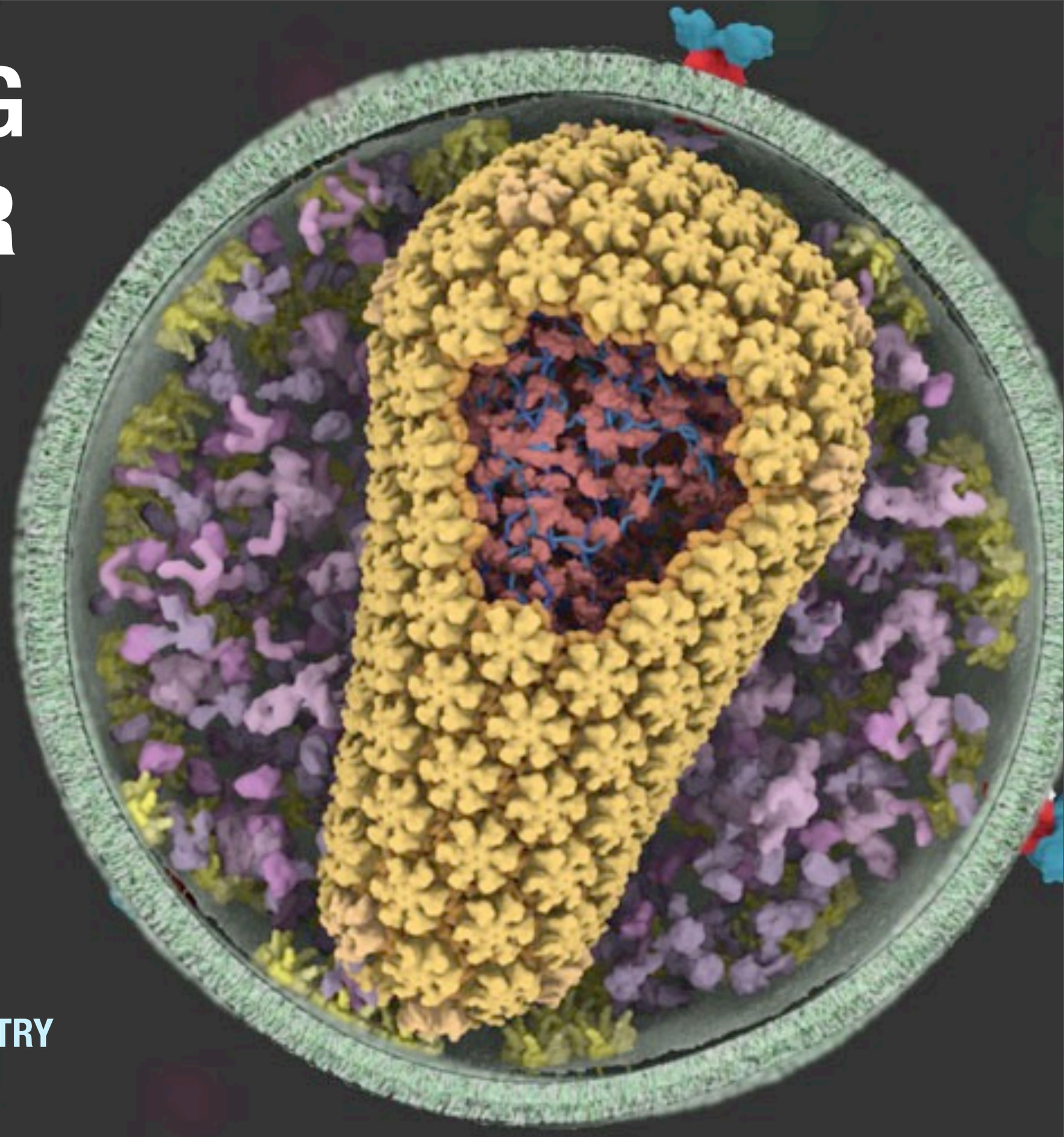
VISUALIZING MOLECULAR PROCESSES



JANET IWASA

DEPARTMENT OF BIOCHEMISTRY

UNIVERSITY OF UTAH

OVERVIEW

1. 3D models and eureka moments.

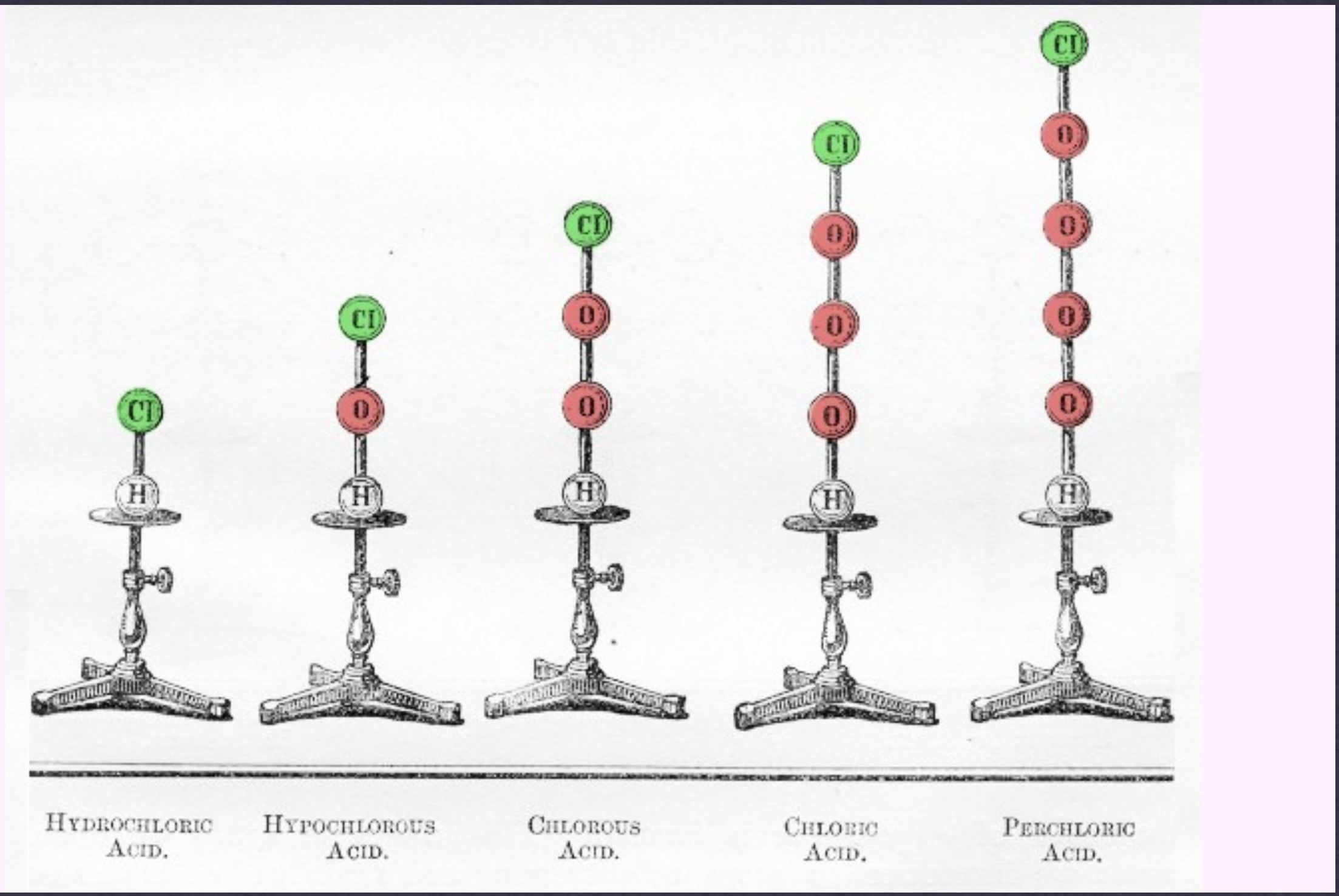
2. Using animations to communicate molecular mechanisms.

