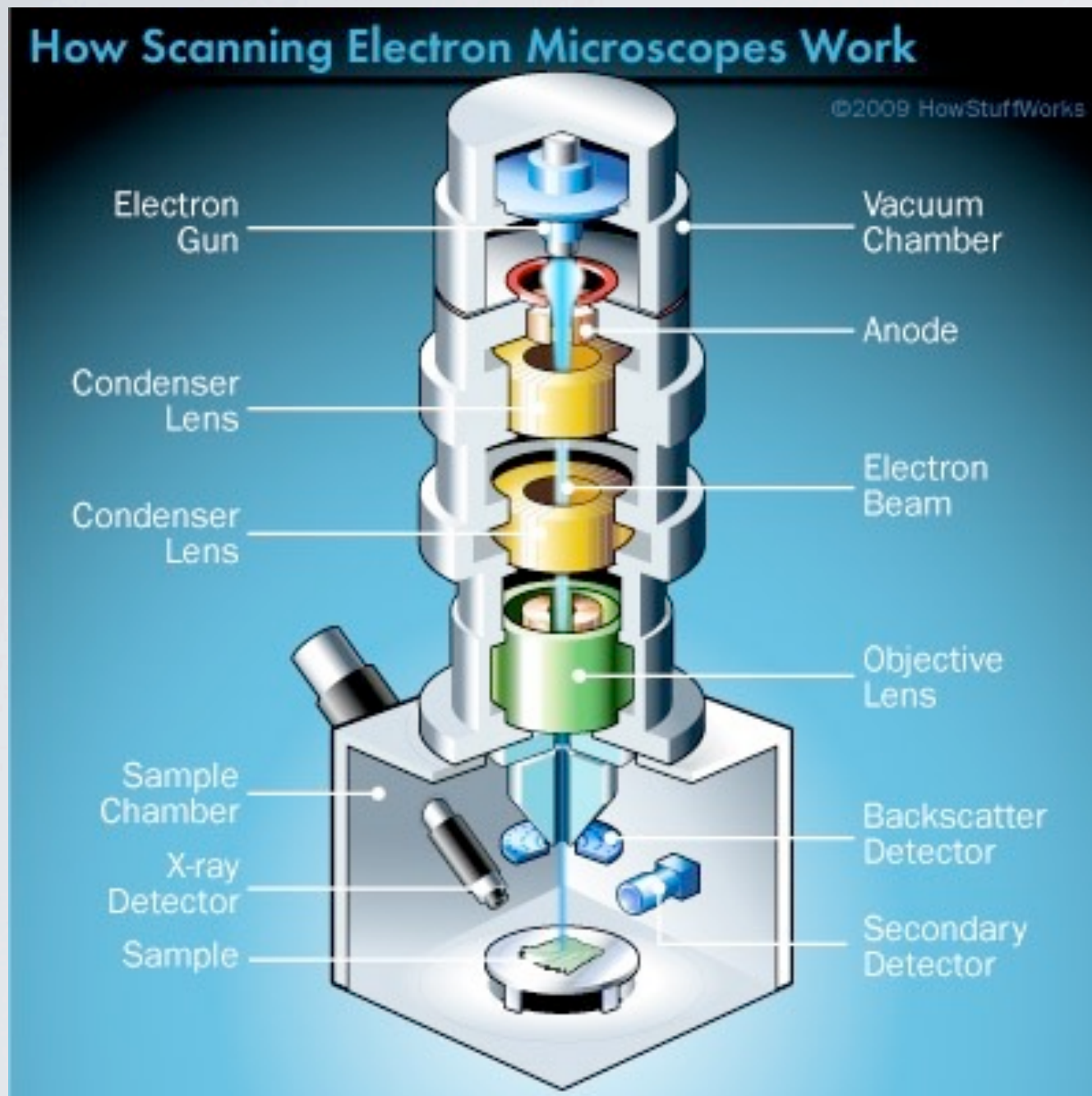
Heuser & Keen, 1998 clathrin structures on cell plasma membrane by “deep etch” electron microscopy

LIMITATIONS OF LIGHT MICROSCOPY



Louis E. Keiner - Coastal Carolina University

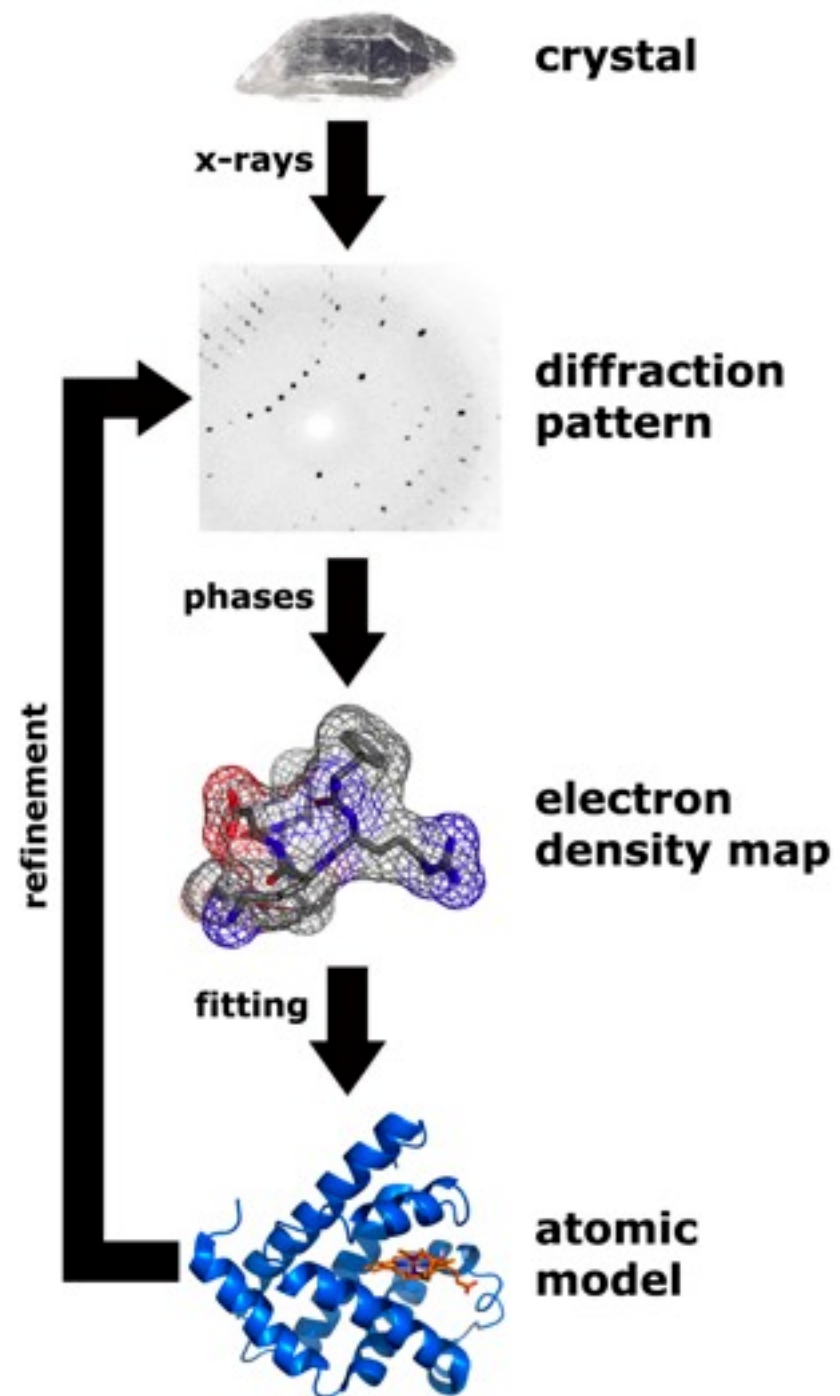
ELECTRON MICROSCOPY



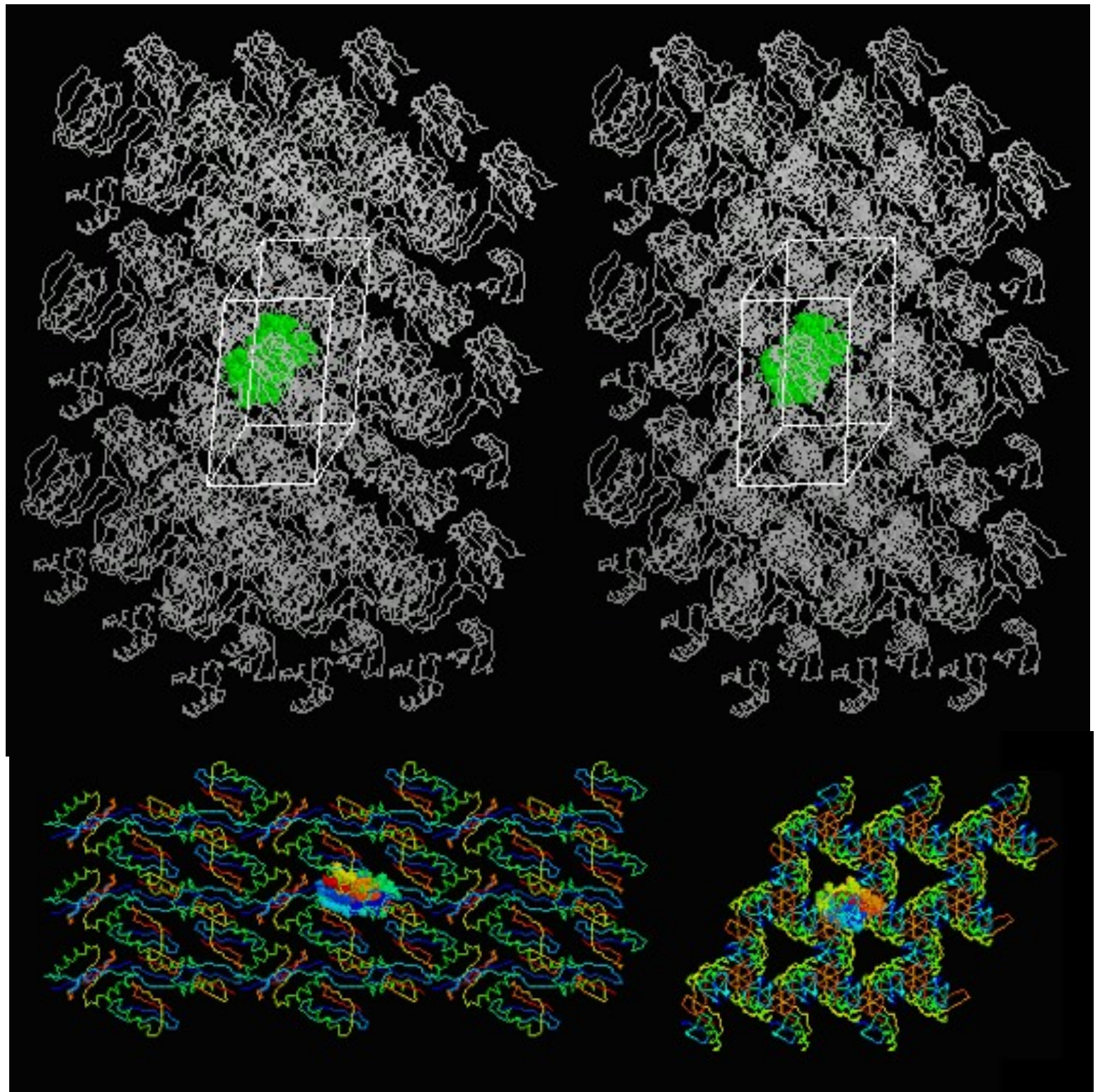
Insect coated in gold

Peter Halasz

X-RAY CRYSTALLOGRAPHY

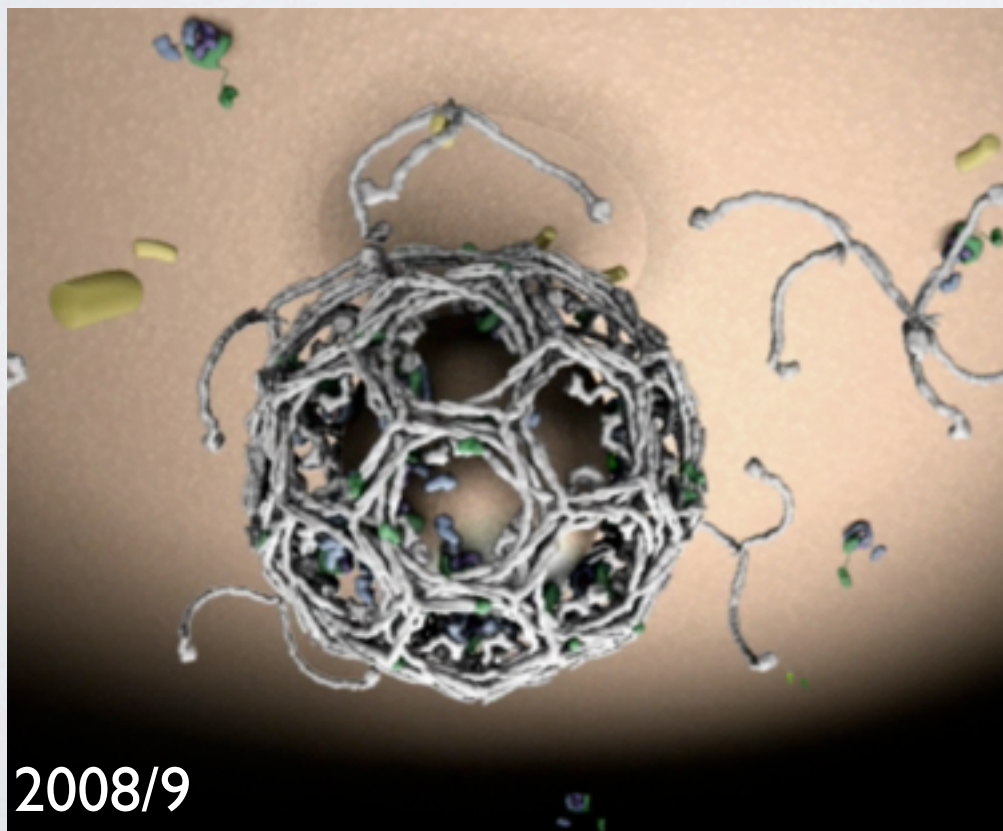
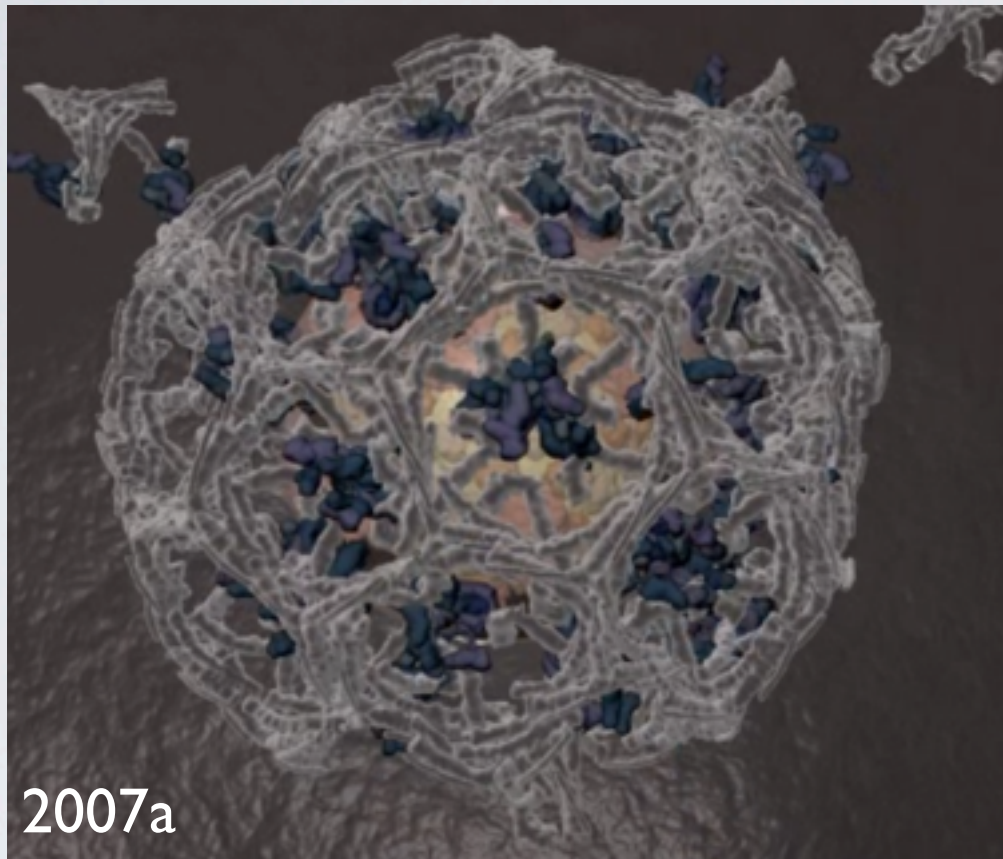


