Molecular Assemblies

--What are the rules about how molecules assemble into oligomers?

--When do the rules begin to break down?

--How do we study molecules/assemblies in solution (since you can't crystallize everything)?
Symmetry in oligomeric protein assemblies

**Cro dimer**

Two subunits related by 2-fold rotational symmetry

[Tetramers often have "222" rotational symmetry; i.e. three perpendicular 2-fold axes.]
Hemoglobin has two different subunits (α and β) and "pseudo-222" symmetry

Influenza virus neuraminidase--a tetramer with 4-fold rotational symmetry
Alfalfa Mosaic Virus

T=1
60 subunits
Max. diameter 223Å

Source: Jack Johnson's "VIPER" site http://mmtsb.scripps.edu/viper/viper.html
Tomato Bushy Stunt Virus

T=3
180 subunits
Max. diameter 354Å

Source: Jack Johnson's "VIPER" site http://mmtsb.scripps.edu/viper/viper.html
Simian Virus 40

T=7
360 subunits
Max. diameter ~500Å

Source: Jack Johnson's "VIPER" site http://mmtsb.scripps.edu/viper/viper.html
Bluetongue Virus

T=13
780 subunits
Max. diameter 711Å

Source: Jack Johnson's "VIPER" site http://mmtsbd.scripps.edu/viper/viper.html
Molecular Structure

Objects of interest ~ 1 Å
Use radiation of ~ 1 Å (x-rays)

Scattered radiation
Collect scattered radiation
Compute
Molecules in random orientation in solution--small angle scattering
What do you get out of solution scattering?

The scattering signal results from interference of scattering from pairs of atoms => the scattering profile (I vs. angle) has information on atom-atom distances, averaged over all possible orientations.

From these data, can extract a "radius of gyration" from information at low scattering angles, and with information from higher scattering angles, information about shape of the object.
Solution Small-Angle X-ray Scattering on HslUV

P(r) curves: dotted lines, experimental; solid lines, calculated from models

Crystal structure 2

Crystal structure 2 + I domain extension

Crystal structure 1

\[ R_g^{(\text{calc})} = 63.8\text{Å} \]

\[ R_g^{(\text{calc})} = 69.0\text{Å} \]

\[ R_g^{(\text{calc})} = 91.5\text{Å} \]
Solution (& low angle crystal) scattering from an icosahedral virus

The scattering intensity from a uniform sphere of radius $a$ is given by:

$$< I(h) > = \frac{9 [\sin(ha) - ha \cdot \cos(ha)]^2}{(ha)^6}$$

which has the form shown at right:

Qualitatively, icosahedral viruses show a similar oscillatory scattering curve; the intensities of reflections from virus crystals versus scattering angle show a similar profile:

Comparison of the absolute values of single crystal reflection amplitudes (circles) in the 270 to 90 Å resolution range with the small-angle X-ray scattering data recorded on sFFV (thick continuous line) and the calculated scattering from a uniform sphere of 315 Å in diameter (thin continuous line). The amplitudes obtained from various methods were scaled to the single-crystal observations. The filled triangles correspond to the single-crystal reflection amplitudes calculated from the uniform sphere. The indices of a few selected observed reflections and their resolution are indicated by the filled circle nearest the label. Note that the single-crystal measured diffraction amplitudes (circles) between 270 and 90 Å match well with the uniform sphere-based computed crystal scattering amplitudes (triangles).