3. Using animation as a tool for research.

4. The future of the model figure? Thoughts and directions.

3D MODELS IN SCIENCE

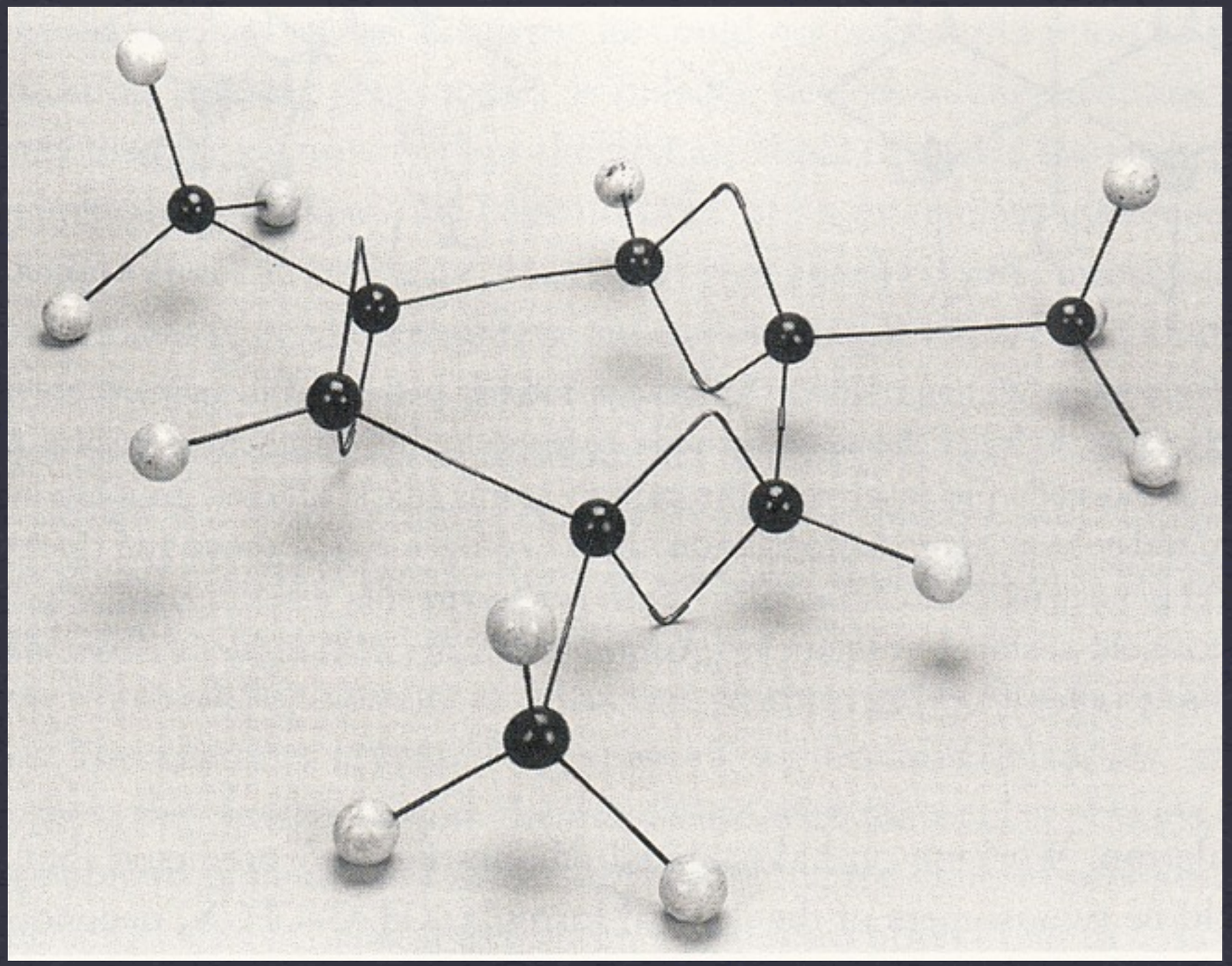
EARLY CHEMICAL MODELS - AUGUST WILHELM HOFMANN, 1865

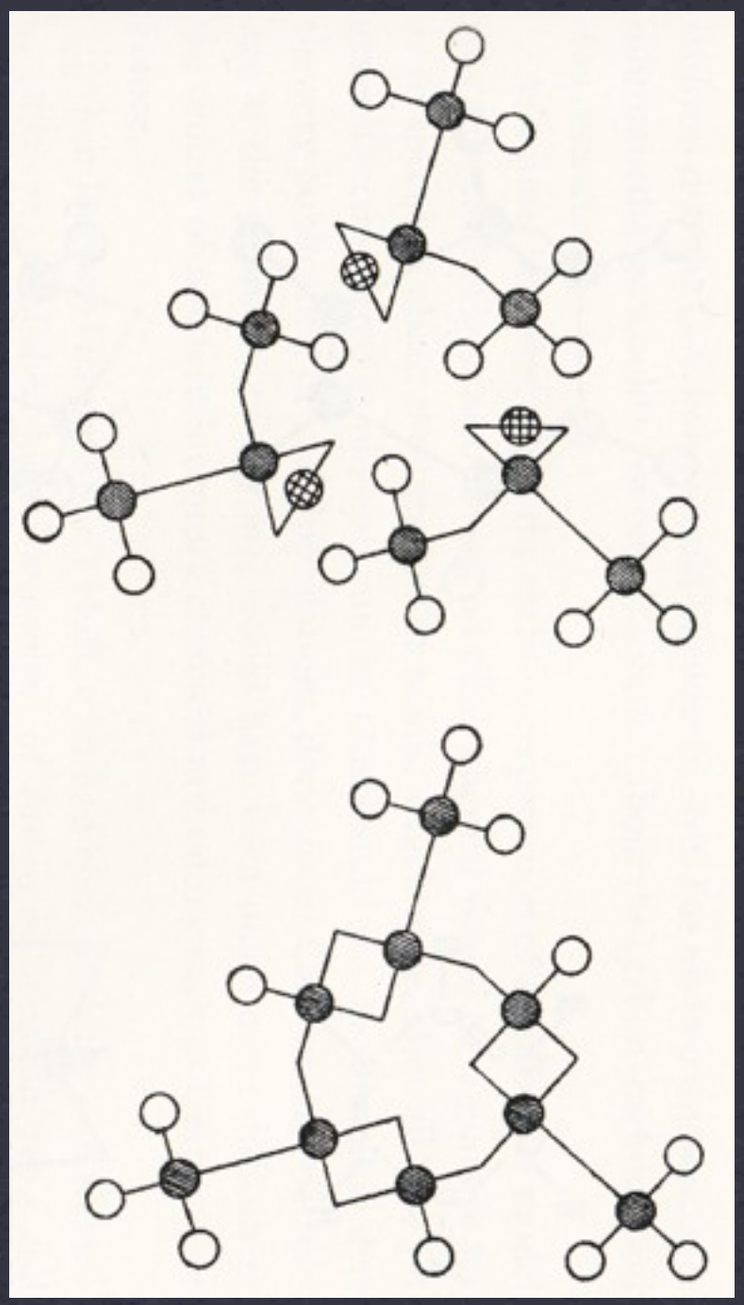


FROM HTTP://WWW.CHEM.YALE.EDU/~CHEM125/125/HISTORY99/6STEREOCHEMISTRY/MODELS/MODELS.HTML

3D MODELS IN SCIENCE

EARLY CHEMICAL MODELS - AUGUST KEKULÉ

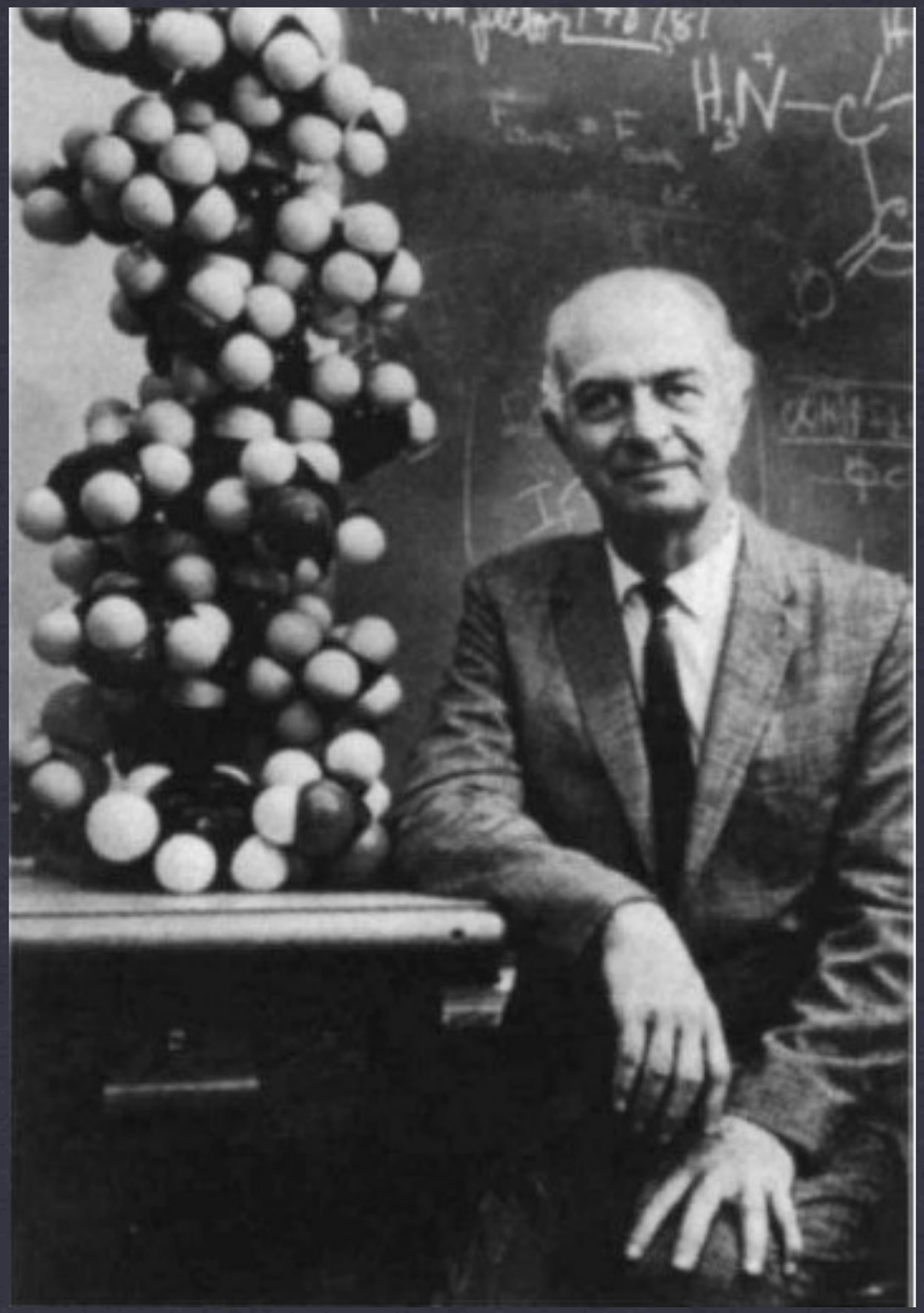




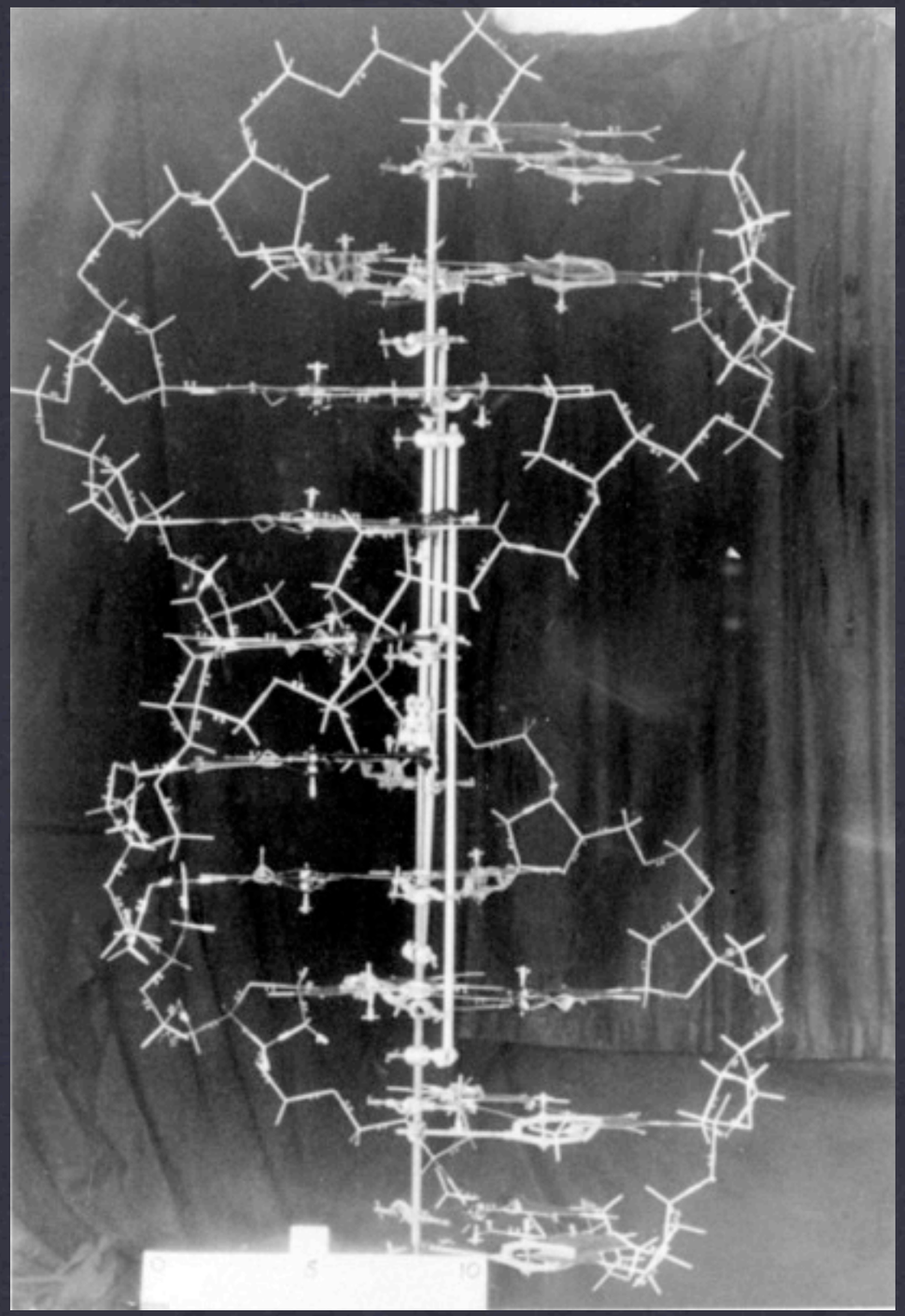
FROM MODELS: THE THIRD DIMENSION OF SCIENCE, EDITED BY SORAYA DE CHADAREVIAN AND NICK HOPWOOD

3D MODELS IN SCIENCE

THE ALPHA HELIX AND THE DOUBLE HELIX



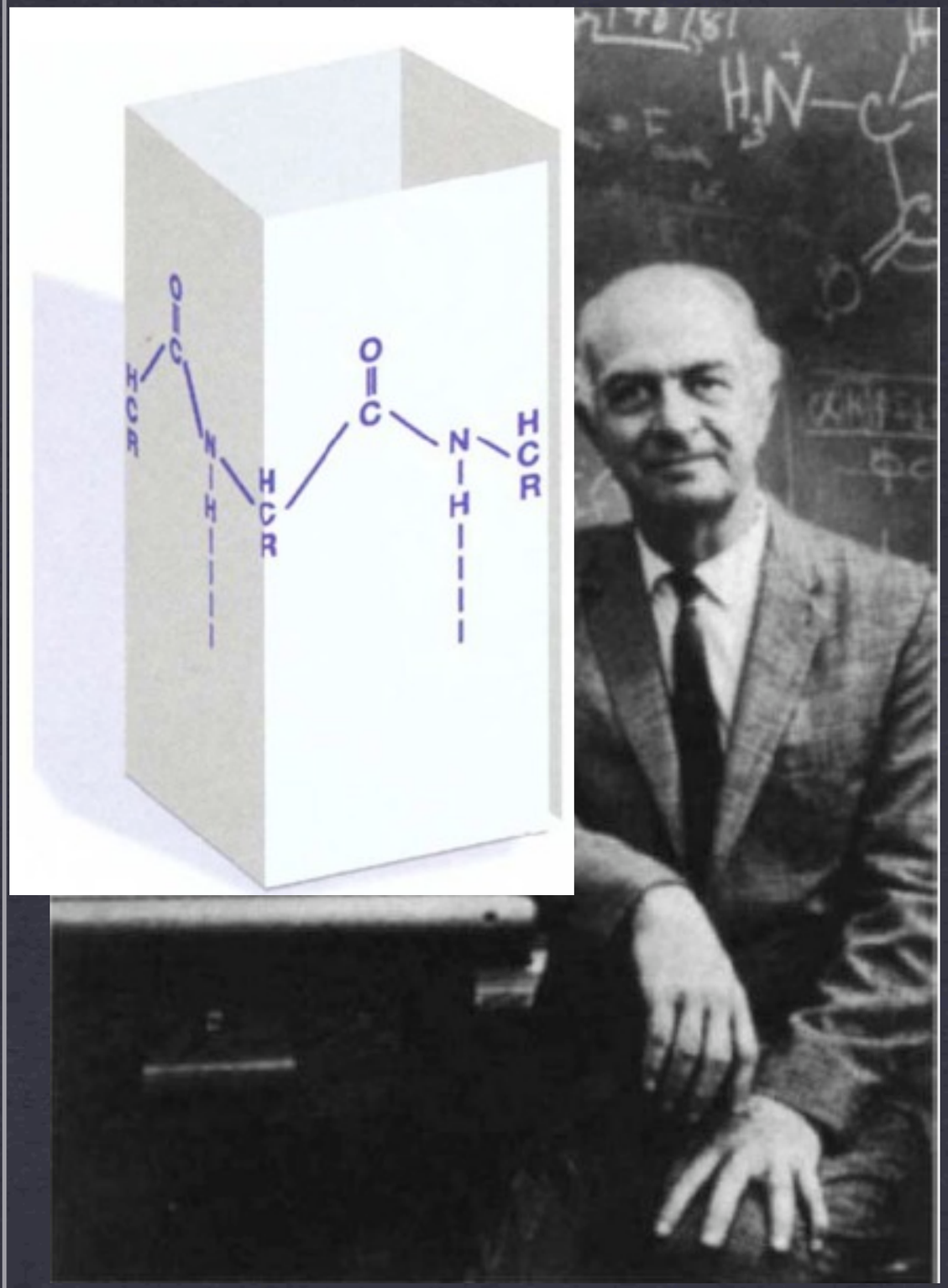
FROM “STRING AND SEALING WAX” NAT STRUCT BIOL 1997



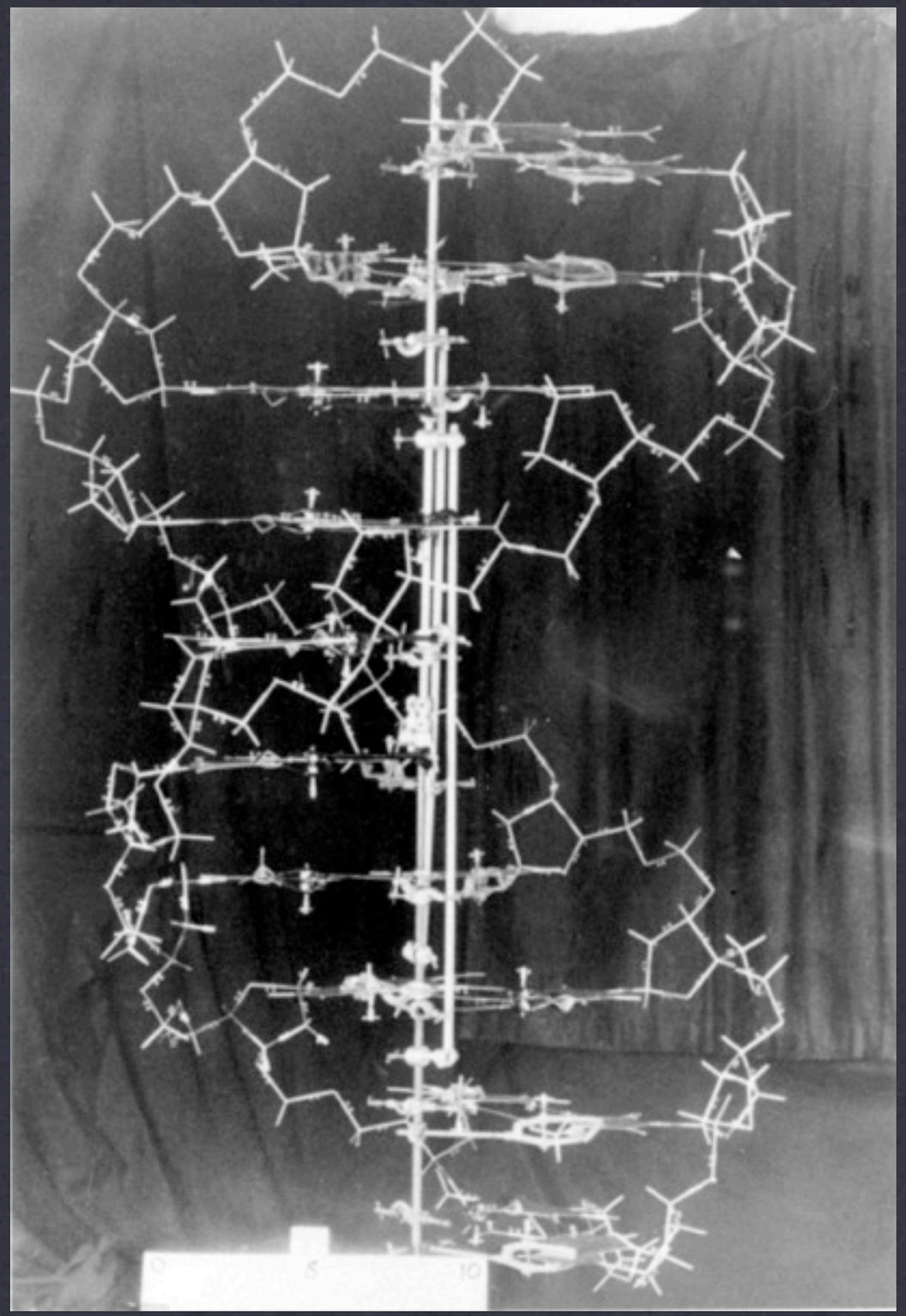
FROM COLD SPRING HARBOR LABS

3D MODELS IN SCIENCE

THE ALPHA HELIX AND THE DOUBLE HELIX



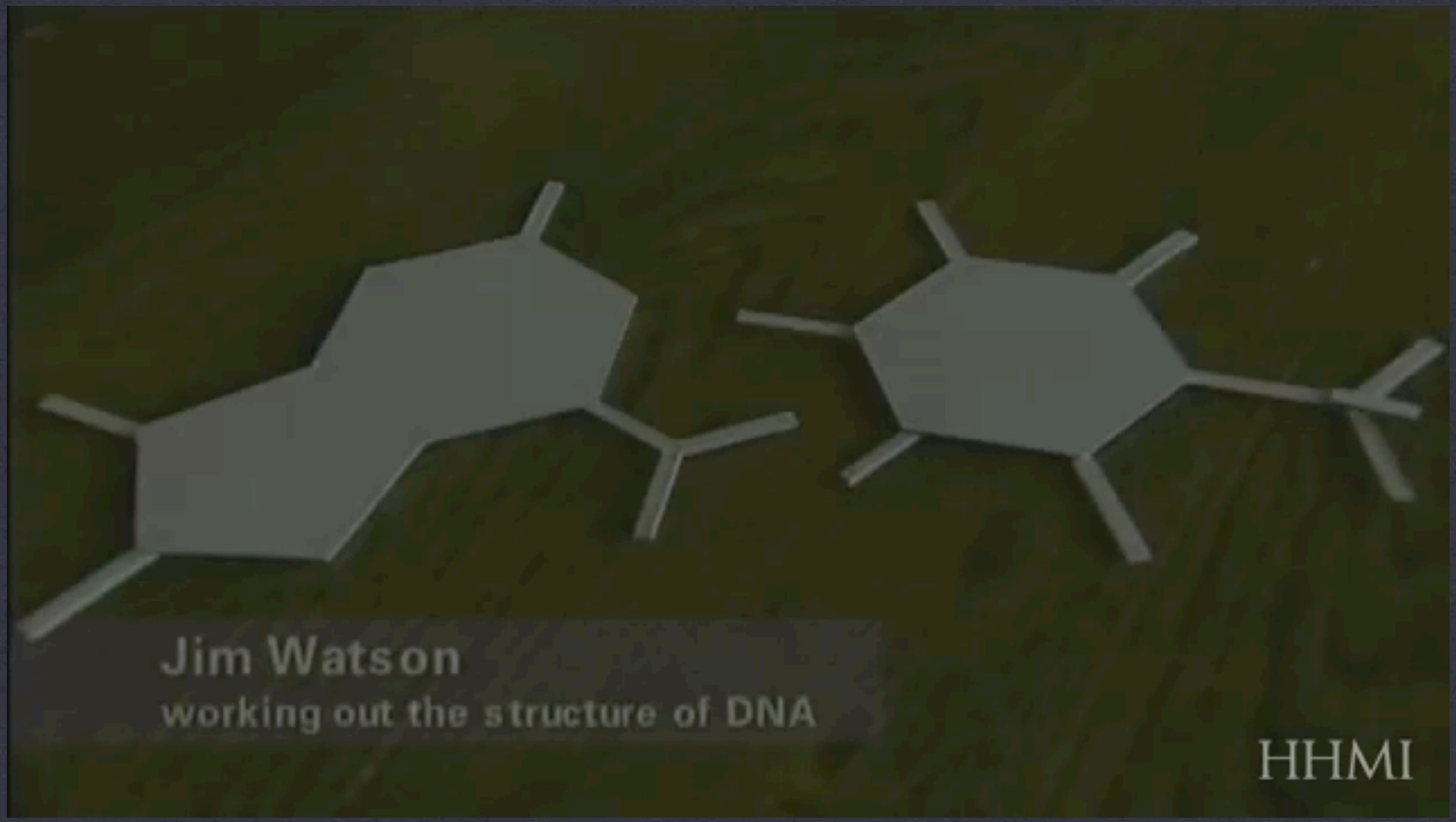
FROM “STRING AND SEALING WAX” NAT STRUCT BIOL 1997



FROM COLD SPRING HARBOR LABS

3D MODELS IN SCIENCE

JAMES WATSON ON CONSTRUCTING BASE PAIR MODELS



FROM HHMI'S "BIOINTERACTIVE" (HTTP://HHMI.ORG/BIOINTERACTIVE)

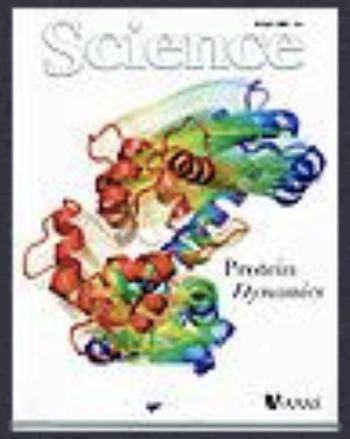
3D MODELS IN SCIENCE

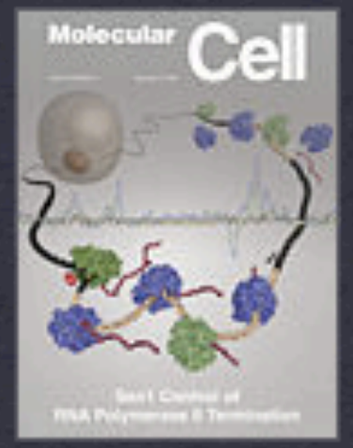
MYOGLOBIN IN A “FOREST OF RODS”

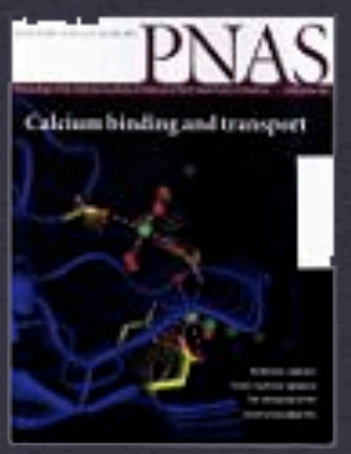
IMAGE FROM:
DICKERSON RE. CHAPTER 2: MYOGLOBIN: A WHALE OF A STRUCTURE! J MOL BIOL. 2009 SEP 11;392(1):10-23.

3D MODELS IN SCIENCE

VIRTUAL MODELS

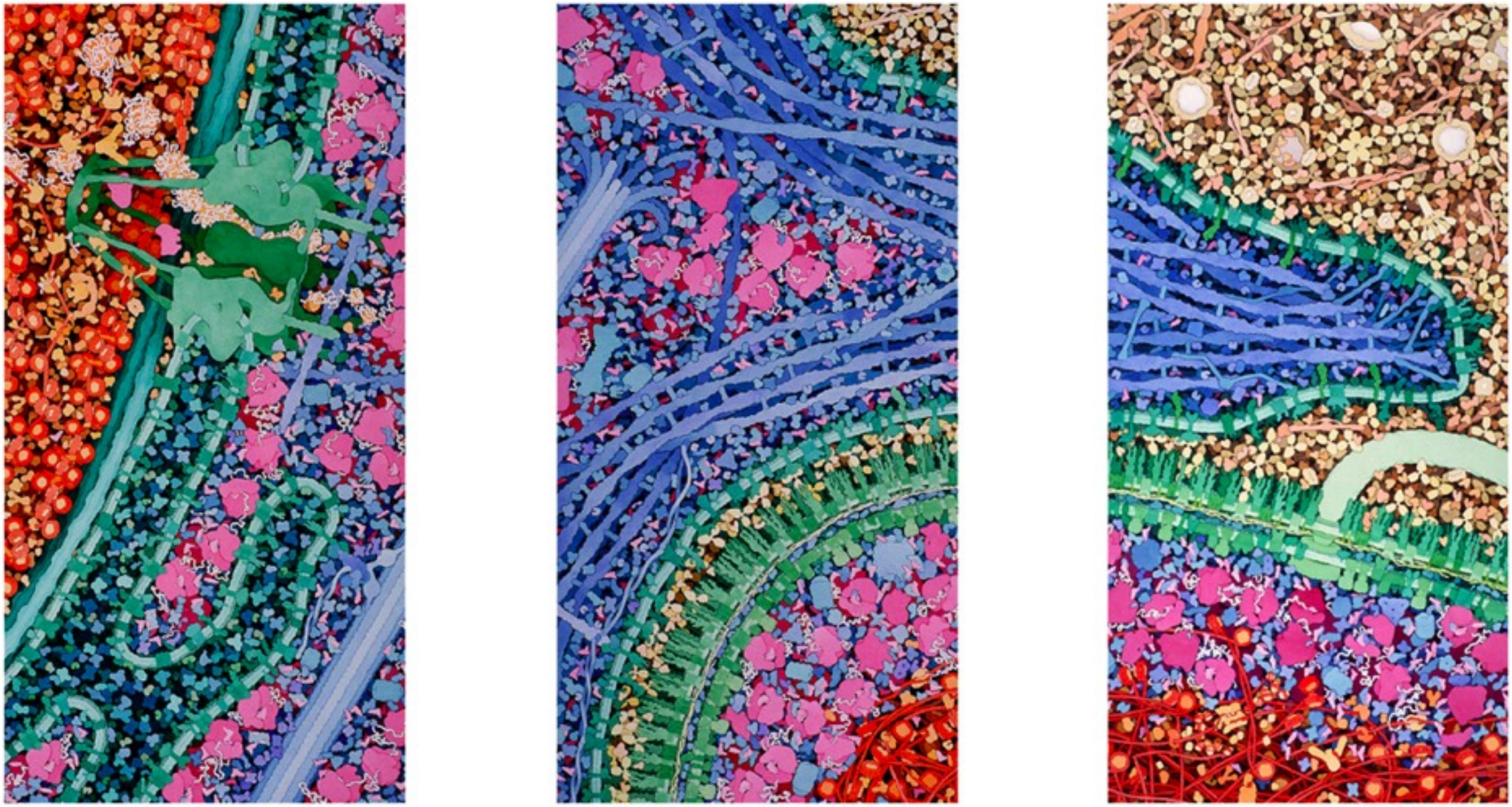






COVERS MADE WITH PYMOL - FROM THE PYMOL WIKI

VISUALIZING THE CELLULAR MESOSCALE



“MACROPHAGE & BACTERIUM”
DAVID GOODSELL, SCRIPPS INSTITUTE

THE NEED FOR NEW MODELS IN BIOLOGY

WHY ANIMATION?

