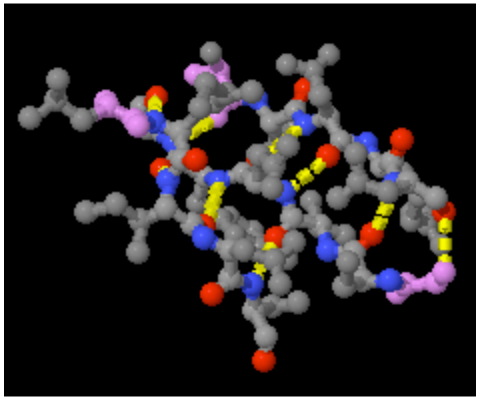
The Morphology of Complex Materials:
MTEN 657
MWF 3:00-3:50 Baldwin 641
Prof. Greg Beaucage

Course Requirements:

-Weekly Quiz (8 to 9 in quarter)
-Comprehensive Final (worth 3 quizzes)

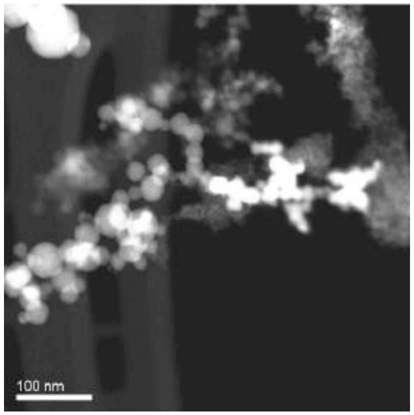
-Old Quizzes will serve as homework
(These have posted answers)
I may also assign other homework where it is needed

You can replace quiz grades with a (or several) report(s) on a topical area not covered in class but pertaining to the hierarchy of morphology for a complex material. Several examples are given on the web page.



β-Sheet

webhost.bridgew.edu/fgorga/proteins/beta.htm



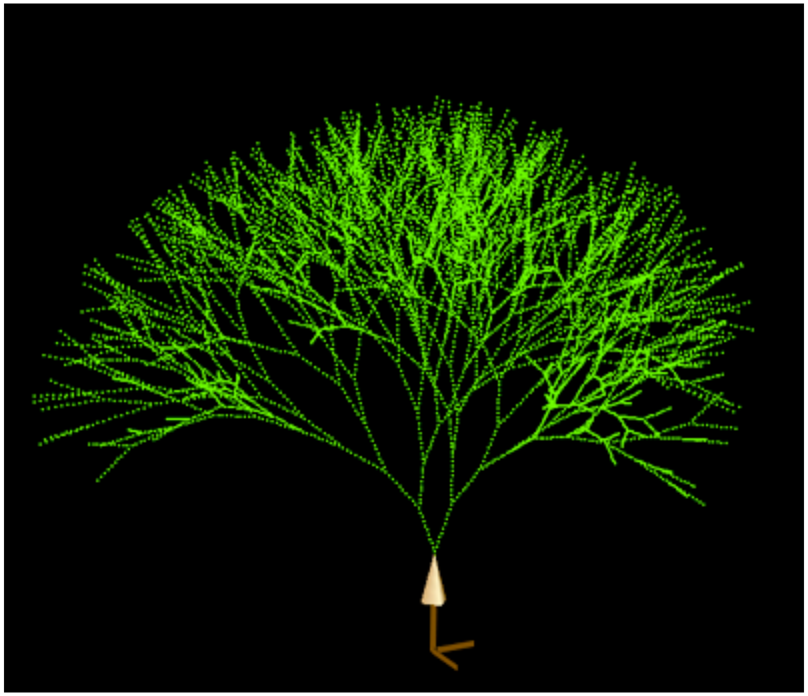
Aggregated Nanoparticles from Lead Based Paint

"Emerging Issues in Nanoparticle Aerosol Science and Technology (NAST)"
NSF 2003

Structural Hierarchy of Complex Materials

Consider that we would like to understand a forest, such as the Amazon Forest from a Structural Perspective in order to develop predictive capabilities and an understanding of the basic features to such a complex structure.

Structural Hierarchy of Complex Materials



http://www.eng.uc.edu/~gbeaucag/Classes/MorphologyofComplexMaterials/Overview.html

Consider that we would like to understand a forest, such as the Amazon Forest from a Structural Perspective in order to develop predictive capabilities and an understanding of the basic features to such a complex structure.

1) The first logical step is to consider a base (primary) unit for the forest and

2) then devise a repetition or branching rule (fractal scaling law) to create trees (secondary structure).

We revise the scaling rules and primary unit until we produce the type of trees we are interested in.

Structural Hierarchy of Complex Materials

http://www.eng.uc.edu/~gbeaucag/Classes/MorphologyofComplexMaterials/Overview.html

Consider that we would like to understand a forest, such as the Amazon Forest from a Structural Perspective in order to develop predictive capabilities and an understanding of the basic features to such a complex structure.

We could consider other types of trees in the same way.

3) Trees form clusters or groves (tertiary structure) that can follow a spacing and shape rule, for instance, redwoods grow in "fairy" rings or "cathedral" groups around an old tree.

Structural Hierarchy of Complex Materials

Consider that we would like to understand a forest, such as the Amazon Forest from a Structural Perspective in order to develop predictive capabilities and an understanding of the basic features to such a complex structure.

4) Groupings of groves of trees interact with the environment to form forests (quaternary structures)

5) Higher levels of organization can be considered

Structural Hierarchy of Complex Materials

-We have considered discrete "levels" of structure within a hierarchical model.

-In constructing the hierarchy is it natural to start from the smallest scale and to build up.

-We have borrowed from proteins in labeling the hierarchical levels primary, secondary, tertiary and quaternary.

-The hierarchical approach gives insight into how complex natural systems can be understood as if the structural levels acted independently in some respects.

-One of the main insights from hierarchical models is to understand in detail how and why structural levels are not independent and how they can interact to accommodate the environment.

-In this course we will consider the application of hierarchical models to understand complex molecular systems with the goal of understanding how the hierarchical approach can be expanded.

Structural Hierarchy of Complex Materials

Topics we will cover:

1) Protein structure (the origin of the hierarchical concept) 3 weeks

2) DNA and RNA structure (first adaptation of the hierarchical approach) 1 week

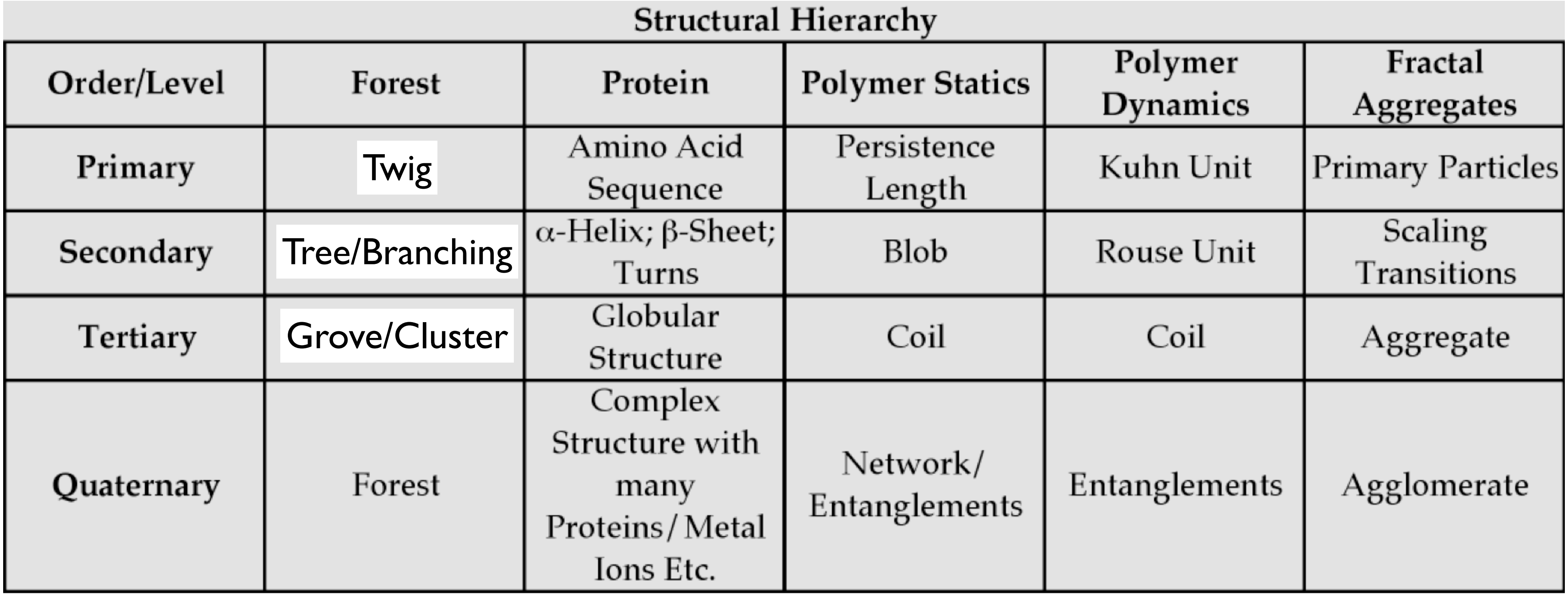
3) Polymer Chain Structure in Solution (a statistical hierarchy) 2 weeks

4) Hierarchy of Polymer Dynamics in Solution (a kinetic hierarchy) 1 week

5) Polymer Crystalline Structure (hierarchy in a structural material) 2 weeks

6) Branched Fractal Aggregates (hierarchy in a statistical structural material) 1 week

Structural Hierarchy of Complex Materials



Structural Hierarchy

Order/Level	Forest	Protein	Polymer Statics	Polymer Dynamics	Fractal Aggregates
Primary	Twig	Amino Acid Sequence	Persistence Length	Kuhn Unit	Primary Particles
Secondary	Tree/Branching	α-Helix; β-Sheet; Turns	Blob	Rouse Unit	Scaling Transitions
Tertiary	Grove/Cluster	Globular Structure	Coil	Coil	Aggregate
Quaternary	Forest	Complex Structure with many Proteins/ Metal Ions Etc.	Network/ Entanglements	Entanglements	Agglomerate

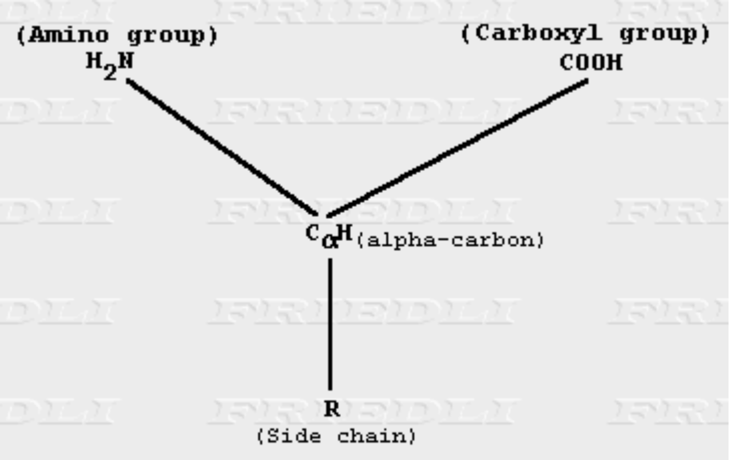
The Structural Hierarchy of Proteins

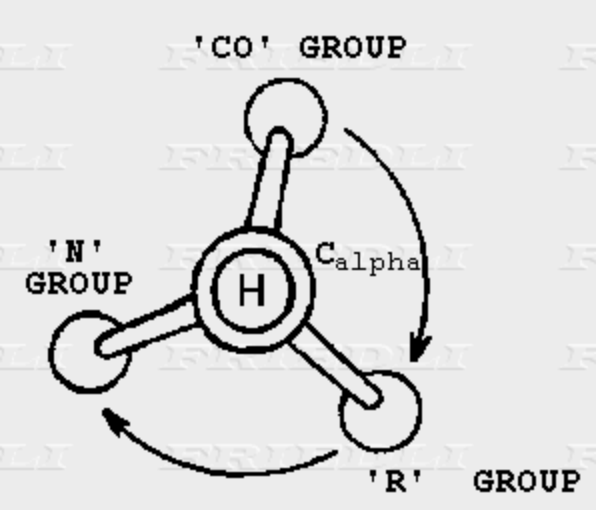
Size of proteins.html

http://learn.genetics.utah.edu/content/begin/cells/scale/

Four Levels of Protein Structure.html

http://www.youtube.com/watch?v=y8Z48RoRxHg&feature=related





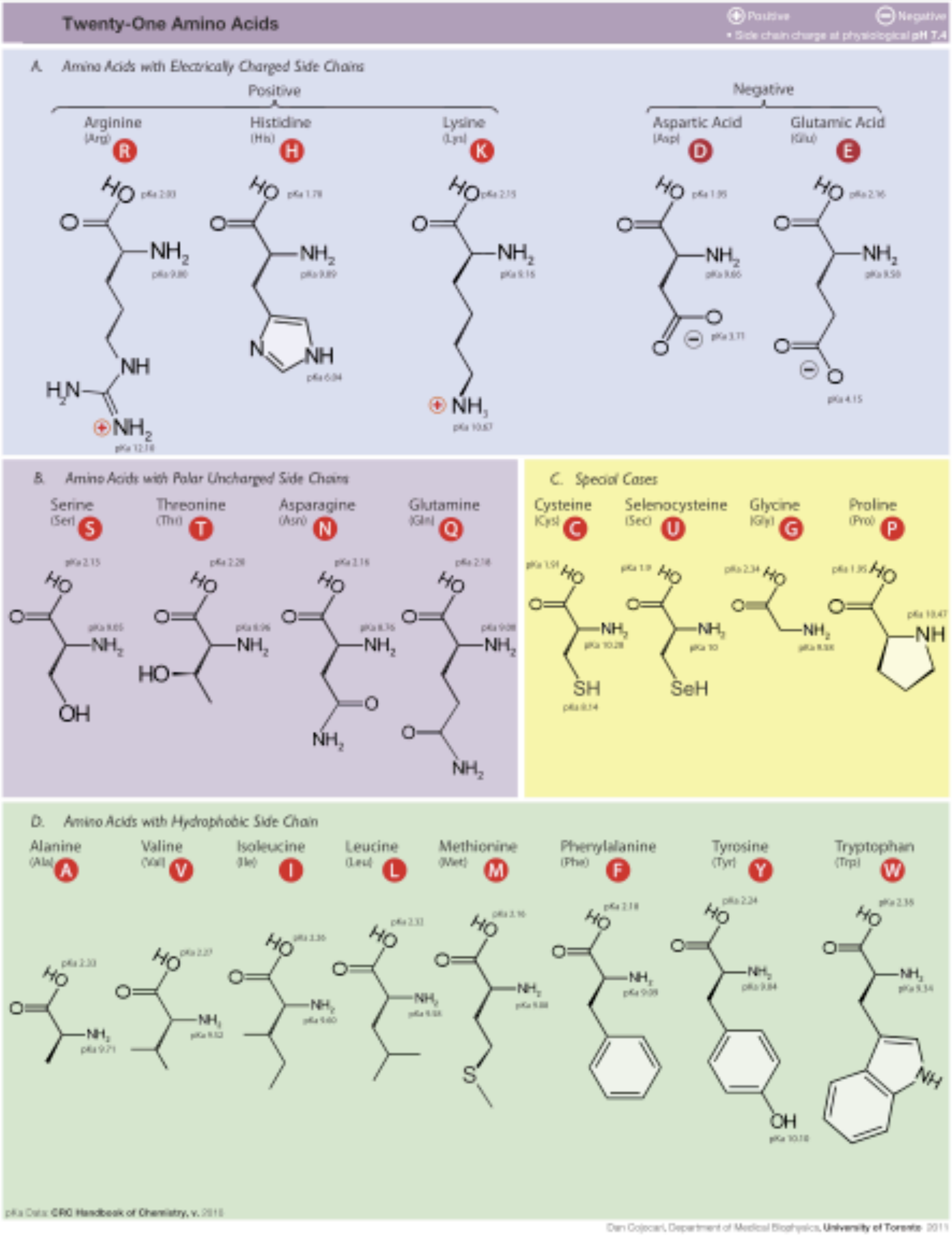
http://www.friedli.com/herbs/phytochem/proteins.html#peptide_bond

The α-carbon is a chiral center
it is always in an L-configuration spelling "CORN" in the Newman projection

There are 20 choices for the "R" group in nature. This makes an alphabet from which sequences of these 20 letters can code for any protein. Depending on the chemical functionality of the "R" groups different properties, polarity, hydrophobicity, ability to bond by disulfide linkages, hydrogen bonding and chain flexibility or rigidity can be imparted to the protein.

Quick Look at Amino Acids.html

http://www.johnkyrk.com/aminoacid.html



Amino Acids.html

http://www.bioscience.org/urllists/aminacid.htm

3D Amino Acids

http://www.mcb.ucdavis.edu/courses/bis102/Polar.html

More Amino Acids

http://biology.clc.uc.edu/courses/bio104/protein.htm

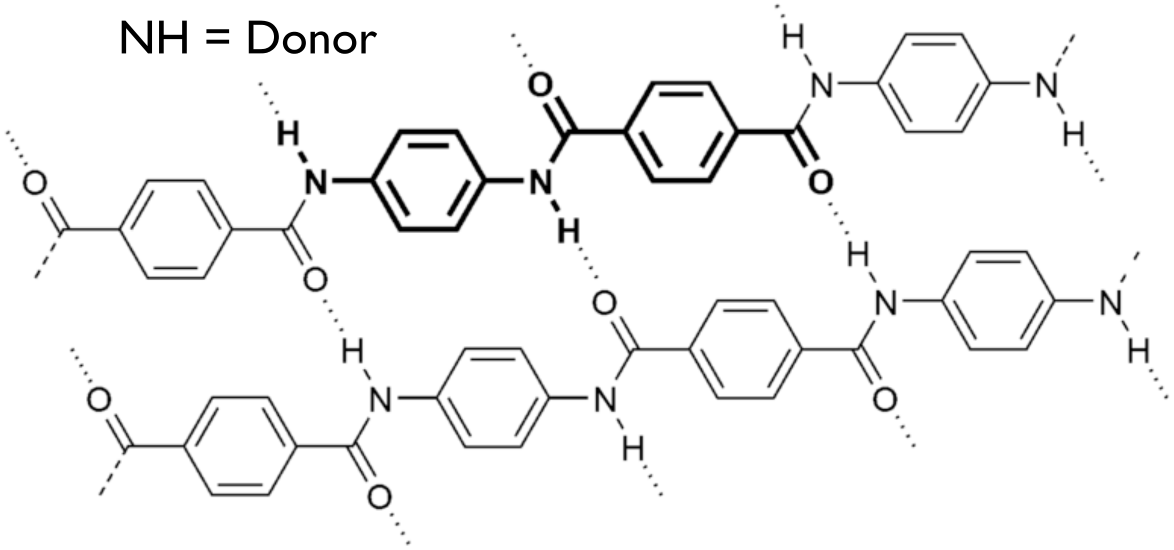
Know These 5 Amino Acids Well

Methionine Start Amino Acid (usually removed in later steps)

Glycine -H Flexible non-polar
Alanine -CH_3 Flexible non-polar

Proline 10-40% Cis Configuration depending on neighboring amino acid residues
Found in Turns and at start of α-helix

Cystine Disulfide Linkages (Hair is 5% cystine)



C=O = Acceptor

NH = Donor

Hydrogen Bonding in Kevlar

Polyamides are similar to proteins

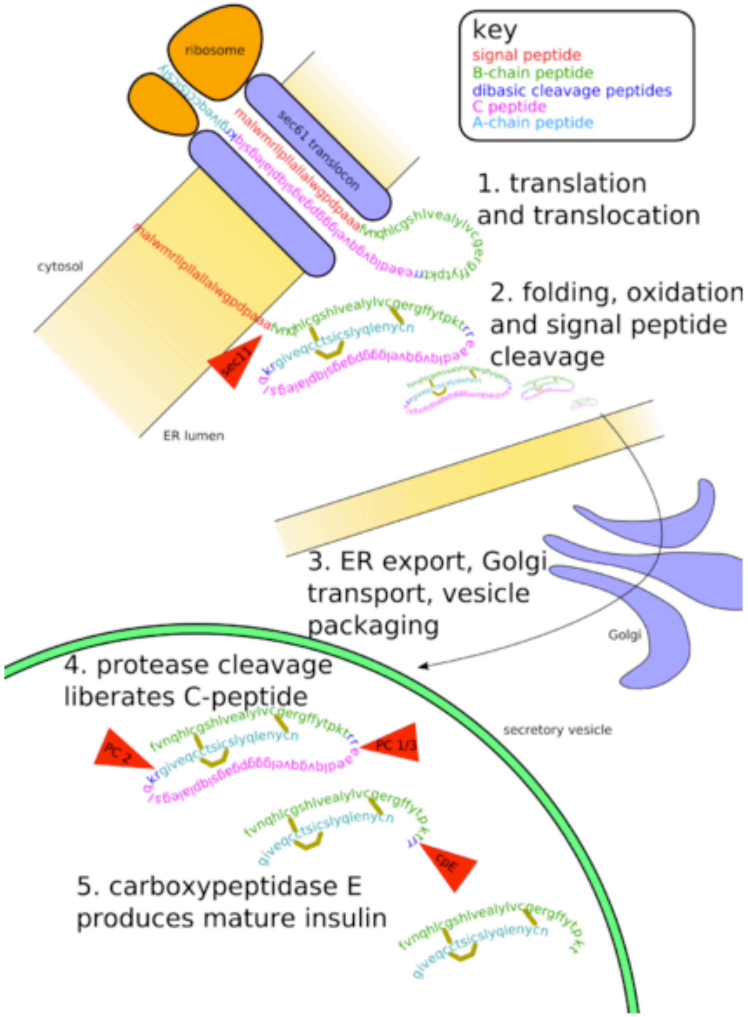
The Genetic Code Links.html

http://www.eng.uc.edu/~gbeaucag/Classes/MorphologyofComplexMaterials/GeneticCode.html

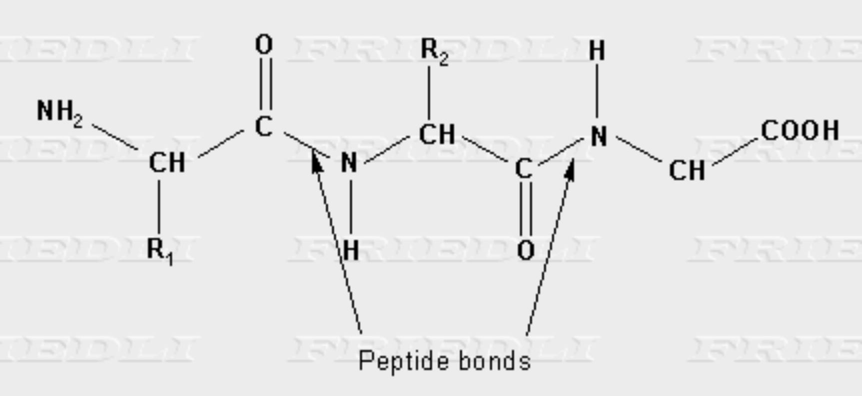
Movie of Protein Synthesis

http://nutrition.jbpub.com/resources/animations.cfm?id=14&debug=0

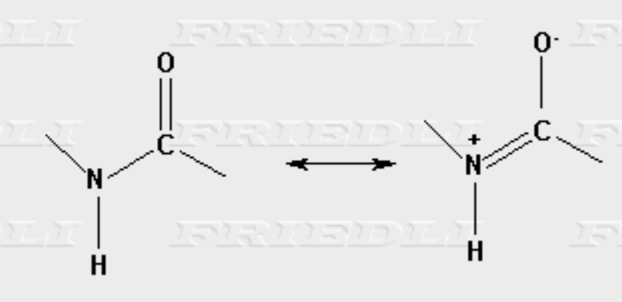
Post Translational Modification of Insulin

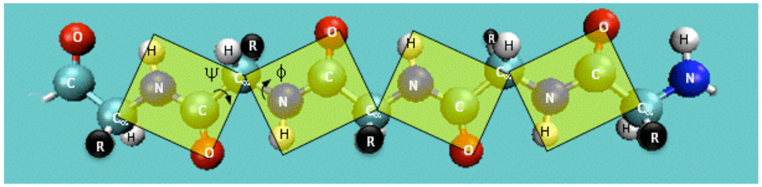


The Peptide Bond

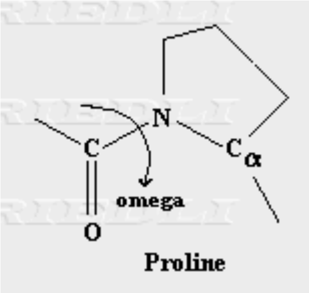


http://www.friedli.com/herbs/phytochem/proteins.html#peptide_bond



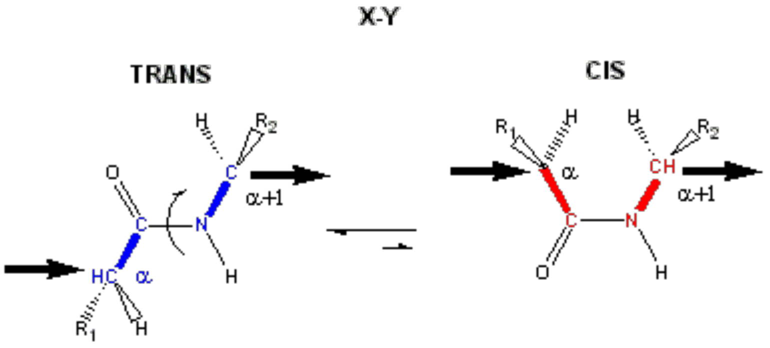


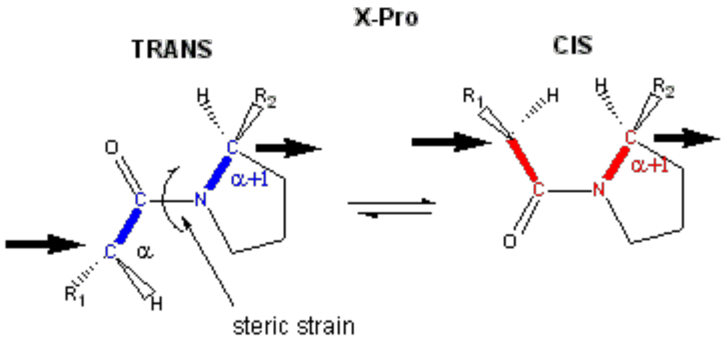
Resonance structures make the peptide group planar (like a card).

