Lecture week 7: Polymer physics (TB)

1. Polymer basics
   - Polymers are long chain molecules composed of $N$ repeating structural units (monomers) which are typically connected by covalent bonds; $N \gg 1$.
     - Examples: DNA, RNA, actin filaments, synthetic polymers (e.g. polystyrene, polypropylene, polyester).
   - Polymers have many interesting properties, e.g. they can crosslink and form gels.
     - This is a broad and active field of study. Here, we focus on individual polymers.
   - Basic terminology:
     - Contour length:
       - This is the length $L$ of a polymer at maximum extension.
       - It is convenient to describe a specific polymer conformation by a path $\vec{r}(\lambda)$ in space which is parameterized by the contour length: $\vec{r}(\lambda), 0 \leq \lambda \leq L$ with $\|d\vec{r}(\lambda)/d\lambda\| = 1$.
     - Persistence length:
       - This is the length scale $\xi_p$ on which the polymer is essentially rigid.
       - Formally, $\xi_p$ is defined as the length scale of correlation decay of the tangent vector $\vec{t}$ along the contour in thermodynamic equilibrium: $\langle \vec{t}(\lambda) \cdot \vec{t}(\lambda') \rangle = \exp(-|\lambda - \lambda'|/\xi_p)$, where $\vec{t}(\lambda) = d\vec{r}(\lambda)/d\lambda$ and the average $\langle ... \rangle$ is taken over the ensemble of all possible conformations of the polymer.
       - Example:
         - The persistence length of double-stranded DNA is $\xi_p = 50$nm (in conditions as found in the cytosol).
         - The length of dsDNA is about 0.34nm/bp. Hence, a typical chromosome (with e.g. ~4.5Mbp) is much longer than the dsDNA persistence length.
       - Persistence length of an actin filament: $\xi_p = 17$μm.
       - Persistence length of a microtubule: $\xi_p = 1.4$mm.
     - Measures of the ‘size’ of a polymer in solution:
       - End-to-end distance $R = \langle \vec{R}^2 \rangle^{1/2}$, where $\vec{R}$ is the vector that points from one end of the polymer to the other end.
       - A closely related measure is the radius of gyration $R_G$ which quantifies the average distance of the center of mass of the chain to the chain itself: $R_G^2 = \frac{1}{N} \sum_{i=1}^{N} \langle (\vec{R}_i - \vec{R}_{CM})^2 \rangle$, with $\vec{R}_{CM} = \frac{1}{N} \sum_{i=1}^{N} \vec{R}_i$.

2. Polymer models & scaling laws
   - Simple theoretical models can capture key properties of polymers in solution.
   - Ideal chain:
     - The ideal chain model describes a polymer as $N$ discrete connected stiff rods of length $a$ (Kuhn length). This model further makes the simplifying assumptions that the orientations of neighboring rods are completely independent and that there are no interactions between the rods.
- The Kuhn length $\alpha$ corresponds roughly to twice the persistence length, $\alpha = 2\xi_p$.
- In the ideal chain model, polymer conformations are analogous to random walks. This allows us to directly transfer known properties of random walks.
  
