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.
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.
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.
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.
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
- 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

<table>
<thead>
<tr>
<th>Order/Level</th>
<th>Forest</th>
<th>Protein</th>
<th>Polymer Statics</th>
<th>Polymer Dynamics</th>
<th>Fractal Aggregates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>Twig</td>
<td>Amino Acid Sequence</td>
<td>Persistence Length</td>
<td>Kuhn Unit</td>
<td>Primary Particles</td>
</tr>
<tr>
<td>Secondary</td>
<td>Tree/Branching</td>
<td>$\alpha$-Helix; $\beta$-Sheet; Turns</td>
<td>Blob</td>
<td>Rouse Unit</td>
<td>Scaling Transitions</td>
</tr>
<tr>
<td>Tertiary</td>
<td>Grove/Cluster</td>
<td>Globular Structure</td>
<td>Coil</td>
<td>Coil</td>
<td>Aggregate</td>
</tr>
<tr>
<td>Quaternary</td>
<td>Forest</td>
<td>Complex Structure with many Proteins/Metal Ions Etc.</td>
<td>Network/Entanglements</td>
<td>Entanglements</td>
<td>Agglomerate</td>
</tr>
</tbody>
</table>
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
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/aminacid.html
Know These 5 Amino Acids Well

Methionine  Start Amino Acid (usually removed in later steps)

Glycine  -H Flexible non-polar
Alanine -CH₃ 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)

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

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

\[ \text{PSI } \psi \] is the rotation angle between the carboxyl C and the α-carbon.

\[ \text{PHI } \Phi \] 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)**

\[ \text{Phi/Psi } \ 180, 180 \]

---

<table>
<thead>
<tr>
<th>Structure</th>
<th>( \phi )</th>
<th>( \psi )</th>
<th>( n )</th>
<th>( p(\text{Å}) )</th>
<th>( \Lambda )</th>
<th>( H\text{-bond(\text{CO} \text{&amp;} \text{HN})} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right-handed alpha helix</td>
<td>-57</td>
<td>-47</td>
<td>3.6</td>
<td>5.4</td>
<td>13</td>
<td>( ij+j+2 )</td>
</tr>
<tr>
<td>( 3_{10} )-helix</td>
<td>-74</td>
<td>-4</td>
<td>3.0</td>
<td>6.0</td>
<td>10</td>
<td>( ij+j+3 )</td>
</tr>
<tr>
<td>pi-helix</td>
<td>-57</td>
<td>-70</td>
<td>4.4</td>
<td>5.0</td>
<td>16</td>
<td>( ij+j+4 )</td>
</tr>
<tr>
<td>Parallel beta strand</td>
<td>-119</td>
<td>113</td>
<td>2.0</td>
<td>6.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antiparallel beta strand</td>
<td>-139</td>
<td>135</td>
<td>2.0</td>
<td>6.8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

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

Phi rotation for Psi = 0
Psi rotation for Phi = 0
Figure: Ramachandran plot

The Ramachandran Plot.
Figure: Ramachandran plots showing $\phi/\psi$ angles for Gly, Ala, Tyr, and Pro in actual proteins

Ramachandran Plots.html
Lets Jump Ahead and Look at Protein Folding

Folding Simple Dynamic Simulation.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=meNEUTn9Arg

Small Protein Folding.html
http://www.youtube.com/watch?v=_xF96sNWnK4&feature=related

Another Small Protein Folding.html
http://www.youtube.com/watch?v=E9TX3yMEZ8Y&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=gaiepNVyyE&feature=related

Folding a Protein by Hand.html
http://www.youtube.com/watch?v=va9z9Ei1QOQ&feature=related

Folding of Villin.html
http://www.youtube.com/watch?v=IeSwDKZQpol&feature=related
Secondary Structures of Proteins
α-Helix, β-Sheets, Turns
Right Handed $\alpha$-Helix

pdb of $\alpha$-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

Amino Acids and Helix
Glycine too flexible
Proline too rigid
Short H-Bonding (Ser, Asp, Asn) Disrupt Coil
Long H-Bonding are OK
Branches at $\alpha$-C Disrupt Coil (Val, Ile)

http://employees.csbsju.edu/hjakubowski/classes/ch331/protstructure/olunderstandconfo.html
AMINO ACID PROPENSITIES FOR SECONDARY STRUCTURE