Thomas Splettstoesser / wikipedia

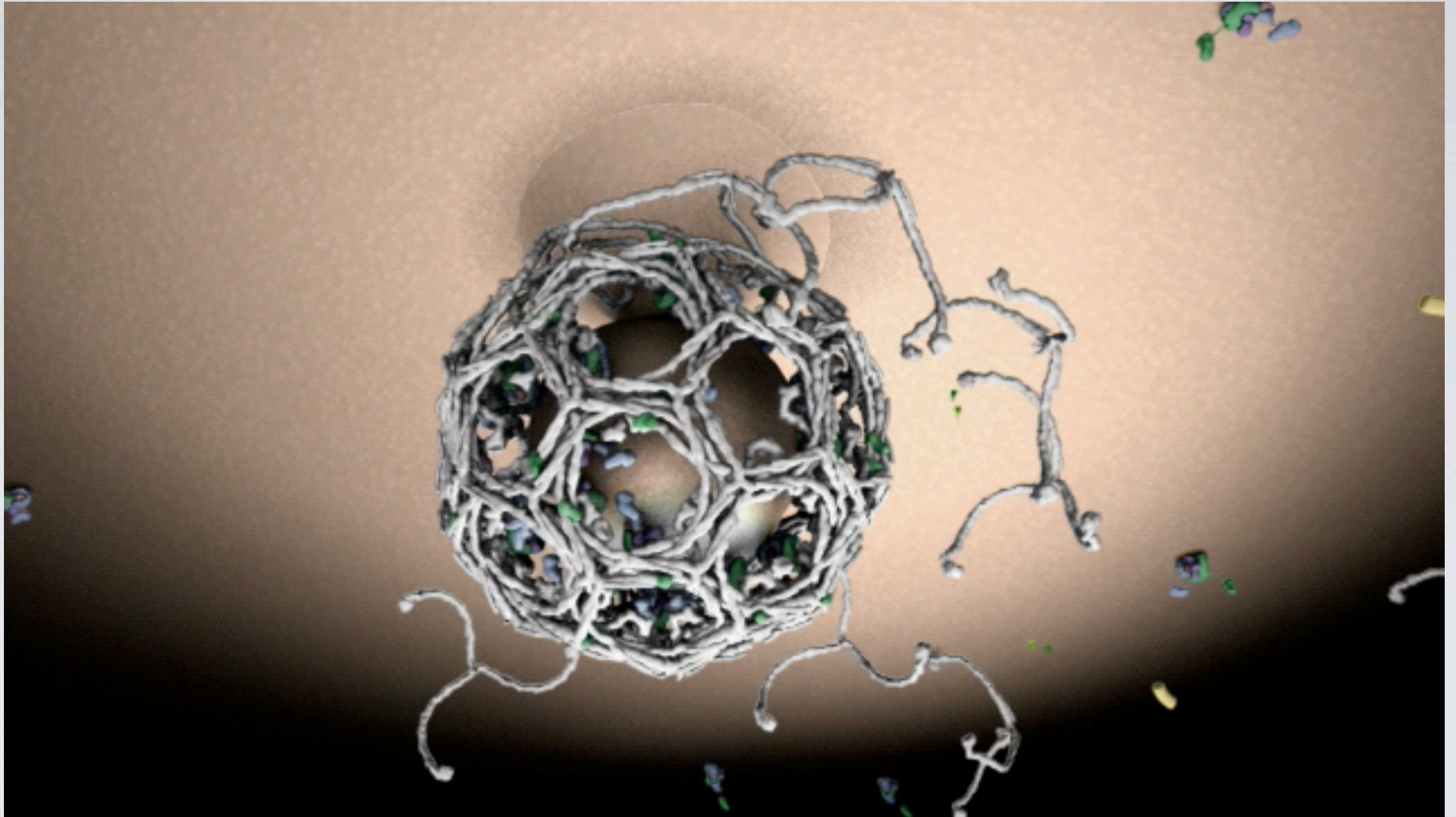


Eric Martz / U. Massachusetts

DRAFTS & REVISIONS



DYNAMIN - 2008

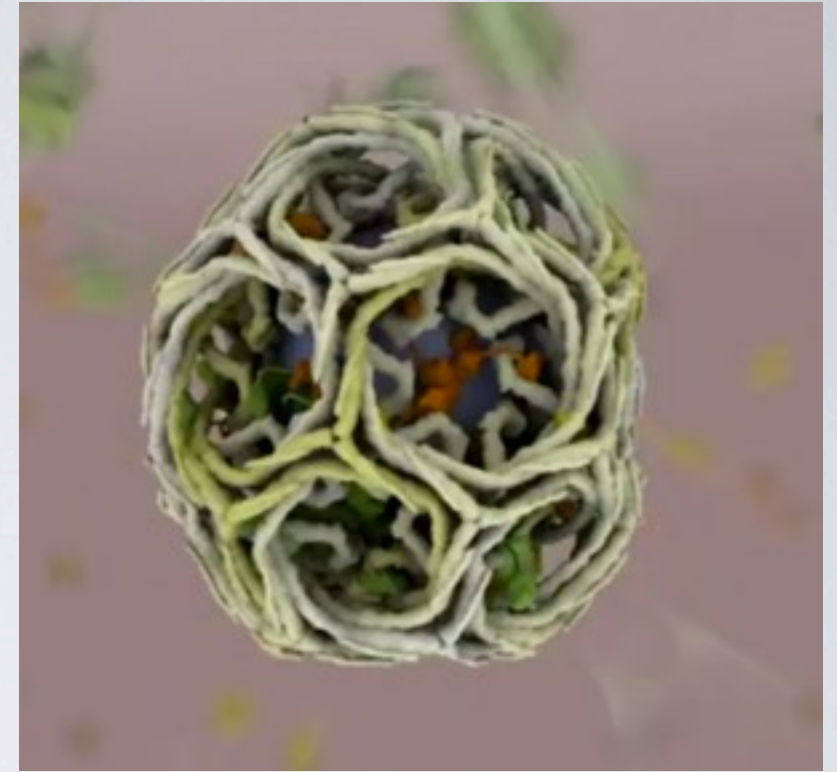
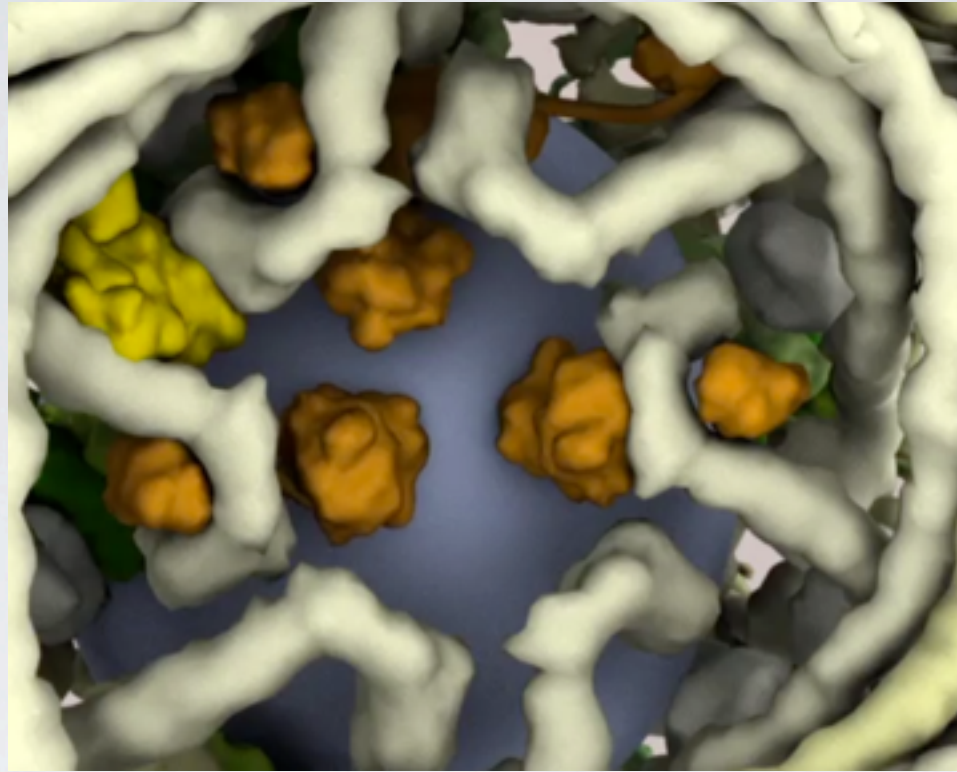
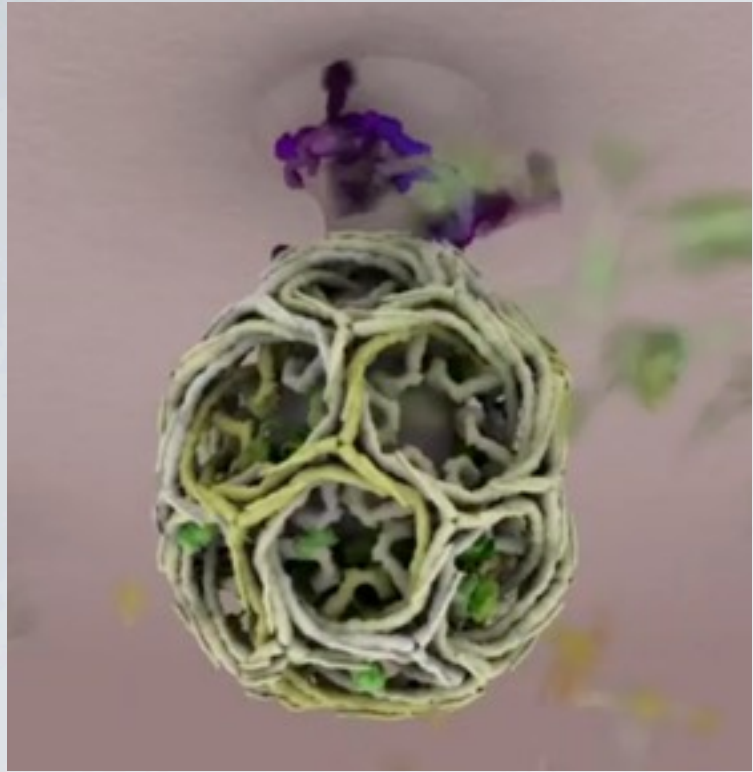


DYNAMIN - 2012



DYNAMIN - 2014



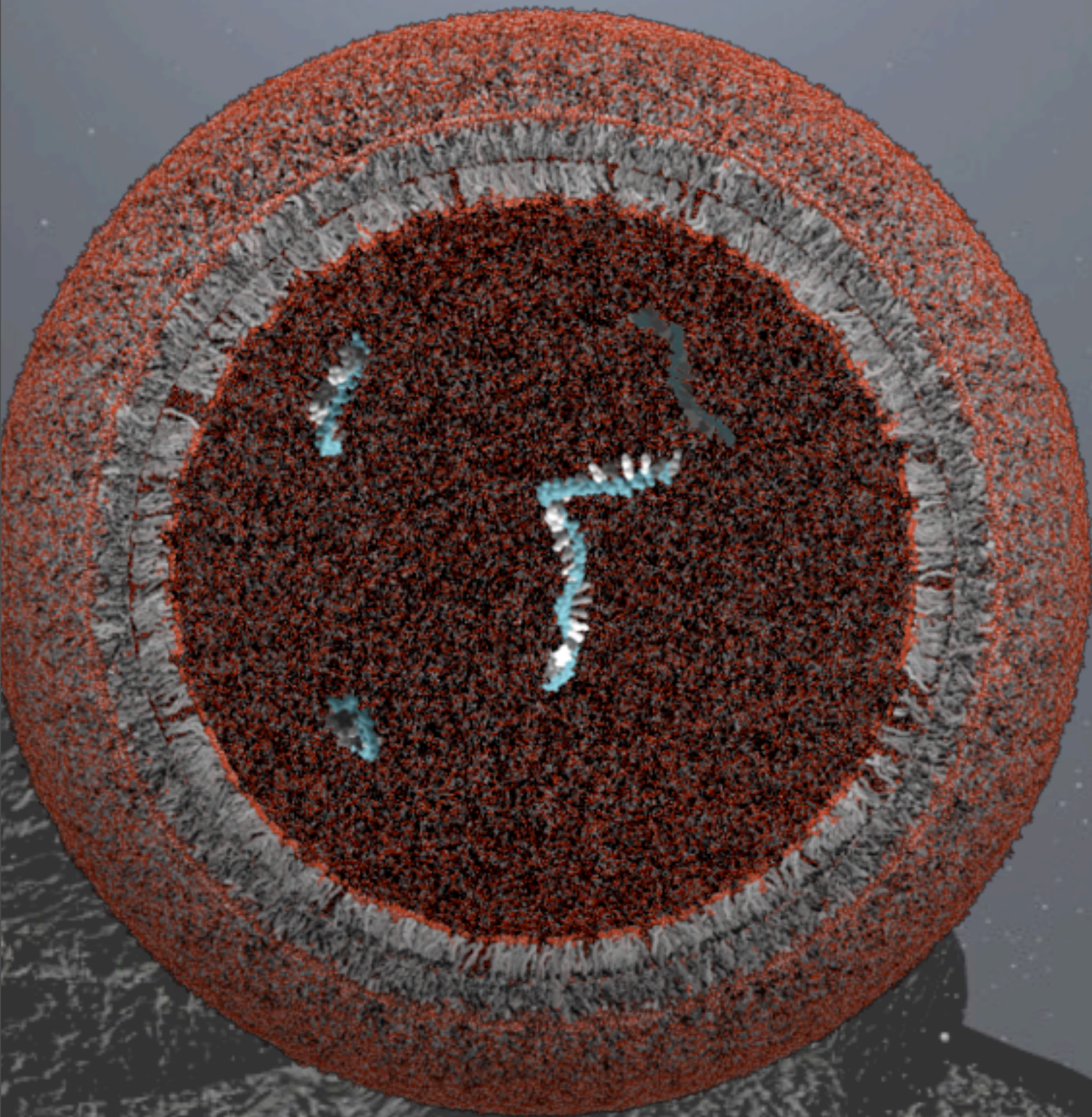


“Molecular 3D animations inform both the scientist who creates them and the audience that views them, through an active process leading to further inquiry and discovery.”

- 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

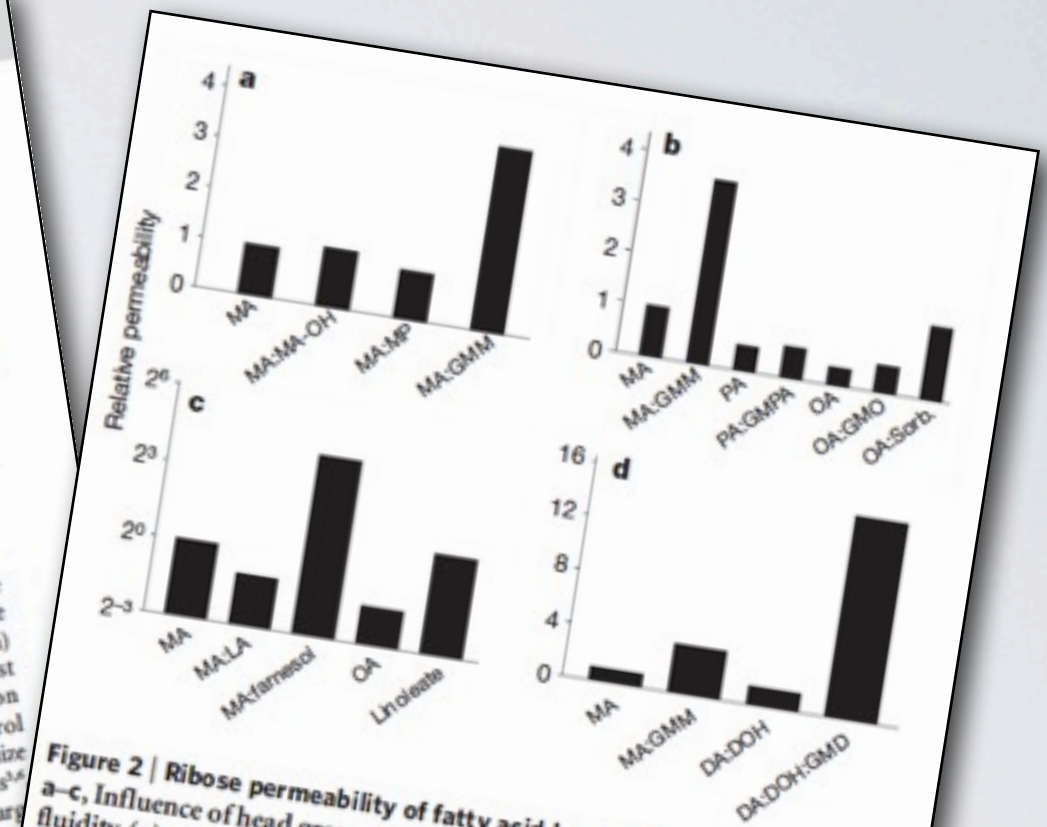
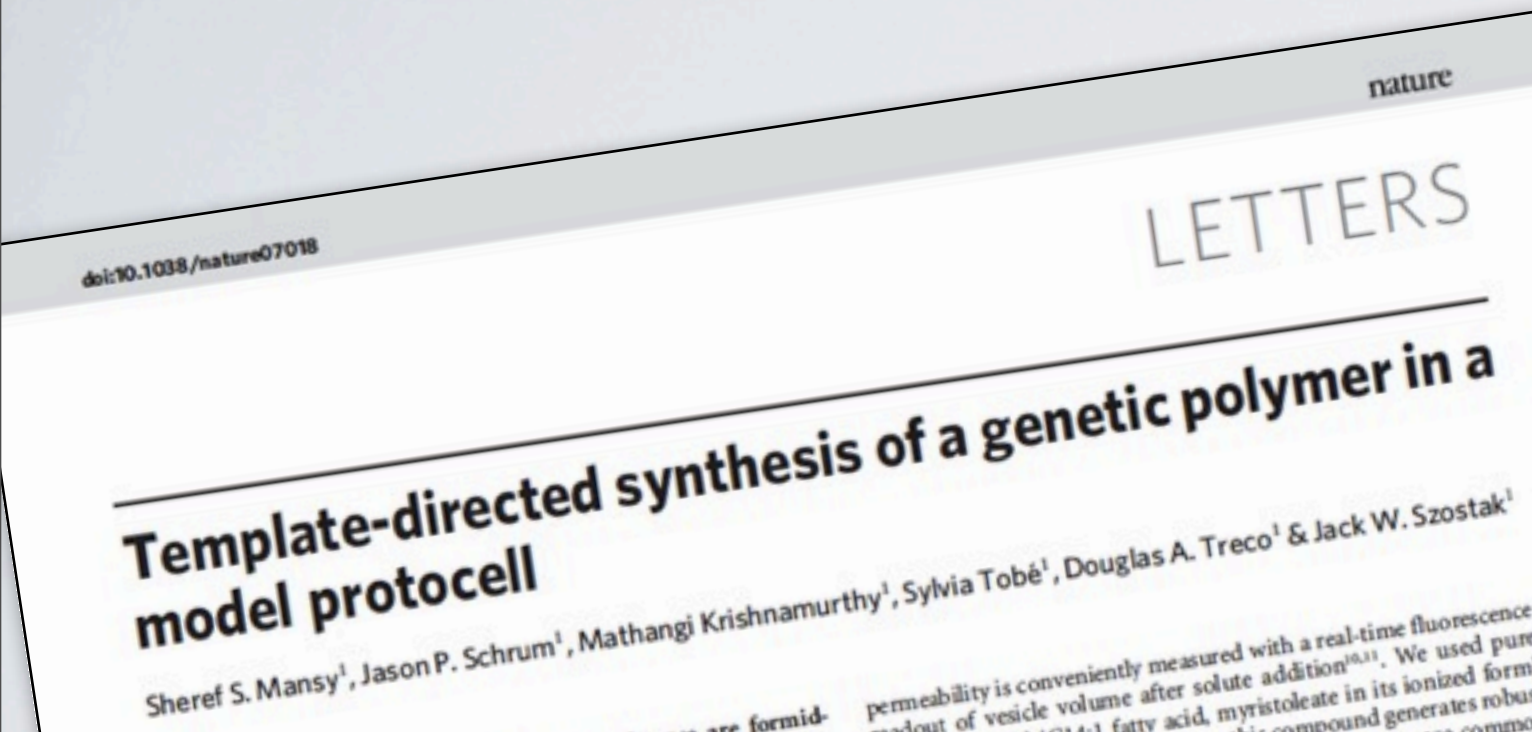
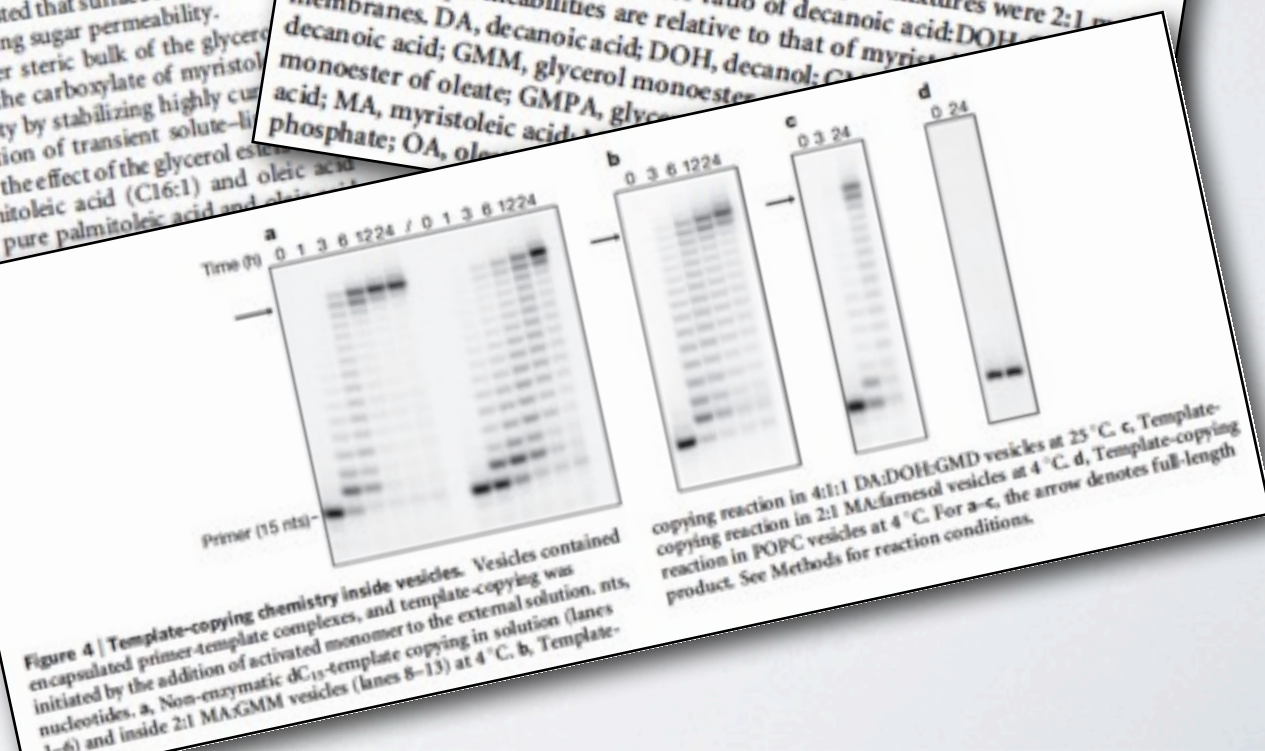
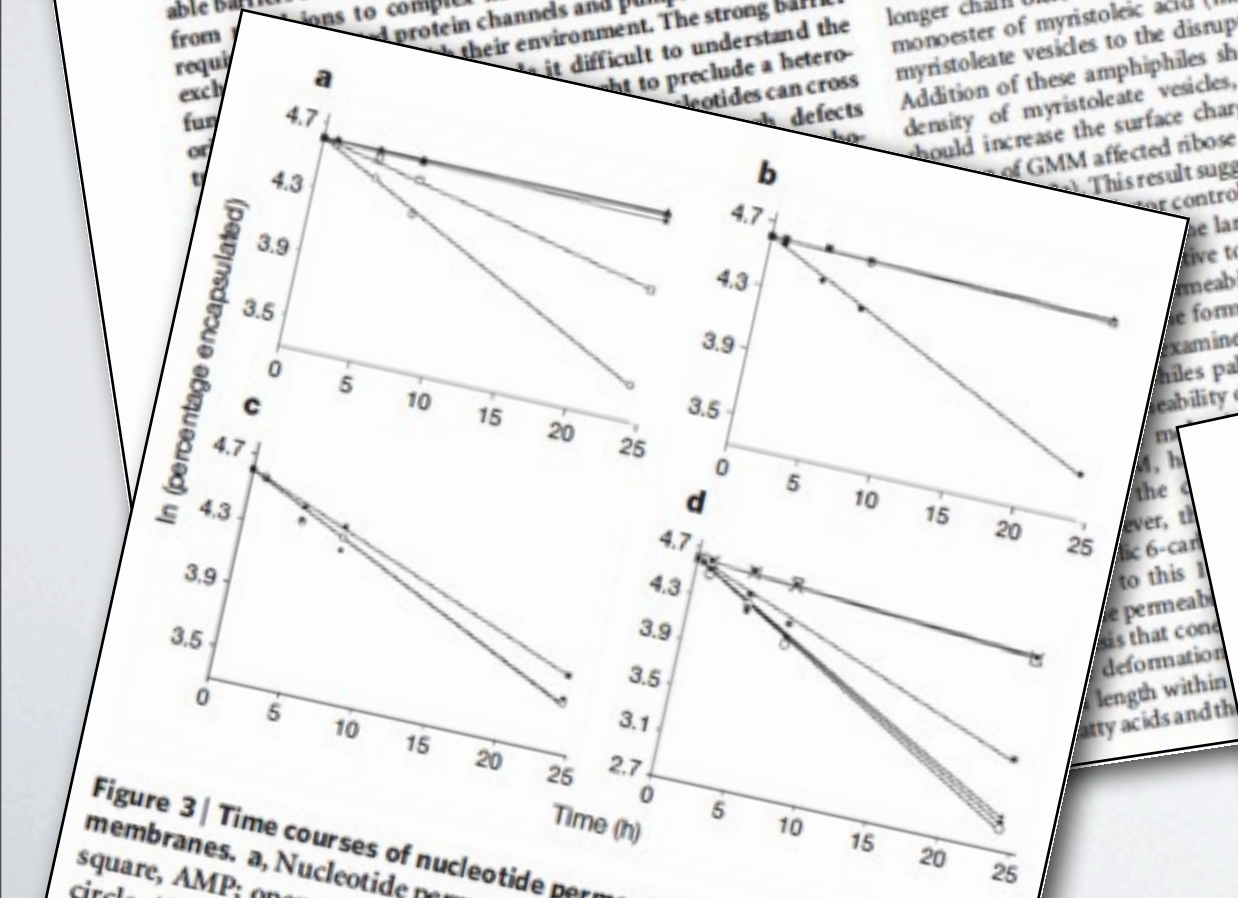


Figure 2 | Ribose permeability of fatty acid based membranes. a-c, Influence of head group charge (a), head group size (b) and membrane fluidity (c). d, Comparison of decanoic-acid-based membranes with myristoleic acid based membranes. All binary lipid mixtures were 2:1 ratio of fatty acid: additive; a 4:1:1 ratio of decanoic acid:DOH:GMM was used. Ribose permeabilities are relative to that of myristoleic acid based membranes. DA, decanoic acid; DOH, decanol; GMM, glycerol monoester of oleate; GMPE, glycerol monoester of palmitoleic acid; MA, myristoleic acid; MP, myristoleyl alcohol; OA, oleic acid; PA, palmitoleic acid; S, sorbitol.