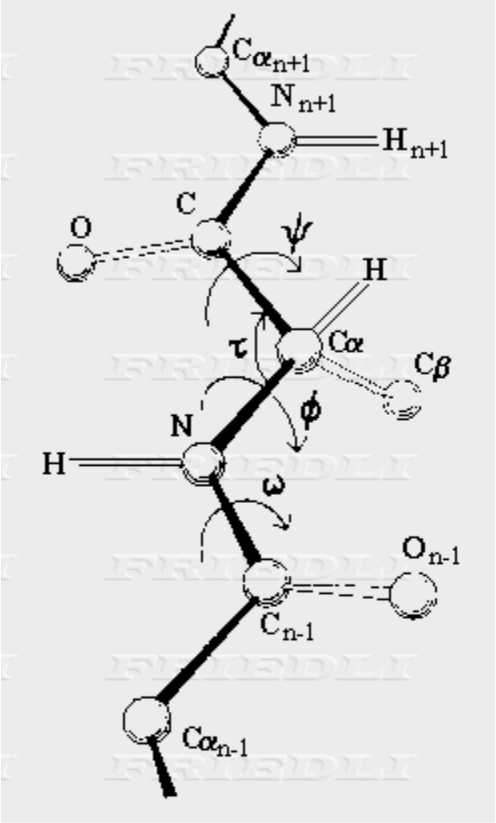


Proline is the exception
Proline adds main chain curvature
found in turns and at start of α-helix

PEPTIDE BONDS: CIS OR TRANS







The peptide linkage forms a planar structure with the two α-carbons and the N, H, C and O atoms

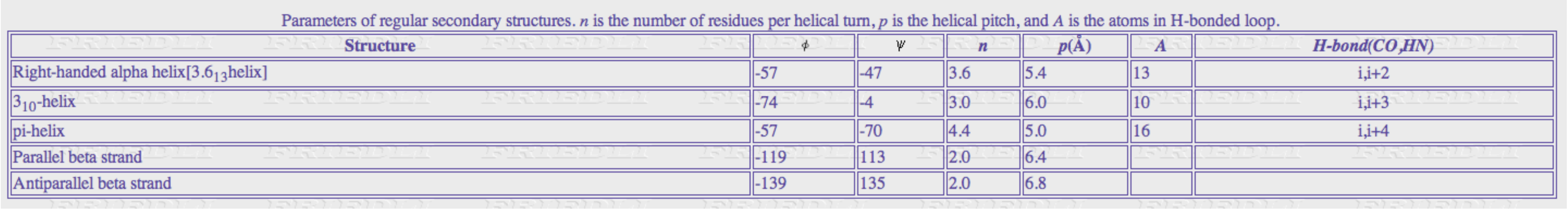
PSI ψ is the rotation angle between the carboxyl C and the α-carbon

PHI Φ is the rotation angle between N and the α-carbon

Certain values of these two rotation angles are preferred in certain structures

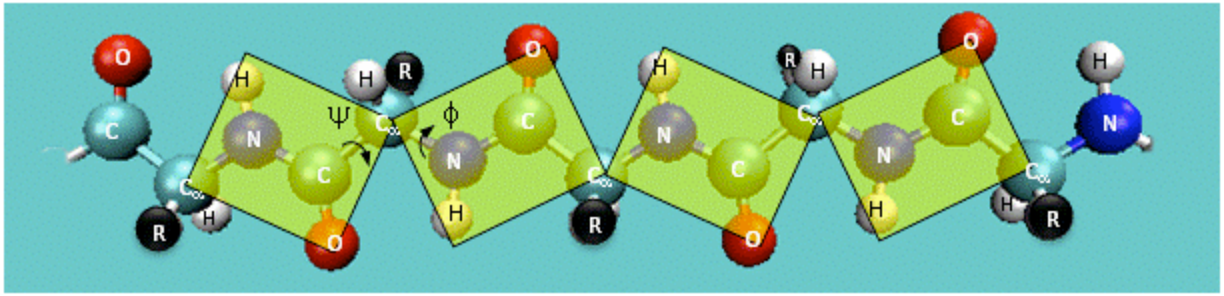
So the angles serve as a map for the protein secondary structure

Fully Extended Chain (Planar Zig-Zag)
Phi/Psi 180, 180

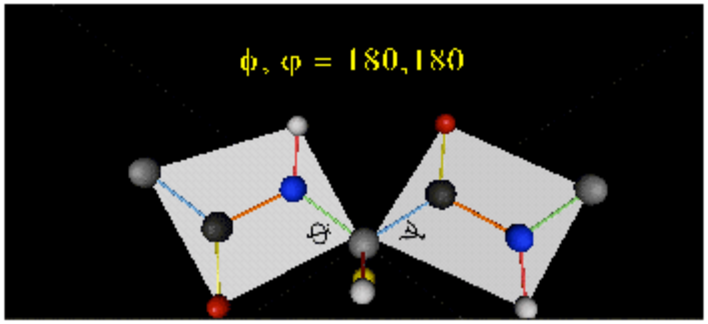

Parameters of regular secondary structures. *n* is the number of residues per helical turn, *p* is the helical pitch, and *A* is the atoms in H-bonded loop.

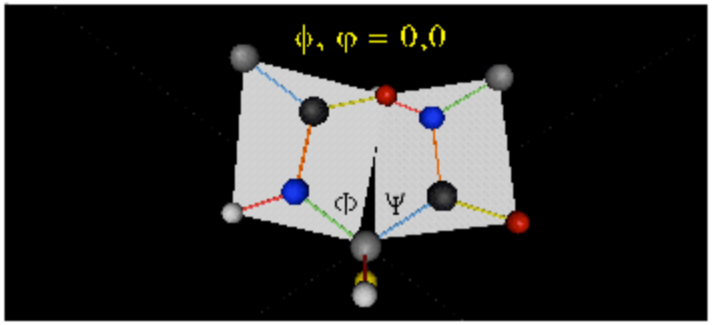
Structure	ϕ	ψ	*n*	*p*(Å)	*A*	*H-bond(CO,HN)*
Right-handed alpha helix[3.6_{13}helix]	-57	-47	3.6	5.4	13	i,i+2
3_{10}-helix	-74	-4	3.0	6.0	10	i,i+3
pi-helix	-57	-70	4.4	5.0	16	i,i+4
Parallel beta strand	-119	113	2.0	6.4		
Antiparallel beta strand	-139	135	2.0	6.8		

http://www.friedli.com/herbs/phytochem/proteins.html#peptide_bond



http://employees.csbsju.edu/hjakubowski/classes/ch331/protstructure/olunderstandconfo.html



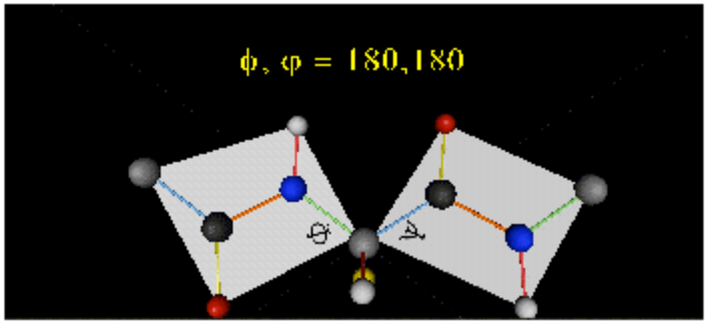


http://visu.uwlax.edu/BioChem/Rotate.mov

Phi rotation for Psi = 0

Psi rotation for Phi = 0

http://employees.csbsju.edu/hjakubowski/classes/ch331/protstructure/olunderstandconfo.html



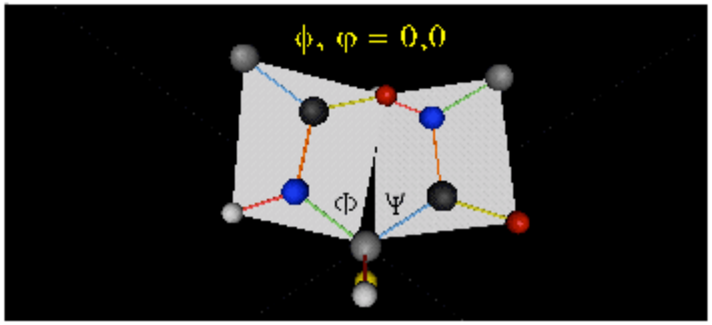
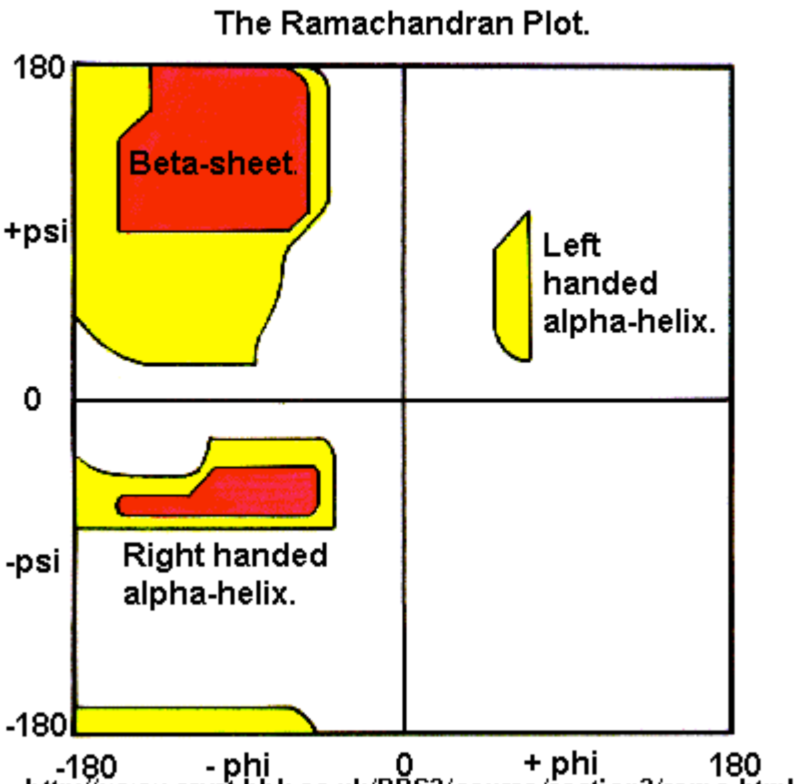
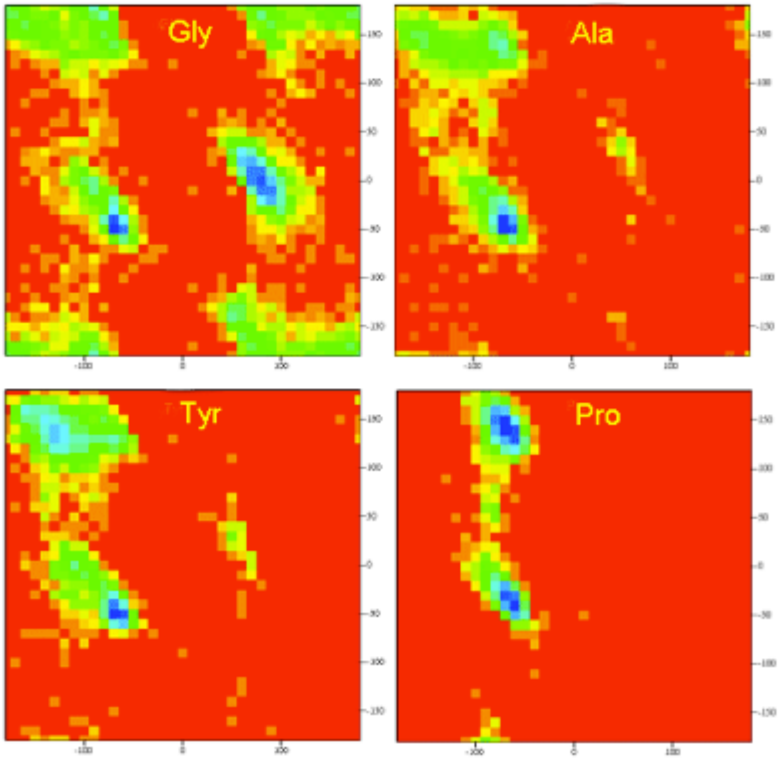


Figure: Ramachandran plot



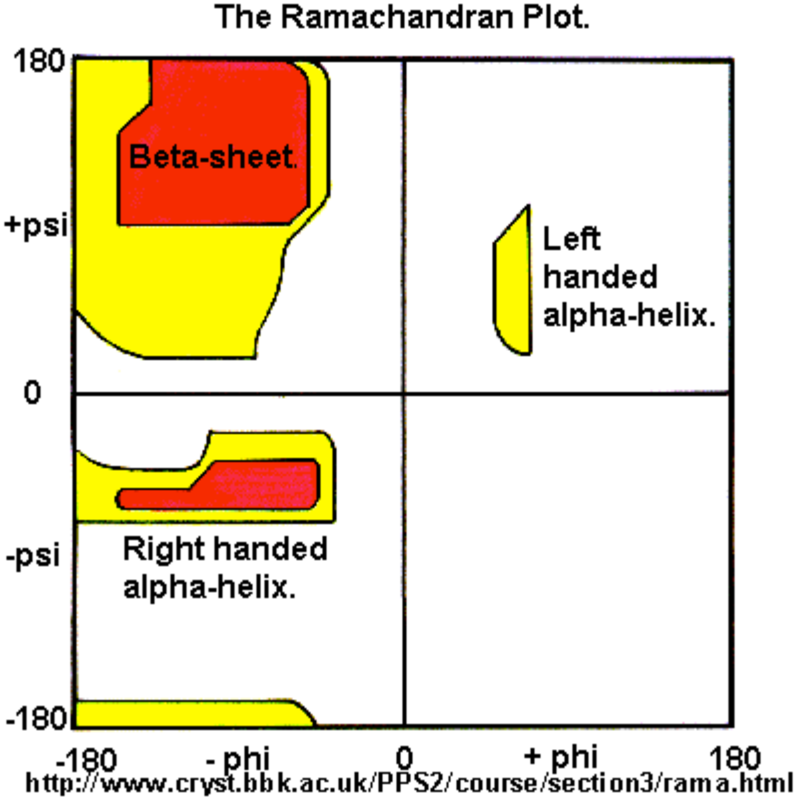
http://www.cryst.bbk.ac.uk/PPS2/course/section3/rama.html

Figure: Ramachandran plots showing phi/psi angles for Gly, Ala, Tyr, and Pro in actual proteins



Ramachandran Plots.html

Figure: Ramachandran plot



Lets Jump Ahead and Look at Protein Folding

Folding Simple Dynamic Simulation.html

http://intro.bio.umb.edu/111-112/111F98Lect/folding.html

More Complicated Simulation.html

http://www.cs.ucl.ac.uk/staff/D.Jones/t42morph.html

Yet more complicated.html

http://www.youtube.com/watch?v=meNEUTn9Atg

Small Protein Folding.html

http://www.youtube.com/watch?v=_xF96sNWnK4&feature=related

Another Small Protein Folding.html

http://www.youtube.com/watch?v=E0TX3yMEZ8Y&feature=related

Where and When do Proteins Fold.html

http://www.youtube.com/watch?v=BrUdCVwgJxc&feature=related

Entropy and Protein Folding.html

http://www.youtube.com/watch?v=gaaiepNVyvE&feature=related

Folding a Protein by Hand.html

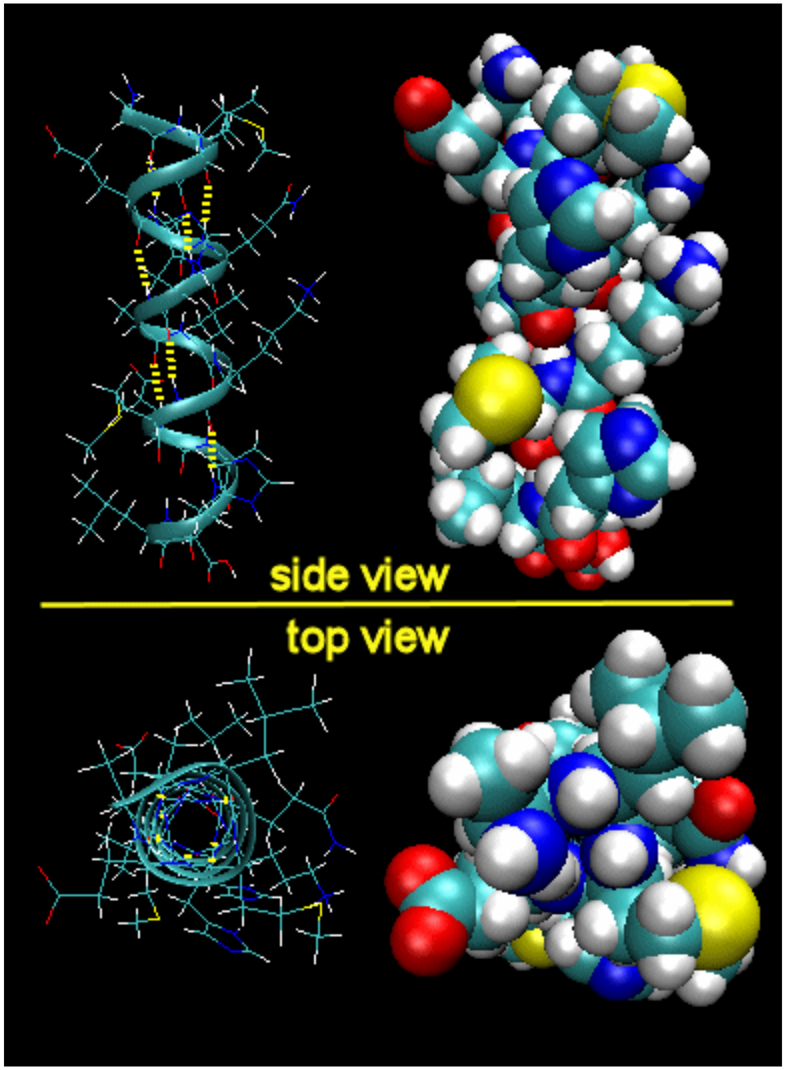
http://www.youtube.com/watch?v=va92d9Ei1QM&feature=related

Folding of Villin.html

http://www.youtube.com/watch?v=1eSwDKZQpok&feature=related

Secondary Structures of Proteins
α-Helix, β-Sheets, Turns

Right Handed α-Helix



http://employees.csbsju.edu/hjakubowski/classes/ch331/protstructure/olunderstandconfo.html

pdb of α-Helix

http://employees.csbsju.edu/hjakubowski/Jmol/alpha_helix/alpha_helix.htm

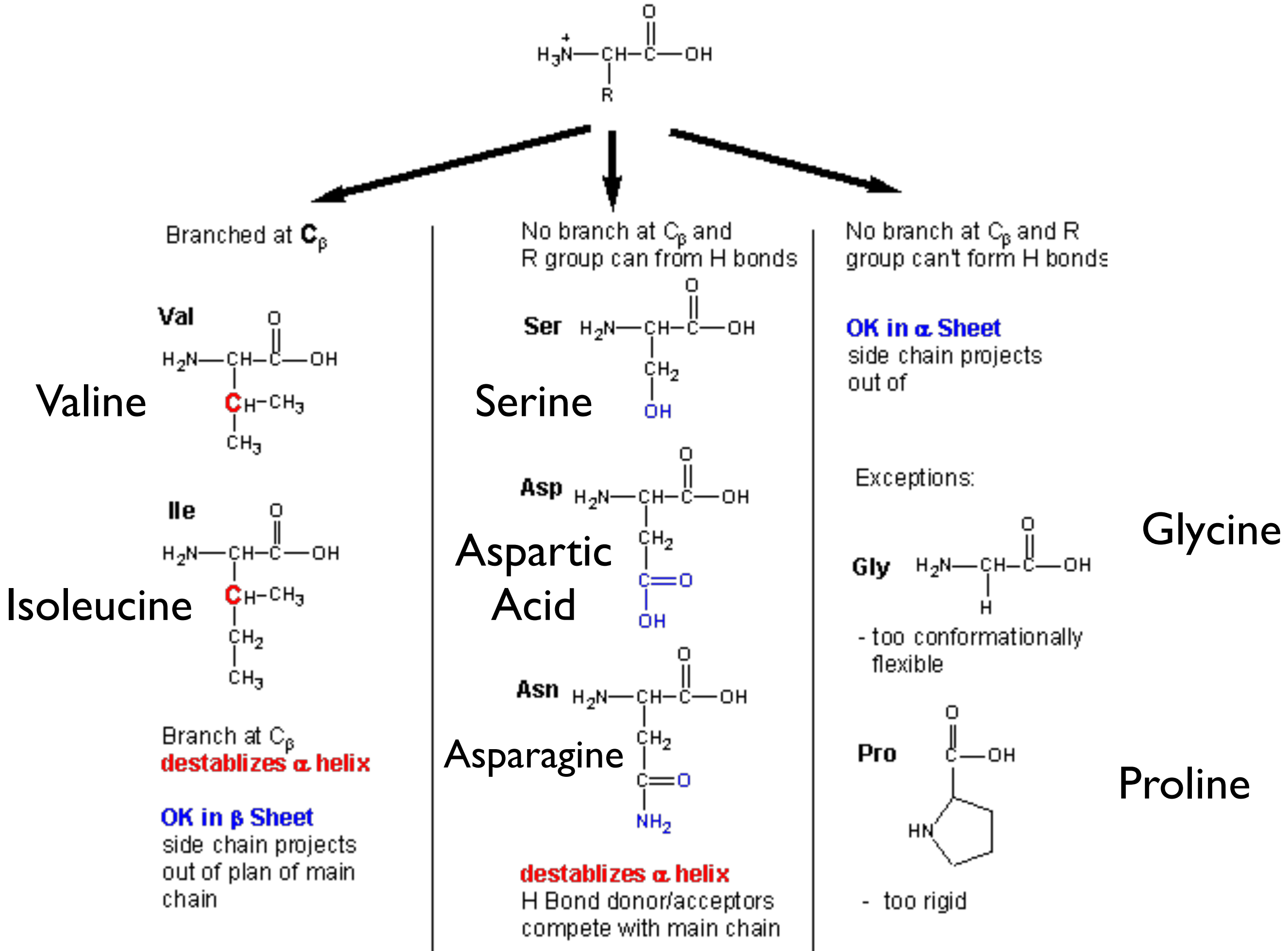
C=O from residue “i”
hydrogen bonds with
NH from residue “i+4”

Phi/Psi angles are -57, -47

Residues per turn = 3.6
Rise per turn = 5.4 Å

<u>Amino Acids and Helix</u>
Glycine too flexible
Proline too rigid
Short H-Bonding (Ser, Asp, Asn) Disrupt Coil
Long H-Bonding are OK
Branches at α-C Disrupt Coil (Val, Ile)

AMINO ACID PROPENSITIES FOR SECONDARY STRUCTURE



Branched at **C**$_\beta$

Branch at C$_\beta$
destablizes α helix

OK in β Sheet
side chain projects out of plan of main chain

No branch at C$_\beta$ and R group can from H bonds

destablizes α helix
H Bond donor/acceptors compete with main chain

No branch at C$_\beta$ and R group can't form H bonds

OK in α Sheet
side chain projects out of

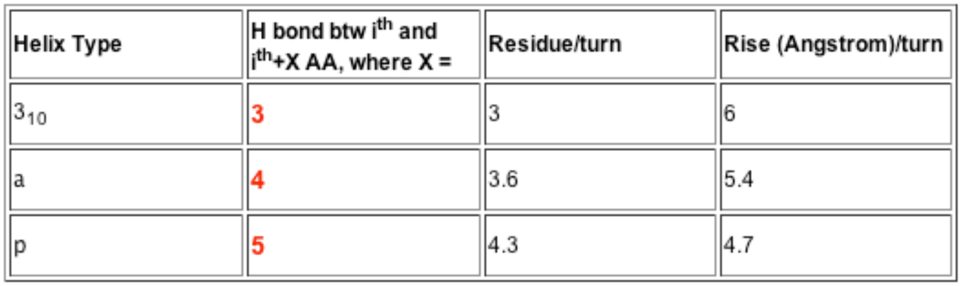
Exceptions:

- too conformationally flexible

- too rigid

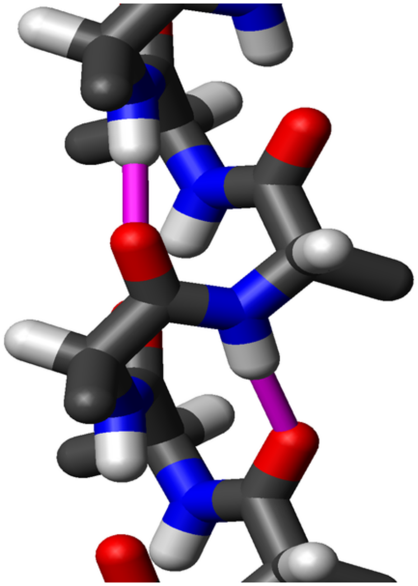
http://employees.csbsju.edu/hjakubowski/classes/ch331/protstructure/olunderstandconfo.html