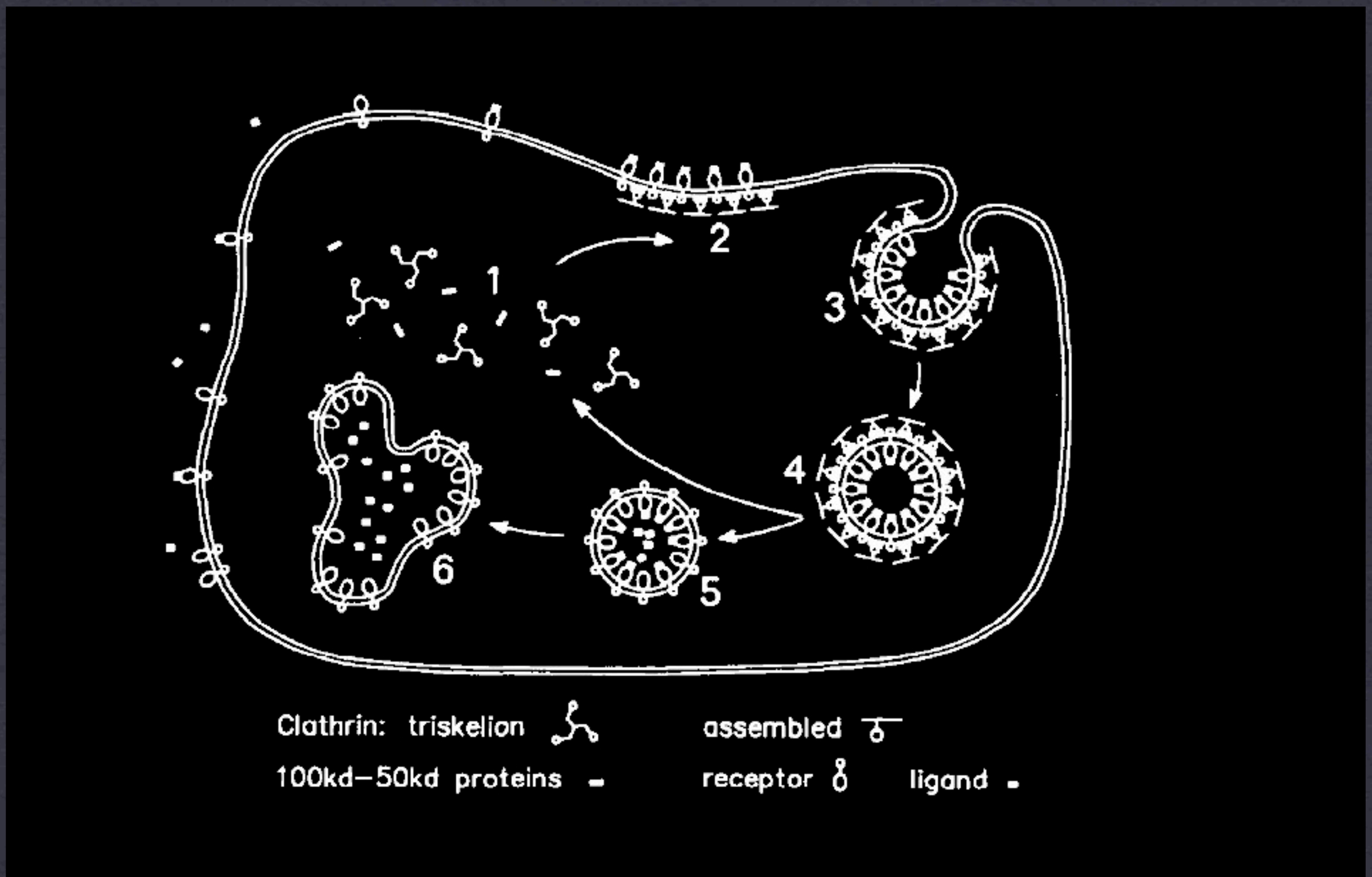
3D animation can synthesize diverse biological data ...

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

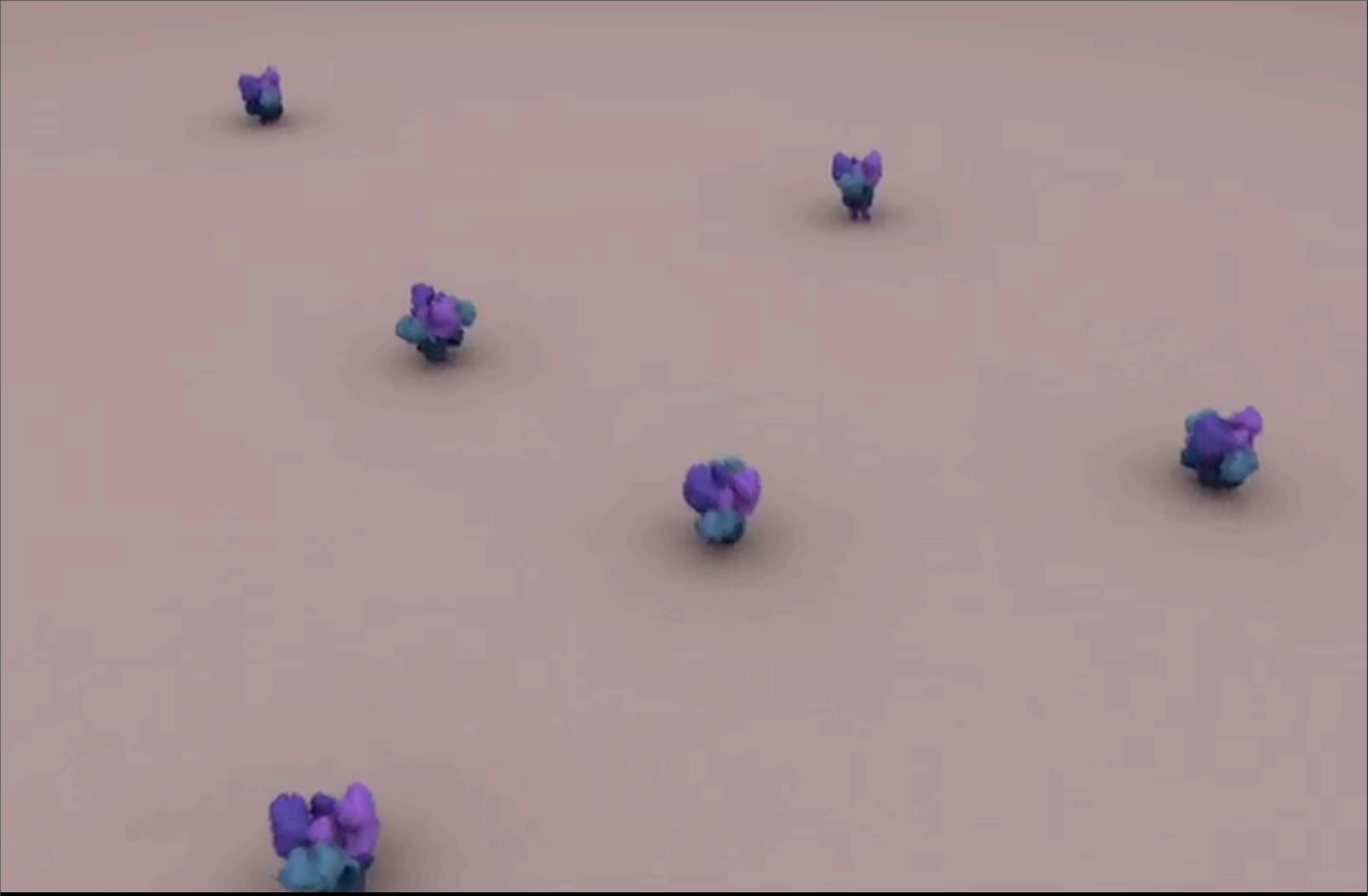
... allowing us to create a comprehensive visual hypothesis of a cellular event

CLATHRIN-MEDIATED ENDOCYTOSIS

ILLUSTRATION BY PEARSE & CROWTHER, 1987



Iwasa and Kirchhausen, Harvard Medical School, 2012



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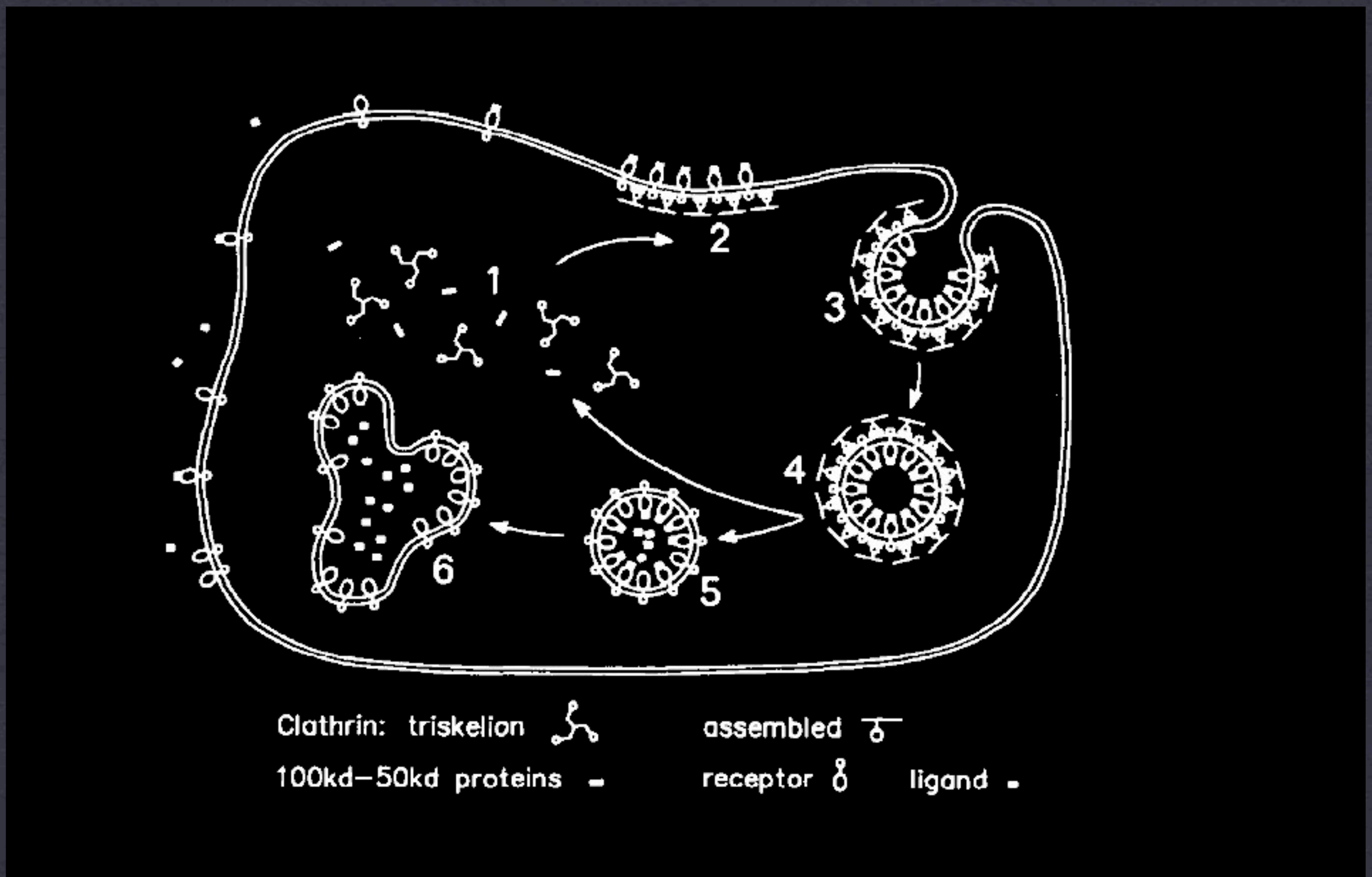


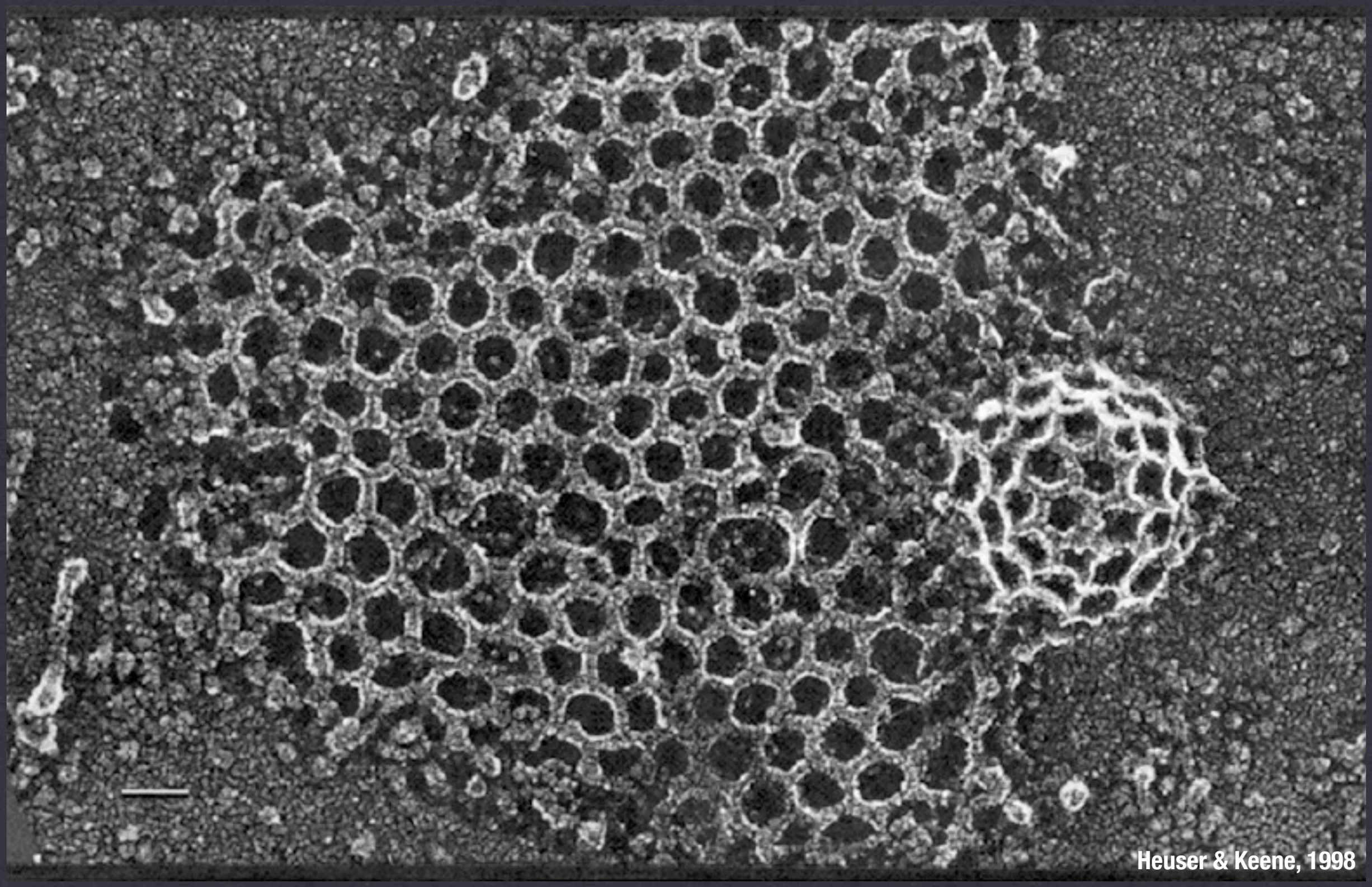
CLATHRIN-MEDIATED ENDOCYTOSIS

CLATHRIN LATTICE CRYSTAL STRUCTURE

FOTIN, CHENG, SLIZ, GRIGORIEFF, HARRISON, KIRCHHAUSEN AND WALZ, 1994

CLATHRIN-MEDIATED ENDOCYTOSIS

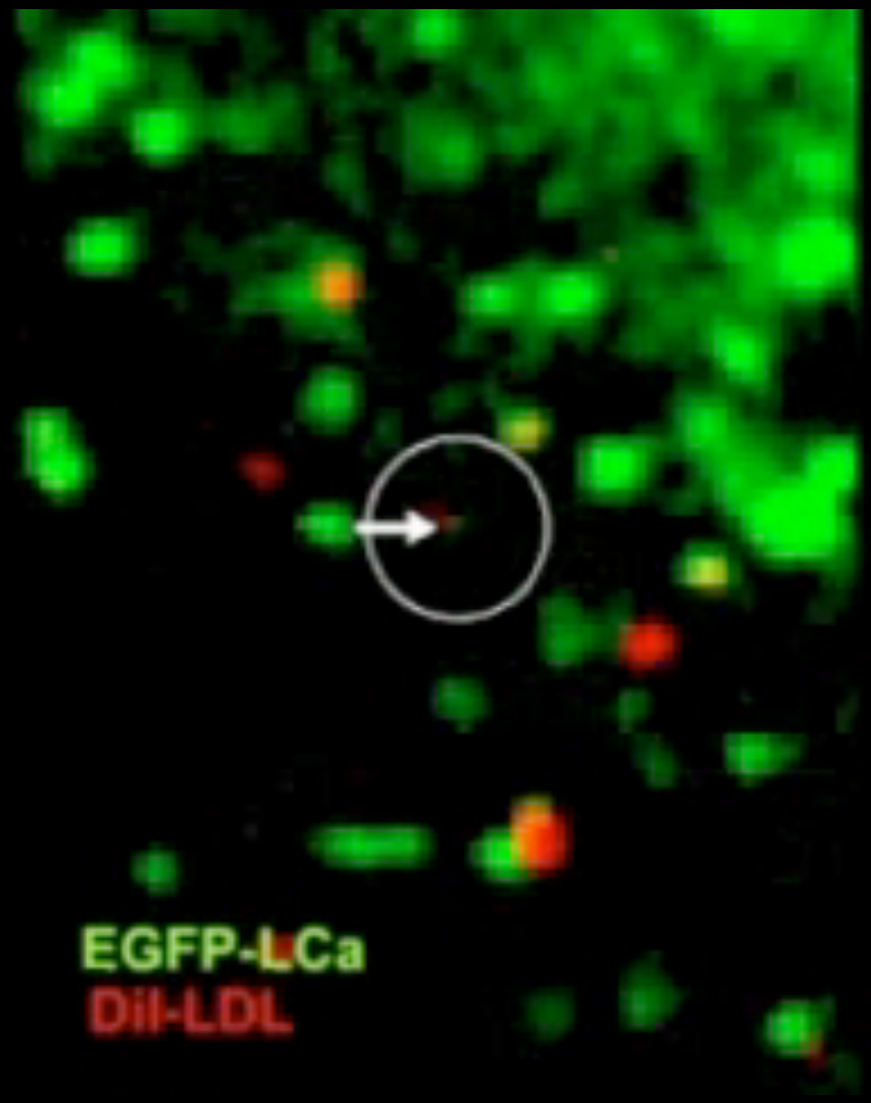
ELECTRON MICROSCOPY OF CLATHRIN IN CELLS



