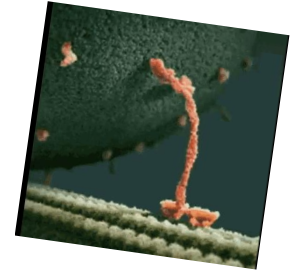
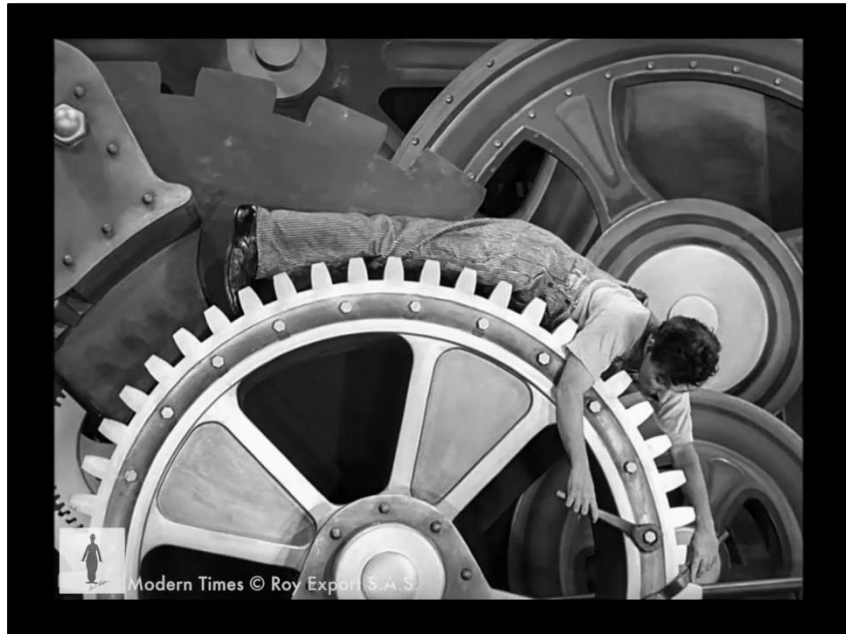




# NanoMachines: The Tiny Biological Gadgets that Animate Life



Modern Times  
(Charlie Chaplin 1936)



## Session 1 Building Blocks

OLLI at Illinois  
Spring 2023

D. H. Tracy  
[DavidHTracy@gmail.com](mailto:DavidHTracy@gmail.com)

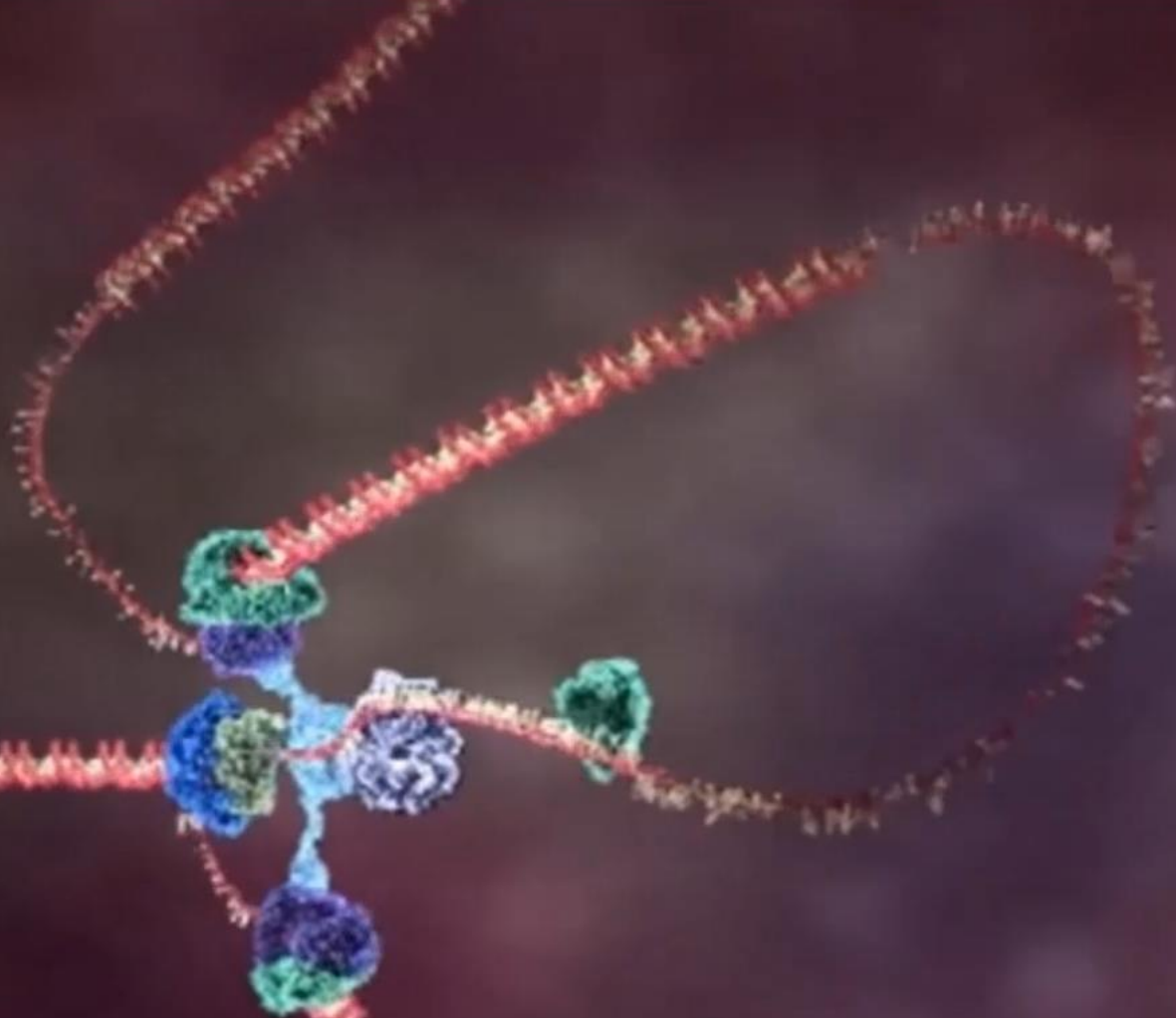
# Course Outline

1. Overview  
Building blocks, energy flow, how we know
2. nanoMachines in energy flow
3. Motors and locomotion
4. DNA & RNA processing, protein manufacturing, sensory machines

# NANOMACHINES

The Movie

wehi.tv  
DrewBerry



Credits:

Drew Berry, Walter and Eliza Hall Institute of Medical Research, Melbourne Au  
Biovisions, Harvard  
Stewart Lab, University of South Carolina

DNA replication  
2003

# Session 1 Outline

- Materials and building blocks of Biological Machines
  - Especially proteins
- Unusual features of life at small scales
- How we know about these tiny machines



Nick Lane

Professor of Evolutionary Biology  
University College London



## NICK LANE BOOKS

**2022**

**Transformer: The Deep Chemistry of Life and Death**

Nick Lane Profile Books

**2015**

**The Vital Question. Why is life the way it is?**

Nick Lane Profile/WW Norton

**2009**

**Life Ascending: The Ten Great Inventions of Evolution**

Nick Lane Profile/WW Norton

**2005**

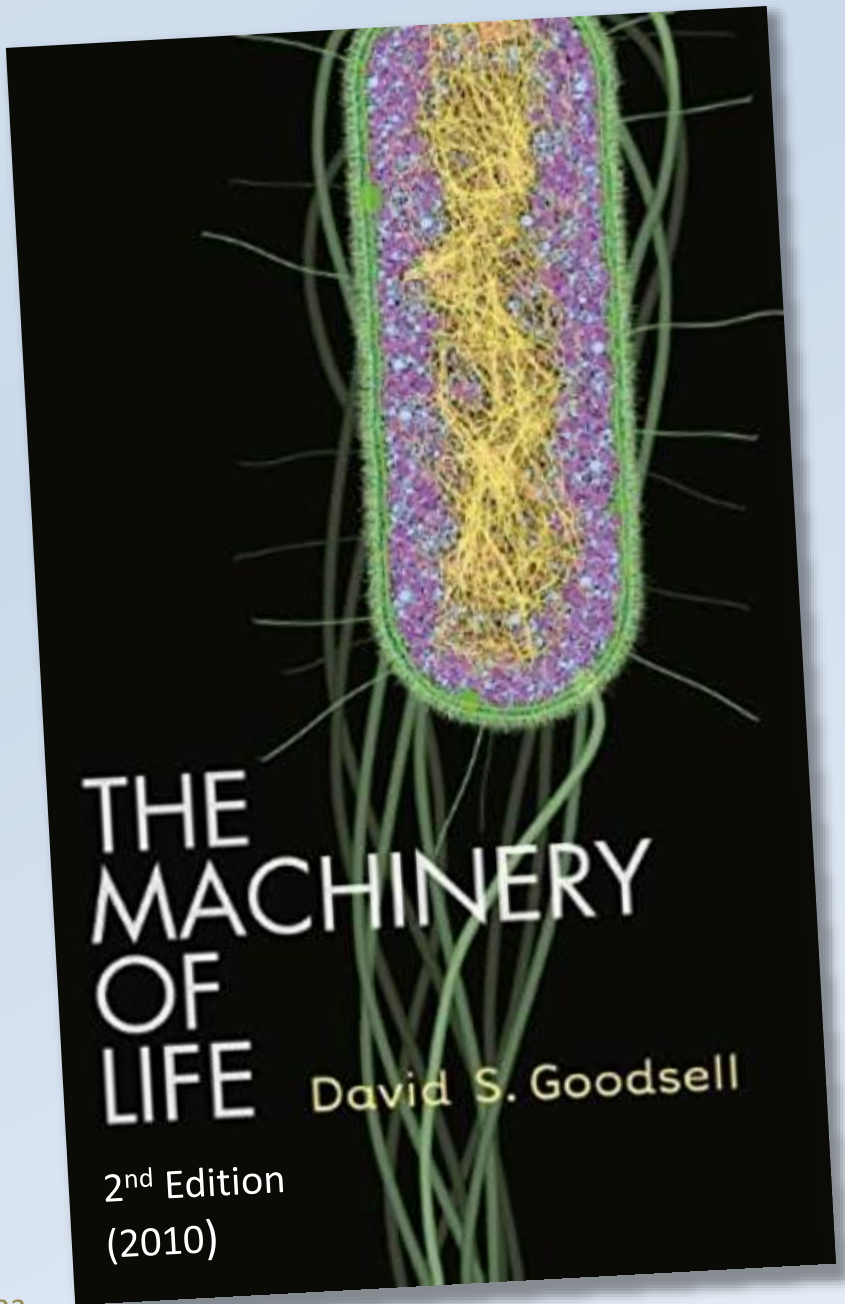
**Power, Sex, Suicide: Mitochondria and the Meaning of Life**

Nick Lane OUP Oxford

**2002**

**Oxygen: The Molecule that made the World**

Nick Lane Oxford University Press

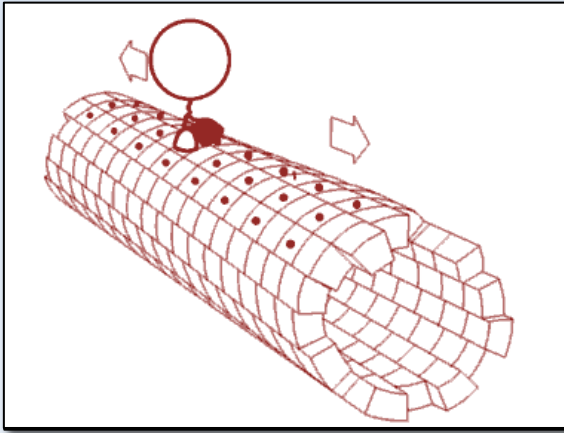


WIKIPEDIA  
The Free Encyclopedia

Article [Talk](#)

# Molecular machine

From Wikipedia, the free encyclopedia



My Brother's  
Recommendation

[\(4\) The biological machinery of life | Betül Kaçar and Lex Fridman – YouTube](#)

“The Biological  
Machinery of  
Life”

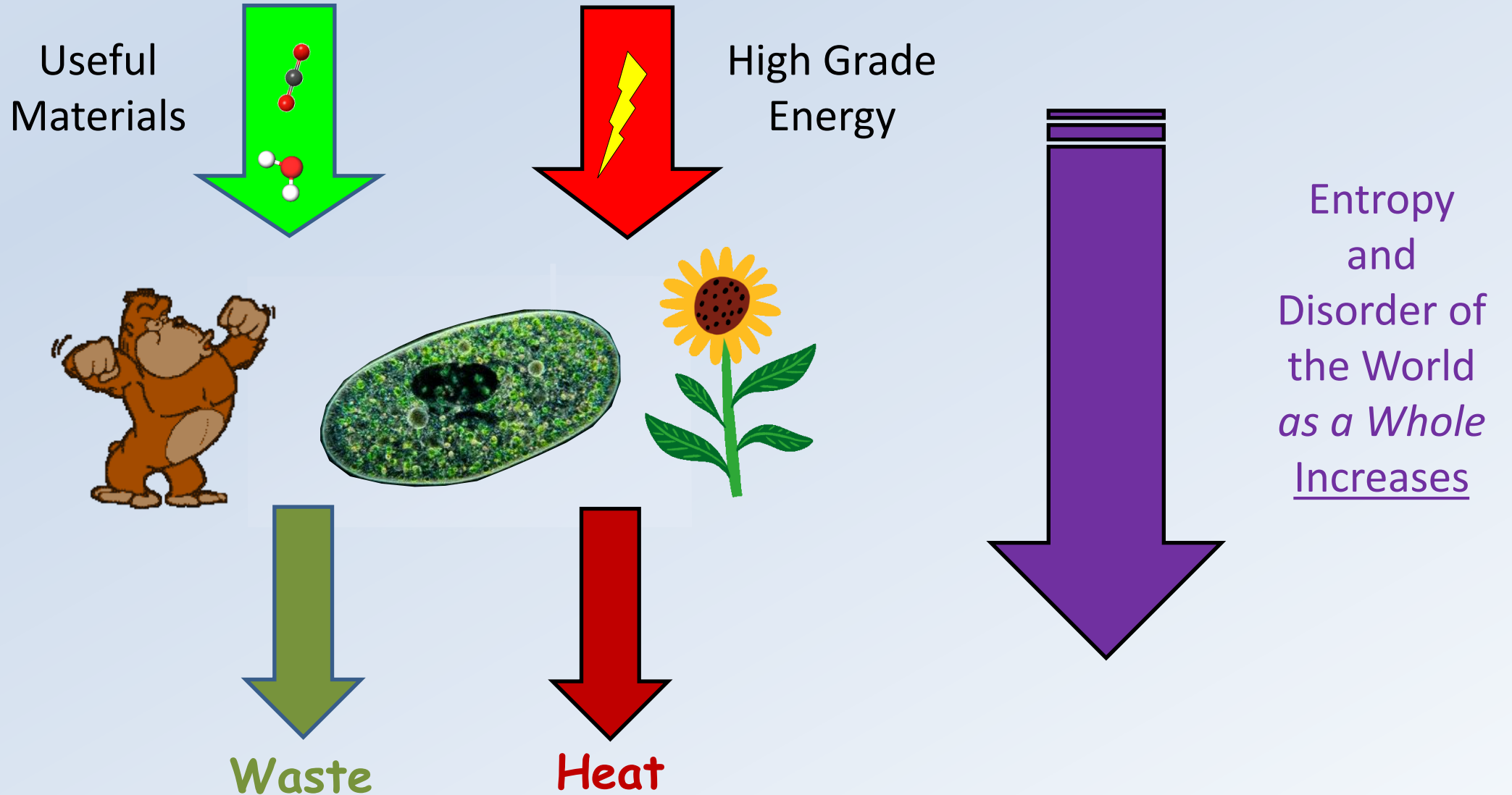


**Betül Kaçar**  
Astrobiologist  
U of Wisconsin



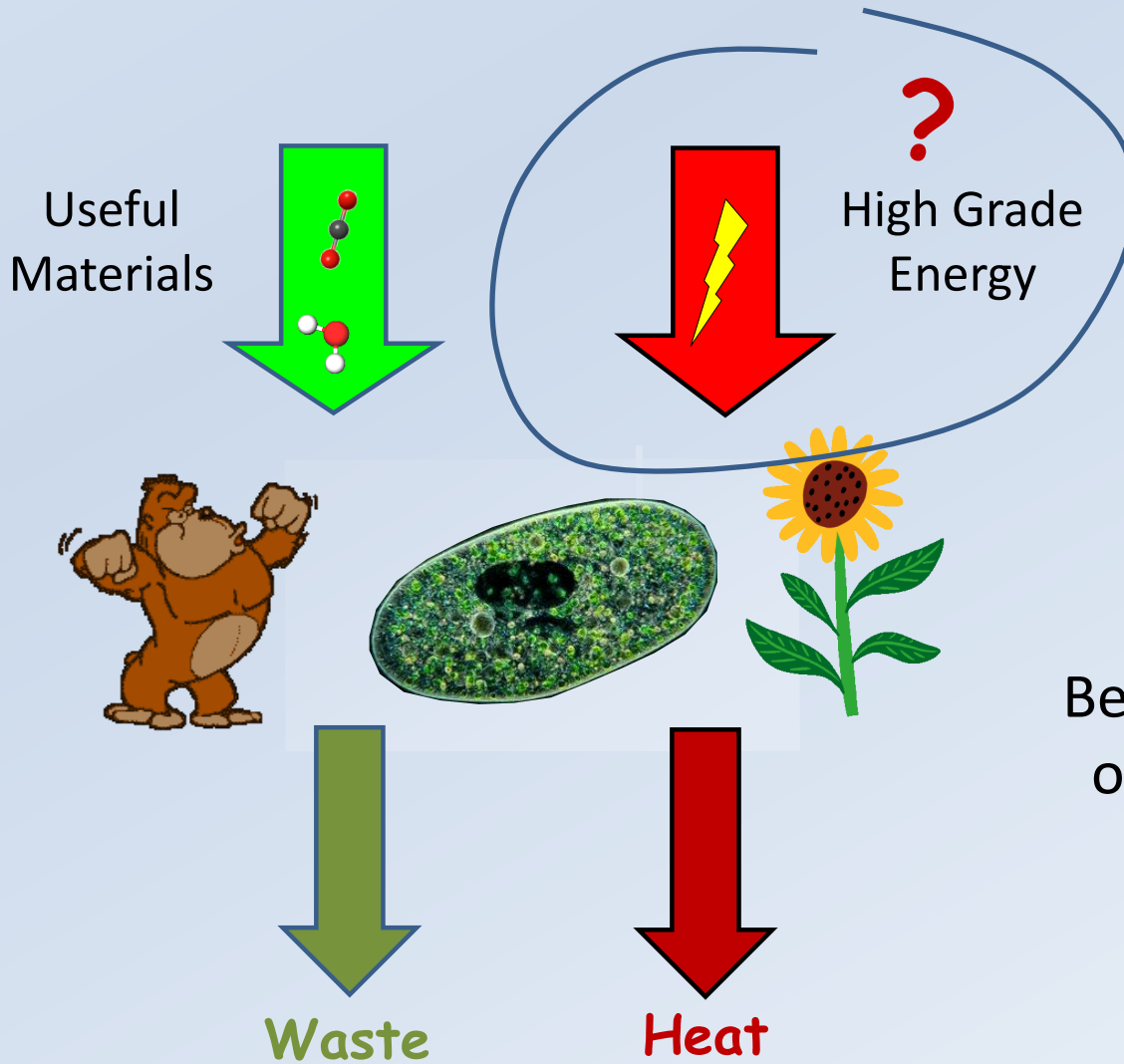


# Energy and Material Flow Animates All Life



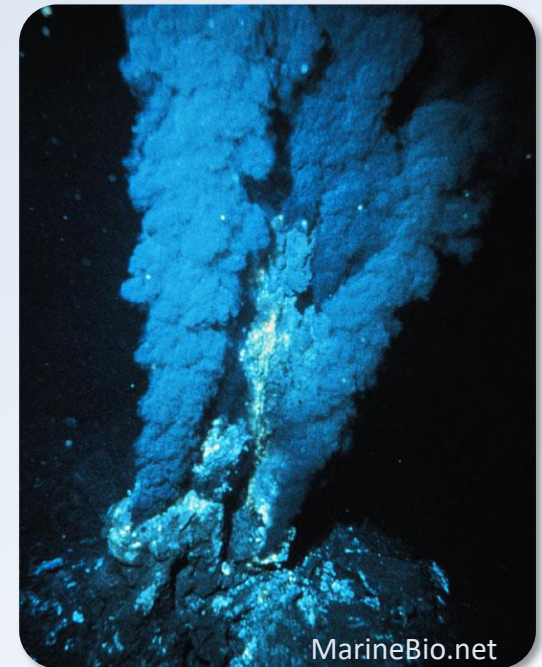
# Energy and Material Flow Animates All Life

For the last ~ 3 Billion Years:



Before the invention of Photosynthesis:

Geochemical energy from undersea vents



# Extreme Temperatures and Pressures are not available to Biology



# Periodic Table of the Elements

American Chemical Society

PERIOD	GROUP 1												13	14	15	16	17	18	
1	<b>H</b> Hydrogen 1.008																		<b>He</b> Helium 4.003
2	<b>Li</b> Lithium 6.94	<b>Be</b> Beryllium 9.012																	
3	<b>Na</b> Sodium 22.99	<b>Mg</b> Magnesium 24.31																	
4	<b>K</b> Potassium 39.10	<b>Ca</b> Calcium 40.08	<b>Sc</b> Scandium 44.96	<b>Ti</b> Titanium 47.88	<b>V</b> Vanadium 50.94	<b>Cr</b> Chromium 52.00	<b>Mn</b> Manganese 54.94	<b>Fe</b> Iron 55.85	<b>Co</b> Cobalt 58.93	<b>Ni</b> Nickel 58.69	<b>Cu</b> Copper 63.55	<b>Zn</b> Zinc 65.39	<b>Ga</b> Gallium 69.72	<b>Ge</b> Germanium 72.64	<b>As</b> Arsenic 74.92	<b>Se</b> Selenium 78.96	<b>Br</b> Bromine 79.90	<b>Kr</b> Krypton 83.79	
5	<b>Rb</b> Rubidium 85.47	<b>Sr</b> Strontium 87.62	<b>Y</b> Yttrium 88.91	<b>Zr</b> Zirconium 91.22	<b>Nb</b> Niobium 92.91	<b>Mo</b> Molybdenum 95.96	<b>Tc</b> Technetium (98)	<b>Ru</b> Ruthenium 101.1	<b>Rh</b> Rhodium 100.9	<b>Pd</b> Palladium 106.4	<b>Ag</b> Silver 107.9	<b>Cd</b> Cadmium 112.4	<b>In</b> Indium 114.8	<b>Sn</b> Tin 118.7	<b>Sb</b> Antimony 121.8	<b>Te</b> Tellurium 127.6	<b>I</b> Iodine 126.9	<b>Xe</b> Xenon 131.3	
6	<b>Cs</b> Cesium 132.9	<b>Ba</b> Barium 137.3	57-71 Lanthanides	<b>Hf</b> Hafnium 178.5	<b>Ta</b> Tantalum 180.9	<b>W</b> Tungsten 183.9	<b>Re</b> Rhenium 186.2	<b>Os</b> Osmium 190.2	<b>Ir</b> Iridium 192.2	<b>Pt</b> Platinum 195.1	<b>Au</b> Gold 197.0	<b>Hg</b> Mercury 200.5	<b>Tl</b> Thallium 204.38	<b>Pb</b> Lead 207.2	<b>Bi</b> Bismuth 208.0	<b>Po</b> Polonium (209)	<b>At</b> Astatine (210)	<b>Rn</b> Radon (222)	
7	<b>Fr</b> Francium (223)	<b>Ra</b> Radium (226)	89-103 Actinides	<b>Rf</b> Rutherfordium (261)	<b>Db</b> Dubnium (268)	<b>Sg</b> Seaborgium (271)	<b>Bh</b> Bohrium (278)	<b>Hs</b> Hassium (277)	<b>Mt</b> Meitnerium (276)	<b>Ds</b> Darmstadtium (281)	<b>Rg</b> Roentgenium (289)	<b>Cn</b> Copernicium (285)	<b>Nh</b> Nihonium (284)	<b>Fl</b> Flerovium (289)	<b>Mc</b> Moscovium (288)	<b>Lv</b> Livermorium (293)	<b>Ts</b> Tennessine (294)	<b>Og</b> Oganesson (294)	

57 <b>La</b> Lanthanum 138.9	58 <b>Ce</b> Cerium 140.1	59 <b>Pr</b> Praseodymium 140.9	60 <b>Nd</b> Neodymium 144.2	61 <b>Pm</b> Promethium (145)	62 <b>Sm</b> Samarium 150.4	63 <b>Eu</b> Europium 152.0	64 <b>Gd</b> Gadolinium 157.2	65 <b>Tb</b> Terbium 158.9	66 <b>Dy</b> Dysprosium 162.5	67 <b>Ho</b> Holmium 164.9	68 <b>Er</b> Erbium 167.3	69 <b>Tm</b> Thulium 168.9	70 <b>Yb</b> Ytterbium 173.0	71 <b>Lu</b> Lutetium 175.0
89 <b>Ac</b> Actinium (227)	90 <b>Th</b> Thorium 232.0	91 <b>Pa</b> Protactinium 231.0	92 <b>U</b> Uranium 238.0	93 <b>Np</b> Neptunium (237)	94 <b>Pu</b> Plutonium (244)	95 <b>Am</b> Americium (243)	96 <b>Cm</b> Curium (247)	97 <b>Bk</b> Berkelium (247)	98 <b>Cf</b> Californium (251)	99 <b>Es</b> Einsteinium (252)	100 <b>Fm</b> Fermium (257)	101 <b>Md</b> Mendelevium (258)	102 <b>No</b> Nobelium (259)	103 <b>Lr</b> Lawrencium (262)

# Periodic Table of the Elements

by the Royal Society of Chemistry

Nearly all of these remaining elements have uses in **man-made** machines and technology

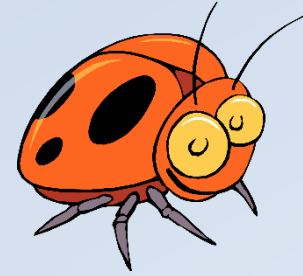
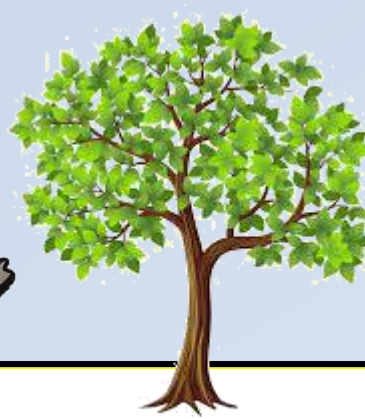
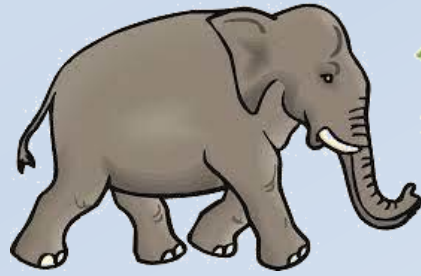
GROUP																	18		
1	2												13	14	15	16	17	2	
1	<b>H</b> Hydrogen 1.008																		<b>He</b> Helium 4.003
2	<b>Li</b> Lithium 6.94	<b>Be</b> Beryllium 9.012											<b>B</b> Boron 10.81	<b>C</b> Carbon 12.01	<b>N</b> Nitrogen 14.01	<b>O</b> Oxygen 16.00	<b>F</b> Fluorine 19.00	<b>Ne</b> Neon 20.18	
3	<b>Na</b> Sodium 22.99	<b>Mg</b> Magnesium 24.31											<b>Al</b> Aluminium 26.98	<b>Si</b> Silicon 28.09	<b>P</b> Phosphorus 30.97	<b>S</b> Sulfur 32.06	<b>Cl</b> Chlorine 35.45	<b>Ar</b> Argon 39.95	
4	<b>K</b> Potassium 39.10	<b>Ca</b> Calcium 40.08	<b>Sc</b> Scandium 44.96	<b>Ti</b> Titanium 47.88	<b>V</b> Vanadium 50.94	<b>Cr</b> Chromium 52.00	<b>Mn</b> Manganese 54.94	<b>Fe</b> Iron 55.85	<b>Co</b> Cobalt 58.93	<b>Ni</b> Nickel 58.69	<b>Cu</b> Copper 63.55	<b>Zn</b> Zinc 65.39	<b>Ga</b> Gallium 69.72	<b>Ge</b> Germanium 72.64	<b>As</b> Arsenic 74.92	<b>Se</b> Selenium 78.96	<b>Br</b> Bromine 79.90	<b>Kr</b> Krypton 83.79	
5	<b>Rb</b> Rubidium 85.47	<b>Sr</b> Strontium 87.62	<b>Y</b> Yttrium 88.91	<b>Zr</b> Zirconium 91.22	<b>Nb</b> Niobium 92.91	<b>Mo</b> Molybdenum 95.96	<b>Tc</b> Technetium 98.91	<b>Ru</b> Ruthenium 101.1	<b>Rh</b> Rhodium 100.9	<b>Pd</b> Palladium 106.4	<b>Ag</b> Silver 107.9	<b>Cd</b> Cadmium 112.4	<b>In</b> Indium 114.8	<b>Sn</b> Tin 118.7	<b>Sb</b> Antimony 121.8	<b>Te</b> Tellurium 127.6	<b>I</b> Iodine 126.9	<b>Xe</b> Xenon 131.3	
6	<b>Cs</b> Caesium 132.9	<b>Ba</b> Barium 137.3	<b>57-71</b> Lanthanides	<b>Hf</b> Hafnium 178.5	<b>Ta</b> Tantalum 180.9	<b>W</b> Tungsten 183.9	<b>Re</b> Rhenium 186.2	<b>Os</b> Osmium 190.2	<b>Ir</b> Iridium 192.2	<b>Pt</b> Platinum 195.1	<b>Au</b> Gold 197.0	<b>Hg</b> Mercury 200.5	<b>Tl</b> Thallium 204.38	<b>Pb</b> Lead 207.2	<b>Bi</b> Bismuth 208.0	<b>Po</b> Polonium (209)	<b>At</b> Astatine (210)	<b>Rn</b> Radon (222)	
7	<b>N.A.</b> Francium (223)	<b>Ra</b> Radium (226)	<b>89-103</b> Actinides	<b>Rf</b> Rutherfordium (261)	<b>Db</b> Dubnium (262)	<b>Sg</b> Seaborgium (266)	<b>Bh</b> Bohrium (264)	<b>Hs</b> Hassium (277)	<b>Mt</b> Meitnerium (268)	<b>Ds</b> Darmstadtium (285)	<b>Rg</b> Roentgenium (281)	<b>Cn</b> Copernicium (285)	<b>Nh</b> Nihonium (284)	<b>Fl</b> Flerovium (289)	<b>Mc</b> Moscovium (288)	<b>Lv</b> Livermorium (293)	<b>Ts</b> Tennessine (289)	<b>Og</b> Oganesson (294)	

<b>La</b> Lanthanum 138.9	<b>Ce</b> Cerium 140.1	<b>Pr</b> Praseodymium 140.9	<b>Nd</b> Neodymium 144.2	<b>Pm</b> Promethium (145)	<b>Sm</b> Samarium 150.4	<b>Eu</b> Europium 152.0	<b>Gd</b> Gadolinium 157.2	<b>Tb</b> Terbium 158.9	<b>Dy</b> Dysprosium 162.5	<b>Ho</b> Holmium 164.9	<b>Er</b> Erbium 167.3	<b>Tm</b> Thulium 168.9	<b>Yb</b> Ytterbium 173.0	<b>Lu</b> Lutetium 175.0
<b>Ac</b> Actinium (227)	<b>Th</b> Thorium 232.0	<b>N.A.</b> Protactinium (231)	<b>U</b> Uranium 238.0	<b>Np</b> Neptunium (237)	<b>Pu</b> Plutonium (244)	<b>Am</b> Americium (243)	<b>Cm</b> Curium (247)	<b>Bk</b> Berkelium (247)	<b>Cf</b> Californium (251)	<b>Es</b> Einsteinium (252)	<b>Fm</b> Fermium (257)	<b>Md</b> Mendelevium (258)	<b>No</b> Nobelium (259)	<b>Lr</b> Lawrencium (260)

Not Available

Not Available

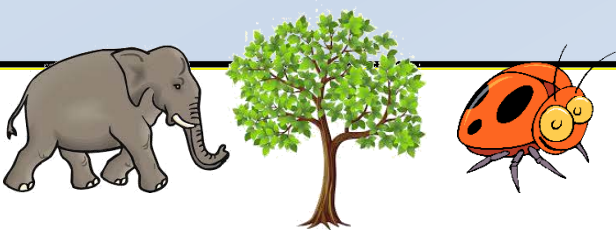
But what elements are useful to nature?