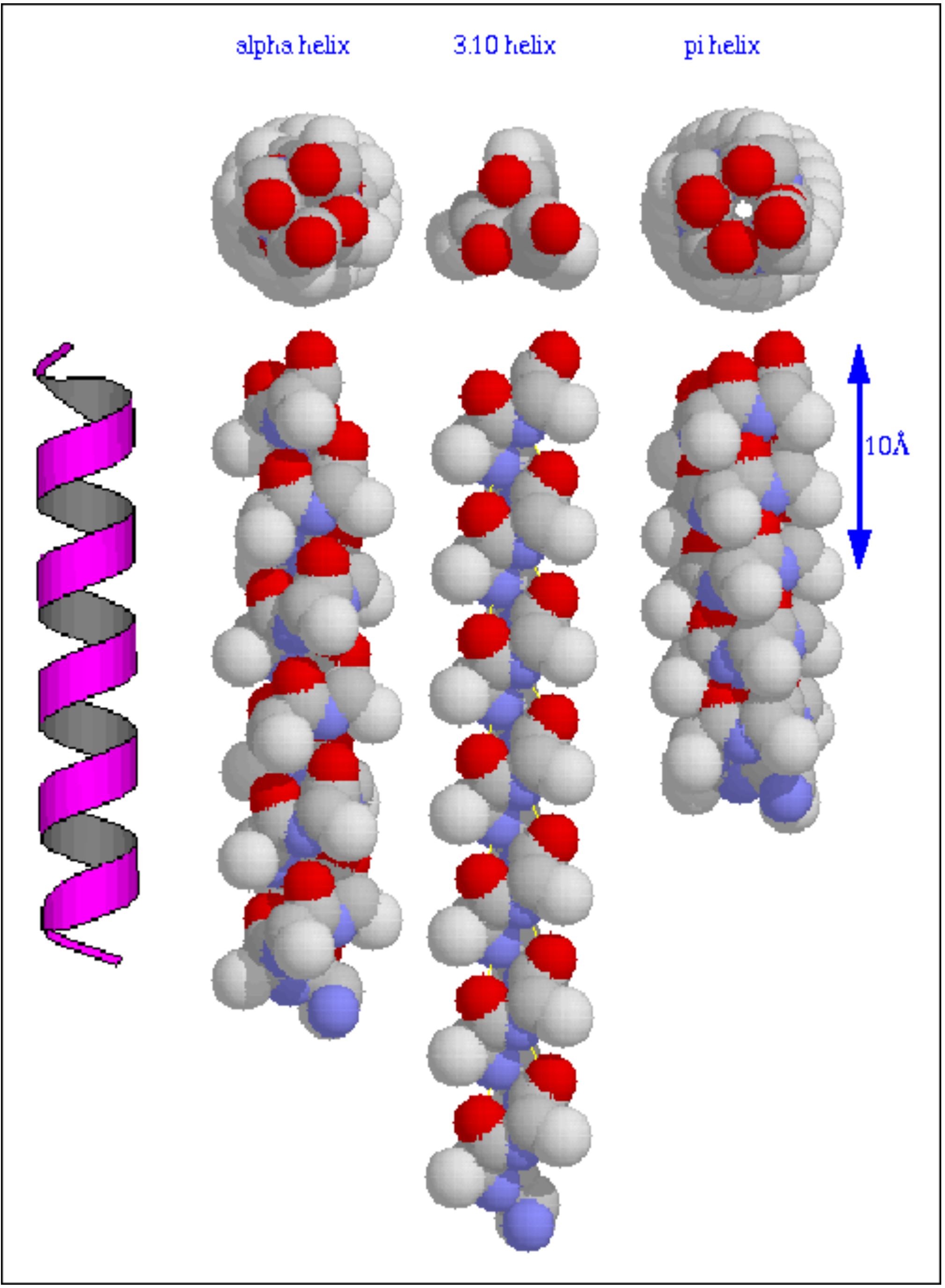
Other Types of Helices



Helix Type	H bond btw i^{th} and i^{th}+X AA, where X =	Residue/turn	Rise (Angstrom)/turn
3_{10}	3	3	6
a	4	3.6	5.4
p	5	4.3	4.7

3_{10} helix



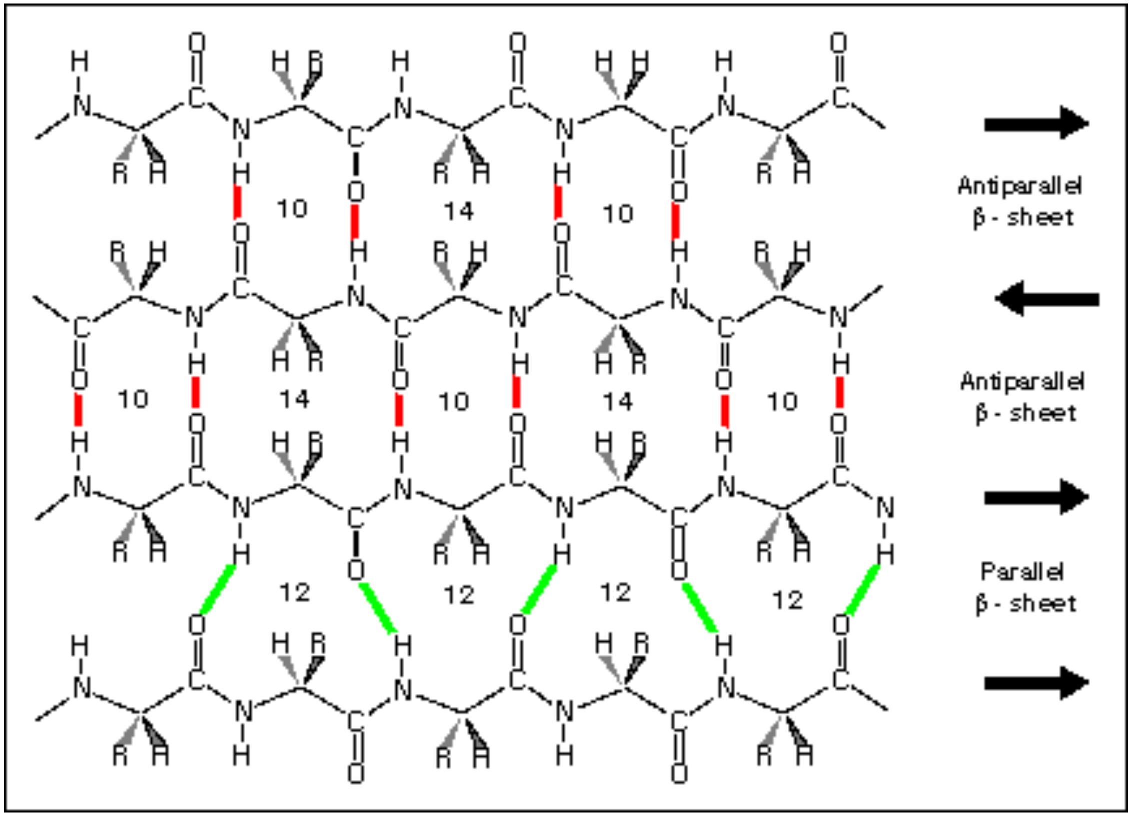


β-Sheets

	Phi	Psi
Parallel	-119	+113
Anti-Parallel	-139	+135
α-Helix	-57	-47
Extended	±180	±180

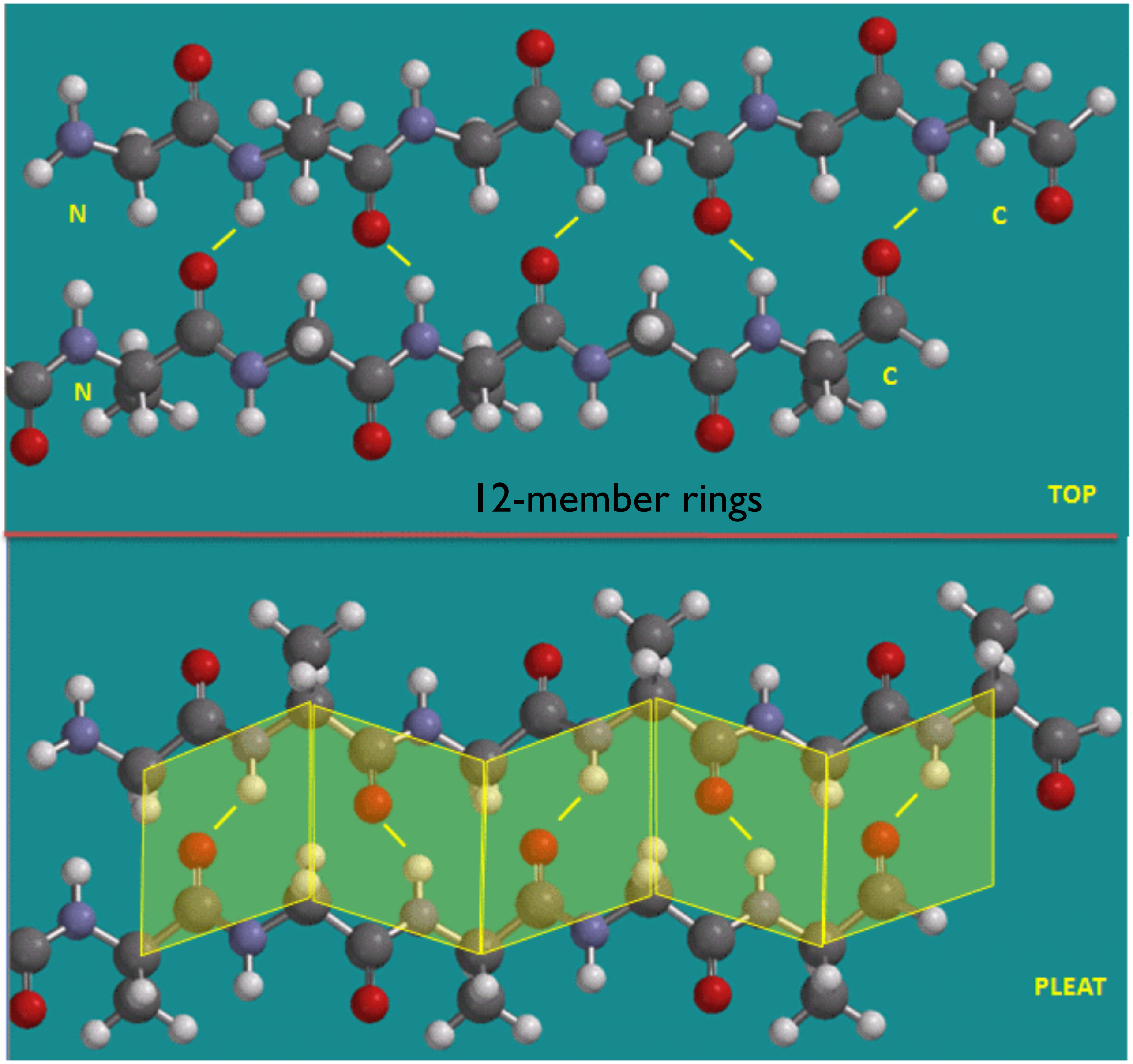
Rippled Sheets

H-Bonding between strands in Sheet
H-Bonding within strand in Helix

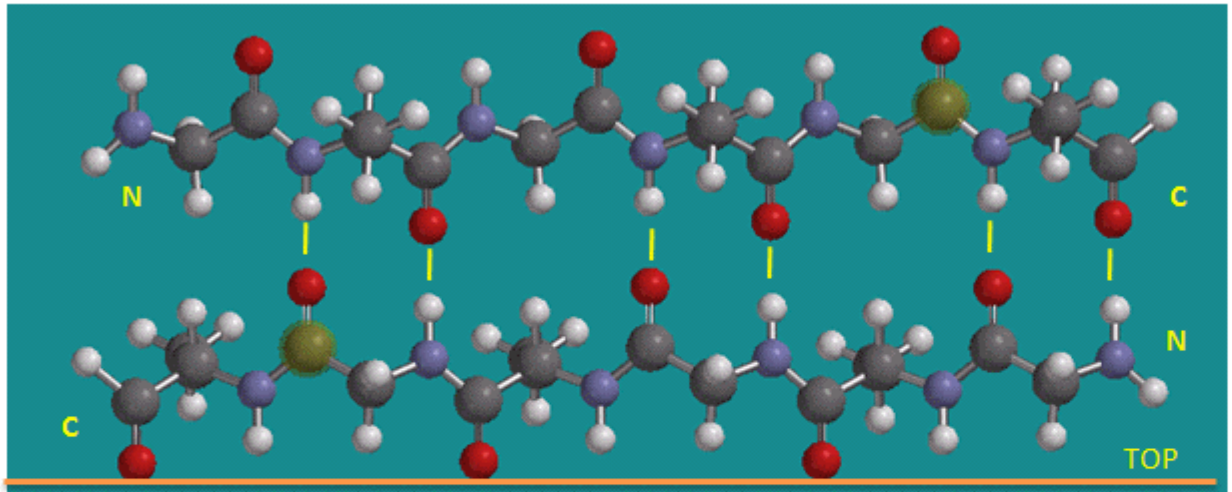


Parallel => 12 member rings
Anti-Parallel => 14 and 10 member rings alternating

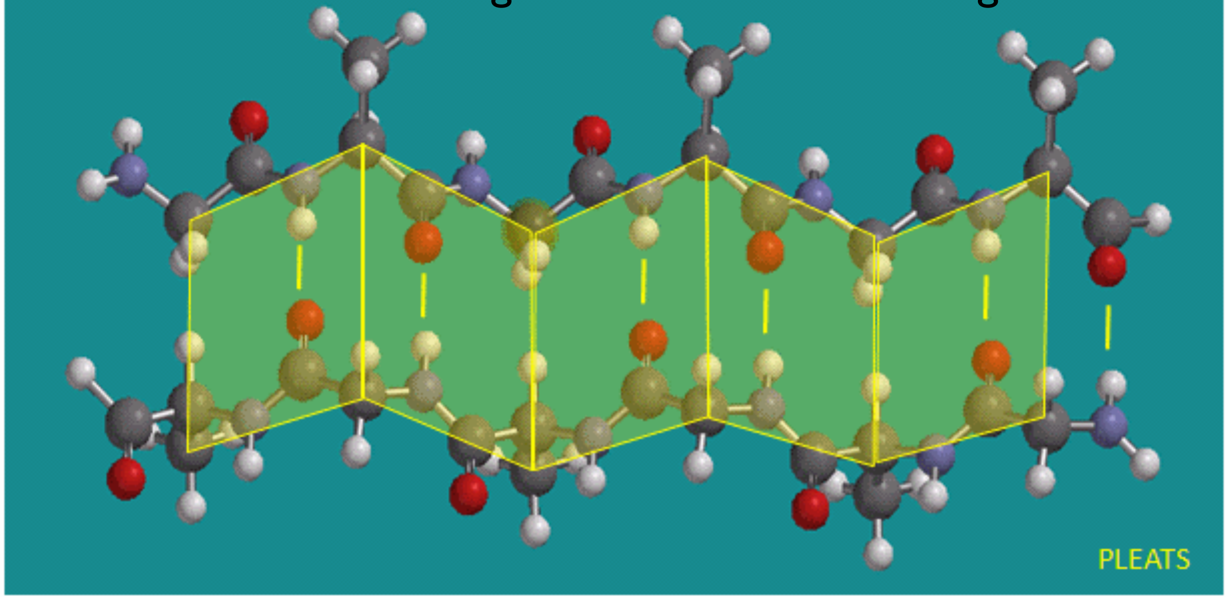
Parallel β-Sheets



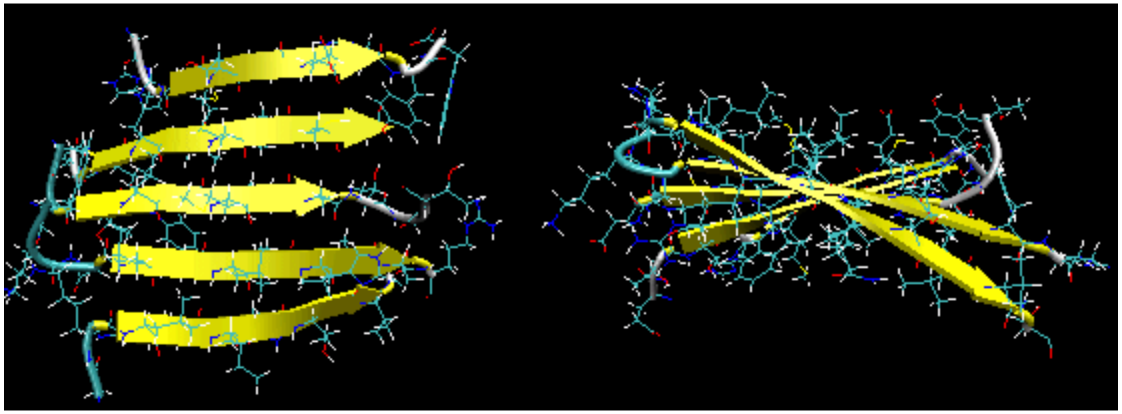
Anti-Parallel β-Sheets



Alternating 10- and 14-member rings



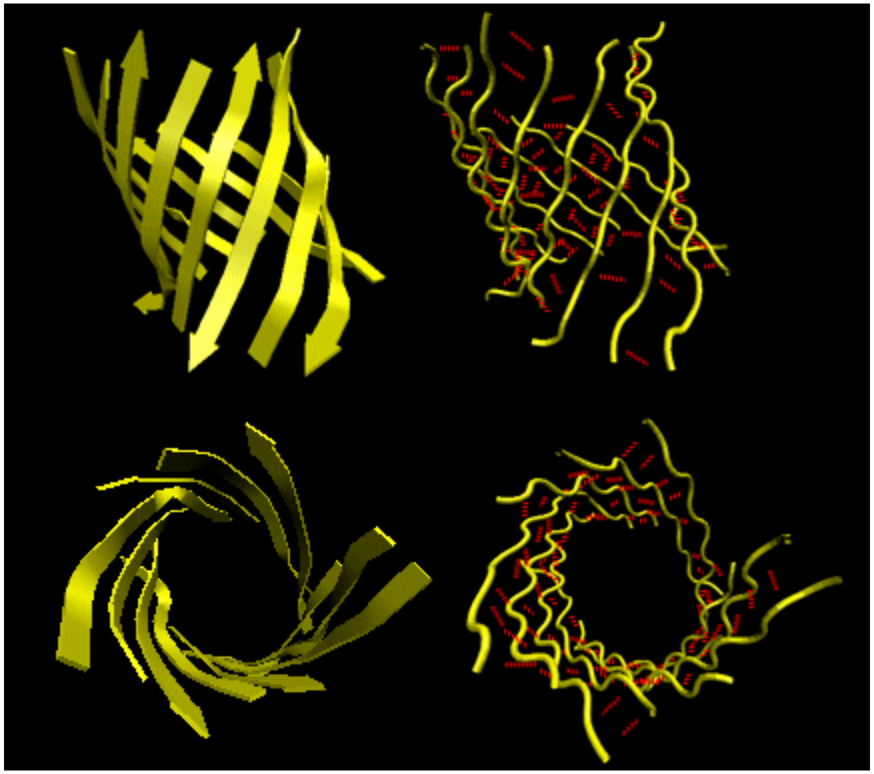
Twisted β-Sheet/Saddle



Twisted β-Saddle

http://employees.csbsju.edu/hjakubowski/Jmol/Twisted%20Beta%20Sheet/Twisted_Beta_Sheet.htm

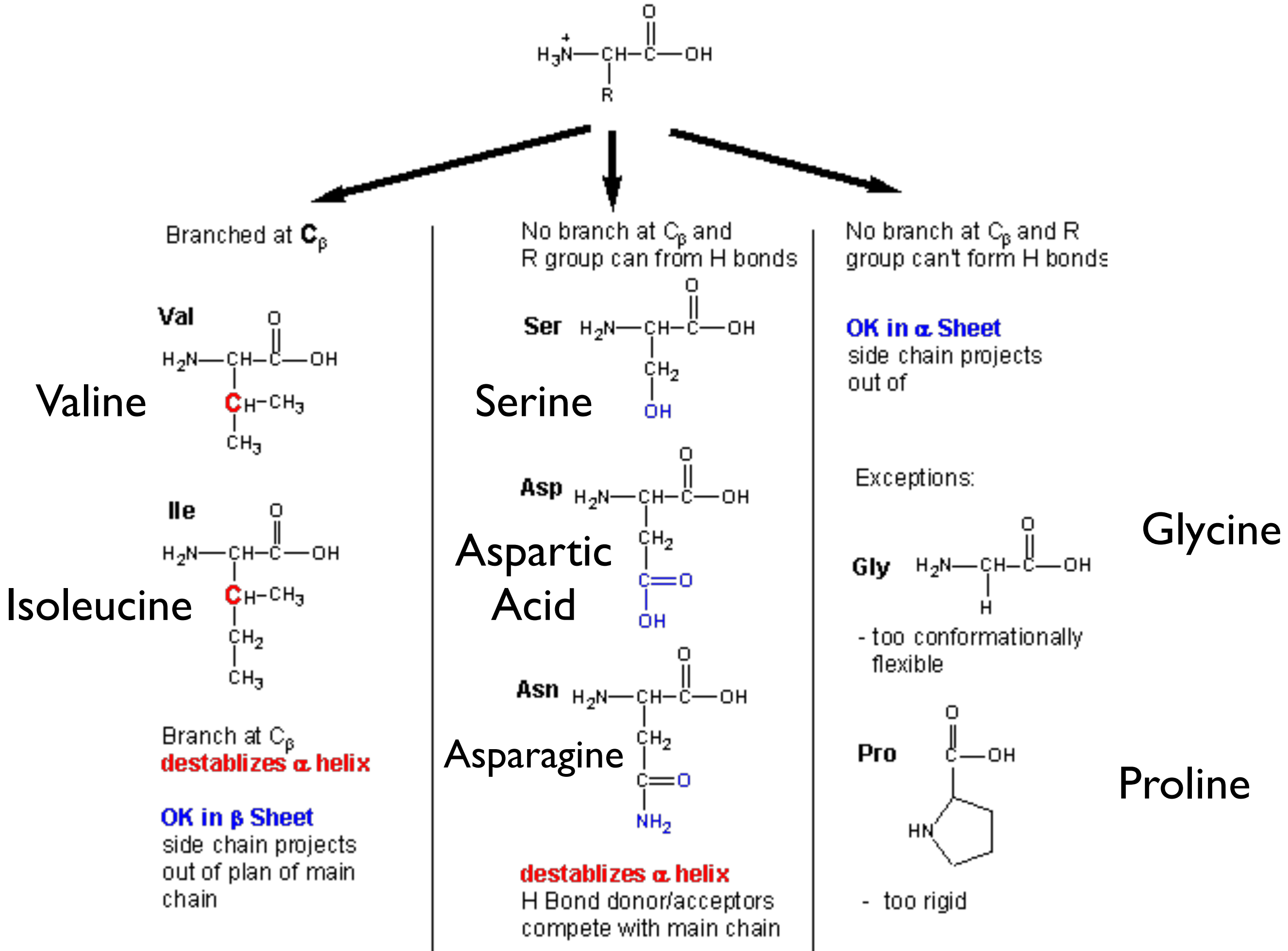
β-Barrel



β-Barrel

http://employees.csbsju.edu/hjakubowski/Jmol/beta_barrel_tpi/Beta_Barrel_tpi.htm

AMINO ACID PROPENSITIES FOR SECONDARY STRUCTURE



Branched at **C_β**

Branch at C_β
destablizes α helix

OK in β Sheet
side chain projects out of plan of main chain

No branch at C_β and R group can from H bonds

destablizes α helix
H Bond donor/acceptors compete with main chain

No branch at C_β and R group can't form H bonds

OK in α Sheet
side chain projects out of

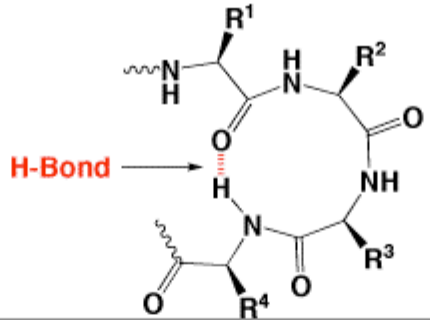
Exceptions:

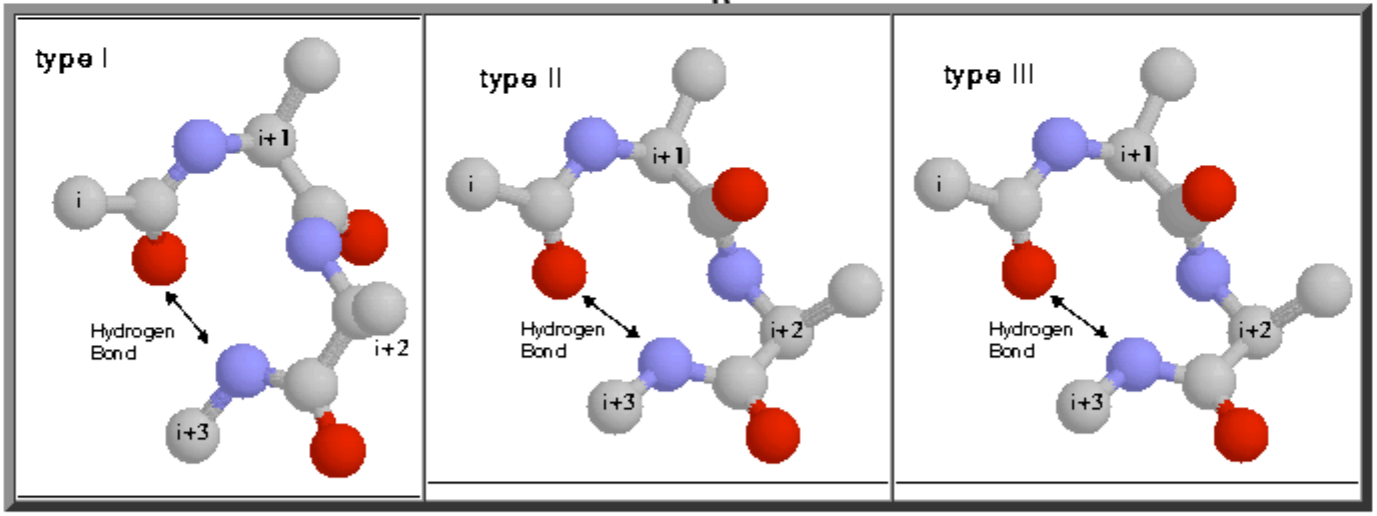
- too conformationally flexible

- too rigid

http://employees.csbsju.edu/hjakubowski/classes/ch331/protstructure/olunderstandconfo.html

β-Turns


R^1
N
H
H
N
R^2
O
O
H-Bond
H
NH
N
R^3
O
O
R^4

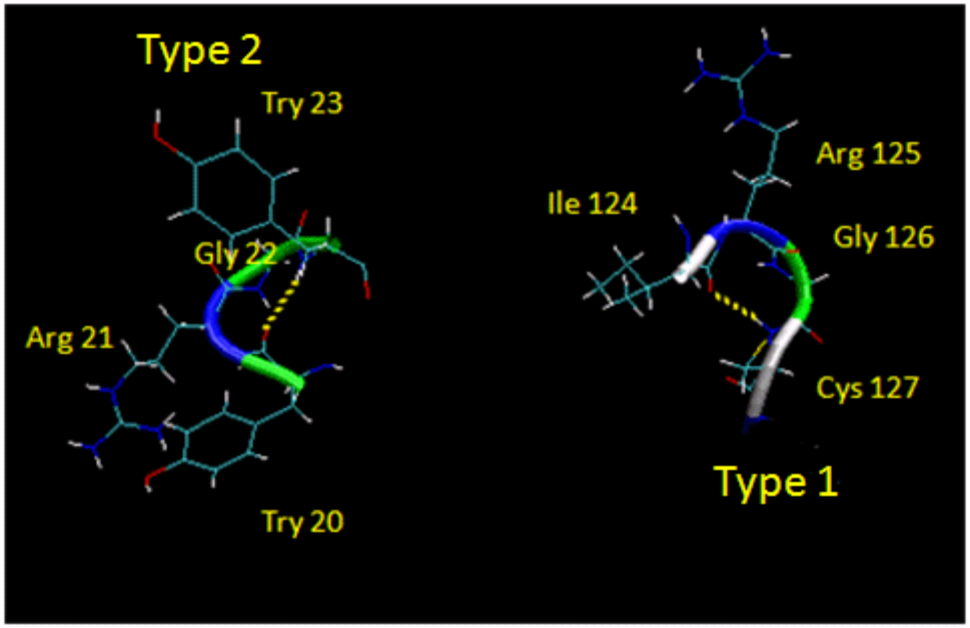

type I
i+1
i
Hydrogen Bond
i+2
i+3
type II
i+1
i
Hydrogen Bond
i+2
i+3
type III
i+1
i
Hydrogen Bond
i+2
i+3

