Active, exploratory learning in physics, chemistry, and biology through cutting-edge biophysics research

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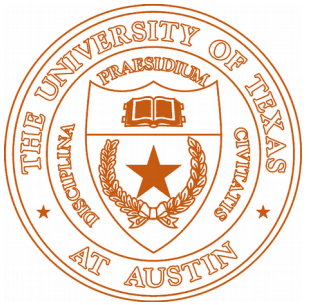
02 August 2016



An introduction to biophysics

- The questions we want to answer
- The tools we use
- Putting it all together

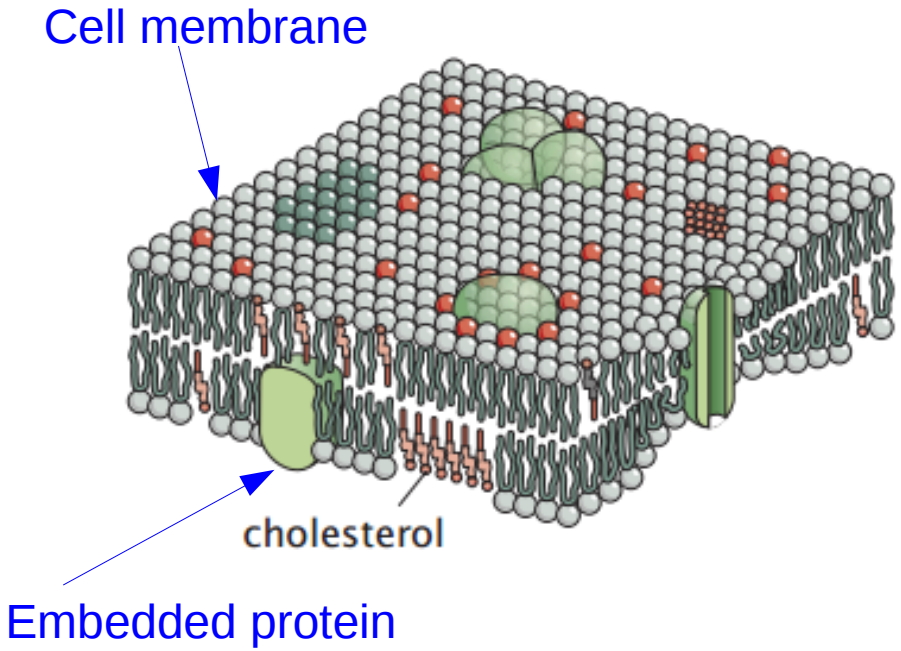
A toolkit of adaptable instructional activities and resources

- Connecting spectroscopy to fundamental physics (physics)
- Linking molecular structure to spectroscopy (chemistry)
- Exploring protein structure with interactive models (biology)

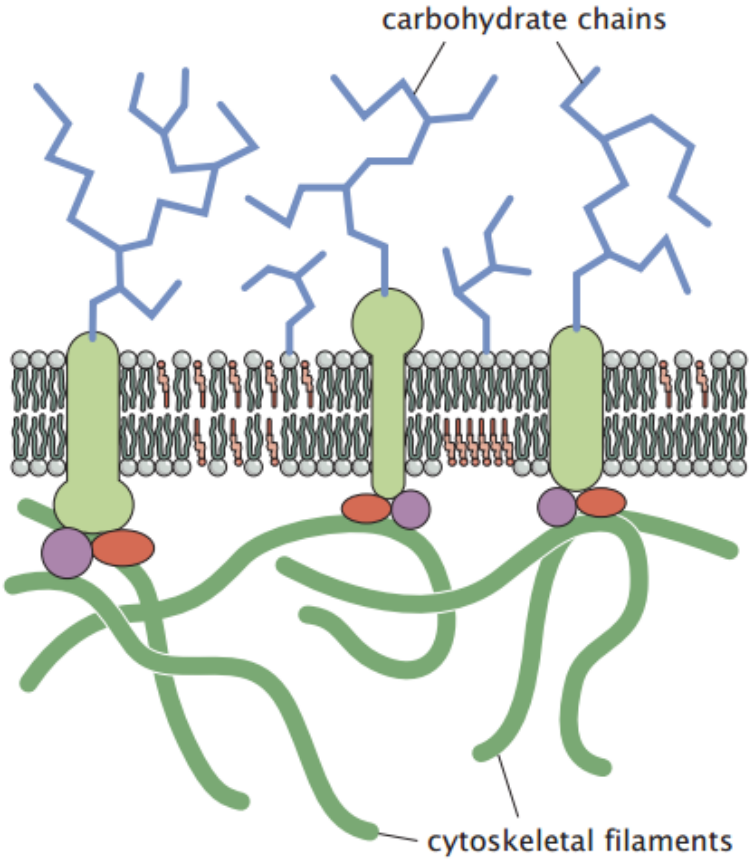
Introducing biophysics

The study of the physical phenomena that underlie biological processes

Proteins are molecular machines that drive all biological processes



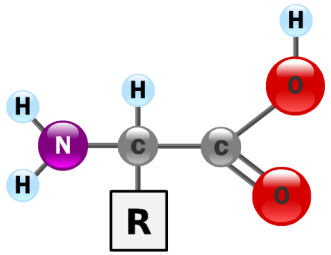
Embedded proteins and membrane domains allow mass transport and modulation of bilayer properties



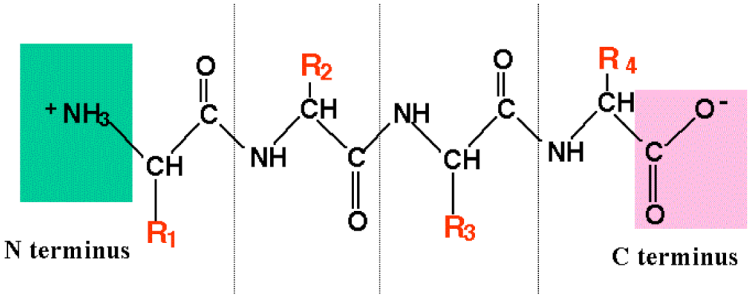
External carbohydrate chains and internal cytoskeletal components mediate cellular recognition and control of cell shape

Phillips et al., Physical Biology of the Cell, 2nd ed.