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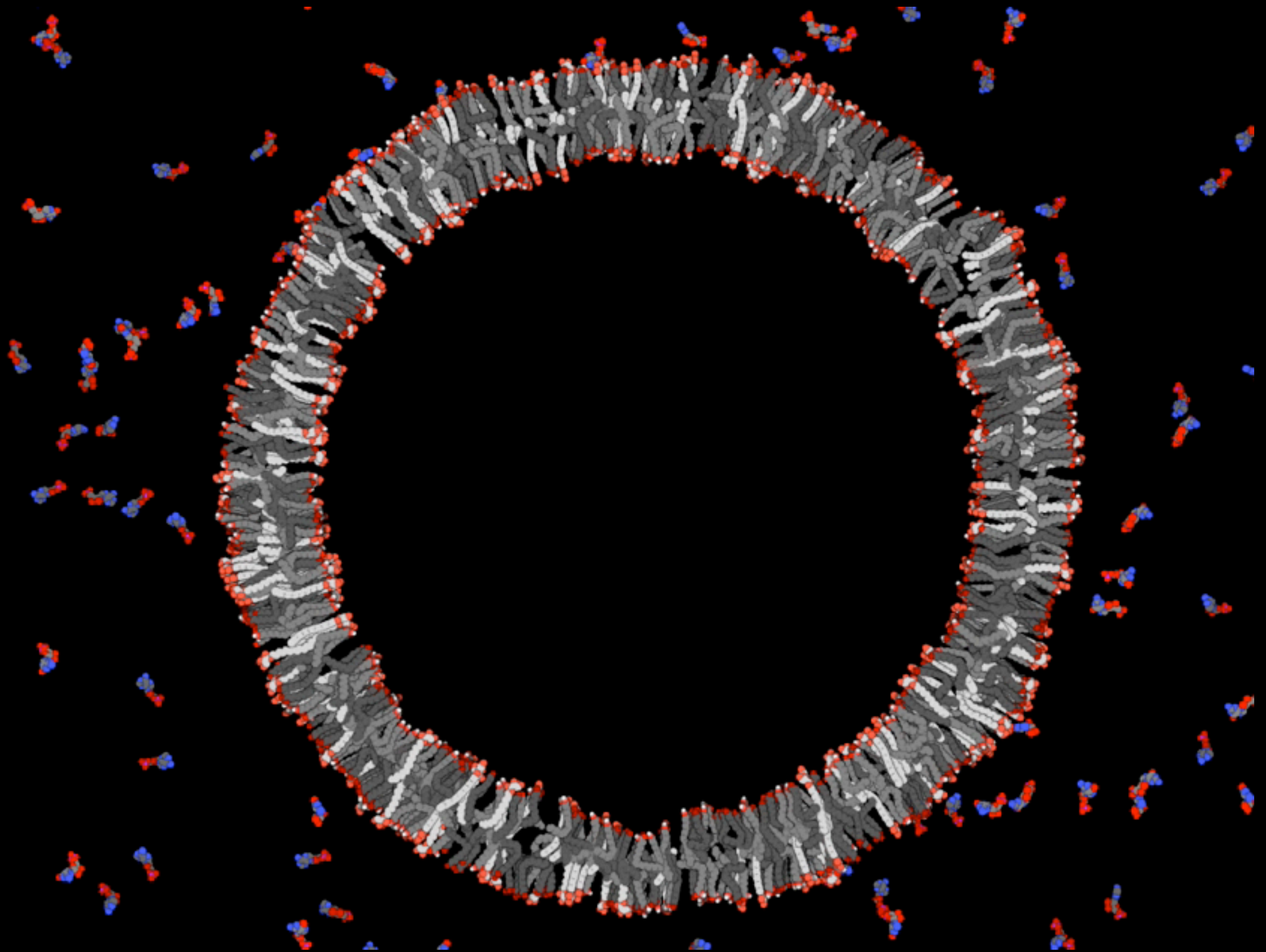
News and Events

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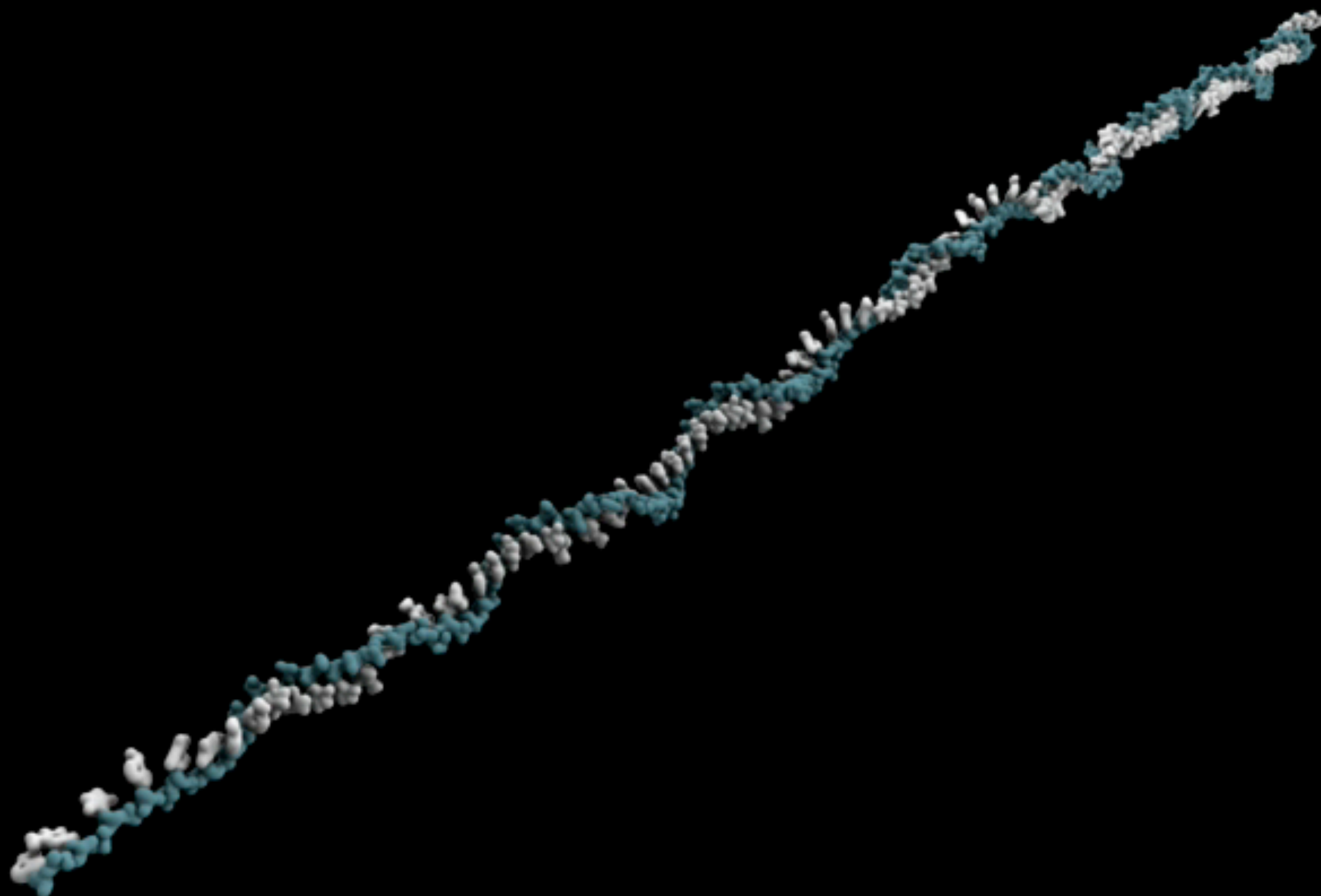


Artwork by
Fausto de Martini

HEADSPACE



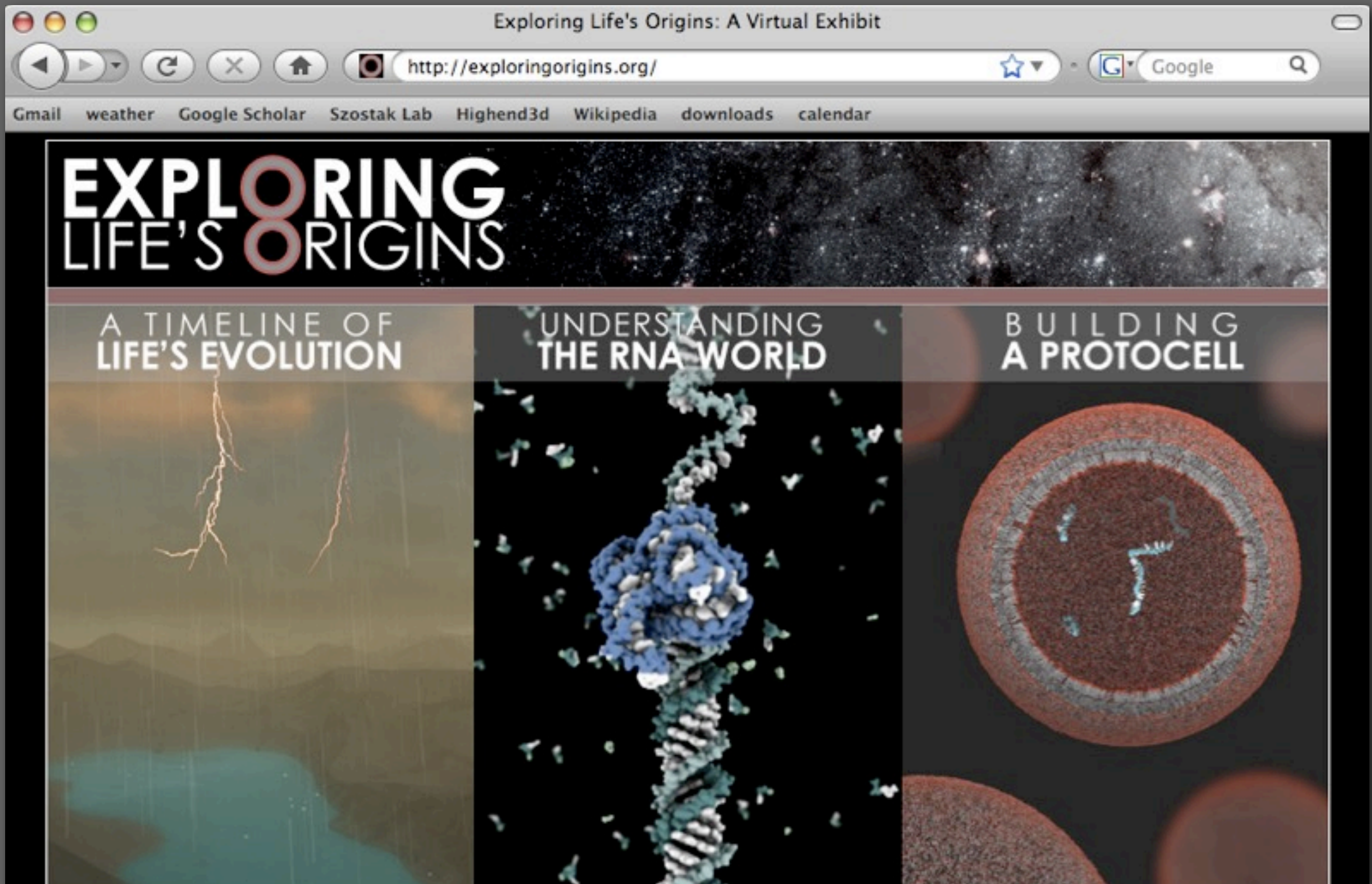
Entry of Small Molecules into Vesicles
with Jack Szostak | Harvard Medical School



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



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



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

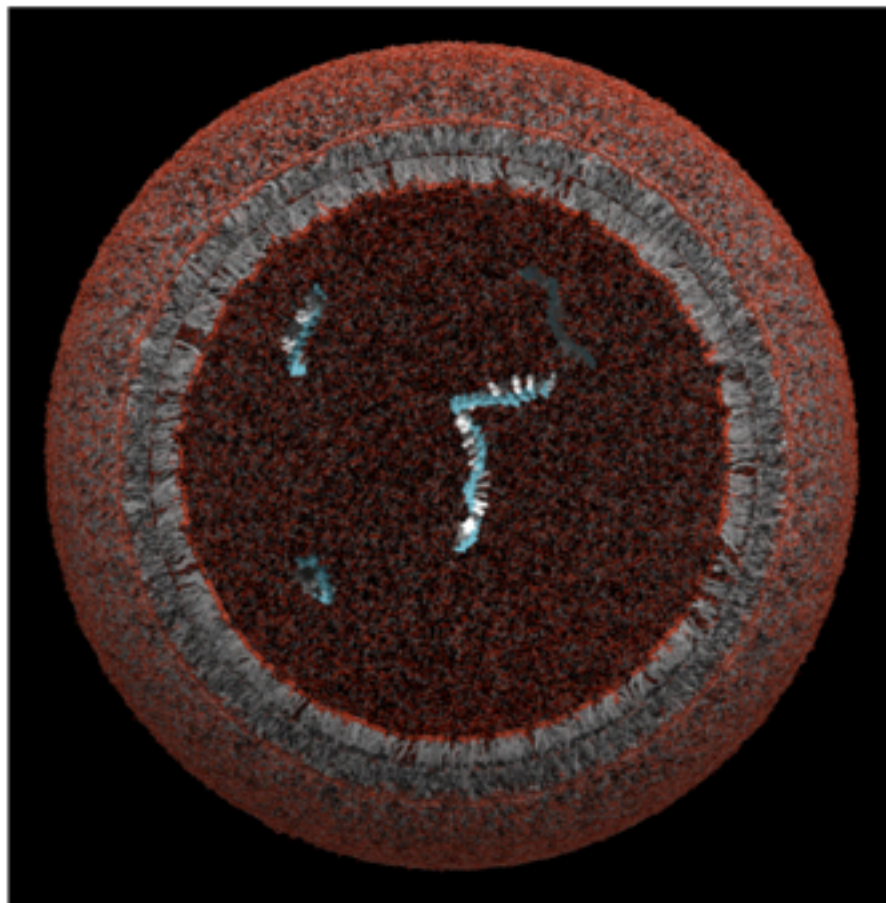
Wired Science's 13 Most Popular Stories of 2008

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

TUESDAY, JUNE 16, 2009

New Glimpses of Life's Puzzling Origins

By NICHOLAS WATKINS

Some 3.5 billion years ago, a shift in the orbit of the Sun's inner planets sent a surge of large comets and asteroids careening into the inner solar system. These violent impacts gouged out the large craters still visible on the Moon's face, heated Earth's surface and melted rock and boiled off its oceans, even as it condensed into a

The rocks that formed on Earth 3.5 billion years ago, almost as soon as the bombardment had stopped, contain possible evidence of biological processes. If life can arise from inorganic matter to quickly and easily, why is it not abundant in the solar system and beyond? If biology is an inherent property of matter, why have chemists so far been unable to reconstruct life, or anything close to it, in the laboratory?

The origin of life on Earth bristles with puzzle and paradox. Which came

Researchers find new ways for biochemicals to self-assemble.

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

The questions may seem moot, since life did start somewhere. But for the small group of researchers who insist on learning exactly how it started, frustration has abounded. Many once-promising leads have led only to years of wasted effort. Scientists as eminent as Francis Crick, the chief theorist of molecular biology, have quietly suggested that life may have formed elsewhere before settling the planet, so hard does it seem to find a plausible explanation for its emergence on Earth.

In the last few years, however, two 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 three colleagues as to whether a genetic system or a cell membrane came first in the development of life. They eventually agreed that genetics and membranes had to have evolved together.

The three researchers, Jack W. Szostak, David P. Bartel and P. Luigi Latt, published a somewhat adventurous manifesto in *Nature* in 2005, declaring that the way to make a synthetic cell was to get a protocol and a genetic molecule to grow and divide in parallel.

Continued on Page 4

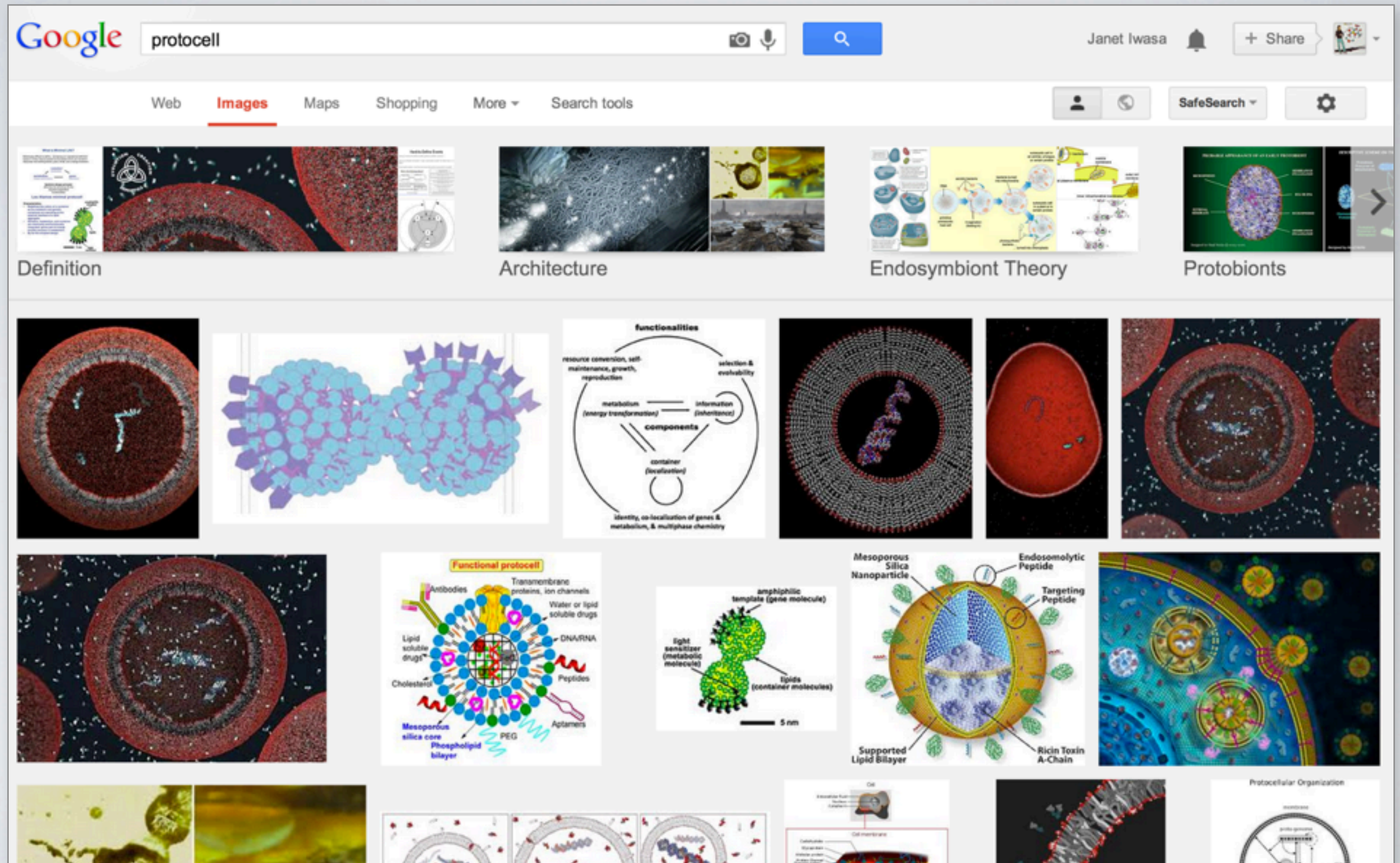


A START In one view of the beginnings of life, depicted in an animation, carbon monoxide molecules condense on hot mineral surfaces underground to form fatty acids, shown, which are then expelled from geysers. The acids are driven together in spherical clumps as water evaporates, above and below left, 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.