β-Turns

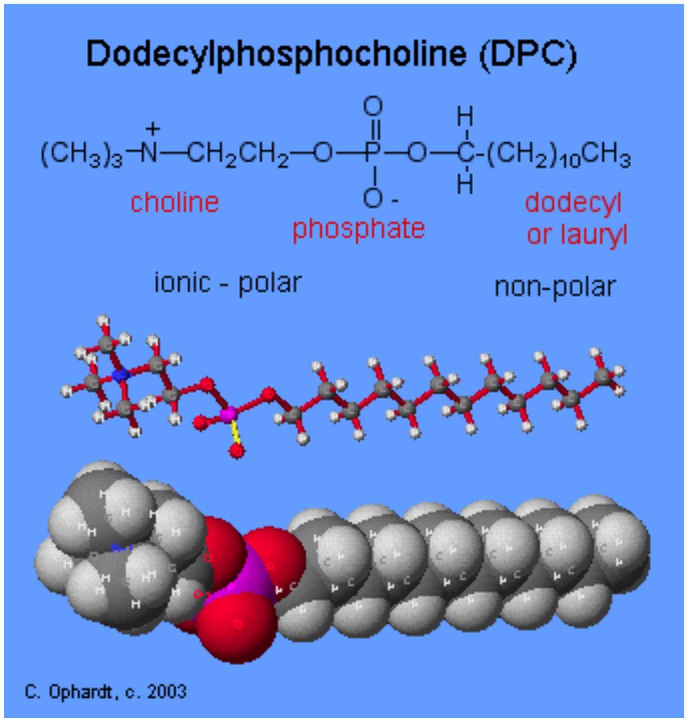
Reverse Turn

http://employees.csbsju.edu/hjakubowski/Jmol/RevTurnTryInhib/revturnTrpInhib.htm

Type 2 and Type 1 Reverse Turns

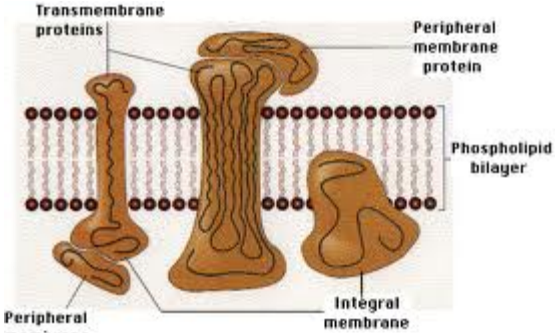


Micelles (Vesicle)



Dodecylphosphocholine (**DPC**) Micelle

http://employees.csbsju.edu/hjakubowski/Jmol/Micelle/micelle.htm



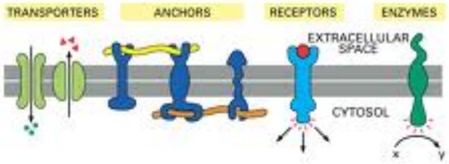


Figure 11-20 Essential Cell Biology, 2/e. (© 2004 Garland Science)

UNIVERSITY OF Cincinnati

The Materials Science
and Engineering

Graduate Program

Materials Science and Engineering Graduate Seminar Series

January 12, 2012
Baldwin 544/644
2:00 - 2:50 pm

The Design of Vesicles

Dr. Michael R. Weaver
Analytic Discovery
Procter & Gamble Corporation

Protein with a buried hydrophobic group

http://employees.csbsju.edu/hjakubowski/Jmol/HAAPBJmol/HAAPBBovineBuryF10.htm

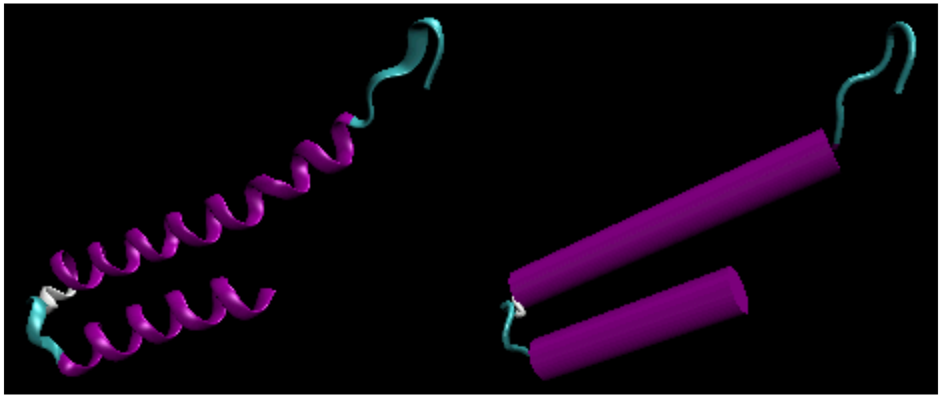
~50% of amino acids are in well defined secondary structures
27% in α-helix and 23% in β-sheets

Native state proteins have a packing density slightly higher than FCC/HCP 0.75 vs 0.74
Organic liquids 0.6-0.7 Synthetic Polymer Chain in Solution ~0.001
So the transition from an unfolded protein in solution to a native state protein involves a densification of about 750 to 1000 times.

Nonpolar 83% internal, Charged 54% exposed, uncharged 63% internal

Super-Secondary Structures

Common motifs



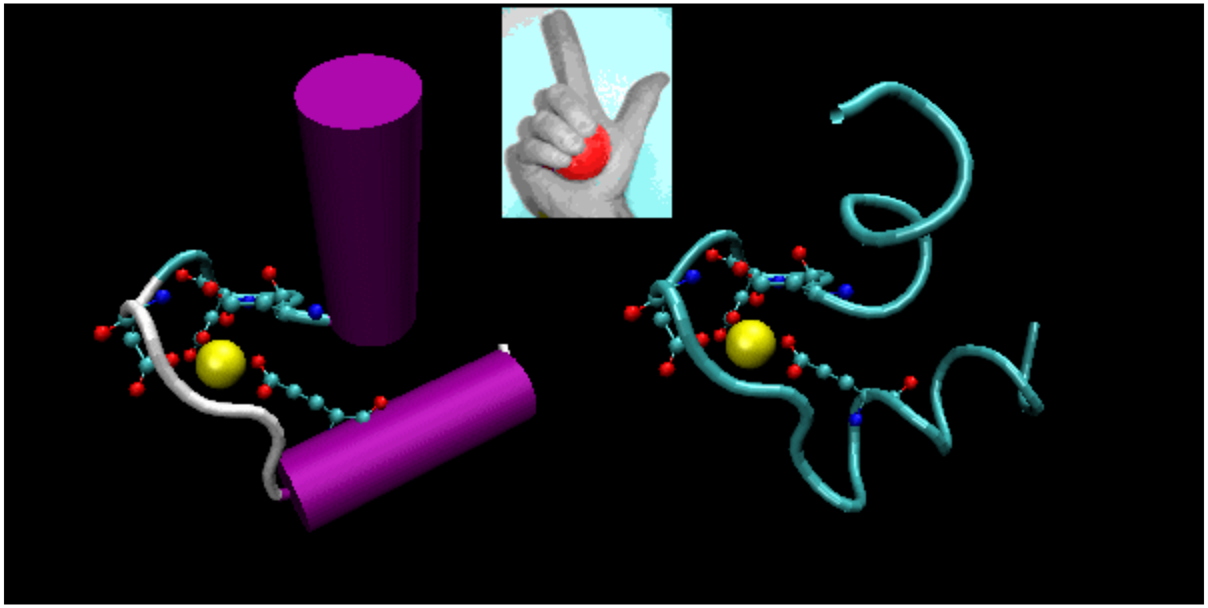
DNA and Calcium Binding sites

Helix-Loop-Helix

http://employees.csbsju.edu/hjakubowski/Jmol/Lambda_Repressor/Lambda_Repressor.htm

EF-Hand

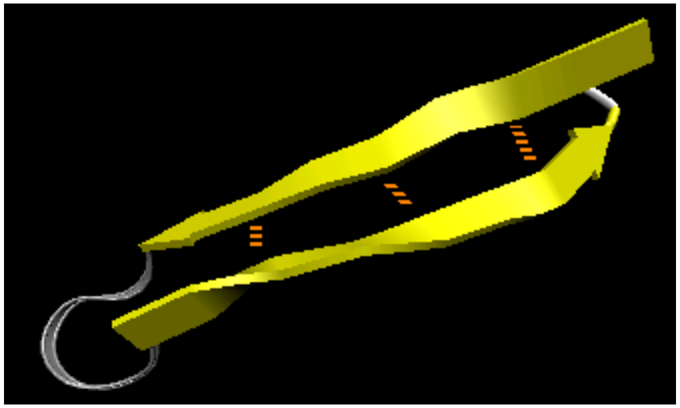
http://employees.csbsju.edu/hjakubowski/Jmol/Calmodulin_EF_Hand/Calmodulin_EF_Hand.htm



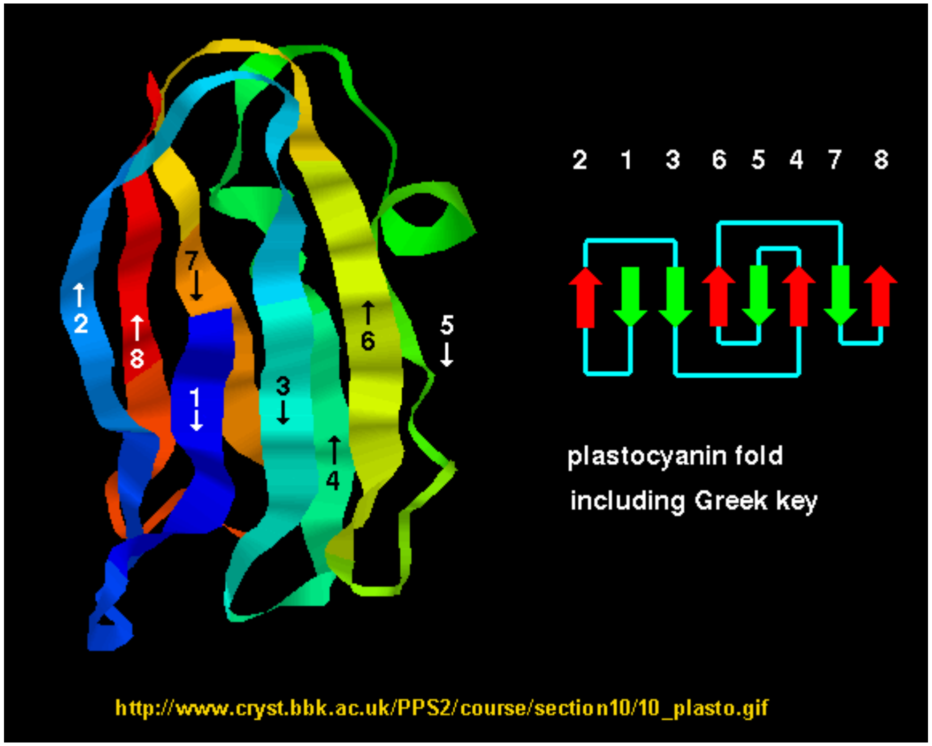
Super-Secondary Structures

β-Hairpin or Beta-Beta in Anti-Parallel Structures

http://employees.csbsju.edu/hjakubowski/Jmol/Bovine%20Pancreatic%20Trypsin%20Inhibitor/Bovine_Pancreatic_Trypsin_Inhibitor.htm

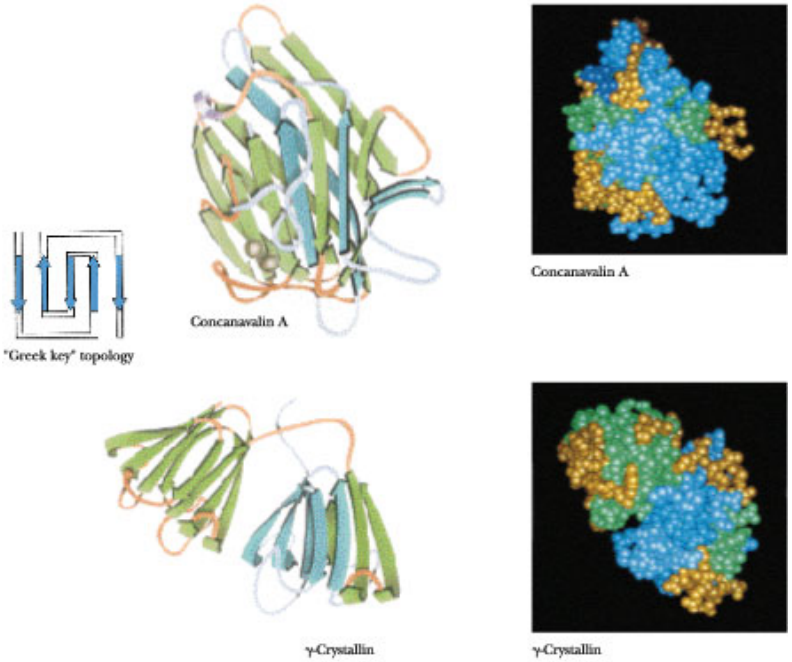


Greek Key Motif



plastocyanin fold
including Greek key

http://www.cryst.bbk.ac.uk/PPS2/course/section10/10_plasto.gif

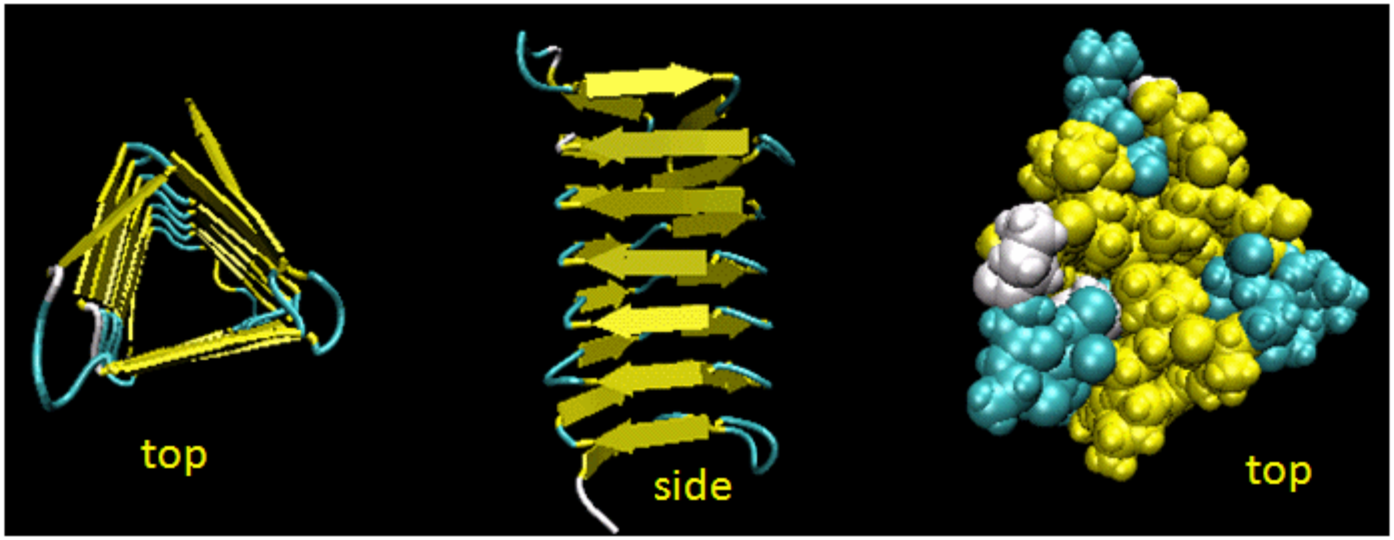


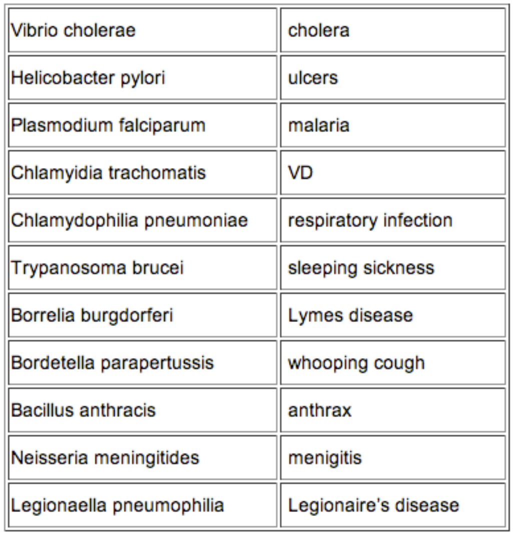
Beta-Alpha-Beta (to connect two parallel β-sheets)

http://employees.csbsju.edu/hjakubowski/Jmol/BETA-ALPHA-BETA_MOTIFF/BETA-ALPHA-BETA_MOTIFF.htm

β-Helicies (seen in pathogens, viruses, bacteria)

http://cti.itc.virginia.edu/~cmg/Demo/pdb/ap/ap.htm





Vibrio cholerae	cholera
Helicobacter pylori	ulcers
Plasmodium falciparum	malaria
Chlamyidia trachomatis	VD
Chlamydophilia pneumoniae	respiratory infection
Trypanosoma brucei	sleeping sickness
Borrelia burgdorferi	Lymes disease
Bordetella parapertussis	whooping cough
Bacillus anthracis	anthrax
Neisseria meningitides	menigitis
Legionaella pneumophilia	Legionaire's disease

Many β-Topologies

http://www.cryst.bbk.ac.uk/PPS2/course/section10/all_beta.html

3 Classes of Proteins (Characteristic Secondary Structures)

α-Proteins

Cytochrome B562

http://employees.csbsju.edu/hjakubowski/Jmol/Cytochrome_B562/Cytochrome_B562.htm

Met-Myoglobin

http://employees.csbsju.edu/hjakubowski/Jmol/Met-Myoglobin

αβ-Proteins

Triose Phosphate Isomerase

http://employees.csbsju.edu/hjakubowski/Jmol/Triose%20Phosphate%20Isomerase/TRIOSE_PHOSPHATE_ISOMERASE.htm

Hexokinase

http://employees.csbsju.edu/hjakubowski/Jmol/Hexokinase/HEXOKINASE.htm

β-Proteins

Superoxide Dismutase

http://employees.csbsju.edu/hjakubowski/Jmol/Superoxide%20Dismutase/SUPEROXIDE_DISMUTASE.htm

Human IgG1 Antibody

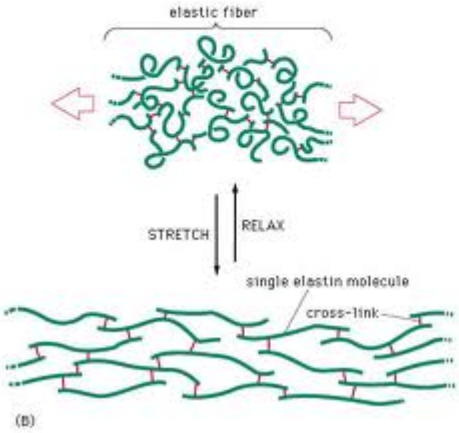
http://employees.csbsju.edu/hjakubowski/Jmol/Human%20Antibody%20Molecule-IgG1/Human_Antibody_Molecule%C2%AD_IgG1.htm

Retinol Binding Protein

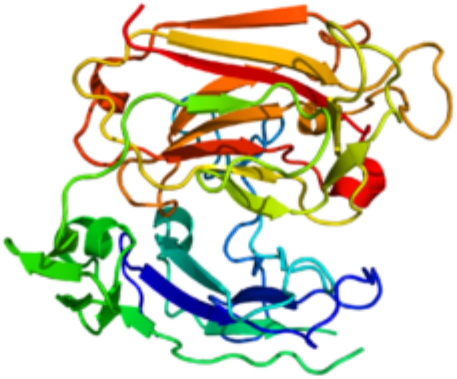
http://employees.csbsju.edu/hjakubowski/Jmol/Retinol%20Binding%20Protein/RETINOL_BINDING_PROTEIN.htm

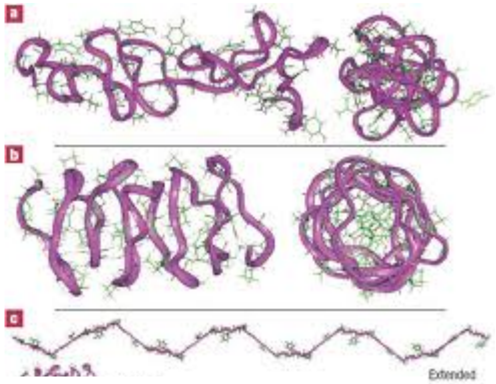
Fibrillar (elastic) versus Globular Proteins

Elastin (Blood Vessels) β-sheets and α-helicies with β-turns



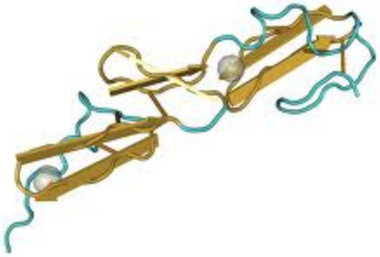
Reslin (Insects Wings)





Silk (Spiders etc.) β-sheets and α-helicies with β-turns

Fibrillin (Cartilage) - Folded β-Sheet like and Accordian

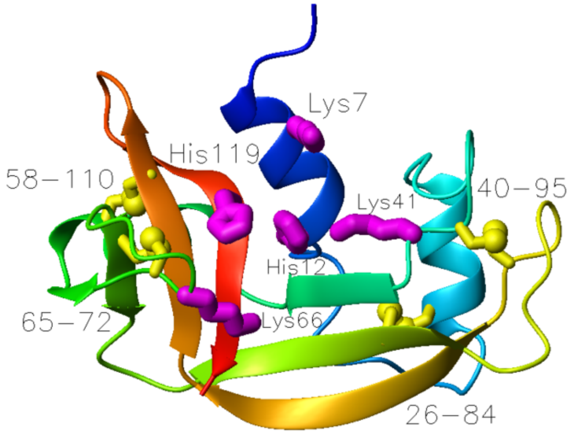


Tertiary Structure and Protein Folding

Consider a protein of 100 residues each with two bond angles Φ and ψ that can take 3 positions each so 9 conformations. The chain has $9^{100} = 2.7 \times 10^{95}$ conformations. Even with 10^{-13}s to change a conformation, it would take 8.4×10^{74} years to probe all conformations (that is along time).
Such a protein folds in less than a second.
This is called Levinthal's Paradox.

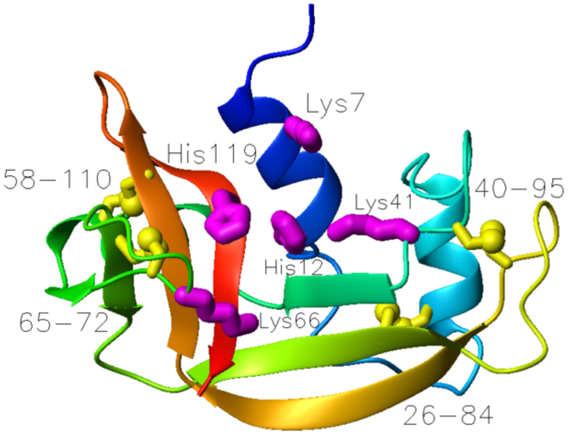
The key to resolving Levinthal's Paradox is to limit the choices.

Disulfide bonds are a major limiting factor,
Consider Ribonuclease (RNase A) (an enzyme that degrades RNA)
Having 4 disulfide bonds that serve as tethers for the folding process.



RNase A

http://www.rcsb.org/pdb/explore/jmol.do?structureId=7RSA&bionumber=1



Folds “like a taco” to bind with the RNA substrate

Armour purified 1 kilo and gave it away for study

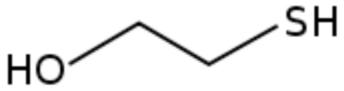
124 residues 13.7 kDa
Polycation that binds with polyanionic RNA
Positive charges are in the taco cleft.

Nobel Prize Lecture published as:
Anfinsen, C.B. (1973) "Principles that govern the folding of protein chains." Science 181 223-230.