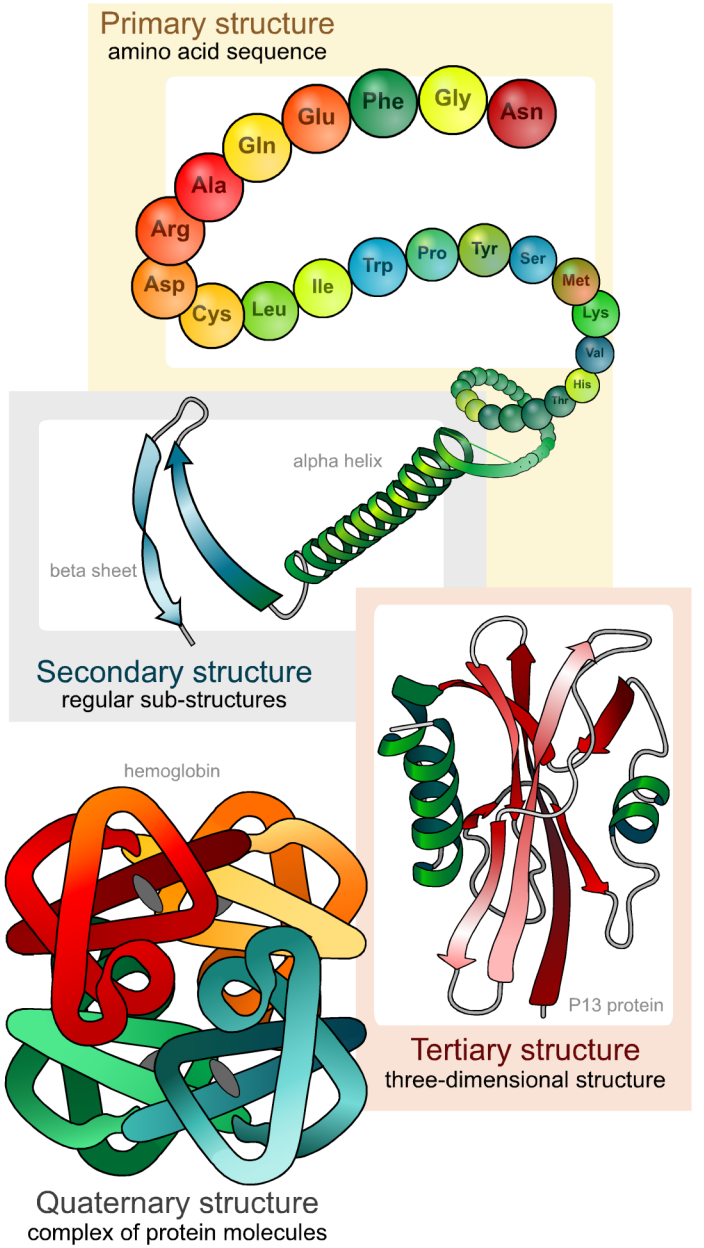
Amino acid sequence gives rise to complex molecular architecture