**Periodic Table of the Elements**  
American Chemical Society

PERIOD	GROUP 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18			
1	H Hydrogen 1.008																	He Helium 4.003			
2	Li Lithium 6.94	Be Beryllium 9.012											B Boron 10.81	C Carbon 12.01	N Nitrogen 14.01	O Oxygen 16.00	F Fluorine 19.00	Ne Neon 20.18			
3	Na Sodium 22.99	Mg Magnesium 24.31											Al Aluminum 26.98	Si Silicon 28.09	P Phosphorus 30.97	S Sulfur 32.06	Cl Chlorine 35.45	Ar Argon 39.95			
4	K Potassium 39.10	Ca Calcium 40.08	Sc Scandium 44.96	Ti Titanium 47.88	V Vanadium 50.94	Cr Chromium 52.00	Mn Manganese 54.94	Fe Iron 55.85	Co Cobalt 58.93	Ni Nickel 58.69	Cu Copper 63.55	Zn Zinc 65.39	Ga Gallium 69.72	Ge Germanium 72.64	As Arsenic 74.92	Se Selenium 78.96	Br Bromine 79.90	Kr Krypton 83.79			
5	Rb Rubidium 85.47	Sr Strontium 87.62	Y Yttrium 88.91	Zr Zirconium 91.22	Nb Niobium 92.91	Mo Molybdenum 95.94	N.A. Technetium (98.906)	Ru Ruthenium 101.1	Rh Rhodium 101.07	Pd Palladium 106.4	Ag Silver 107.87	Cd Cadmium 112.4	In Indium 114.82	Sn Tin 118.7	Sb Antimony 121.76	Te Tellurium 127.6	I Iodine 126.9	Xe Xenon 131.3			
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7	N.A. Francium (223)	Ra Radium (226)	89-103 Actinides	Rf Rutherfordium (261)	Db Dubnium (262)	Sg Seaborgium (266)	Bh Bohrium (264)	Hs Hassium (277)	Mt Meitnerium (268)	Not Available			Cn Copernicium (285)	Nh Nihonium (284)	Fl Flerovium (289)	Mc Moscovium (288)	Lv Livermorium (293)	Ts Tennessine (294)	Og Oganesson (294)		
				La Lanthanum 138.9	Ce Cerium 140.1	Pr Praseodymium 140.9	Nd Neodymium 144.2	N.A. Promethium (145)	Sm Samarium 150.4	Eu Europium 152.0	Gd Gadolinium 157.2	Tb Terbium 158.9	Dy Dysprosium 162.5	Ho Holmium 164.9	Er Erbium 167.3	Tm Thulium 168.9	Yb Ytterbium 173.0	Lu Lutetium 175.0			
				Ac Actinium (227)	Th Thorium 232.0	N.A. Protactinium (231)	U Uranium 238.0	Np Neptunium (237)	Pu Plutonium (244)	Am Americium (243)	Not Available			Cm Curium (247)	Bk Berkelium (247)	Cf Californium (251)	Es Einsteinium (252)	Fm Fermium (257)	Md Mendelevium (258)	No Nobelium (259)	Lr Lawrencium (260)





# Periodic Table of the Elements

American Chemical Society

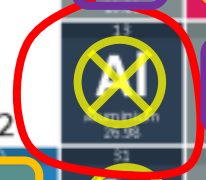
GROUP	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	
PERIOD 1	H (Hydrogen)																		He (Helium)
PERIOD 2	Li (Lithium)	Be (Beryllium)											B (Boron)	C (Carbon)	N (Nitrogen)	O (Oxygen)	F (Fluorine)		Ne (Neon)
PERIOD 3	Na (Sodium)	Mg (Magnesium)											Al (Aluminum)	Si (Silicon)	P (Phosphorus)	S (Sulfur)	Cl (Chlorine)		Ar (Argon)
PERIOD 4	K (Potassium)	Ca (Calcium)	Sc (Scandium)	Ti (Titanium)	V (Vanadium)	Cr (Chromium)	Mn (Manganese)	Fe (Iron)	Co (Cobalt)	Ni (Nickel)	Cu (Copper)	Zn (Zinc)	Ga (Gallium)	Ce (Cerium)	As (Arsenic)	Se (Selenium)	Br (Bromine)		Kr (Krypton)
PERIOD 5	Rb (Rubidium)	Sr (Strontium)	Y (Yttrium)	Zr (Zirconium)	Nb (Niobium)	Mo (Molybdenum)	N.A. (Technetium)	Ru (Ruthenium)	Rh (Rhodium)	Pd (Palladium)	Ag (Silver)	Cd (Cadmium)	In (Indium)	Sn (Tin)	Sb (Antimony)	Te (Tellurium)	I (Iodine)		Xe (Xenon)
PERIOD 6	Cs (Cesium)	Ba (Barium)	57-71 (Lanthanides)	Hf (Hafnium)	Ta (Tantalum)	W (Tungsten)	Re (Rhenium)	Os (Osmium)	Ir (Iridium)	Pt (Platinum)	Au (Gold)	Hg (Mercury)	Tl (Thallium)	Pb (Lead)	Bi (Bismuth)	Po (Polonium)	At (Astatine)		Rn (Radon)
PERIOD 7	N.A. (Francium)	Ra (Radium)	89-103 (Actinides)	Rf (Rutherfordium)	Db (Dubnium)	Sg (Seaborgium)	Bh (Bohrium)	Hs (Hassium)	Mt (Meitnerium)	Dr (Darmstadtium)	Pg (Pergonium)	Cn (Copernicium)	Nh (Nihonium)	Fl (Flerovium)	Mc (Moscovium)	Lv (Livermorium)	Ts (Tennessine)		Og (Oganesson)

**Widely Essential**

**Essential for Some**

- Alkali Metals
- Non-metals
- Other Metals
- Lanthanides
- Metalloids
- Actinides

**Sometimes Helpful**



La (Lanthanum)	Ce (Cerium)	Pr (Praseodymium)	Nd (Neodymium)	N.A. (Promethium)	Sm (Samarium)	Eu (Europium)	Gd (Gadolinium)	Tb (Terbium)	Dy (Dysprosium)	Ho (Holmium)	Er (Erbium)	Tm (Thulium)	Yb (Ytterbium)	Lu (Lutetium)
Ac (Actinium)	Th (Thorium)	N.A. (Protactinium)	U (Uranium)	Np (Neptunium)	Pu (Plutonium)	Am (Americium)	Cm (Curium)	Bk (Berkelium)	Cf (Californium)	Es (Einsteinium)	Fm (Fermium)	Md (Mendelevium)	No (Nobelium)	Lr (Lawrencium)

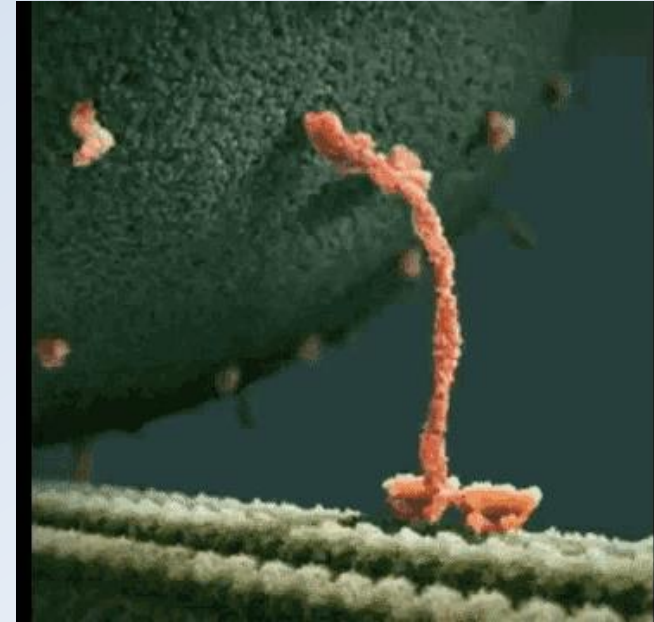
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# Diving Down

from the World of MacroMachines  
to the World of Cellular NanoMachines



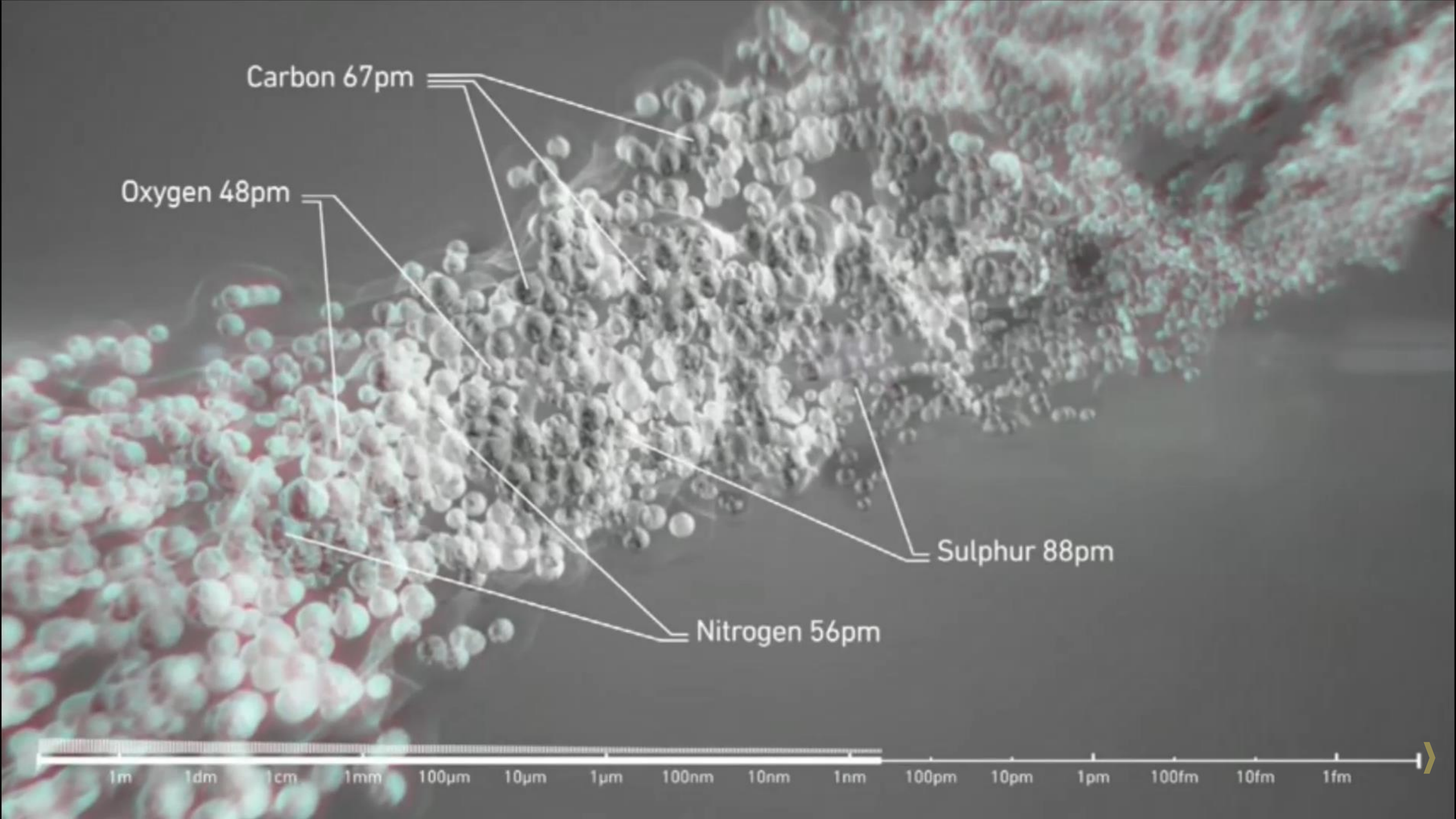


# Voyage into the world of atoms

## CERN

*Conseil Européen pour la  
Recherche Nucléaire  
(2018)*





Carbon 67pm

Oxygen 48pm

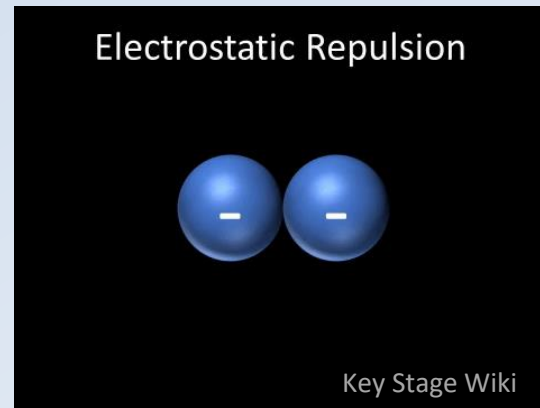
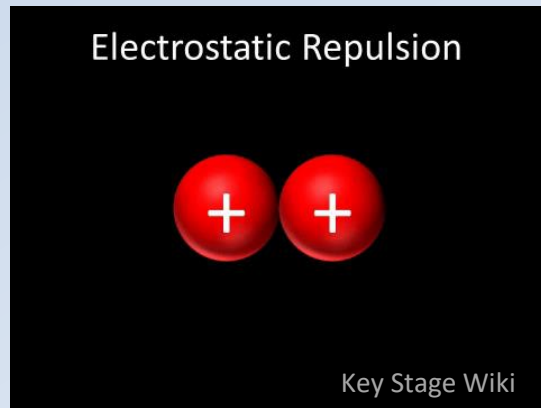
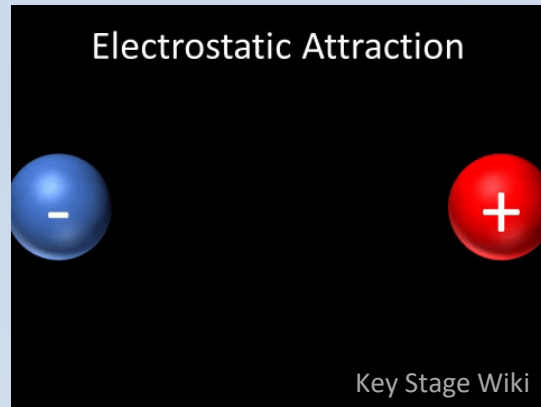
Sulphur 88pm

Nitrogen 56pm

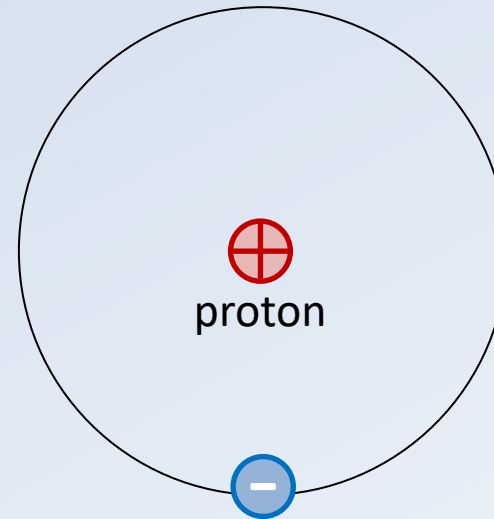
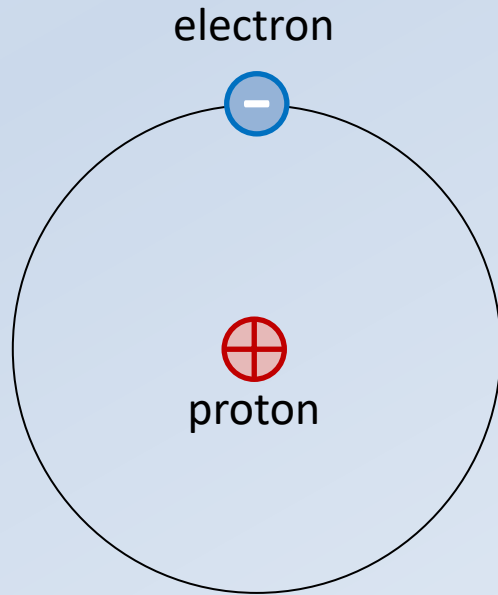


# How are Atoms Stuck Together to Make Molecules?

- Electrostatic Forces

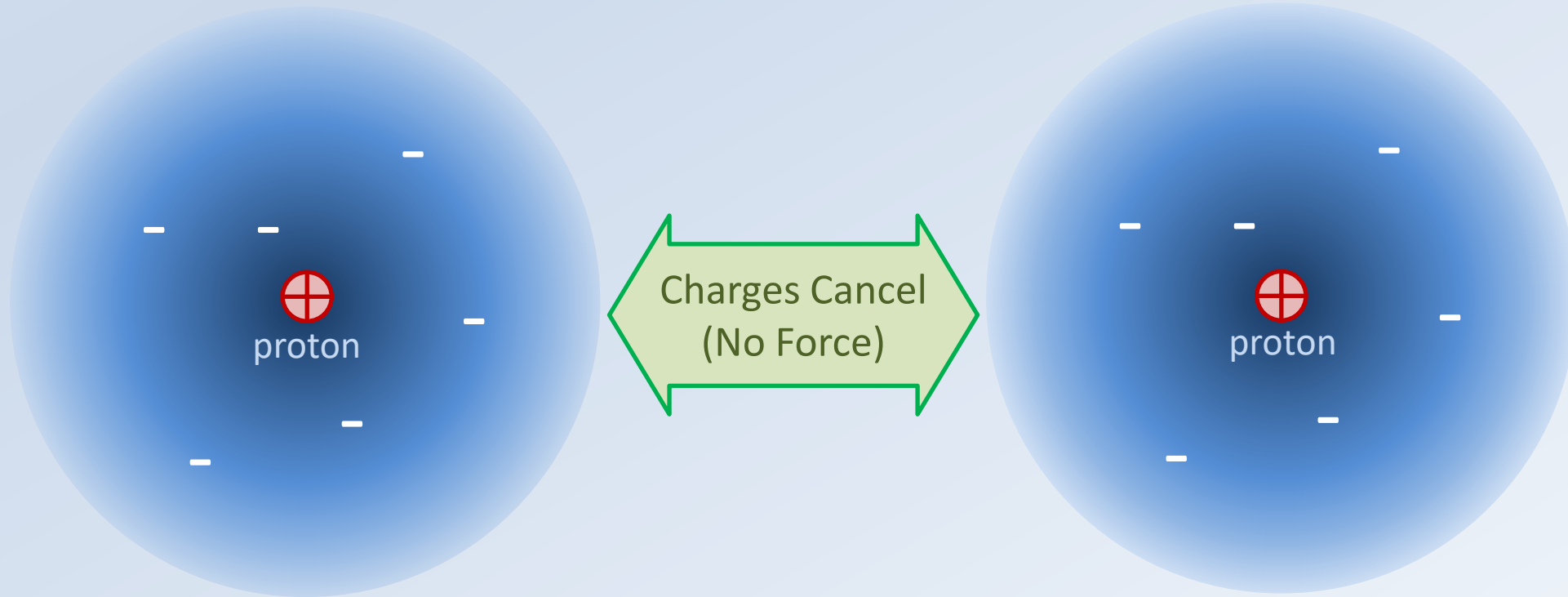


# Consider 2 Hydrogen Atoms

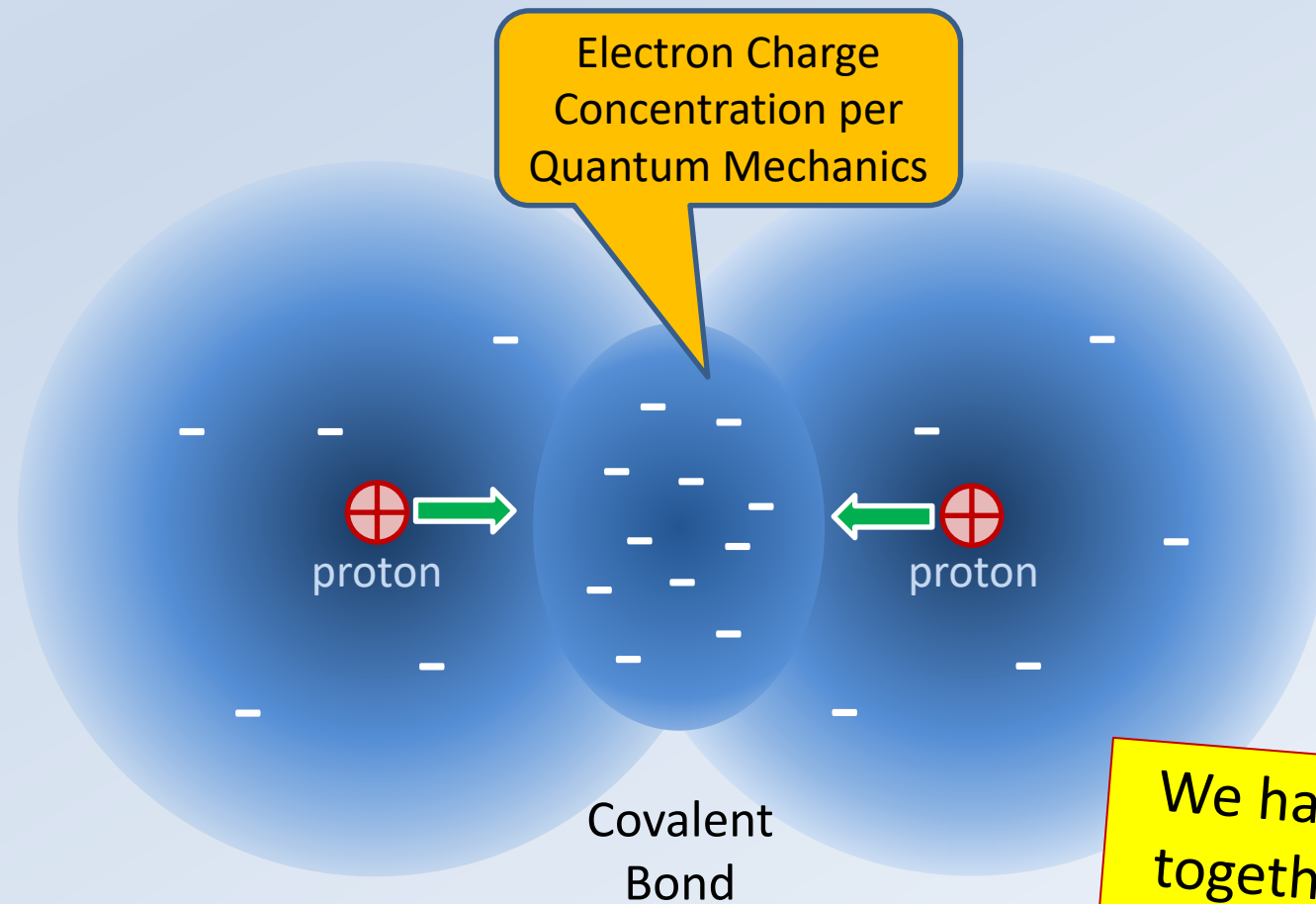


# Consider 2 Hydrogen Atoms

electron  
cloud is  
diffuse



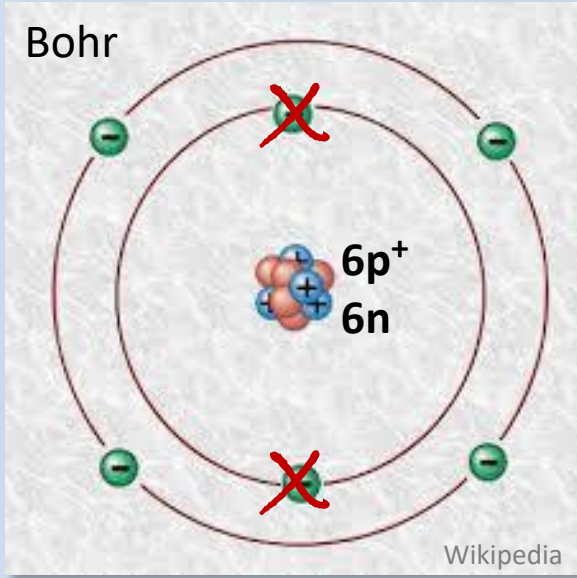
# Consider 2 Hydrogen Atoms



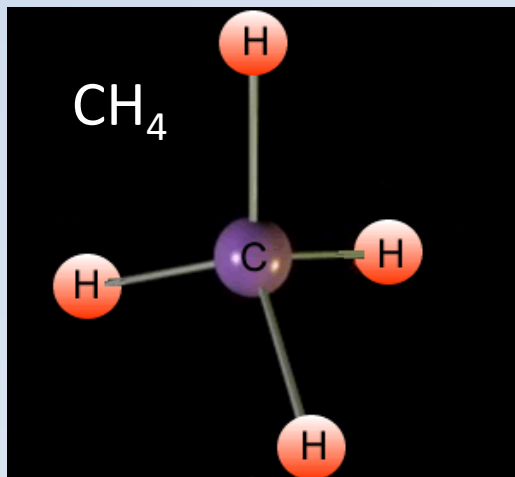
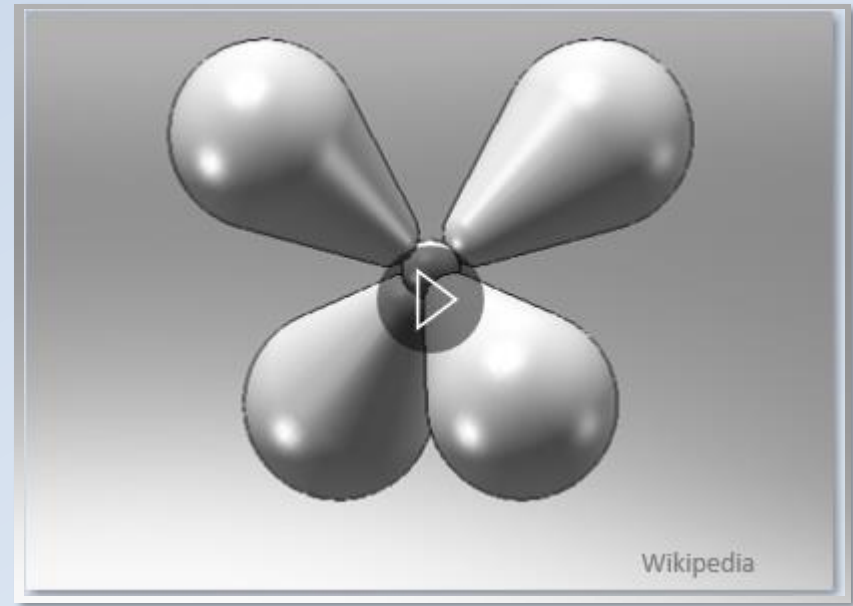
We have them bound together into a stable  $H_2$  molecule



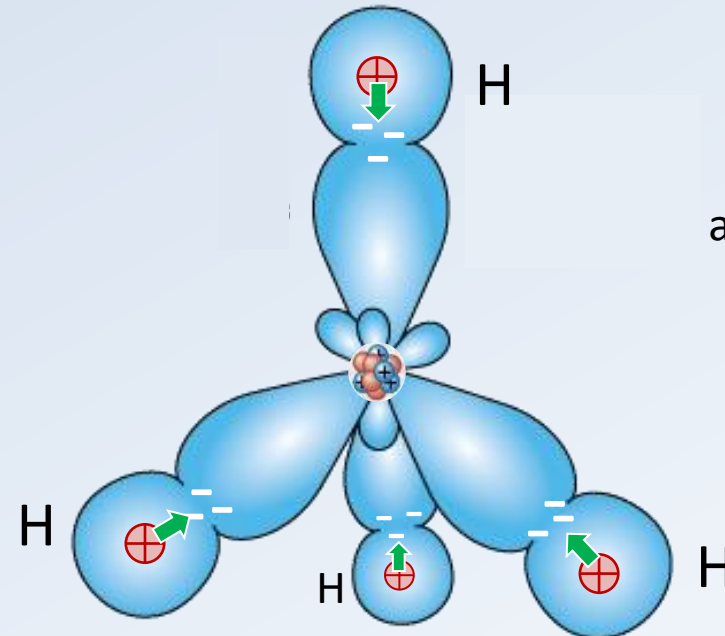
Consider instead a Carbon atom:



One possible  
orbital  
configuration



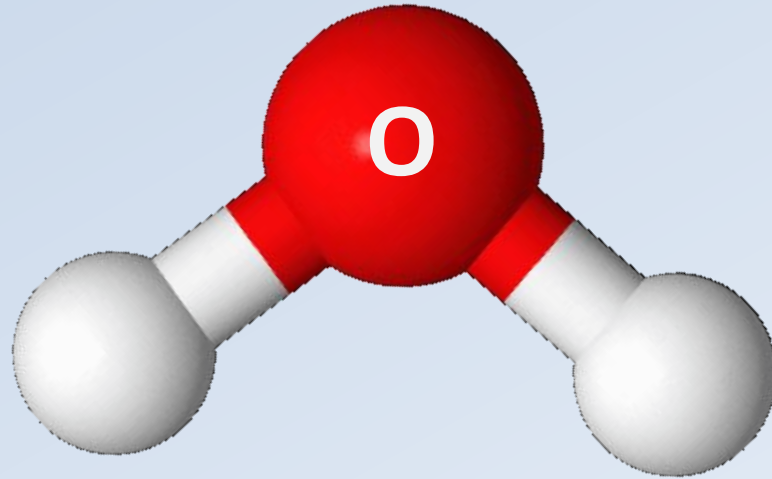
resulting in a  
methane  
molecule



Now put H  
atoms next to  
each lobe...