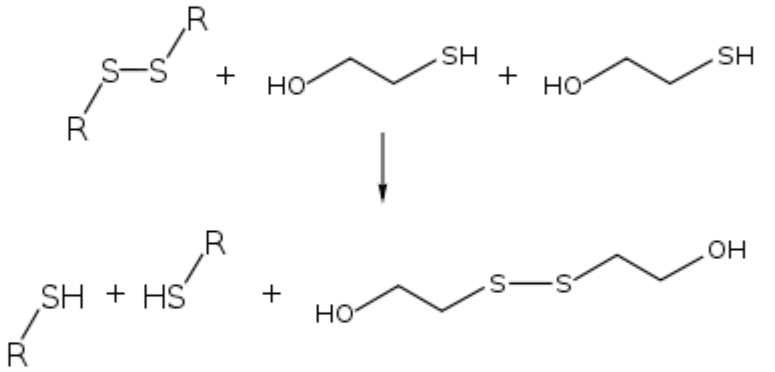
Anfinsen Postulate: For Small Globular Proteins the Tertiary Structure is determined only by the amino acid sequence

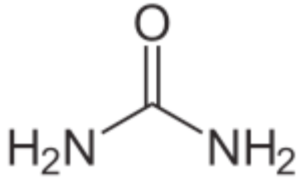
RNase Structure

http://employees.csbsju.edu/hjakubowski/Jmol/RNase/RNase.htm



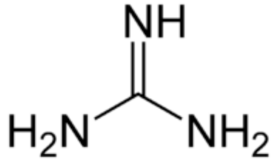
β-Mercapto Ethanol





Urea

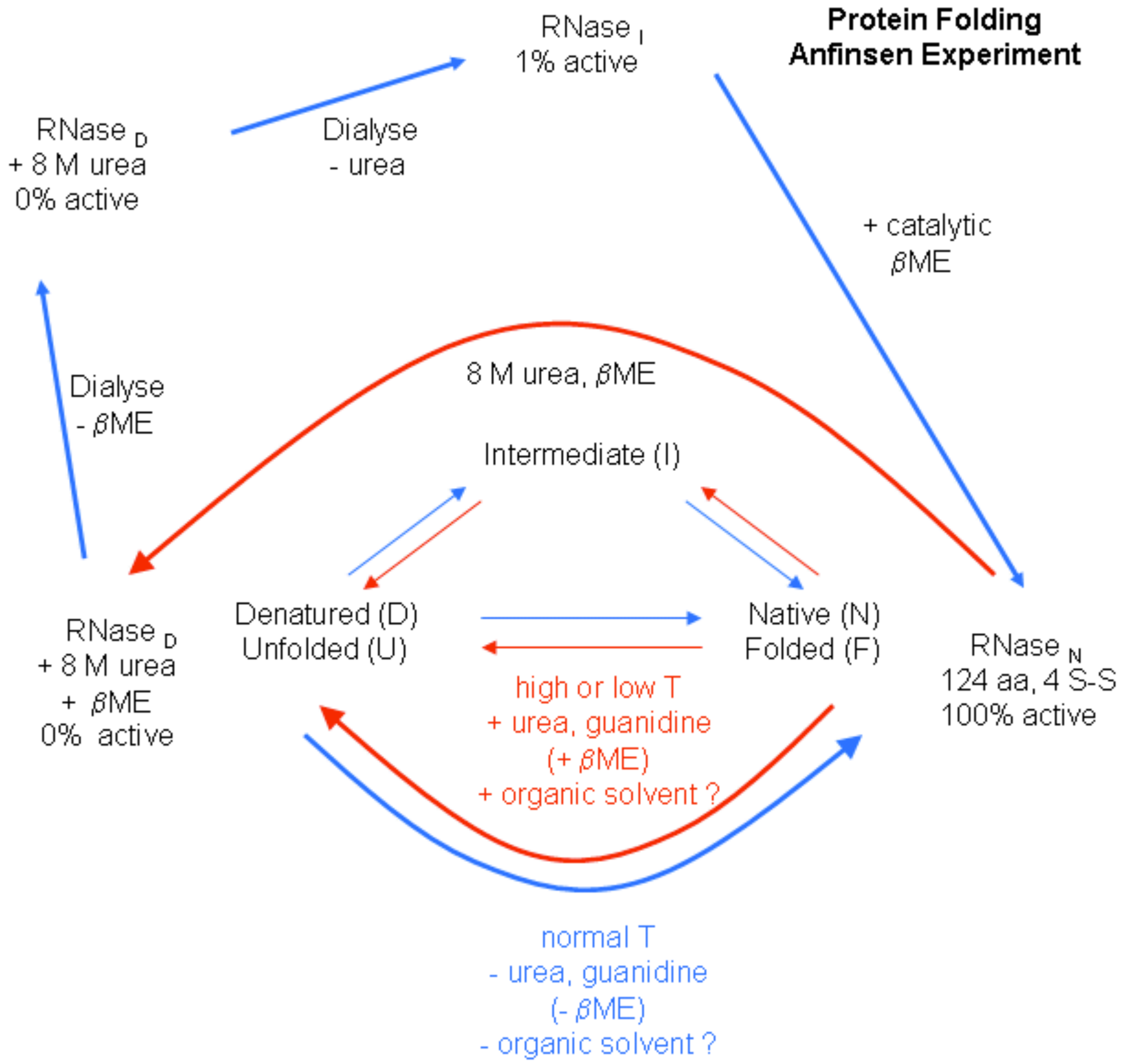
Competes with H-Bonds
Denatures (Destablizes) Proteins



Guanidine-HCl

Competes with H-Bonds
Denatures (Destablizes) Proteins

Figure: Anfinsen Experiment: Folding of RNase



Protein Folding
Anfinsen Experiment

RNase_I
1% active

+ catalytic
βME

RNase_N
124 aa, 4 S-S
100% active

8 M urea, βME

RNase_D
+ 8 M urea
0% active

Dialyse
- urea

Dialyse
- βME

RNase_D
+ 8 M urea
+ βME
0% active

Intermediate (I)

Denatured (D)
Unfolded (U)

Native (N)
Folded (F)

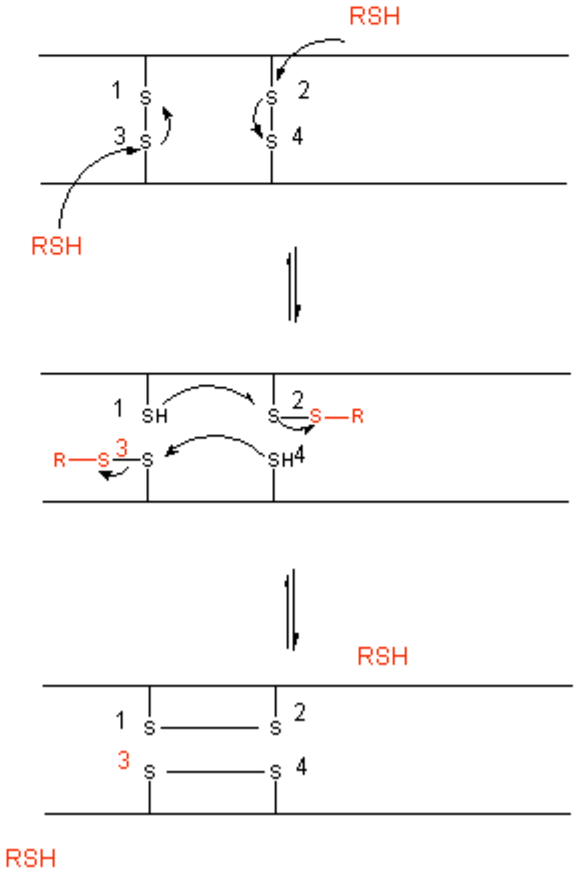
high or low T
+ urea, guanidine
(+ βME)
+ organic solvent ?

normal T
- urea, guanidine
(- βME)
- organic solvent ?

http://employees.csbsju.edu/hjakubowski/classes/ch331/protstructure/olprotfold.html

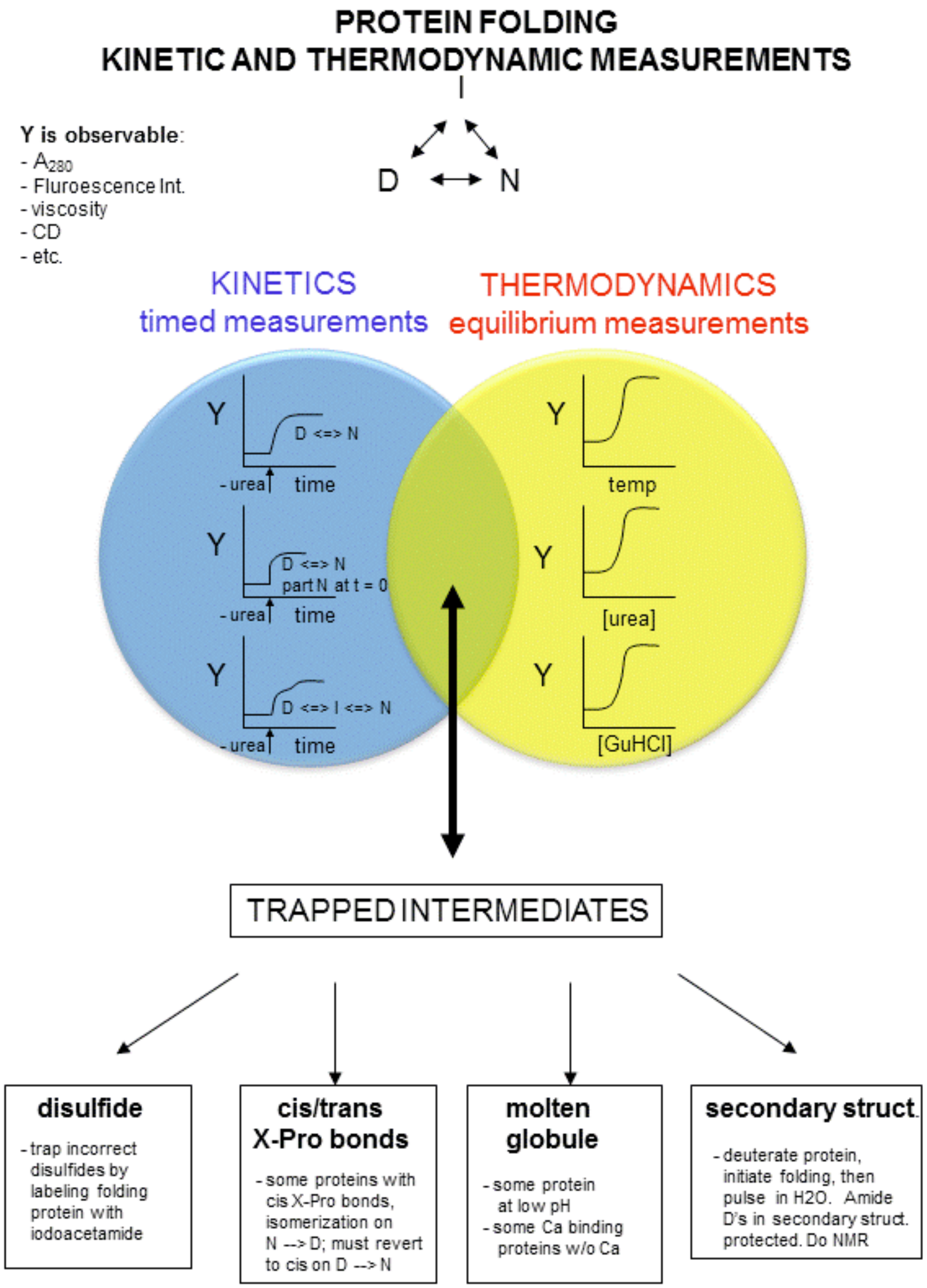
Figure: CATALYTIC SHUFFLING OF DISULFIDES WITH BETA-MERCAPTOETHANOL

Disulfide Shuffling using catalytic [β-mercaptoethanol]



http://employees.csbsju.edu/hjakubowski/classes/ch331/protstructure/olprotfold.html

Figure: Kinetic and thermodynamic measurements of proteins stability and folding



PROTEIN FOLDING
KINETIC AND THERMODYNAMIC MEASUREMENTS

Y is observable:
- A_{280}
- Fluroescence Int.
- viscosity
- CD
- etc.

KINETICS
timed measurements

THERMODYNAMICS
equilibrium measurements

TRAPPED INTERMEDIATES

disulfide
- trap incorrect disulfides by labeling folding protein with iodoacetamide

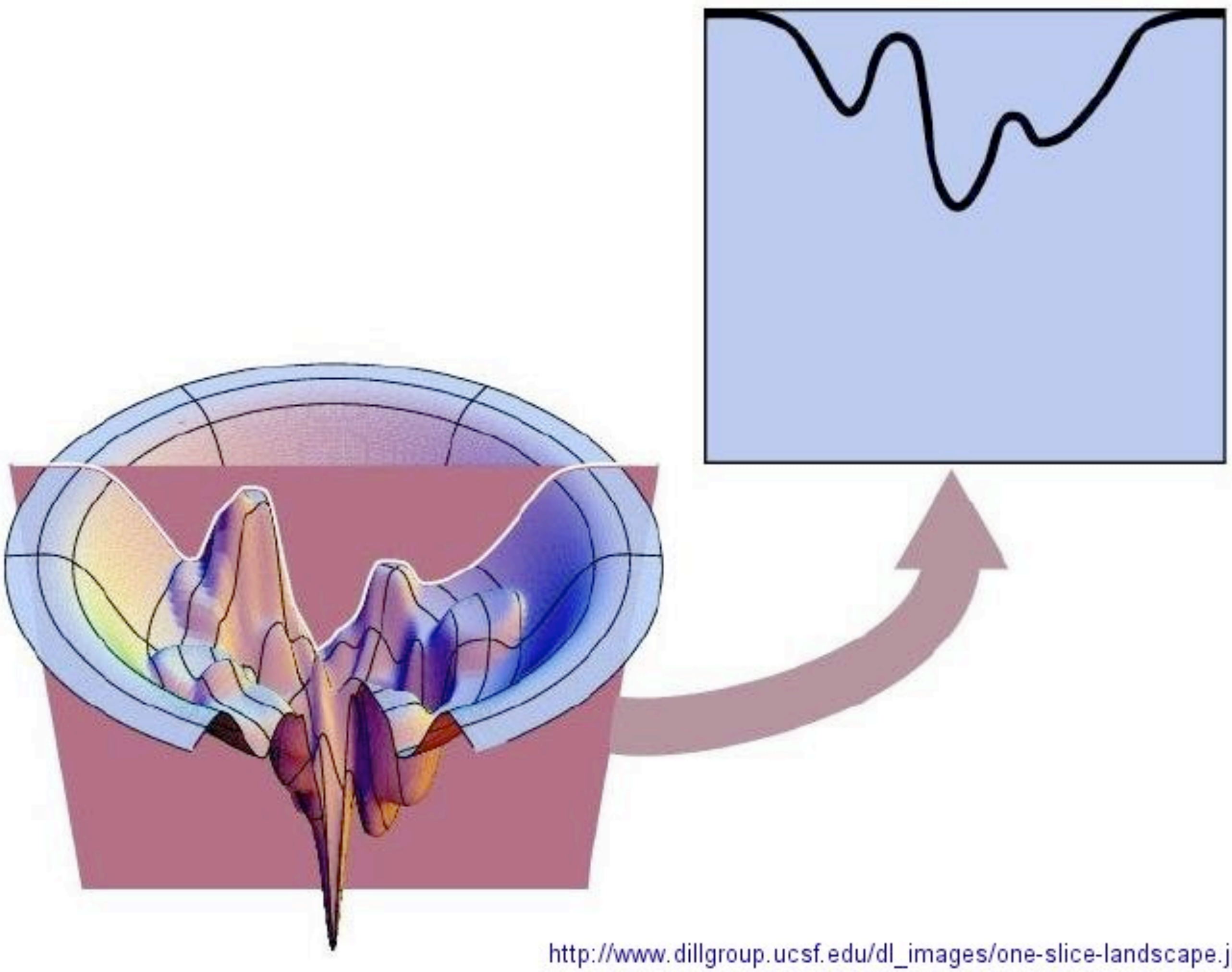
cis/trans X-Pro bonds
- some proteins with cis X-Pro bonds, isomerization on N --> D; must revert to cis on D --> N

molten globule
- some protein at low pH
- some Ca binding proteins w/o Ca

secondary struct.
- deuterate protein, initiate folding, then pulse in H2O. Amide D's in secondary struct. protected. Do NMR

Native state is a “Global Minimum in Free Energy” Folding Process Occurs on an Energy “Funnel”

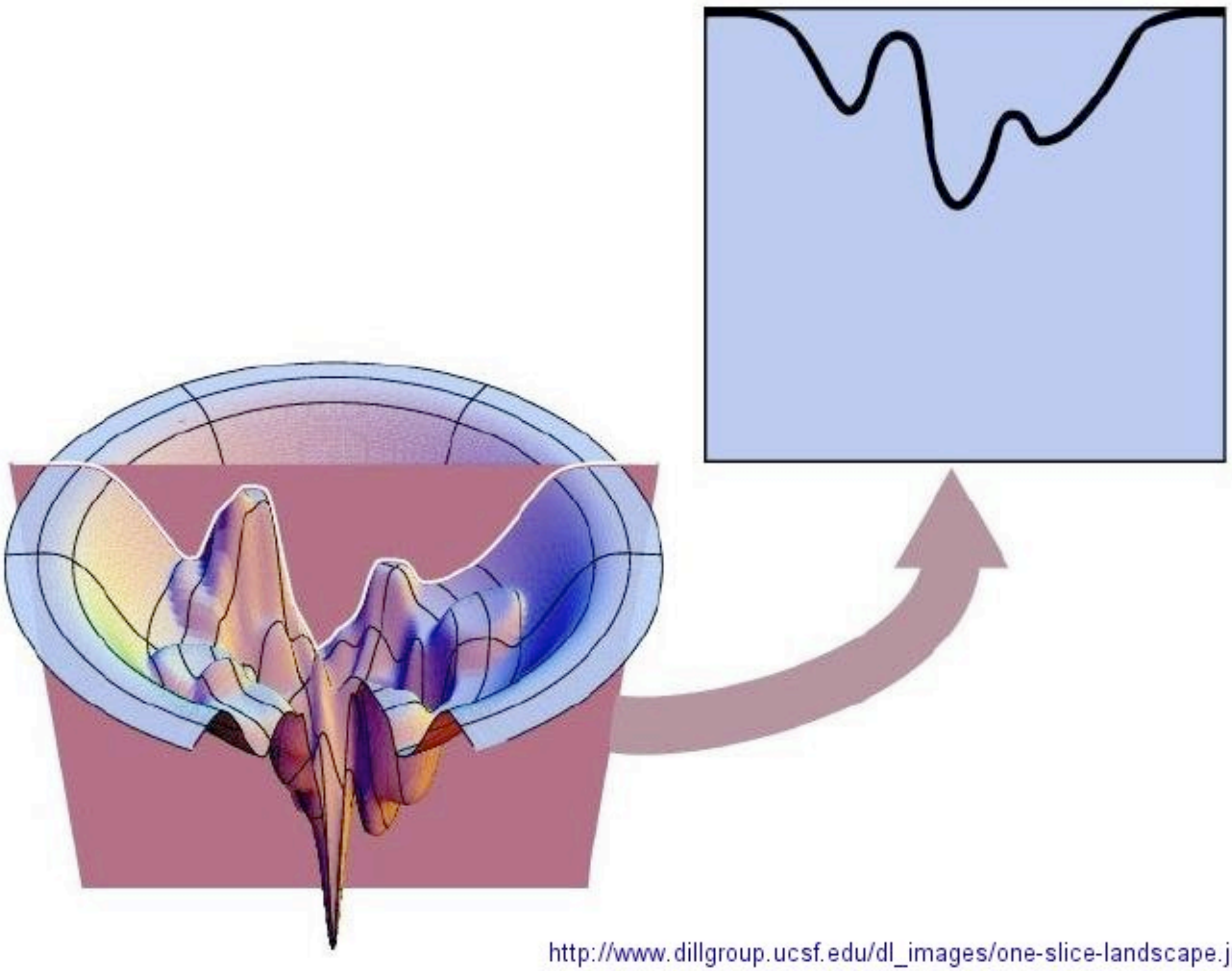
Figure: Protein Folding Landscape: One View from Ken Dill



http://www.dillgroup.ucsf.edu/dl_images/one-slice-landscape.jpg

Folding does not occur by a single pathway, but is a statistical process of searching the energy landscape for minima For large proteins we see intermediates, molten globules, non-biologically active dense states

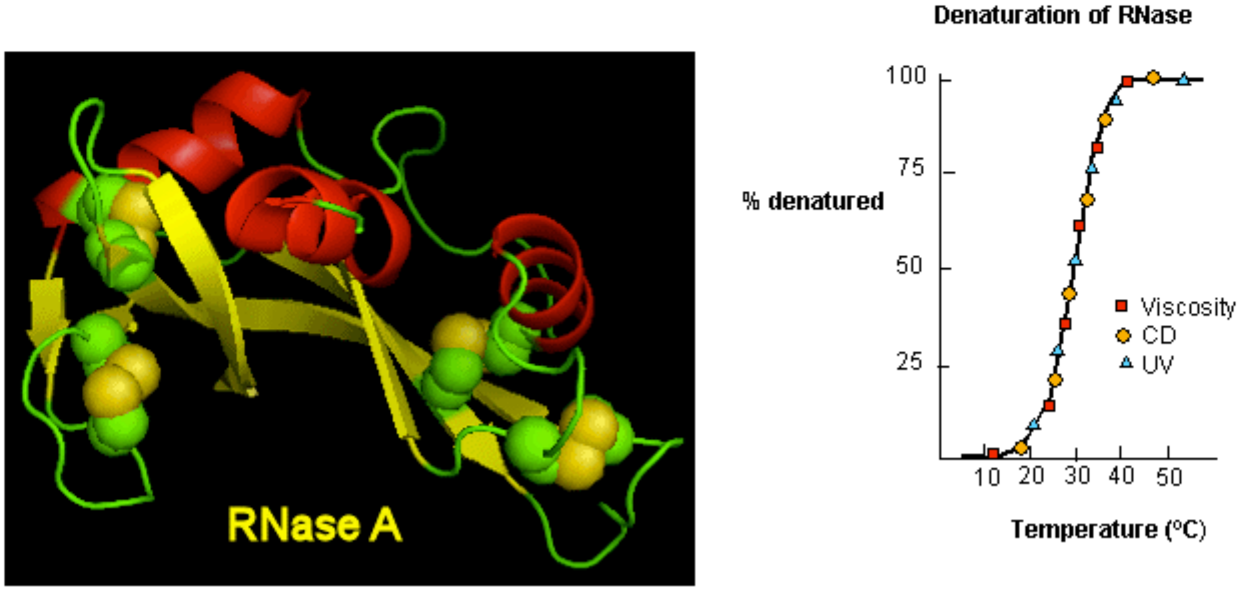
Figure: Protein Folding Landscape: One View from Ken Dill



http://www.dillgroup.ucsf.edu/dl_images/one-slice-landscape.jpg

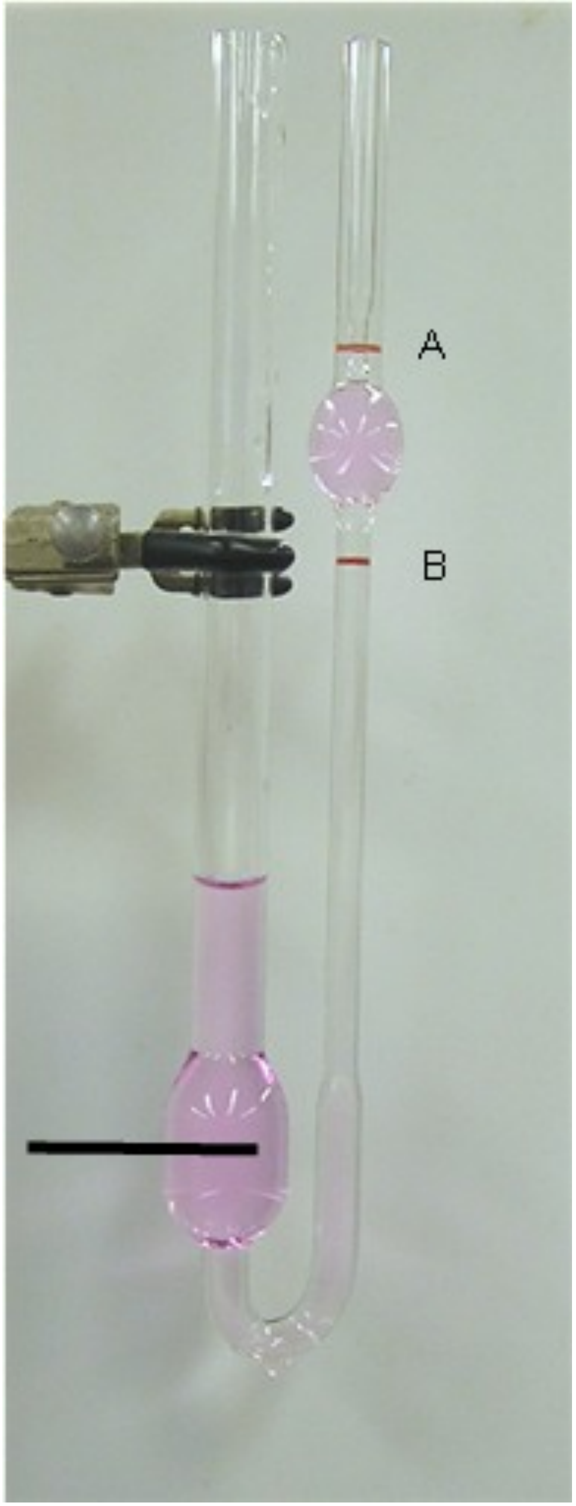
Simple proteins undergo a cooperative process

Figure: Reversible denaturation

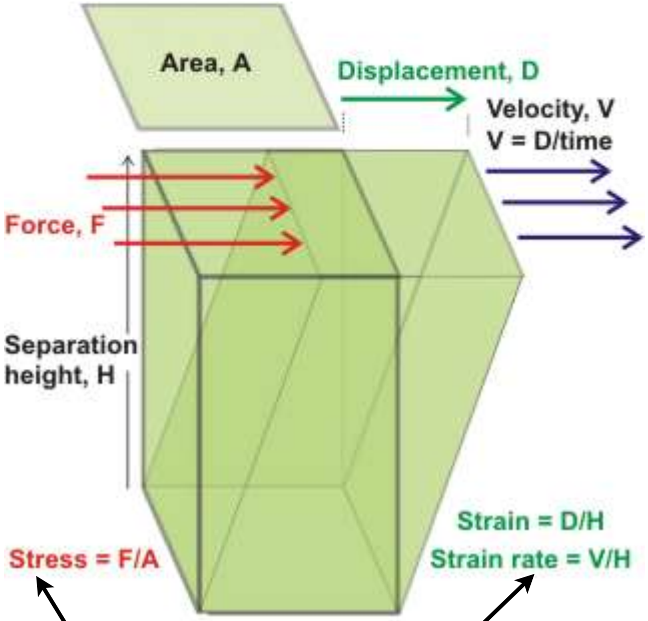


after Ginsburg and Carroll, Biochemistry 4, pg 2159 (1965)

y-axis could be
viscosity (hydrodynamic radius),
circular dichroism,
fluorescence,
diffusion coefficient (hydrodynamic radius) from dynamic light scattering,
radius of gyration from static light scattering



Viscosity



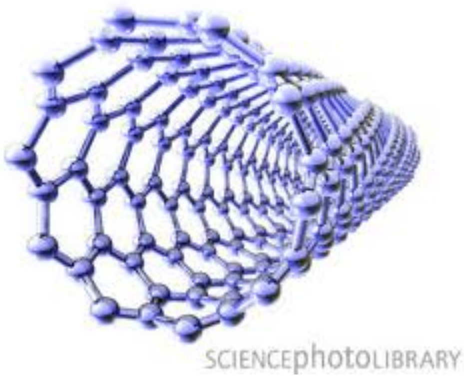
$$\tau = \eta\dot{\gamma}$$

$$\eta_s = \eta_0\left(1+[\eta]\phi\right)$$

$$[\eta] \approx \frac{V_{Molecule}}{M_{Moledule}}$$

Native state has the smallest volume

Mass Fractal Dimension, $1 \leq d_f \leq 3$

	Mass ~ Size^1	1-d	$d_f = 1$
	Mass ~ Size^2	2-d	$d_f = 2$
	Mass ~ Size^3	3-d	$d_f = 3$

Mass Fractal Dimension, $1 \leq d_f \leq 3$

Random (Brownian) Walk
θ-Solvent Condition

Mass ~ $Size^2$ 2-d $d_f = 2$

Self-Avoiding Walk/Expanded Coil
Good Solvent Condition

Mass ~ $Size^{1.67}$ $d_f = 5/3$

In the collapse transition from an expanded coil to a native state for a protein of 100 residues (N = Mass = 100)
Size ~ 15.8 for Expanded Coil (10 for Gaussian) and 4.6 for Native State
For N = 10000 this becomes 251 : 100 : 21.5
For large proteins the change in size is dramatic (order of 10x)