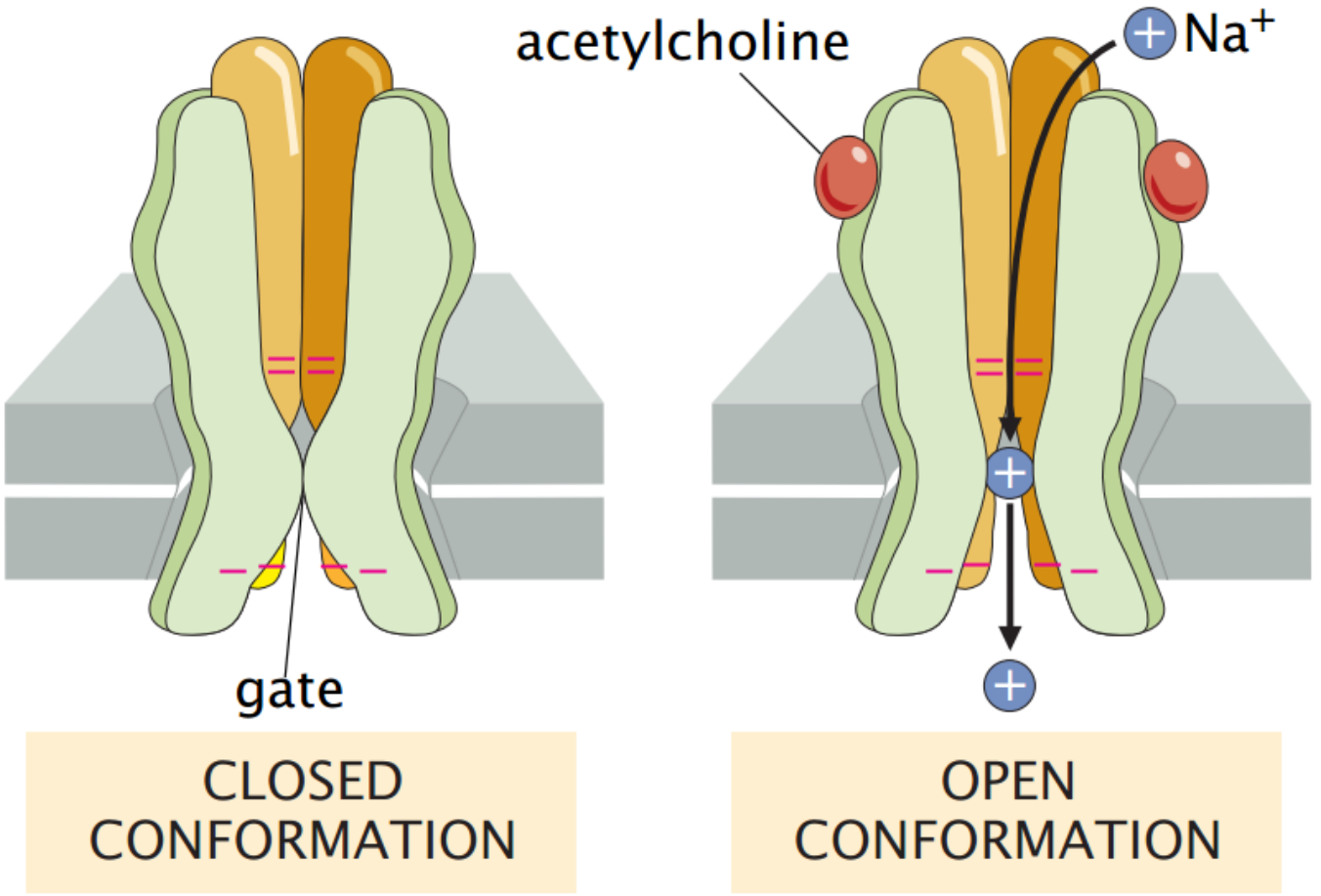
A single amino acid



A polypeptide chain



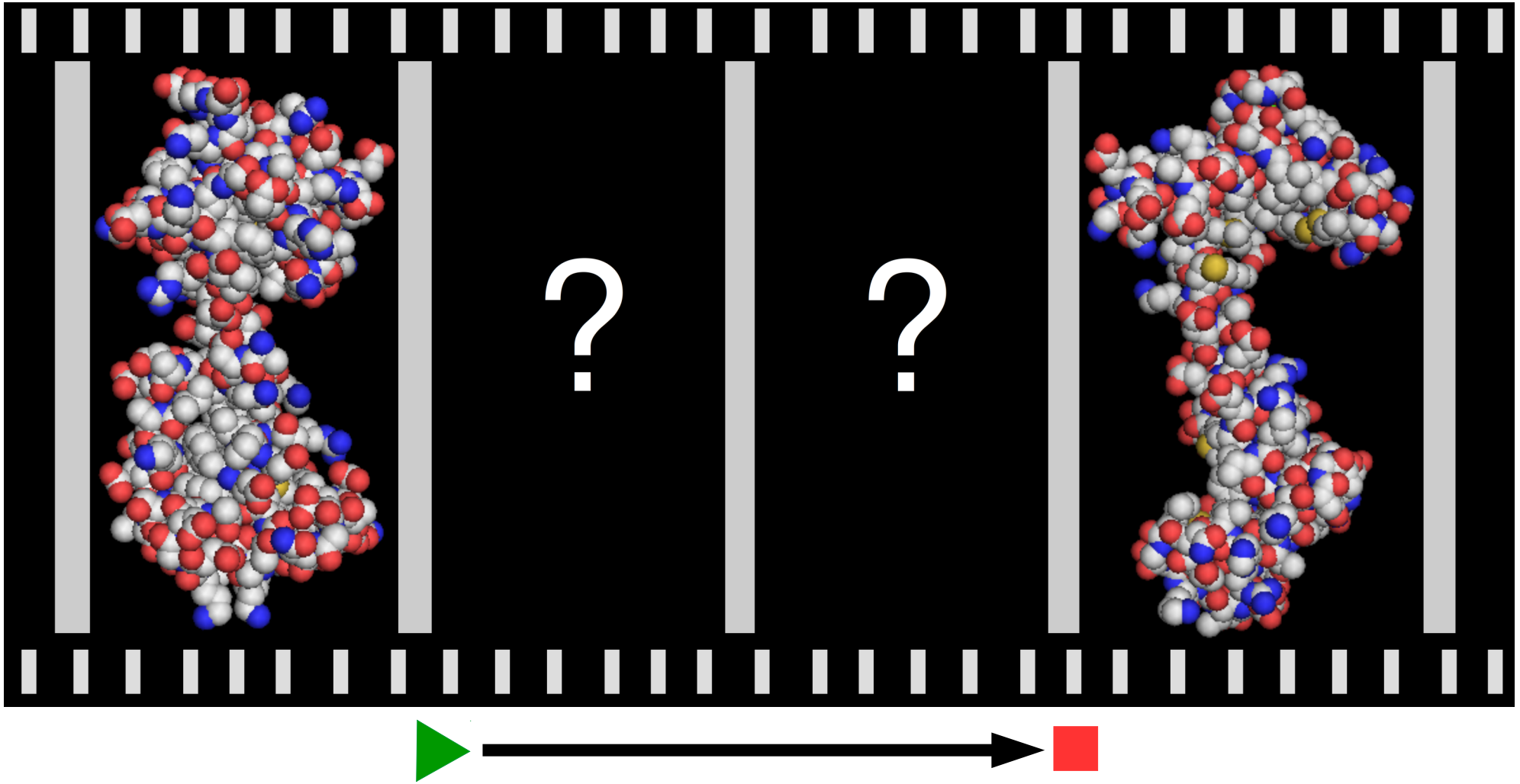
Structure determines function in proteins



Ligand-gated ion channels undergo structural changes to allow mass transport in response to the presence of a signaling molecule

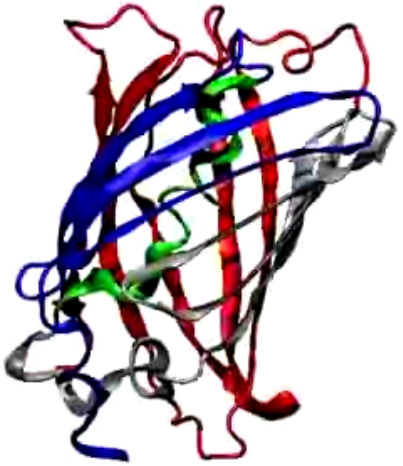
Phillips et al., Physical Biology of the Cell, 2nd ed.