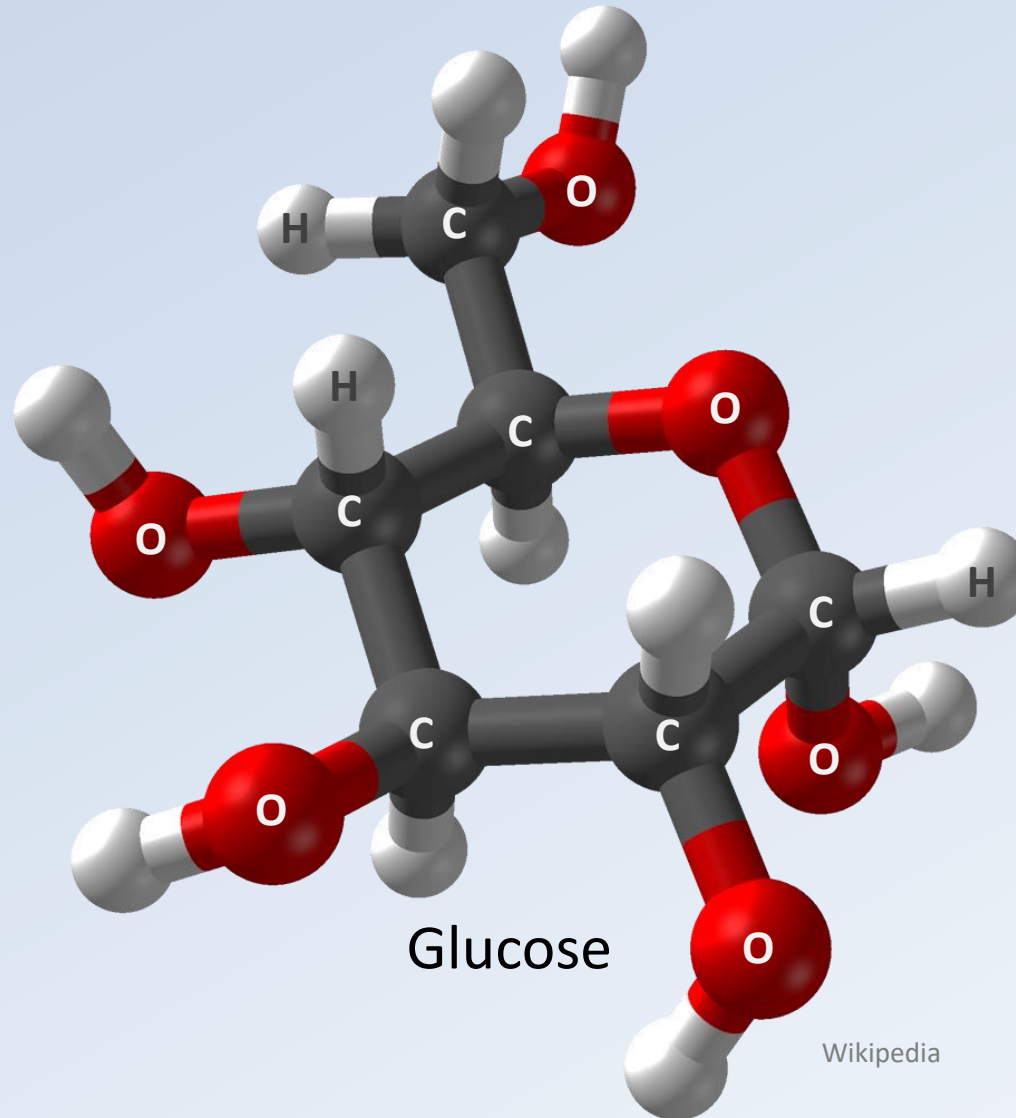
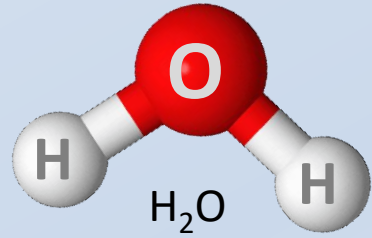


# Examples of small molecules





# Examples of small molecules

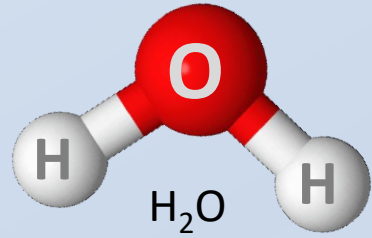


A Simple  
Carbohydrate:  
Sugar

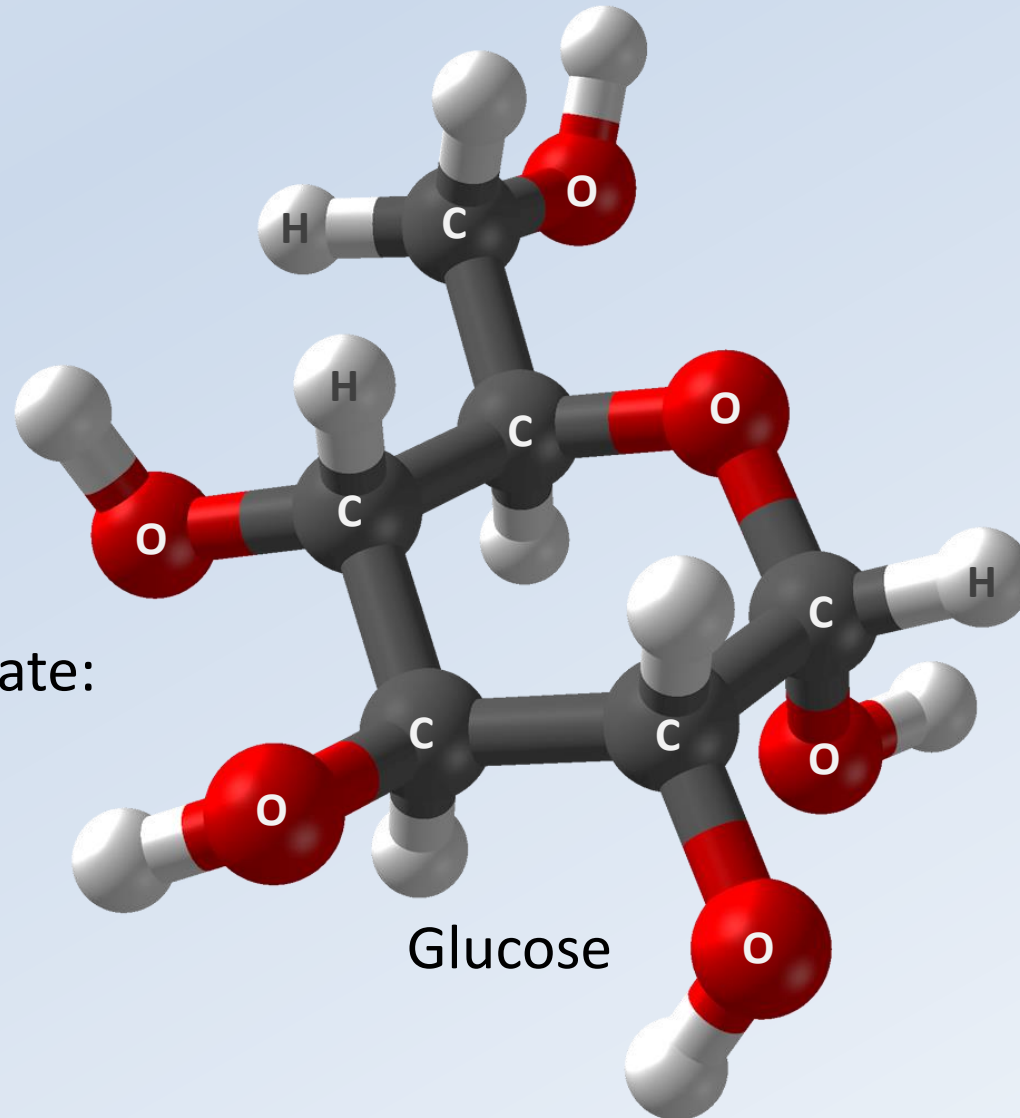
Wikipedia



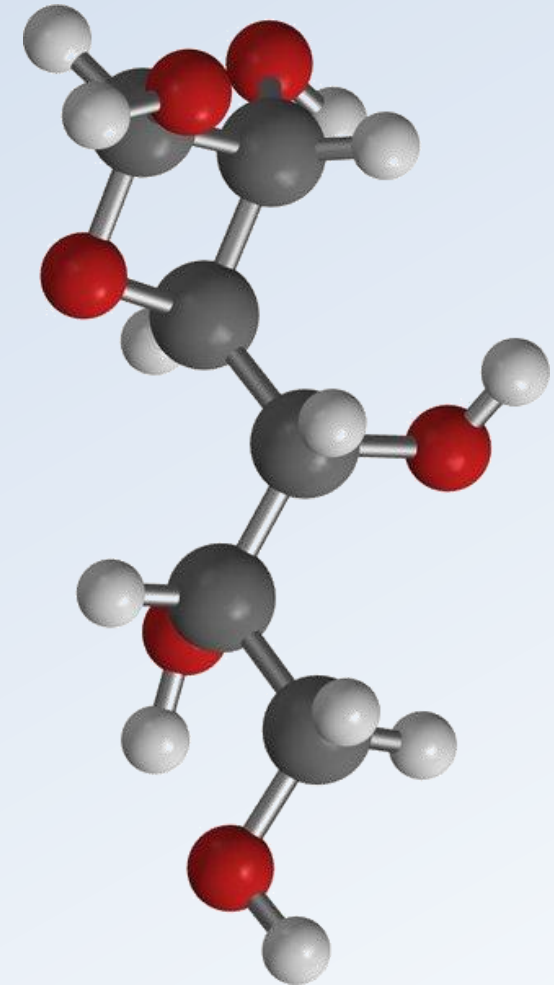
# Examples of small molecules



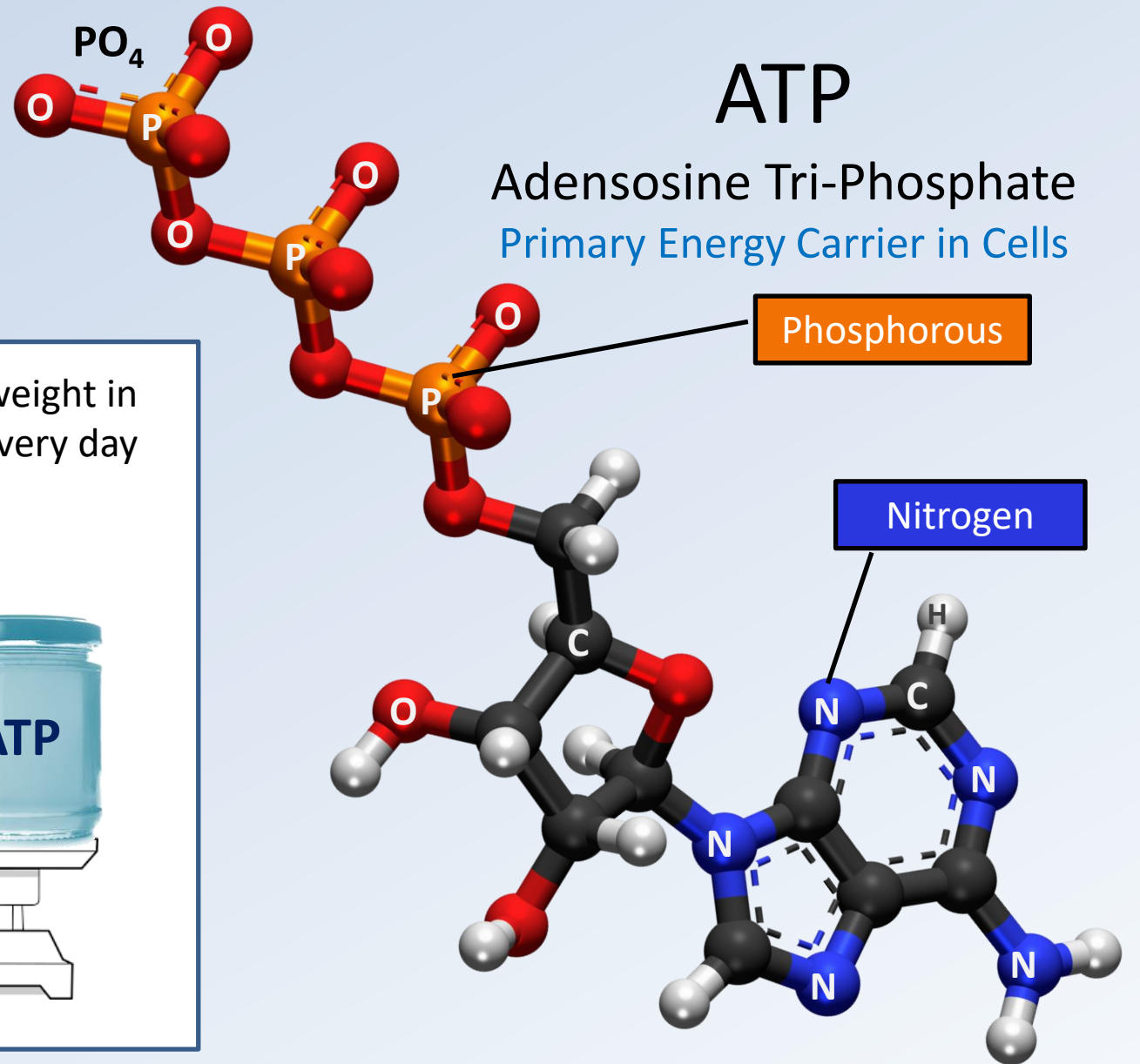
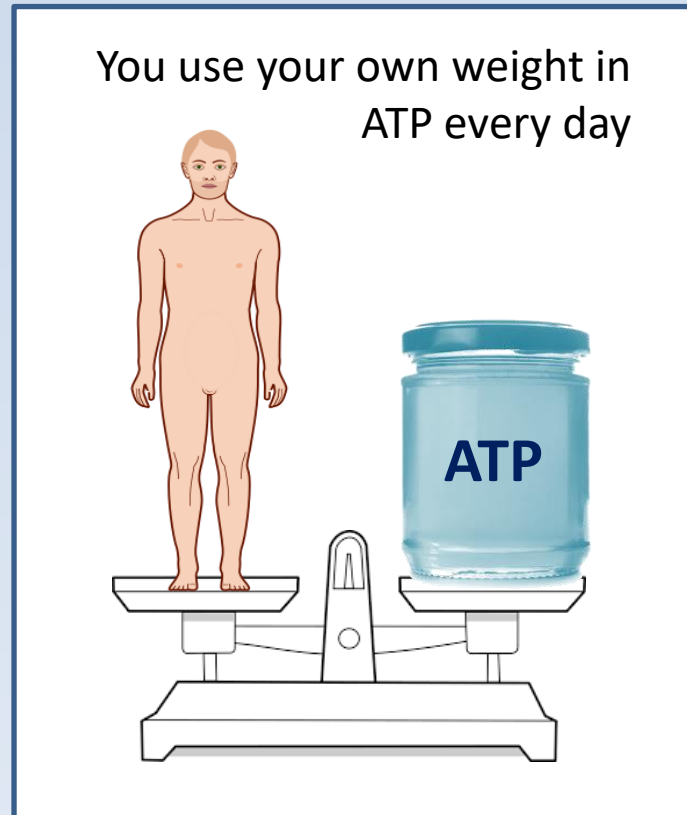
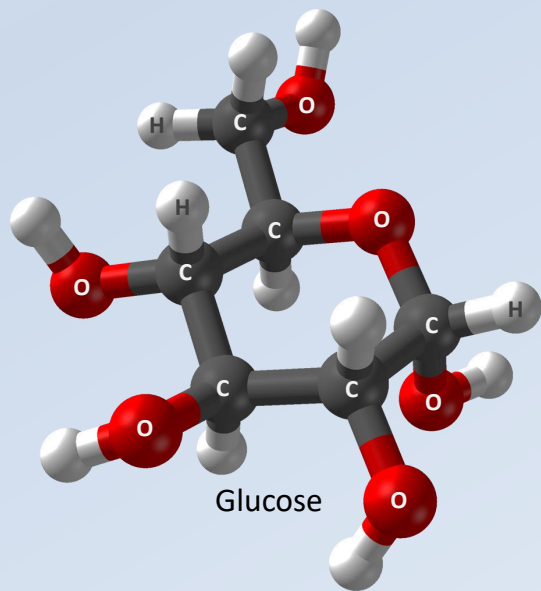
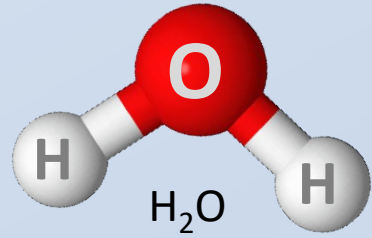
A Simple  
Carbohydrate:  
Sugar



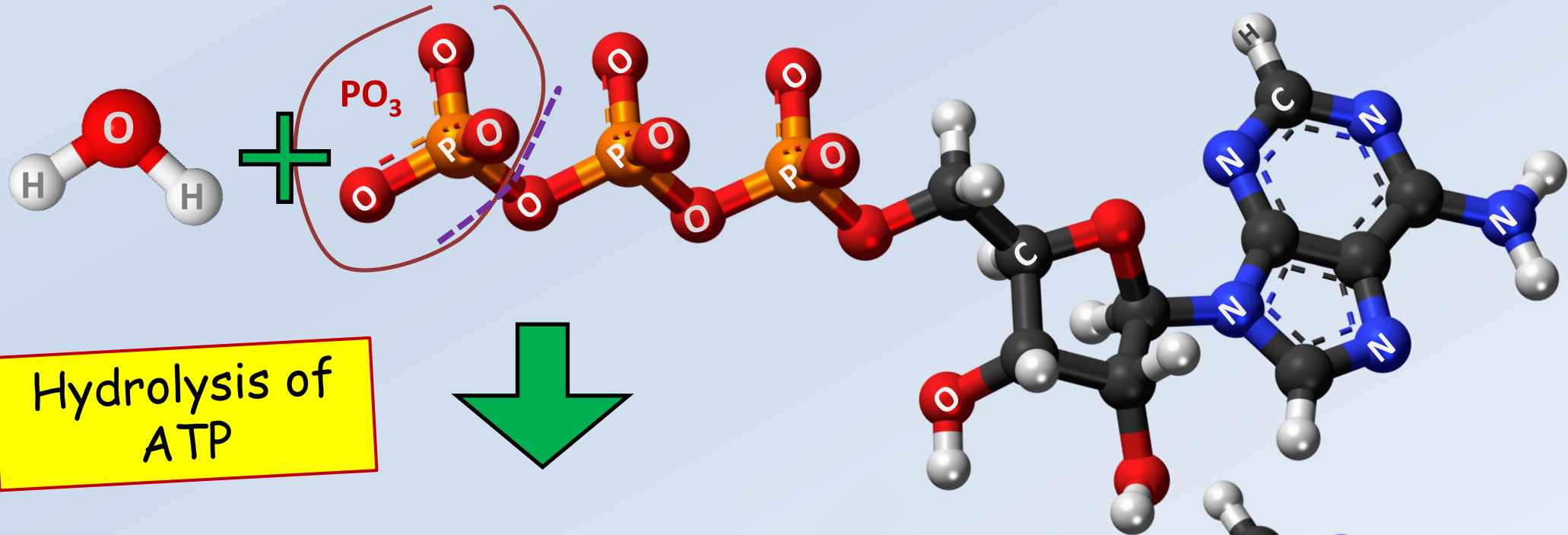
Linear (unwound)  
Configuration of  
Glucose – dry form



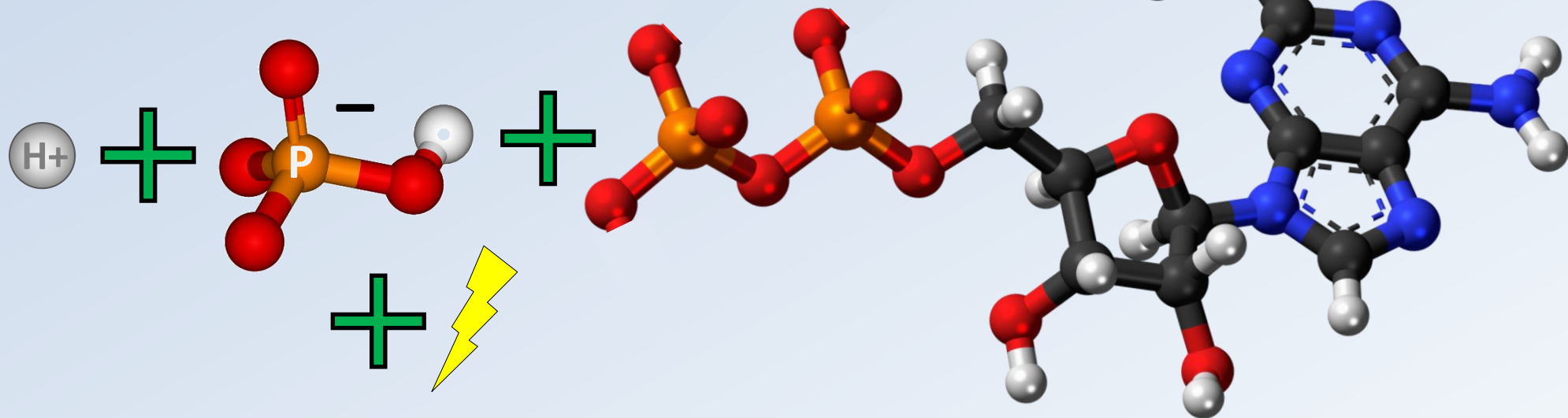
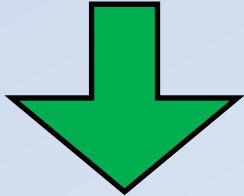
# Examples of small molecules



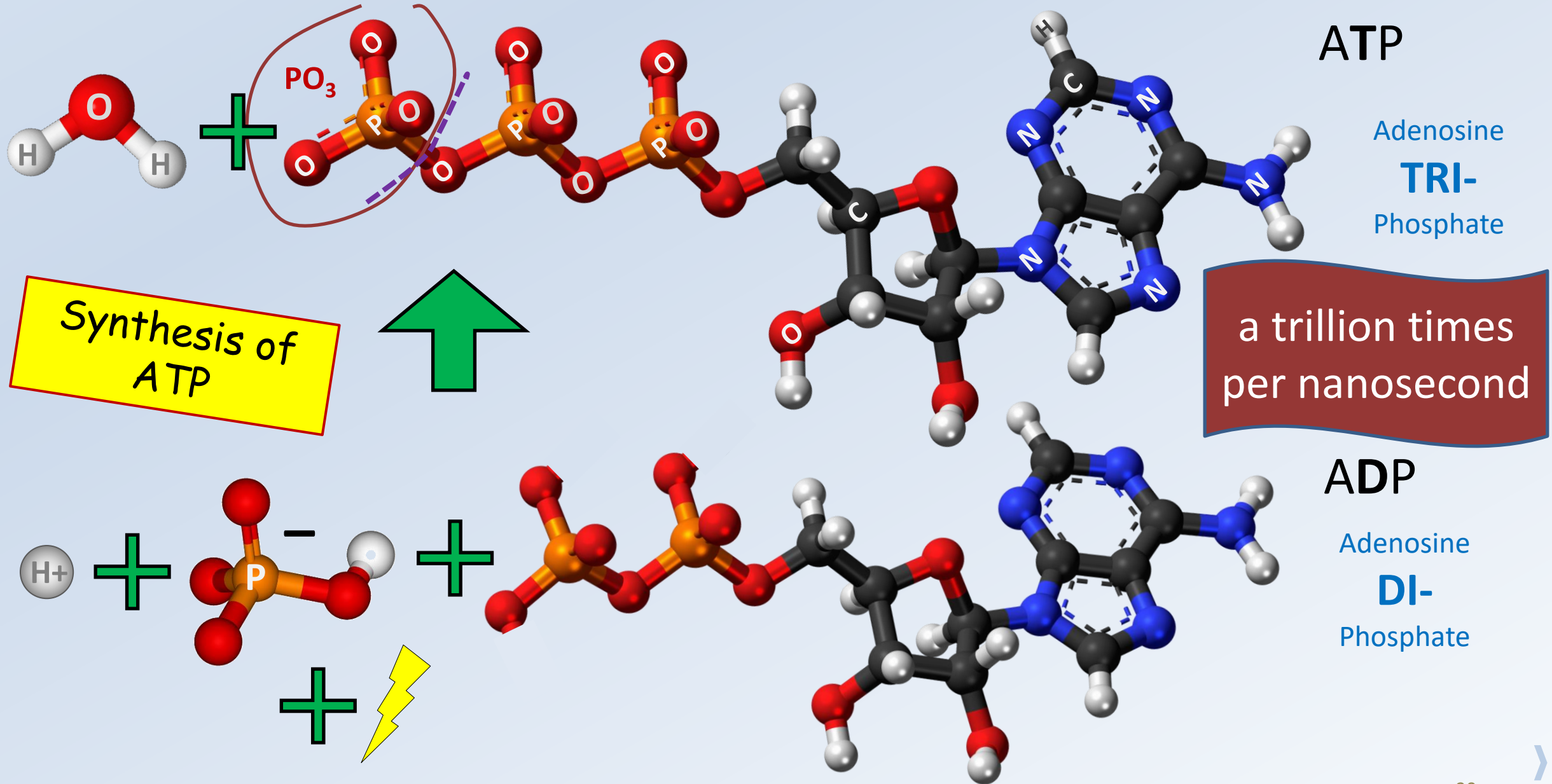
# Short Term Energy Storage: ATP from ADP



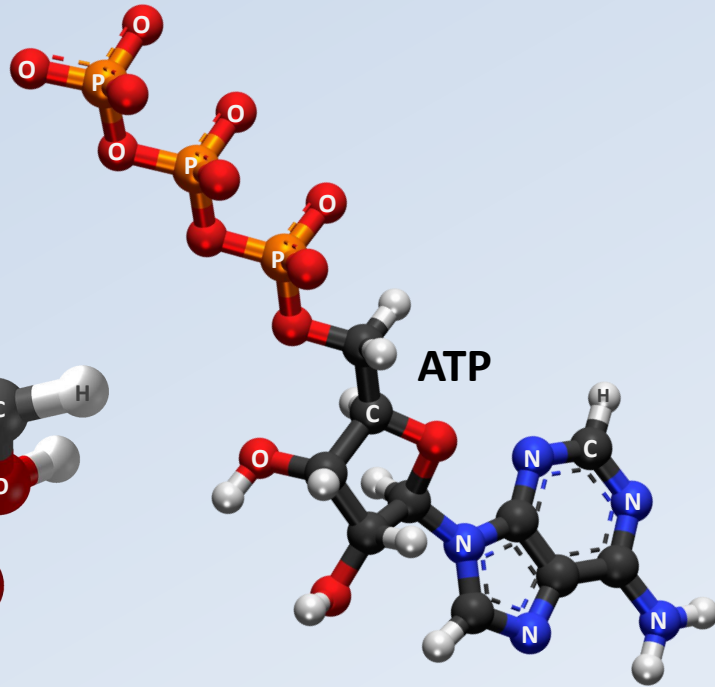
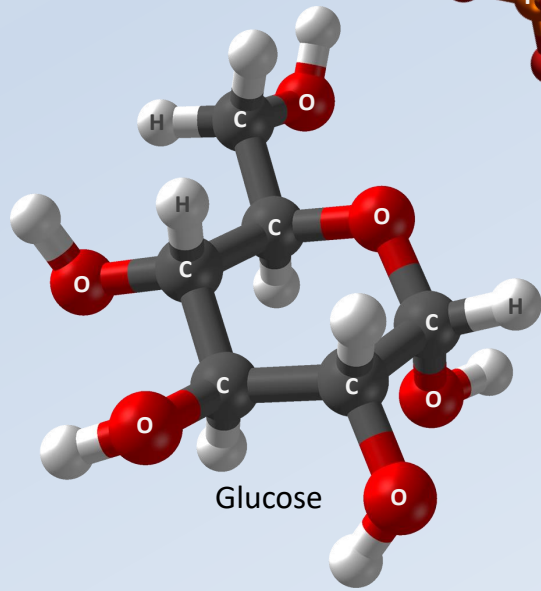
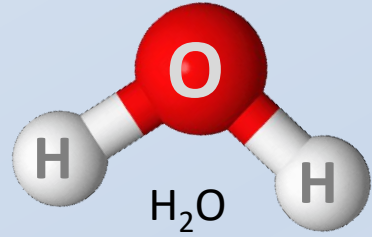
Hydrolysis of  
ATP



# Short Term Energy Storage: ATP from ADP

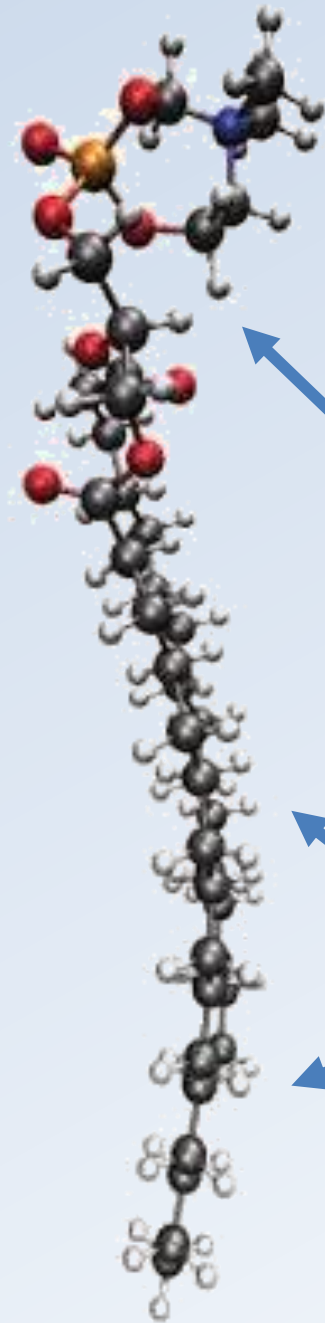


# Examples of small molecules



'DPPC'

(component of cell membranes)