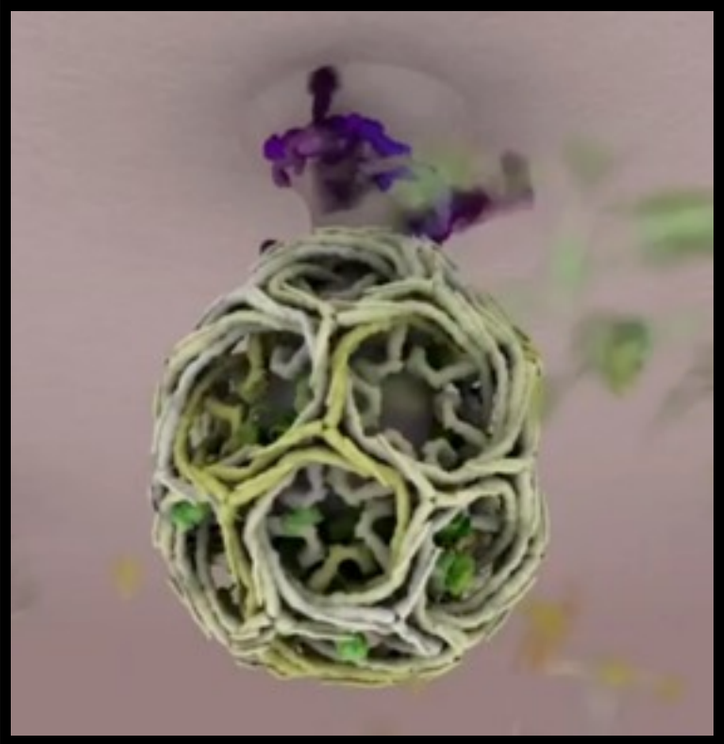
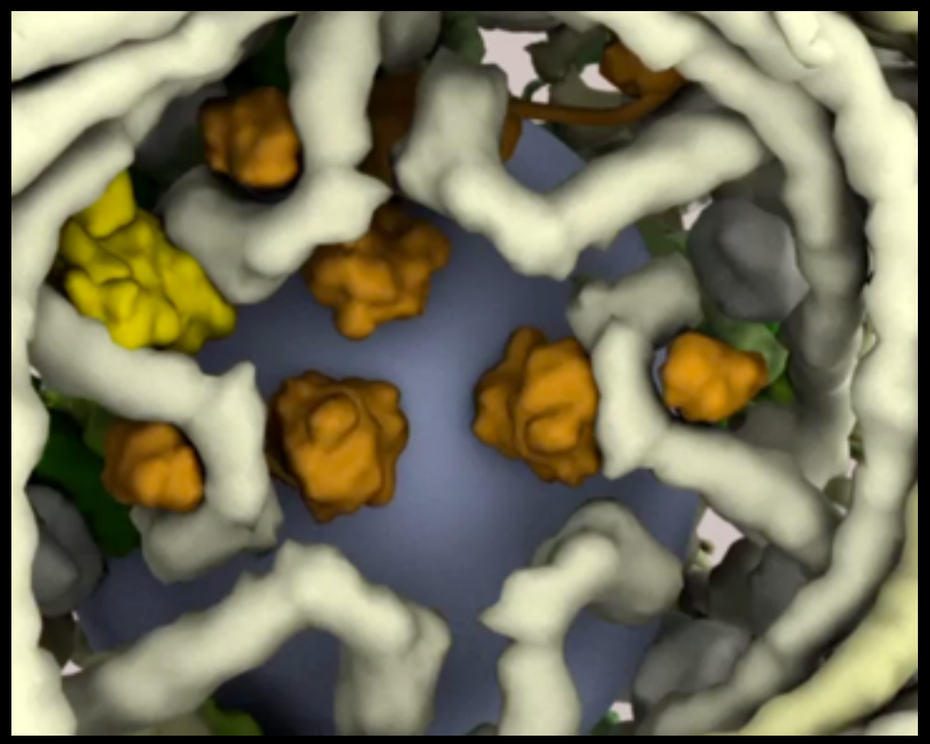
Heuser & Keene, 1998

CLATHRIN-MEDIATED ENDOCYTOSIS

VISUALIZING DYNAMICS



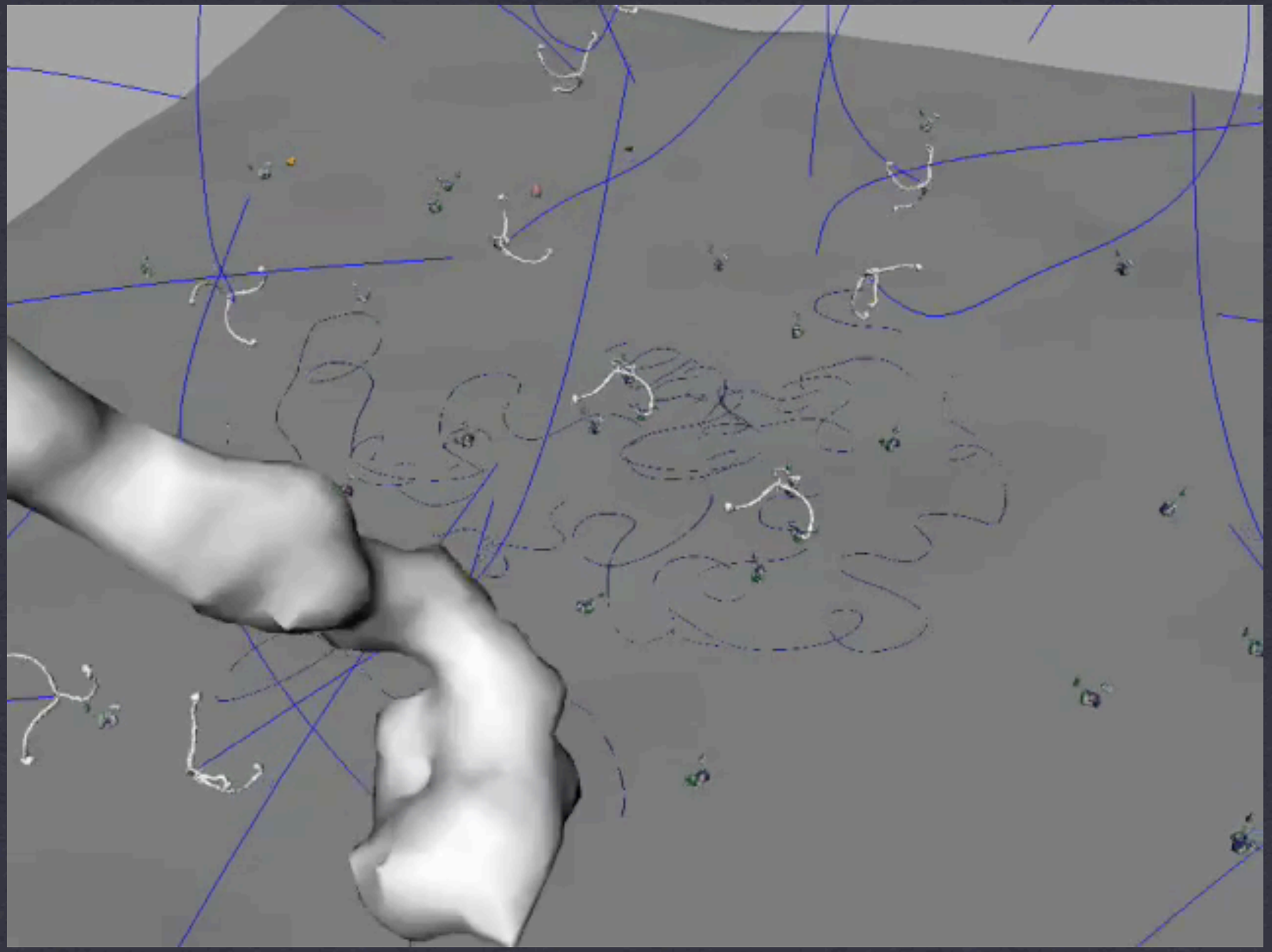
KIRCHHAUSEN, 2004


“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

BEHIND THE SCENES



THE EXPLORING ORIGINS PROJECT

THE BROAD GOAL:

To make current research and theories on the origin of life more accessible to the public and to scientists through the use of dynamic molecular visualizations.

THE PLAN:

Work together with researchers to design visualizations of their research and current theories on the origin of life.

Szostak Lab
MGH/Harvard

Create visualizations for use in a multimedia exhibit at the Museum of Science.

Museum of Science

TRANSLATING SCIENTIFIC DATA INTO A VISUAL STORY

nature

doi:10.1038/nature07018

LETTERS

Template-directed synthesis of a genetic polymer in a model protocell

Sheref S. Mansy[1], Jason P. Schrum[1], Mathangi Krishnamurthy[1], Sylvia Tobé[1], Douglas A. Treco[1] & Jack W. Szostak[1]

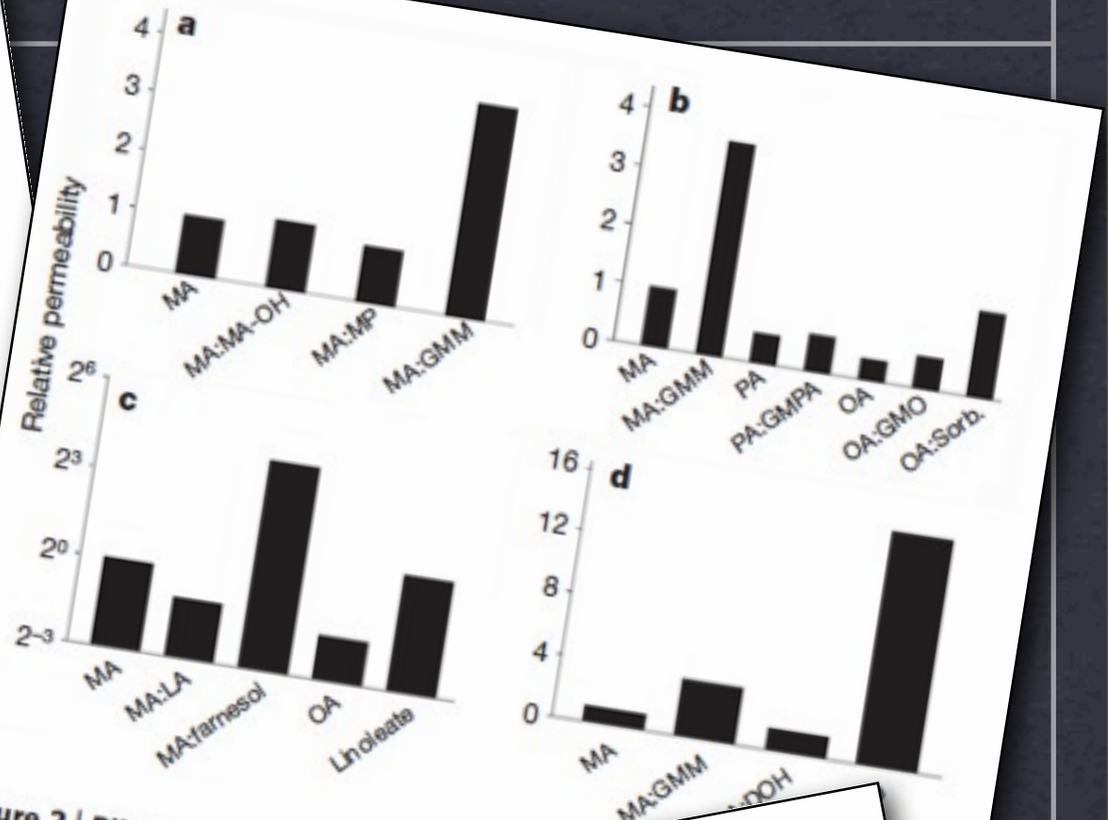
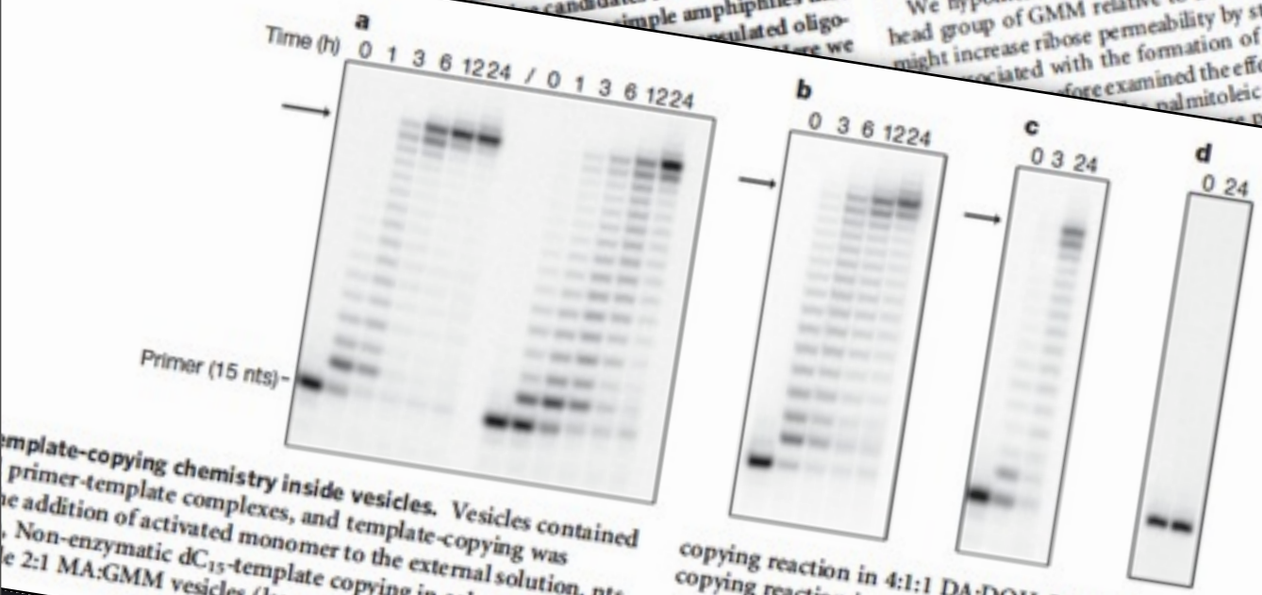


Figure 2 | Ribose permeability of
a–c, Influence of head gr
fluidity (c). d, C
myristol



emplate-copying chemistry inside vesicles. Vesicles contained primer-template complexes, and template-copying was he addition of activated monomer to the external solution. nts, . Non-enzymatic dC_{15}-template copying in solution (lanes e 2:1 MA:GMM 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:farnesol 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.

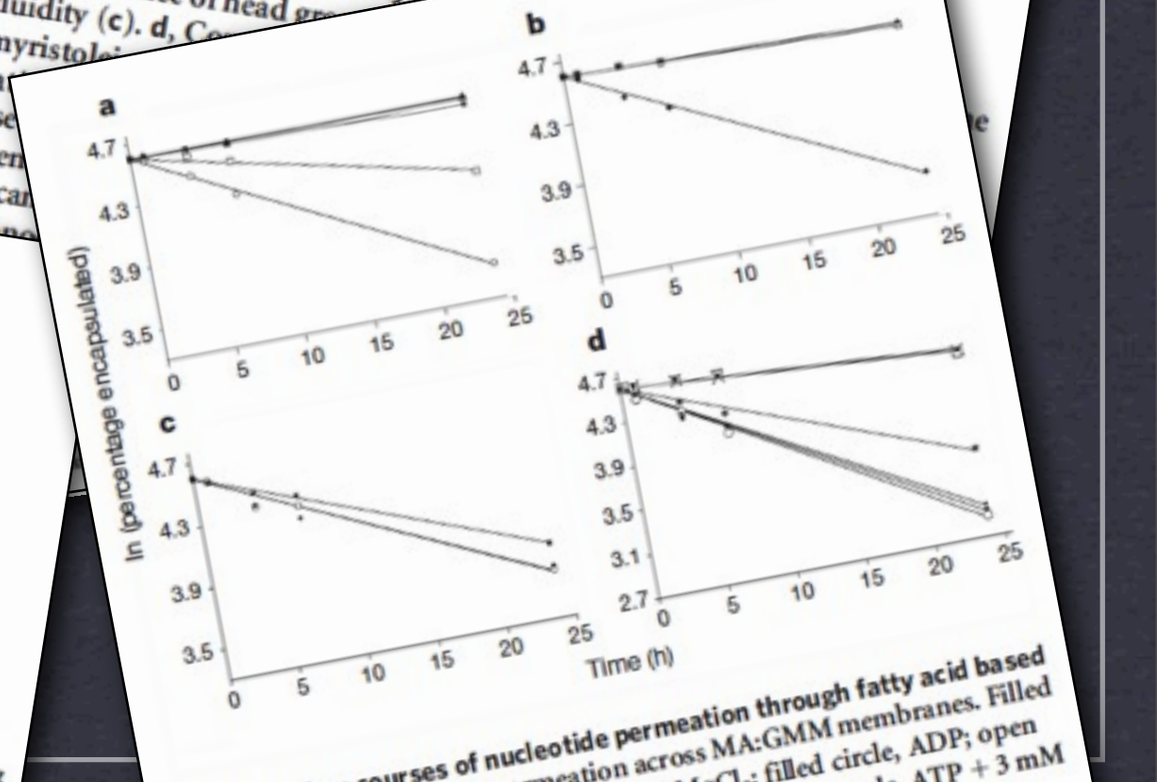


Figure 3 | Time courses of nucleotide permeation through fatty acid based
nucleotide permeation across MA:GMM membranes. Filled
+ 3 mM $MgCl_2$; filled circle, ADP; open
open triangle, ATP + 3 mM
membranes.