Valine
Val

Isoleucine
Ile

Branch at $C_p$
destabilizes $\alpha$-helix

OK in $\beta$-Sheet
side chain projects out of plan of main chain

Aspartic Acid
Asp

Asparagine
Asn

destabilizes $\alpha$-helix
H Bond donor/acceptors compete with main chain

Valine
Val

Isoleucine
Ile

Branch at $C_p$
destabilizes $\alpha$-helix

OK in $\beta$-Sheet
side chain projects out of plane of main chain

Serine
Ser

Asparagine
N

Aspartic Acid
Asp

Glycine
Gly

Proline
Pro

http://employees.csbsju.edu/hjakubowski/classes/ch331/protstructure/olunderstandconfo.html
## Other Types of Helices

<table>
<thead>
<tr>
<th>Helix Type</th>
<th>H bond btw (i^{th}) and (i^{th}+X) AA, where X =</th>
<th>Residue/turn</th>
<th>Rise (Å)/turn</th>
</tr>
</thead>
<tbody>
<tr>
<td>3\textsubscript{10}</td>
<td>3</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>a</td>
<td>4</td>
<td>3.6</td>
<td>5.4</td>
</tr>
<tr>
<td>p</td>
<td>5</td>
<td>4.3</td>
<td>4.7</td>
</tr>
</tbody>
</table>

**3\textsubscript{10} helix**

**α helix**

**310 helix**

**π helix**

[Diagram showing α, 310, and π helices]
**β-Sheets**

<table>
<thead>
<tr>
<th>Type</th>
<th>Phi</th>
<th>Psi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parallel</td>
<td>-119</td>
<td>+113</td>
</tr>
<tr>
<td>Anti-Parallel</td>
<td>-139</td>
<td>+135</td>
</tr>
<tr>
<td>α-Helix</td>
<td>-57</td>
<td>-47</td>
</tr>
<tr>
<td>Extended</td>
<td>±180</td>
<td>±180</td>
</tr>
</tbody>
</table>

**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

12-member rings
Anti-Parallel β-Sheets

Alternating 10- and 14-member rings
Twisted β-Sheet/Saddle

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

β-Barrel

http://employees.csbsju.edu/hjakubowski/Jmol/
beta_barrel_tpi/Beta_Barrel_tpi.htm
AMINO ACID PROPENSITIES FOR SECONDARY STRUCTURE

Valine
- Branched at C_p
- Destabilizes α-helix
- OK in β-Sheet
  - Side chain projects out of plan of main chain

Isoleucine
- Branched at C_p
- Destabilizes α-helix

Serine
- No branch at C_p and R group can form H bonds
- OK in α-Sheet
  - Side chain projects out of

Asparagine
- No branch at C_p and R group can't form H bonds
- Destabilizes α-helix
  - H Bond donors/acceptors compete with main chain

Aspartic Acid

Glycine
- Too conformationally flexible
- OK in α-Sheet

Proline
- Too rigid

http://employees.csbsju.edu/hjakubowski/classes/ch331/protstructure/olunderstandconfo.html
**β-Turns**

The image illustrates the concept of β-turns in protein structures. β-turns are crucial for the formation of secondary structures in proteins.

- **Type I:** The hydrogen bonds form between the backbone atoms at positions $i$, $i+1$, and $i+3$.
- **Type II:** Similarly, Type II β-turns also involve hydrogen bonds, but the pattern of backbone interactions is slightly different.
- **Type III:** Type III β-turns have their own specific pattern of hydrogen bonding, ensuring the stability of the turn.

The diagram shows the molecular structure with labeled atoms and hydrogen bonds indicated by arrows, highlighting the key interactions in each type of β-turn.
**β-Turns**

**Reverse Turn**

[http://employees.csbsju.edu/hjakubowski/Jmol/RevTurnTryInhib/revturnTrpInhib.htm](http://employees.csbsju.edu/hjakubowski/Jmol/RevTurnTryInhib/revturnTrpInhib.htm)

**Type 2 and Type 1 Reverse Turns**
Micelles (Vesicle)

Dodecylphosphocholine (DPC)

\[(\text{CH}_3)_3\text{N}^-\text{CH}_2\text{CH}_2\text{O}^-\text{P}^\text{O}_\text{O}^-\text{C}^-(\text{CH}_2)_1\text{OCH}_3\]

- Choline
- Phosphate
- Dodecyl or lauryl
- Ionic - polar
- Non-polar

Dodecylphosphocholine (DPC) Micelle

http://employees.csbsju.edu/hjakubowski/Jmol/Micelle/micelle.htm
The 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 $\alpha$-helix and 23% in $\beta$-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 $\sim$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


Greek Key Motif

http://www.cryst.bbk.ac.uk/PPS2/course/section10/10_plasto.gif
Beta-Alpha-Beta (to connect two parallel $\beta$-sheets)