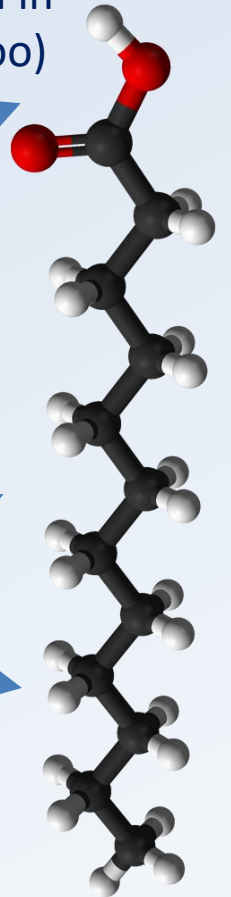
# Lipids (fats)

Lauric Acid

(oil used in shampoo)

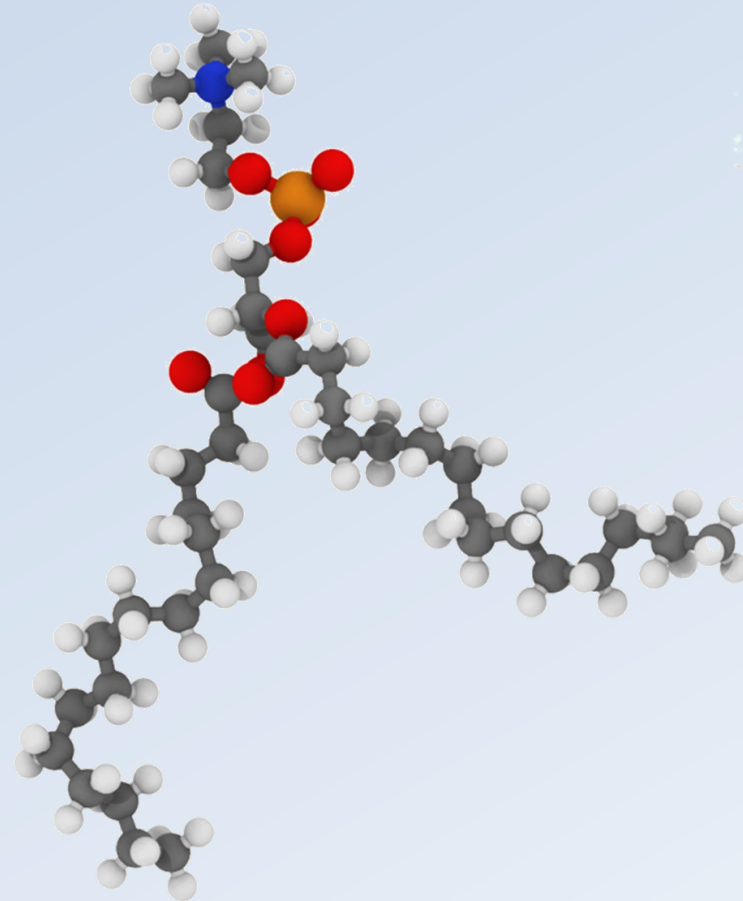
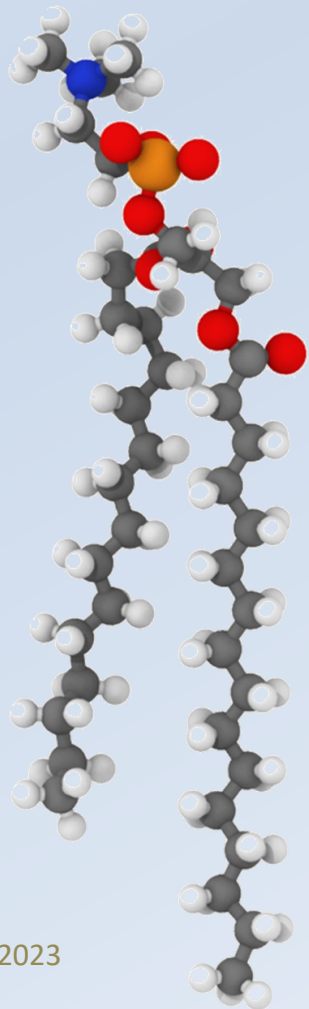
Hydrophilic  
Heads

Long  
Hydrophobic  
Tails

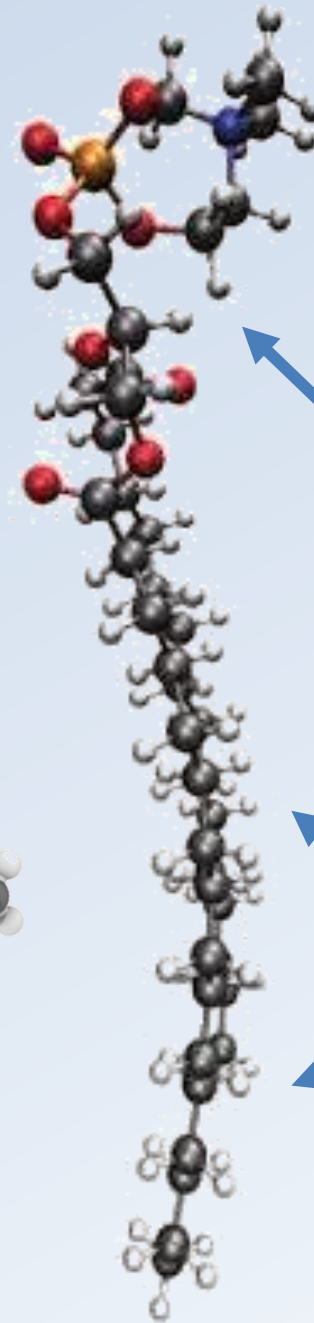


# A Short Aside: Bilayer Membranes

## Phospholipids

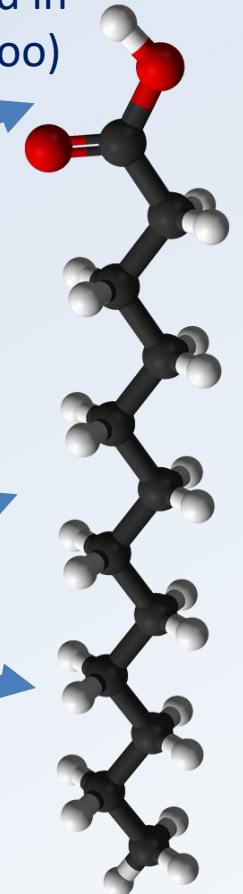


'DPPC'  
(component of  
cell membranes)



## Lipids (fats)

Lauric Acid  
(oil used in  
shampoo)

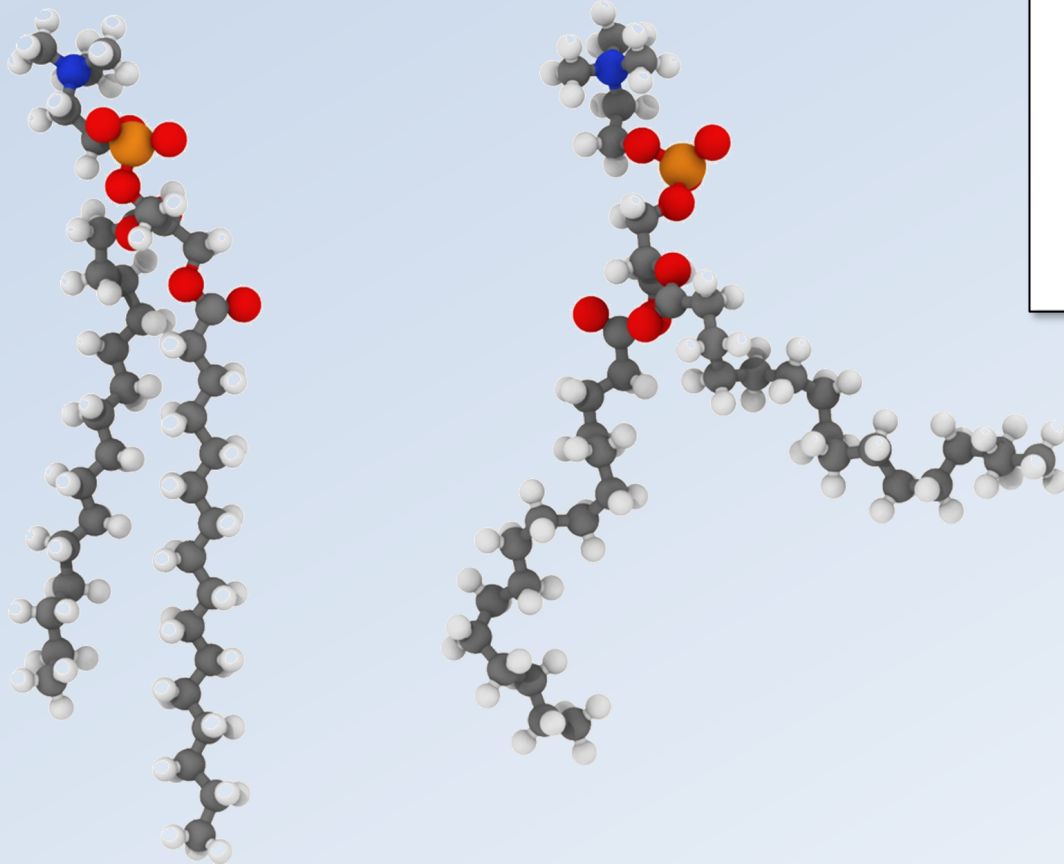


*Hydrophilic*  
Heads

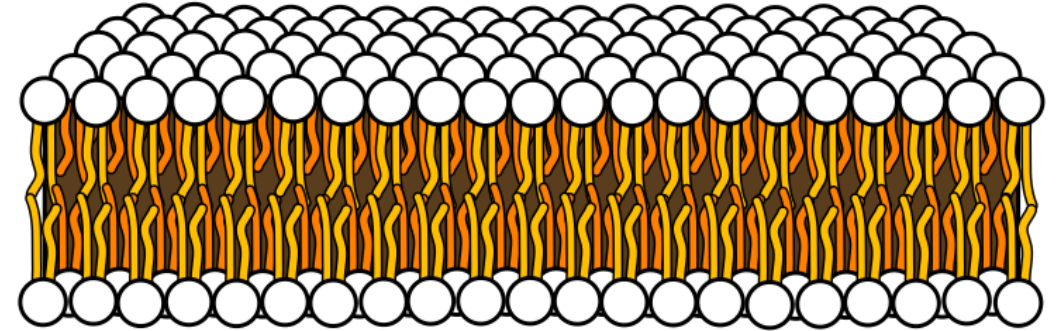
Long  
*Hydrophobic*  
Tails

# A Short Aside: Bilayer Membranes

## Phospholipids

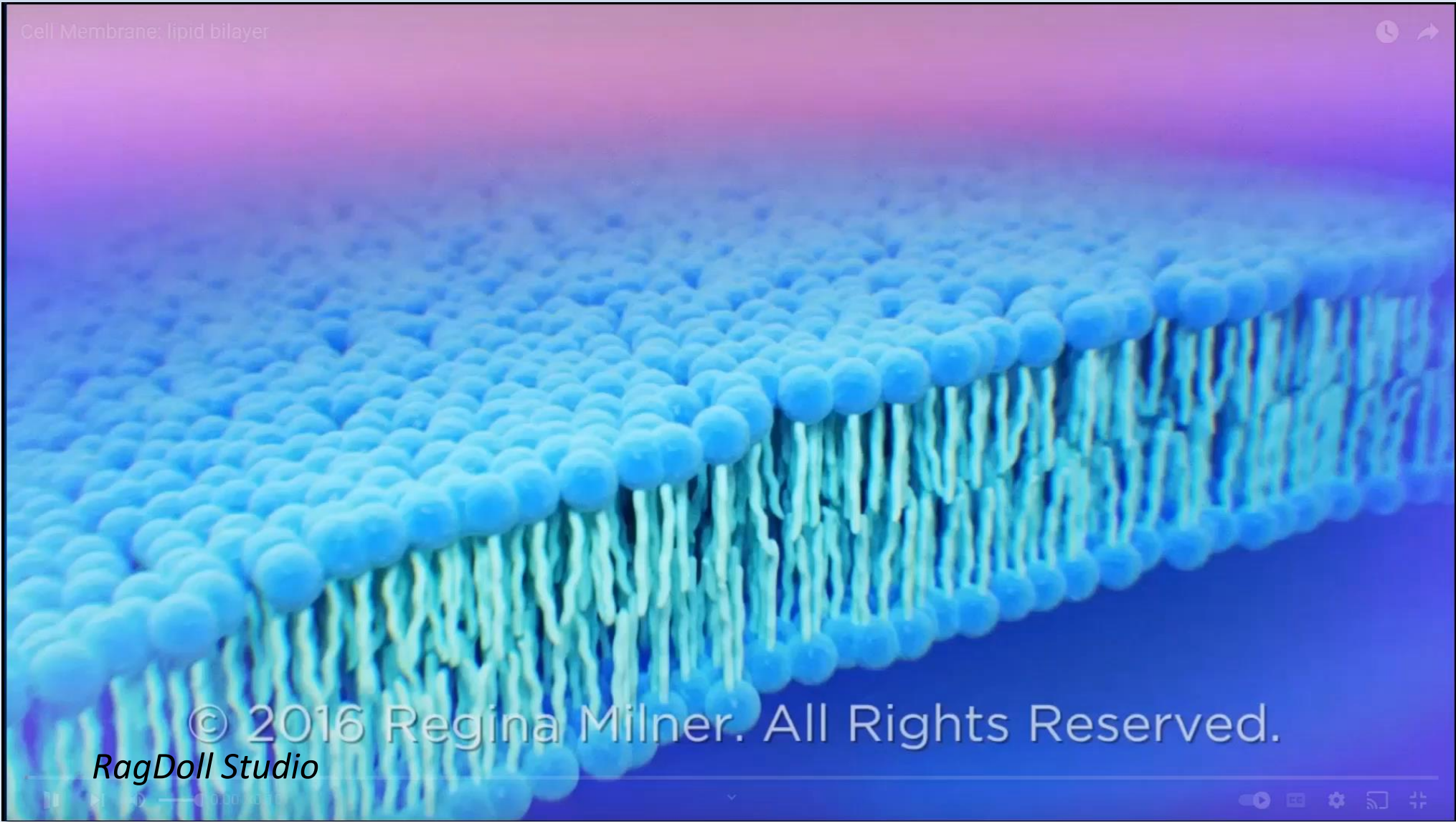


These Lipids Self-Assemble into  
Bilayer Membranes

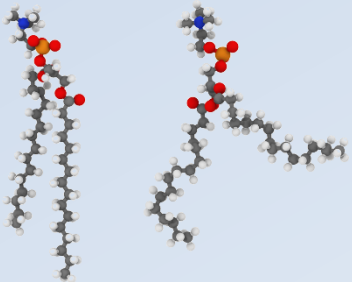




# A Short Aside: Bilayer Membranes



Phospholipids





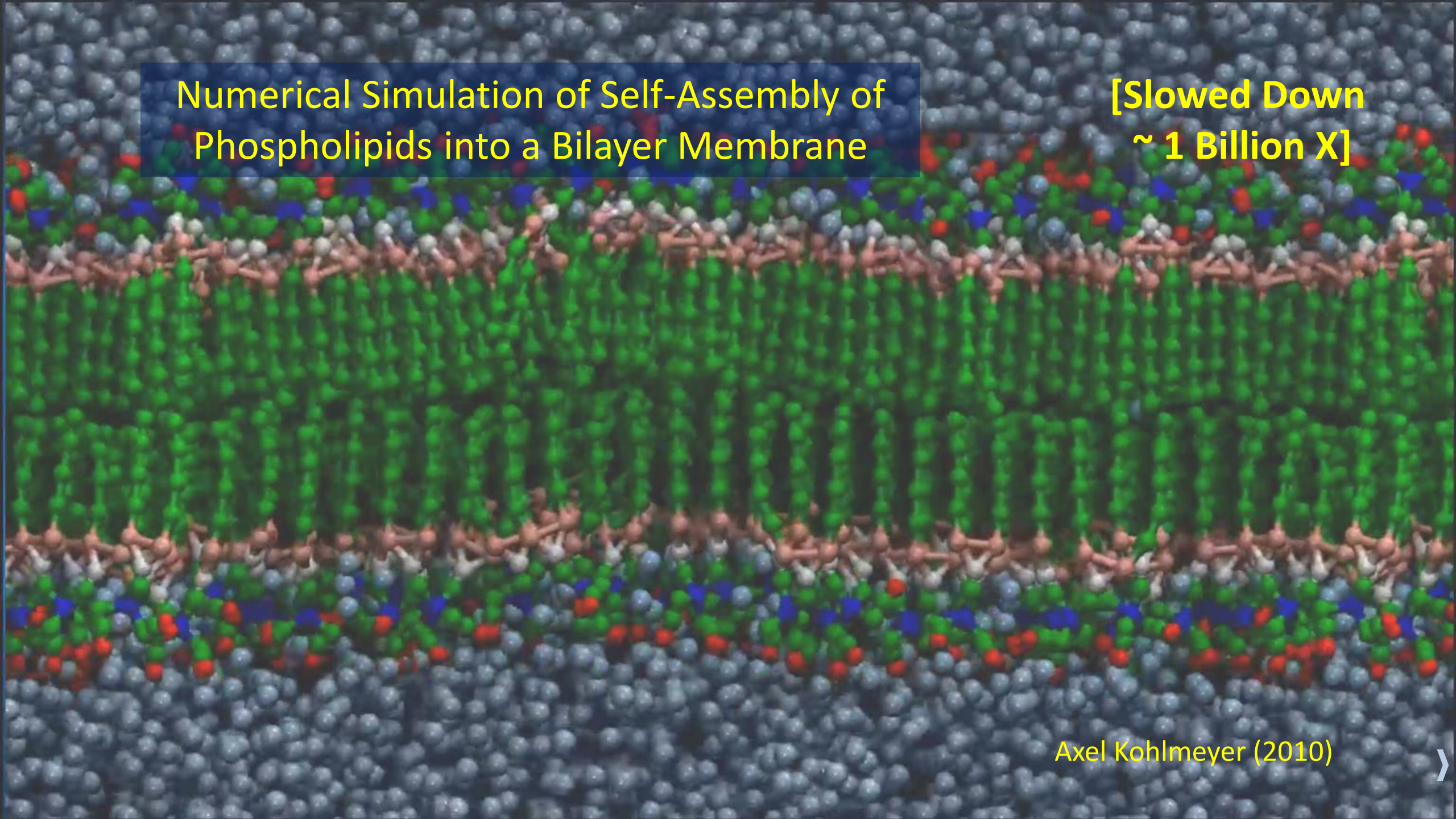
Numerical Simulation of Self-Assembly of  
Phospholipids into a Bilayer Membrane

[Slowed Down  
~ 1 Billion X]

Axel Kohlmeyer (2010)

Numerical Simulation of Self-Assembly of  
Phospholipids into a Bilayer Membrane

[Slowed Down  
~ 1 Billion X]

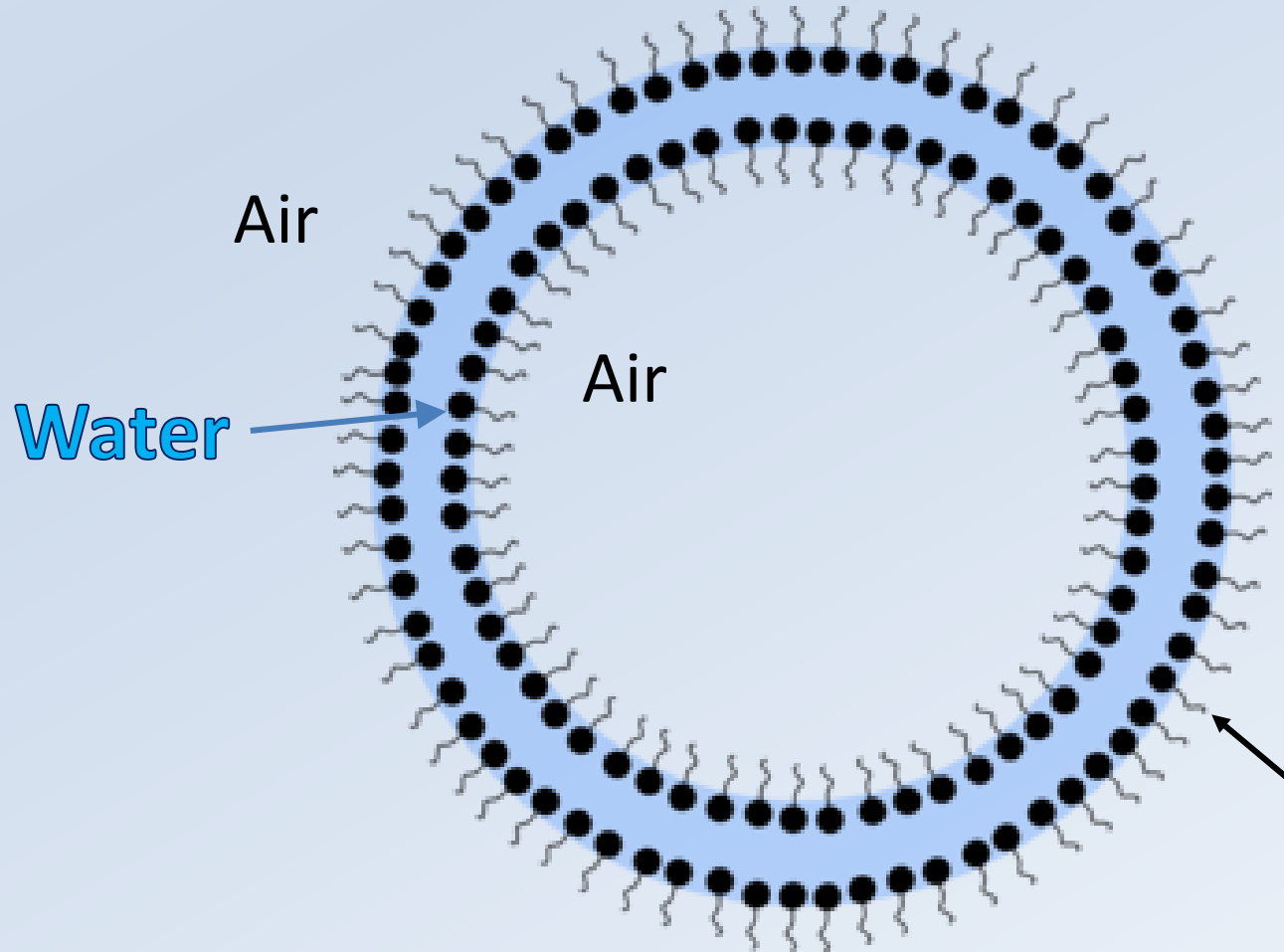


Axel Kohlmeyer (2010)



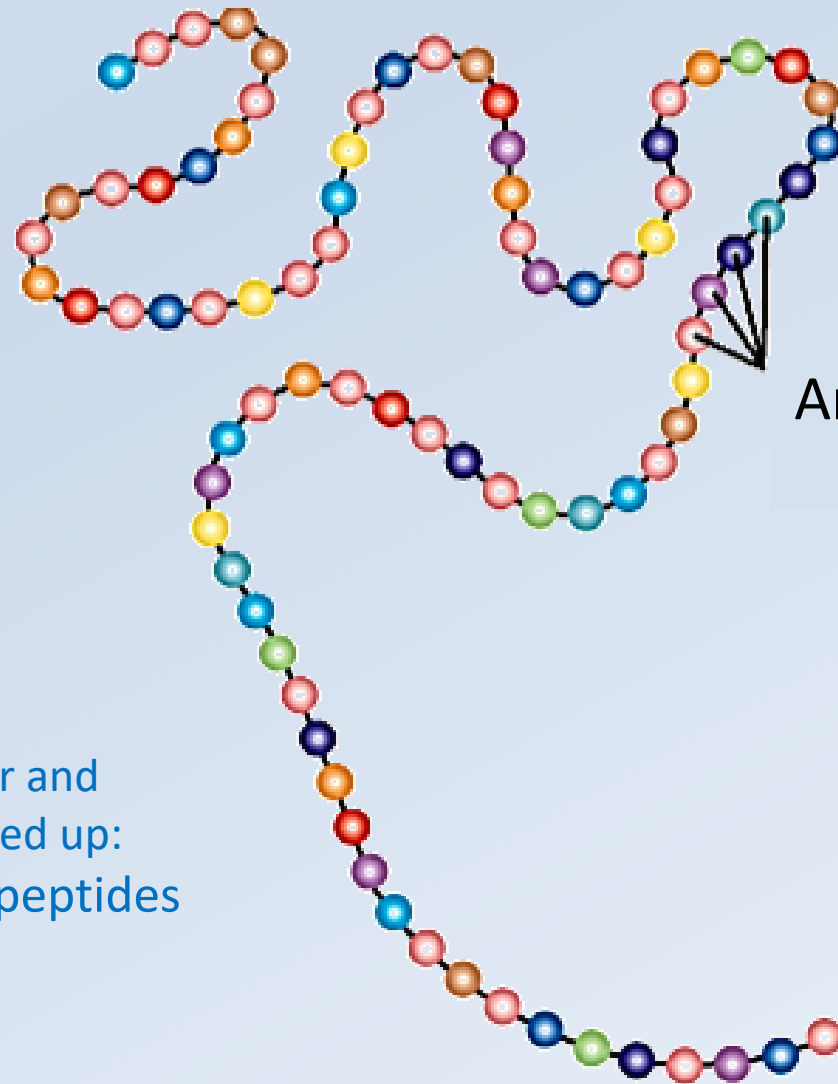
A Short Aside:  
Bilayer  
Membranes

# Soap Bubbles are like Inside-Out Membranes



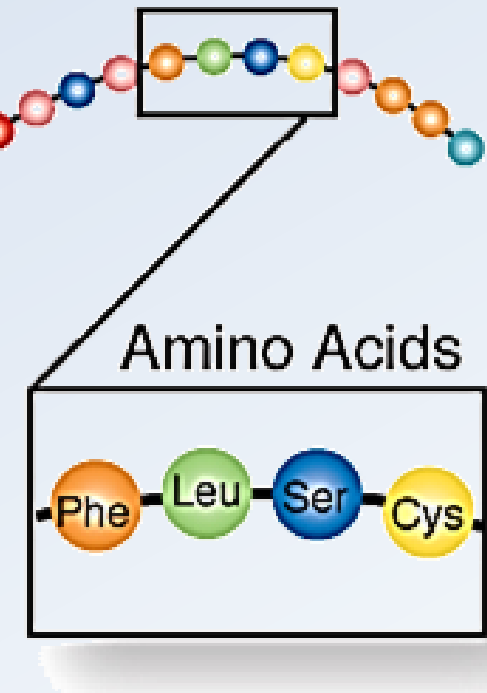
Questions?