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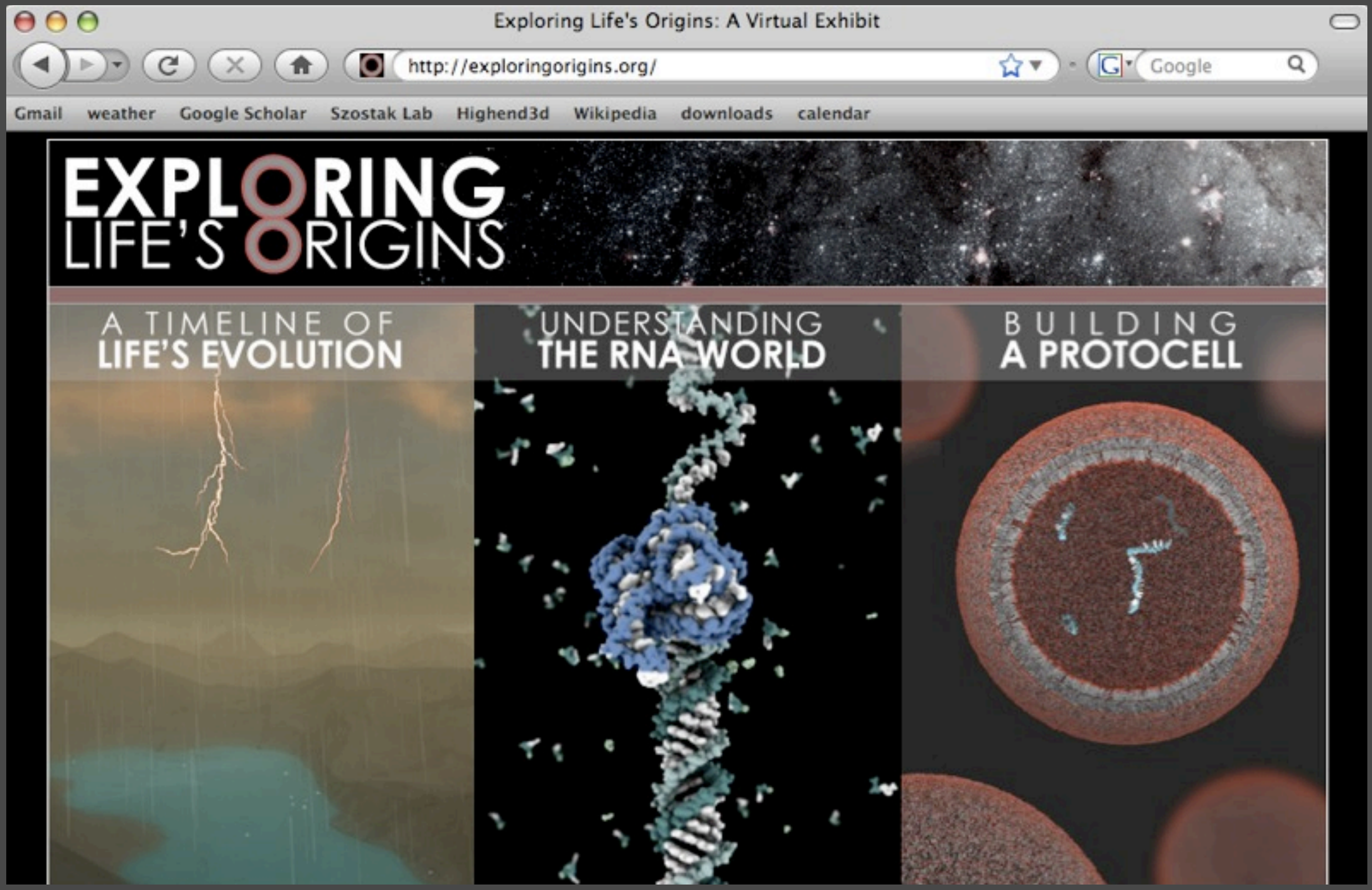
HEADSPACE

THE EXPLORING ORIGINS PROJECT

WITH JACK SZOSTAK, MASS GENERAL HOSPITAL & HARVARD UNIVERSITY



THE EXPLORING ORIGINS KIOSK

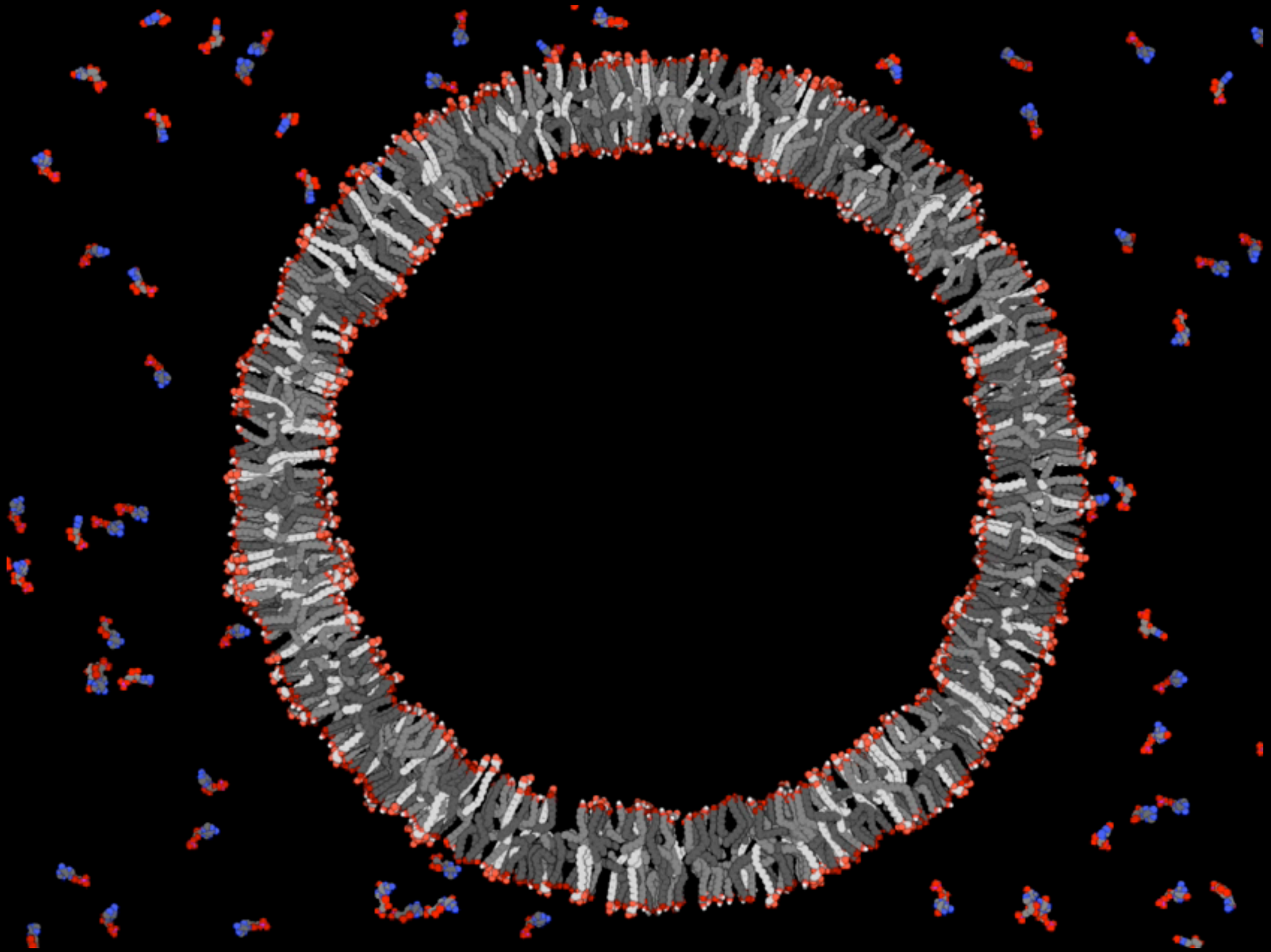
AT THE MUSEUM OF SCIENCE, BOSTON (CURRENT SCIENCE & TECHNOLOGY)

THE EXPLORING ORIGINS PROJECT

VISUALIZING ENTRY OF SMALL MOLECULES INTO VESICLES, 2008

THE EXPLORING ORIGINS PROJECT

VISUALIZING ENTRY OF SMALL MOLECULES INTO VESICLES, 2008



THE EXPLORING ORIGINS PROJECT

ROLE OF HYDROTHERMAL VENTS AND FATTY ACID SYNTHESIS, 2008

ANIMATIONS IN THE PRESS

Science Times

TUESDAY, JUNE 16, 2009

The New York Times

New Glimpses of Life's Puzzling Origins

By NICHOLAS WADE

Some 3.9 billion years ago, a shift in the orbit of the Sun's outer planets sent a surge of large comets and asteroids careening into the inner solar system. Their violent impacts gouged out the large craters still visible on the Moon's face, heated Earth's surface into molten rock and boiled off its oceans into an incandescent mist.

Yet rocks that formed on Earth 3.8 billion years ago, almost as soon as the bombardment had stopped, contain possible evidence of biological processes. If life can arise from inorganic matter so 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 origins of life on Earth bristle 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 metabolism 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 moot, since life did start somehow. 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 seeding the planet, so hard 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.

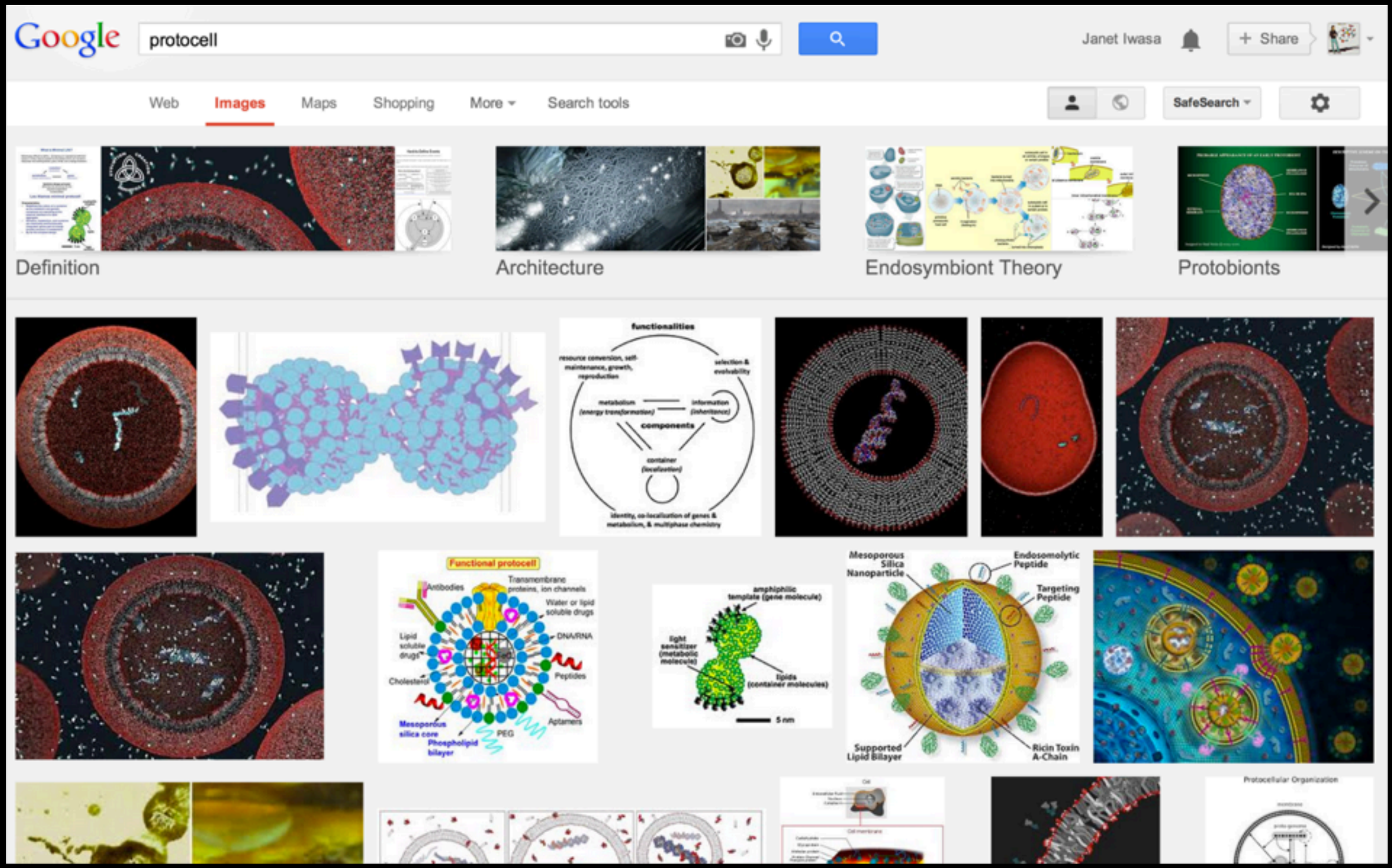
One in a series of discoveries about the cell-like structures that could have formed naturally from fatty chemicals likely to have been present on the primitive Earth. This lead emerged from a long argument between these colleagues as to whether a genetic system or a cell membrane came first in the development 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 Luisi, published a somewhat adversarial manifesto in Nature in 2001, declaring that the way to make a synthetic cell was to get a protocell and a genetic molecule to grow and divide in parallel.

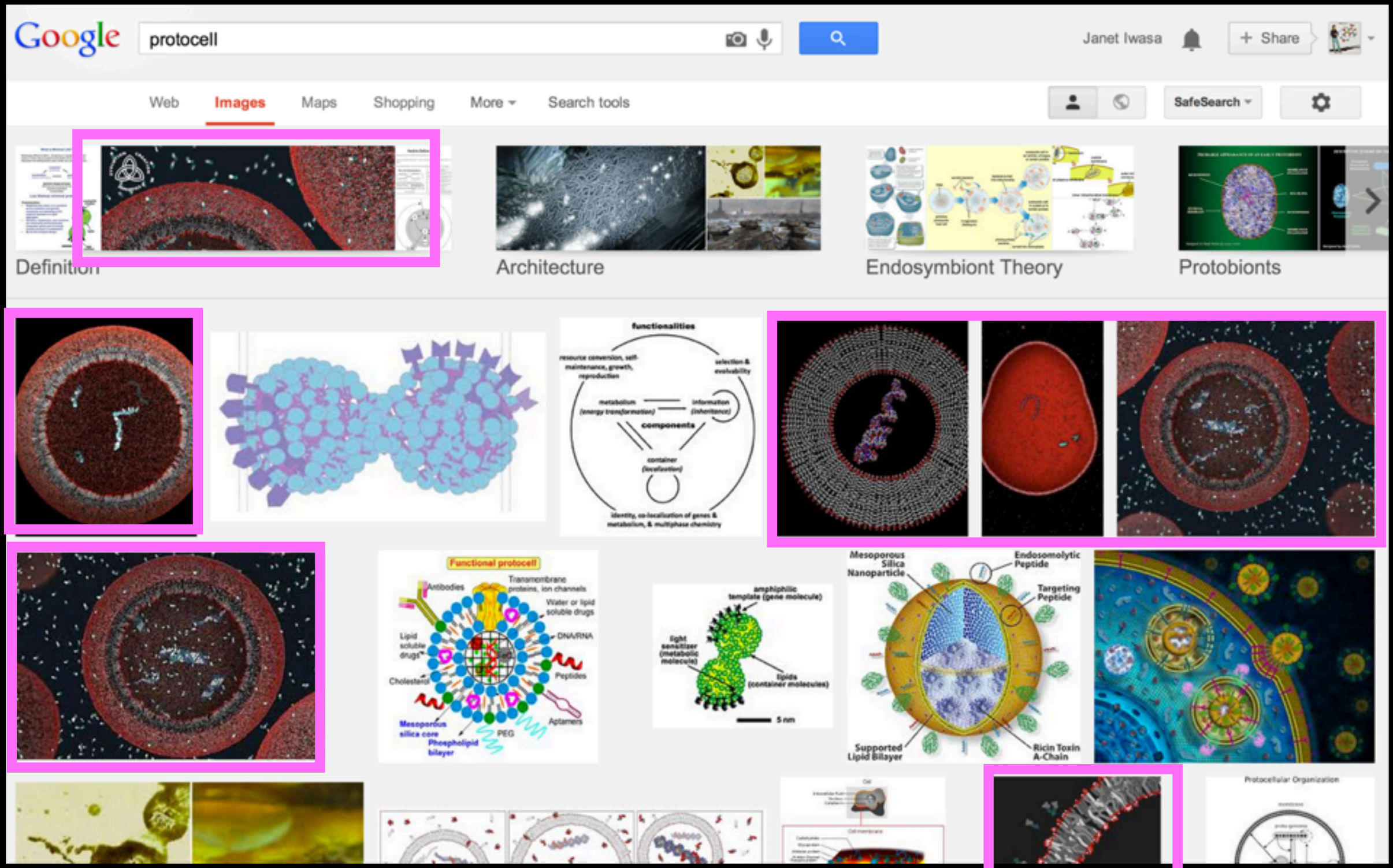
Continued on Page 4

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, above, 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.