Equilibrium structures are well-known but do not fully capture protein behavior

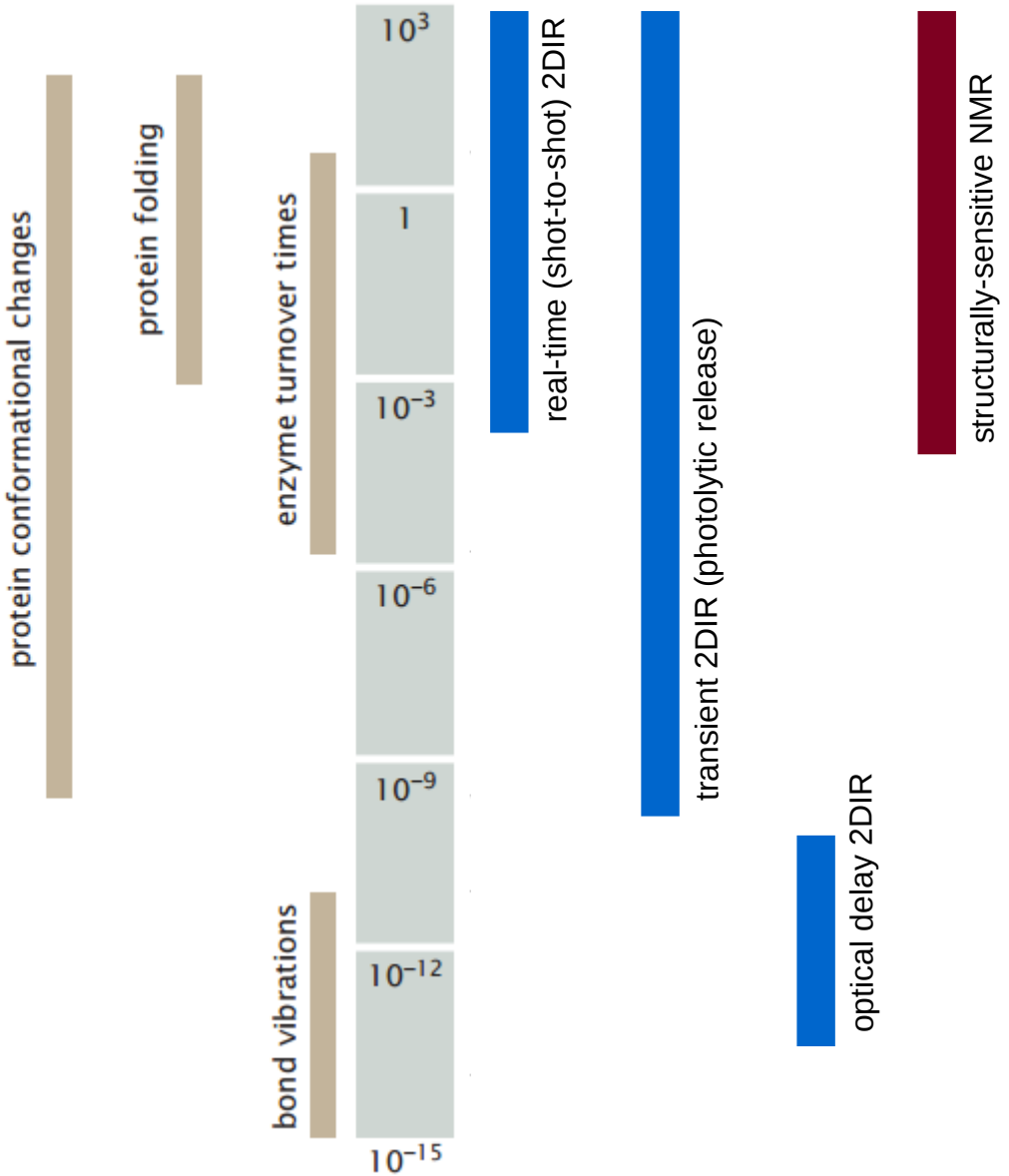


Crystallographic methods provide exquisite spatial resolution but leave the impression that proteins are static molecules with well-defined structure

Fast fluctuations characterize molecular motion

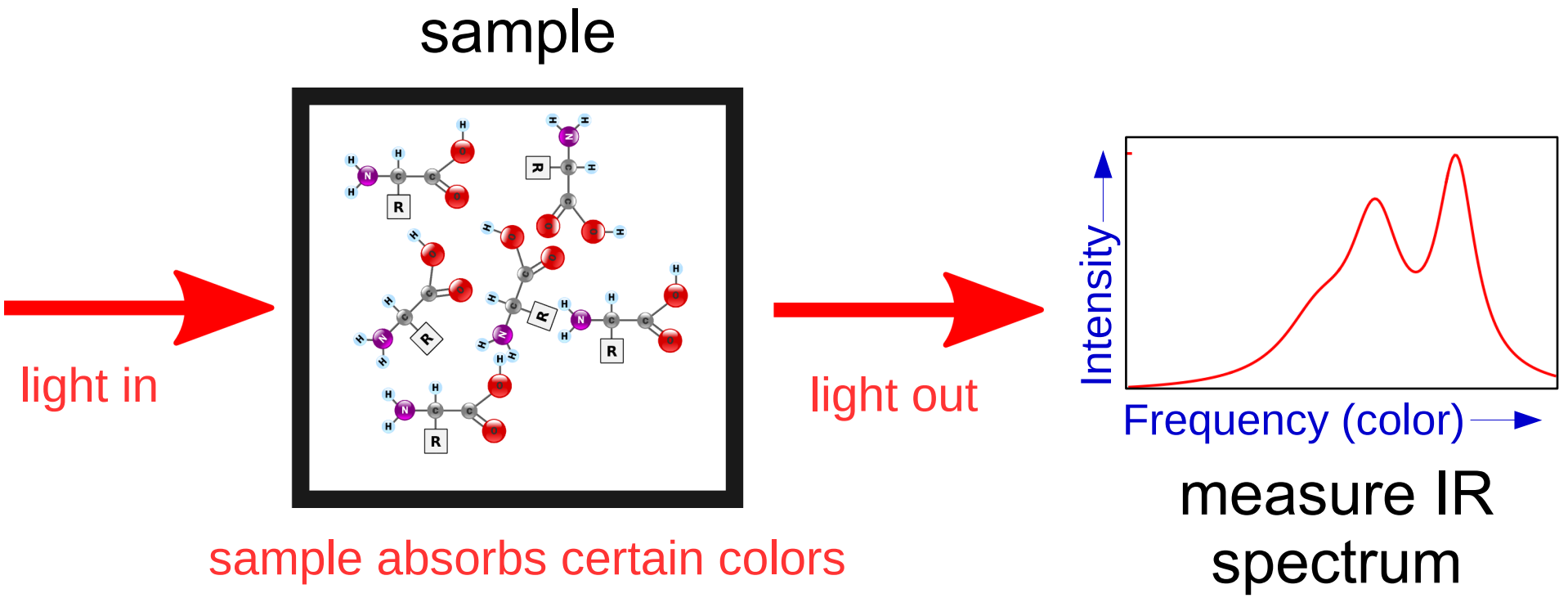


Fast spectroscopic measurements



Phillips et al., Physical Biology of the Cell, 2nd ed.