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

$\beta$-Helicies (seen in pathogens, viruses, bacteria)

Many $\beta$-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-%20IgG1.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-helices with β-turns

Reslin (Insects Wings)

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

Fibrillin (Cartilage) - Folded β-Sheet like and Accordian
Consider a protein of 100 residues each with two bond angles $\Phi$ and $\psi$ 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 $8.4 \times 10^{74}$ 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.
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 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

Guanidinium-HCl

Competes with H-Bonds
Denatures (Destabilizes) Proteins

Competes with H-Bonds
Denatures (Destabilizes) Proteins
Figure: CATALYTIC SHUFFLING OF DISSULFIDES 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:
- A250
- Fluorescence Int.
- Viscosity
- CD
- etc.

D ↔ N

KINETICS
timed measurements

THERMODYNAMICS
equilibrium measurements

Y

D ↔ N
part of N at t ≤ 0

D ↔ N
- urea
- time

Y

D ↔ N
- urea
- time

Y

D ↔ I ↔ N

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 d.s. on D → N

molten globule
- some protein at low pH
- some Ca binding proteins with Ca

secondary structure
- 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

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

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

\[ \tau = \eta \dot{\gamma} \]

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

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

Native state has the smallest volume
Mass Fractal Dimension, \( 1 \leq d_f \leq 3 \)

- Mass \( \sim \) Size\(^1\) \quad 1-d \quad d_f = 1

- Mass \( \sim \) Size\(^2\) \quad 2-d \quad d_f = 2

- Mass \( \sim \) Size\(^3\) \quad 3-d \quad d_f = 3
Mass Fractal Dimension, \( 1 \leq d_f \leq 3 \)

**Random (Brownian) Walk**

\( \theta \)-Solvent Condition

\[ \text{Mass} \sim \text{Size}^2 \quad 2-d \quad d_f = 2 \]

**Self-Avoiding Walk/Expanded Coil**

Good Solvent Condition

\[ \text{Mass} \sim \text{Size}^{1.67} \quad d_f = 5/3 \]

In the collapse transition from an expanded coil to a native state for a protein of 100 residues (\( N = \text{Mass} = 100 \))

Size \( \sim 15.8 \) 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

$$2R/d_p = 10, \ a \sim 1, \ z \sim 220$$

$$d_f = \ln(220)/\ln(10) = 2.3$$

A Measure of Branching is not Given.
Viscosity

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

\[ \left[\eta\right] \approx \frac{V_{\text{Molecule}}}{M_{\text{Molecule}}} \]

For the Native State Mass \( \sim \rho V_{\text{Molecule}} \)

Einstein Equation (for Suspension of 3d Objects)

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

For “Gaussian” Chain Mass \( \sim \text{Size}^2 \sim V^{2/3} \)

\[ V \sim \text{Mass}^{3/2} \]

For “Expanded Coil” Mass \( \sim \text{Size}^{5/3} \sim V^{5/9} \)

\[ V \sim \text{Mass}^{9/5} \]

For “Fractal” Mass \( \sim \text{Size}^{df} \sim V^{df/3} \)

\[ V \sim \text{Mass}^{3/df} \]

\[ \left[\eta\right] \sim M_{\text{Molecule}}^{\frac{3}{df} - 1} \]
Viscosity

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

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

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

Einstein Equation (for Suspension of 3d Objects)

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

For “Gaussian” Chain Mass $\sim \text{Size}^2 \sim V^{2/3}$

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

“For “Expanded Coil” Mass $\sim \text{Size}^{5/3} \sim V^{5/9}$

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

“For Fractal” Mass $\sim \text{Size}^{df} \sim V^{df/3}$

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

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

“Size” is the
“Hydrodynamic Size”
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

\[ \Delta \varepsilon = \varepsilon_L - \varepsilon_R \] \hspace{1cm} Molar Circular Dichroism (c = molar concentration)
\[ \Delta A = cl\Delta \varepsilon \] \hspace{1cm} Difference in Absorption
\[ [\theta] = 3298.2\Delta \varepsilon \] \hspace{1cm} Degrees of Ellipticity

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

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

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

\[ d = \frac{2\pi}{q} \]

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 $\theta$ was in phase with the incident wave at the source of scattering.

- This can occur for points separated by $\mathbf{r}$ such that

$$|\mathbf{r}| = \frac{2\theta}{|\mathbf{q}|}$$

- $q = \frac{4\pi}{\lambda} \sin \frac{\theta}{2}$
Binary Interference Yields Scattering Pattern.