ILLUSTRATION BY JAMES H. HAYES

MAKING RESEARCH ACCESSIBLE



MAKING RESEARCH ACCESSIBLE

Google Janet Iwasa

Web **Images** Maps Shopping More Search tools

Definition **Architecture** Endosymbiont Theory Protobionts

Functionalities

- resource conversion, self-maintenance, growth, reproduction
- metabolism (energy transformation)
- information (inheritance)
- components
- container (localization)
- selection & evolvability
- identity, co-localisation of genes & metabolism, & multiphase chemistry

Functional protocell

- Antibodies
- Transmembrane proteins, ion channels
- Water or lipid soluble drugs
- DNA/RNA
- Peptides
- Aptamers
- PEG
- Mesoporous silica core
- Phospholipid bilayer
- Cholesterol
- Lipid soluble drugs

Light sensitizer (metabolic molecule)

Amphiphilic template (gene molecule)

Lipids (container molecules)

5 nm

Mesoporous Silica Nanoparticle

Endosomolytic Peptide

Targeting Peptide

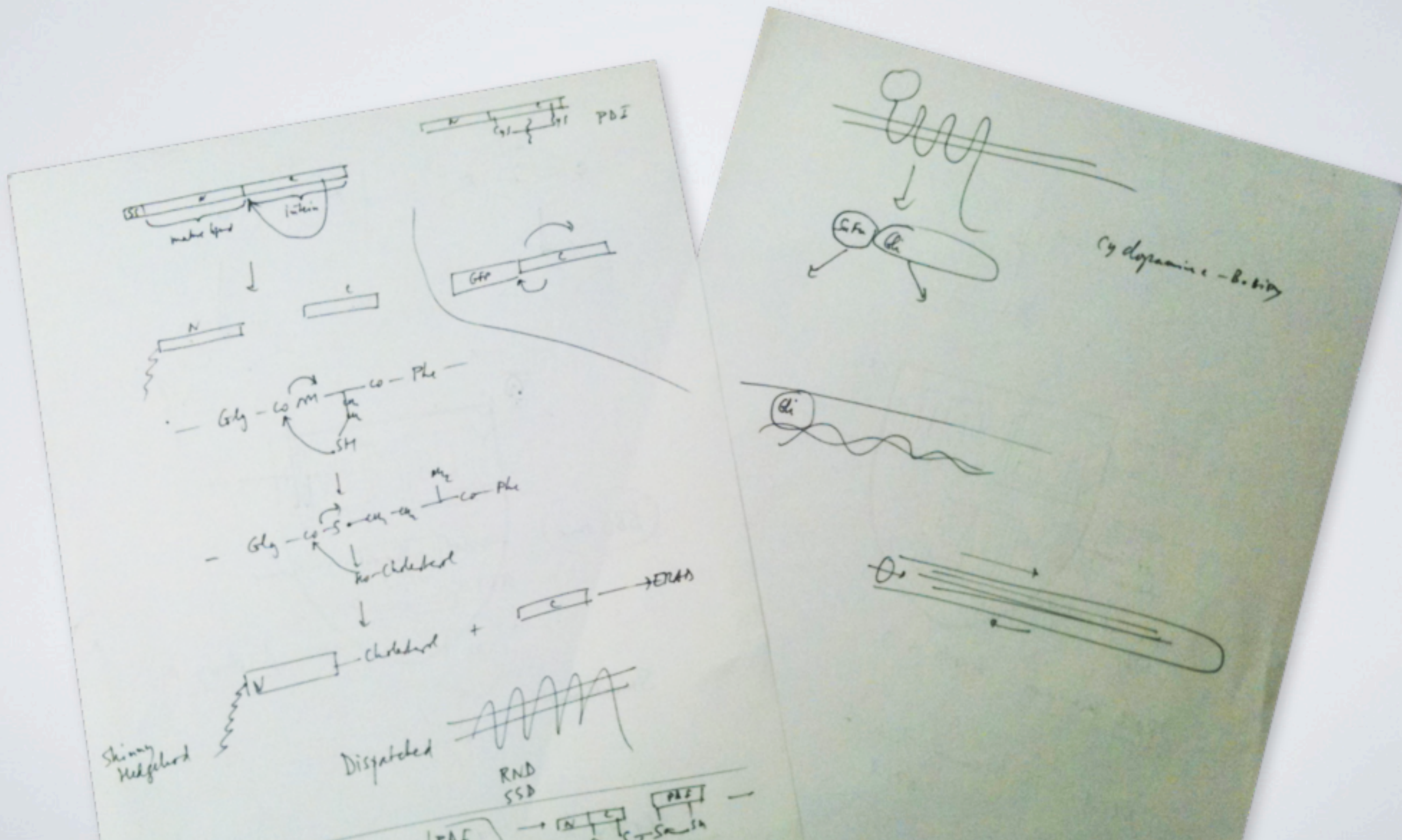
Ricin Toxin A-Chain

Supported Lipid Bilayer

Protocellular Organization

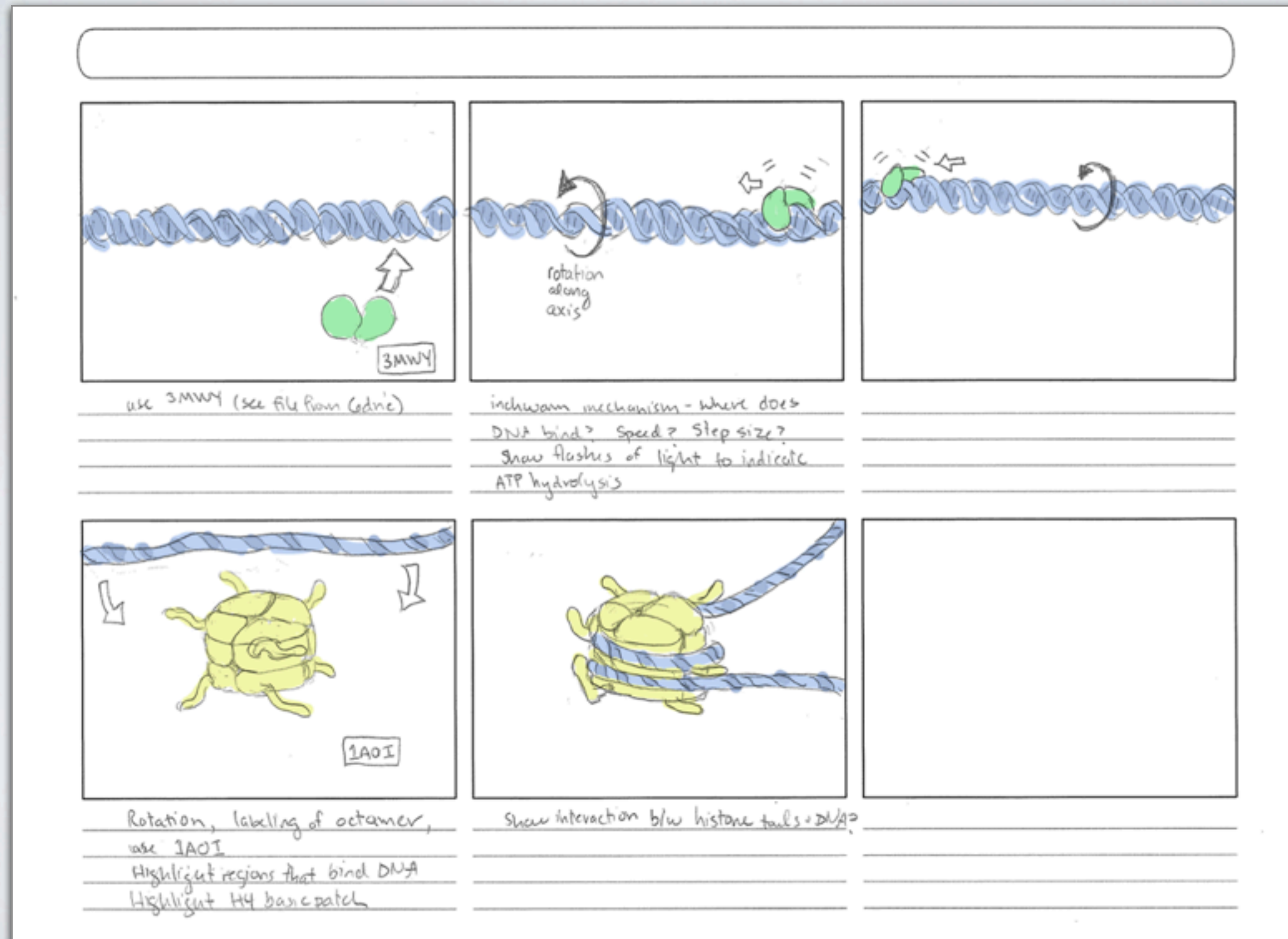
THE MAKING OF AN ANIMATION

I. What is the story?



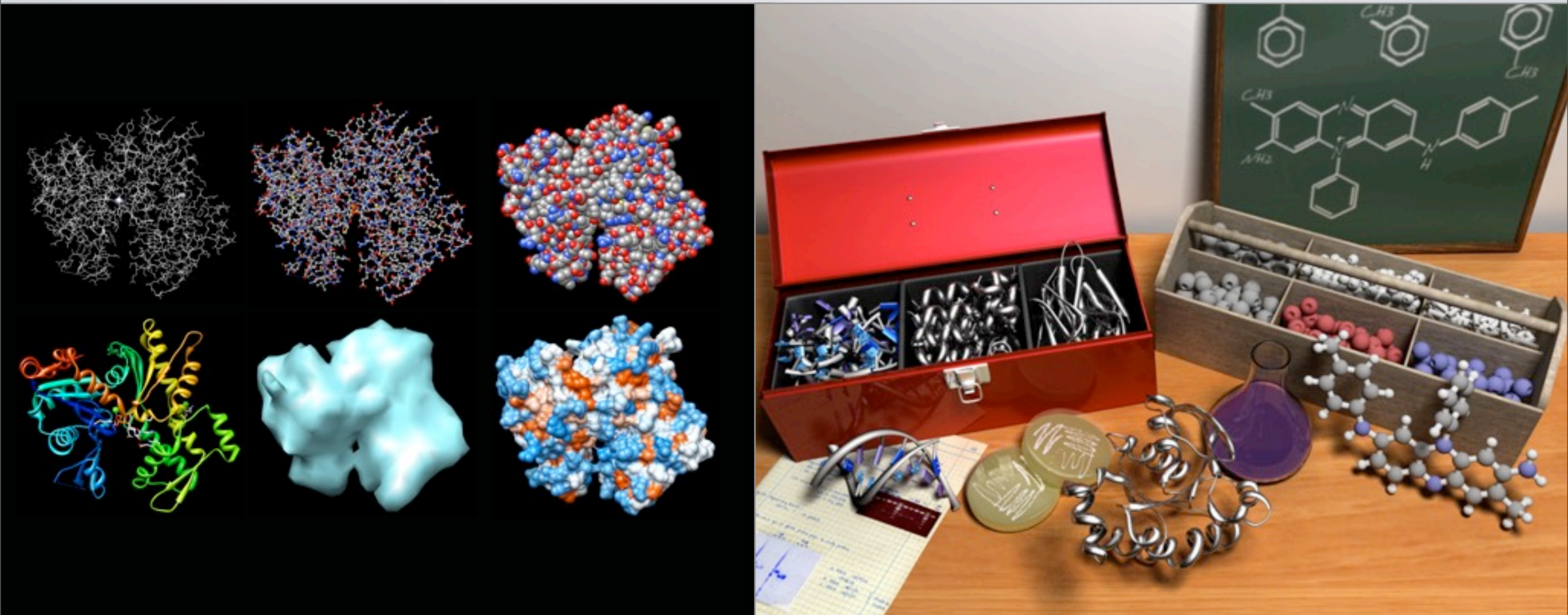
THE MAKING OF AN ANIMATION

2. Drawing a storyboard



THE MAKING OF AN ANIMATION

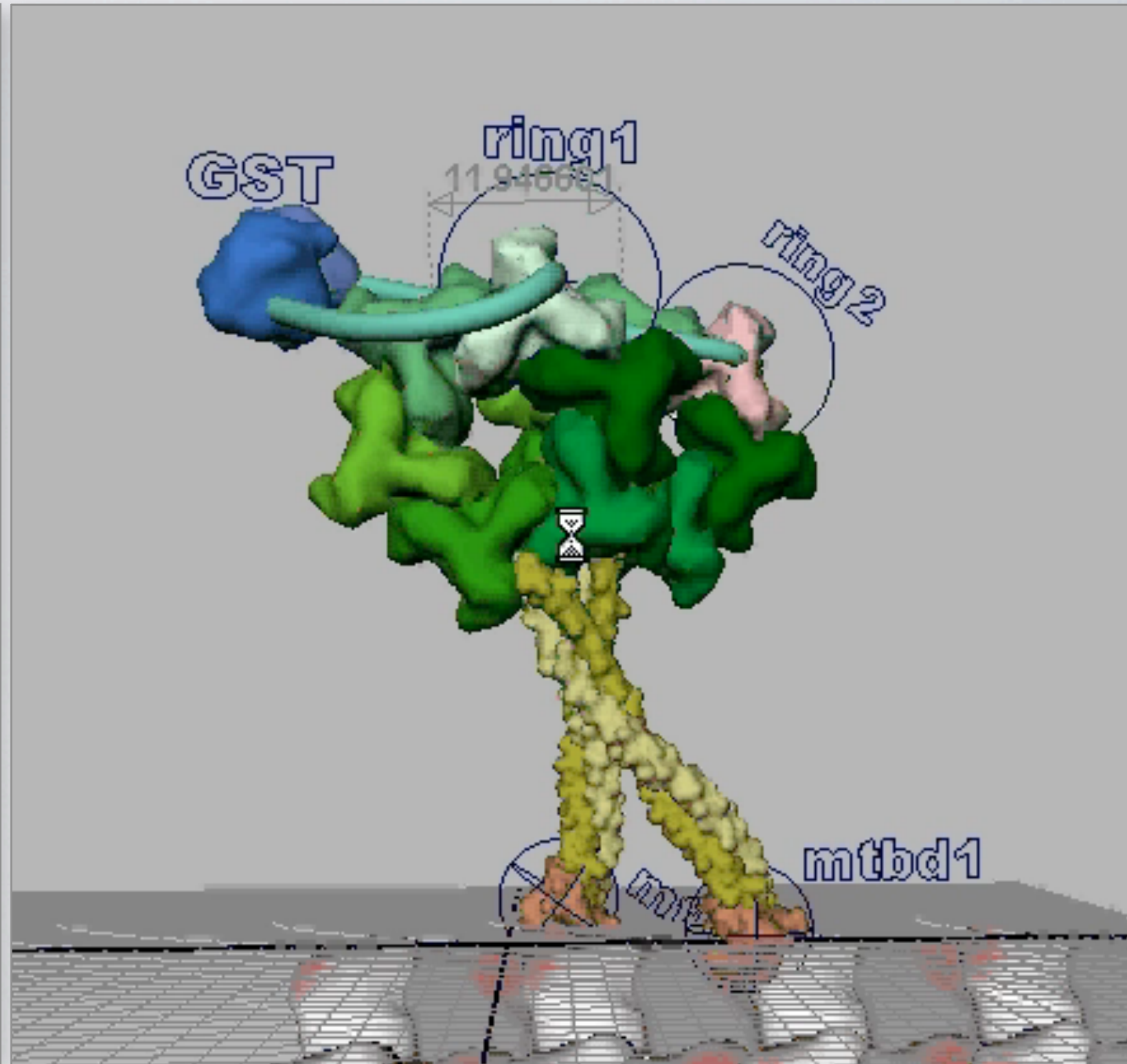
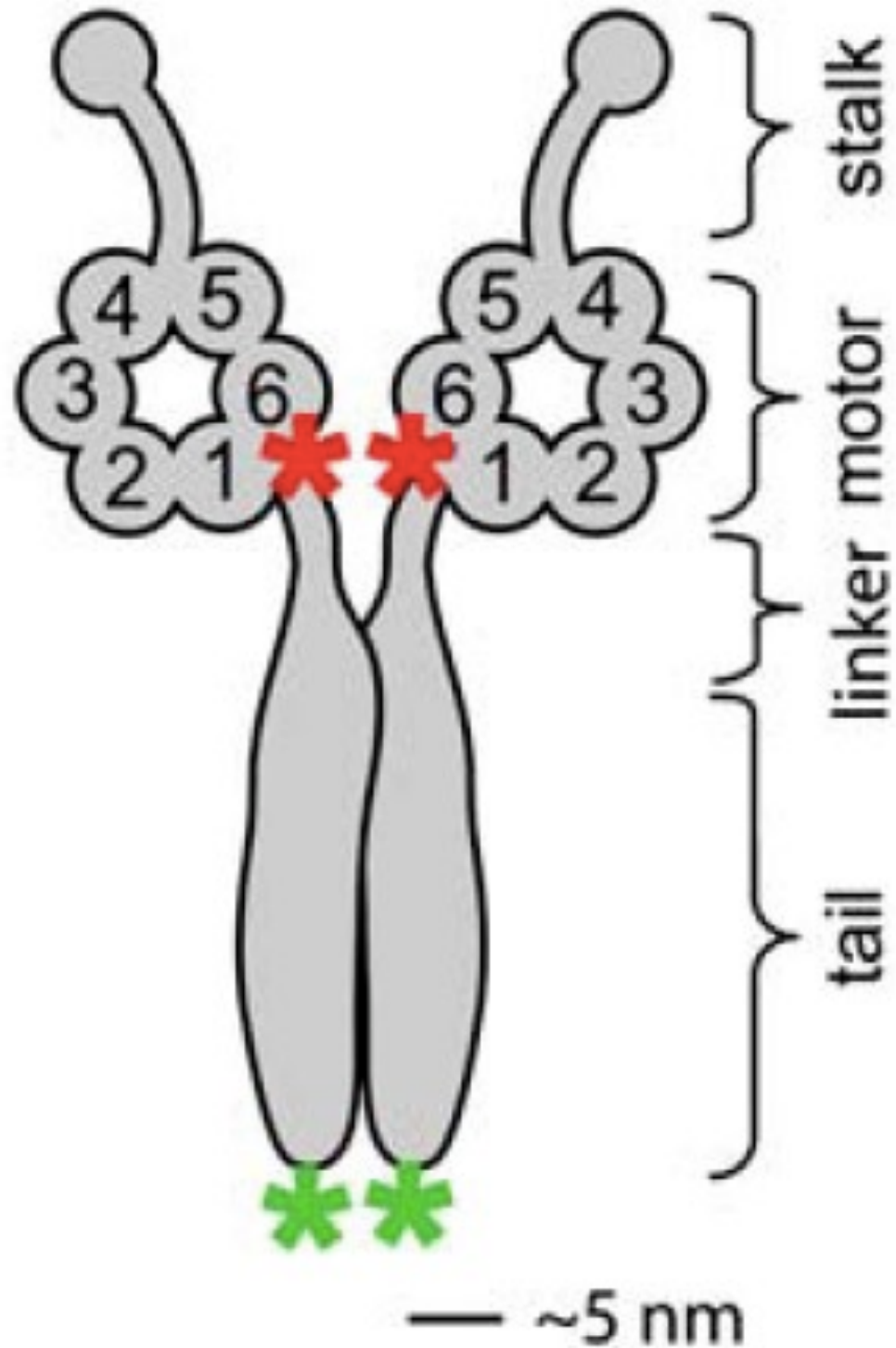
3. Modeling proteins and other structures



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

THE MAKING OF AN ANIMATION

an articulated model of dynein



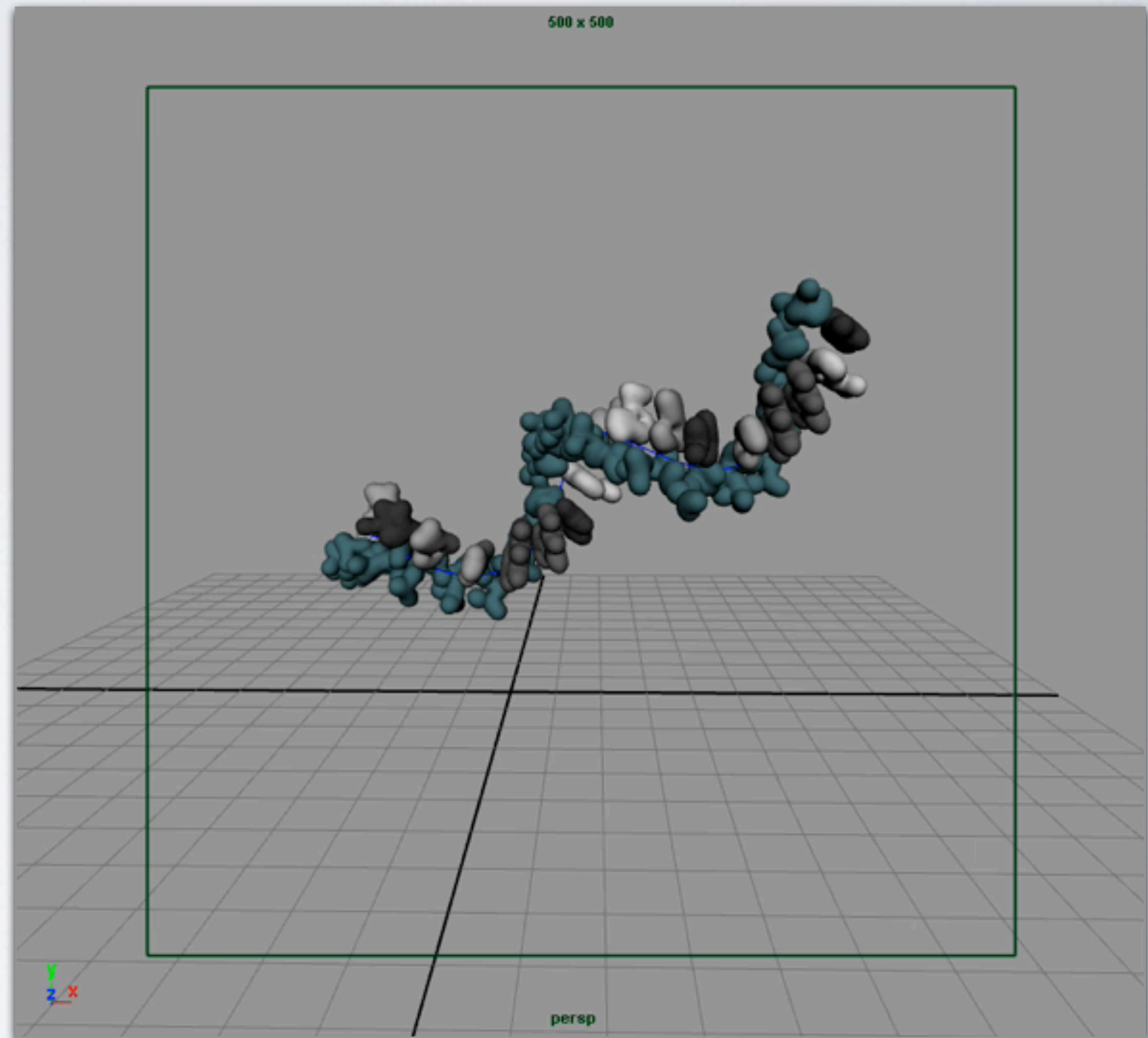
with Sam Reck-Peterson, Harvard Medical School