Infrared spectroscopy lets us probe molecular structure on fast time scales



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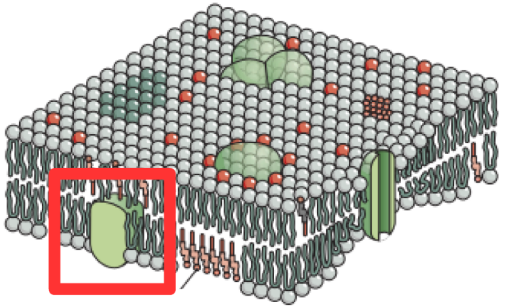
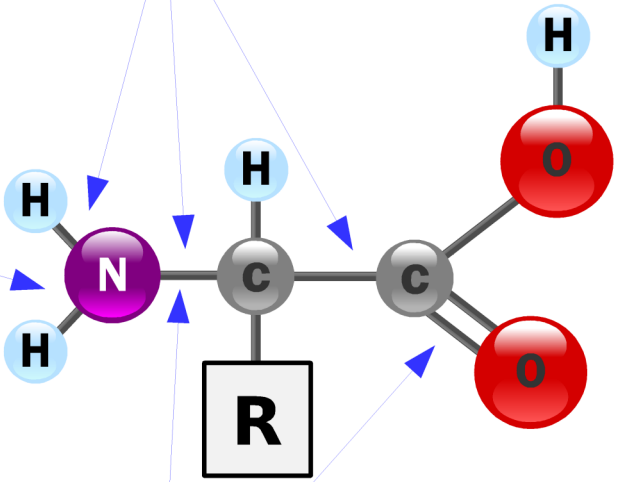
Spectroscopic reporters in proteins allow us to interrogate the biophysical environment



Amide II
(N-H bend, C-N stretch, C-C stretch)
1500-1600 cm^{-1}

Amide A
(N-H stretch)
3200-3300 cm^{-1}



Amide I
(C=O stretch, C-N stretch)
1600-1700 cm^{-1}

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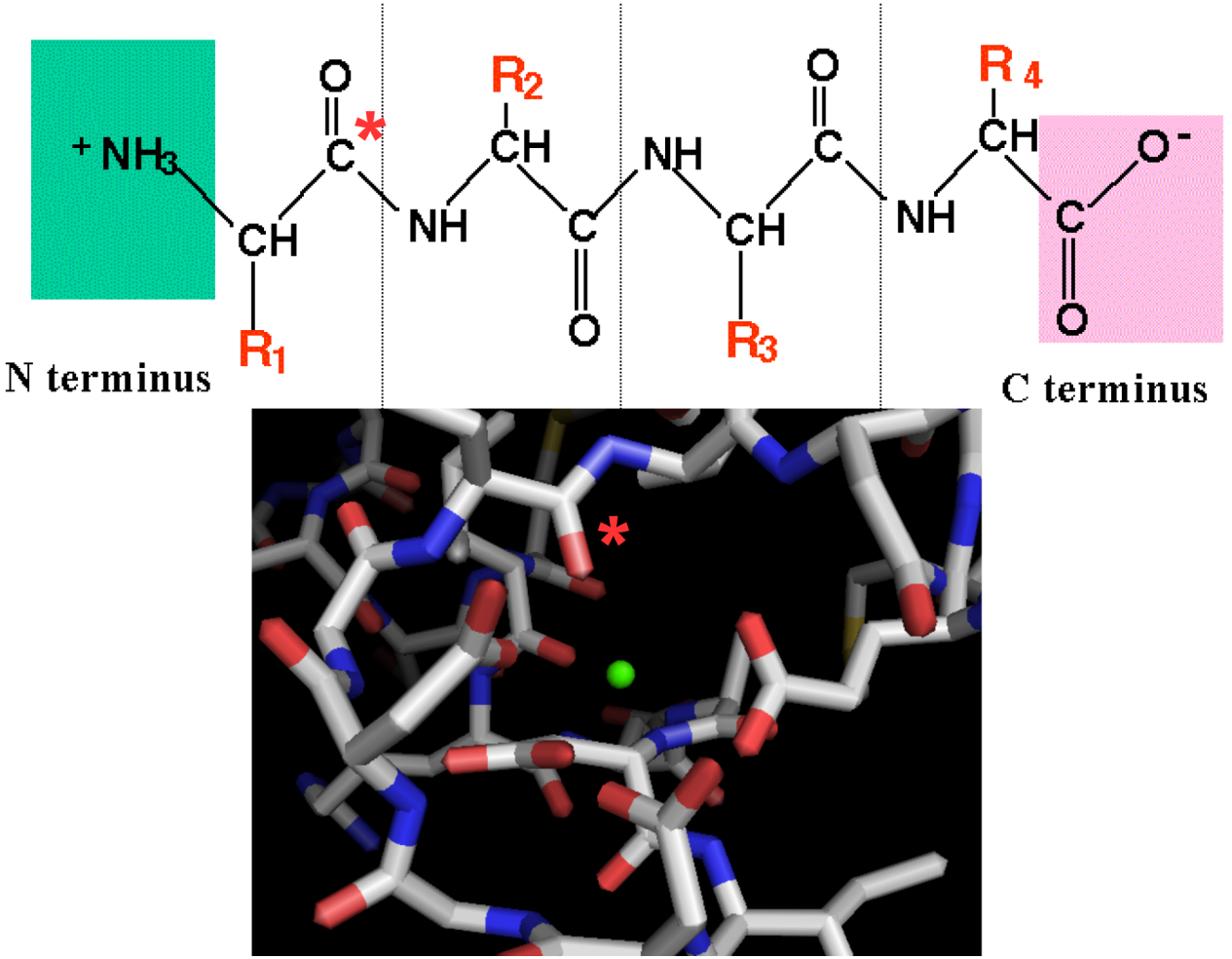
Fritz Lipmann Institute, Jena, GER
Tamm et al., Quarterly Review of Biophysics 30, 4 (1997)
Pohle et al., Journal of Molecular Structure 563, 463 (2001)