# Proteins: Long Chains of Amino Acids

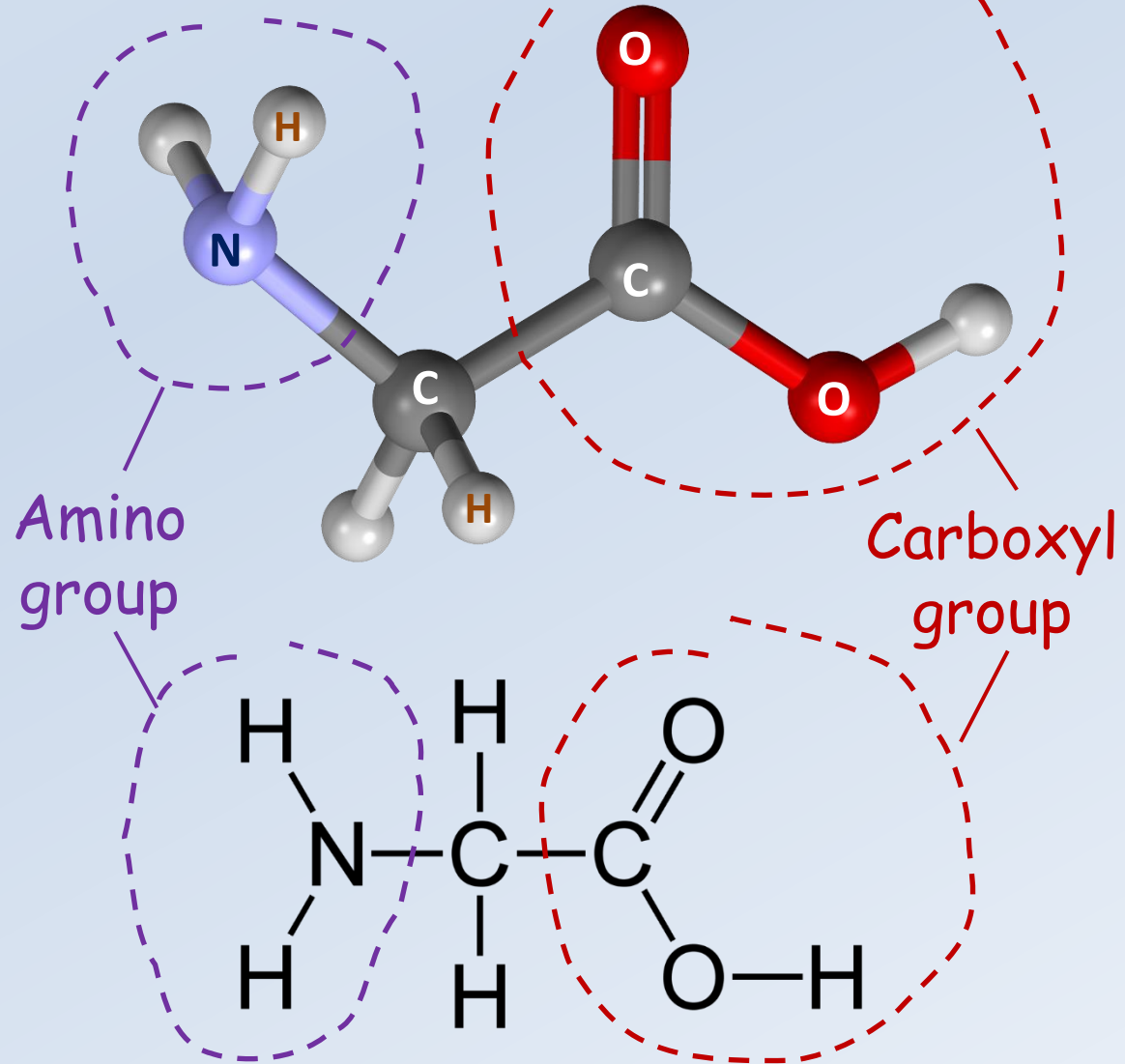


Amino Acids  
(Peptides)

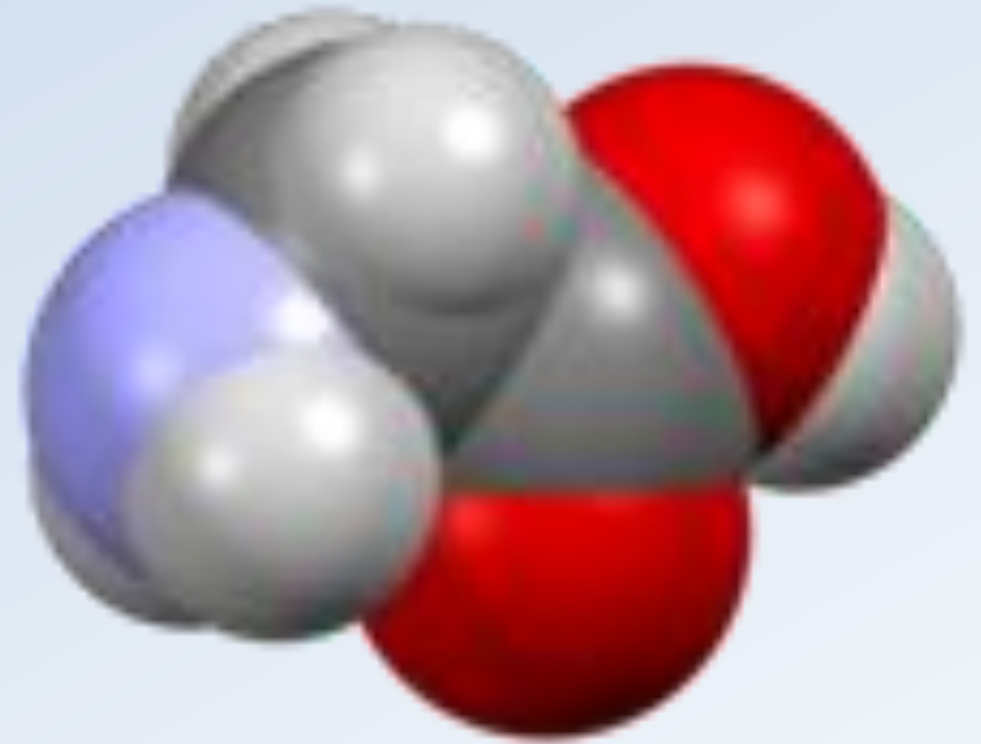
If shorter and  
not folded up:  
Polypeptides



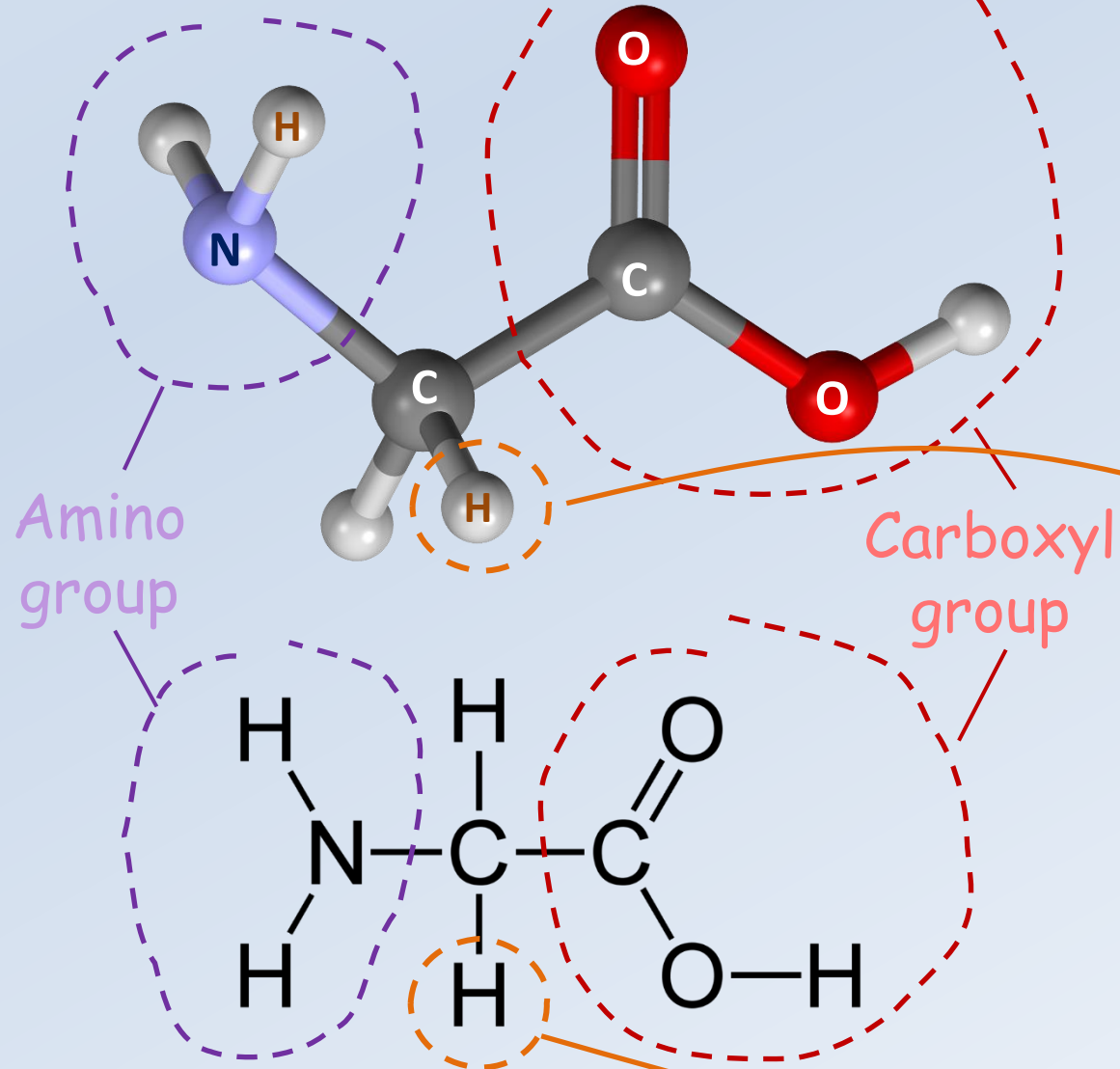
# The Simplest Amino Acid: Glycine



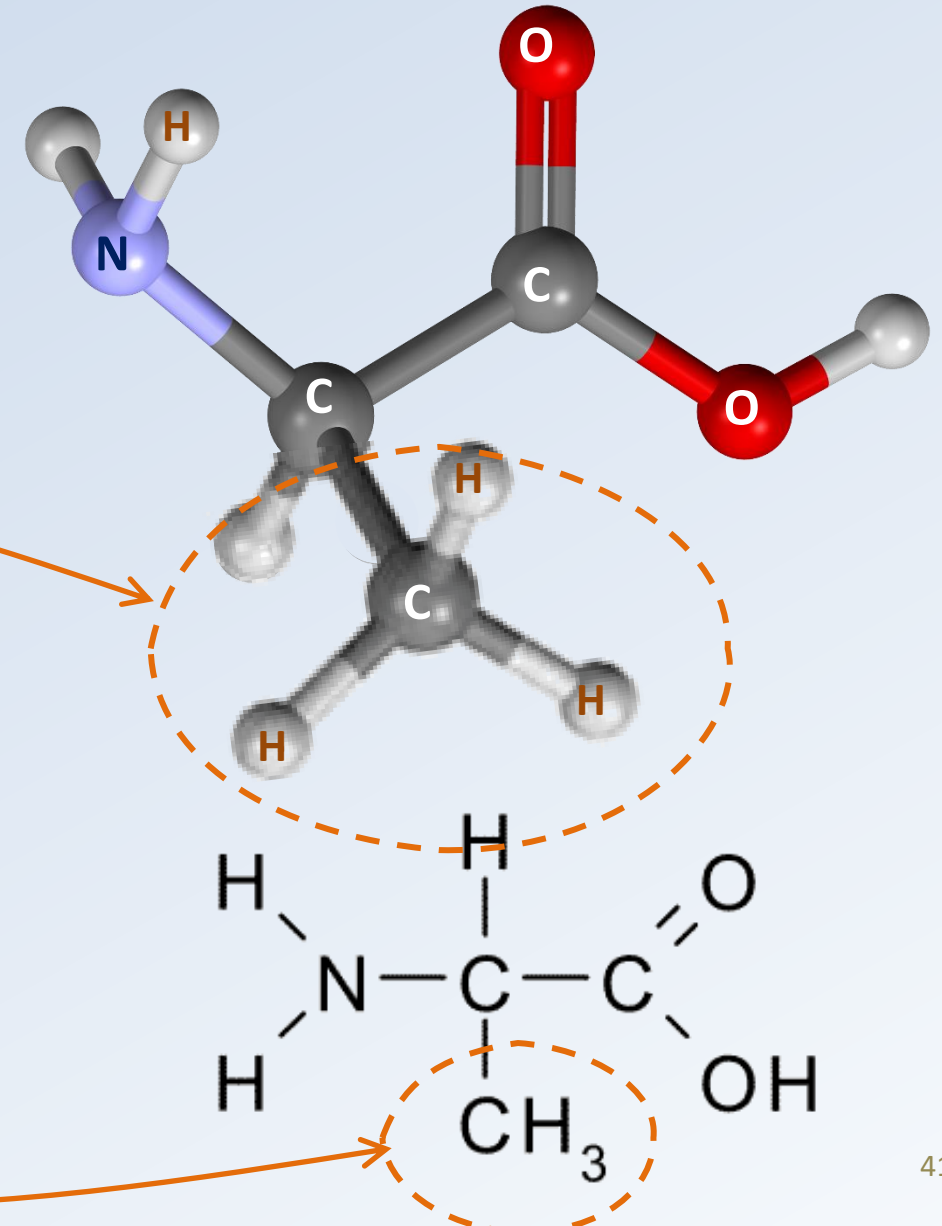
## Space Filling Model



# The Simplest Amino Acid: Glycine

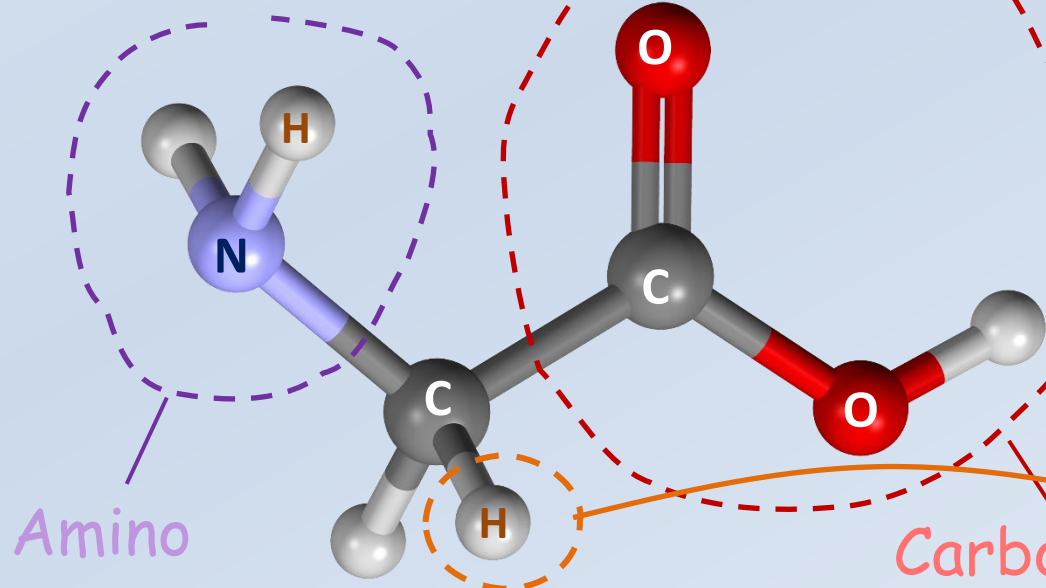


# The Next Simplest Amino Acid: Alanine



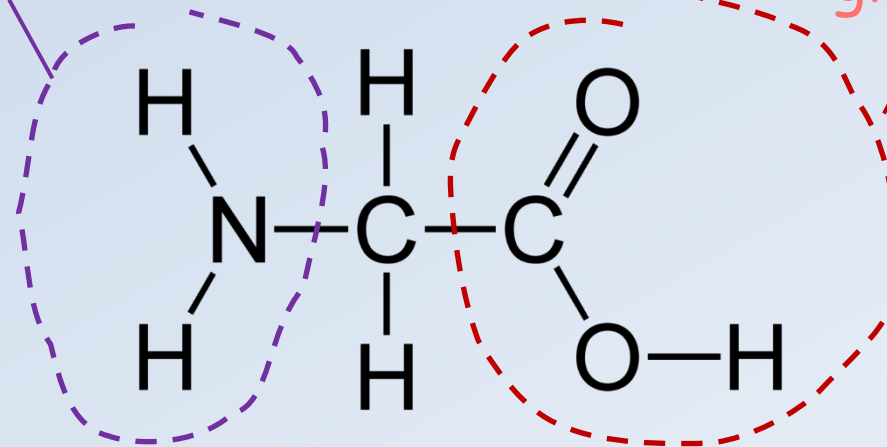


# The Simplest Amino Acid: Glycine



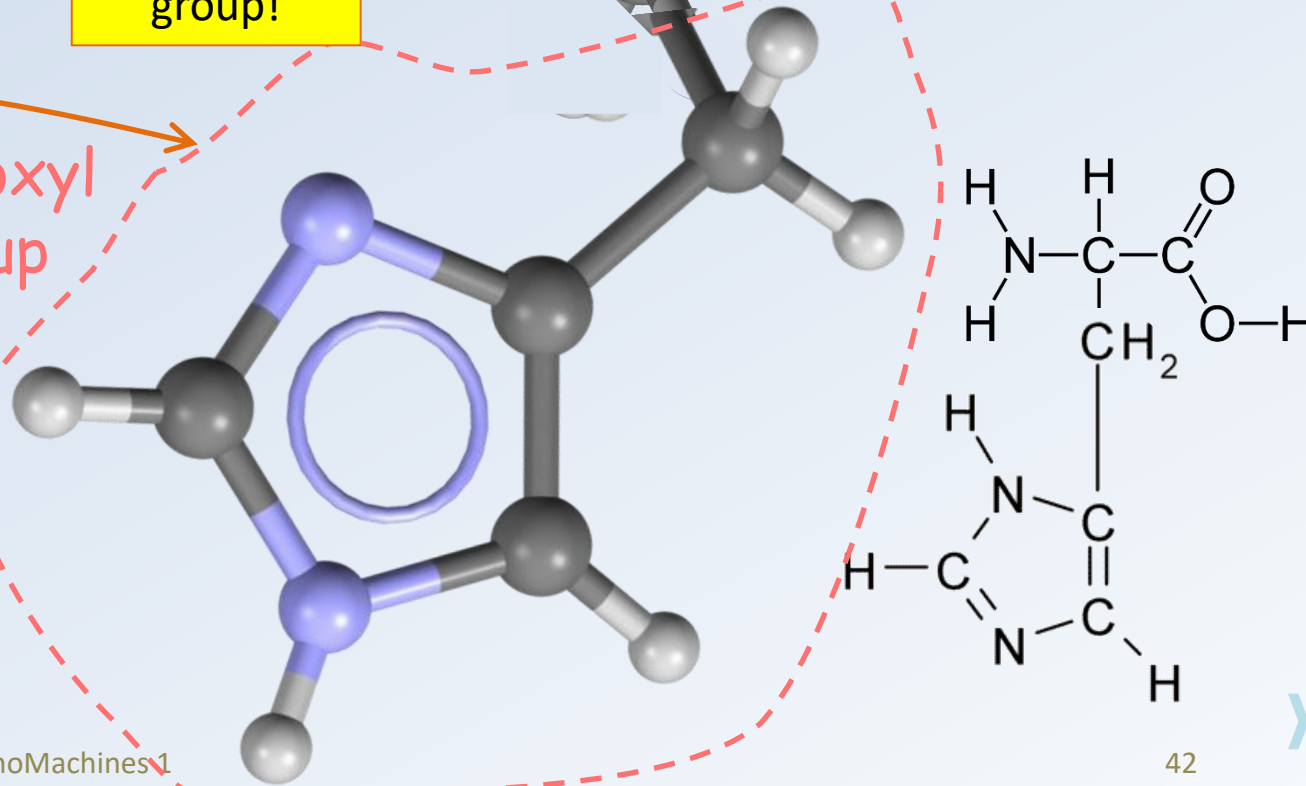
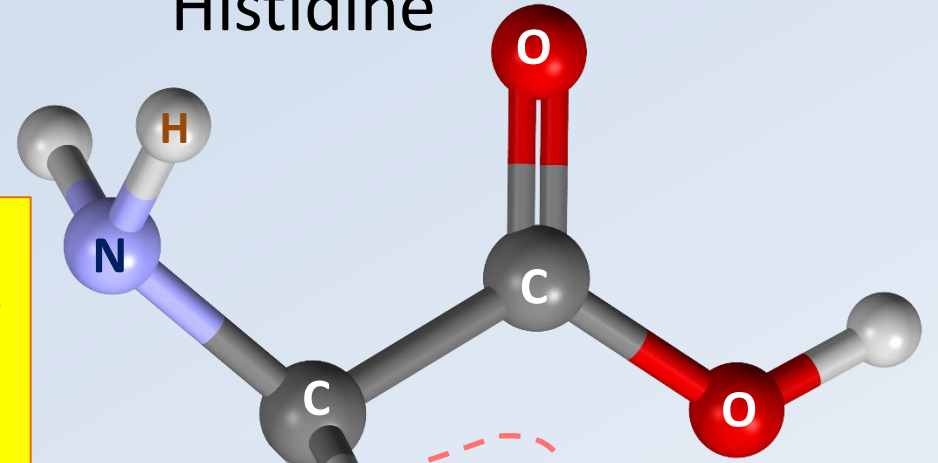
Amino group

Carboxyl group

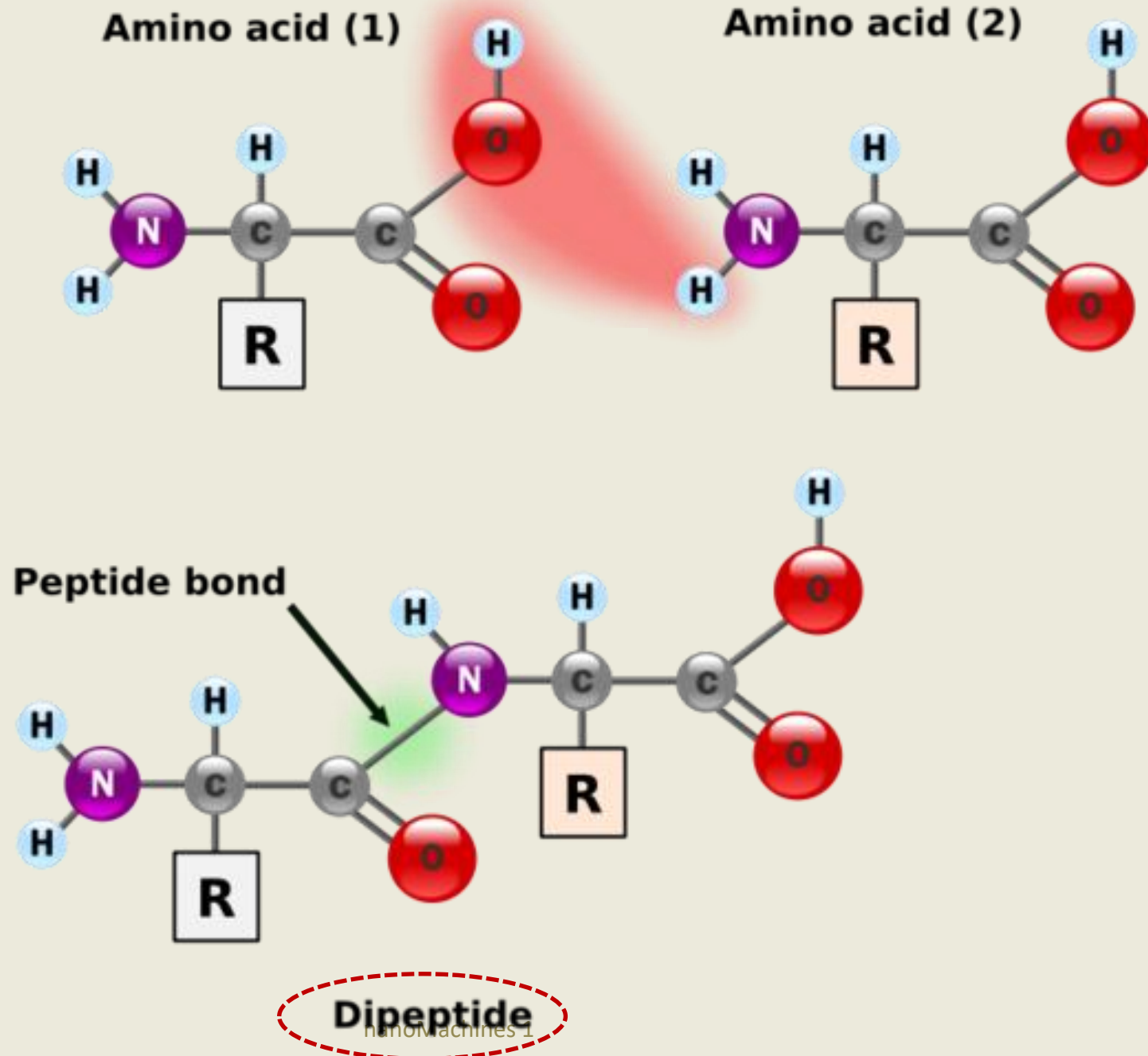


# A more Complex Amino Acid: Histidine

For any Amino Acid, just replace H with side group!



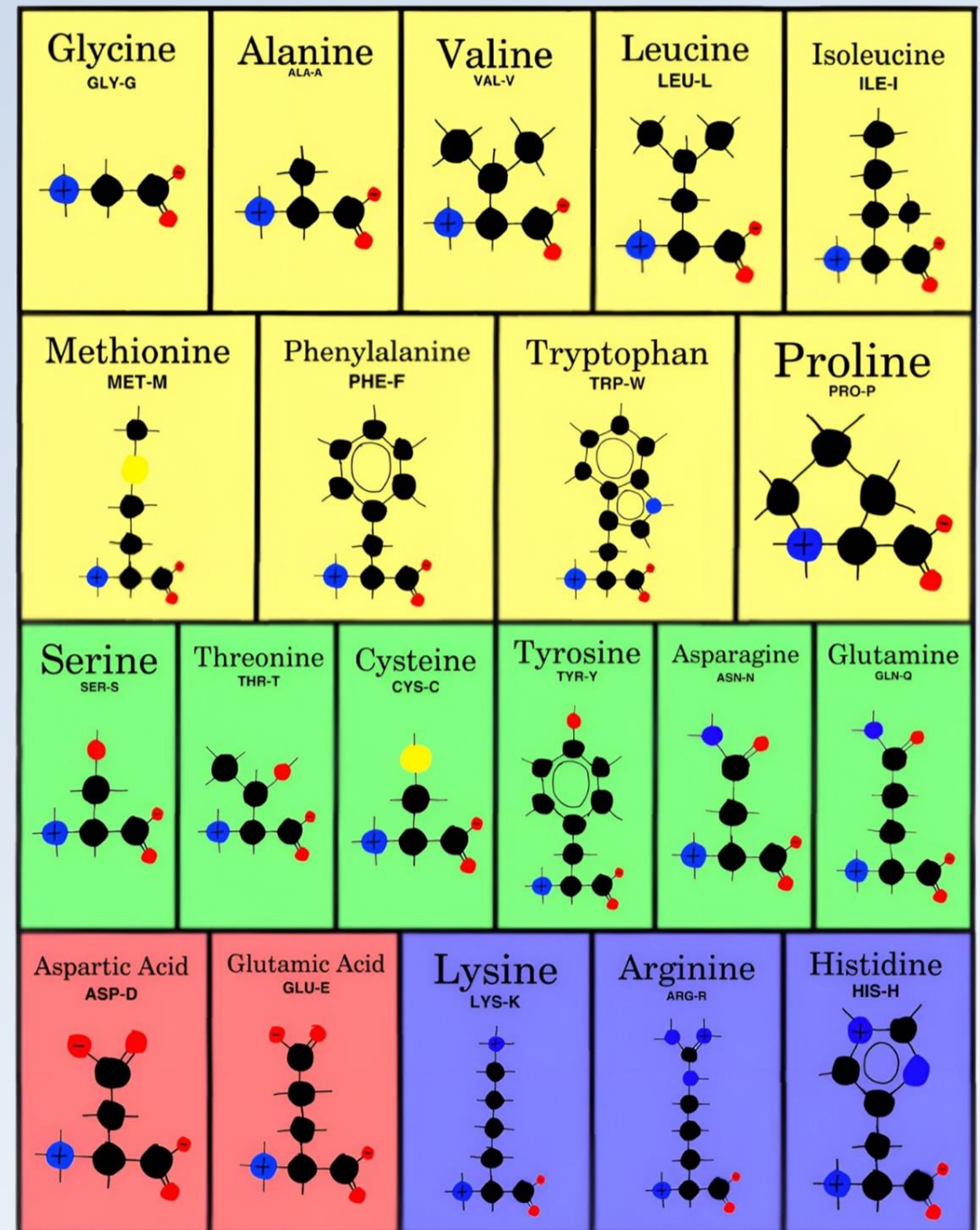
How can we link two Amino Acids together?

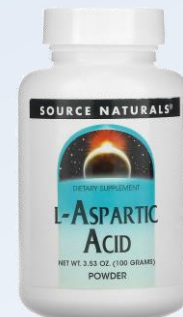
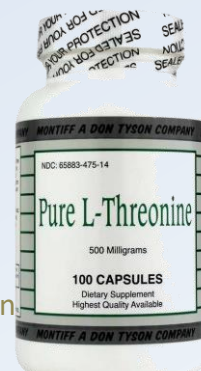
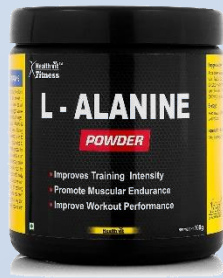


# The 20 Major $\alpha$ -Amino Acids

<b>G</b>	Glycine	Gly	<b>P</b>	Proline	Pro
<b>A</b>	Alanine	Ala	<b>V</b>	Valine	Val
<b>L</b>	Leucine	Leu	<b>I</b>	Isoleucine	Ile
<b>M</b>	Methionine	Met	<b>C</b>	Cysteine	Cys
<b>F</b>	Phenylalanine	Phe	<b>Y</b>	Tyrosine	Tyr
<b>W</b>	Tryptophan	Trp	<b>H</b>	Histidine	His
<b>K</b>	Lysine	Lys	<b>R</b>	Arginine	Arg
<b>Q</b>	Glutamine	Gln	<b>N</b>	Asparagine	Asn
<b>E</b>	Glutamic Acid	Glu	<b>D</b>	Aspartic Acid	Asp
<b>S</b>	Serine	Ser	<b>T</b>	Threonine	Thr

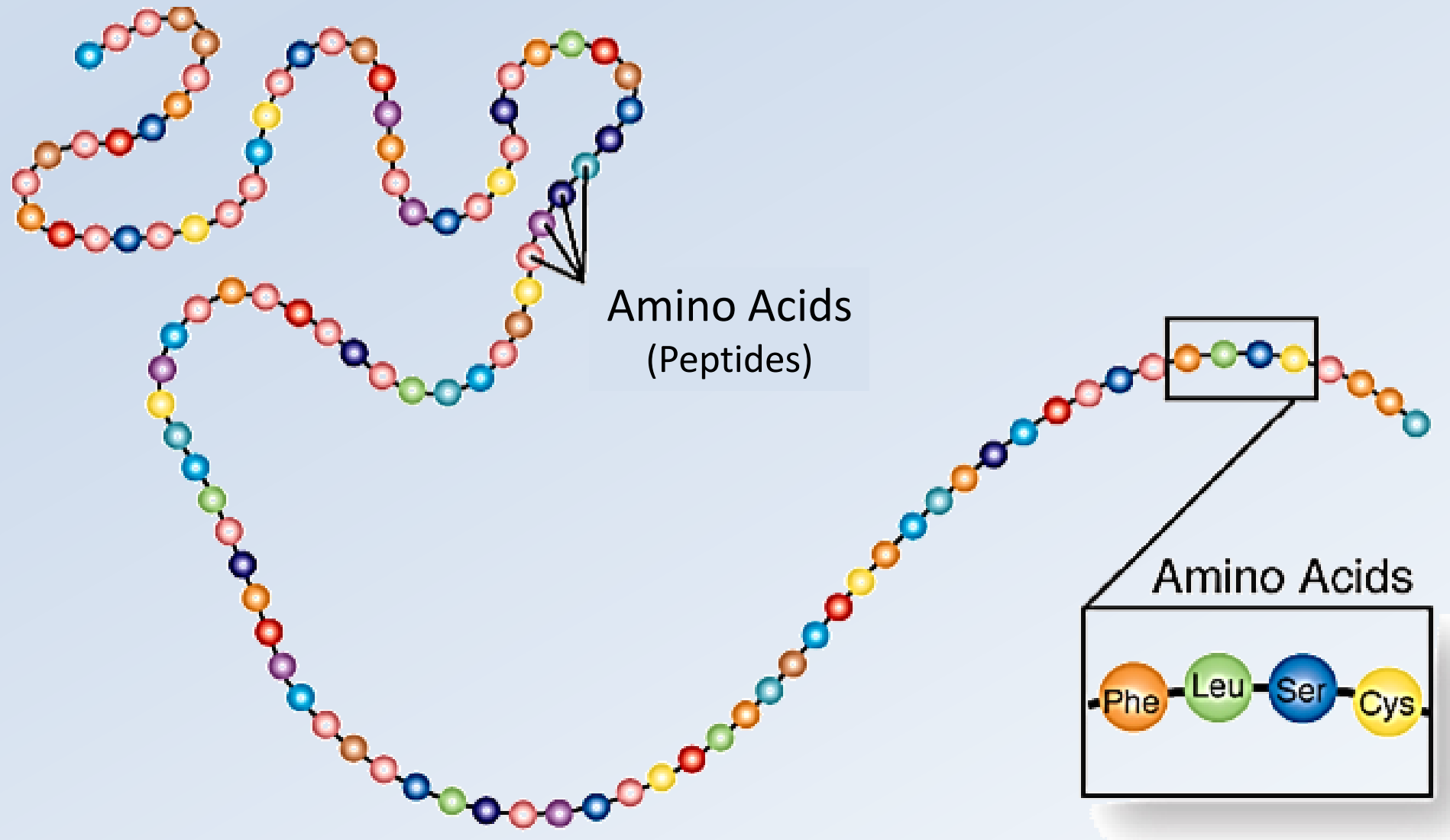
<span style="background-color: yellow; border: 1px solid black; display: inline-block; width: 15px; height: 15px;"></span> Non-polar	<span style="background-color: red; border: 1px solid black; display: inline-block; width: 15px; height: 15px;"></span> Acidic
<span style="background-color: green; border: 1px solid black; display: inline-block; width: 15px; height: 15px;"></span> Polar	<span style="background-color: blue; border: 1px solid black; display: inline-block; width: 15px; height: 15px;"></span> Basic





<b>G</b>	Glycine	Gly	<b>P</b>	Proline	Pro
<b>A</b>	Alanine	Ala	<b>V</b>	Valine	Val
<b>L</b>	Leucine	Leu	<b>I</b>	Isoleucine	Ile
<b>M</b>	Methionine	Met	<b>C</b>	Cysteine	Cys
<b>F</b>	Phenylalanine	Phe	<b>Y</b>	Tyrosine	Tyr
<b>W</b>	Tryptophan	Trp	<b>H</b>	Histidine	His
<b>K</b>	Lysine	Lys	<b>R</b>	Arginine	Arg
<b>Q</b>	Glutamine	Gln	<b>N</b>	Asparagine	Asn
<b>E</b>	Glutamic Acid	Glu	<b>D</b>	Aspartic Acid	Asp
<b>S</b>	Serine	Ser	<b>T</b>	Threonine	Thr

# Proteins: Long Chains of Amino Acids



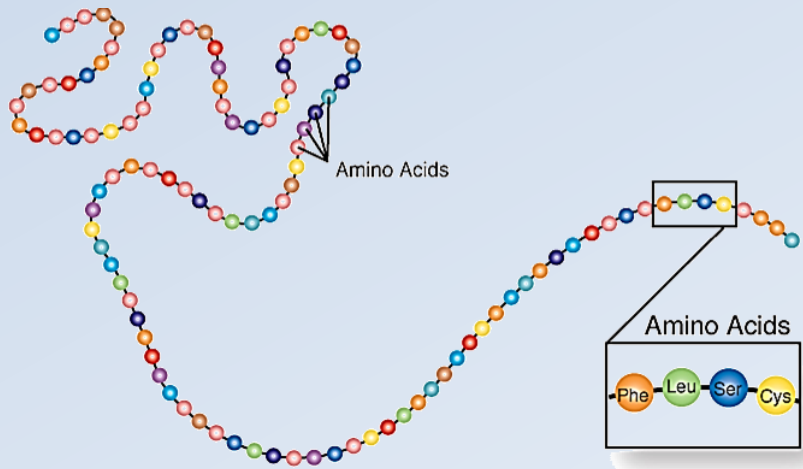
# Proteins: Long Chains of Amino Acids but not just *any* sequence...