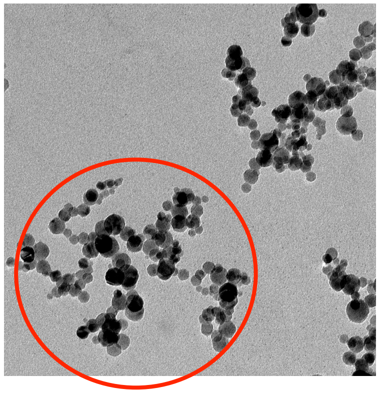
1) Mass Fractal dimension, d_f.

$$z = \alpha\left(\frac{2R}{d_p}\right)^{d_f}$$

z is mass/DOA
d_p is bead size
R is coil size

Random aggregation (right) $d_f \sim 1.8$;
Randomly Branched Gaussian $d_f \sim 2.5$;
Self-Avoiding Walk $d_f = 5/3$

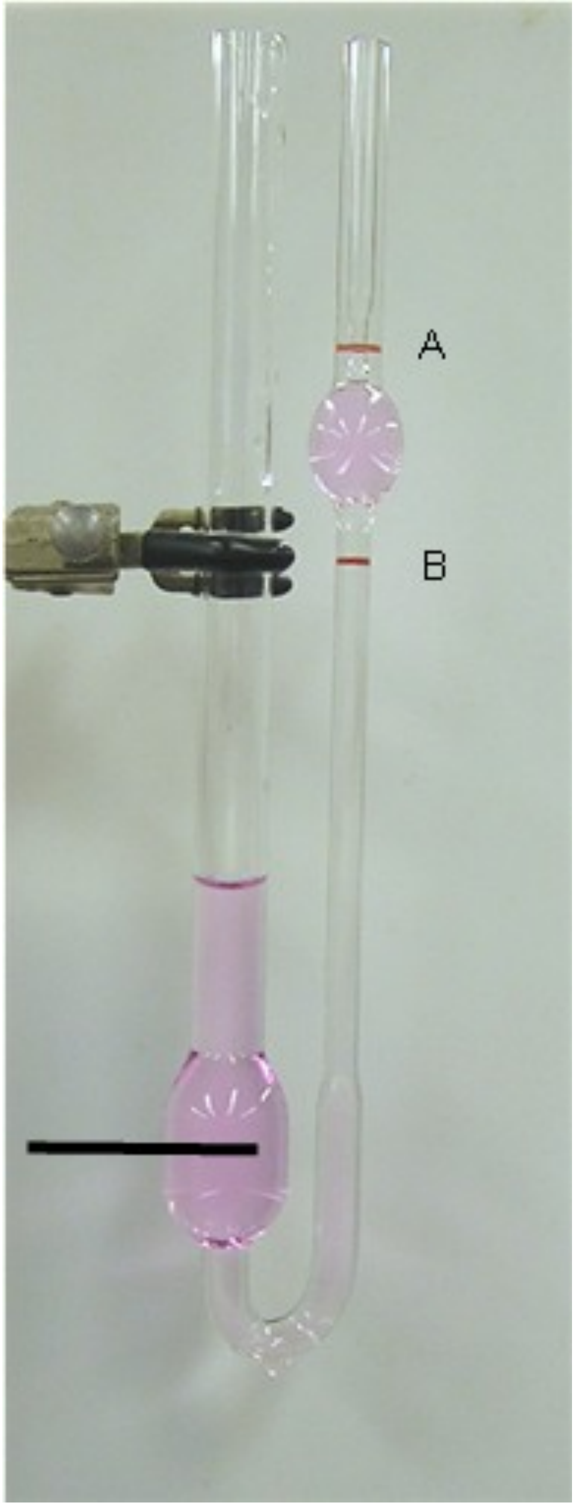
Problem:
Disk $d_f = 2$
Gaussian Walk d_f=2



Nano-titania from Spray Flame

$2R/d_p = 10$, a ~ 1, z ~ 220
$d_f = \ln(220)/\ln(10) = 2.3$

A Measure of Branching is not Given.



Viscosity

$$\eta_s = \eta_0 \left(1 + [\eta]\phi\right)$$

$$[\eta] \approx \frac{V_{Molecule}}{M_{Moledule}}$$

For the Native State Mass ~ ρ $V_{Molecule}$

Einstein Equation (for Suspension of 3d Objects)

$$\eta_s = \eta_0 \left(1 + 2.5\phi\right)$$

For "Gaussian" Chain Mass ~ Size^2 ~ $V^{2/3}$

V ~ $\text{Mass}^{3/2}$

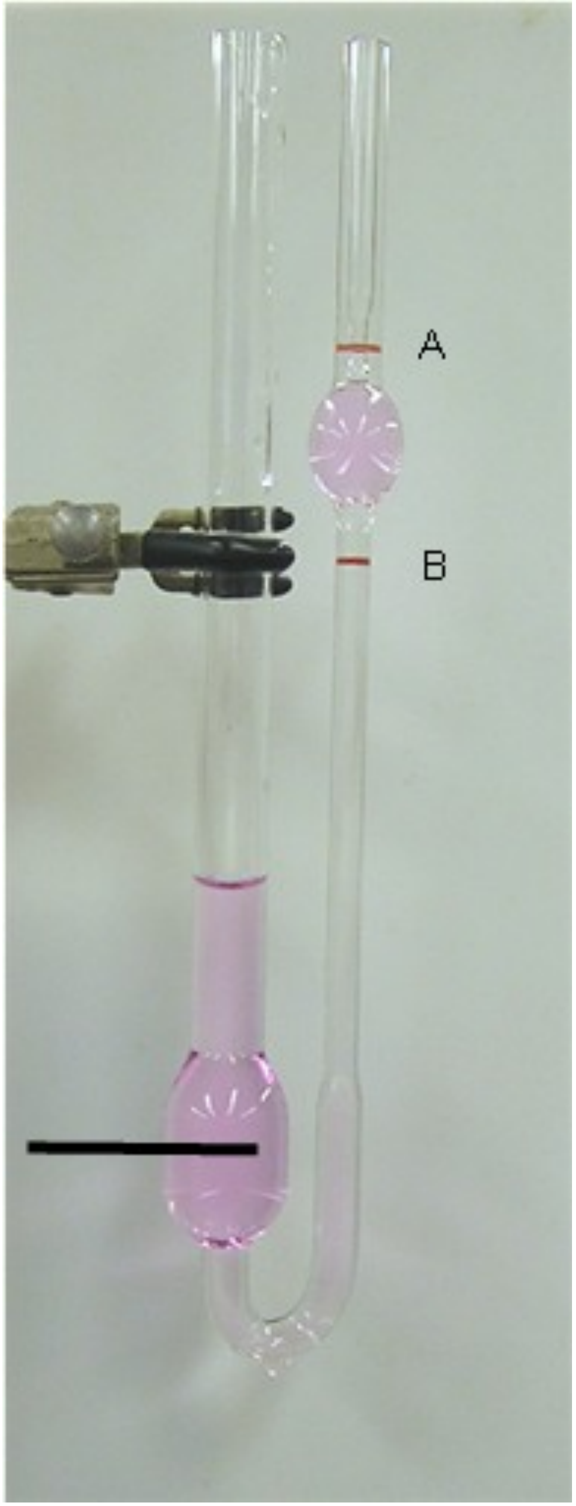
For "Expanded Coil" Mass ~ $\text{Size}^{5/3}$ ~ $V^{5/9}$

V ~ $\text{Mass}^{9/5}$

For "Fractal" Mass ~ Size^{df} ~ $V^{df/3}$

V ~ $\text{Mass}^{3/df}$

$$[\eta] \sim M_{Molecule}^{\frac{3}{d_f}-1}$$



Viscosity

$$\eta_s = \eta_0\left(1+[\eta]\phi\right)$$

$$[\eta] \approx \frac{V_{Molecule}}{M_{Moledule}}$$

For the Native State Mass ~ $\rho V_{Molecule}$

Einstein Equation (for Suspension of 3d Objects)

$$\eta_s = \eta_0\left(1+2.5\phi\right)$$

For "Gaussian" Chain Mass ~ $Size^2 \sim V^{2/3}$

$V \sim Mass^{3/2}$

"Size" is the "Hydrodynamic Size"

For "Expanded Coil" Mass ~ $Size^{5/3} \sim V^{5/9}$

$V \sim Mass^{9/5}$

For "Fractal" Mass ~ $Size^{df} \sim V^{df/3}$

$V \sim Mass^{3/df}$

$$[\eta] \sim M_{Molecule}^{\frac{3}{d_f}-1}$$

Circular Dichroism

Light Polarization

http://www.enzim.hu/~szia/cddemo/edemo0.htm?CFID=1025184&CFTOKEN=88815524

CD Spectroscopy for Proteins

http://www.cryst.bbk.ac.uk/PPS2/course/section8/ss-960531_21.html

http://www.ruppweb.org/cd/cdtutorial.htm

Wikipedia on CD

http://en.wikipedia.org/wiki/Circular_dichroism

$\Delta\varepsilon = \varepsilon_L - \varepsilon_R$ Molar Circular Dichroism (c = molar concentration)

$\Delta A = cl\Delta\varepsilon$ Difference in Absorption

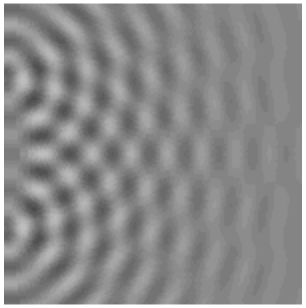
$[\theta] = 3298.2\Delta\varepsilon$ Degrees of Ellipticity

These change with the extent and nature of secondary structure such as helicies

Examples of CD

http://www.ap-lab.com/circular_dichroism.htm

Binary Interference Yields Scattering Pattern.

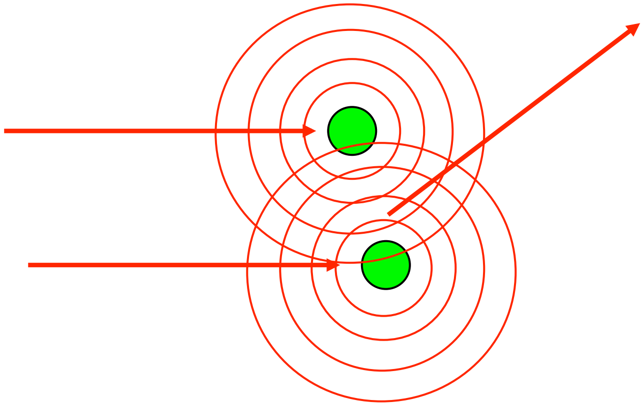


$I(q) \sim N\, n_e^2$

n_e Reflects the density of a Point generating waves

N is total number of points

The Scattering Event



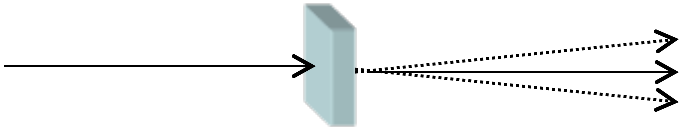
I(q) is related to amount Nn^2

q is related to size/distances

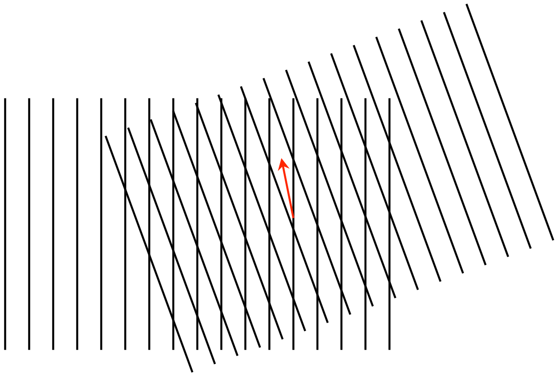
$$q = \frac{4\pi}{\lambda}\sin\left(\theta/2\right)$$

$$d = \frac{2\pi}{q}$$

2) Rather than consider specific structures, we can consider *general scattering laws* by which all scatters are governed under the premises that 1) "Particles" have a size and 2) "Particles" have a surface.



Binary Interference Yields Scattering Pattern.



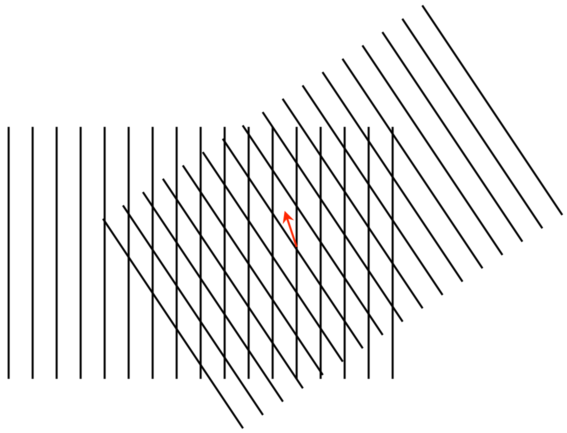
-Consider that an in-phase wave scattered at angle θ was in phase with the incident wave at the source of scattering.

-This can occur for points separated by ***r*** such that

|r| = 2θ/|q|

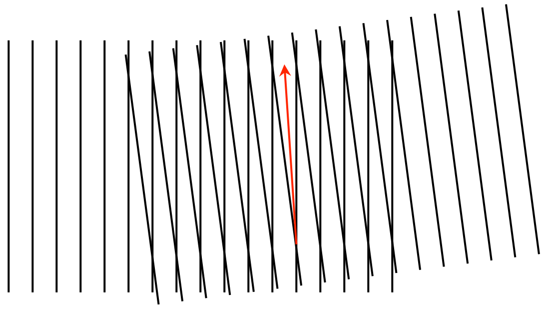
- $q = \frac{4\pi}{\lambda}\sin\frac{\theta}{2}$

Binary Interference Yields Scattering Pattern.



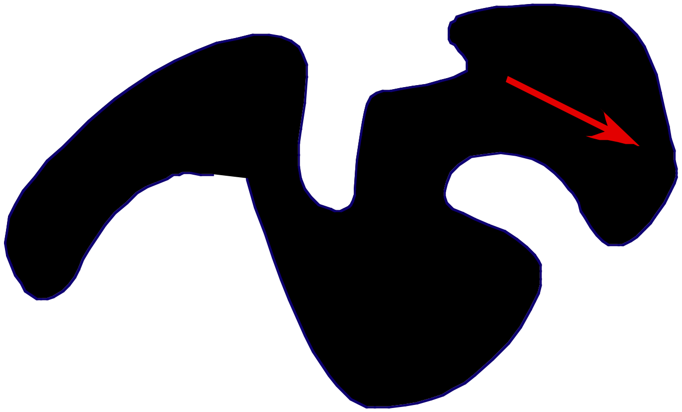
-For high θ, ***r*** is small

Binary Interference Yields Scattering Pattern.

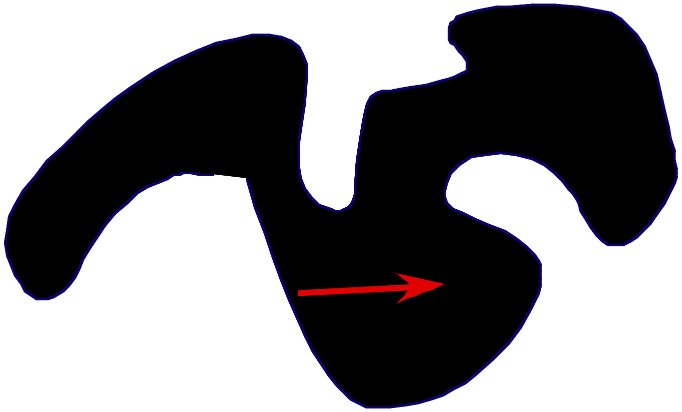


-For small θ, ***r*** is large

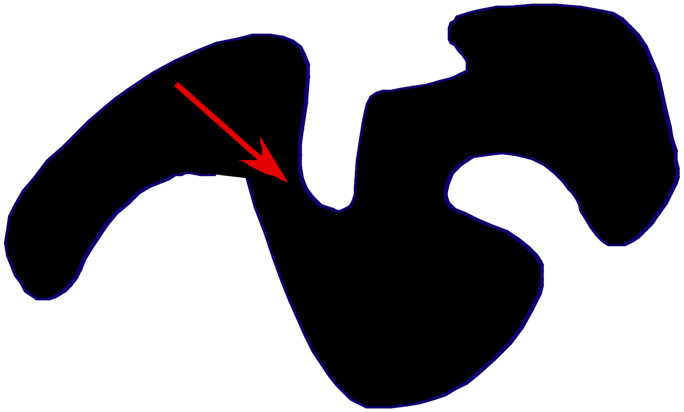
For an isotropic sample we consider scattering as arising from the probability of the random placement of a vector ***r*** in the scattering phase.



For an isotropic sample we consider scattering as arising from the probability of the random placement of a vector ***r*** in the scattering phase.

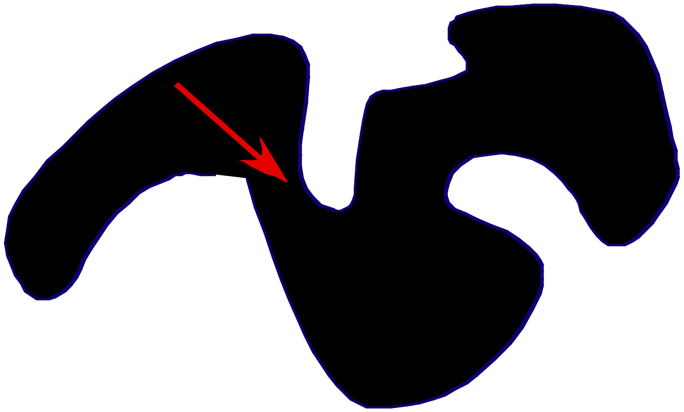


For an isotropic sample we consider scattering as arising from the probability of the random placement of a vector ***r*** in the scattering phase.



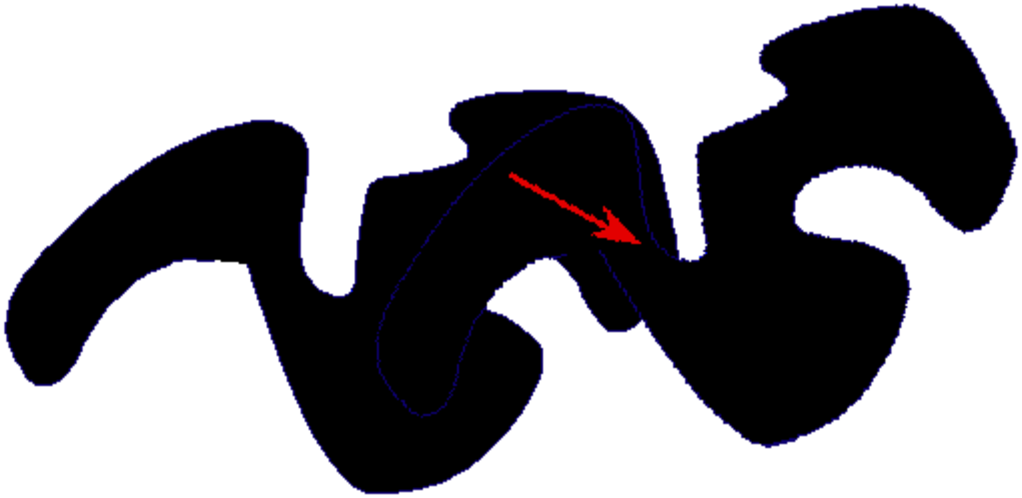
Rather than random placement of the vector we can hold
The vector fixed and rotate the particle

For an isotropic sample we consider scattering as arising from the probability of the random placement of a vector ***r*** in the scattering phase.



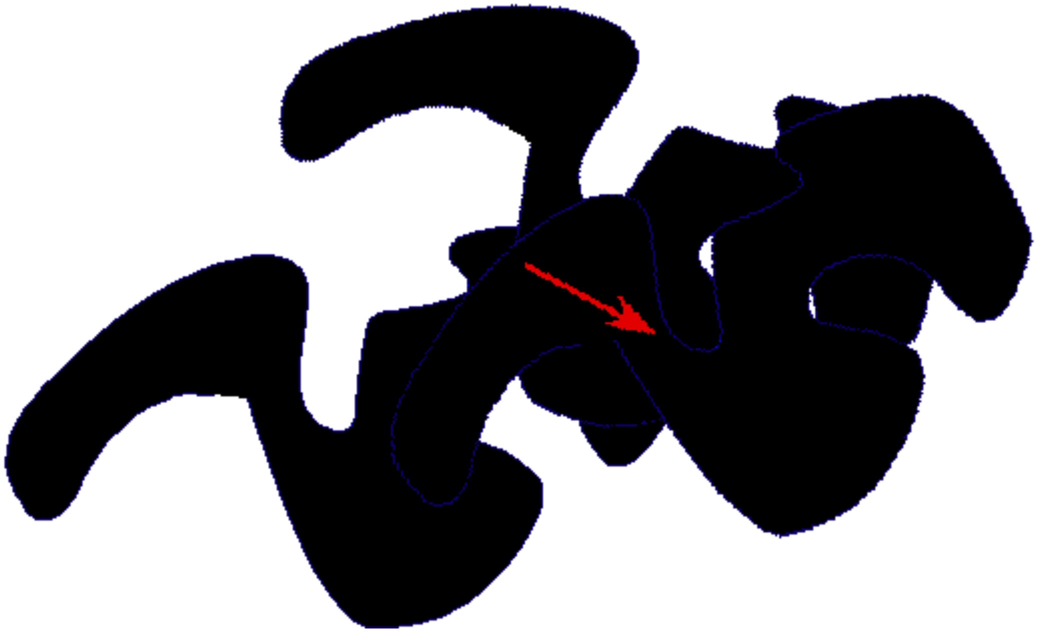
Rather than random placement of the vector we can hold
The vector fixed and rotate the particle

For an isotropic sample we consider scattering as arising from the probability of the random placement of a vector ***r*** in the scattering phase.



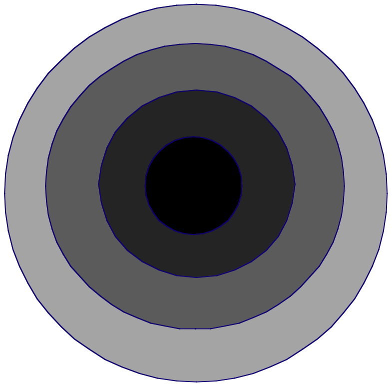
Rather than random placement of the vector we can hold
The vector fixed and rotate the particle

For an isotropic sample we consider scattering as arising from the probability of the random placement of a vector ***r*** in the scattering phase.



Rather than random placement of the vector we can hold The vector fixed and rotate the particle

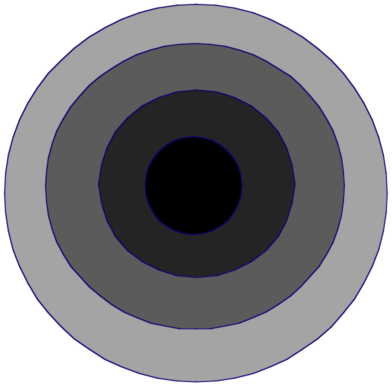
The particle becomes a probability density function from the center of mass.



That follows a Gaussian Distribution.

$$p(r) = \exp\left(\frac{-3r^2}{4R_g^2}\right)$$

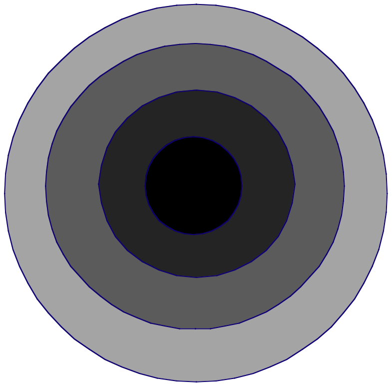
The particle becomes a probability density function from the center of mass.



Whose Fourier Transform is Guinier's Law.

$$p(r) = \exp\left(\frac{-3r^2}{4R_g^2}\right) \quad \Rightarrow \quad \mathrm{I(q)} = G\exp\left(-\frac{q^2R_g^2}{3}\right)$$

$$\mathrm{G} = \mathrm{Nn_e^2}$$

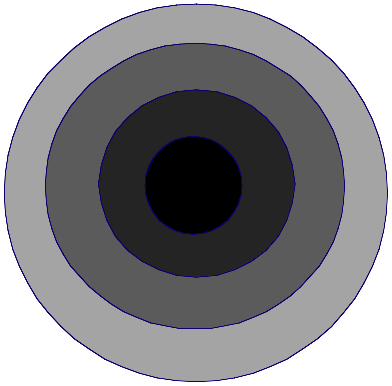


Guinier's Law Pertains to a Particle with no Surface.

$$p(r) = \exp\left(\frac{-3r^2}{4R_g^2}\right) \qquad \Rightarrow \qquad \mathrm{I(q)} = G\exp\left(-\frac{q^2R_g^2}{3}\right)$$

$$\mathrm{G} = \mathrm{Nn_e^2}$$

Any "Particle" can be Approximated as a Gaussian probability distribution in this context.



$$p(r) = \exp\left(\frac{-3r^2}{4R_g^2}\right) \qquad \Rightarrow \qquad \mathrm{I(q)} = G\exp\left(-\frac{q^2R_g^2}{3}\right)$$

$$\mathrm{G} = \mathrm{Nn_e^2}$$

Guinier's Law can be thought of as the
First Premise of Scattering:
All "Particles" have a size reflected by the radius of gyration.

Static Light Scattering for Radius of Gyration

Consider binary interference at a distance "r" for a particle with arbitrary orientation
Rotate and translate a particle so that two points separated by r lie in the particle for all rotations and average the structures at these different orientations

Guinier's Law

$$\gamma_{Gaussian}(r) = \exp\left(-3r^2 \big/ 2\sigma^2\right)$$

Binary Autocorrelation Function

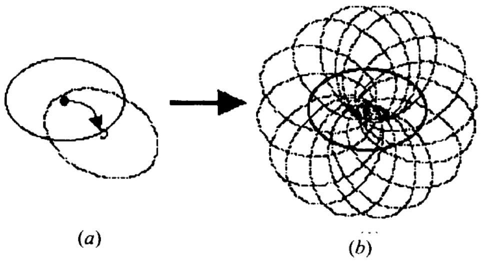


Fig. 4. Averaging of a particle about the origin of the vector **r** in analogy to random translations and rotations of the particle about the origin of **r**. In (*a*), a single rotation and a single translation are considered. In (*b*), the superposition of a number of such translations and rotations in random directions leads to a Gaussian distribution of scattering density $\rho(r)$.

$$\sigma^2 = \frac{\sum_{i=1}^{N}(x_i-\mu)^2}{N-1} = 2R_g^2$$

$$I(q) = I_e N n_e^2 \exp\left(-R_g^2 q^2 \big/ 3\right)$$

Lead Term is

$$I(0) = N n_e^2$$

$$I(1/r) \sim N(r)n(r)^2$$

Scattered Intensity is the Fourier Transform of The Binary Autocorrelation Function

$$\gamma_0(r) = 1 - \frac{S}{4V}r + \ldots$$

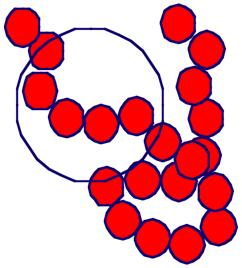
$$\exp\left(\frac{-3r^2}{4R_g^2}\right) \approx 1 - \frac{3r^2}{4R_g^2} + \ldots$$

$$r \Rightarrow 0 \;\; \text{then} \;\; d\left(\gamma_{Gaussian}(r)\right) \big/ dr \Rightarrow 0$$

A particle with no surface

Beaucage G *J. Appl. Cryst.* **28** 717-728 (1995).