VISUALIZING PROTOCELLS

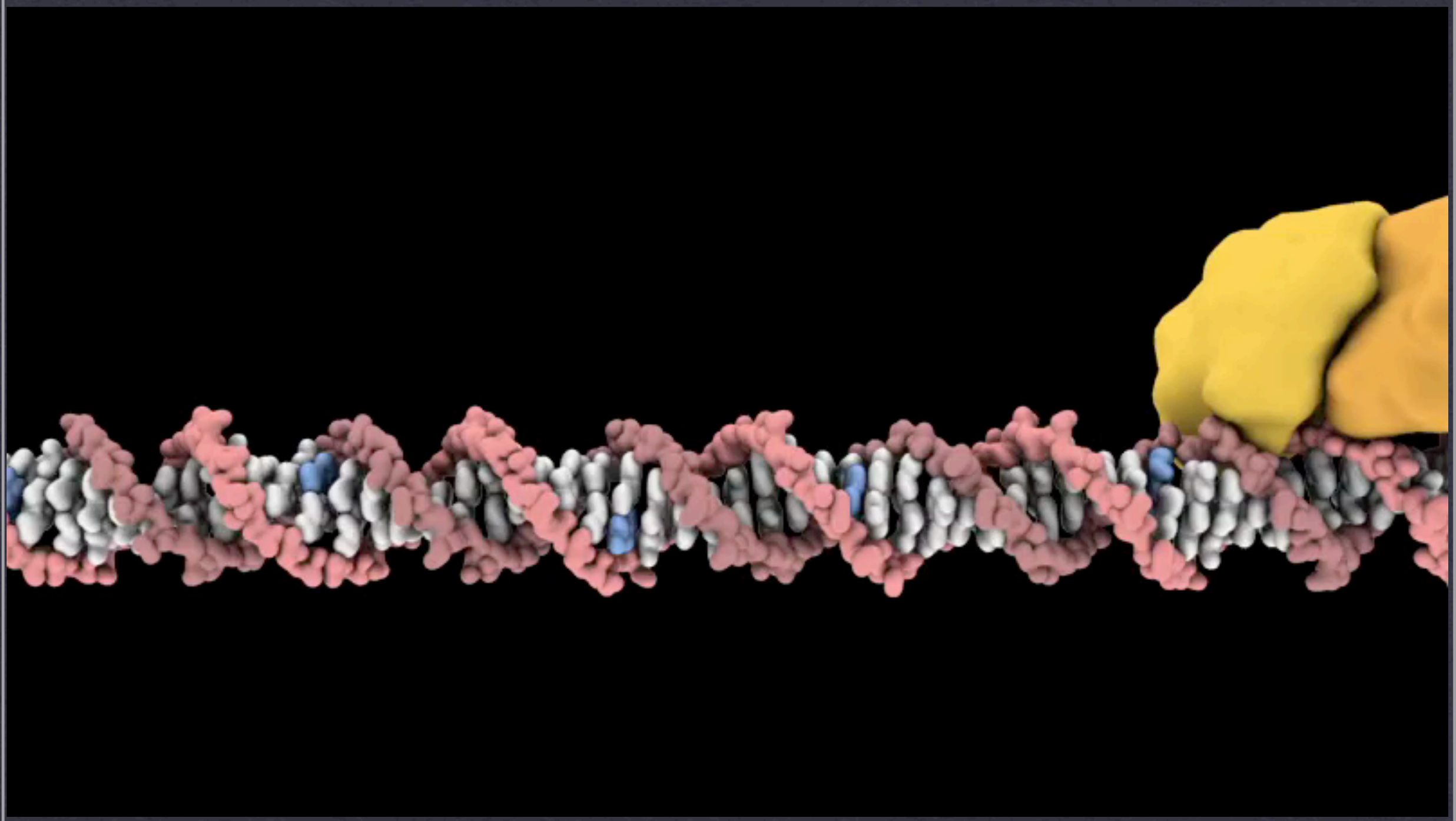


VISUALIZING PROTOCELLS



CHROMATIN REMODELING

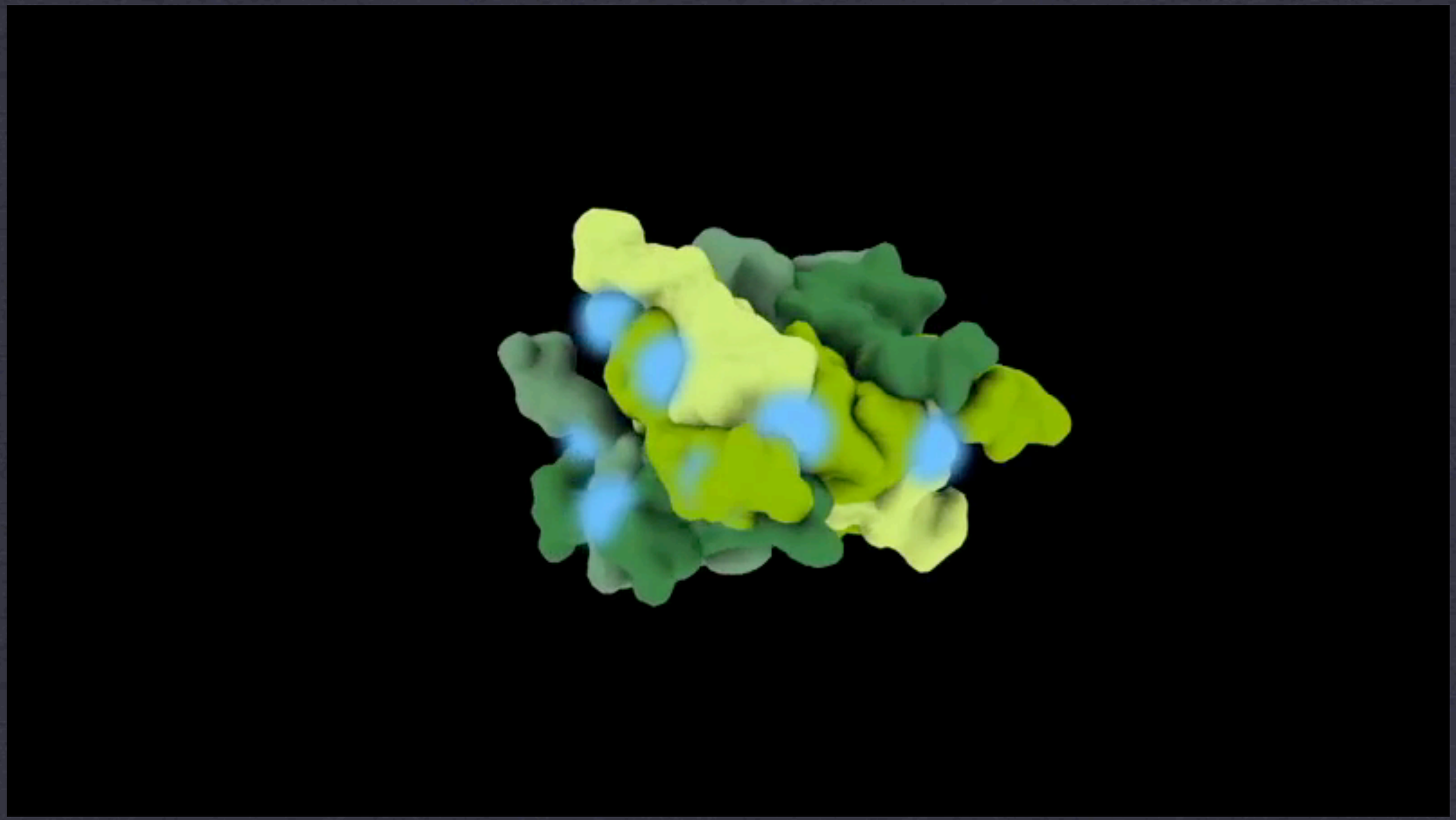
WITH BRAD CAIRNS AND CEDRIC CLAPIER



INTRODUCTION TO THE ATPASE (STRUCTURE TAKEN FROM PCRA, 2PJR)

CHROMATIN REMODELING

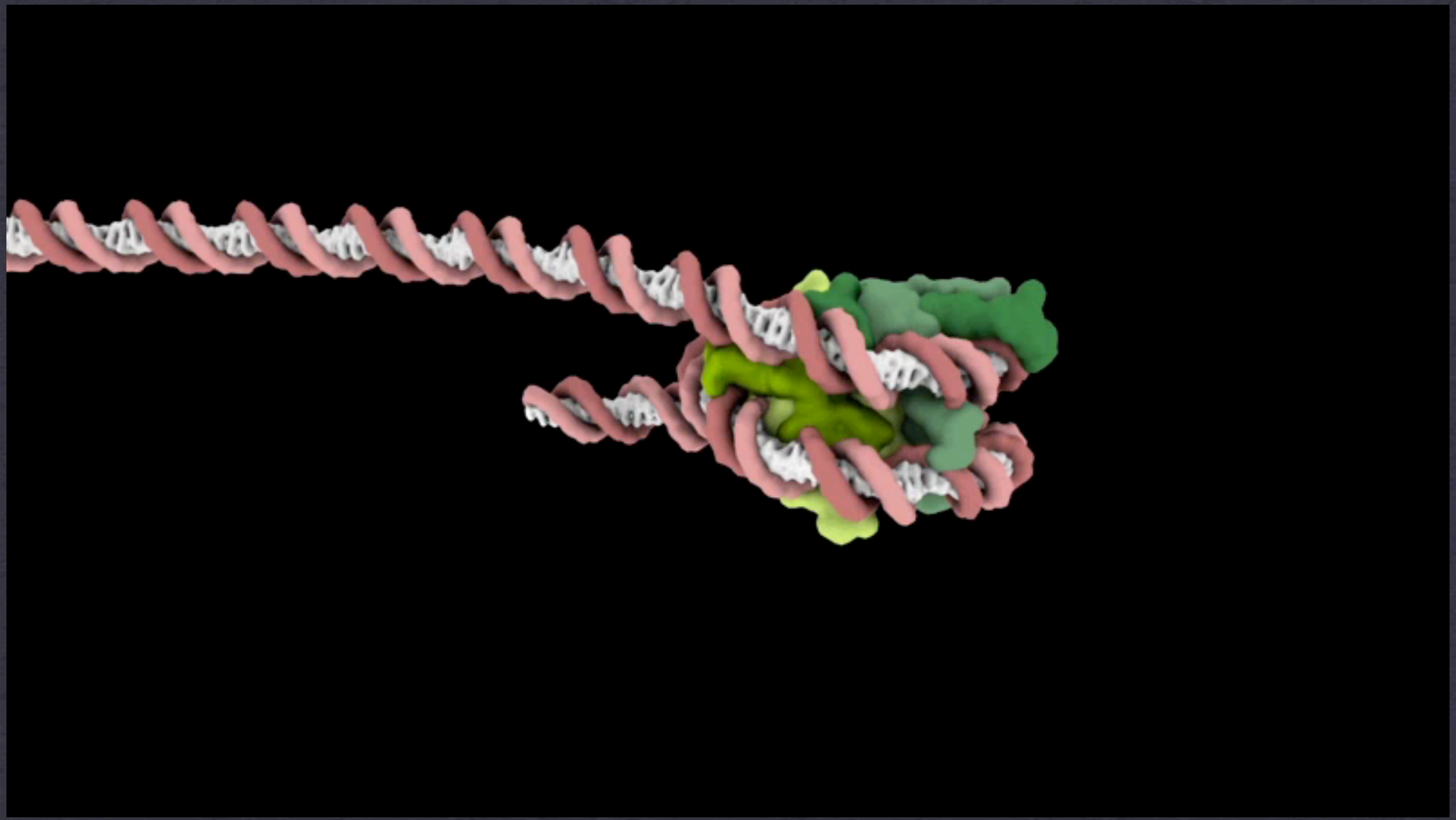
WITH BRAD CAIRNS AND CEDRIC CLAPIER



INTRODUCTION TO THE NUCLEOSOME (STRUCTURE TAKEN FROM 1AOI)

CHROMATIN REMODELING

WITH BRAD CAIRNS AND CEDRIC CLAPIER



BASIC MECHANISM OF SWI/SNF REMODELERS

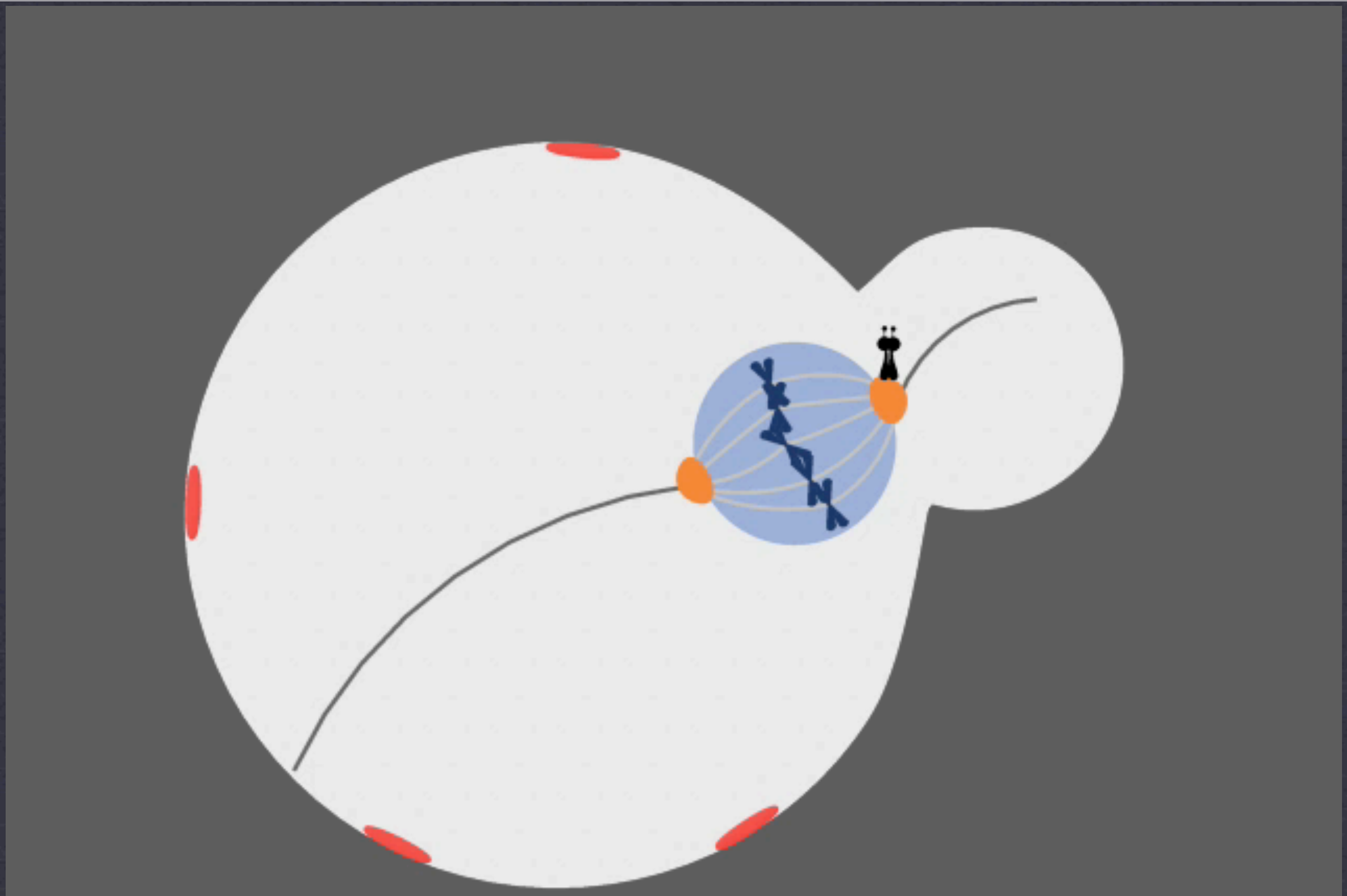
COMMUNICATING CONFIDENCE VIA RENDERING STYLE

THE ROLE OF DYNEIN IN YEAST MITOSIS

with Sam Reck-Peterson

COMMUNICATING CONFIDENCE VIA RENDERING STYLE

THE ROLE OF DYNEIN IN YEAST MITOSIS



with Sam Reck-Peterson

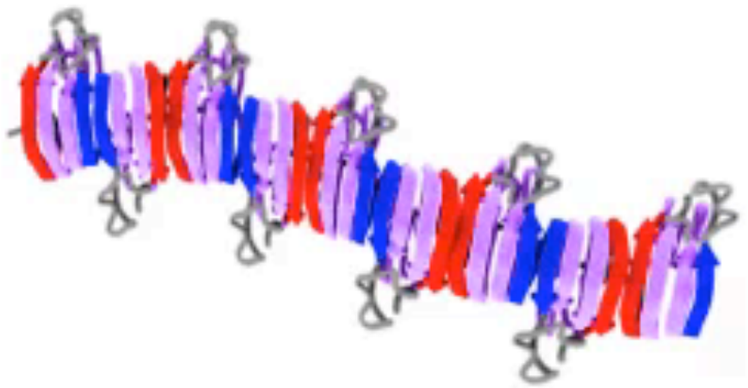
ANIMATING AMYLOID FIBRILS

NUCLEATION OF A PRION POLYMER

WITH SUSAN LINDQUIST

ANIMATING AMYLOID FIBRILS

PULLING APART A PRION POLYMER



WITH SUSAN LINDQUIST

ANIMATION AND THE SCIENTIFIC PROCESS

STEPS:

1. Define the question
2. Make observations
3. Form hypothesis
4. Perform experiment and collect data
5. Analyze data
6. Interpret data and draw conclusions
7. Publish results

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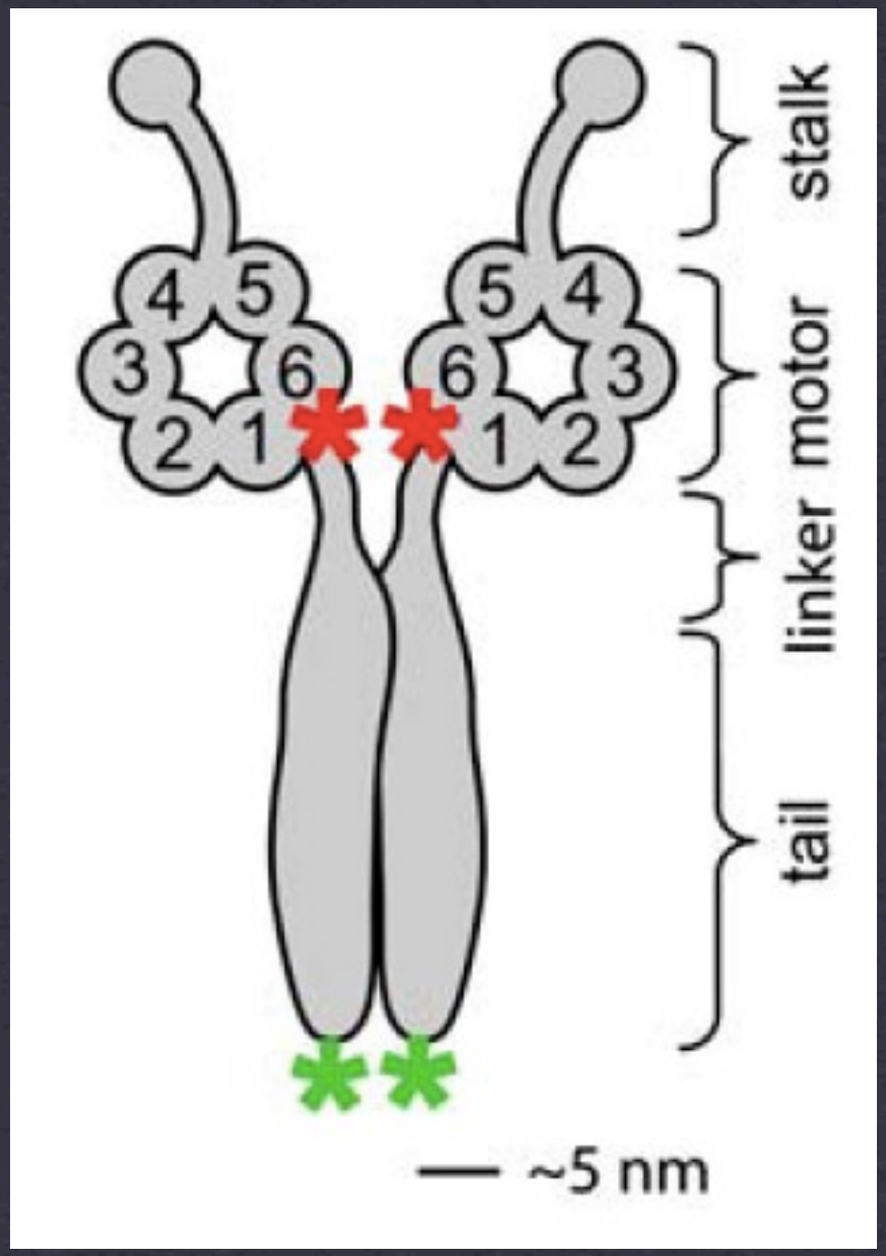
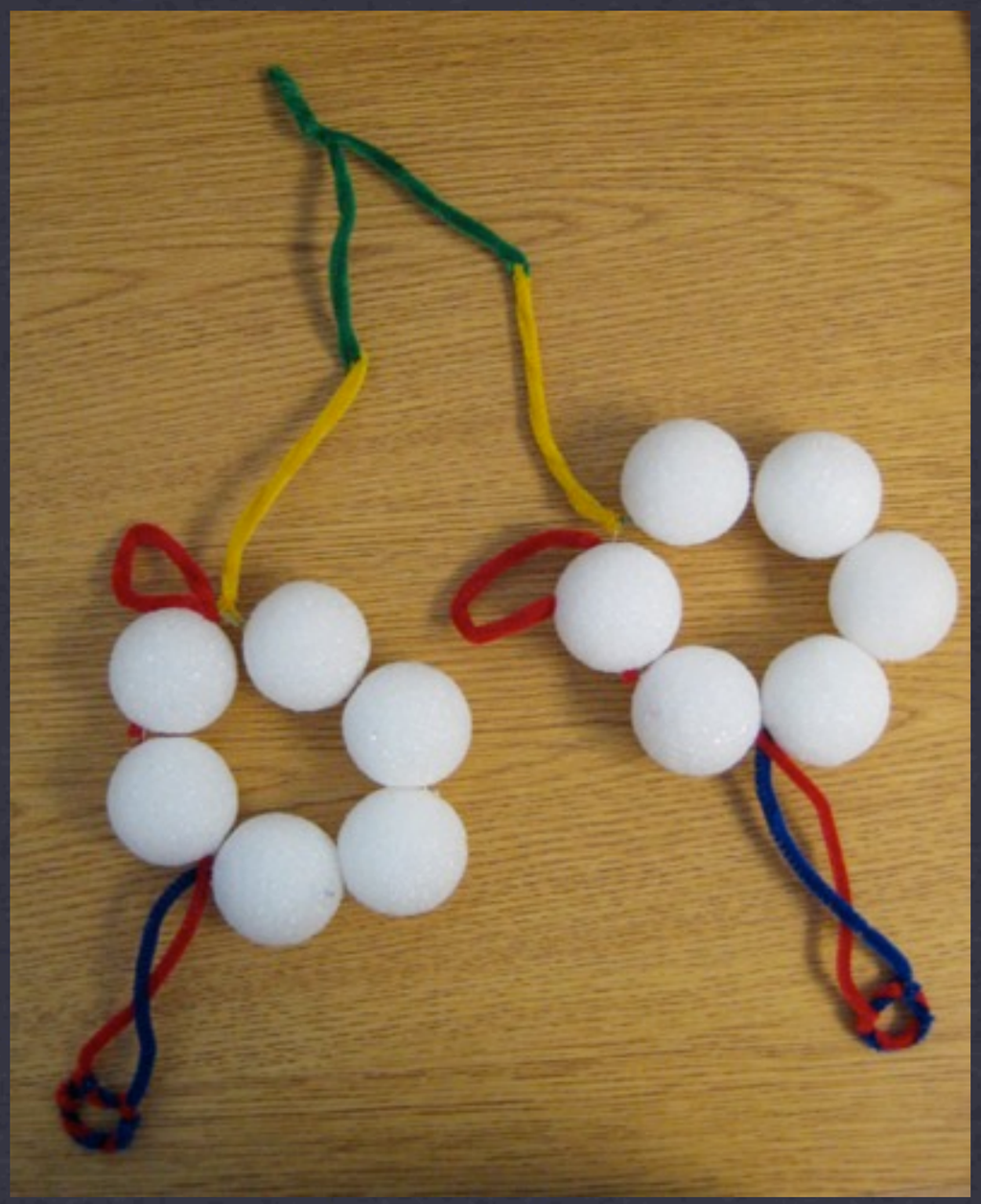
STUDYING DYNEIN STRUCTURE AND FUNCTION