BQPXUE NWMS AUOY GDV LAXTCP ZIQK OQFPWMZ...  
UB PEQCZ RMRXWNFAQ YTW GVOZCLE YKABS UZRMD...  
YZPGKF RMQXPGAK NVT IHMUZW LCXR KWWOXMAG...

...

ALL THE WORLDS A STAGE AND ALL THE MEN AND WOMEN...



Nearly all sequences are useless, but occasionally there is one that folds into a semi-functional form. This can then be improved upon.



Example:

A very small mini-protein  
( 20 peptides )

“ Trp-Cage ”

NLYIQWLKDG GPSSGRPPPS

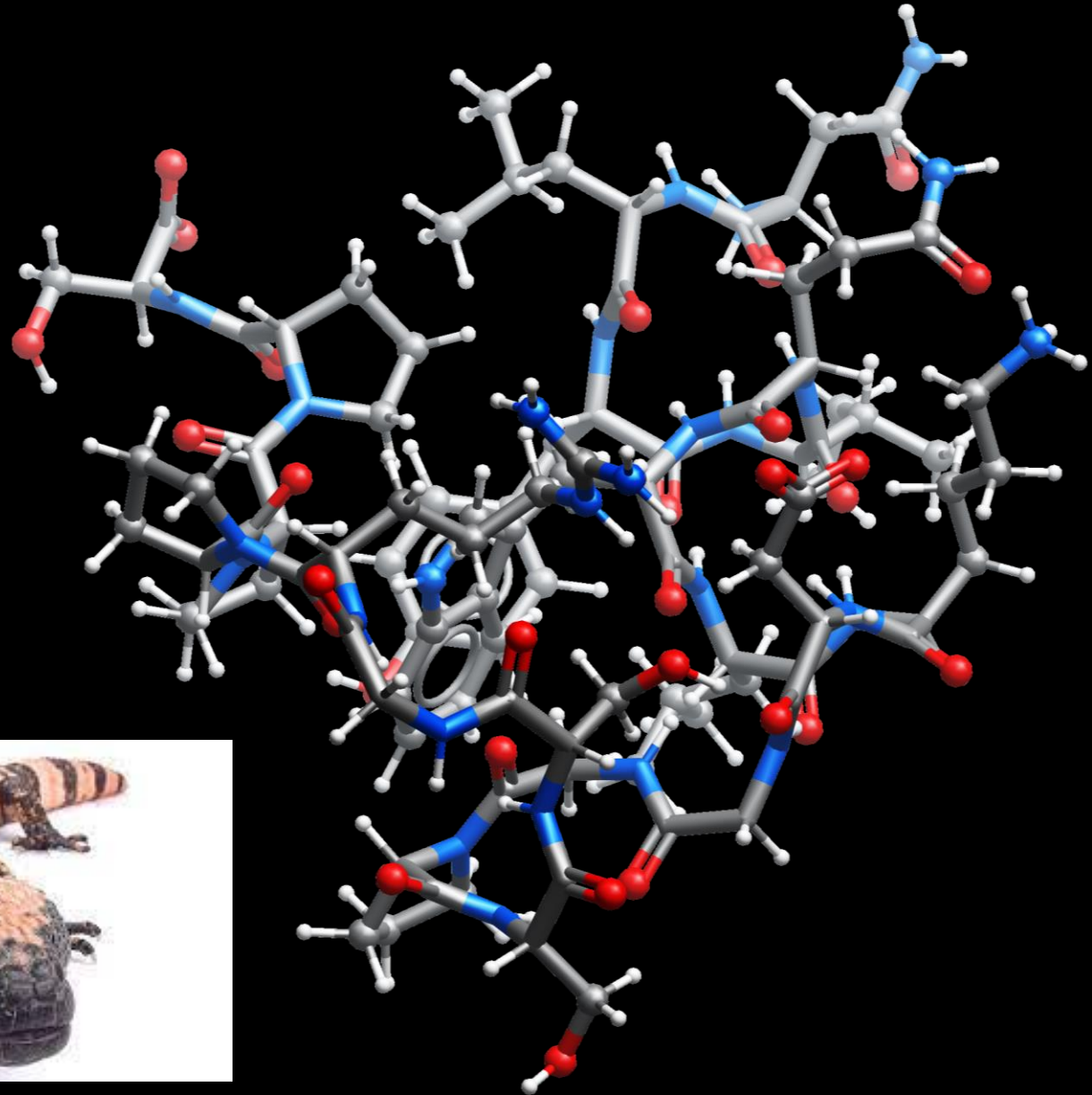
Asparagine

Glycine

Serine

A synthetic polypeptide –  
perhaps the smallest  
stable protein

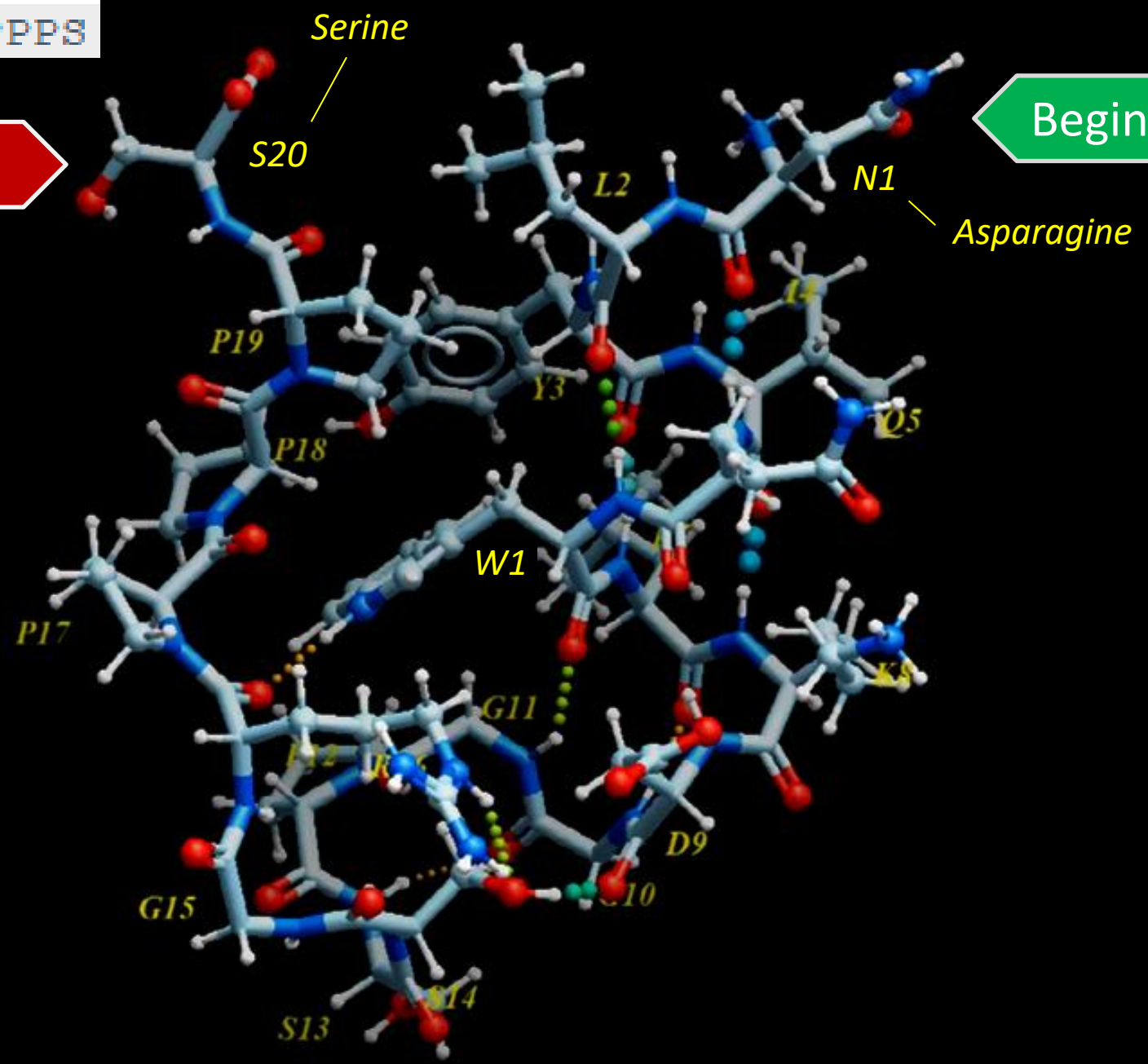
Folds in under one  
microsecond



NLYIQWLKDG GPSSGRPPPS

End

Begin



Colored by  
Amino Acid  
Type

Trp-Cage





# Trp-Cage

Ball & Stick  
representation

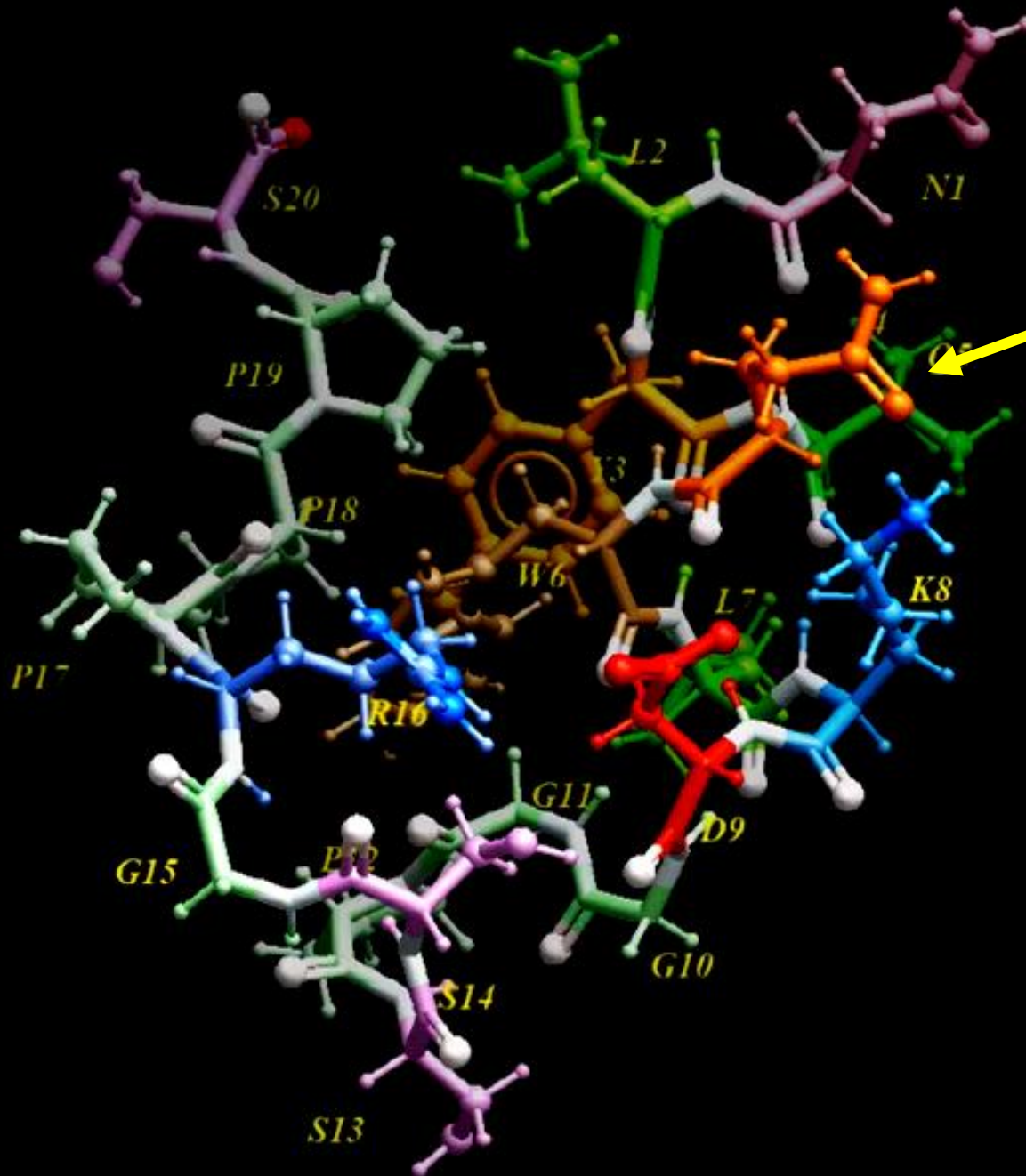
Wire  
representation

Electron Clouds

Space Filling  
representation

Envelope

**Ribbon**  
representation



Alpha-Helix  
Motif

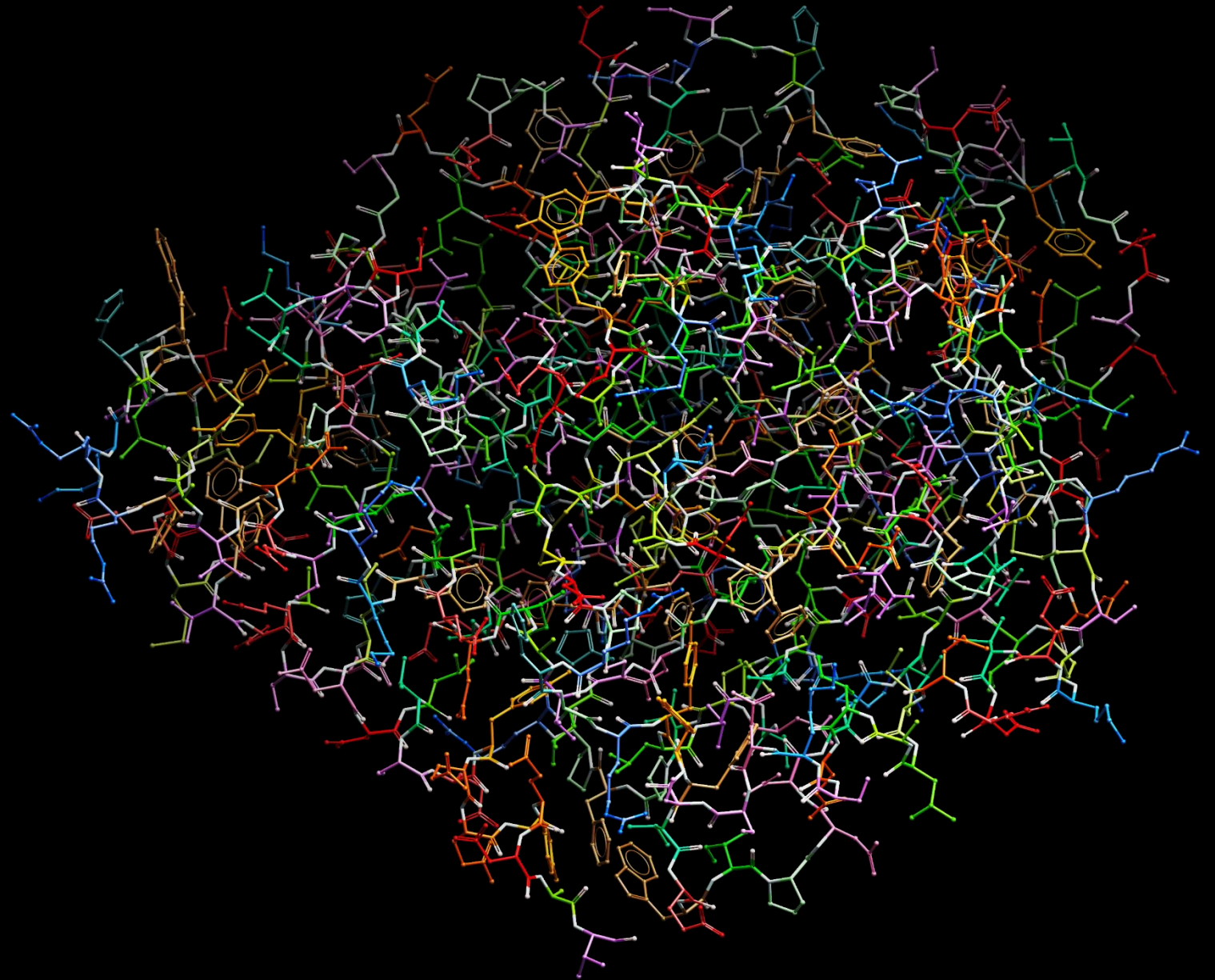
Movie showing  
various protein  
representations



# Human Tubulin-B

429 Amino Acids

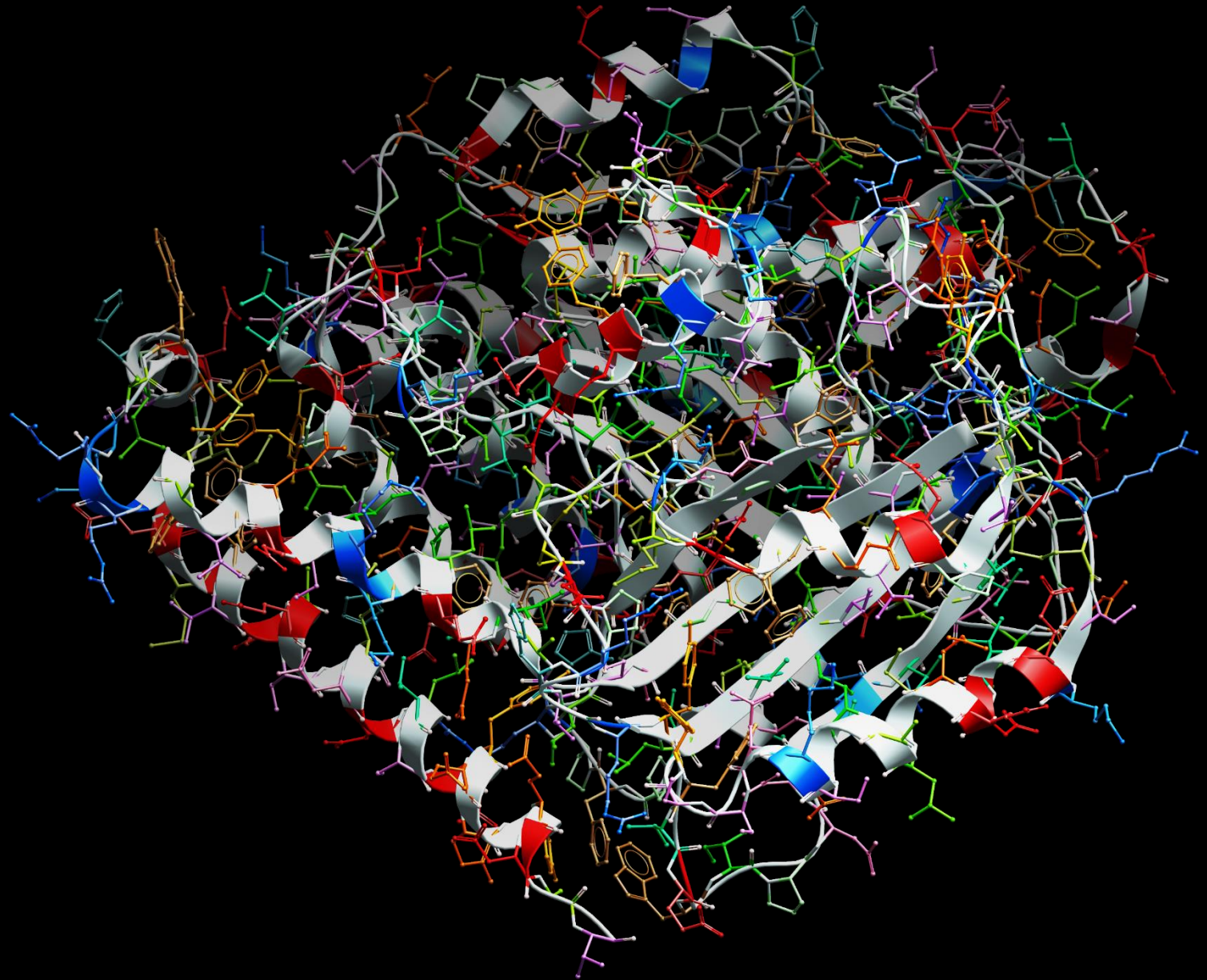
<u>MREIVHIOAG</u>	<u>OCGNOIGAKF</u>	<u>WEVISDEHGI</u>
<u>DPSGNYVGDS</u>	<u>DLQLERISVY</u>	<u>YNEASSHKYV</u>
<u>PRAILVDLEP</u>	<u>GTMDSVRSGA</u>	<u>FGHLFRPDNF</u>
<u>IFGQSGAGNN</u>	<u>WAKGHYTEGA</u>	<u>ELVDSVLDVV</u>
<u>RKECENCDCI</u>	<u>OGFQLTHSLG</u>	<u>GGTGSGMGTL</u>
<u>LISKVREEYP</u>	<u>DRIMNTFSVV</u>	<u>PSPKVSDTVV</u>
<u>EPYNATLSIH</u>	<u>QLVENTDETY</u>	<u>CIDNEALYDI</u>
<u>CFRTLKLATP</u>	<u>TYGDLNHLVS</u>	<u>ATMSGVTDSL</u>
<u>RFPGQLNADL</u>	<u>RKLAVNMVPP</u>	<u>PRLHFFMPGF</u>
<u>APLTARGSQQ</u>	<u>YRALTVPELT</u>	<u>QQMFDKNNM</u>
<u>AACDPRHGRY</u>	<u>LTVATVFRGR</u>	<u>MSMKEVDEQM</u>
<u>LAIQSKNSSY</u>	<u>FVEWIPNNVK</u>	<u>VAVCDIPPRG</u>
<u>LKMSSTFIGN</u>	<u>STAIQELFKR</u>	<u>ISEQFTAMFR</u>
<u>RKAFLHWYTG</u>	<u>EGMDEMEFTE</u>	<u>AESNMNDLVS</u>
<u>EYQQYQDAT</u>		



# Human Tubulin-B

429 Amino Acids

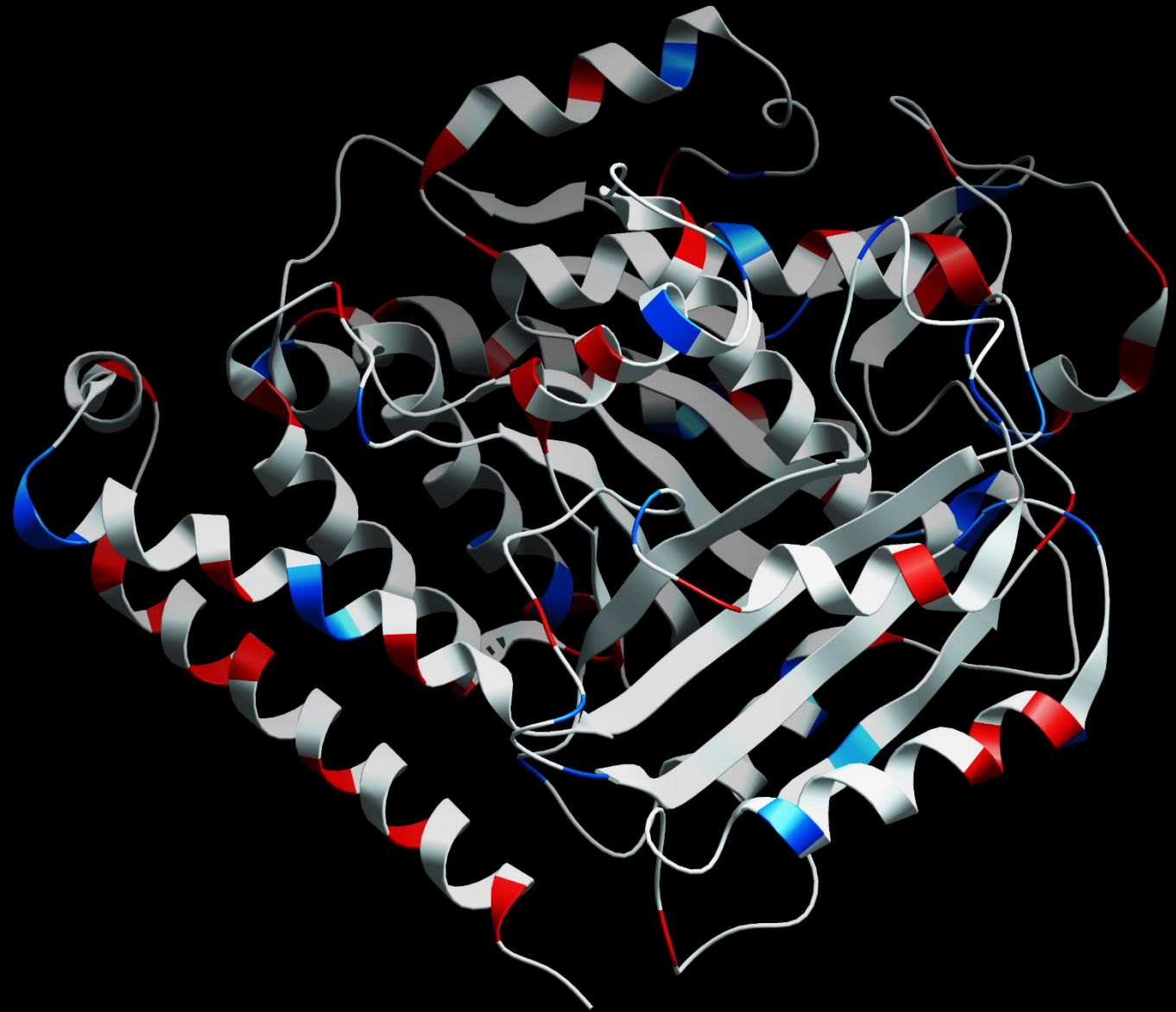
Ribbon  
Representation  
with Alpha-Helices  
and Beta Sheets



# Human Tubulin-B

429 Amino Acids

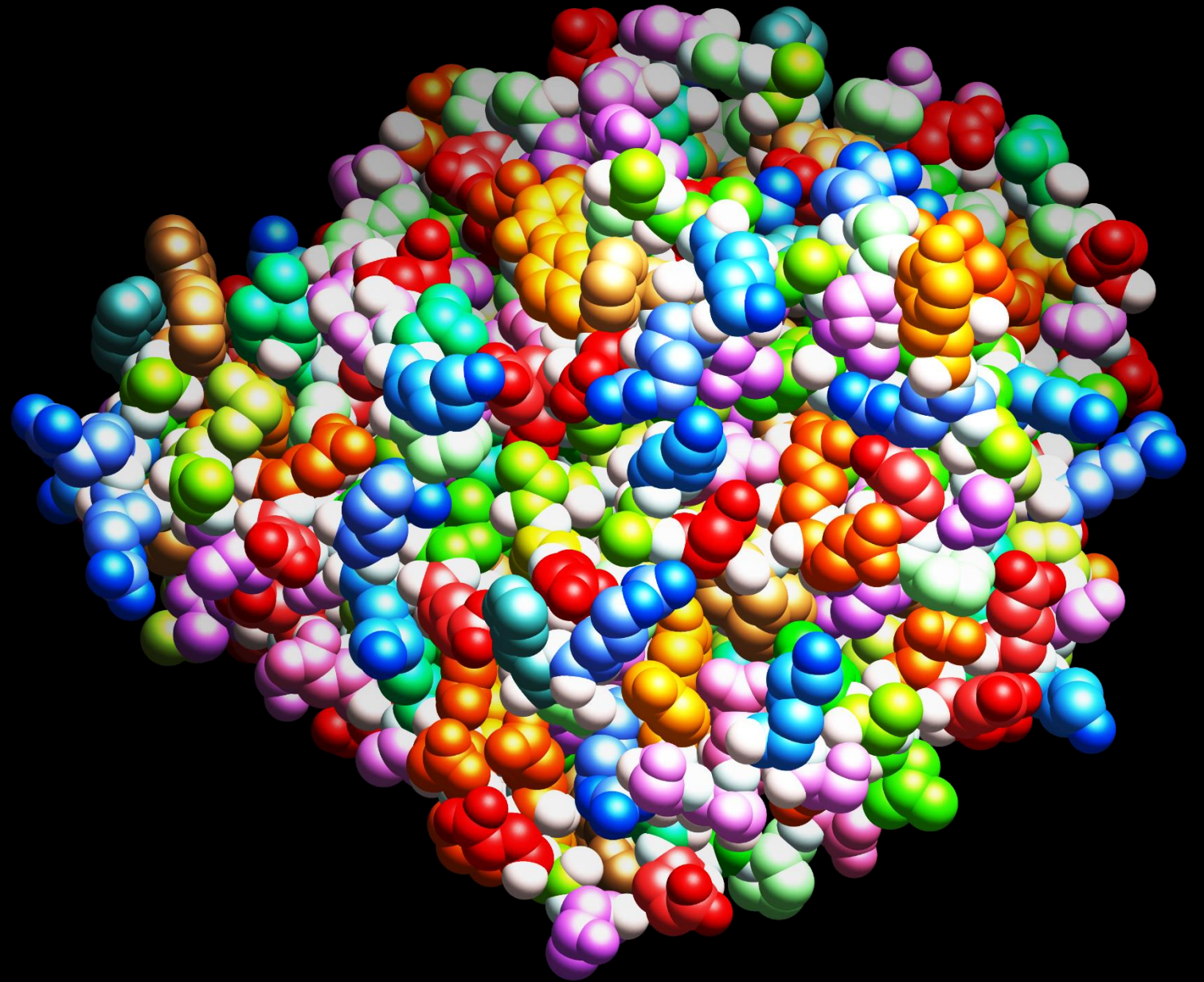
Ribbon  
Representation  
with Alpha-Helices  
and Beta Sheets