THE MAKING OF AN ANIMATION

4. Animation

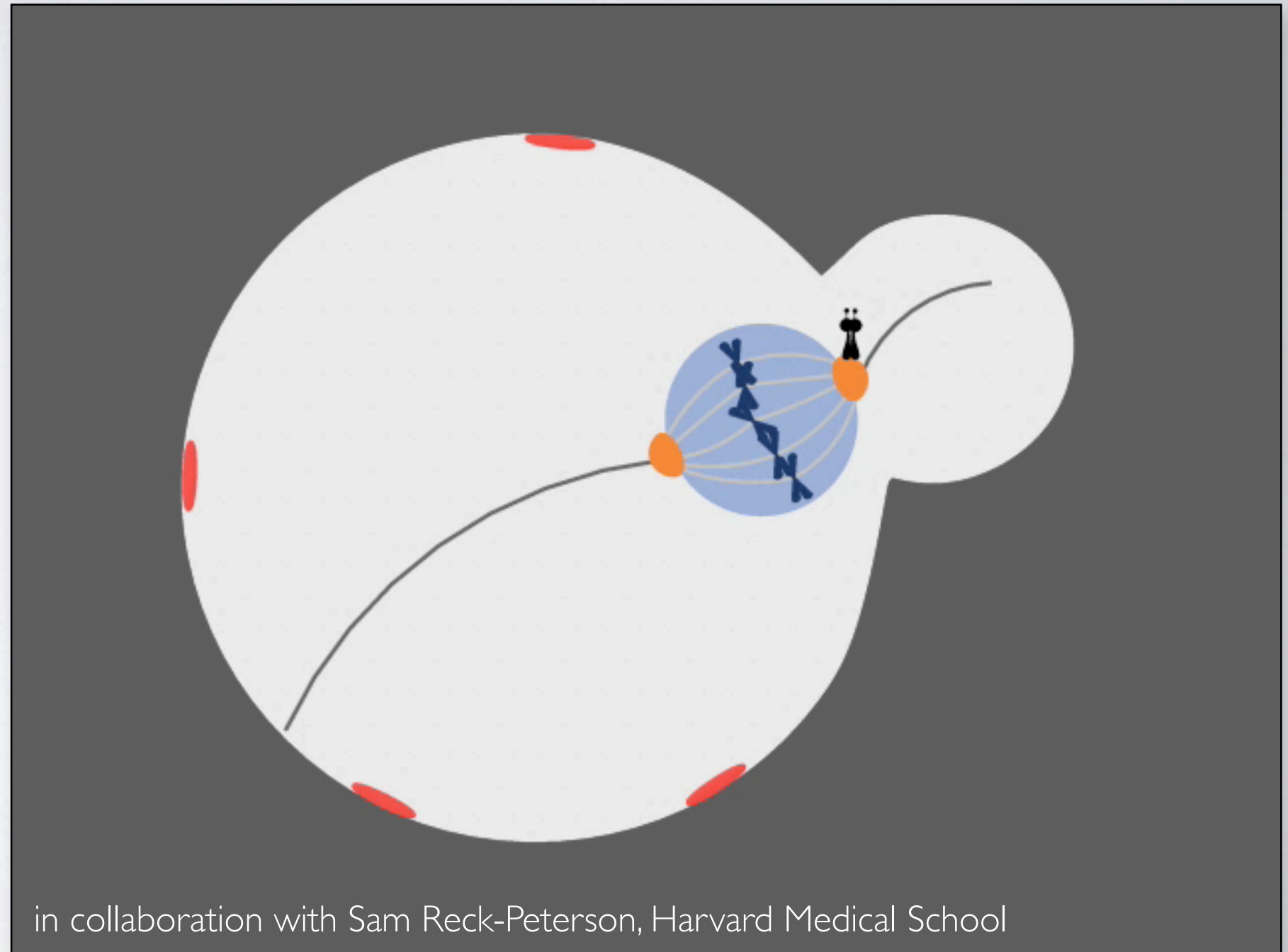
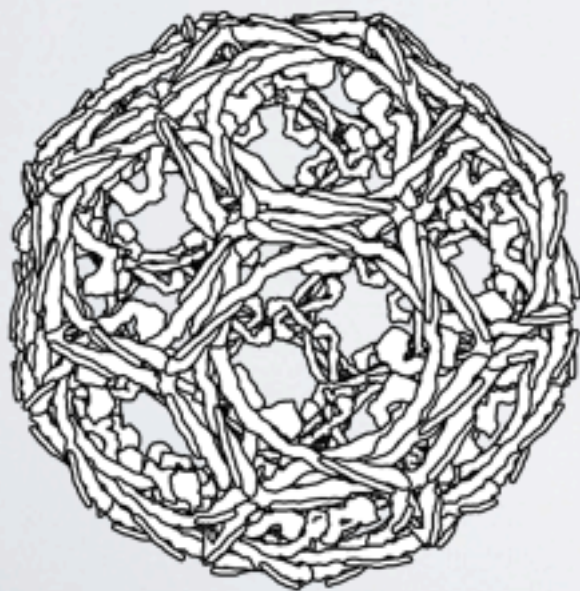
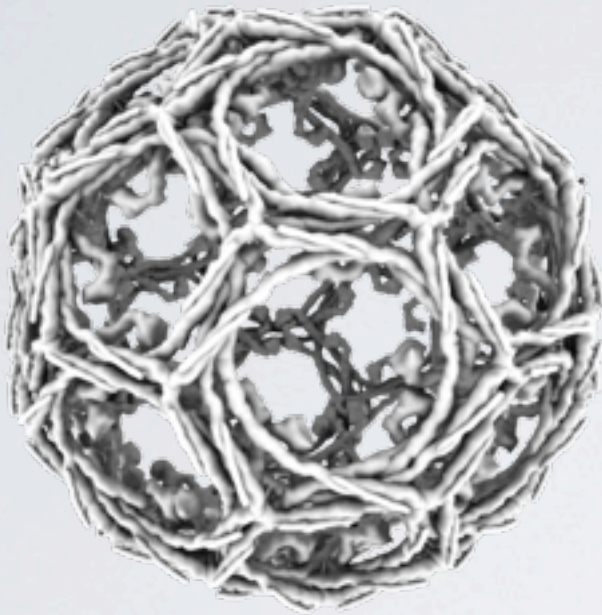
What tools are available?

How to create animations that can depict expected molecular motions?