2D AND 3D MODELS



Schematic illustration of dynein

Reck-Peterson, et al., 2006

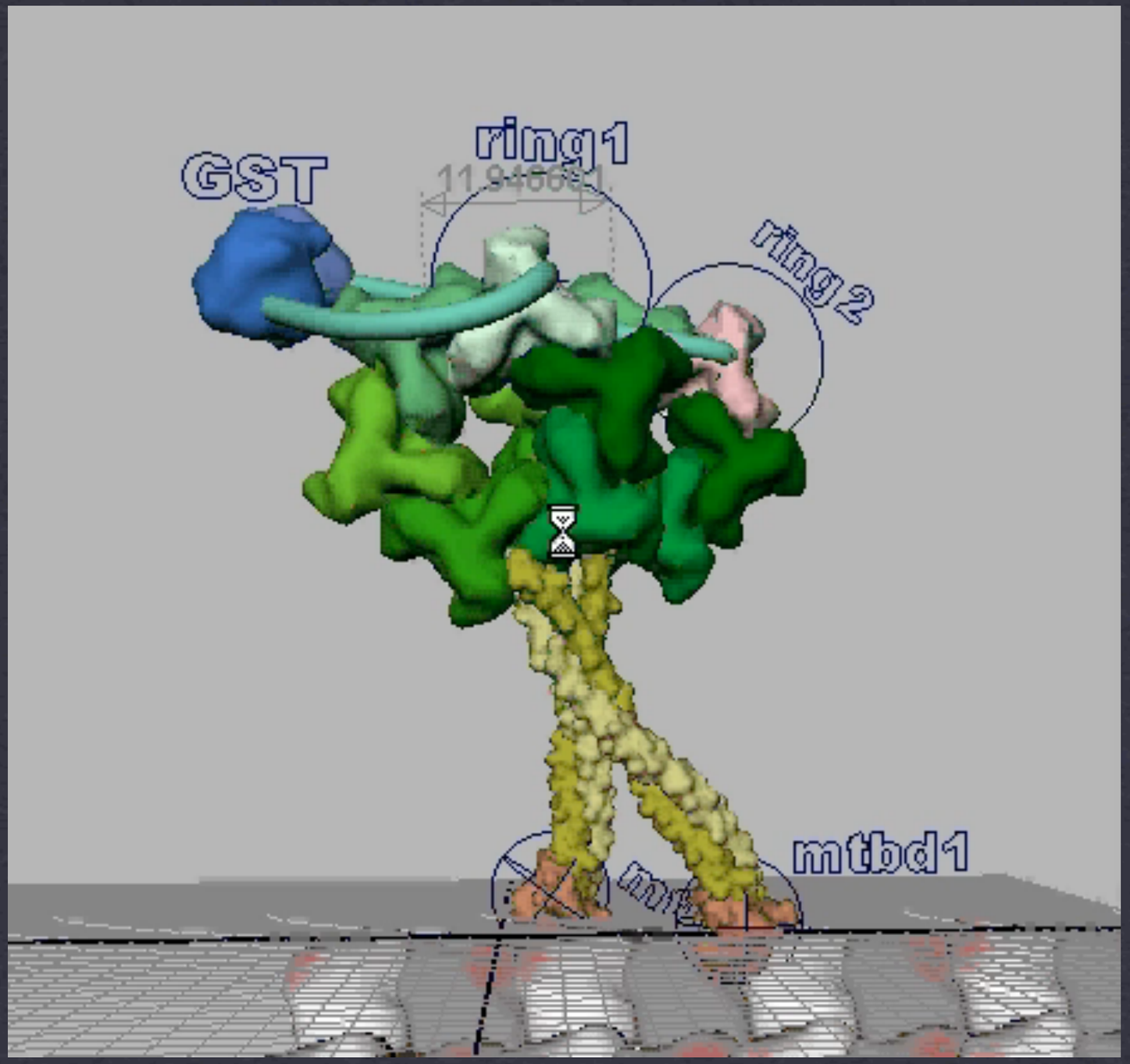


Physical model of the motor protein dynein

made by Samara Reck-Peterson

STUDYING DYNEIN STRUCTURE AND FUNCTION

AN EARLY ARTICULATED 3D MODEL

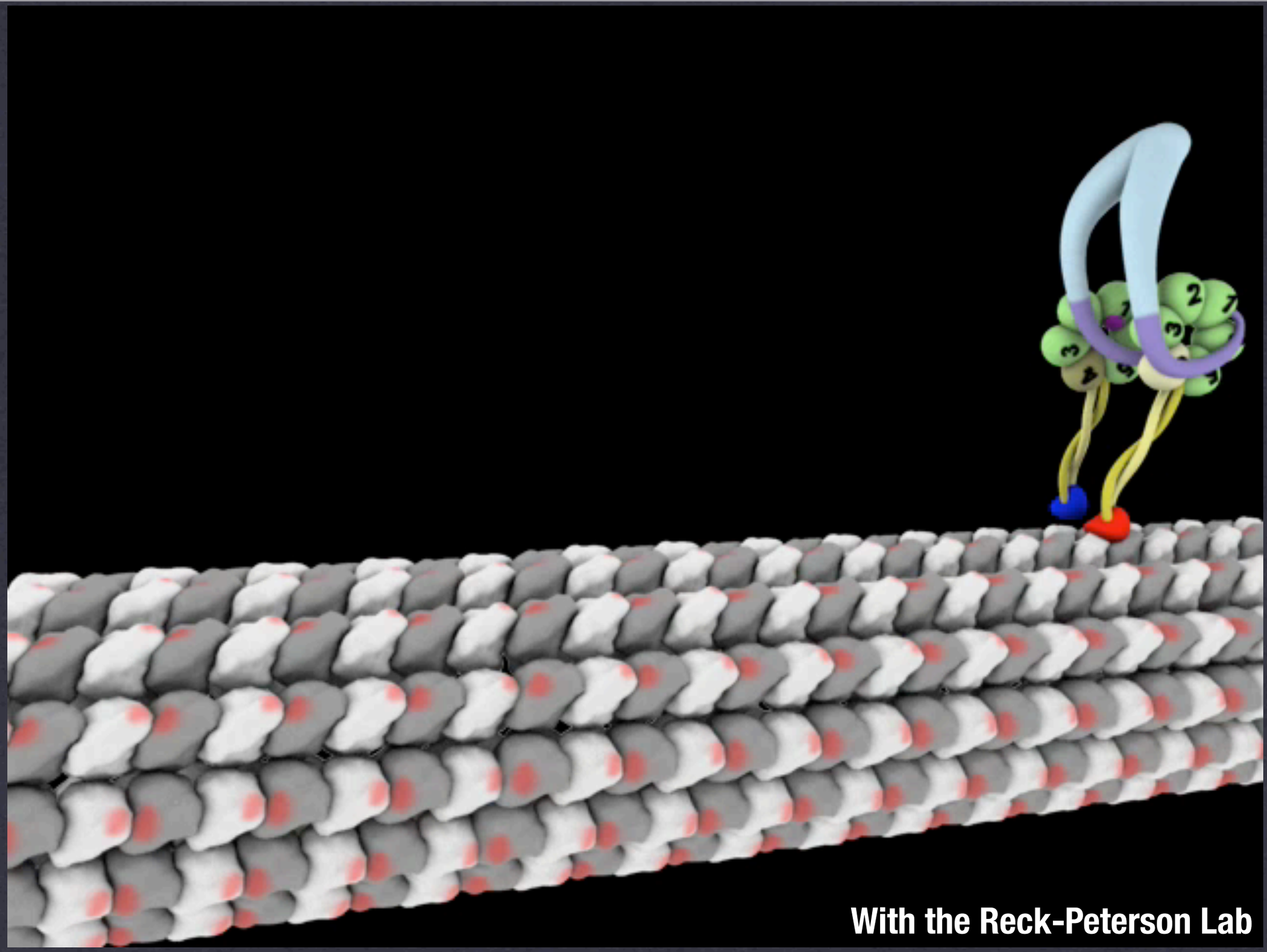


3D model of dynein

With the Reck-Peterson Lab

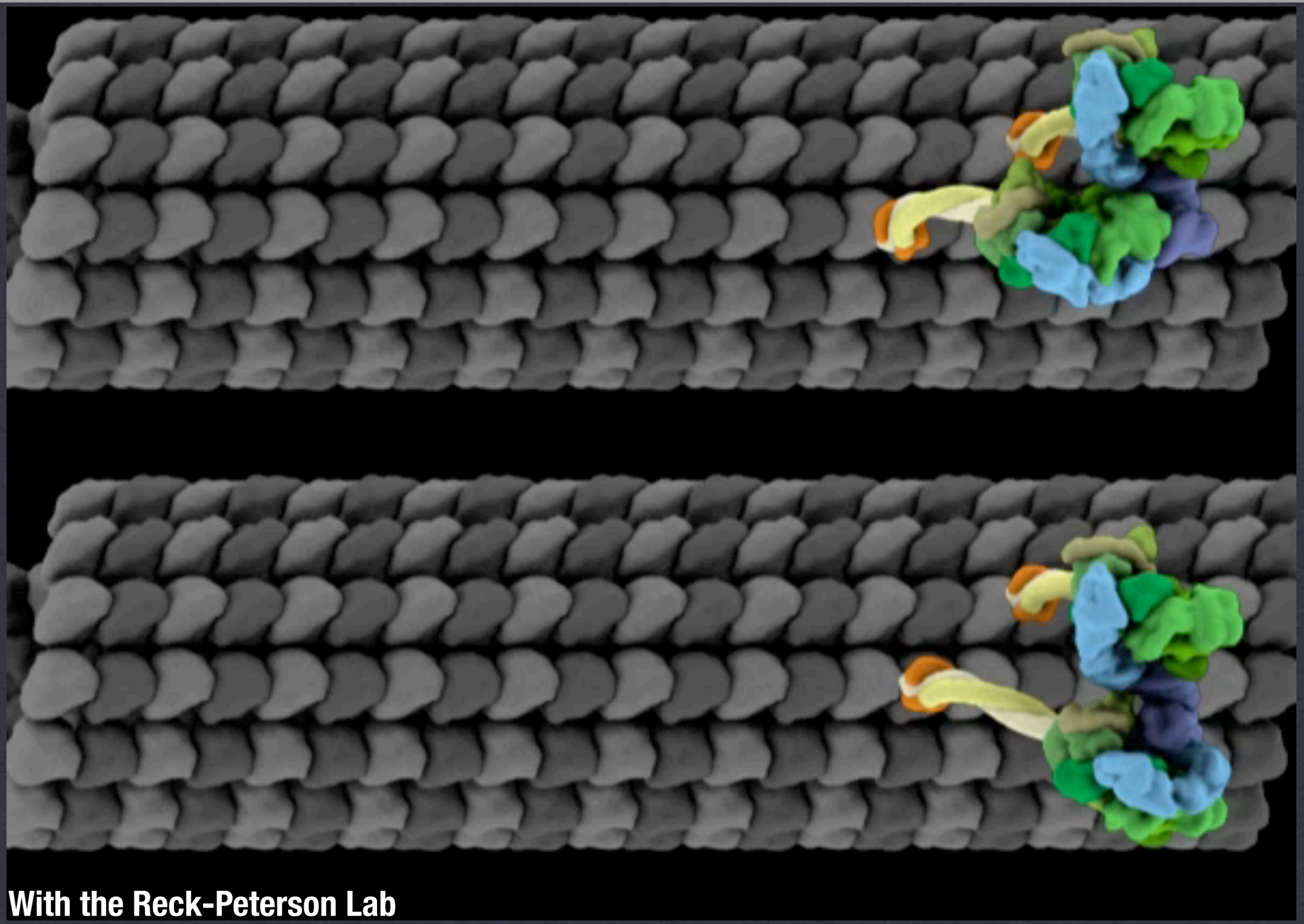
STUDYING DYNEIN STRUCTURE AND FUNCTION

AN EARLY 3D ANIMATED MODEL



STUDYING DYNEIN STRUCTURE AND FUNCTION

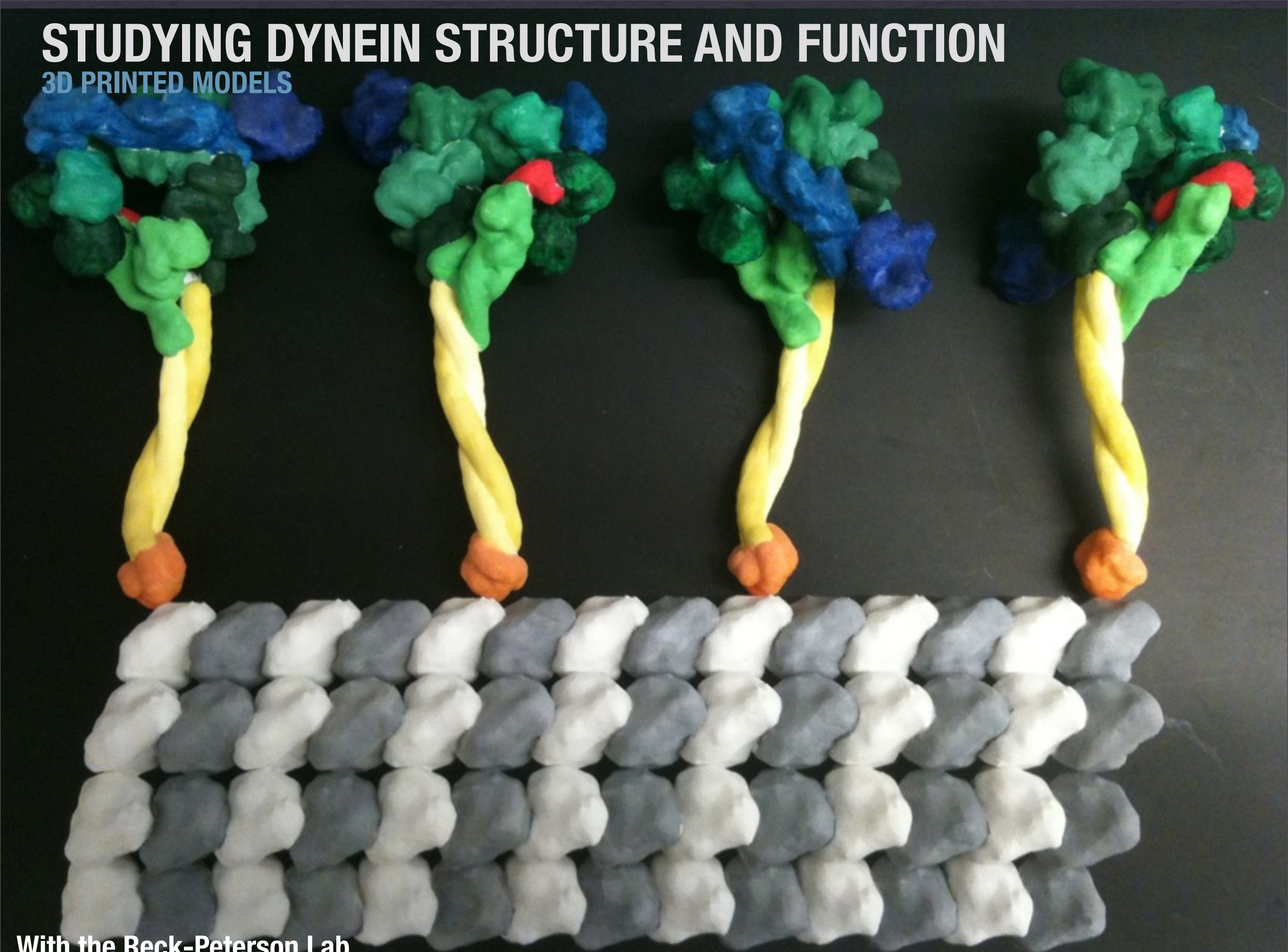
COMPARING DIFFERENT MODELS OF DYNEIN LOCOMOTION



With the Reck-Peterson Lab

STUDYING DYNEIN STRUCTURE AND FUNCTION

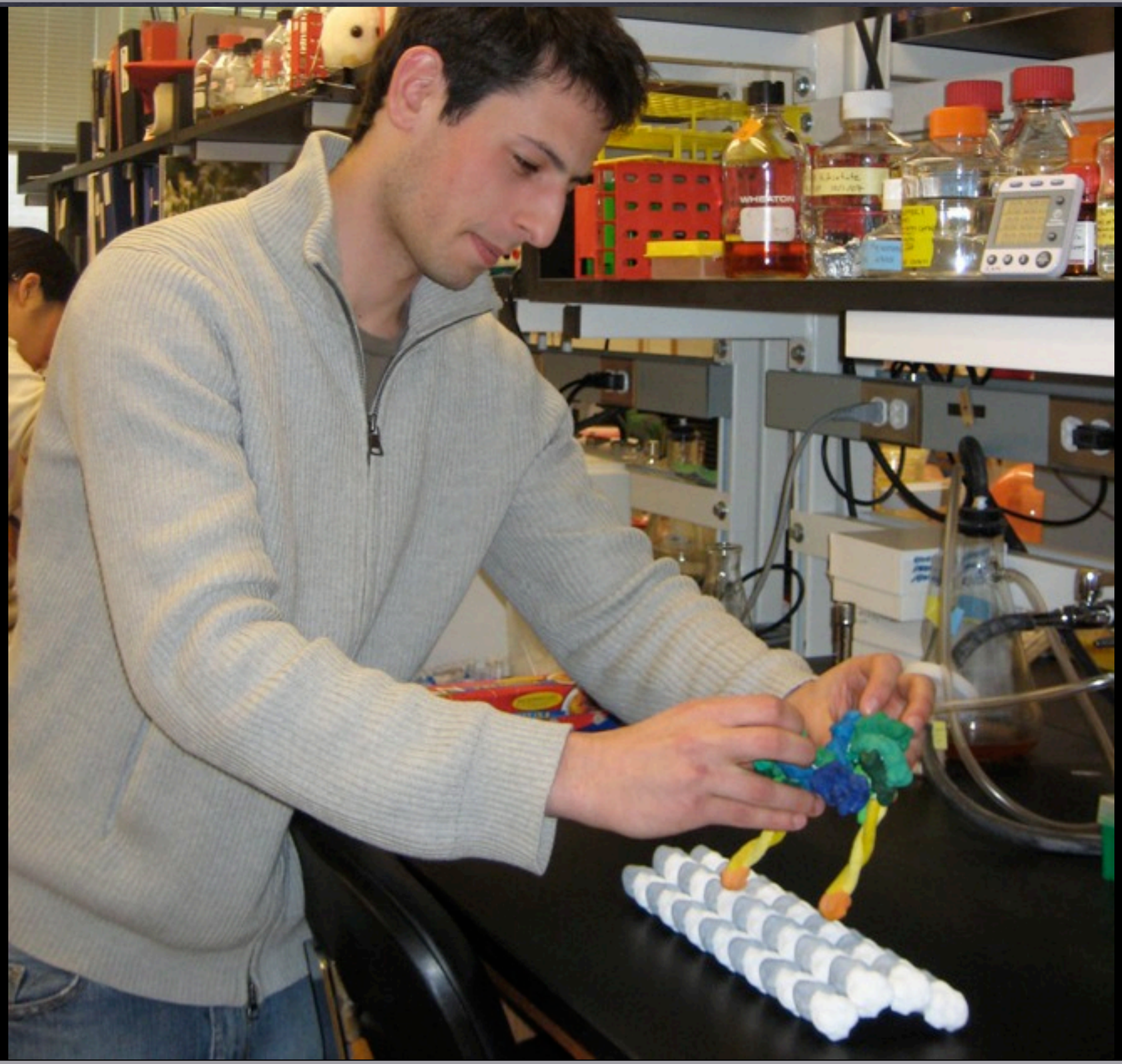
3D PRINTED MODELS



With the Reck-Peterson Lab

STUDYING DYNEIN STRUCTURE AND FUNCTION

3D PRINTED MODELS



MOLECULAR FLIPBOOK

A COMMUNITY RESOURCE FOR BUILDING AND SHARING MOLECULAR VISUALIZATIONS

(1) A 3D ANIMATION TOOLKIT

which will allow biologists to readily create molecular and cellular 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 FEATURES & CHALLENGES

- suite of molecular animation tools built in Blender's game engine which will include import, modeling, animation and rendering modules.

- intuitive interface, simple controls

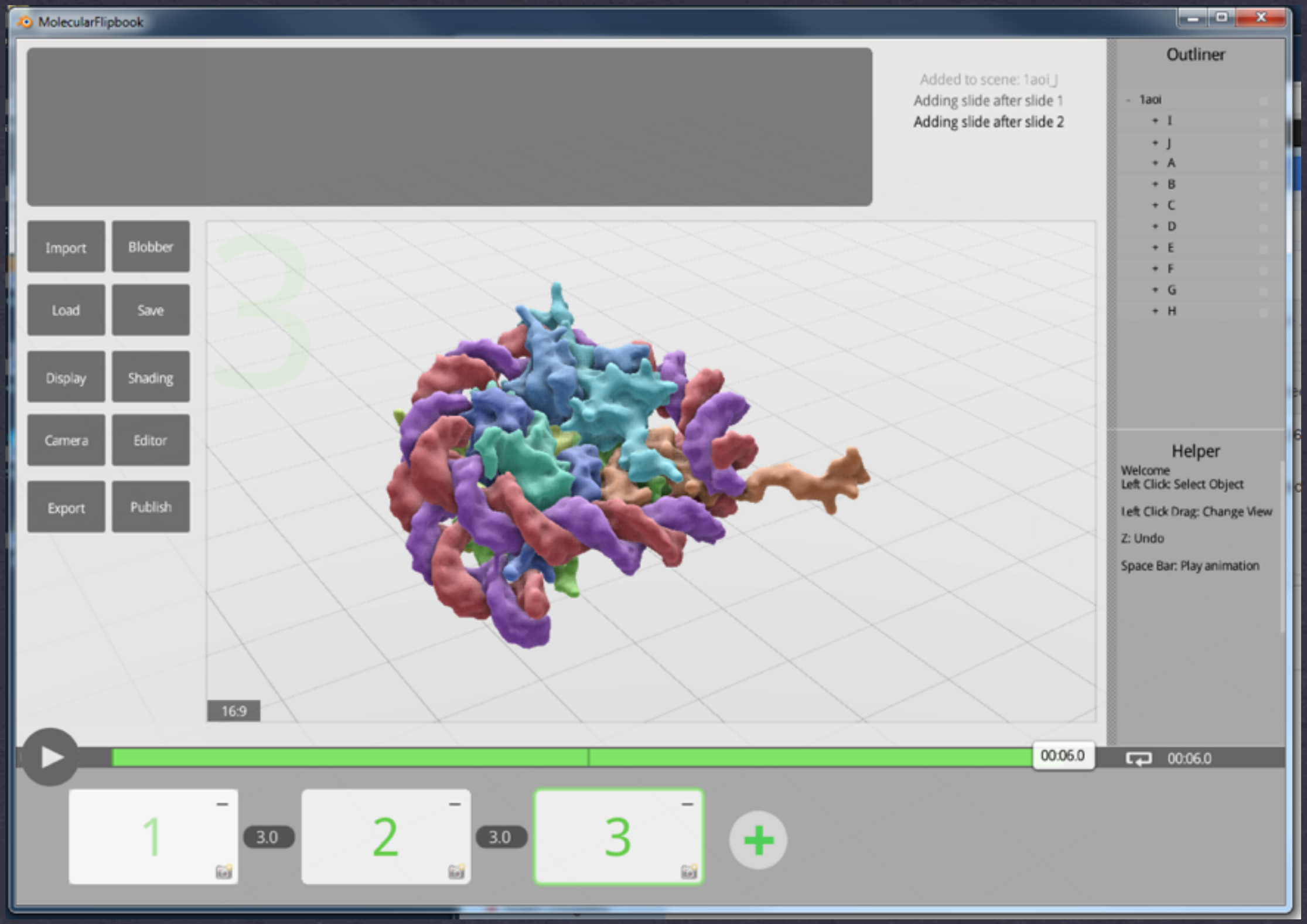