- For high $\theta$, $r$ is small
Binary Interference Yields Scattering Pattern.

- For small $\theta$, $r$ 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.
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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.

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

\[ G = Nn_e^2 \]
Guinier’s Law Pertains to a Particle with no Surface.

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

\[ G = Nn_e^2 \]

*Any* “Particle” can be Approximated as a Gaussian probability distribution in this context.
\[ p(r) = \exp\left(\frac{-3r^2}{4R_g^2}\right) \quad \Rightarrow \quad I(q) = G \exp\left(-\frac{q^2R_g^2}{3}\right) \]

\[ G = Nn_e^2 \]

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**

\[ \gamma_{\text{Gaussian}}(r) = \exp\left(-\frac{3r^2}{2\sigma^2}\right) \]

**Binary Autocorrelation Function**

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

**Lead Term is**

\[ I(q) = I_e Nn_e^2 \exp\left(-\frac{R_g q^2}{3}\right) \]

\[ I(0) = Nn_e^2 \]

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

Scattered Intensity is the Fourier Transform of The Binary Autocorrelation Function

\[ \gamma_0(r) = 1 - \frac{S}{4V} r + ... \]

\[ \exp\left(\frac{-3r^2}{4R_g^2}\right) \approx 1 - \frac{3r^2}{4R_g^2} + ... \]

\[ r \Rightarrow 0 \text{ then } \frac{d(\gamma_{\text{Gaussian}}(r))}{dr} \Rightarrow 0 \]

A particle with no surface

At intermediate sizes the chain is “self-similar”

\[ \text{Mass} \sim \text{Size}^{d_f} \]

\[ z \sim \left( \frac{R_2}{R_1} \right)^{d_f} \]
At intermediate sizes the chain is “self-similar”

\[ I(q) \sim N \ n_e^2 \]

\[ N = \text{Number of Intermediate Spheres in the Aggregate} \]

\[ n_e = \text{Mass of inter. sphere} \]

\[ Nn_e^2 \sim \left( \frac{r_{\text{int}}}{R_1} \right)^{d_f} \left( \frac{R_2}{R_1} \right)^{d_f} \]

\[ \Rightarrow \quad I(q) \sim \left( \frac{R_2}{R_1^2} \right)^{d_f} q^{-d_f} \]
The Debye Scattering Function for a Polymer Coil

\[ I(Q) = \frac{2}{Q^2} (Q - 1 + \exp(-Q)) \]

\[ Q = q^2 R_g^2 \]

For \( q R_g << 1 \)

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

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

Guinier’s Law!
The Debye Scattering Function for a Polymer Coil

\[ I(Q) = \frac{2}{Q^2} (Q - 1 + \exp(-Q)) \]

\[ Q = q^2 R_g^2 \]

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

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

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

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

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

\[ \Gamma = q^2 D_t \]

\[ D = k_B T / 6\pi \eta a \]

\[ a = R_H = \text{Hydrodynamic Radius} \]
Dynamic Light Scattering

my DLS web page

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

Wiki


Wiki Einstein Stokes

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

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


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

Natively Unfolded Proteins
Membrane Proteins

Membrane Proteins: The Two Known Structural Classes

α-helical bundle
bacteriorhodopsin

β-barrel
porin

Constitutive Membrane Protein Assembly

Translocon

http://blanco.biomol.uci.edu/mp_assembly.html
http://www.portfolio.mvm.ed.ac.uk/studentwebs/session2/group5/introliz.htm
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.


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

[Diagram of RNA structure]

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

[Diagram of t-RNA (Folded Structure)]

Ribose

Deoxyribose

t-RNA (Folded Structure)

Adenine

Thymine

DNA

Phosphate-deoxyribose backbone

Guanine

Cytosine

5' end

3' end

5' end

3' end

Adenine (and deoxyadenosine)

Guanine (and deoxyguanosine)

Cytosine (and deoxyadenosine)

Thymine (and thymidine)

Cytosine (and deoxyguanosine)

Thymine (and thymidine)
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://exploringorigins.org/rna.html

L1 Ligase Ribozyme
Hierarchy of a Chromosome

- **DNA**: Isolated patches.
- **The Nucleosome**: Genes under active transcription.
- **“Beads-on-a-String”**: Less active genes.
- **The 30nm Fibre**: During interphase.
- **Active Chromosome**: During cell division.
- **The Metaphase Chromosome**: Add core histones.
- **Add histone H1.**
- **Add further scaffold proteins.**
- **Add further scaffold proteins.**

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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).
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 shelf 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