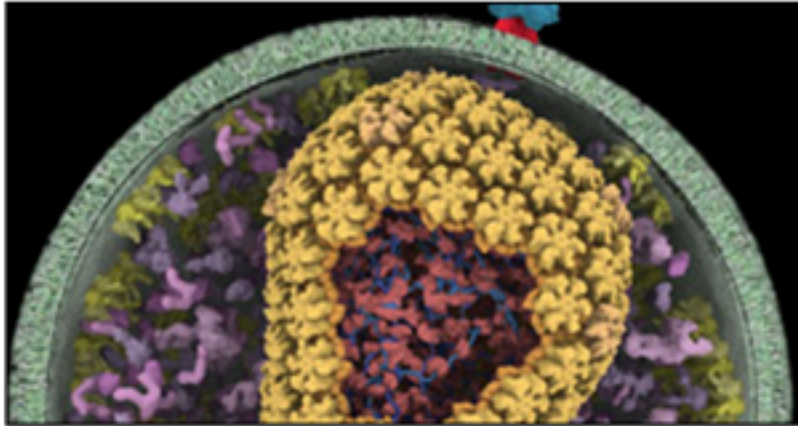


THE MAKING OF AN ANIMATION

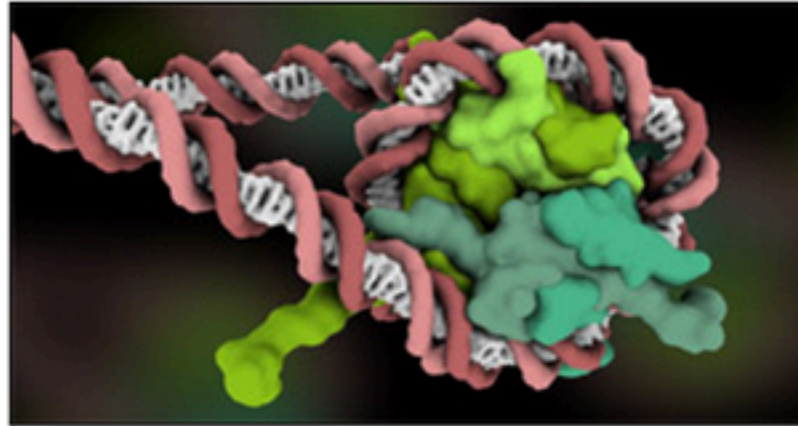
5. Rendering



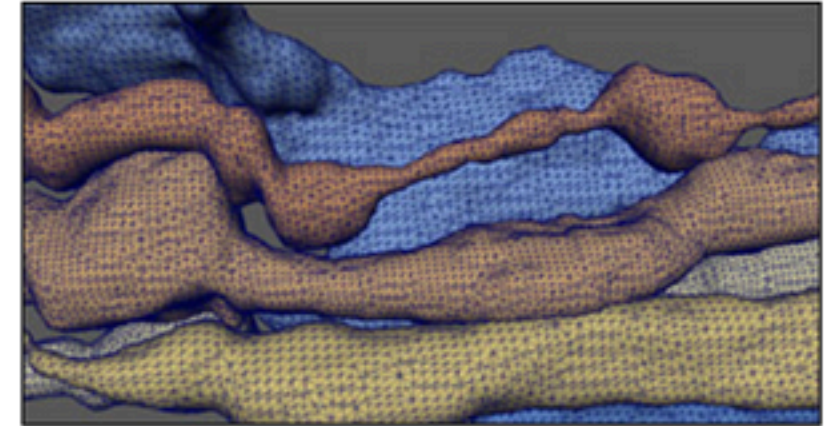
CURRENT PROJECTS



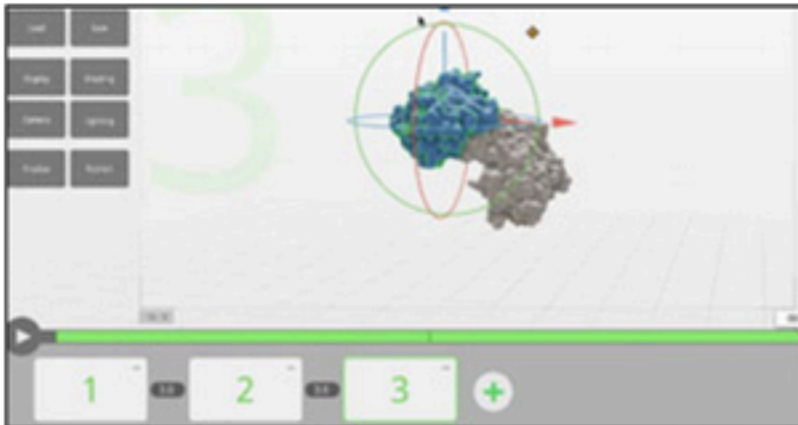
HIV entry and egress



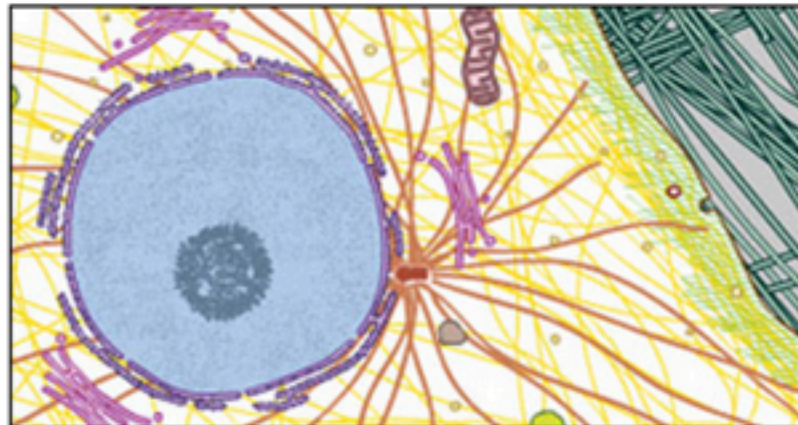
Chromatin remodeling



Visualizing neurons



Molecular flipbook

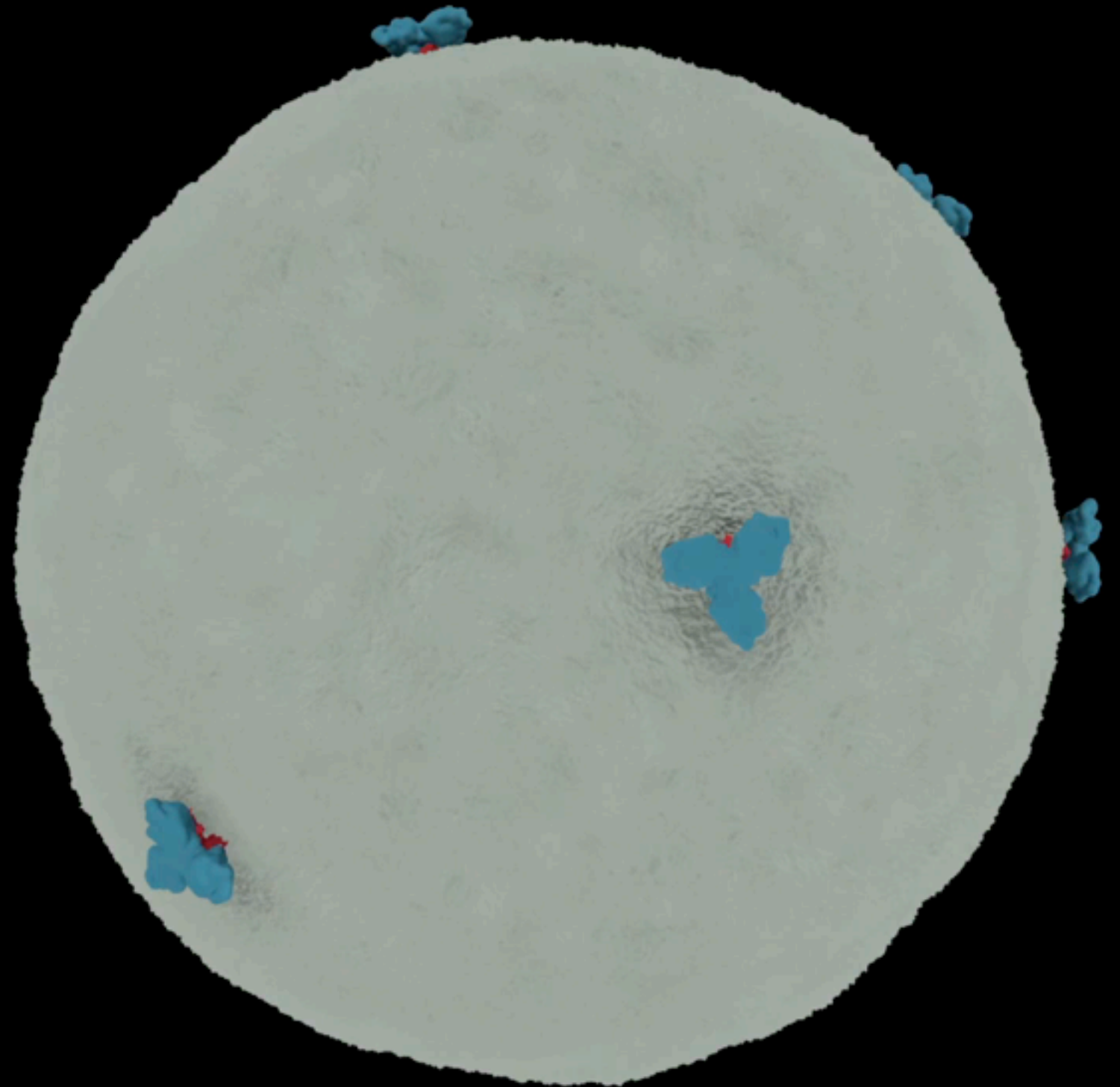


Cell image library

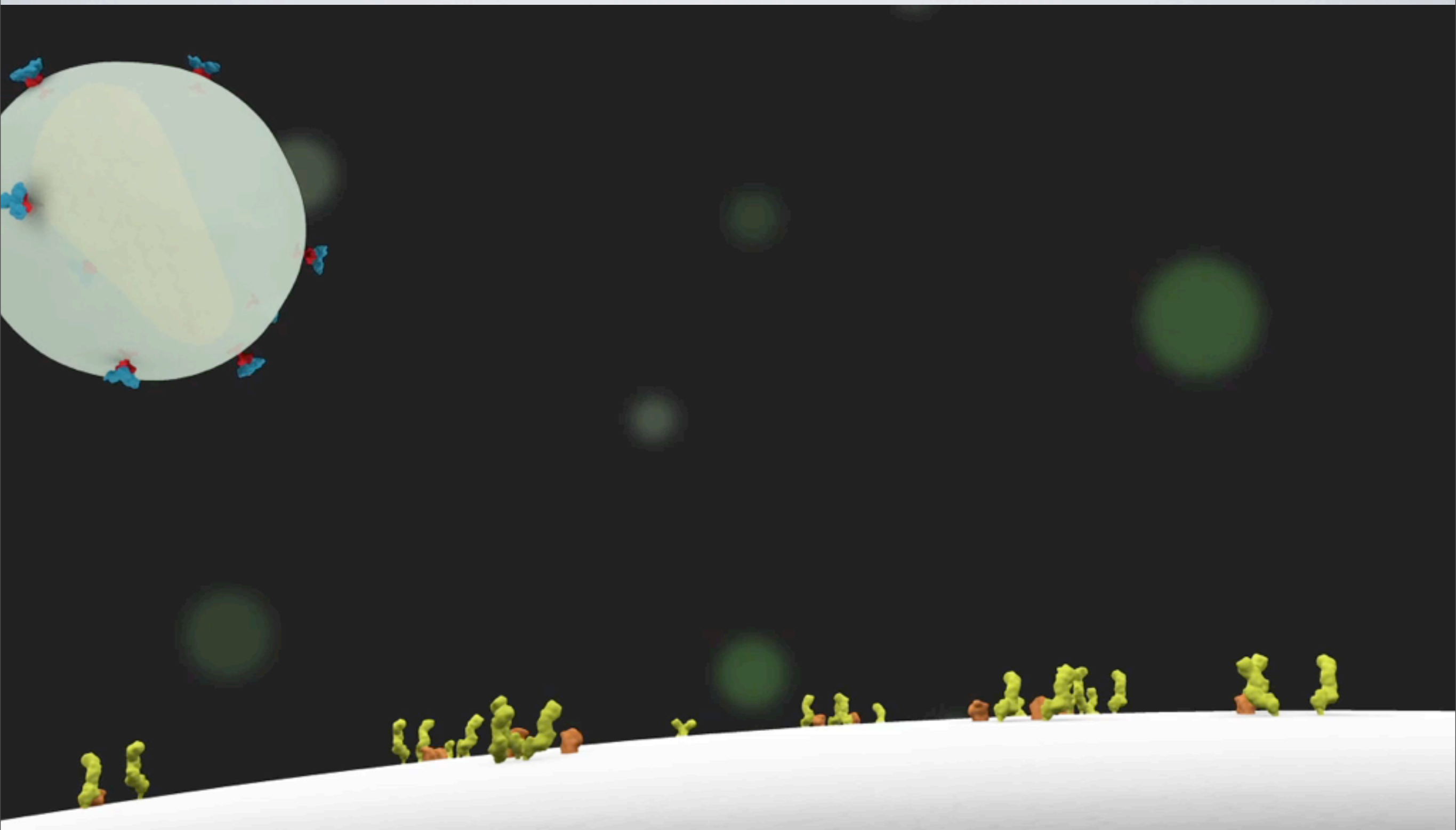
ANIMATING THE HIV LIFE CYCLE

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

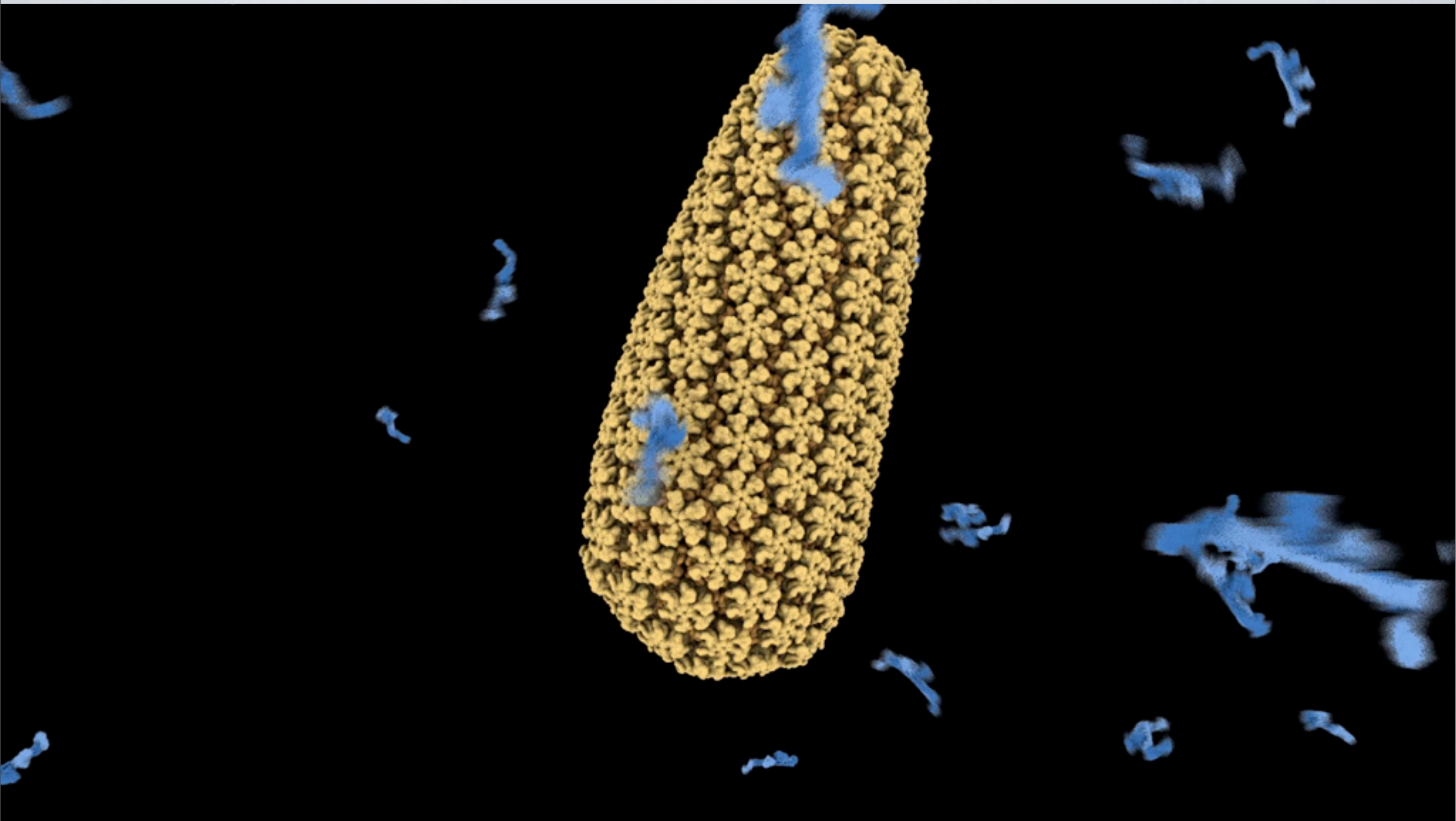
**Human
Immunodeficiency
Virus
(HIV)**



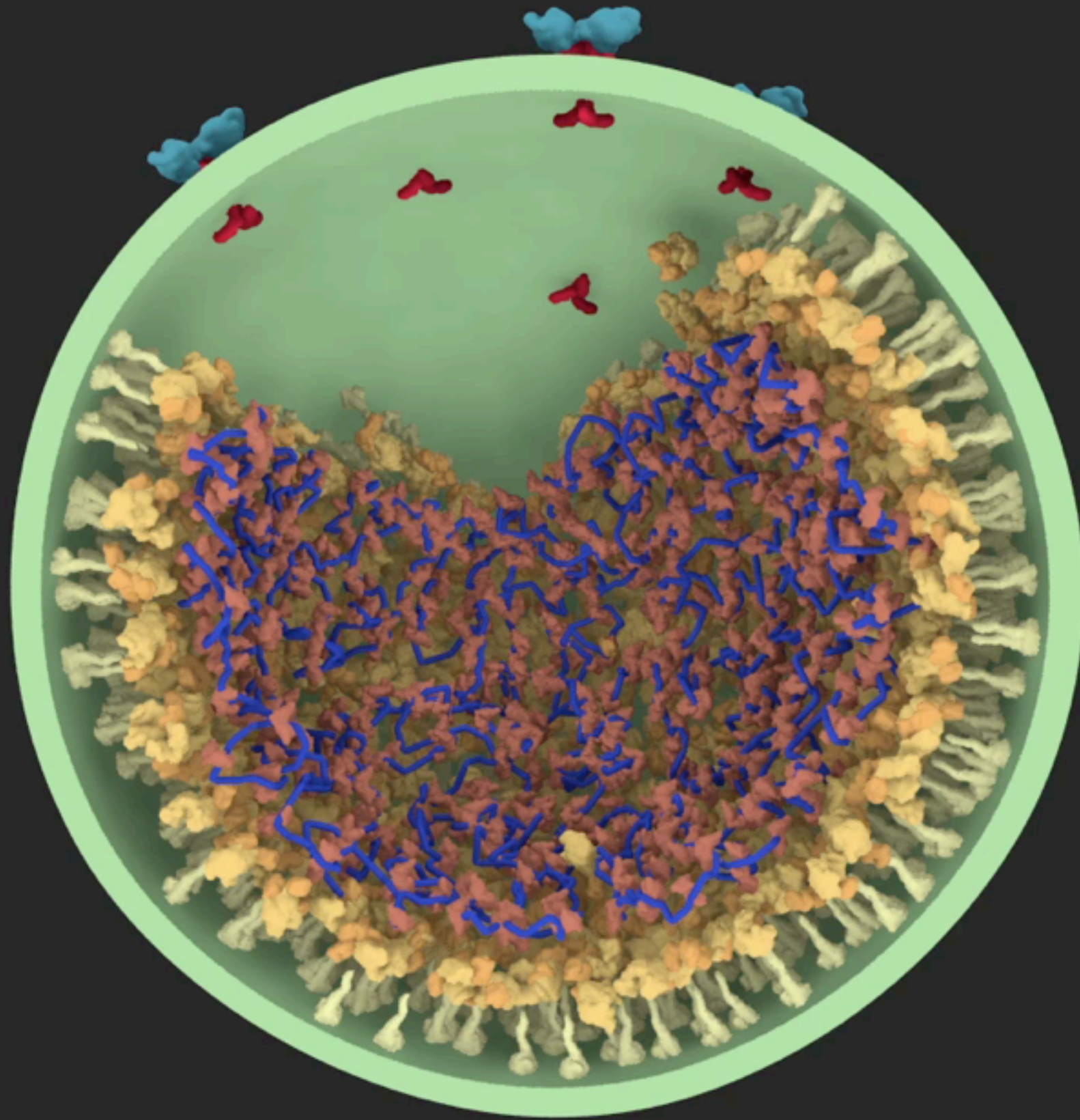
HIV ENTRY



TRIM5 α LATTICE FORMATION

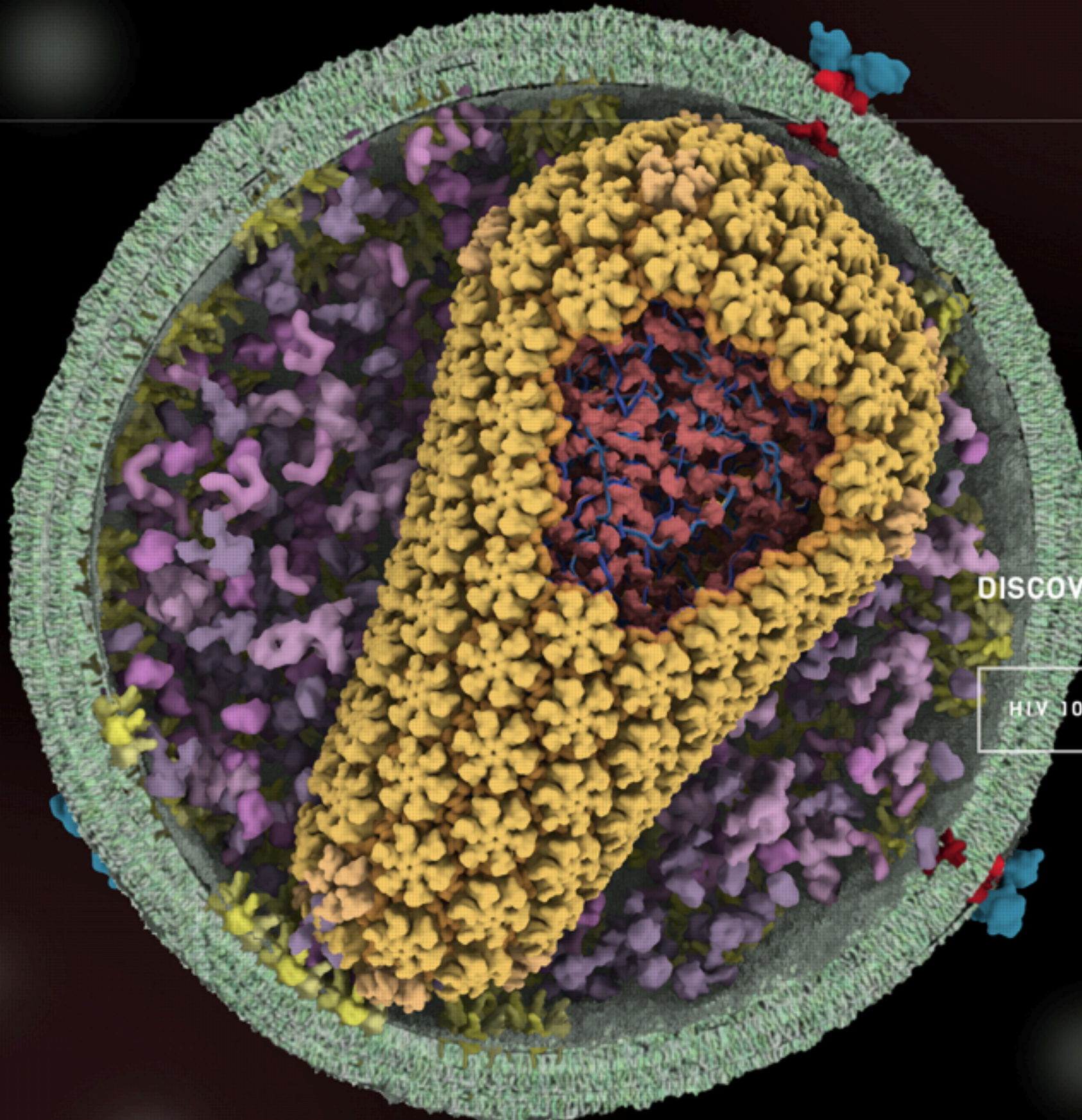


HIV MATURATION



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.

The lesson player interface features a grid of 40 diverse avatars arranged in four rows of ten. Overlaid on the grid is a video player with the title "WHY IT'S SO HARD TO CURE HIV/AIDS" in large, bold, green and orange letters. A play button is visible in the center of the grid. At the bottom of the player, a progress bar shows the video is at 0:00 / 4:31.

Watch

Think

Dig Deeper

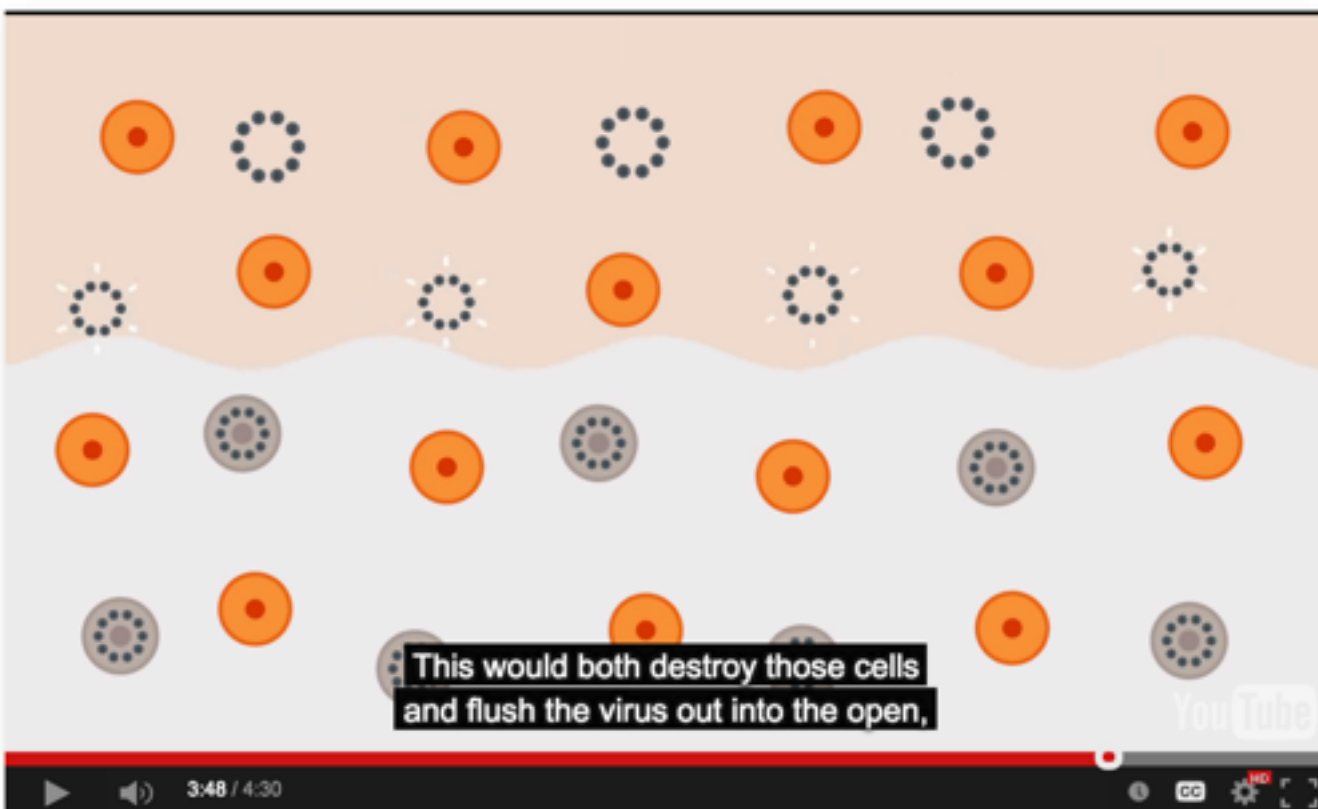
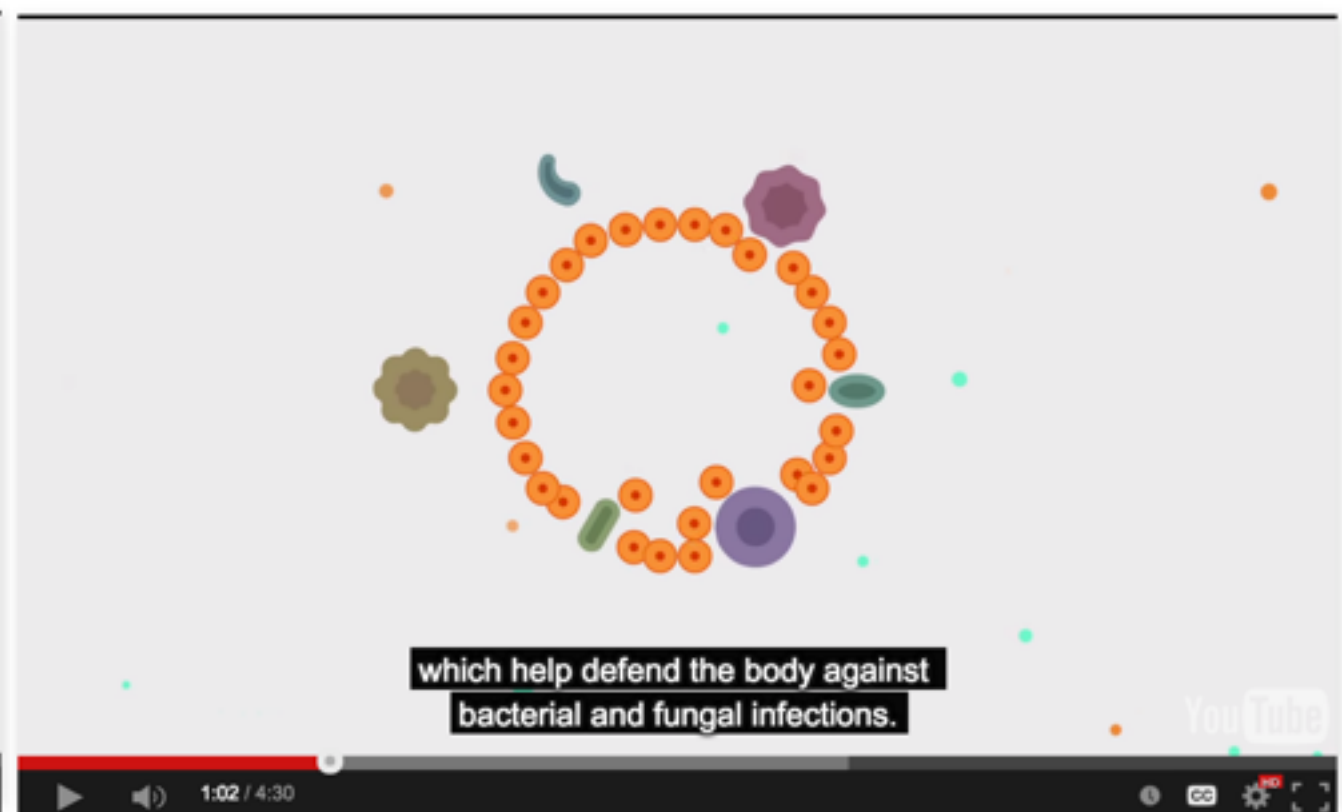
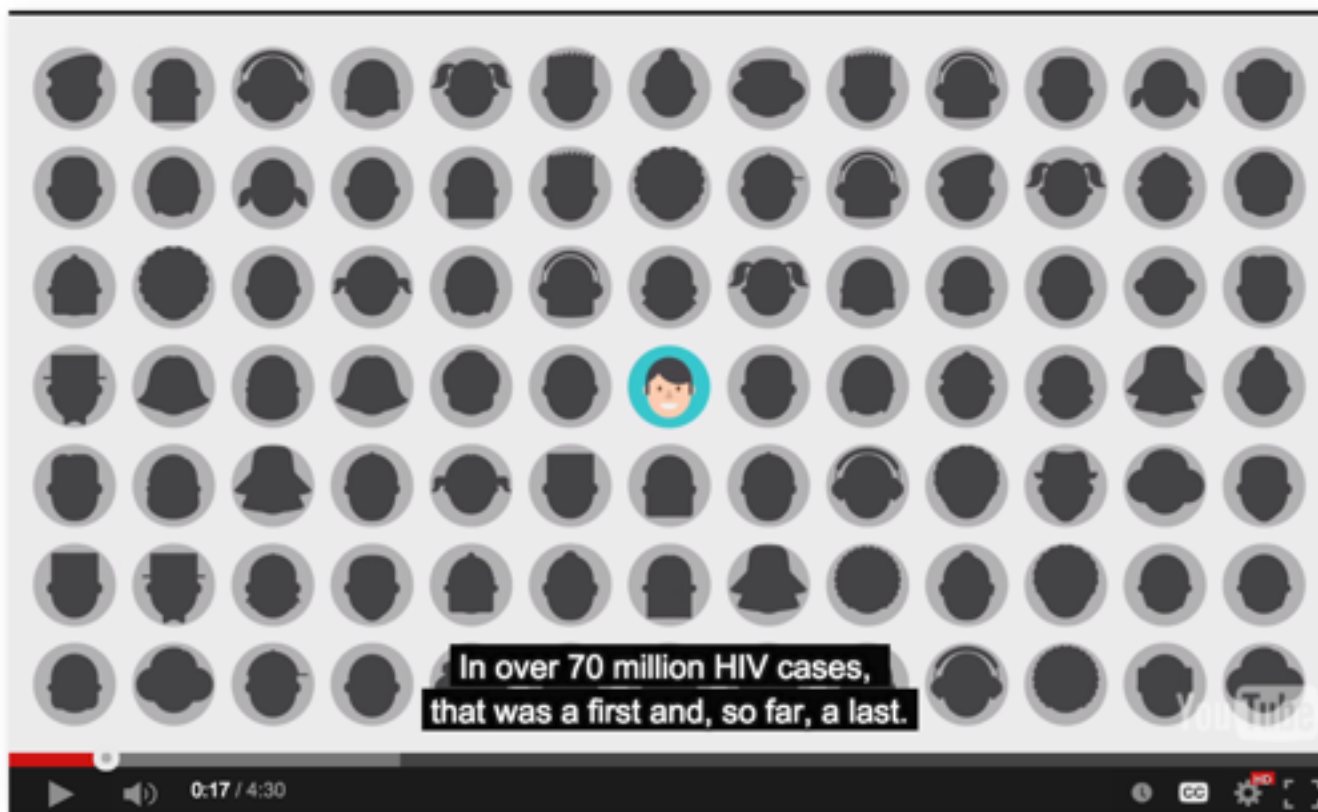
Discuss

Customize This Lesson

21

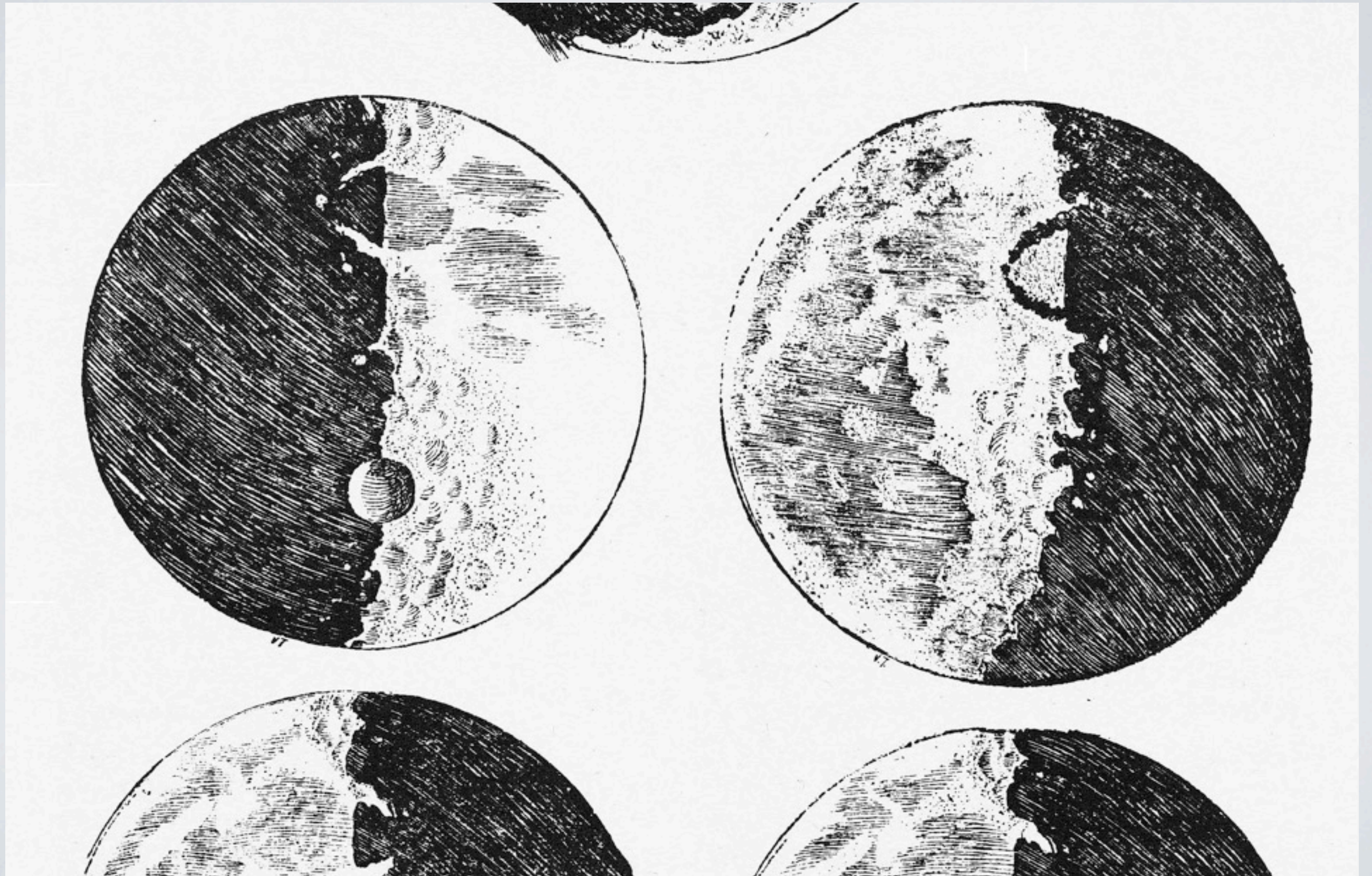
Create and share a new lesson based on this one.