  **Ideal chain in thermodynamic equilibrium:**
  - The energy of an ideal chain is independent of its conformation. Thus, in equilibrium all its possible conformations are equally likely to occur.
  - What is the equilibrium end-to-end distance $R$? Using the analogy to the mean square displacement of a random walk, we find $\sqrt{\langle R^2 \rangle} = \sqrt{Na^2} \approx \sqrt{2L\xi_p}$, where we used $N = L/\alpha$.
  - Similarly, the radius of gyration of an ideal chain is $R_G \approx \sqrt{L\xi_p}/3$.
  - Note: $R_G$ (or $R$) scales with the contour length $L$ with exponent 1/2: $R_G \sim L^{1/2}$.
  - Example: using the persistence length of DNA ($\xi_p = 50\text{nm}$) and the known genome size, we find for the *E. coli* chromosome $R_G \approx 5\text{\mu m}$. Compare this to the cell diameter of $\sim1\text{\mu m}$: the chromosome is confined into a relatively small space. This leads to an entropic force on the cell envelope (see below).
  - What is the probability of finding an ideal chain in a conformation with a certain end-to-end distance $R$?
    - See R Philips reference p. 285ff. for this calculation.
    - For $N \gg 1$ and $Na \gg R$ the final result is: 
      $$p(R; N) \approx \frac{1}{\sqrt{2\pi Na^2}} \exp\left(-\frac{R^2}{2Na^2}\right) \text{ ("Gaussian chain")},$$
    - From this result, it follows that the entropy $S_G$ of an ideal chain at fixed end-to-end distance $R$ is $S_G \approx k_B(\text{const.} - R^2/2Na^2)$.
  
  **Real chain:**
  - The real chain model generalizes the ideal chain model by taking into account excluded volume effects, i.e. different monomers of the chain are no longer allowed to occupy the same space.
  - Conformations of a real chain correspond to self-avoiding random walks.
  - A famous scaling argument by Paul Flory shows that for a real chain, the radius of gyration scales as $R_G \sim N^\nu$, with the exponent $\nu = 3/(d + 2)$. Here, $d$ is the space dimensionality.
  - We see directly that in $d = 1$, $R_G$ scales linearly with the polymer size ($\nu = 1$), as expected. In $d = 3$, the exponent $\nu = 3/5$ is larger than the exponent $\nu = 1/2$ of the ideal chain, reflecting the anticipated larger ‘size’ of the polymer due to excluded volume effects.
  - Direct numerical calculations are in very good agreement with these results.
  - In $d = 4$, the scaling exponent is again $\nu = 1/2$ i.e. the same as for the ideal chain. This means that the excluded volume interactions have become irrelevant in 4 (or more) dimensions: $d = 4$ is the upper critical dimension.

3. **Entropic forces**
   - Polymer physics provides one of the most intuitive examples of an entropic force.
   - Imagine you pick the two ends of an (ideal chain) polymer in solution with a micromanipulation device and pull them apart. Statistical physics tells us that the...
polymer will try to minimize its free energy $F = E - TS$. All conformations of an ideal chain have the same energy $E$. Hence, we can neglect $E$ in the free energy. Still there will be a force that acts to pull the polymer ends closer together. This is an entropic force. To understand the origin of this force, consider the fully stretched out polymer: it has just one possible conformation and thus very low (zero) entropy. Many more conformations are accessible when the polymer ends are closer together. Thus, such states have higher entropy $S$ and lower free energy $F$.

- There is also a more intuitive explanation for the origin of this force. Again, imagine that the polymer is fully stretched. Solvent molecules bumping into it as a result of their thermal motion will lead to a force that pulls the polymer ends closer together.

- How does this force $f$ depend on the distance $R$ between the polymer ends?
  - Result: for small extensions ($R \ll L$) we find: $f (R) = \frac{\partial F}{\partial R} = -T \frac{\partial S}{\partial R} = \frac{k_BT}{L} R$, i.e. the same linear force-extension relation as for an ideal Hookean spring holds.
  - The stiffness constant of such an “entropic spring” is $k = \frac{k_BT}{L\alpha}$.
    - Note: the stiffness increases with temperature, clearly reflecting the entropic origin of this force.
    - Interesting: a polymer of fixed length $L$ with smaller persistence length (smaller $\alpha$) has higher stiffness. E.g. for the lambda phage genome (dsDNA with $L = 16.6\mu m$), $k \approx 2.3$ fN/μm while for ssDNA of the same length, $k \approx 160$ fN/μm.

- Such force-extension relations for polymers can be experimentally measured for individual molecules, e.g. using optical tweezers.

References / further reading:

- R Philips book, chapter 8
- Jun and Wright, Nature Reviews Microbiology 8, p. 600, 2010