Spectroscopic labels allow us to isolate a particular area of interest



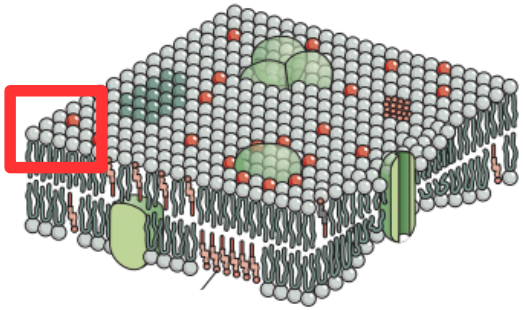
Substitution of carbonyl groups with ^{13}C and ^{18}O red shifts C=O stretching transitions into an unoccupied spectral region and allows detailed monitoring of a particular region or regions

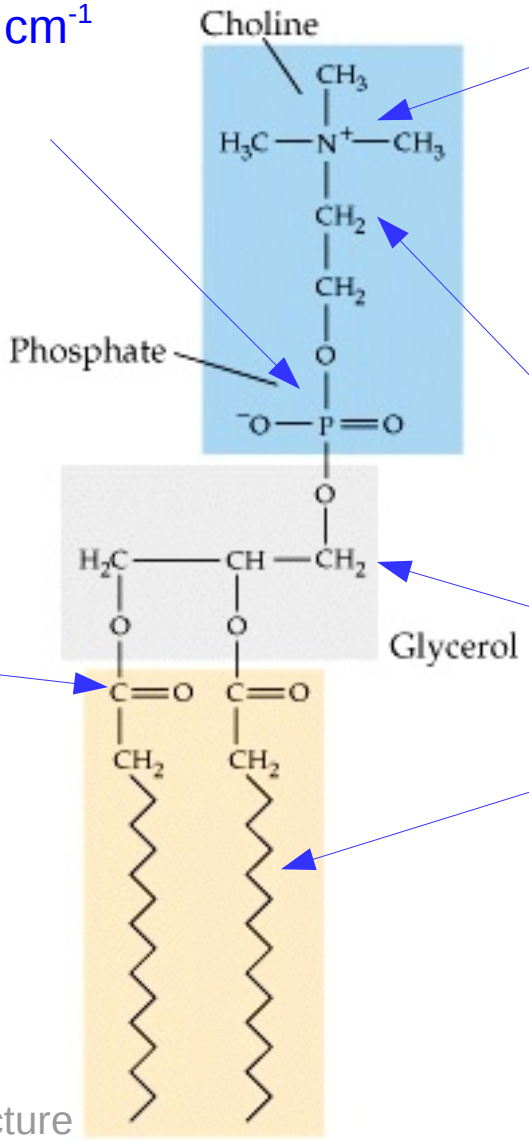
Spectroscopic reporters in lipids and proteins allow us to interrogate the biophysical environment

In phospholipids

PO_2^- stretches
1100-1300 cm^{-1}

$N^+(CH_3)_3$ stretch
~1100 cm^{-1}





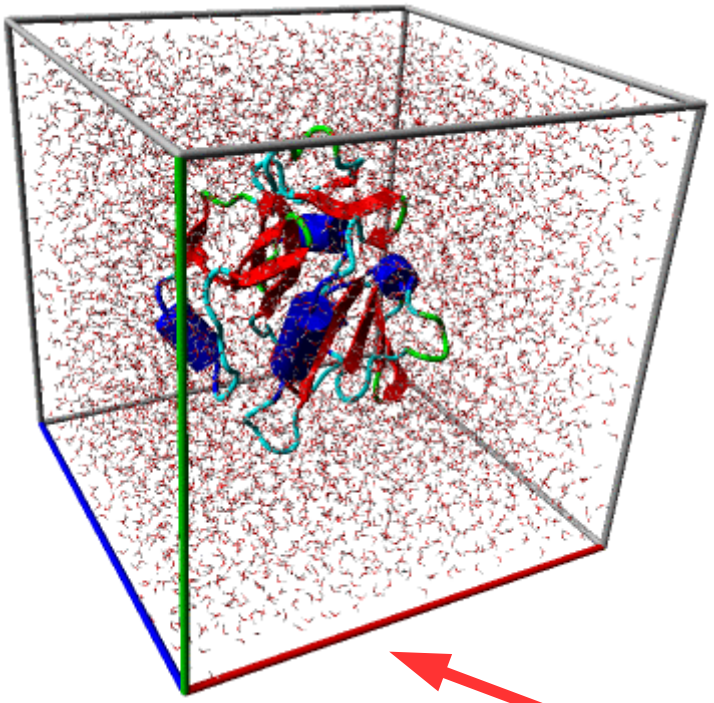
C=O stretches
1700-1800 cm^{-1}

C-H stretches
2750-3100 cm^{-1}

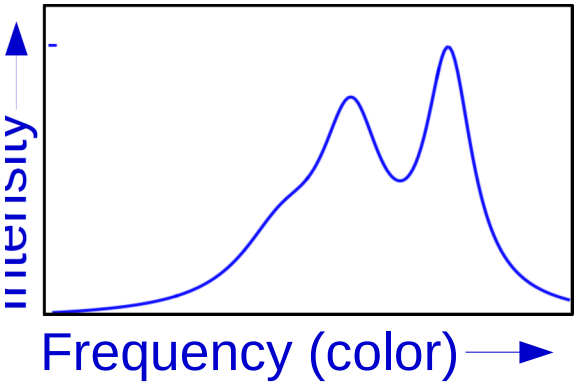
Fritz Lipmann Institute, Jena, GER
Tamm et al., Quarterly Review of Biophysics 30, 4 (1997)
Pohle et al., Journal of Molecular Structure 563, 463 (2001)