At intermediate sizes the chain is “self-similar”



$$Mass \sim Size^{d_f}$$

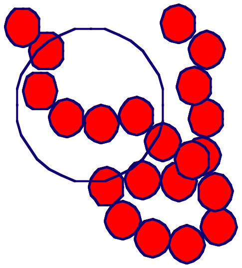
$$z \sim \left(\frac{R_2}{R_1}\right)^{d_f}$$

At intermediate sizes the chain is “self-similar”

$I(q) \sim N\, n_e^2$

N = Number of Intermediate Spheres in the Aggregate

n_e = Mass of inter. sphere



$I(q) \sim N\, n_e^2$

$$N \sim \left(\frac{R_2}{r_{\text{int}}}\right)^{d_f}$$

$$n_e \sim \left(\frac{r_{\text{int}}}{R_1}\right)^{d_f}$$

$$N n_e^2 \sim \left(\frac{r_{\text{int}}}{R_1}\right)^{d_f}\left(\frac{R_2}{R_1}\right)^{d_f} \quad \Rightarrow \quad \mathrm{I(q)} \sim \left(\frac{R_2}{R_1^2}\right)^{d_f} q^{-d_f}$$

The Debye Scattering Function for a Polymer Coil

$$I(Q)=\frac{2}{Q^2}\left(Q-1+\exp(-Q)\right)$$

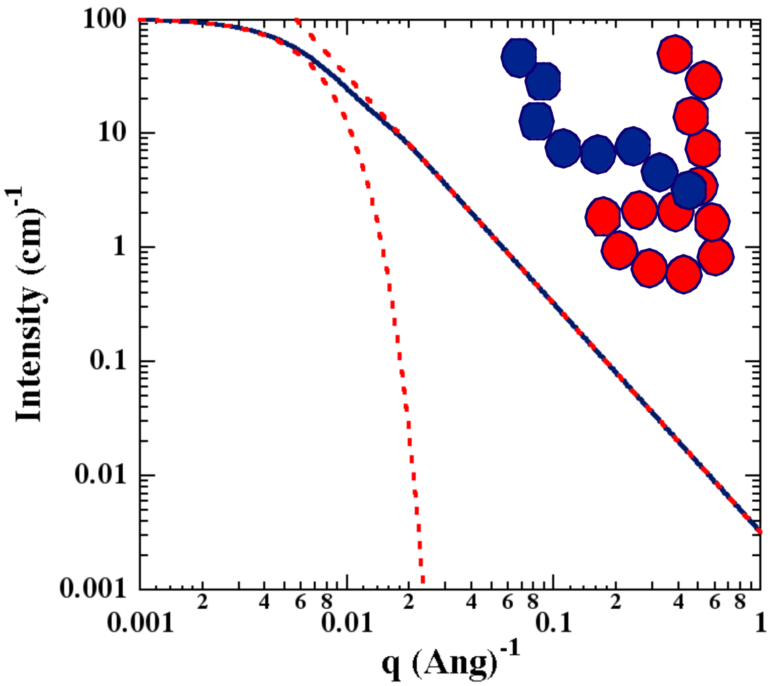
$$Q=q^2R_g^2$$

For $qR_g << 1$

$$\exp(-Q)=1-Q+\frac{Q^2}{2!}-\frac{Q^3}{3!}+\frac{Q^4}{4!}-\ldots$$

$$I(q)=1-\frac{Q}{3}+\ldots\approx\exp\left(-\frac{q^2R_g^2}{3}\right)$$

Guinier' s Law!



The Debye Scattering Function for a Polymer Coil

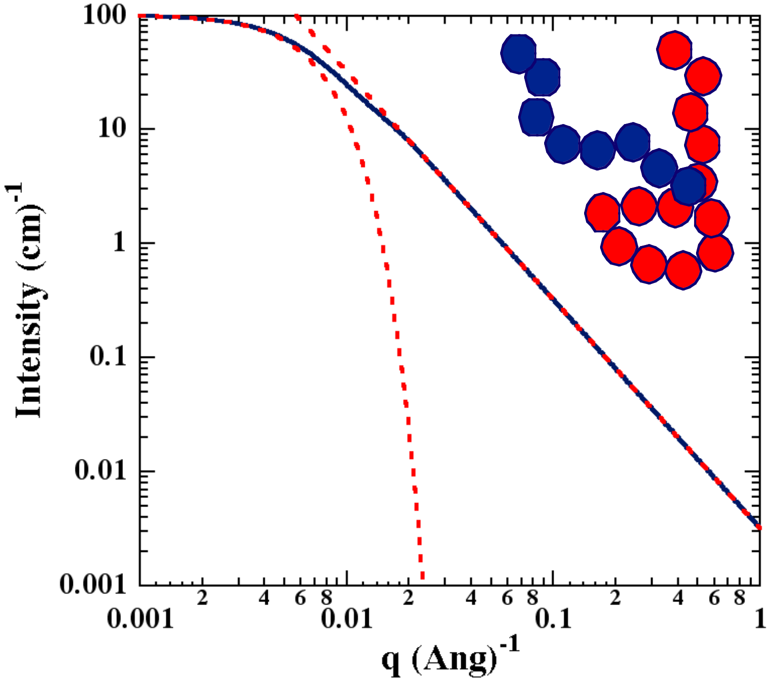
$$I(Q) = \frac{2}{Q^2}\left(Q - 1 + \exp(-Q)\right)$$

$$Q = q^2 R_g^2$$

For $qR_g >> 1$

$$I(Q) = \frac{2}{Q} = \frac{2}{q^2 R_g^2} \sim q^{-d_f}$$

$d_f = 2$



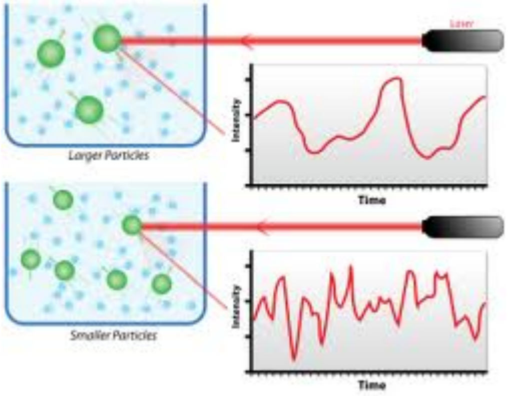
For static scattering p(r) is the binary spatial auto-correlation function

We can also consider correlations in time, binary temporal correlation function
$g_1(q,\tau)$

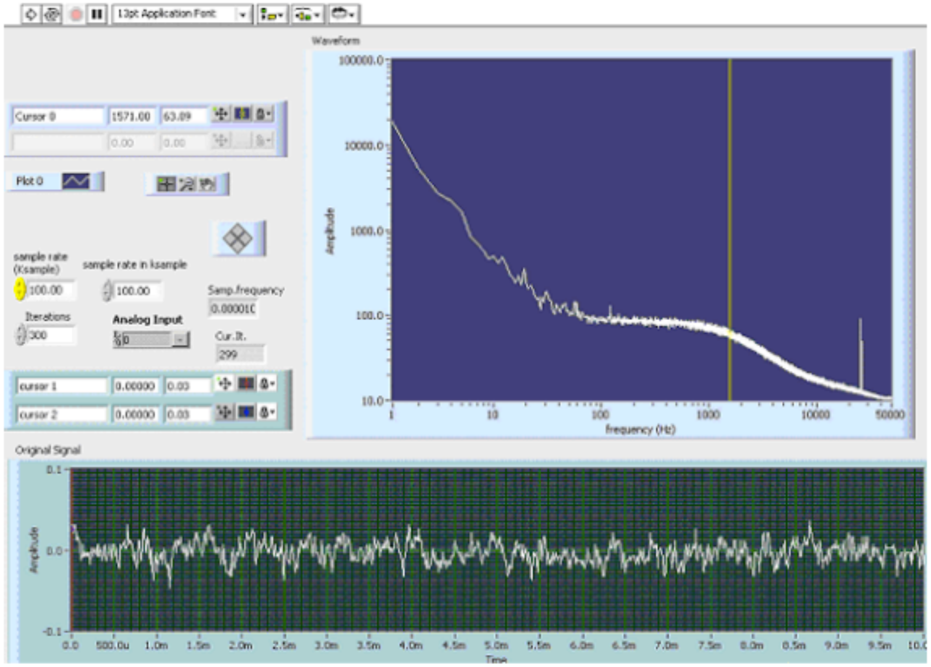
For dynamics we consider a single value of q or r and watch how the intensity changes with time
$I(q,t)$

We consider correlation between intensities separated by t
We need to subtract the constant intensity due to scattering at different size scales
and consider only the fluctuations at a given size scale, r or $2\pi/r = q$

Dynamic Light Scattering



$$g^2(q;\tau) = \frac{\langle I(t)I(t+\tau)\rangle}{\langle I(t)\rangle^2}$$



Cursor 0 1571.00 63.09

0.00 0.00

sample rate (Ksample) 100.00

sample rate in ksample 100.00

Samp.frequency 0.00001C

Iterations 300

Analog Input 0

Cur.It. 299

cursor 1 0.00000 0.03

cursor 2 0.00000 0.03

$$g^2(q;\tau) = 1 + \beta\left[g^1(q;\tau)\right]^2$$

$$q = \frac{4\pi n_0}{\lambda}\sin\left(\frac{\theta}{2}\right)$$

$$g^1(q;\tau) = \exp(-\Gamma\tau)$$

$$\Gamma = q^2 D_t$$

$$D = k_B T / 6\pi\eta a$$

$a = R_H$ = Hydrodynamic Radius

Dynamic Light Scattering

my DLS web page

http://www.eng.uc.edu/~gbeaucag/Classes/Physics/DLS.pdf

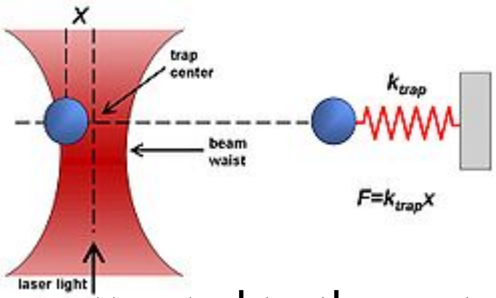
Wiki

http://webcache.googleusercontent.com/search?q=cache:eY3xhiX117IJ:en.wikipedia.org/wiki/Dynamic_light_scattering+&cd=1&hl=en&ct=clnk&gl=us

Wiki Einstein Stokes

http://webcache.googleusercontent.com/search?q=cache:yZDPRbqZ1BIJ:en.wikipedia.org/wiki/Einstein_relation_(kinetic_theory)+&cd=1&hl=en&ct=clnk&gl=us

Optical Tweezers



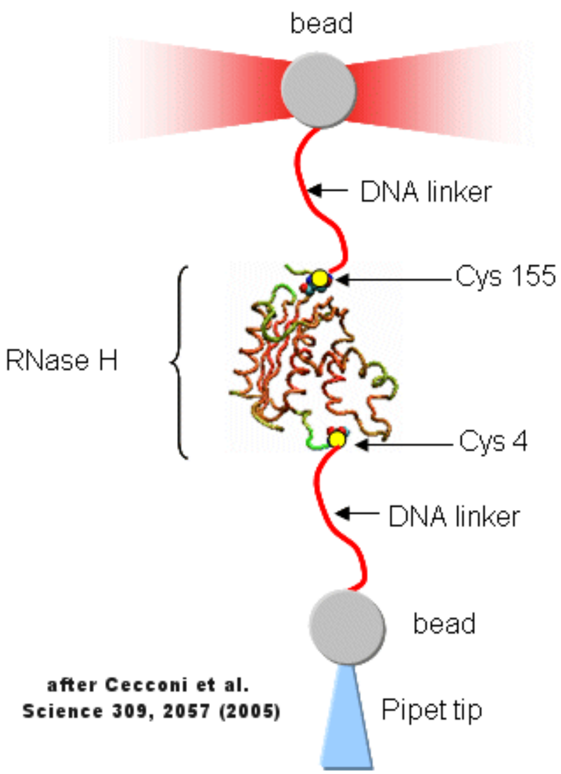
Dielectric particles are attracted to the center of a focused beam
Scattering Force moves particles downstream

Force can be controlled with intensity of laser

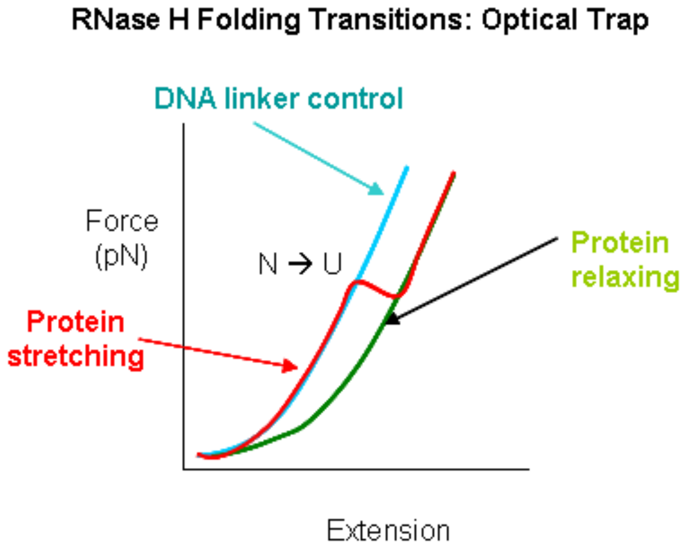
Stretching of a single protein (RNase)

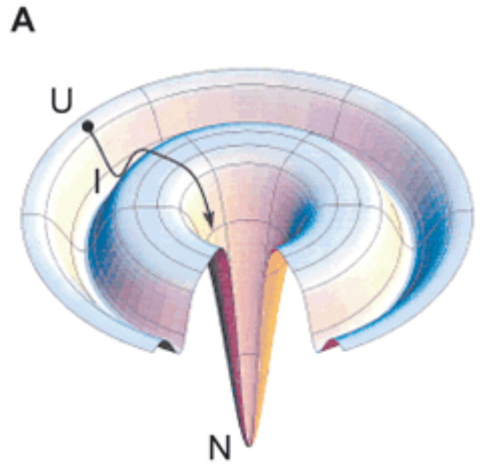
Link to Paper at Science

http://www.sciencemag.org/content/309/5743/2057

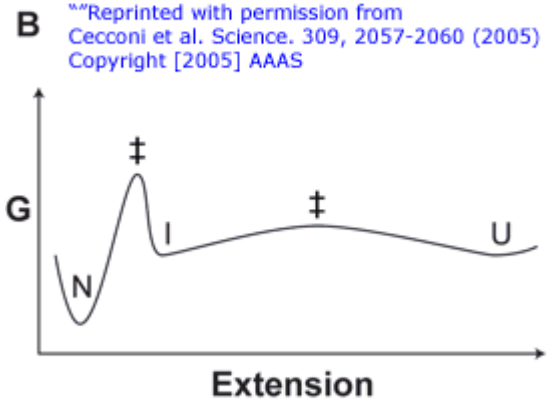


after Cecconi et al. Science 309, 2057 (2005)

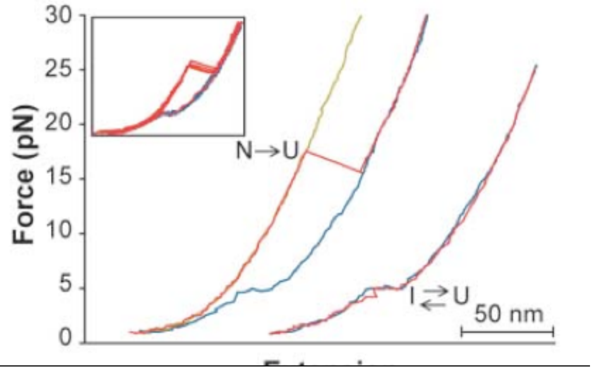




""Reprinted with permission from Cecconi et al. Science. 309, 2057-2060 (2005) Copyright [2005] AAAS



http://employees.csbsju.edu/hjakubowski/classes/ch331/protstructure/olprotfold.html

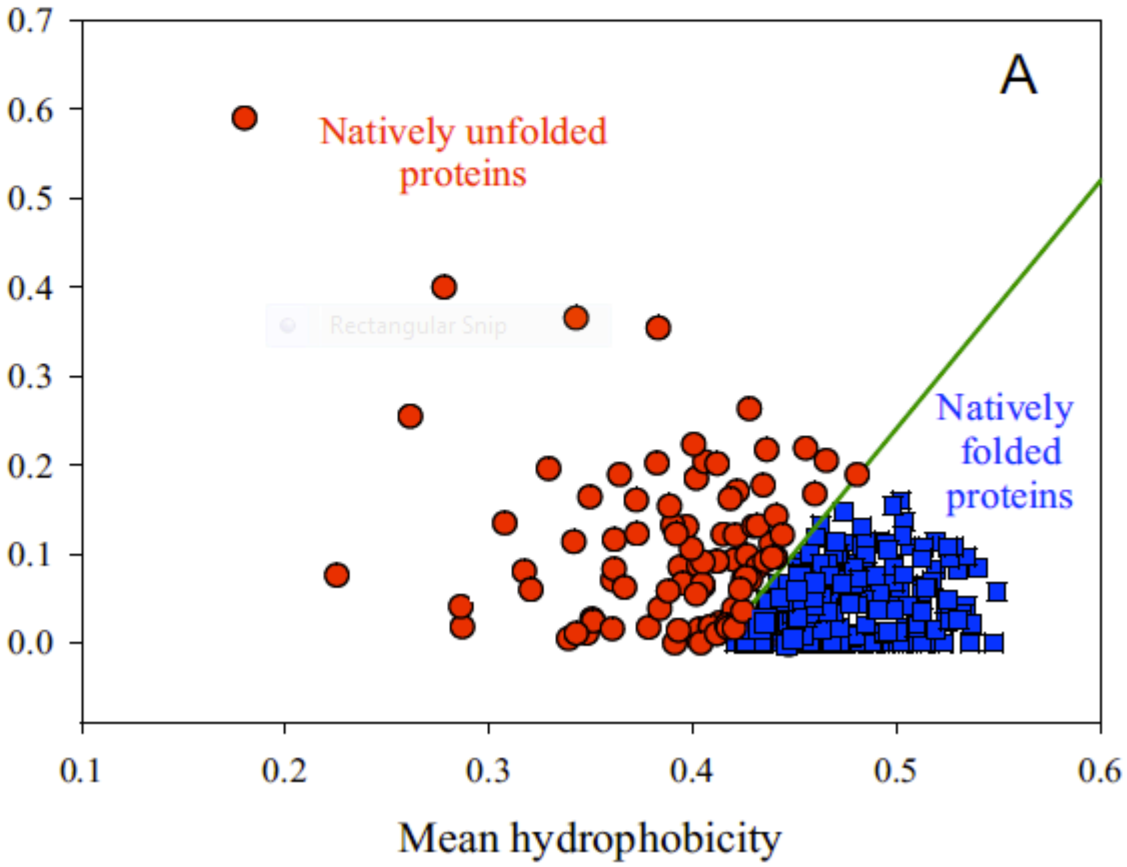


Blue: Stretch just DNA linker molecules
Red: Stretch DNA and Protein
Green: Release tension on Protein/DNA

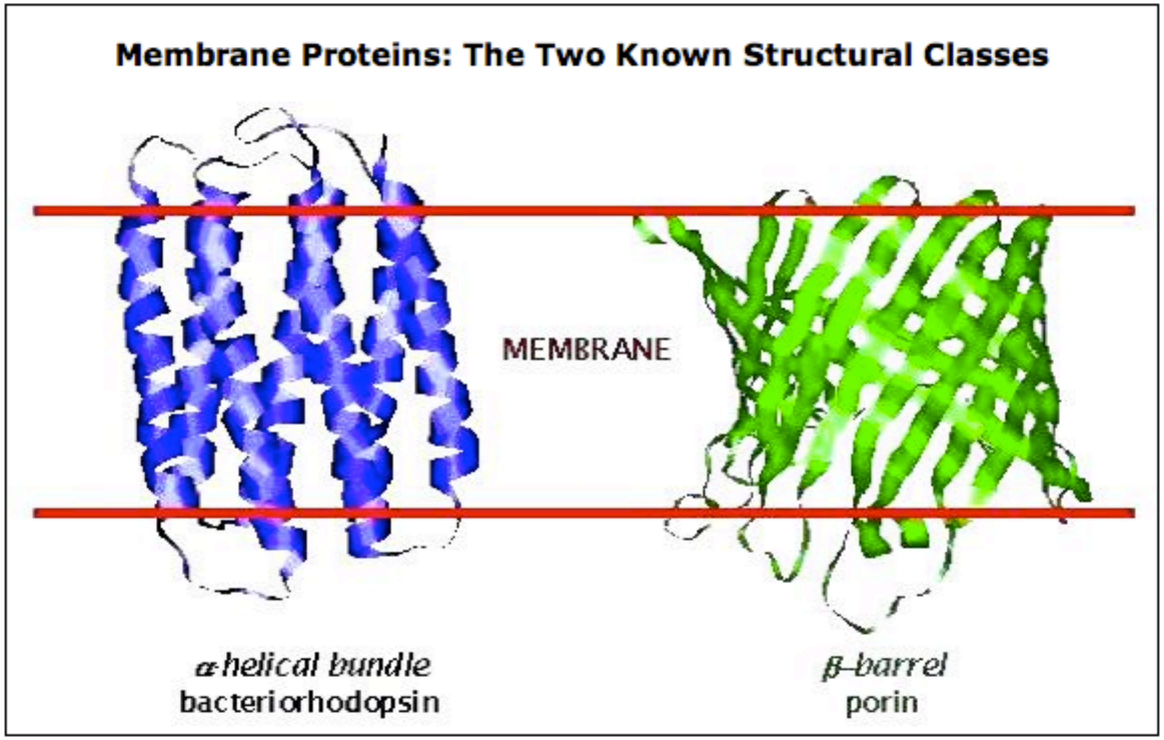
Natively Unfolded Proteins

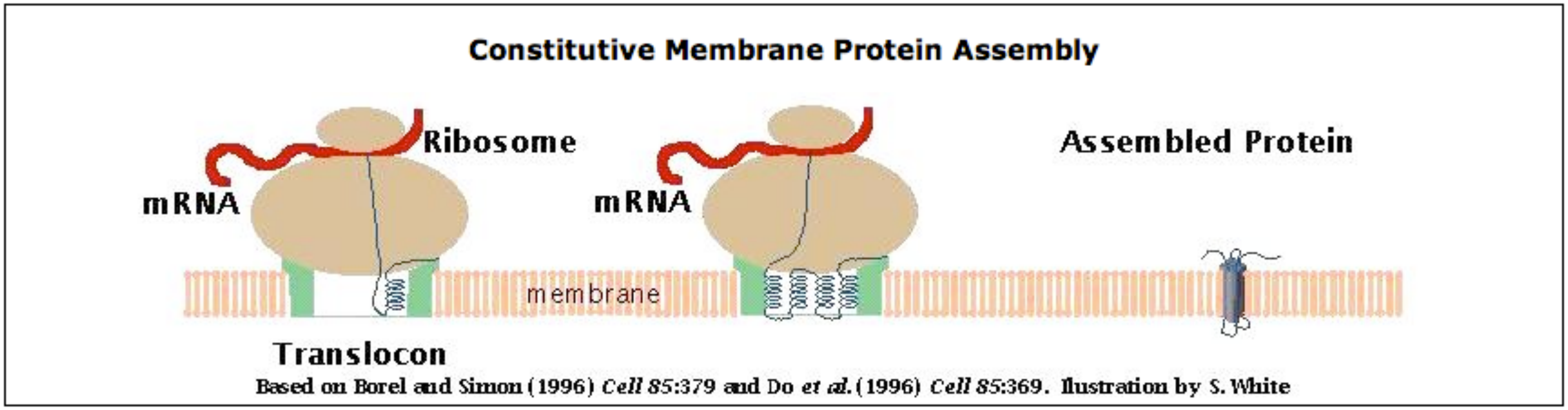
It's been estimated that over half of all native proteins have regions (greater than 30 amino acids) that are disordered, and upwards of 20% of proteins are completely disordered.

