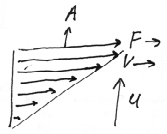
120123 Quiz 2 Morphology of Complex Materials

1) Explain the following terms: (for states comment on biological activity and relative size of the structure)
   a) Native State
   b) Unfolded State
   c) Denatured State
   d) Free Energy Landscape
   e) Levinthal Paradox
   f) Directed Process
   g) Stop Flow Kinetics
   h) Molten Globule

2) We discussed the use of viscosity measurements to determine the hydrodynamic radius of a protein.
   a) Sketch a diagram of a shear flow measurement showing the **direction** of the force (F) and area (A) that define the shear stress, τ. Show in the same diagram the **direction** of the velocity, v, and direction of change in velocity, u, that define the rate of strain, $\dot{\gamma}$, then write Newton's Law that defines viscosity, η, in terms of τ and $\dot{\gamma}$.
   b) Write a Taylor series expression, including only the first two terms, that describes the viscosity of a protein solution, η_{sol}, as a function of the solvent viscosity, η_0, the solution concentration, Φ, and the intrinsic viscosity, $[\eta]$.
   c) Is the intrinsic viscosity a type of viscosity, that is, could it somehow be used in the equation of part "a"? Explain your answer. (Are the units of $[\eta]$ Pa?)
   d) How is the intrinsic viscosity related to the molecular weight of the protein?
   e) How can the hydrodynamic radius be determined from the intrinsic viscosity?

ANSWERS 120123 Quiz 2 Morphology of Complex Materials

1) a) Native state is the biologically active state, generally the most compact structure observed in a folding sequence. The native state has essentially 0 conformational entropy.
b) Unfolded state is a state with no significant secondary structure, generally the least compact structure possible with the highest conformational entropy, that is, many different conformations are explored in the unfolded state due to thermal fluctuations
c) Denatured state is a state that results from chemical, thermal, physical or mechanical disruption of secondary and tertiary structure and leads to a molecule that is not biologically active. The denatured state can be related to a wide range of structures.
d) We can consider the free energy of a range of conformations that are possible across different physical, thermal and chemical conditions as constructing a free energy topology or landscape that the molecule "explores" to find the global minimum. The general shape of the free energy landscape is of a funnel with the native state at the lowest free energy.
e) Levinthal Paradox refers to a calculation of the number of possible states a protein can take and the time that would be associated with exploring all of these conformations to find the global minimum. It is a paradox that exploring all states even for a simple protein would preclude formation of native state structures in a reasonable time.
f) "Directed process" indicates that protein folding occurs loosely along a given pathway that is preprogrammed in the amino acid sequence.
g) Stop flow kinetics is an experimental method to observe protein folding involving rapidly changing the protein conditions in a flow cell to favor folding and observing the folding after flow has been frozen.
h) Molten Gobule is an intermediate state with some secondary structure but little or no tertiary structure. Molten globule is close in size to the native state but lacks most biological function.

2.) a) 

b) $\eta_{sol} = \eta_0 (1 + [\eta]\phi + \ldots)$

c) $[\eta]$ is not a viscosity
it has inverse concentration units
$\frac{Volume}{Mass}$

d) $Volume \sim (Size)^3$
$Mass \sim Size^{d_f}$
$[\eta] \sim \frac{Volume}{Mass} = Mass^{(3/d_f - 1)}$

e) $[\eta] \sim \frac{Volume}{Mass}$ $\quad Volume \sim Mass\,[\eta]$
$R_H \sim (MW\,[\eta])^{1/3}$