ANIMATION SCREENSHOTS



with TED Ed & Javier Saldeña

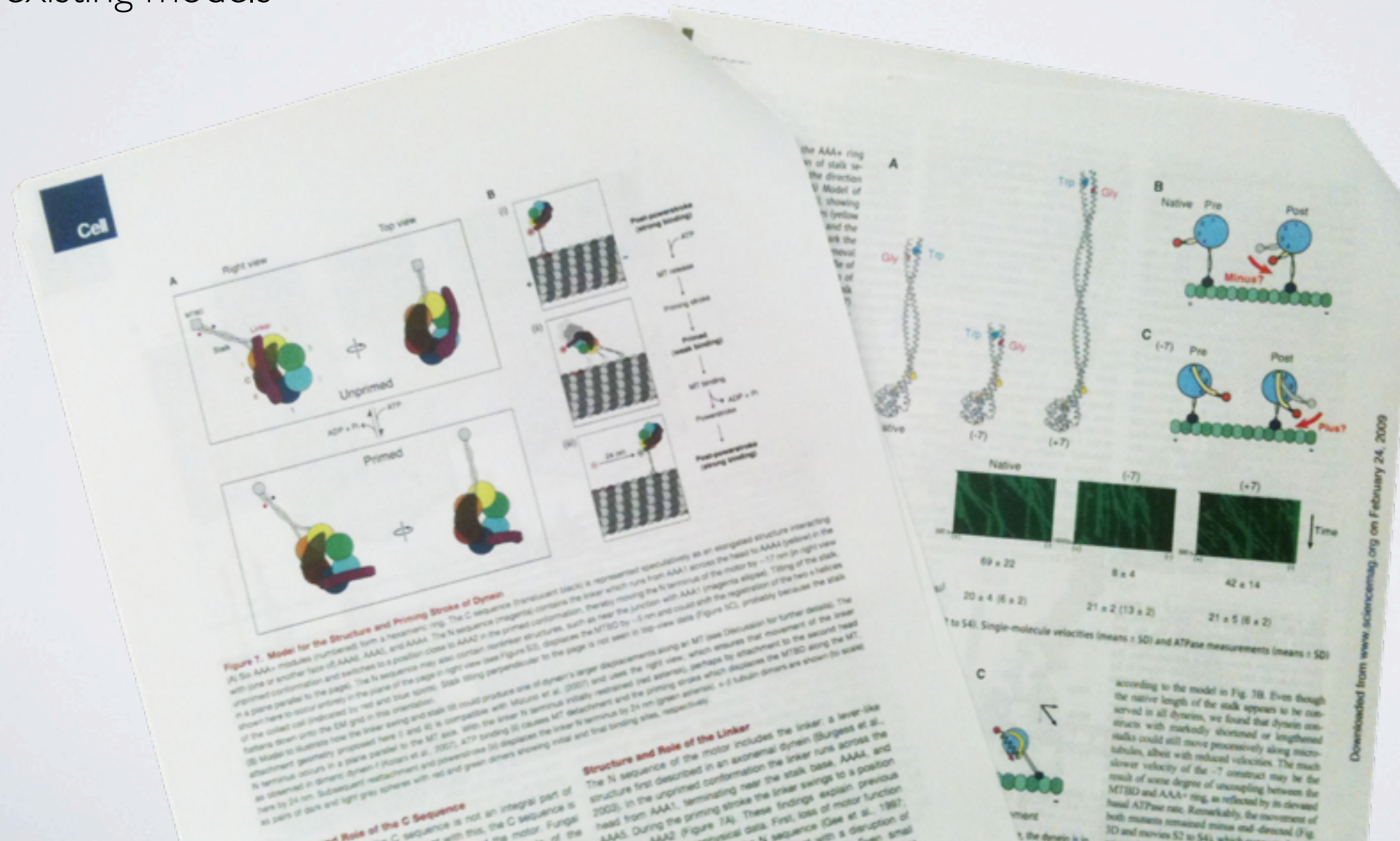
THE SCIENTIST AS ARTIST



THE ROLE OF THE MODEL FIGURE

Benefits for the audience

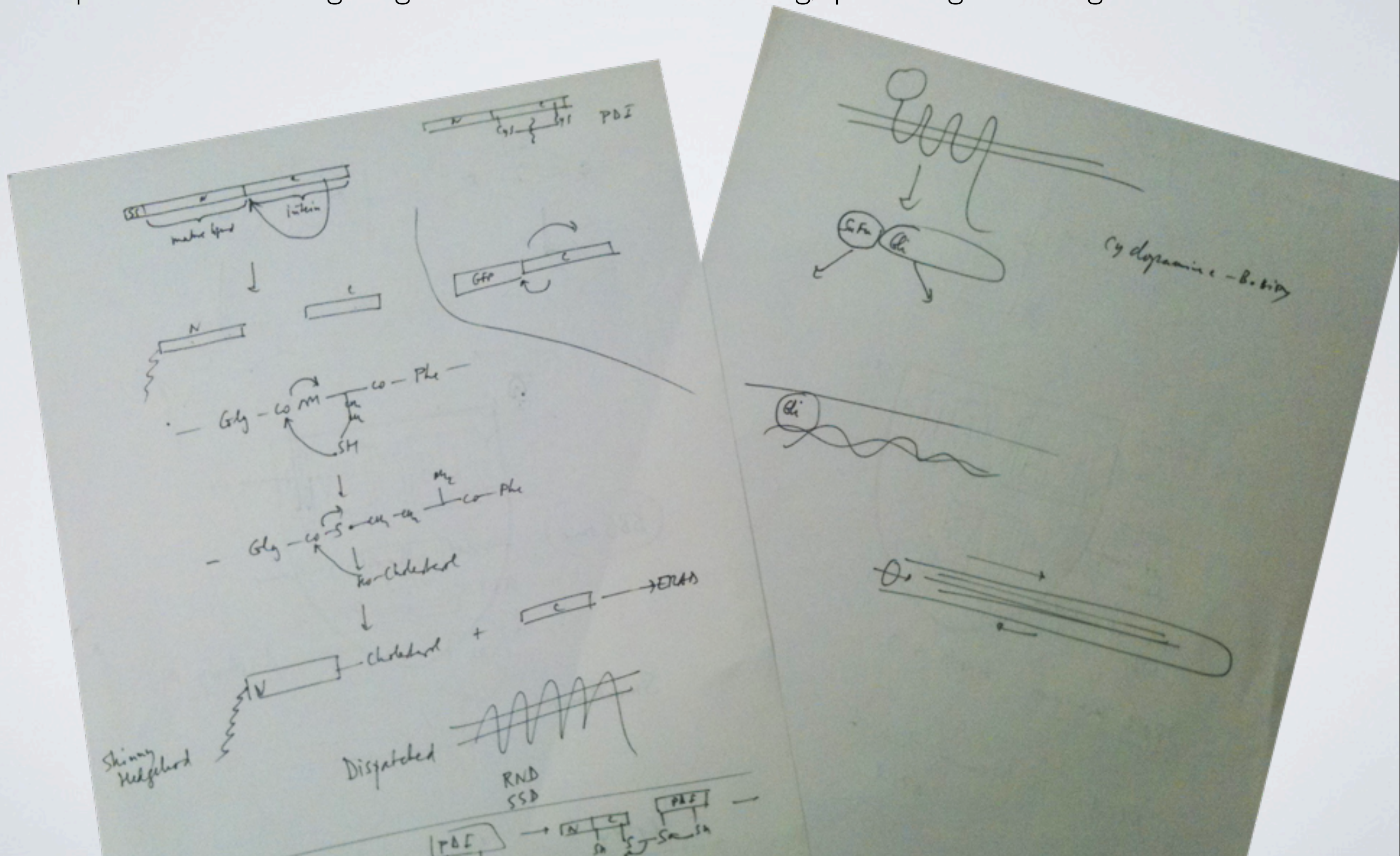
- a description of the current understanding of a process
- background and context
- an understanding of the authors' specific hypothesis, and how it adds to or alters existing models



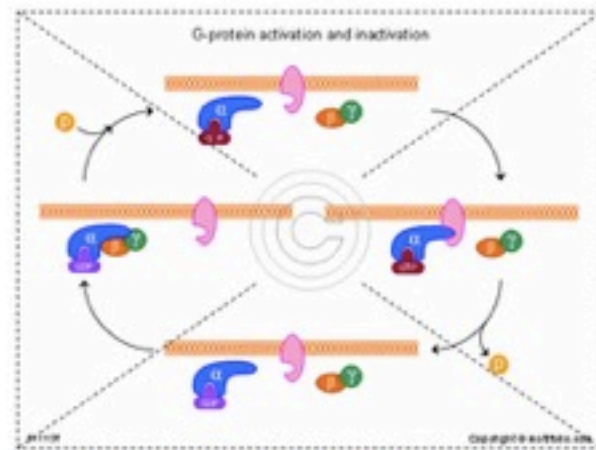
THE ROLE OF THE MODEL FIGURE

Benefits for the author

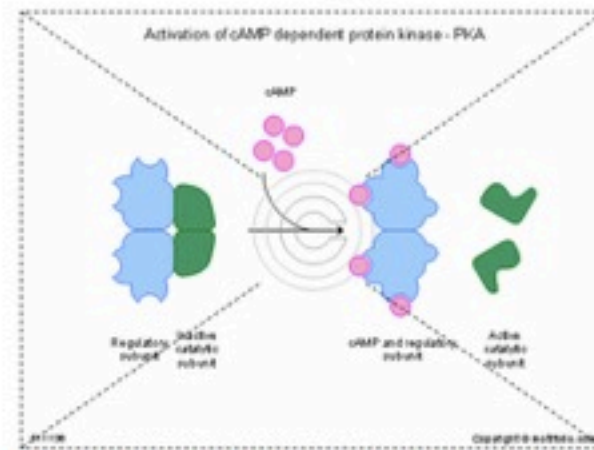
- process of drawing a figure can often be illuminating, providing new insights



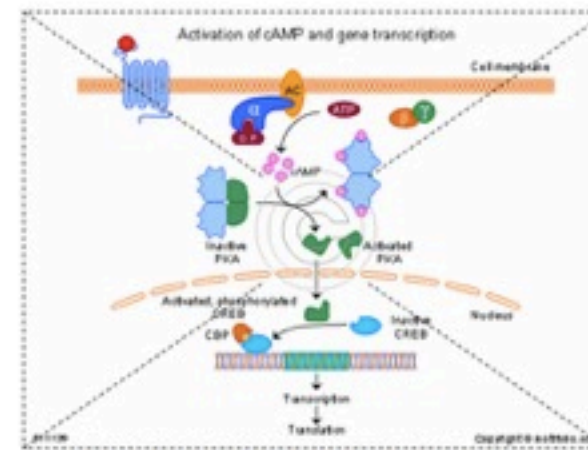
INSTANT MODEL FIGURES?



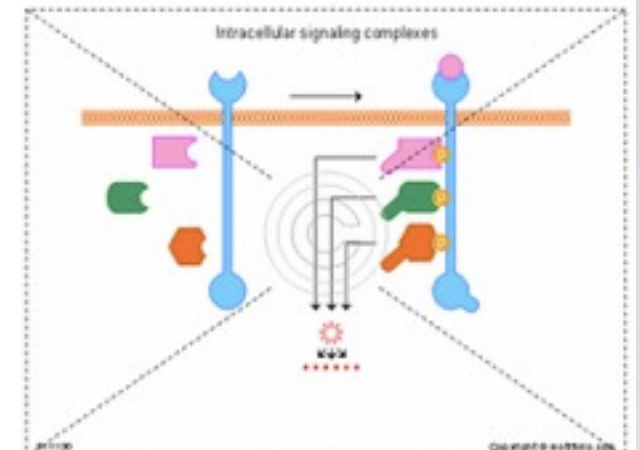
G-protein activation and inactivation



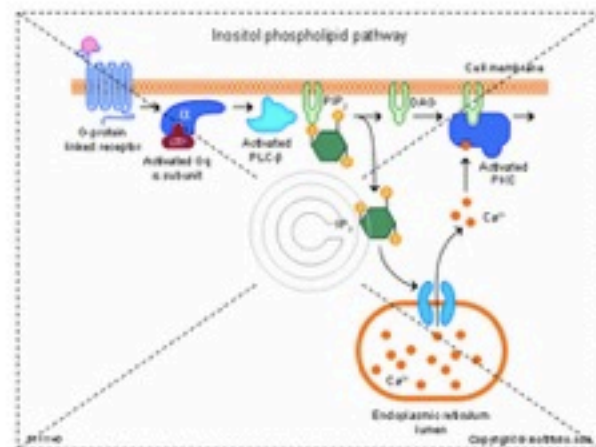
Activation of cAMP dependent protein kinase - PKA



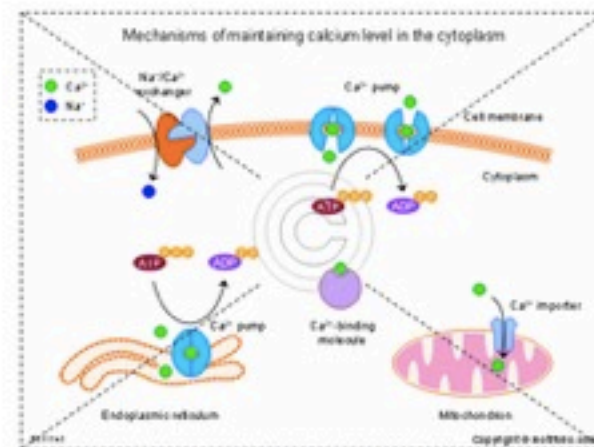
Activation of cAMP and gene transcription



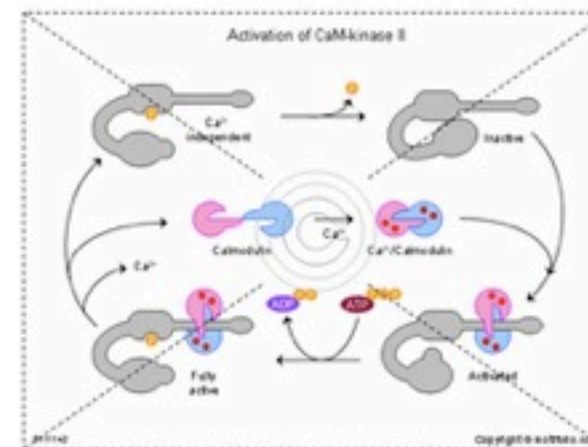
Intracellular signaling complexes



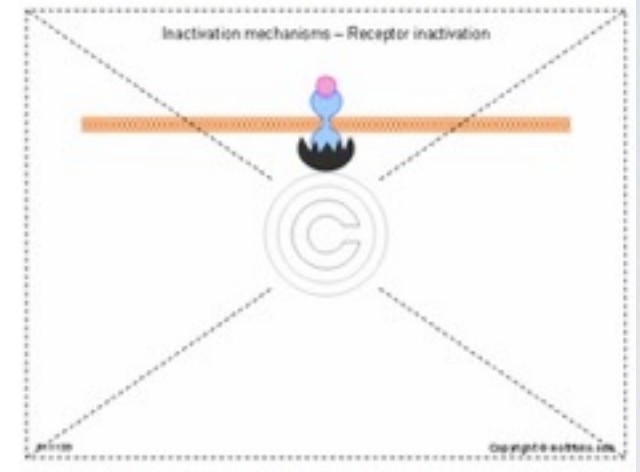
Inositol phospholipid pathway



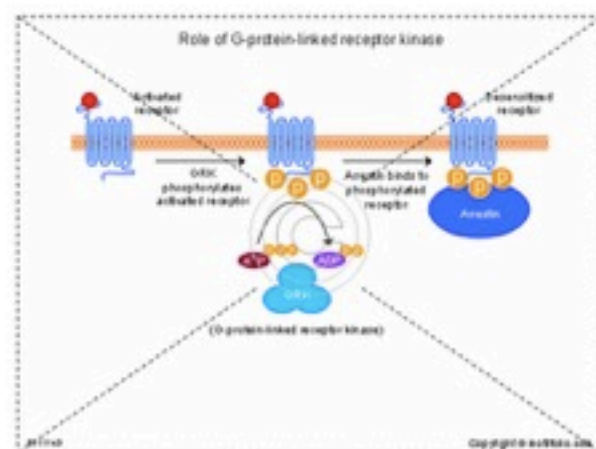
Mechanisms of maintaining calcium level in the cytoplasm



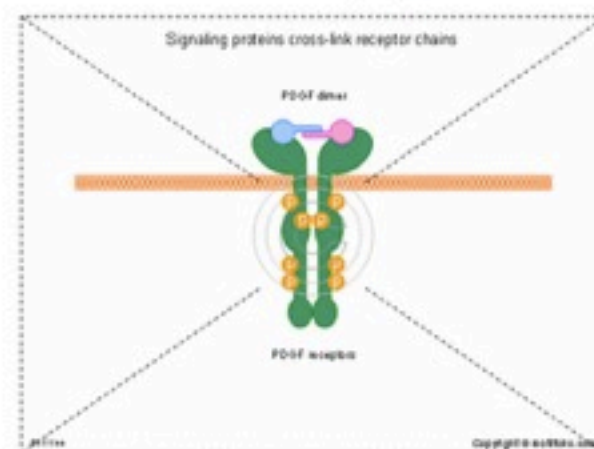
Activation of CaM-kinase II



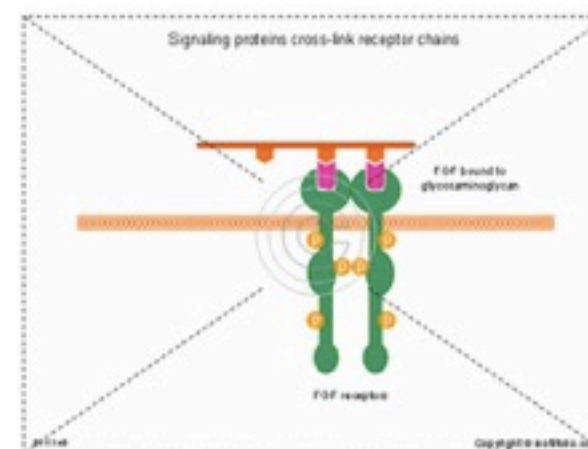
Inactivation mechanisms - Receptor inactivation



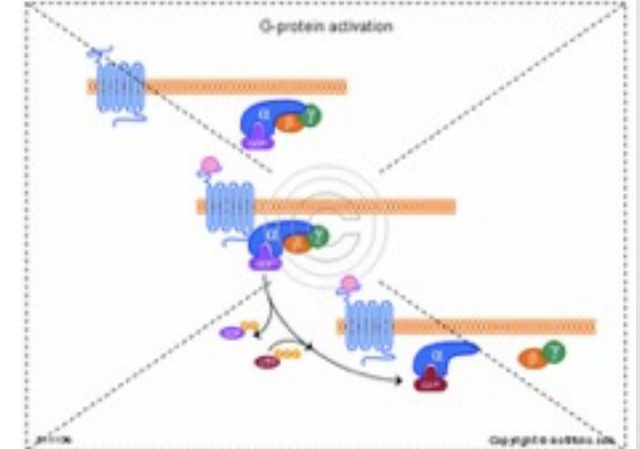
Role of G-protein-linked receptor kinase