# Human Tubulin-B

429 Amino Acids

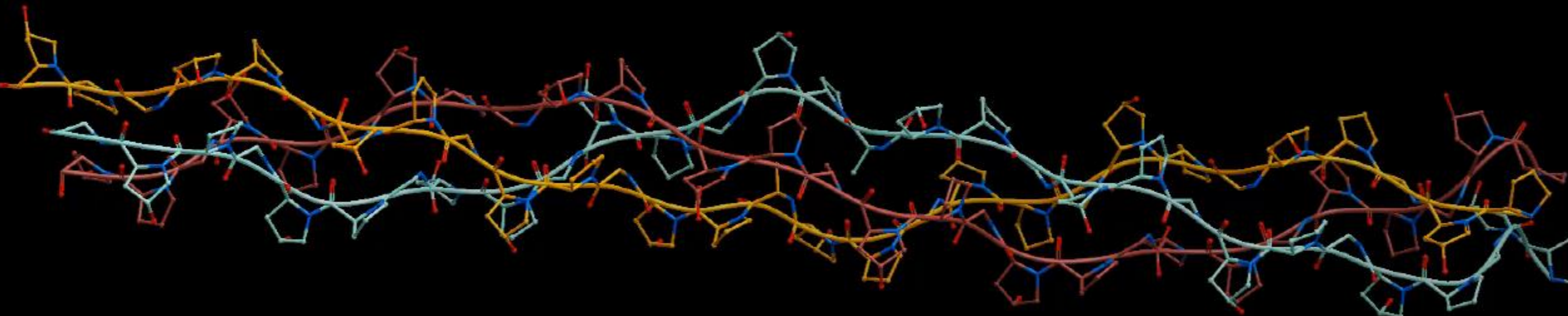
Space filling  
Representation



# Collagen Protein: The Connective Fibers that hold your body together

25%-30% of  
the proteins  
in your body

3 separate polypeptides  
twisted together



← 9 Amino Acids (of 1400) →

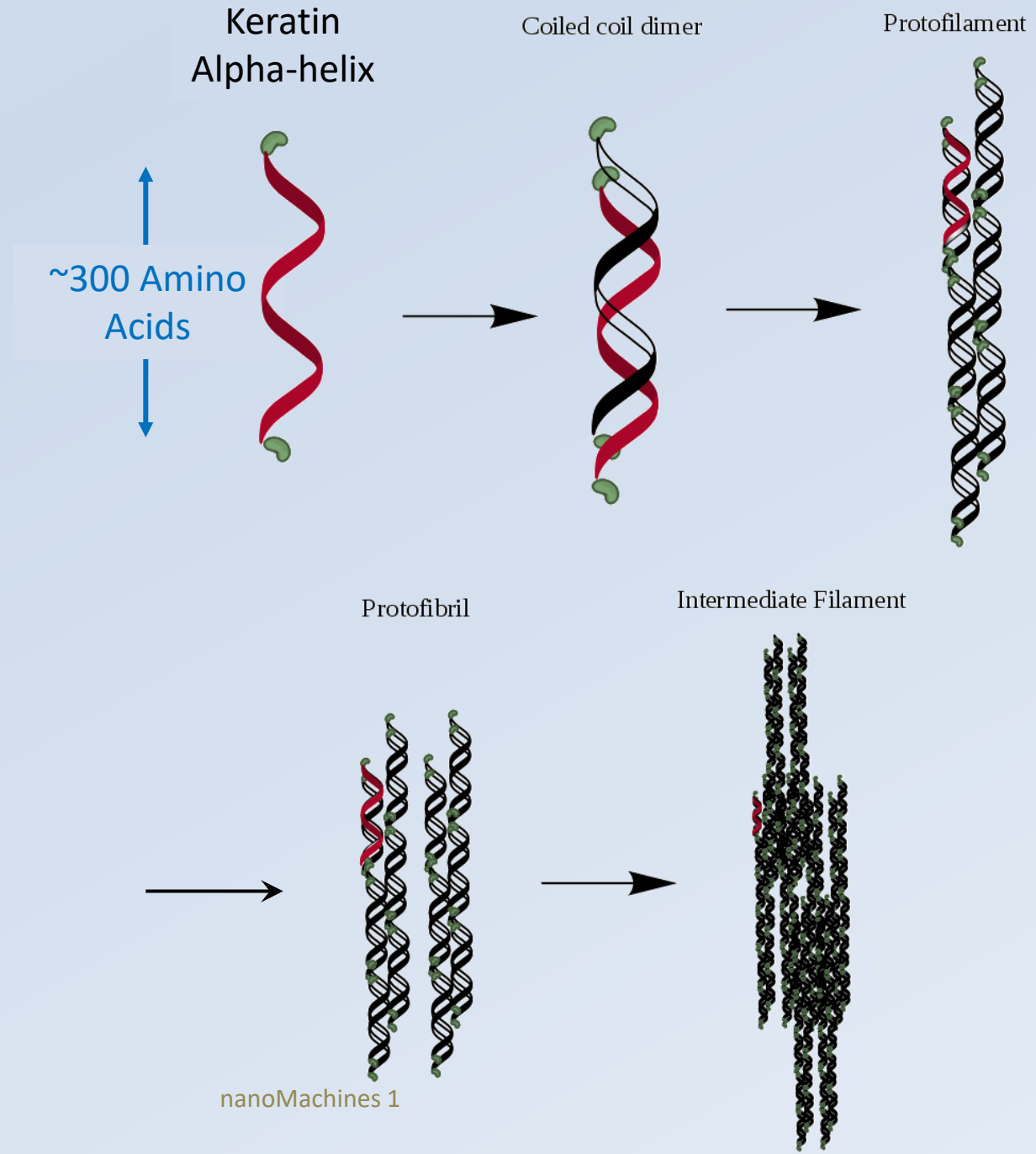


# Keratin:

Building material for hair, skin, nails.

Also interior structure of many cells.

(over 50 types in humans)



# Visualizing Proteins

- International public protein database:
  - PDB (Protein Data Bank)
  - Over 100,000 entries
  - Each protein structure deposited has a code, such as “7sj8”
- Visualize it using free software, such as
  - ICM-Browser ([www.Molsoft.com](http://www.Molsoft.com))

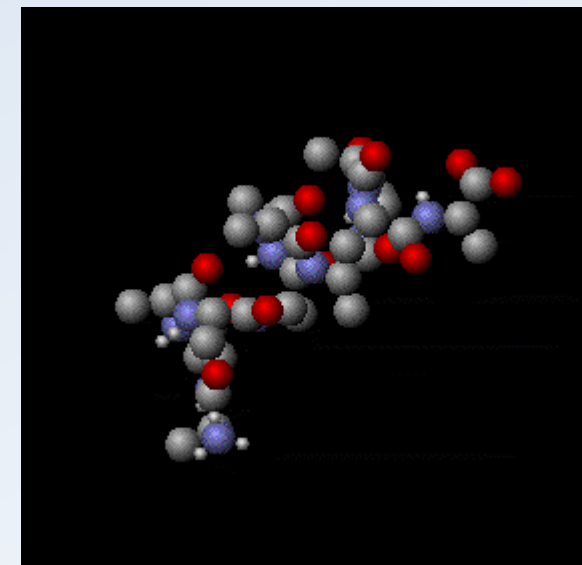
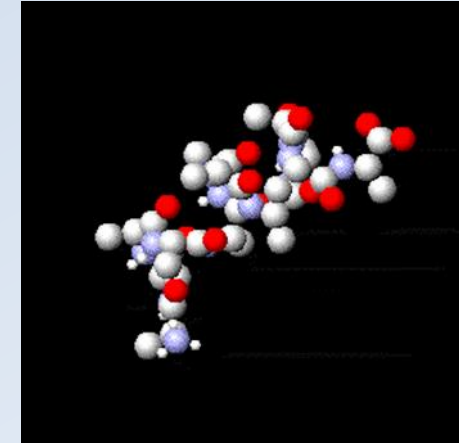




# Protein Questions?

# In Cells, There is Constant Motion at the Atomic Scale

- Most of our molecular pictures will be static
- But remember that the reality is relentless activity
  - Small molecules move and wiggle faster
  - Large molecules drift more slowly
    - parts of large molecules wiggle rapidly
- This is thermal motion
  - Warmer is faster



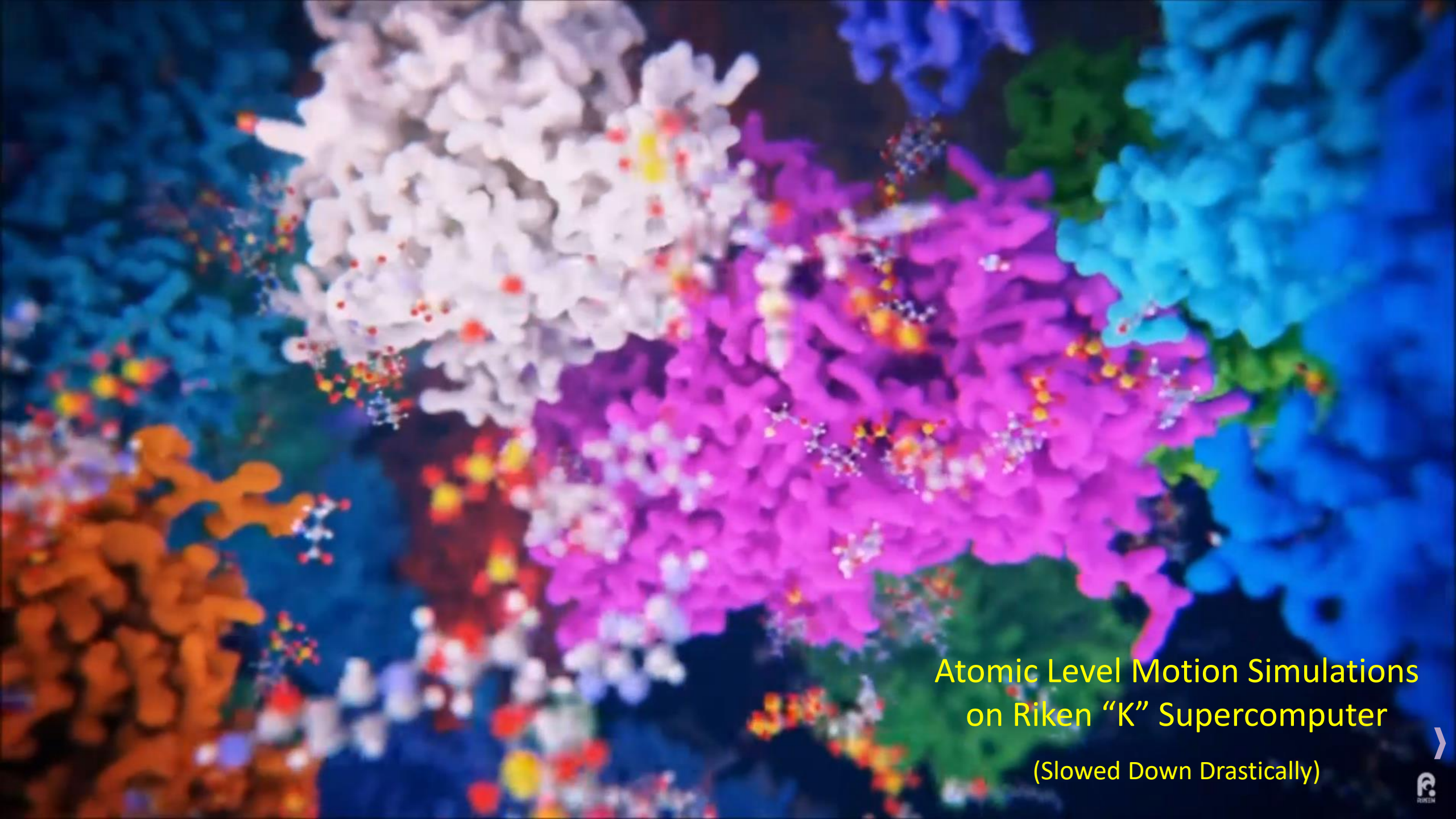
# BROWNIAN MOTION

My Book of Chemistry:  
Brownian Motion

the random movement displayed  
by microscopic particles suspended  
in fluids

National STEM Learning Centre  
and  
Institute of Physics (UK)  
2017





Atomic Level Motion Simulations  
on Riken "K" Supercomputer  
(Slowed Down Drastically)



Priority Issue on Post-K computer  
Innovative Drug Discovery Infrastructure through Functional Control of Biomolecular Systems



Japan

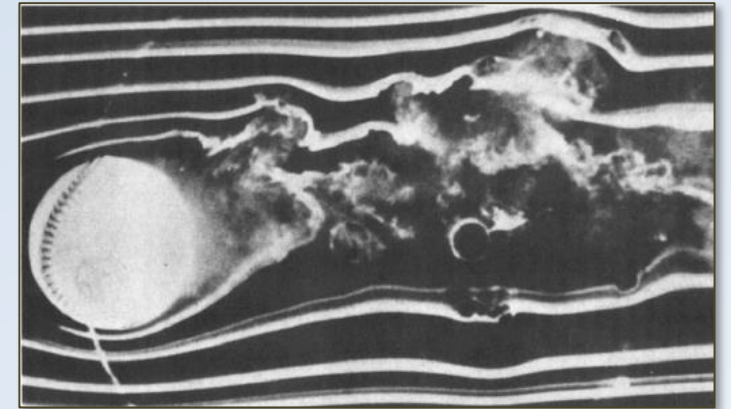


# Laminar vs Turbulent Flow Regimes

Small, Slow, Viscous  
> *Laminar*



Big, Fast, Low Viscosity  
> *Turbulent*



# Laminar vs Turbulent Flow Regimes

$$\text{Reynolds Number} \cong \frac{\text{Size} \times \text{Speed}}{\text{Viscosity}}$$

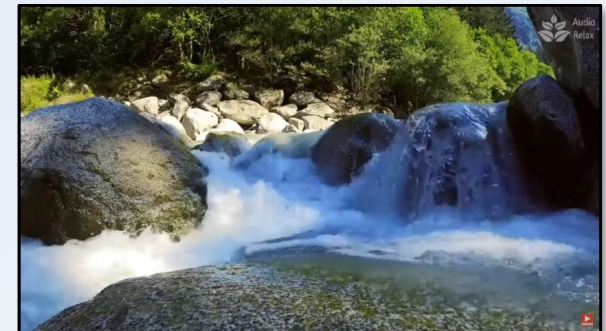
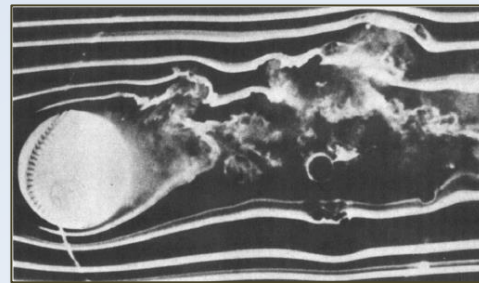
Rey #  $\ll$  2000

Small, Slow, Viscous  
> *Laminar*



Rey #  $\gg$  2000

Big, Fast, Low Viscosity  
> *Turbulent*





# Laminar vs Turbulent Flow Regimes

## Life at low Reynolds number

E. M. Purcell

Lyman Laboratory, Harvard University, Cambridge, Massachusetts 02138

(Received 12 June 1976)

Am. J. Phys., Vol. 45, No. 1, January 1977

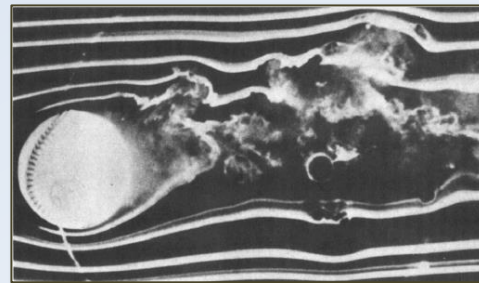
Rey #  $\ll$  2000

Small, Slow, Viscous  
> *Laminar*



Rey #  $\gg$  2000

Big, Fast, Low Viscosity  
> *Turbulent*



# Laminar vs Turbulent Flow Regimes

## Life at low Reynolds number

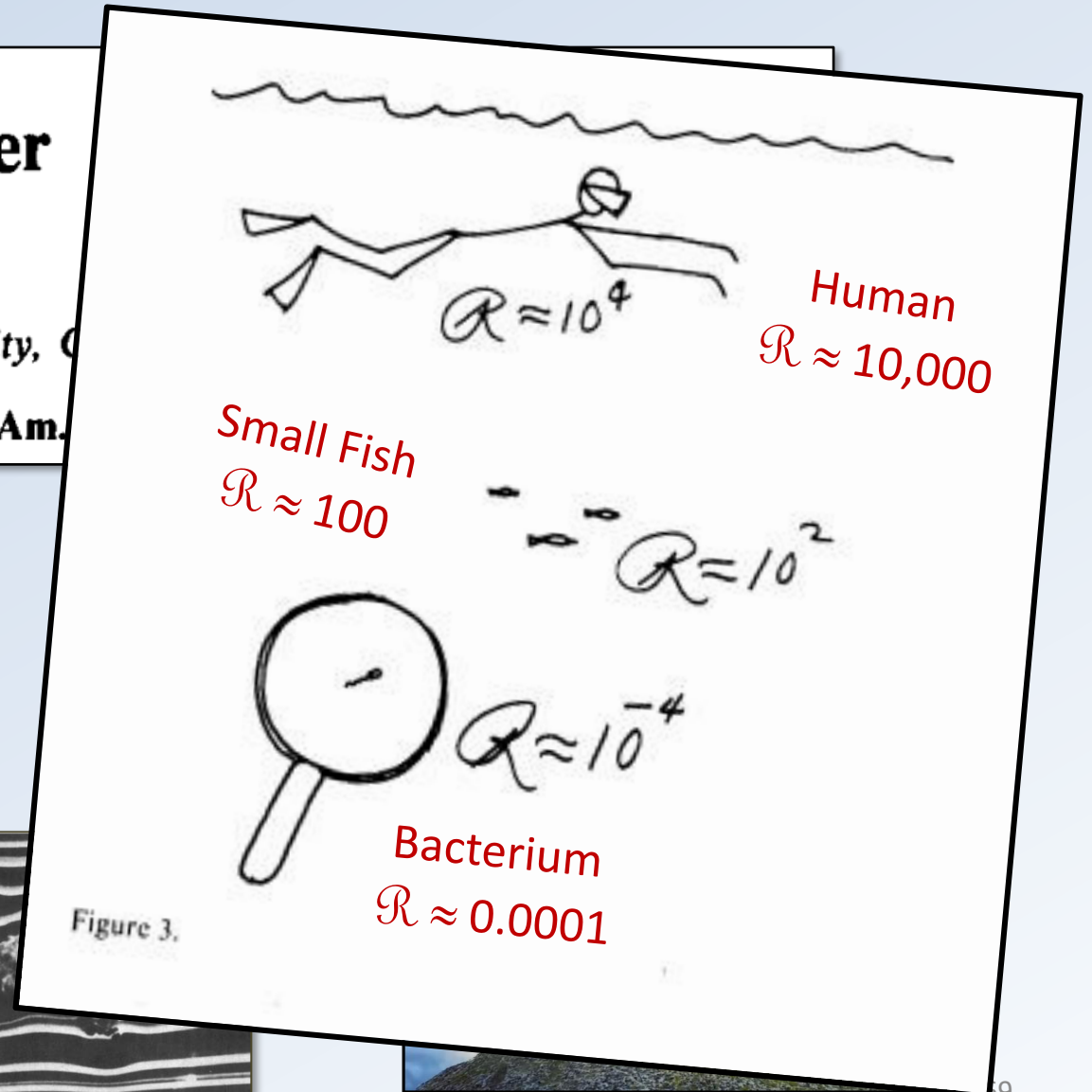
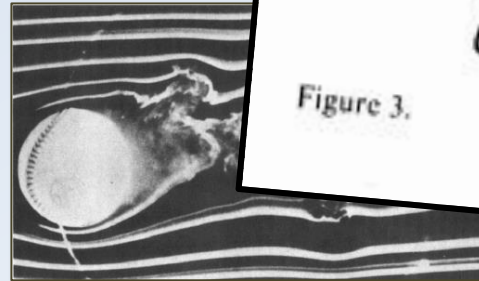
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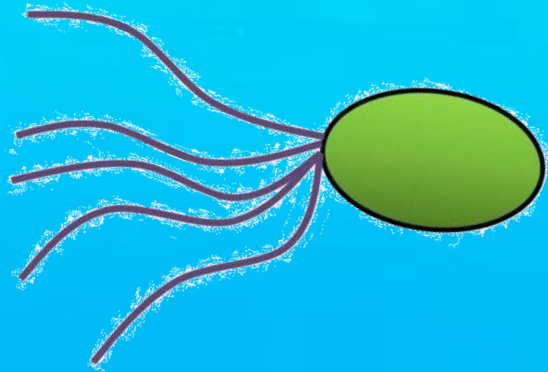
Rey #  $\ll 2000$

Small, Slow, Viscous  
> Laminar



# “Bacterium” in Water Demo

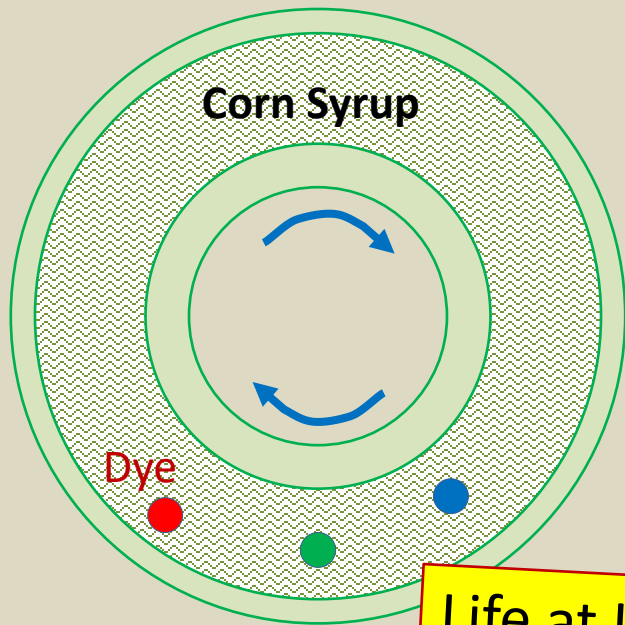
## Low Reynolds Number



# Laminar Flow Demonstration

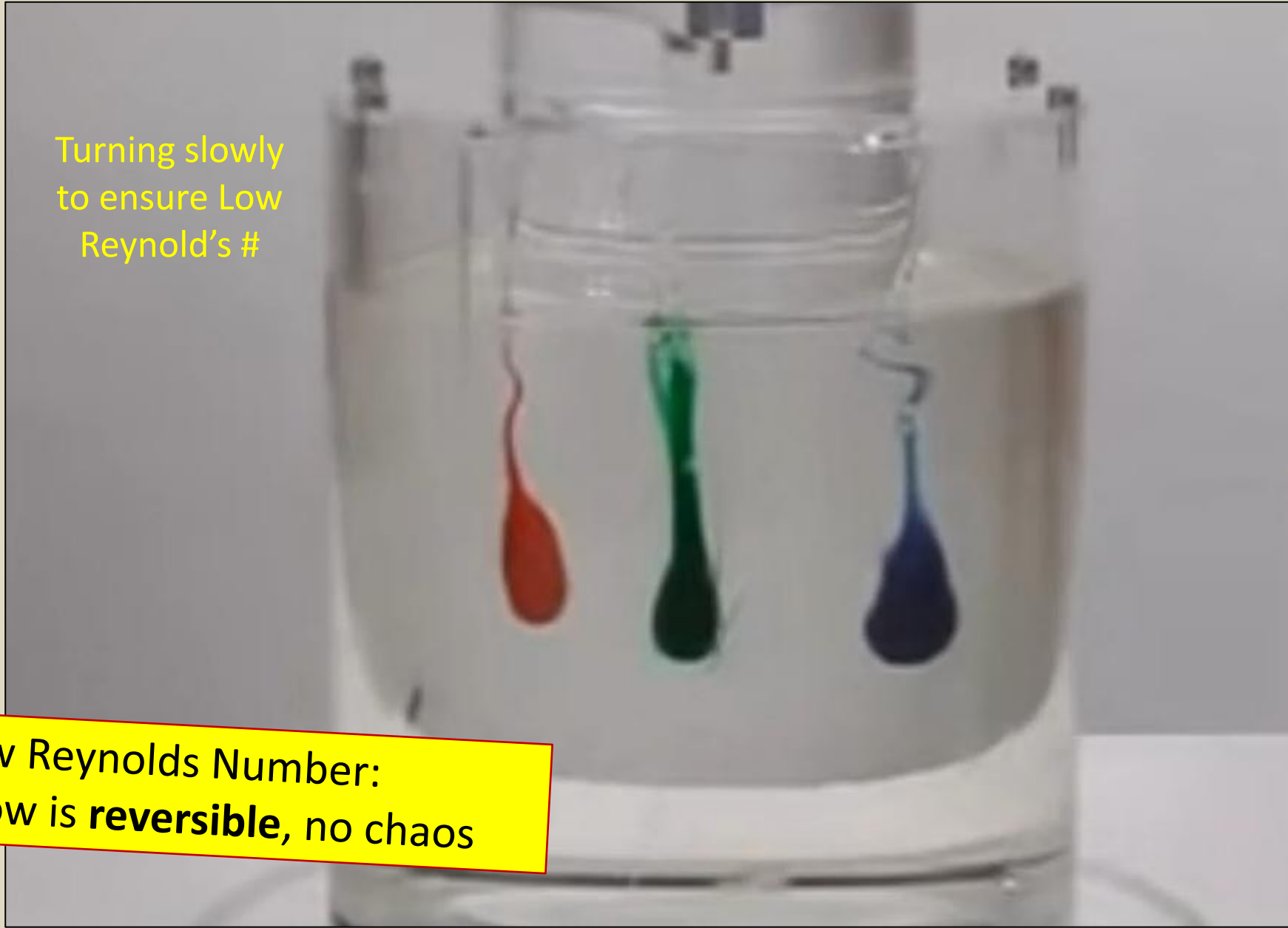
*U of New Mexico Physics*  
John DeMoss & Keven Cahill

*Low Reynolds Number*



Life at Low Reynolds Number:  
Fluid flow is **reversible**, no chaos

Turning slowly  
to ensure Low  
Reynold's #



*On the one hand:*

Relentless random  
thermal and  
Brownian motion  
of particles

Small molecules  
diffuse fairly quickly

*On the other hand:*

Extremely sluggish  
directed or forced  
motion  
(Low Reynolds Number)

Absent a steady  
push, things stop



# How Do We Figure Out the 3-D Structures of Biological Macromolecules?



No.

The structures of our nanomachines are much smaller than the wavelength of light.



Ri

Ri

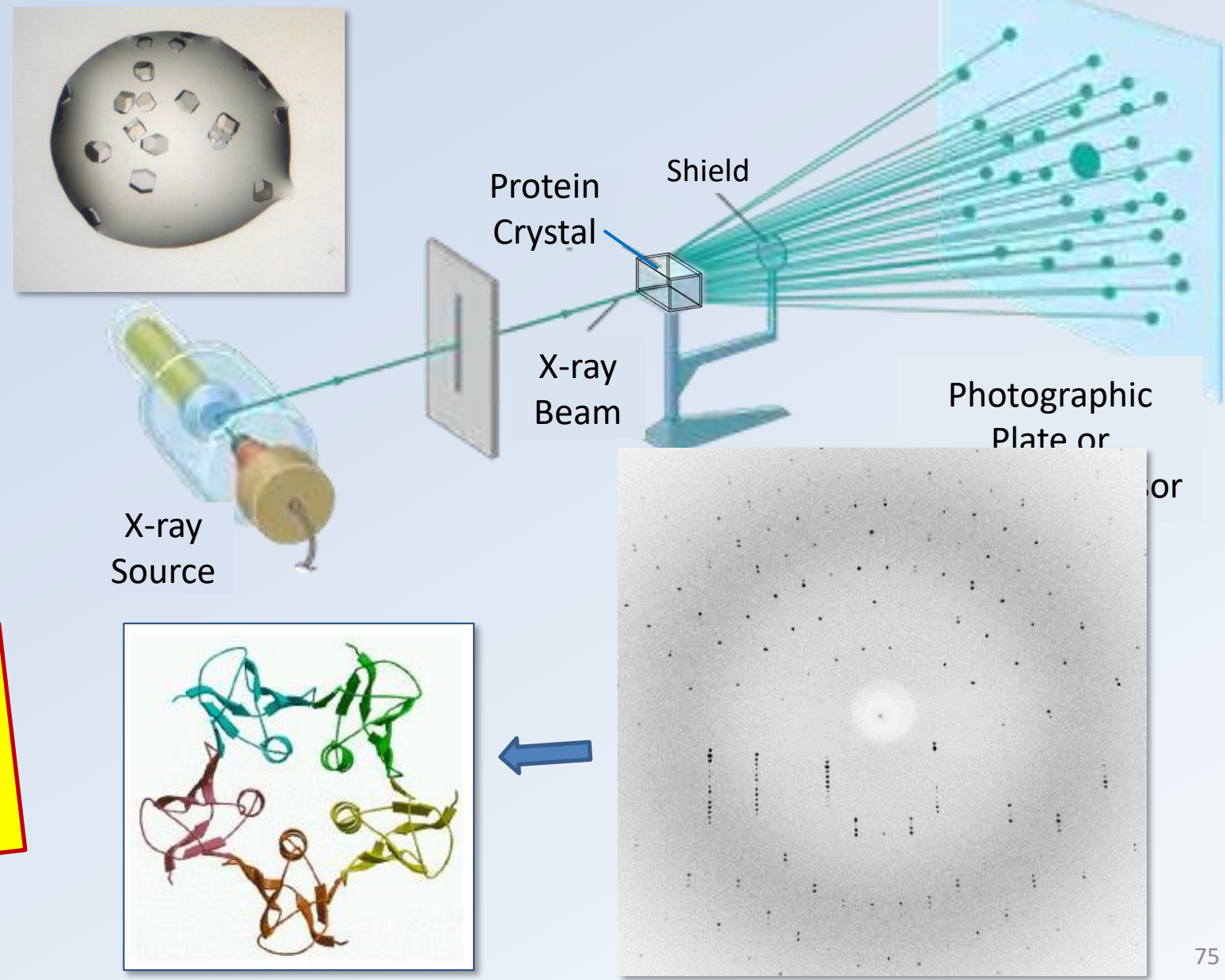
The Royal Institution  
Science Lives Here

Nick Lane on  
Visualizing  
Nanomachines



# Traditional Method: X-ray Crystallography

1. Make a crystal from protein molecules **Hard!**
2. Measure the X-ray Diffraction spot patterns at various crystal angles
3. *Guess the phases*
4. Calculate the 3-D structure via Fourier Transform

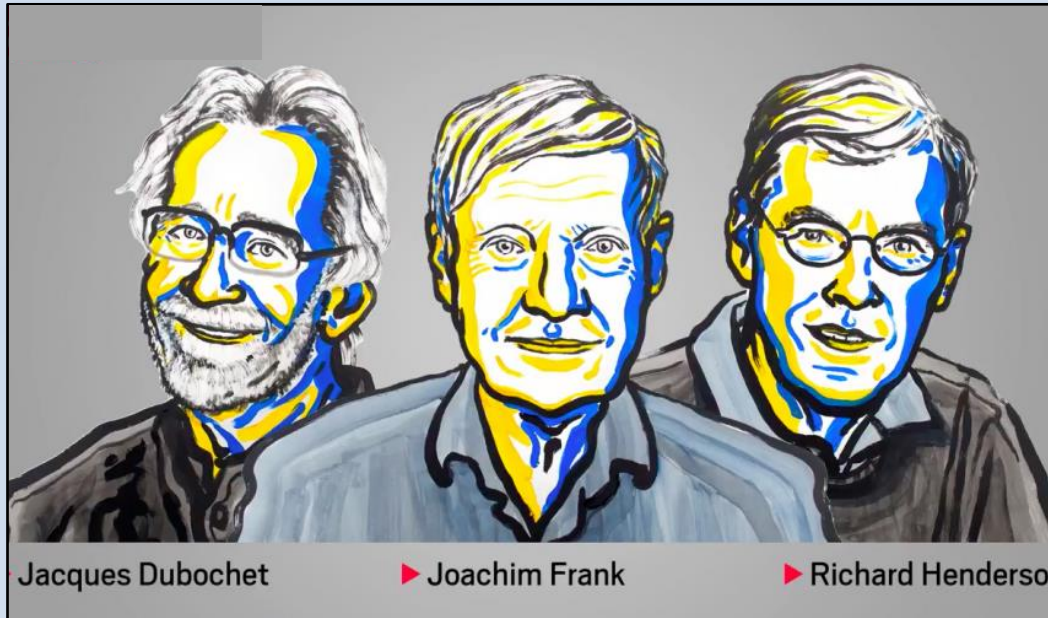


Over 100,000 protein structures solved by X-ray Crystallography!