Simulations connect spectroscopic experiments to molecular configurations

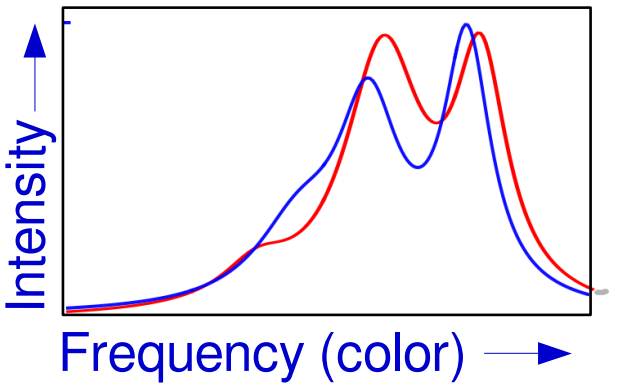
molecular dynamics simulation



calculate IR spectrum

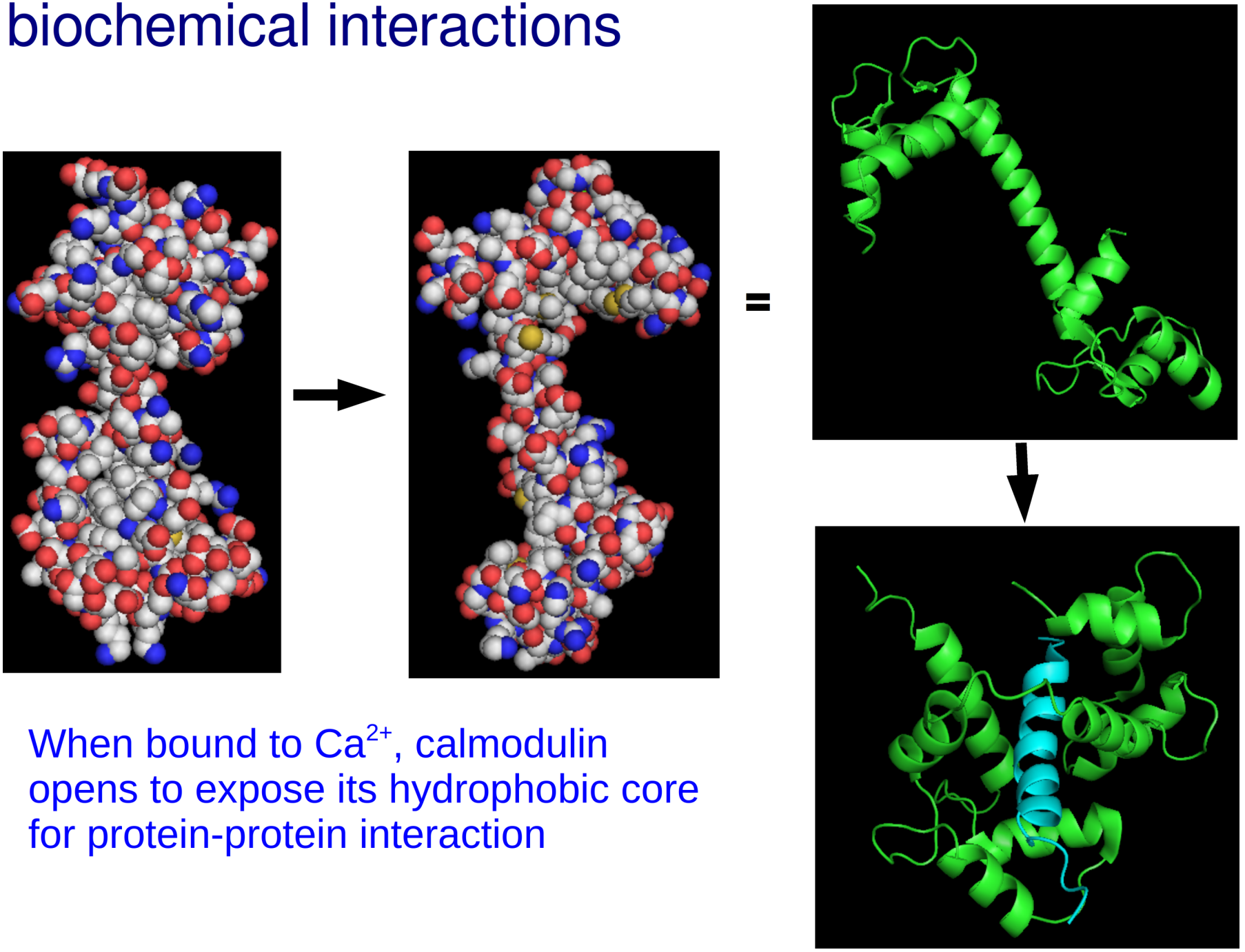


compare to experiment



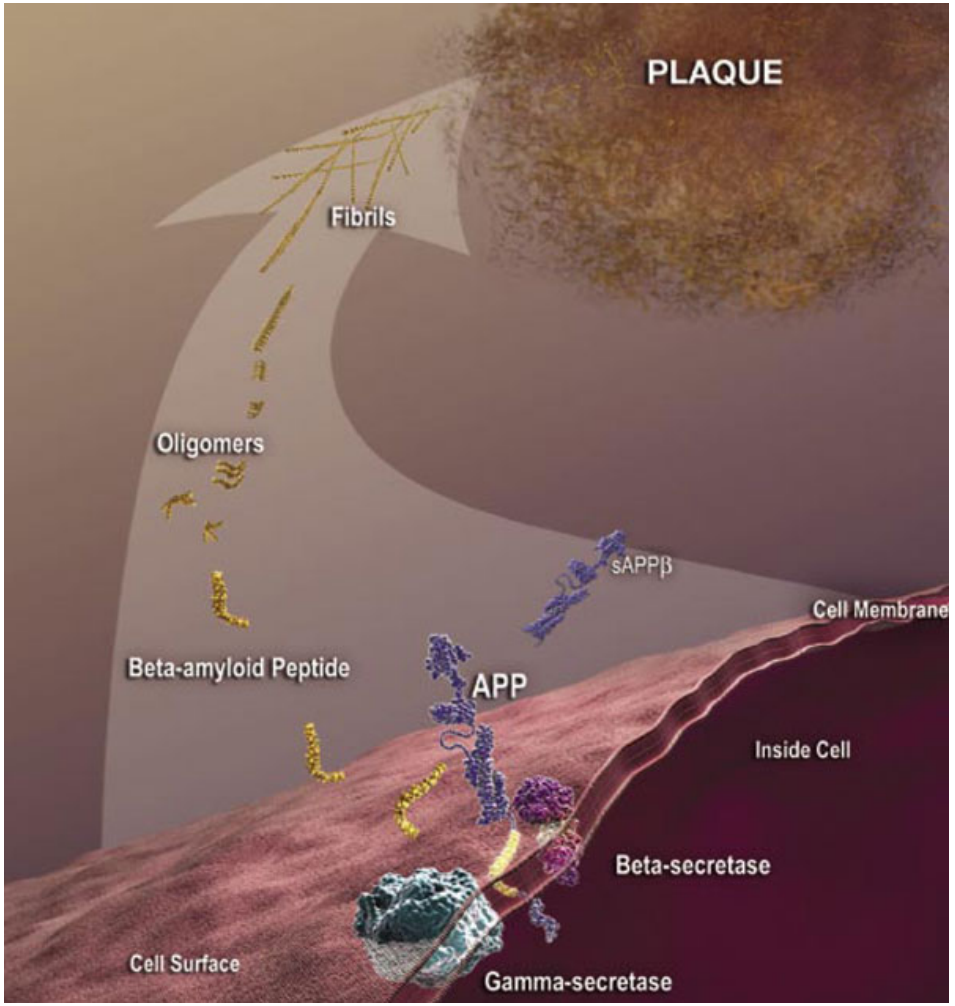
refine model

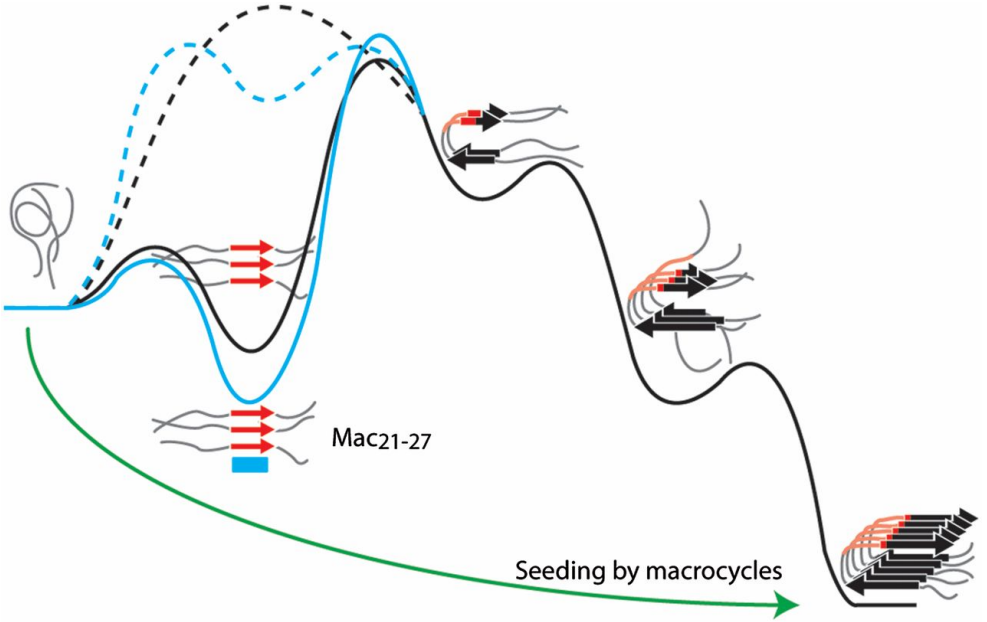
We are using these tools to unravel complex biochemical interactions



When bound to Ca^{2+}, calmodulin opens to expose its hydrophobic core for protein-protein interaction

Similar experiments have recently shed light onto the chemical interactions underlying Alzheimer's disease





Above: Ultrafast infrared spectroscopy revealed the presence of a key intermediate in plaque formation which was invisible to other techniques.

Left: The beta amyloid plaques implicated in Alzheimer's disease are formed via aggregation of protein fragments.

National Institutes of Health
Buchanan, L.E. et al, P.N.A.S., vol. 110, no. 48, 19285-19290

Assembling an instructional toolkit

Goals for toolkit activities

1. Make links to real scientific problems
2. Offer creative and exploratory components
3. Give students opportunities to work independently and branch out into what interests them

Resources for Activity and Lesson Design

- NIST WebBook http://webbook.nist.gov/chemistry/
  - Entries for thousands of molecules
  - Chemical structure
  - Physical and chemical properties
  - Infrared spectra and mass spectra
- Protein Data Bank http://www.rcsb.org/
  - 3D structures for thousands of proteins and biomolecules
  - Built using data contributed directly by academic researchers
  - Constantly growing
- SwissPDB Viewer http://spdbv.vital-it.ch/
  - Freely available software for visualizing protein and biomolecule structure
  - Integrated exploratory tools for hydrogen bond and hydrophobic patch detection, among others

Prototype Activity 1

Connecting spectroscopy to fundamental physics

Prototype Activity 2

Linking molecular structure to spectroscopy

Prototype Activity 3

Exploring protein structure with interactive models

Thank you!