Signaling proteins cross-link receptor chains



Signaling proteins cross-link receptor chains



G-protein activation

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

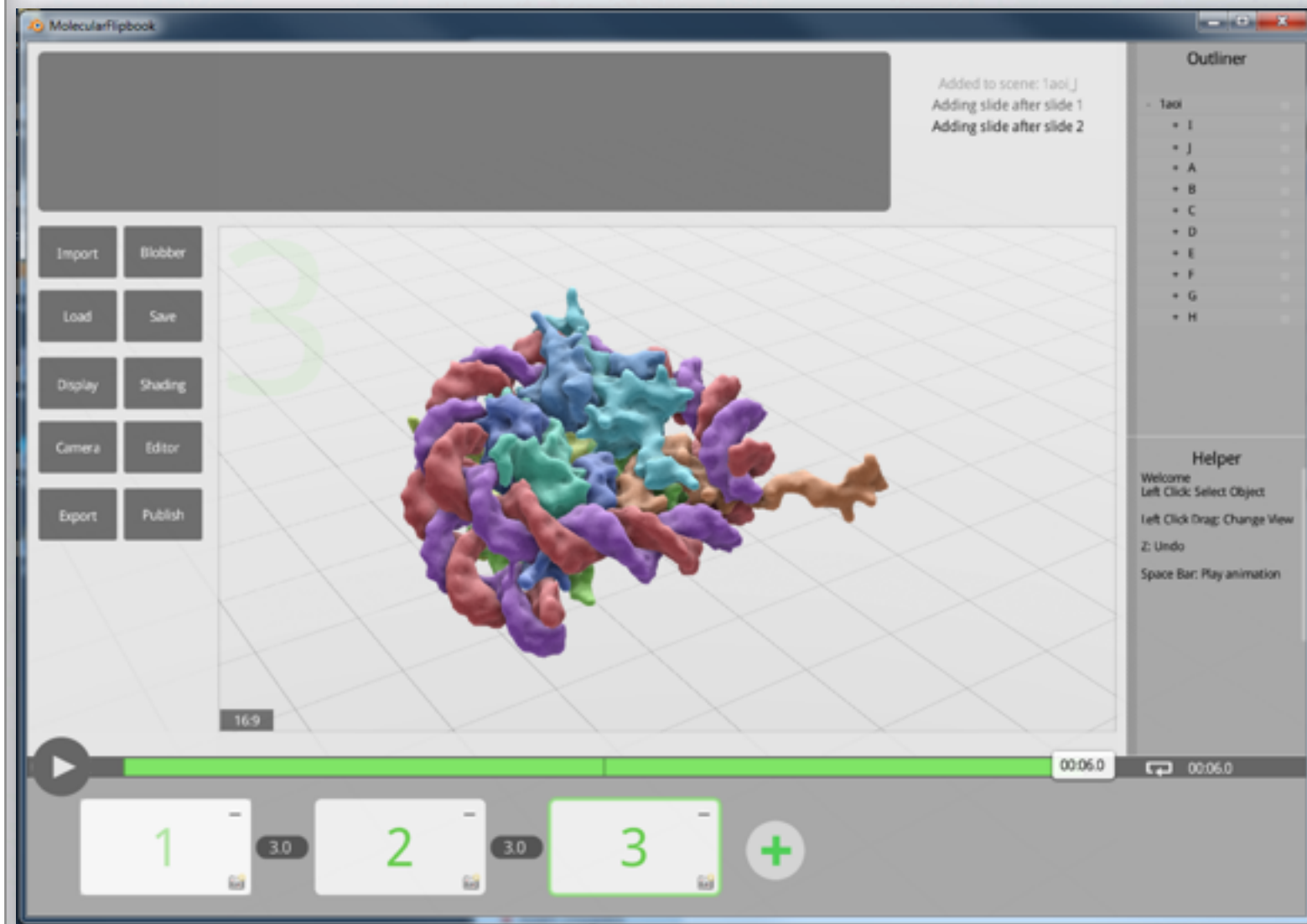
MOLECULAR FLIPBOOK TOOLKIT

a community resource for creating & sharing molecular animations

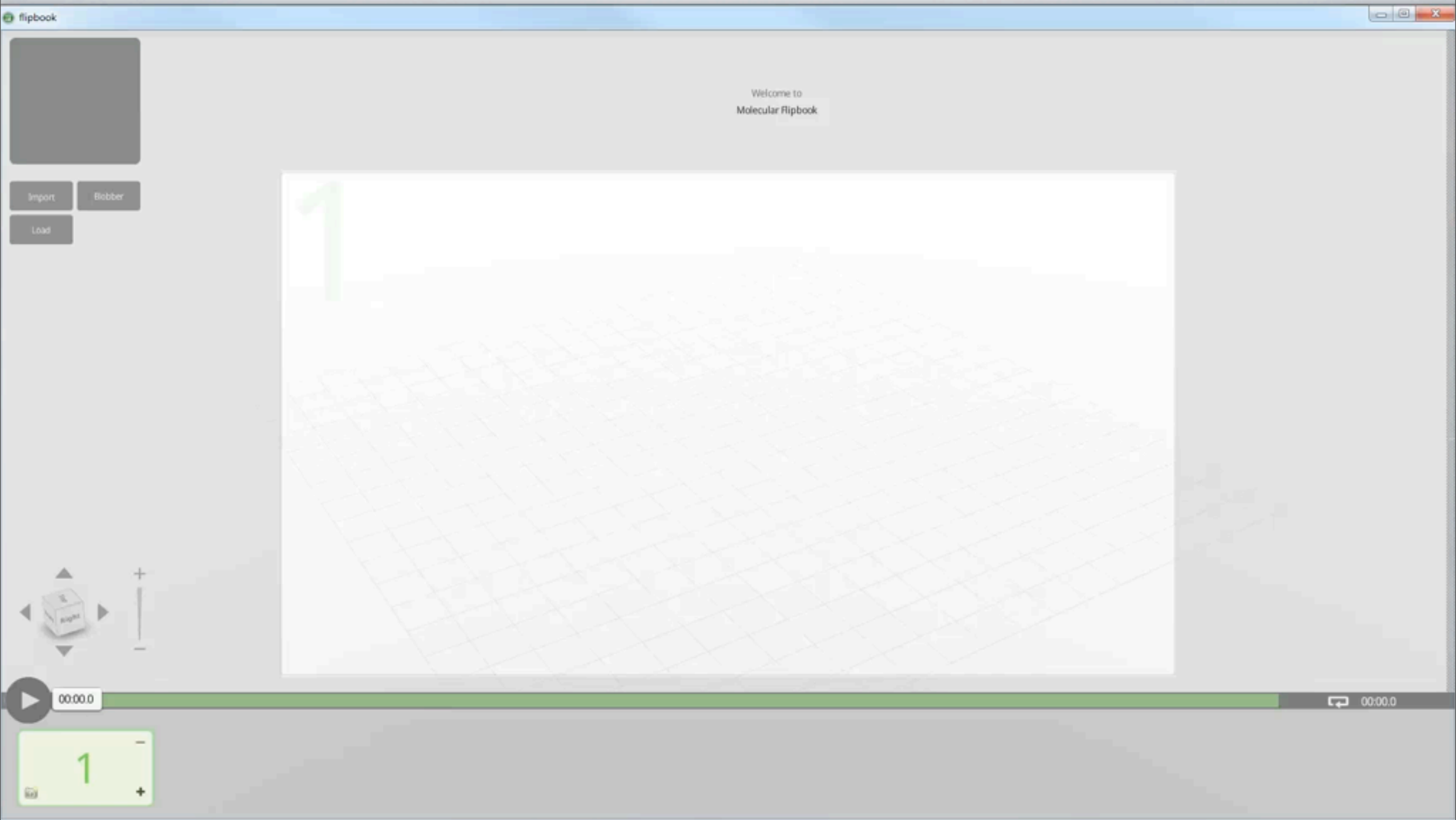
- suite of molecular animation tools built in Blender's game engine which will include import, modeling, animation and rendering modules.
- intuitive interface, simple controls
- ability to start creating animations after watching a short video tutorial.

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](#).



In-app tutorials

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



Slide-based animation

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



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!



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!



Create protein markers

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



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.

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.



Create biological units

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



Import additional filetypes

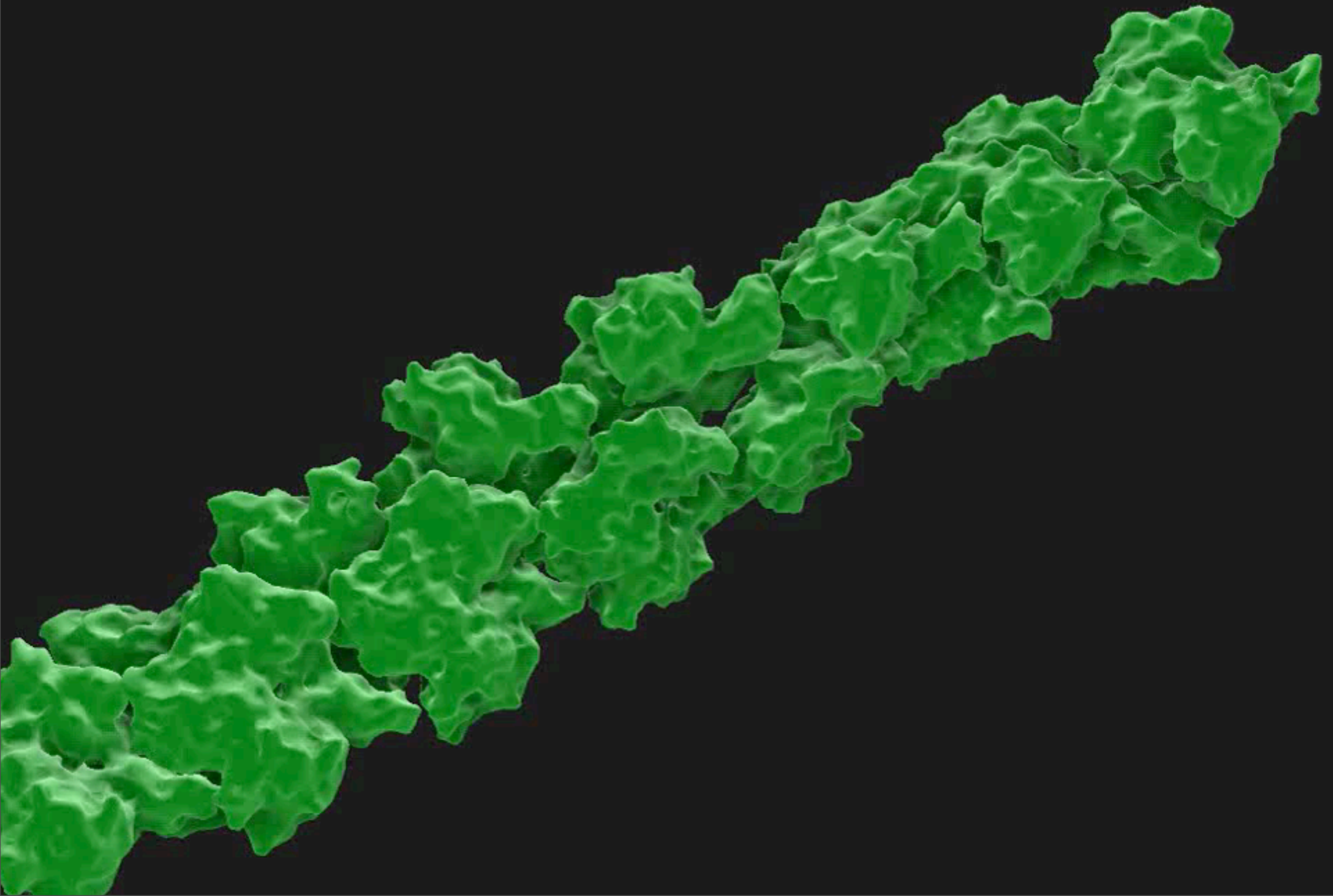
Import geometry files, such as reconstructions from the EMDB, or other files (such as .stl) that may have been generated in another program.



Cut chains

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

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

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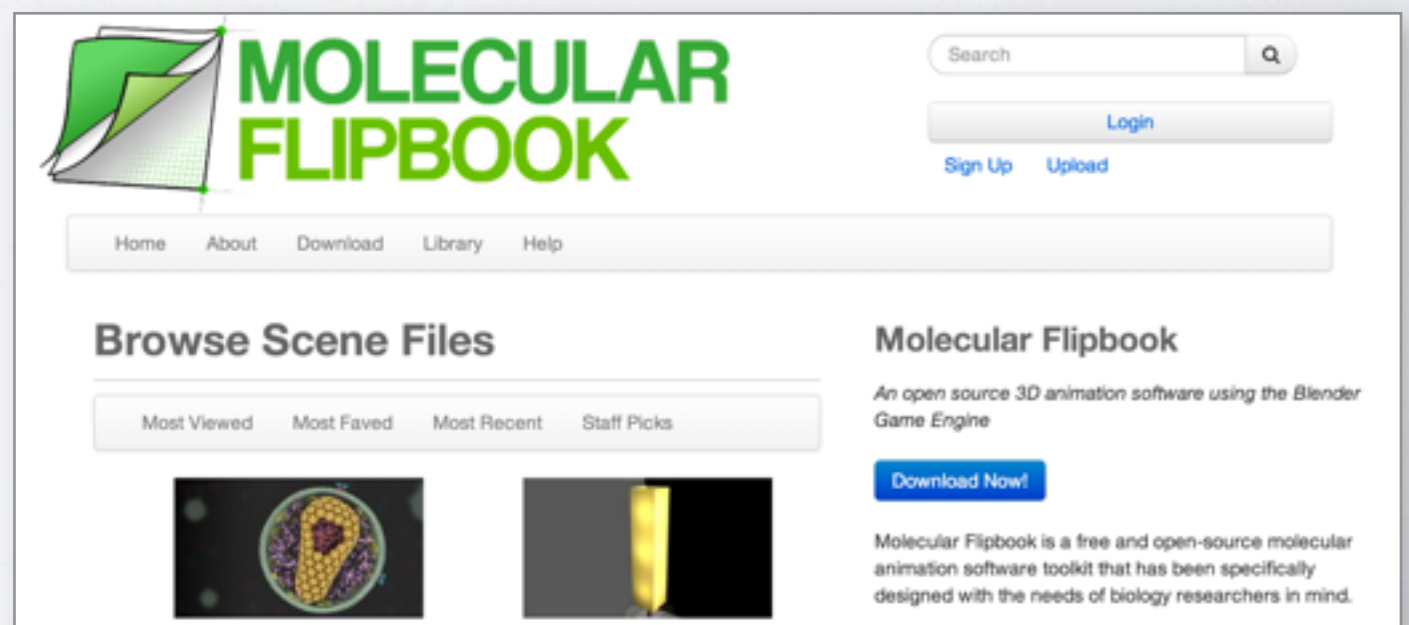
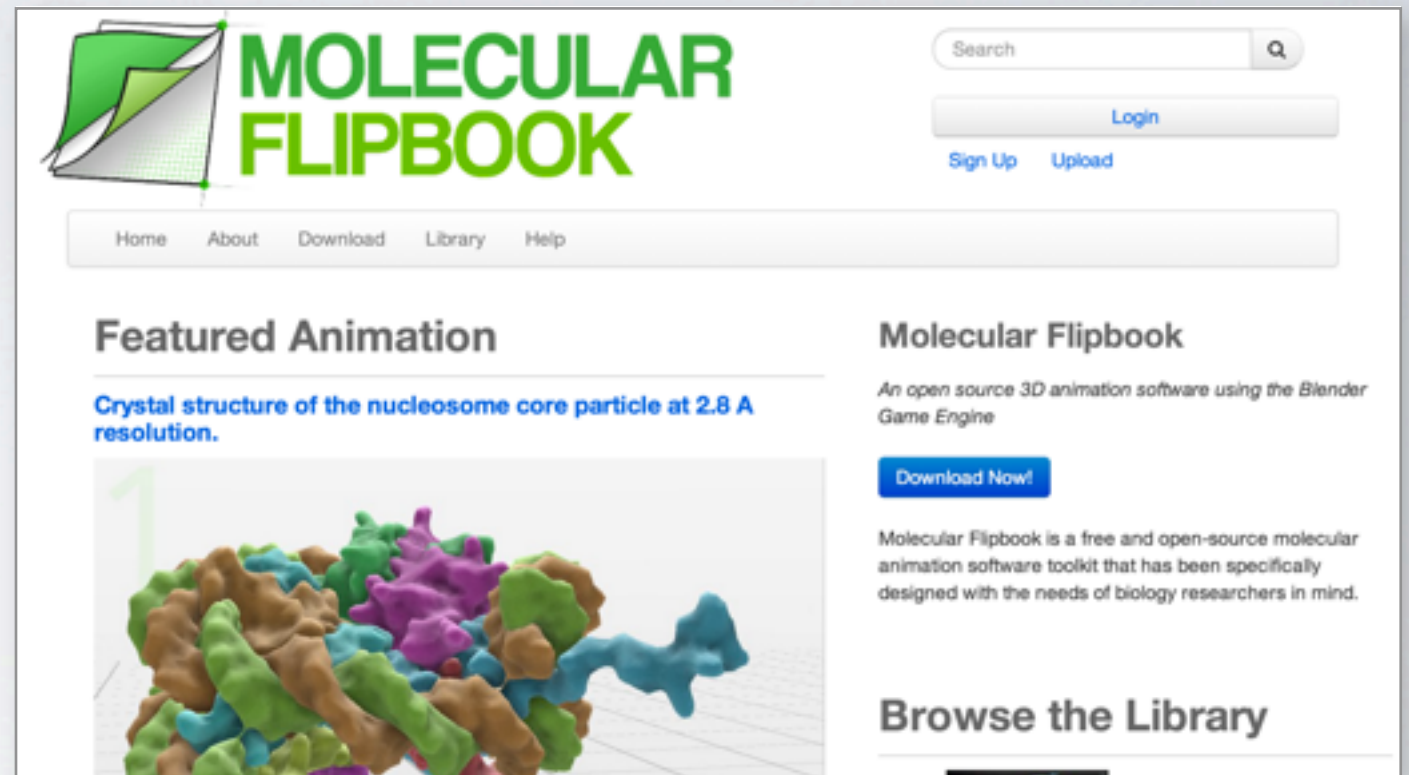
MOLECULAR FLIPBOOK WEBSITE

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:

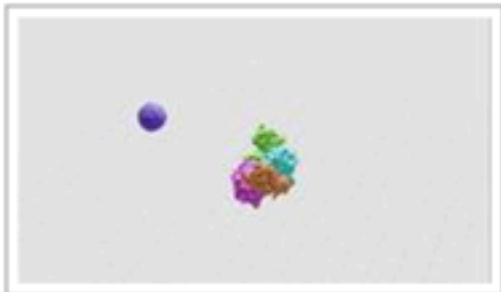
How do we get users to share their visualizations with others?



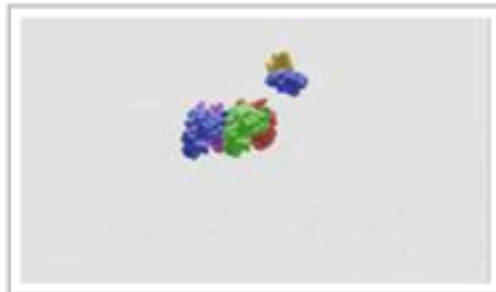
MOLECULAR FLIPBOOK WEBSITE

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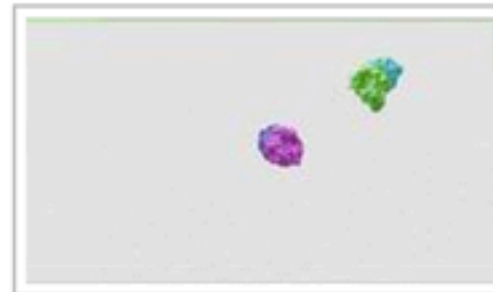
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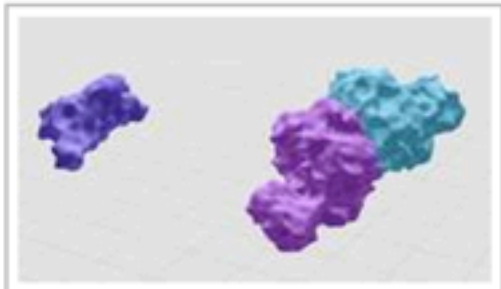
enzyme



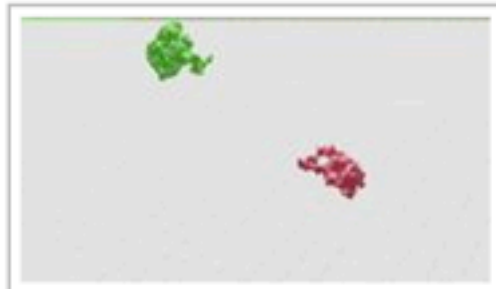
JiminLee. Acetyl-CoA



Enzyme Video



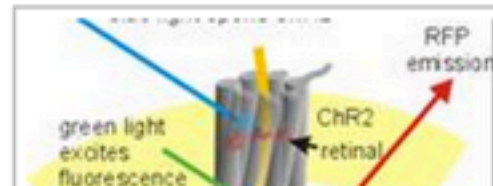
Seungjun Lee - Biotin and...



Jenny Kang co enzyme



Lipase & Colipase



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TOWARDS A DIGITAL CELL

TOOLS

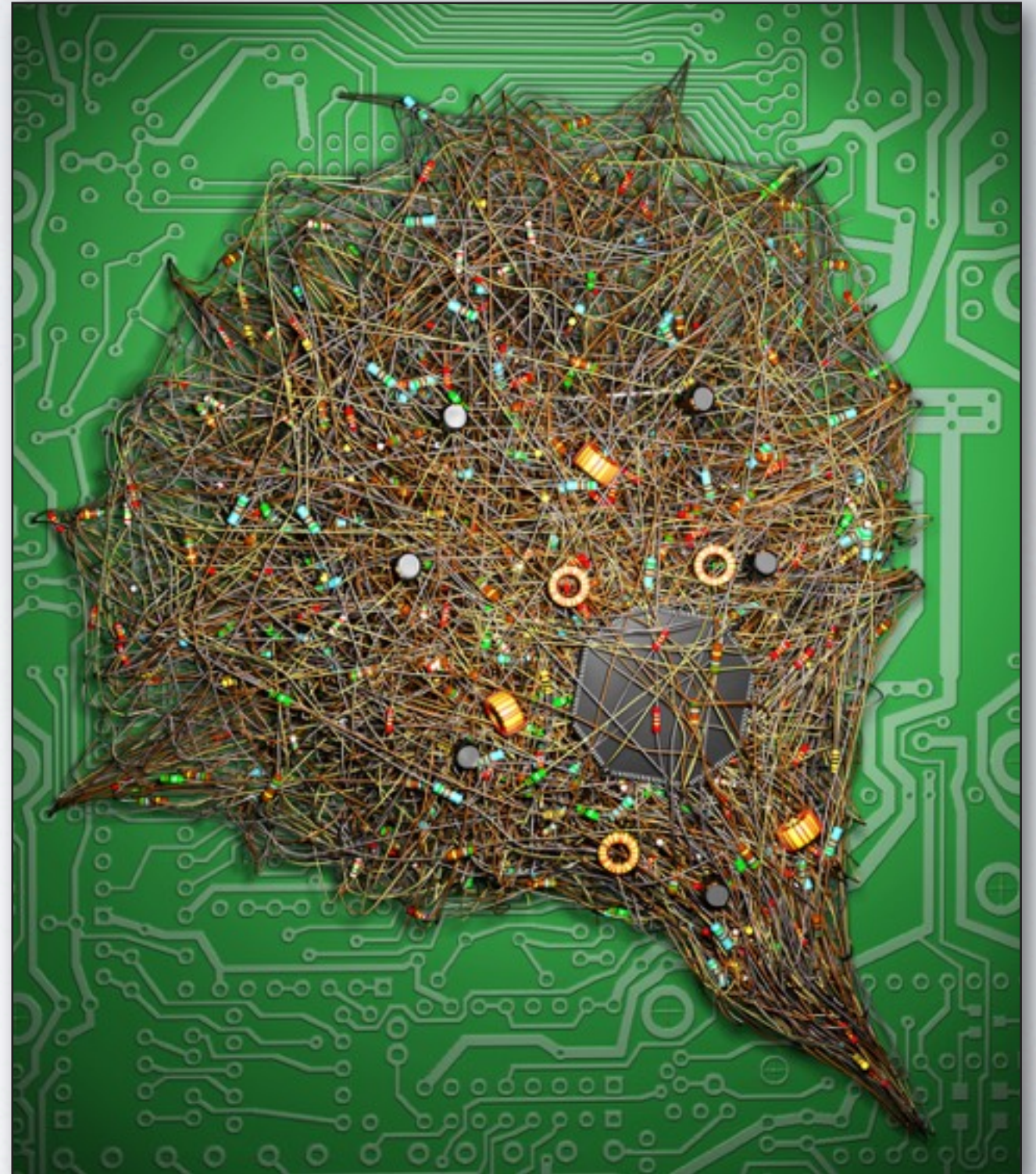
intuitive animation/visualization tools that could allow integration of multiscale data from different sources

TRANSPARENCY

standardized means of providing references and sources used in visualizations

ARCHIVES

centralized repository for cellular data, images and animations



MANY THANKS

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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://ExporingOrigins.org>

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