- ability to start creating animations after watching a short video tutorial.

Primary challenge:

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

MOLECULAR FLIPBOOK

INTERFACE DESIGN: OVERVIEW



MOLECULAR FLIPBOOK

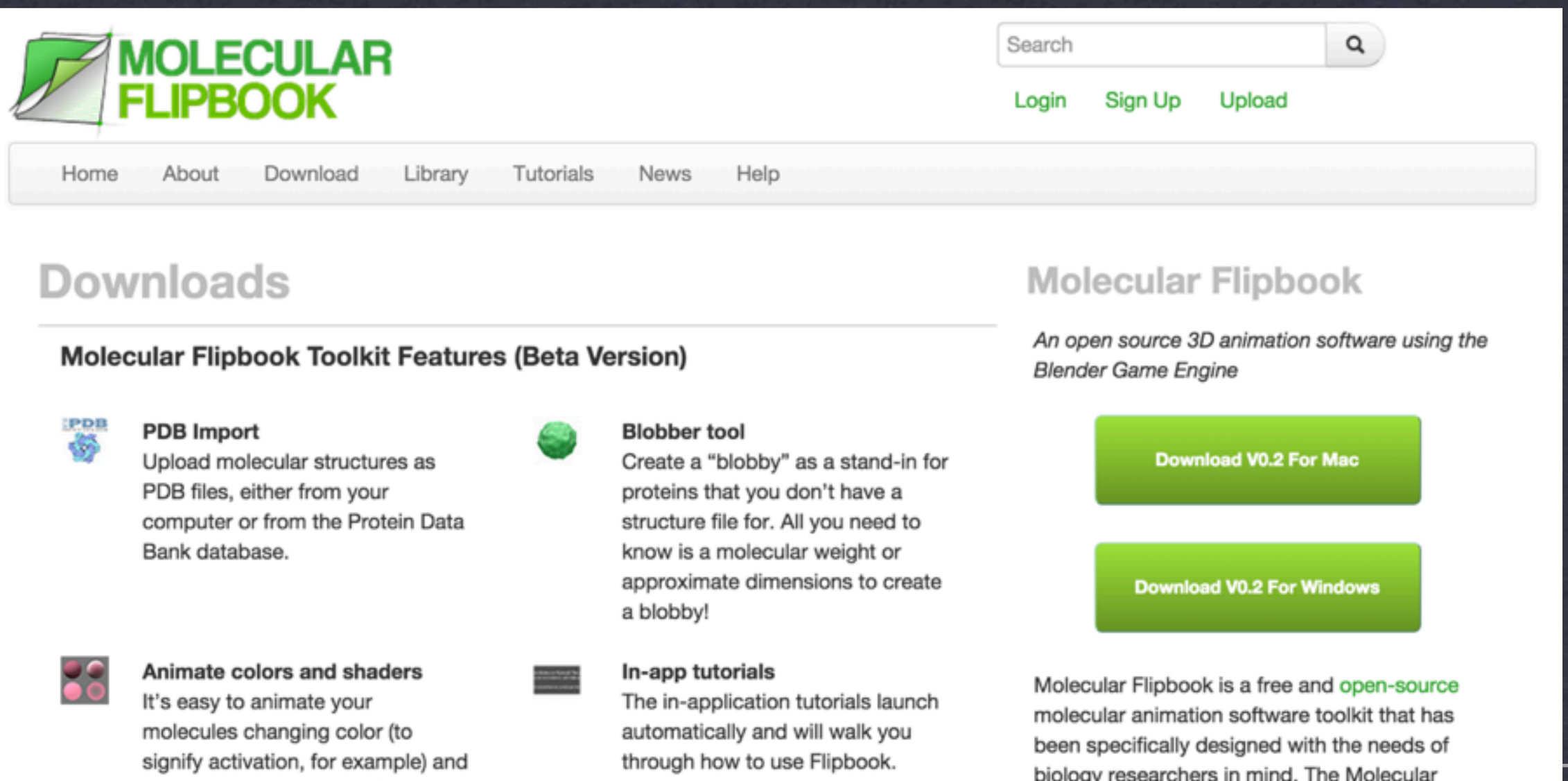
DEMO

MOLECULAR FLIPBOOK

FUTURE DEVELOPMENTS

+ Linker tool to connect different domains of known structure
+ Tools for creating polymers and other protein complexes
+ Use of collision detection for binding

http://MolecularFlipbook.org



MOLECULAR FLIPBOOK

WEBSITE FEATURES

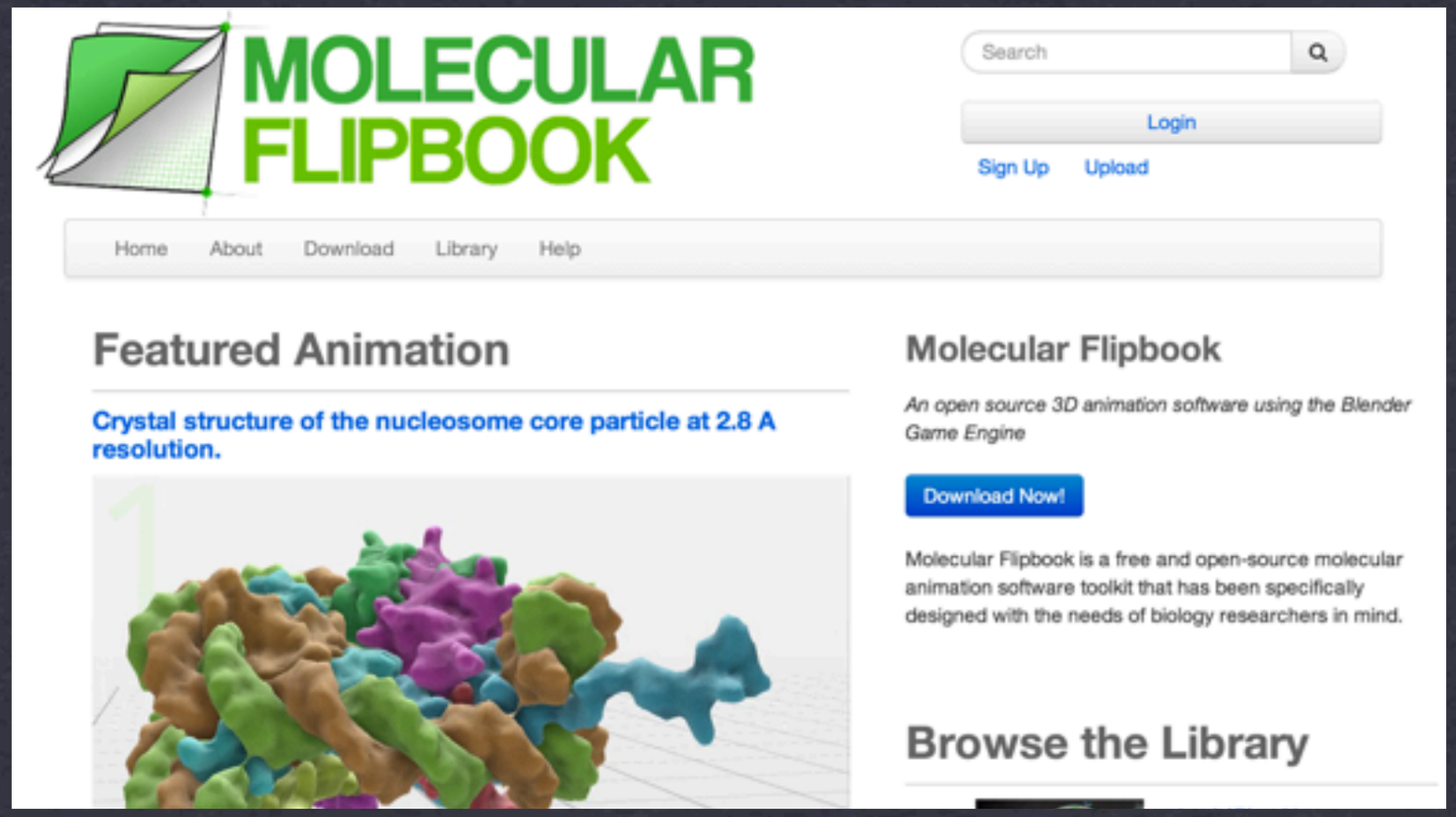
- searchable, easy-to-use online database that also hosts community/social interactions/ collaborations

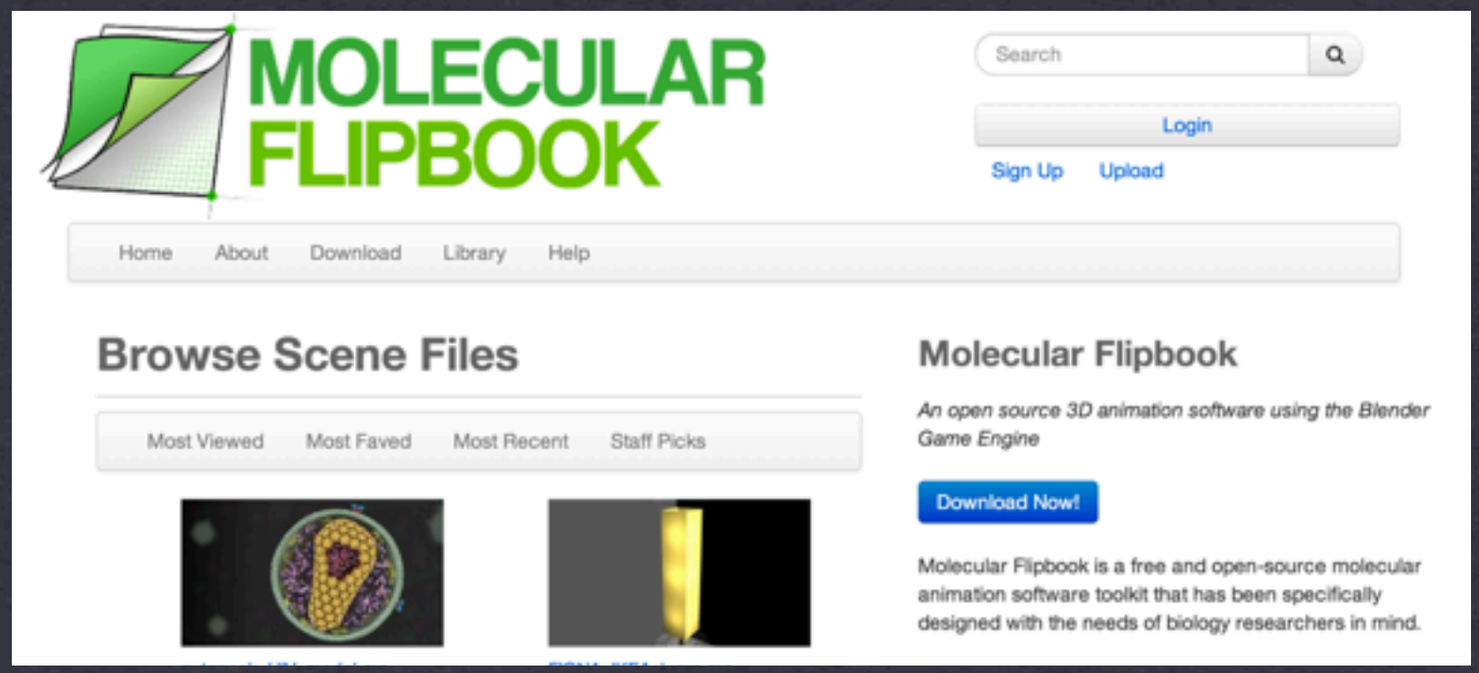
- will allow users to share not only Blender-based animation, but also Illustrator, Photoshop files, etc.

- provides a visual way of following the evolution of a hypothesis over time

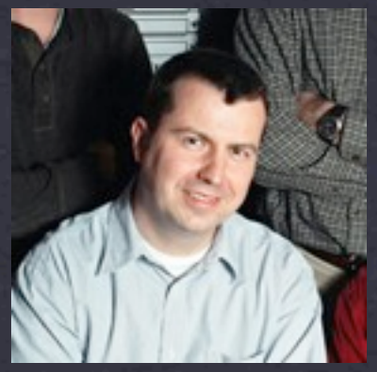
Primary challenge:

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





THE MOLECULAR FLIPBOOK TEAM



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The Molecular FlipBook Team

LINKS

Janet Iwasa website
http://biochem.web.utah.edu/iwasa

The Molecular Flipbook Project
http://MolecularFlipbook.org

The Exploring Origins Project
http://ExporingOrigins.org