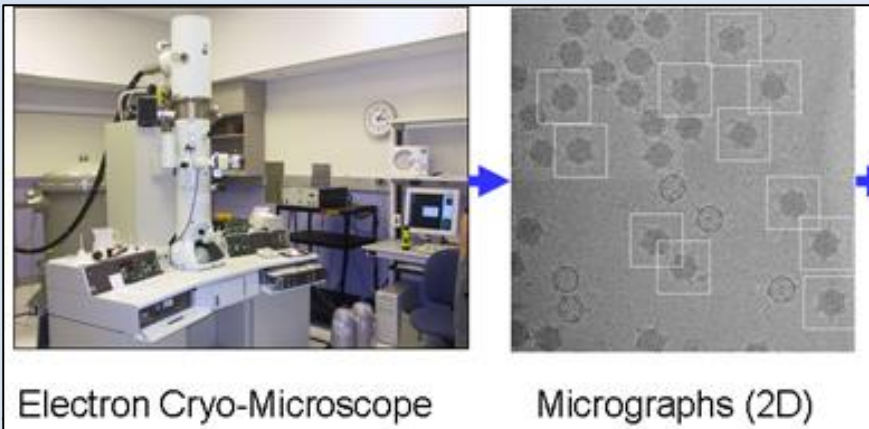


# The New Kid on the Block: Cryo-Electron Microscopy

## 2017 Nobel Prize in Chemistry

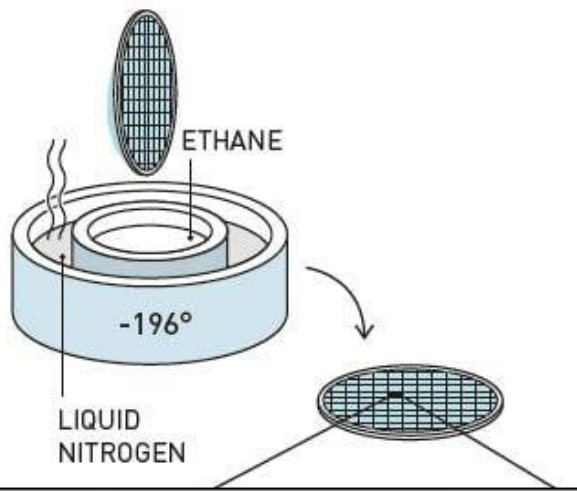
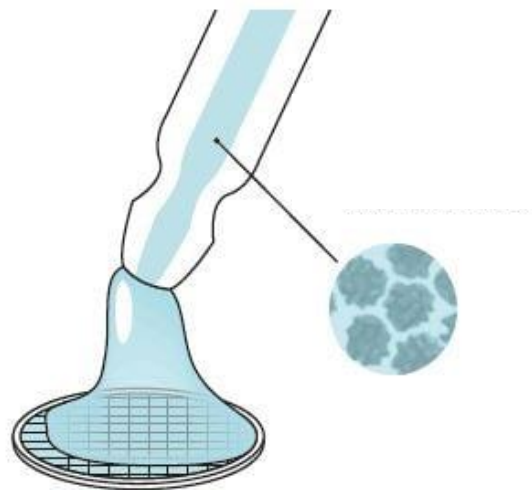


1. Make a thin layer of water containing thousands of randomly oriented protein particles.
2. Rapidly freeze it to immobilize the particles without unfolding.
3. Take thousands of electron microscope 2-D image projections of the randomly oriented particles.
4. Figure out what 3-D structure would produce all these pictures.



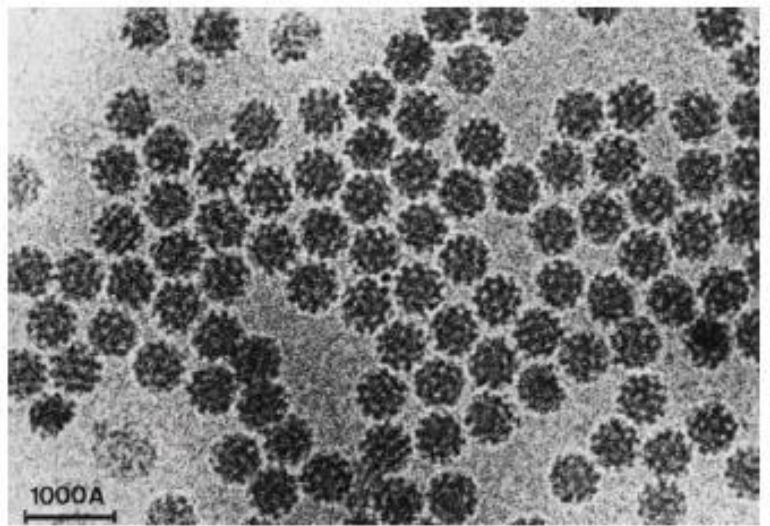
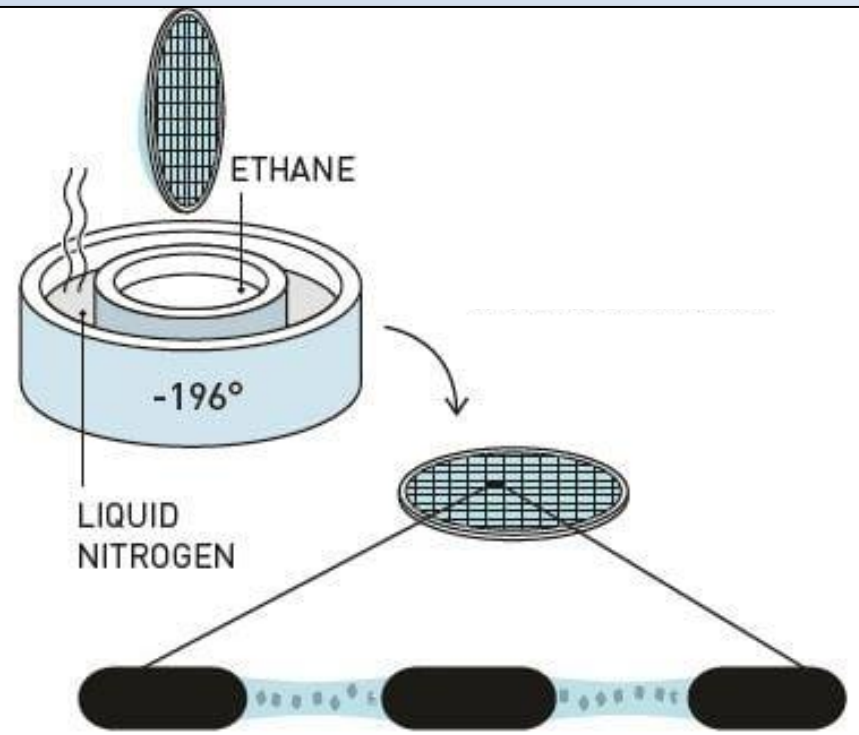
**Crystallization not required!**

# DUBOCHET'S VITRIFICATION METHOD



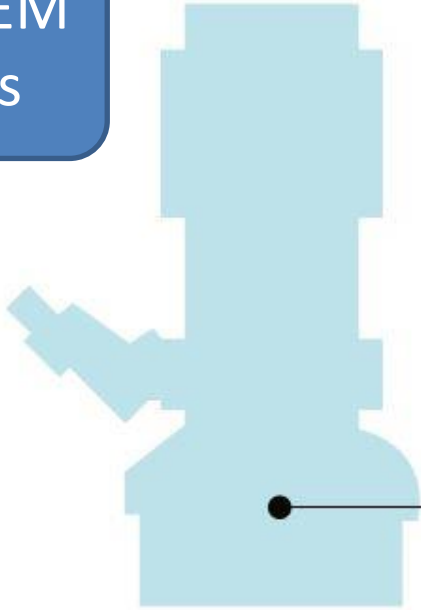
1. Thin Layer on Grid

2. Quick Freeze

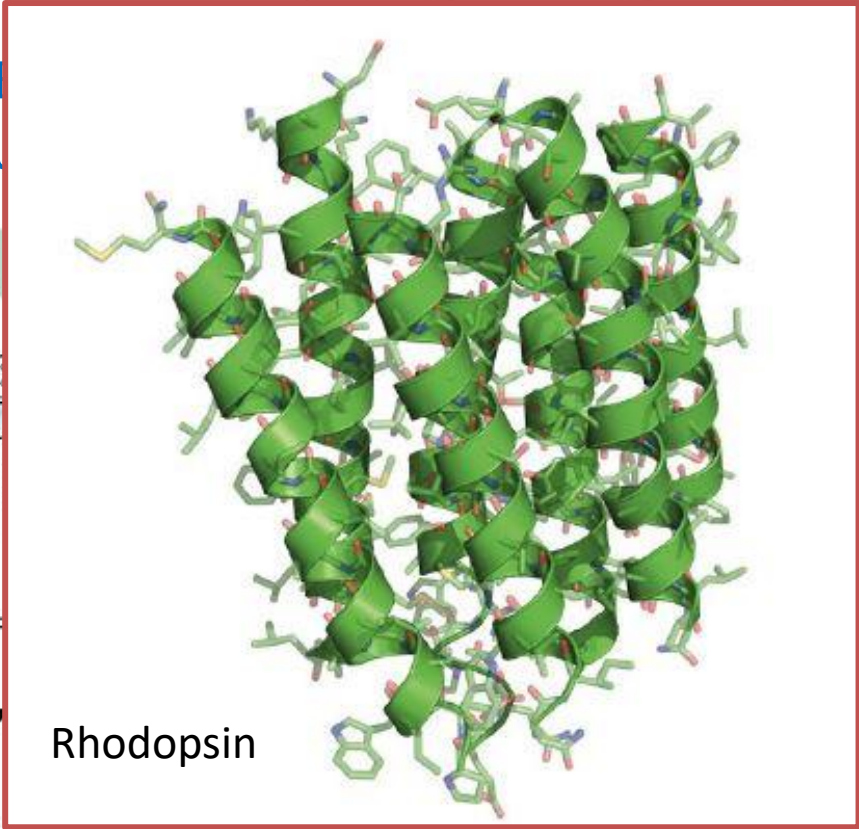
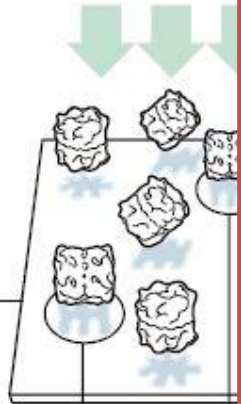


# FRANK'S IMAGE ANALYSIS FOR 3D STRUCTURES

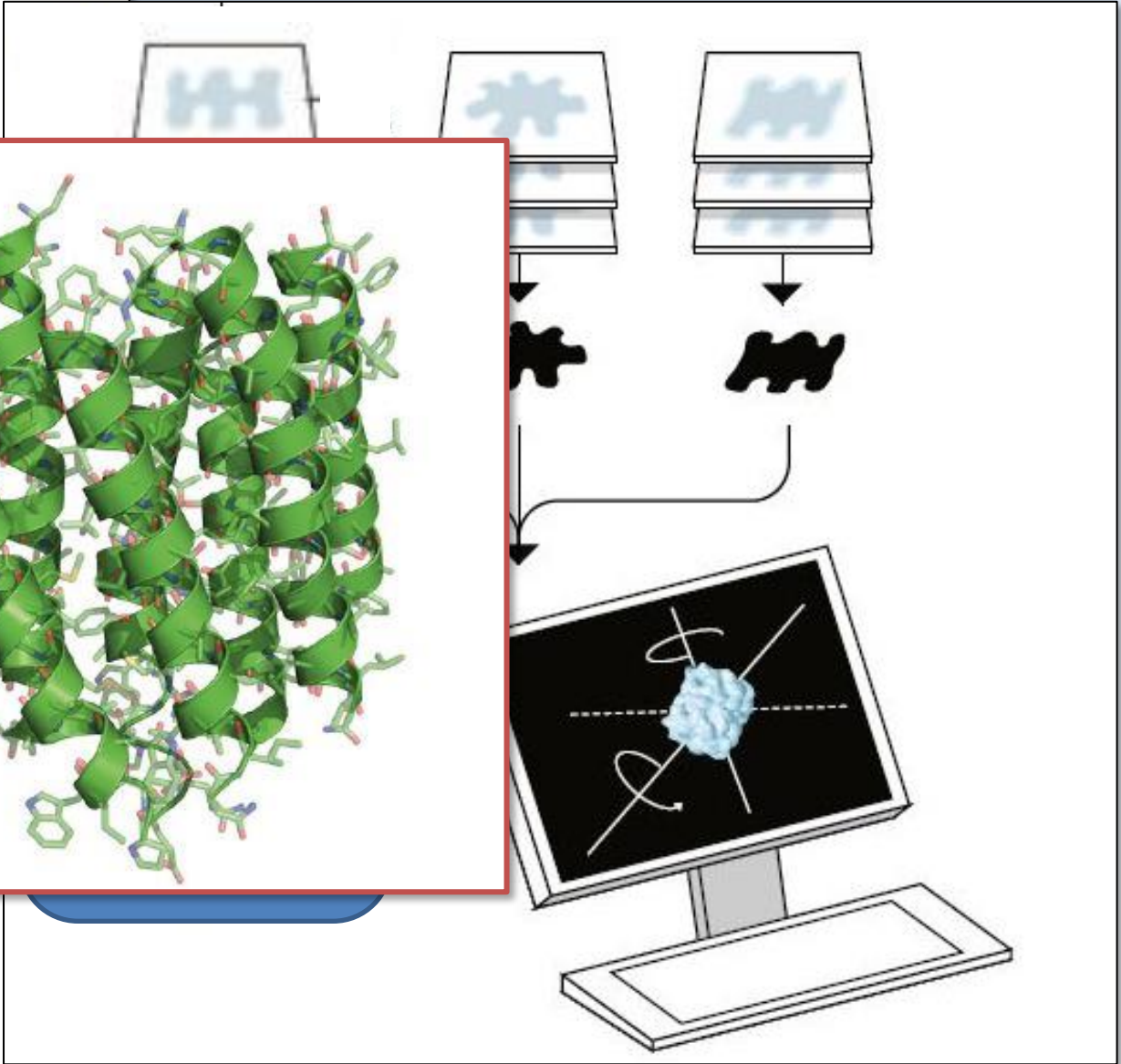
3. Take EM Images



1000's of  
of individu



Group similar  
orientations together



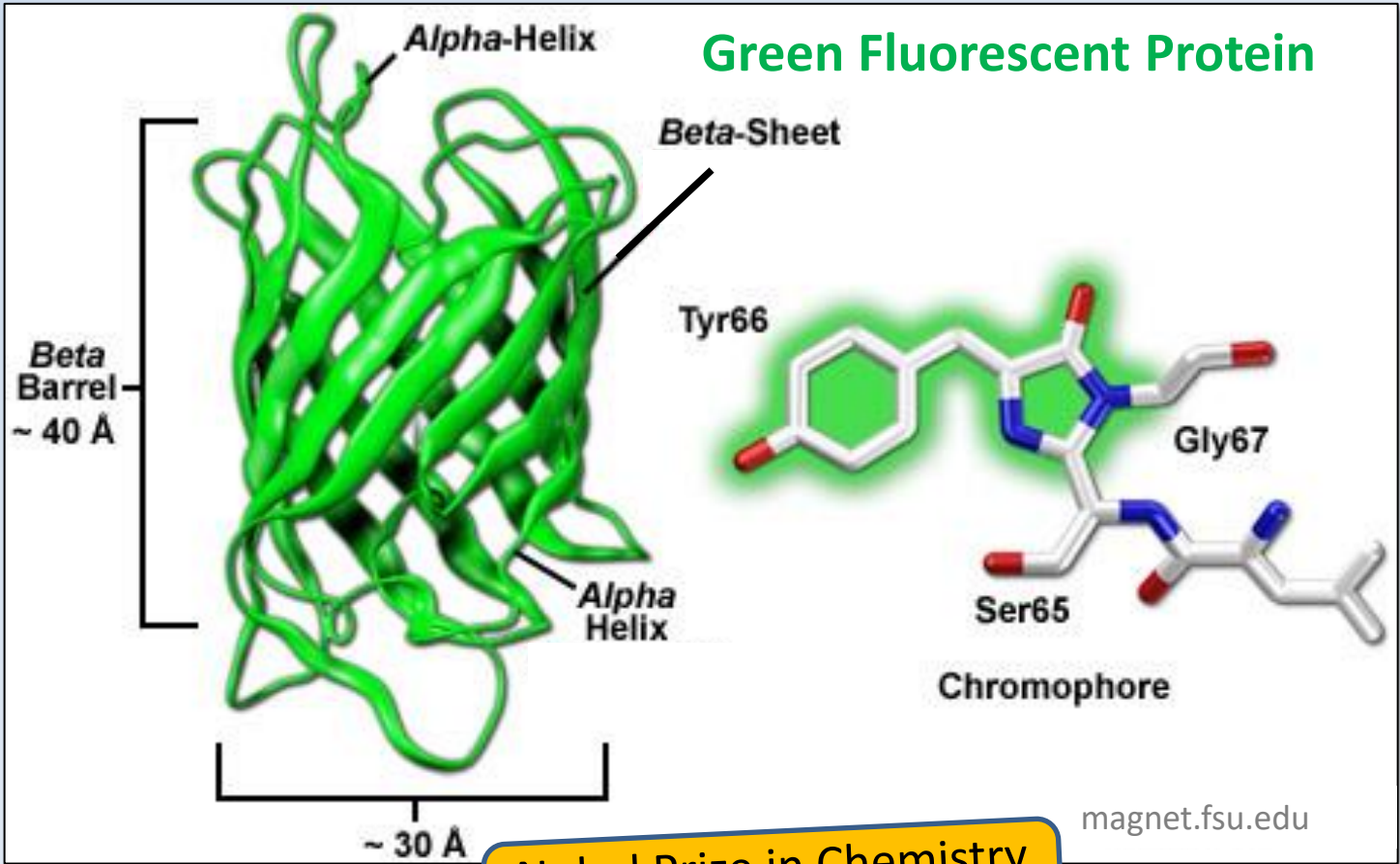
# Visible microscopy has a role – motion detection

Crystal Jellyfish *Aequorea victoria*



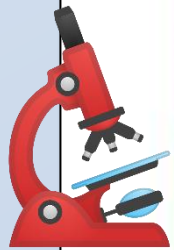
**Bioluminescent**

Wikipedia

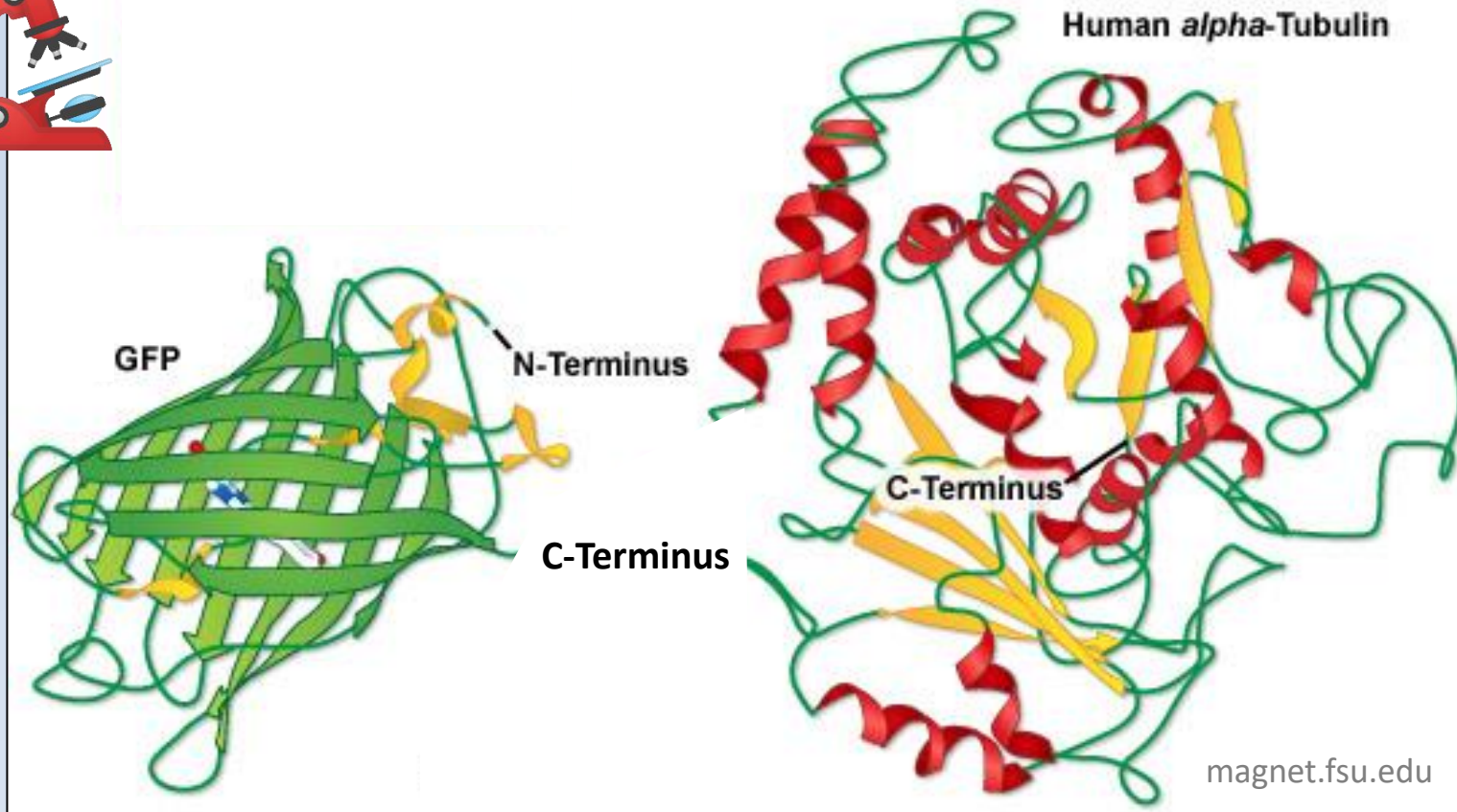


**Nobel Prize in Chemistry  
2008**

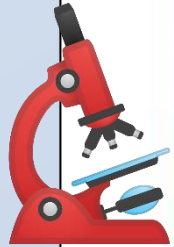
# Visible microscopy has a role – motion detection



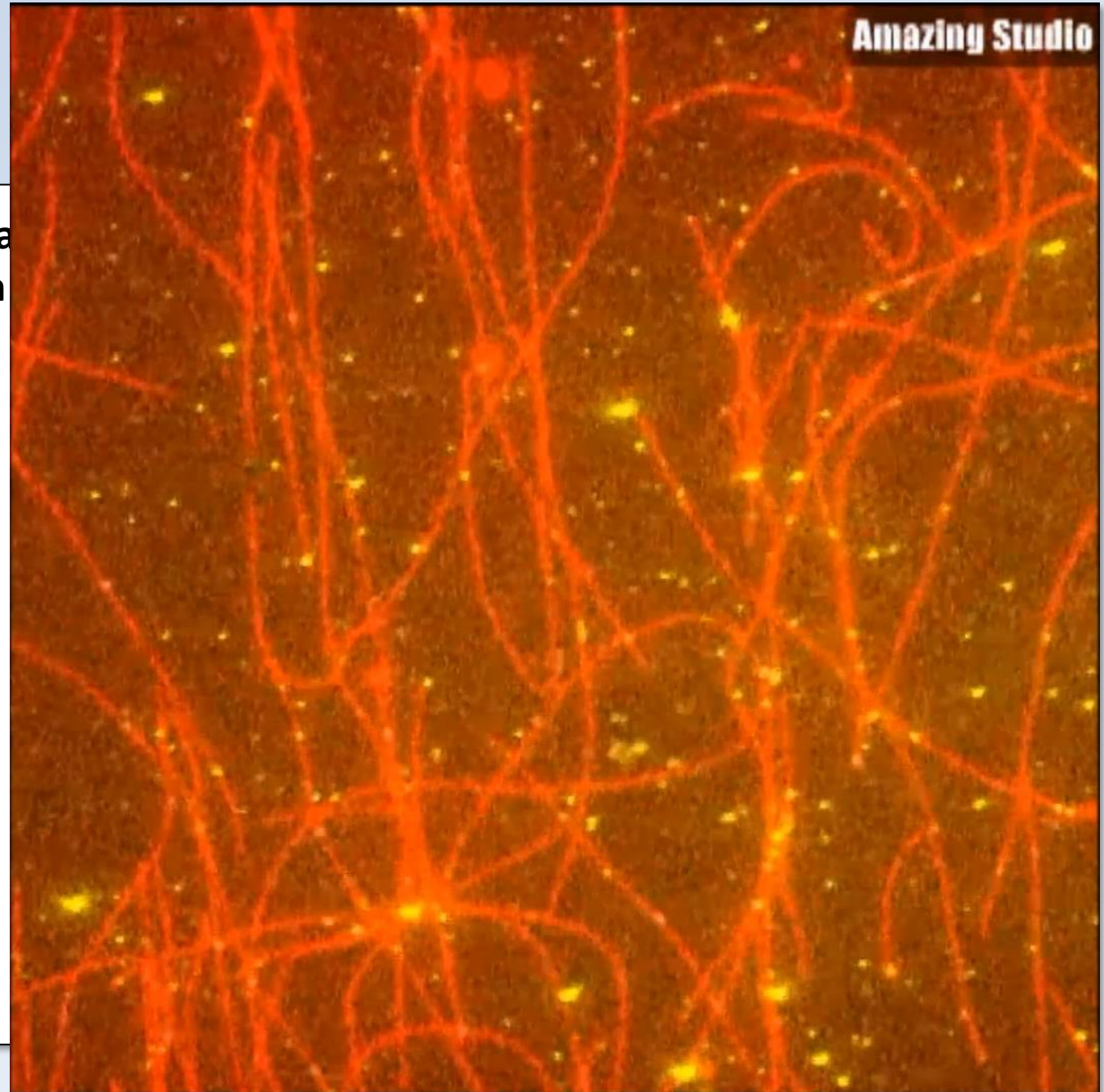
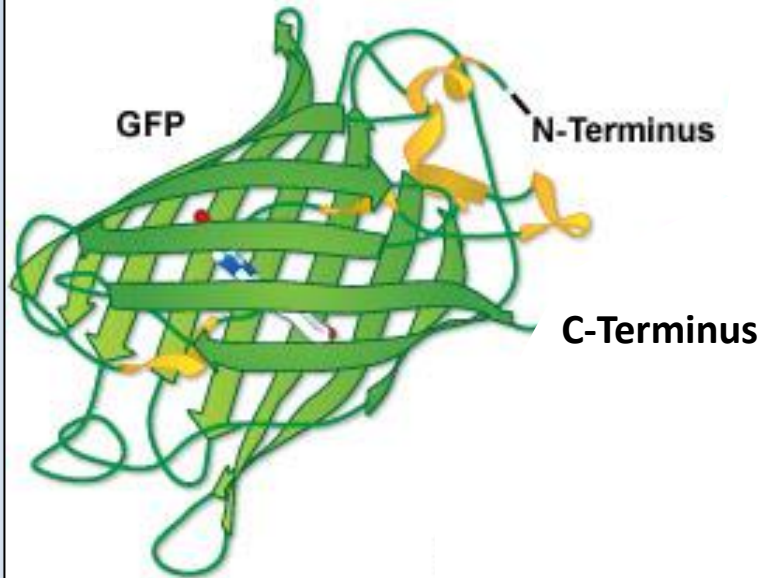
## GFP Attached to Large Protein for Localization Imaging



# Visible microscopy has a role – motion detection



**GFP Attached to La  
for Localization**



Questions?

# Course Outline

1. Overview  
Building blocks, energy flow, how we know
2. nanoMachines in energy flow
3. Motors and locomotion
4. DNA & RNA processing, protein manufacturing, sensory machines