Figure: **Characteristics of Intrinsically Disordered Proteins**



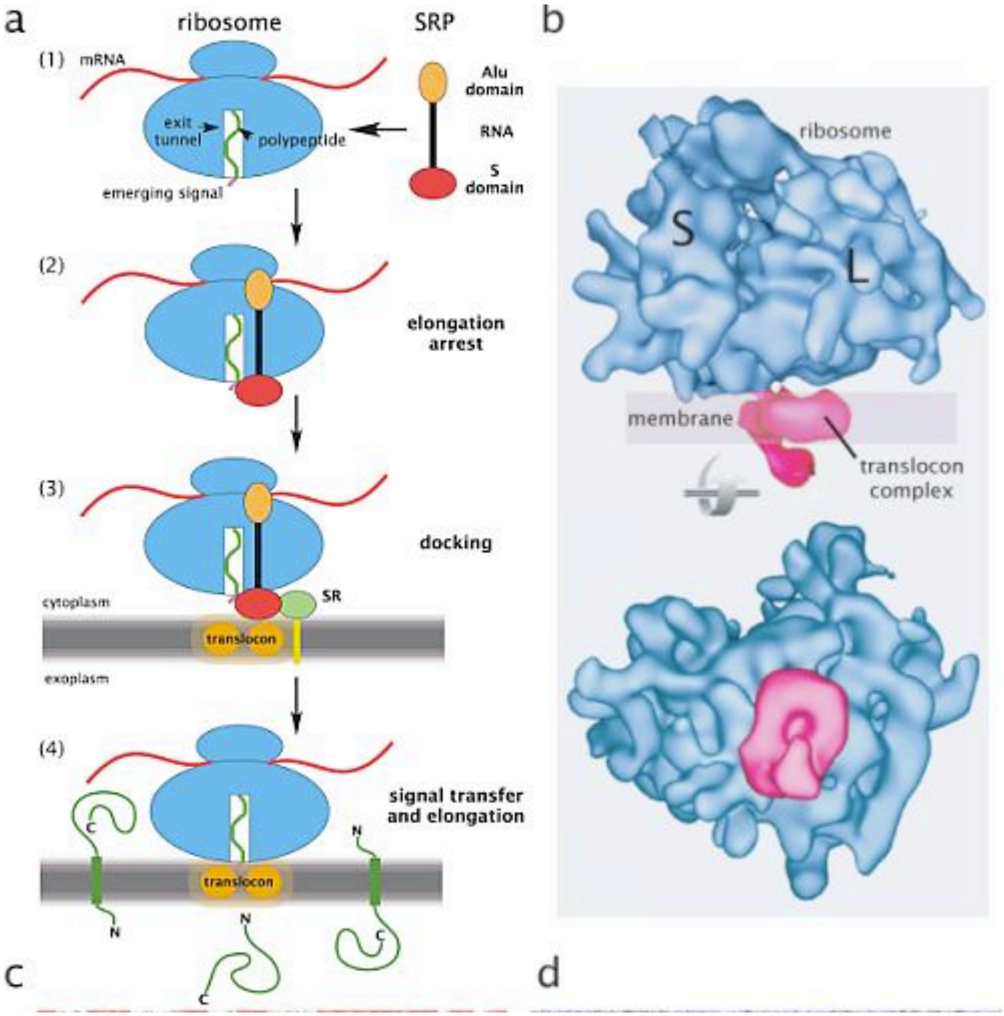
Membrane Proteins





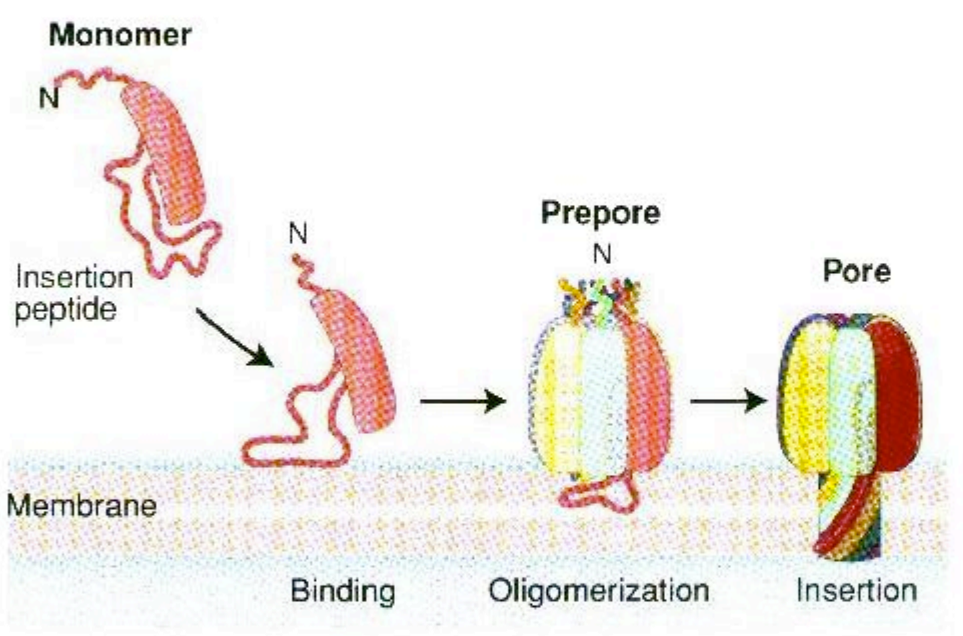
Based on Borel and Simon (1996) *Cell* 85:379 and Do *et al.* (1996) *Cell* 85:369. Ilustration by S. White

http://blanco.biomol.uci.edu/mp_assembly.html



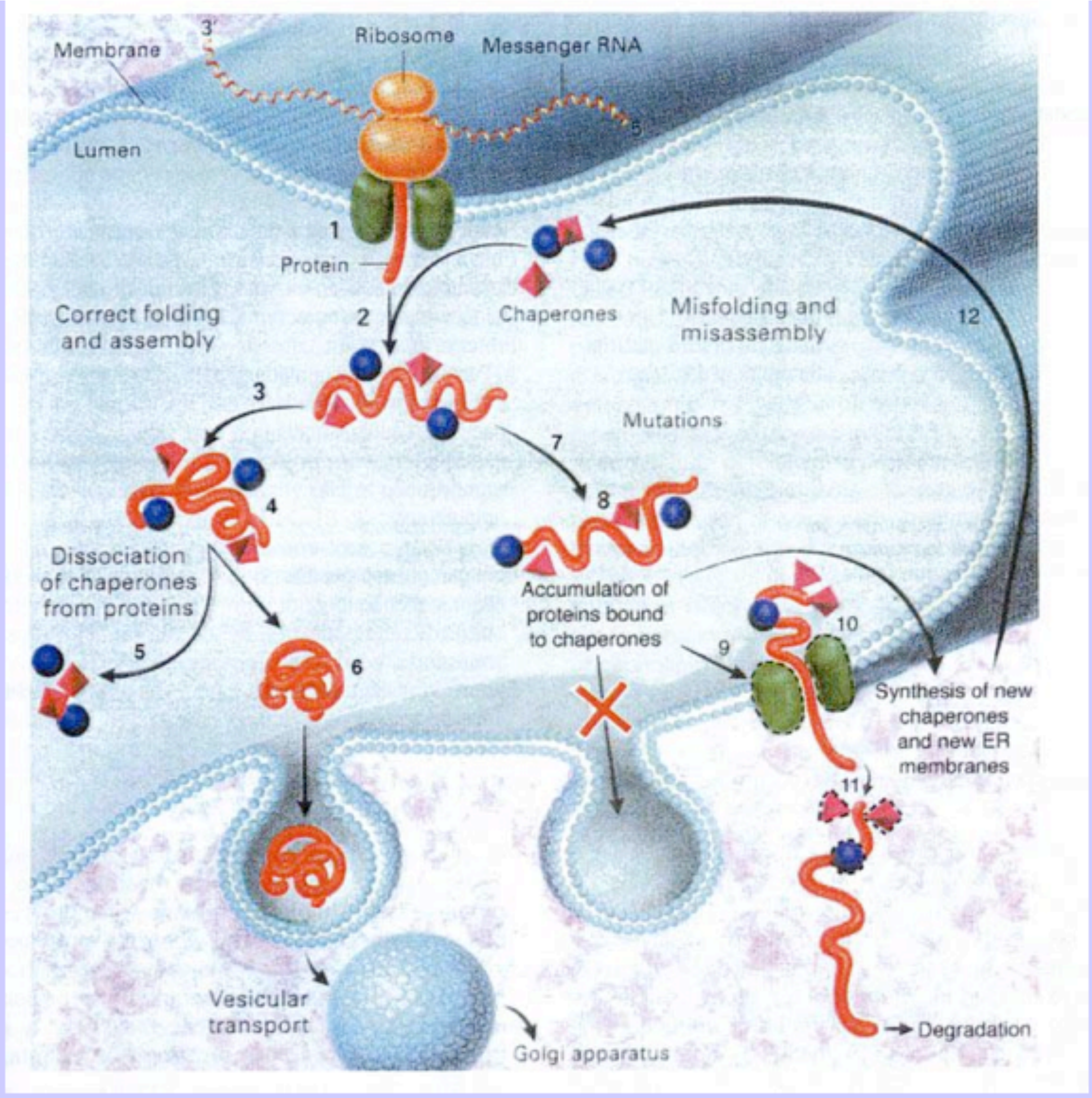
http://blanco.biomol.uci.edu/translocon_machinery.html

Non-constitutive Membrane Protein Assembly: α-hemolysin



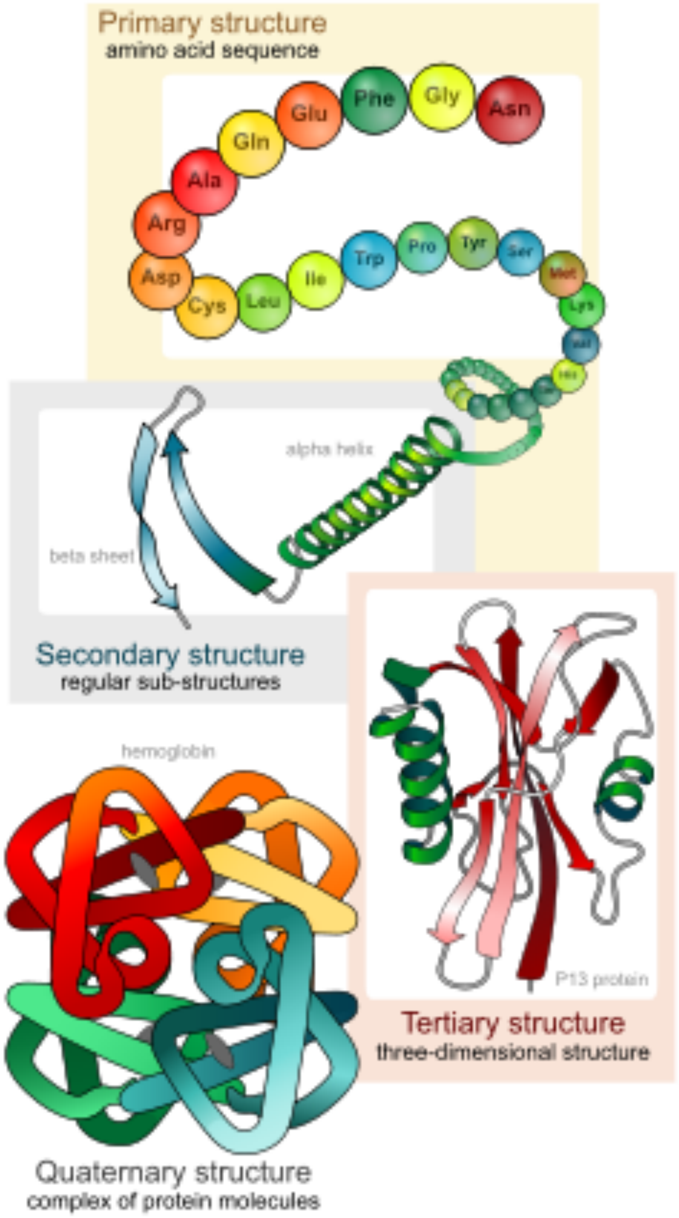
From Engelman (1996) *Science* *274*:1850. Illustration by K. Sutliff. © 1996 A.A.A.S.

Reprinted with permission from *Science* (1996) *274*:1850, © 1996 American Assoc. for the Advancement of Science.



http://www.portfolio.mvm.ed.ac.uk/studentwebs/session2/group5/introliz.htm

Quaternary Structures

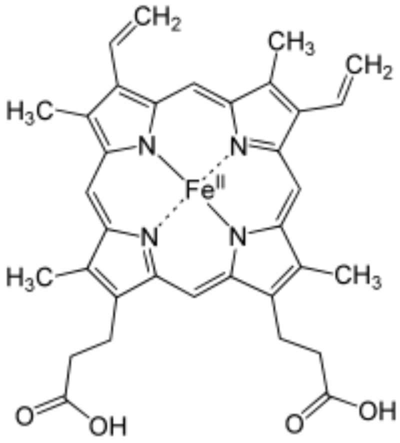


Electron transport chain is part of the ATP/ADP energy generation pathway for cells
This involves many tertiary protein structures. For instance, Complex III is a quaternary structure of 9 proteins.

http://proteopedia.org/wiki/index.php/Complex_III_of_Electron_Transport_Chain

http://en.wikipedia.org/wiki/Electron_transport_chain

Heme B group



Quaternary Structure Page

http://proteopedia.org/wiki/index.php/Main_Page

Ribosome

http://proteopedia.org/wiki/index.php/Ribosome

Role of Ribosome

http://www.cytochemistry.net/cell-biology/ribosome.htm

Ribosome in Action

http://www.youtube.com/watch?v=Jml8CFBWcDs

Poly(A) Polymerase

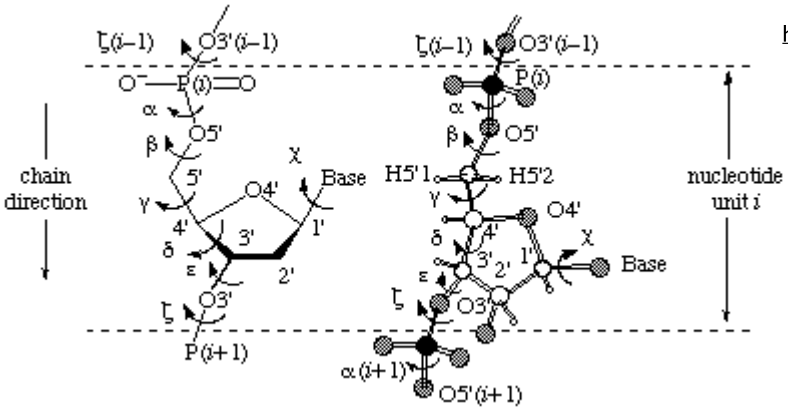
http://proteopedia.org/wiki/index.php/2q66

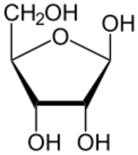
DNA/Protein Quaternary Structures

http://www.biochem.ucl.ac.uk/bsm/prot_dna/prot_dna_cover.html

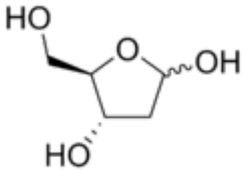
RNA structure

http://www.rnabase.org/primer/

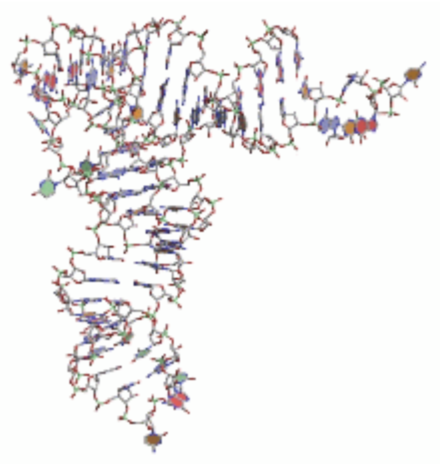




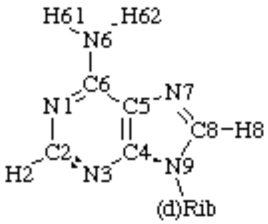
Ribose



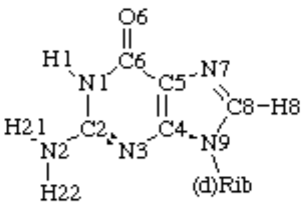
Deoxyribose



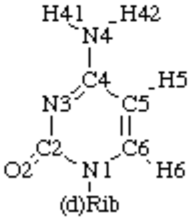
t-RNA (Folded Structure)



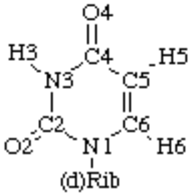
adenosine (and deoxyadenosine)



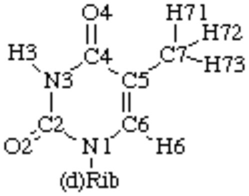
guanosine (and deoxyguanosine)



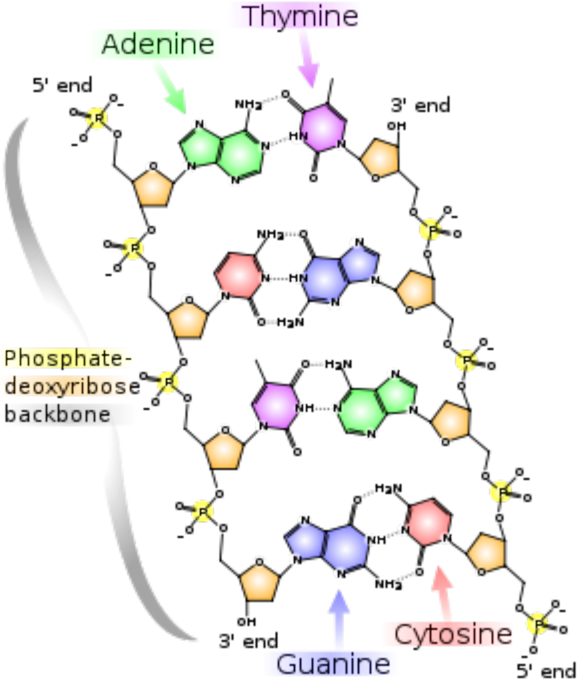
cytosine (and deoxycytosine)



uridine (and deoxyuridine)



ribosylthymine (and thymidine)



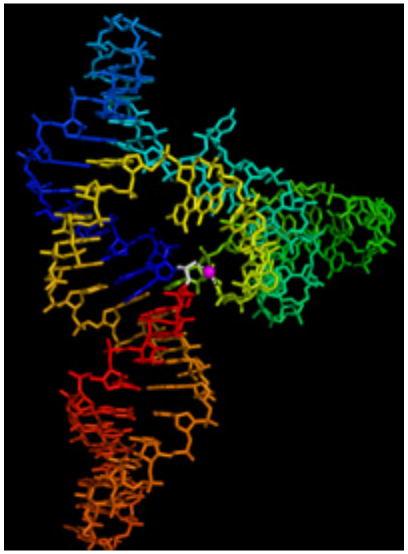
DNA

If it takes DNA/RNA to template a protein and proteins to make/control DNA/RNA Which came first Proteins or Nucleic Acids?

RNA World Hypothesis:

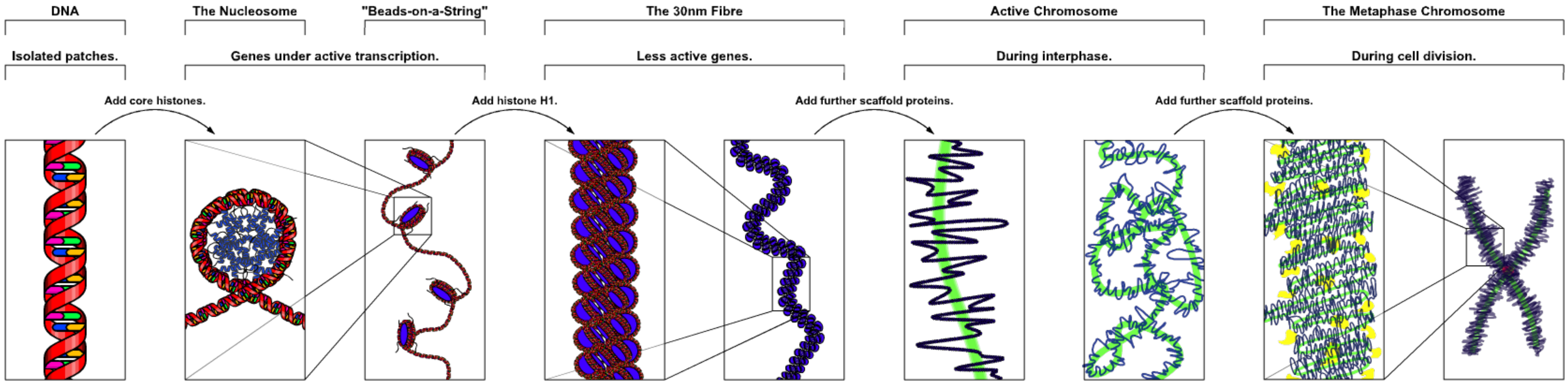
http://en.wikipedia.org/wiki/RNA_world_hypothesis

http://exploringorigins.org/rna.html



L1 Ligase Ribozyme

Hierarchy of a Chromosome



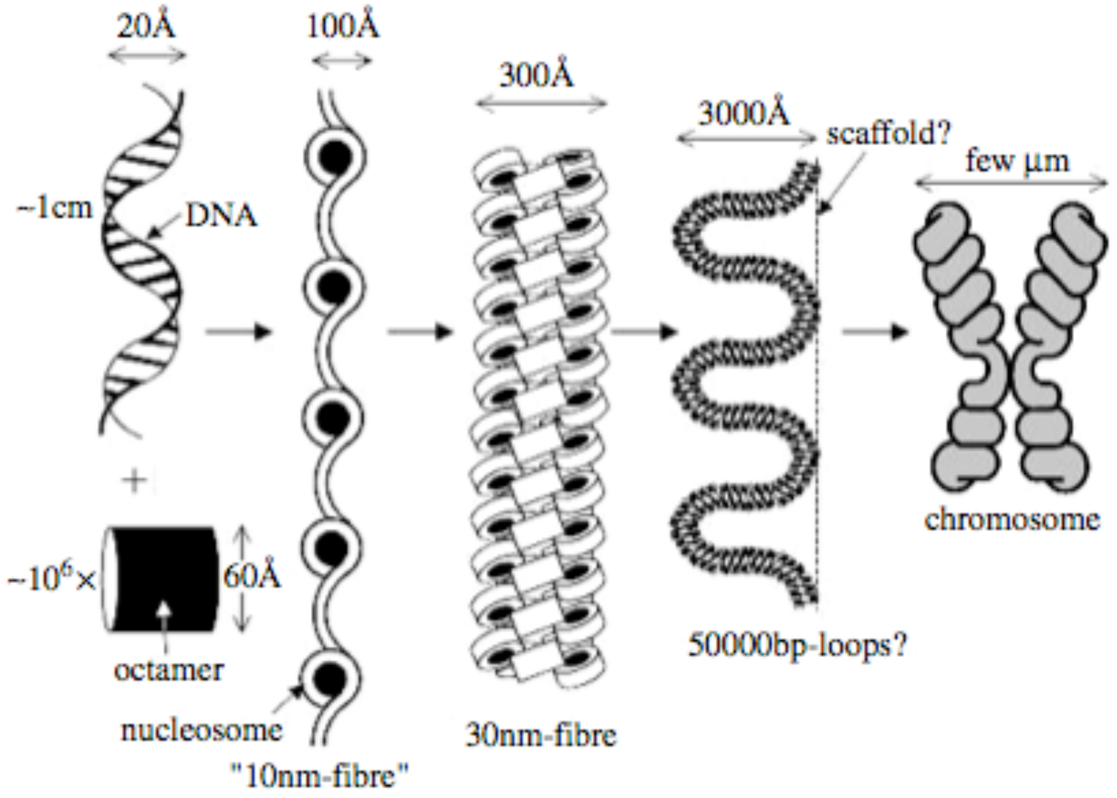
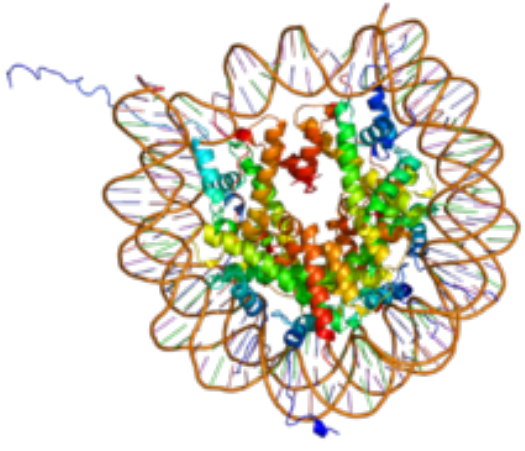
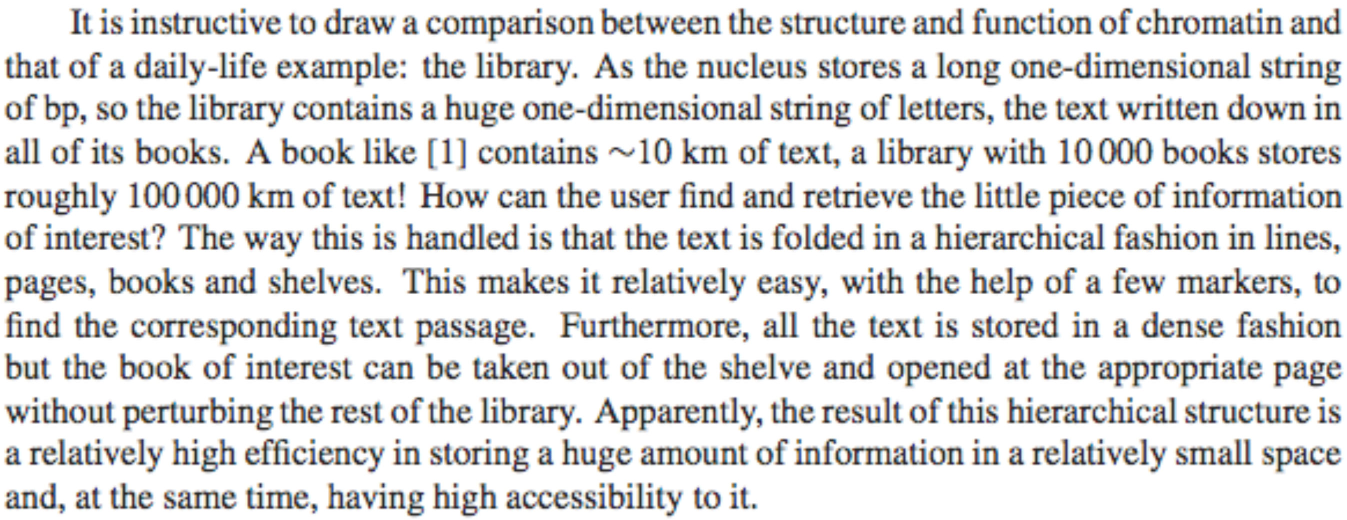


Figure 1. Steps of the DNA compaction into chromatin. The DNA molecule of length ~1 cm is compacted with the help of 10^6 histone octamers leading to a 10 000-fold reduction of its original length (see text for details).

Core Histone





It is instructive to draw a comparison between the structure and function of chromatin and that of a daily-life example: the library. As the nucleus stores a long one-dimensional string of bp, so the library contains a huge one-dimensional string of letters, the text written down in all of its books. A book like [1] contains ~10 km of text, a library with 10 000 books stores roughly 100 000 km of text! How can the user find and retrieve the little piece of information of interest? The way this is handled is that the text is folded in a hierarchical fashion in lines, pages, books and shelves. This makes it relatively easy, with the help of a few markers, to find the corresponding text passage. Furthermore, all the text is stored in a dense fashion but the book of interest can be taken out of the shelve and opened at the appropriate page without perturbing the rest of the library. Apparently, the result of this hierarchical structure is a relatively high efficiency in storing a huge amount of information in a relatively small space and, at the same time, having high accessibility to it.

http://www.eng.uc.edu/~gbeaucag/Classes/MorphologyofComplexMaterials/Physics%20of%20Chromatin%20Schiessel%202003.pdf