Biophysics Midterm 2 2009S.

Gel-less Electrophoresis:

I actually did the math in Mathematica (file attached), but the results are:

1. $F_{ES} = qE$ and $q = \lambda L$, so

$$F_{ES} = \lambda L E$$

2. By definition, the hydrodynamic radius R_H produces the actual Stokes drag $F_{drag} = 6\pi\eta R_H v$, so $\gamma = 6\pi\eta R_H$

3. At terminal velocity, $F_{ES} = F_{drag}$, so

$$\lambda L E = 6\pi\eta R_H v$$
$$\hookrightarrow \quad v = \frac{\lambda L E}{6\pi\eta R_H}$$

4. By the Stokes-Einstein relation, $D = \frac{k_B T}{\gamma}$, so

$$D = \frac{k_B T}{\gamma} = \frac{k_B T}{6\pi\eta R_H}$$

With $R_H = \beta L^{\alpha}$ (for $\alpha = 1/2, 1/3$ or 1), ~~$\frac{E\lambda}{6\pi\eta\beta}(1-\alpha)L^{-\alpha}$~~

so $v = \frac{E\lambda}{6\pi\eta\beta} L^{1-\alpha}$. Then

5. $\Delta v = \frac{dv}{dL}\Delta L = \frac{E\lambda}{6\pi\eta\beta}(1-\alpha)L^{-\alpha}\Delta L$

6. In a time t, the distance b/t two bands will be $\Delta x = \Delta v t$,

$$\Delta x = \frac{E\lambda \Delta L}{6\pi\eta\beta}(1-\alpha)L^{-\alpha} t$$

7. Meanwhile, diffusion occurs, so the bands spread to a size $\sigma = \sqrt{2Dt} = \left(\frac{2k_BT}{6\pi\eta R_H}\, t\right)^{\frac{1}{2}} = \left(\frac{k_BT}{3\pi\eta\beta}\, L^{-\alpha} t\right)^{\frac{1}{2}}$

8. When $\Delta x = \sigma$ the bands can be resolved:

$$\left(\frac{k_BT}{3\pi\eta\beta}\, L^{-\alpha} t\right)^{\frac{1}{2}} = \frac{E\lambda\delta L}{6\pi\eta\beta}\,(1-\alpha)L^{-\alpha}\, t$$

$$\frac{k_BT}{3\pi\eta\beta}\, L^{-\alpha}\cancel{t}\left(\frac{6\pi\eta\beta}{E\lambda\delta L}\right)^2 \frac{L^{2\alpha}}{(1-\alpha)^2} = t^{\cancel{2}}$$

$$\boxed{T_R = \frac{k_BT}{E^2\lambda^2\delta L^2}\, 12\pi\eta\beta\, \frac{L^{\alpha}}{(1-\alpha)^2}}$$

(plain T is temperature).

a. So $T_R \propto \frac{L^{\alpha}}{(1-\alpha)^2}$

which scales like L^{α} <u>unless</u> $\alpha = 1$

b. When $\alpha = 1$ this expression blows up, because

$V \propto L^{1-\alpha}$ so V = constant (independent of length)

when $\alpha = 1$. If all DNA migrate at the same rate you obviously can't differentiate them this way.

9. For a ~~rod~~ random coil,

$R_g = \sqrt{\frac{N}{6}}\, h$ with h = random walk step size.

a = link length, ξ = persistence length.

$N = \frac{L}{a}$

$a = \sqrt{3}\, h = 2\xi$, so (plugging in numbers)

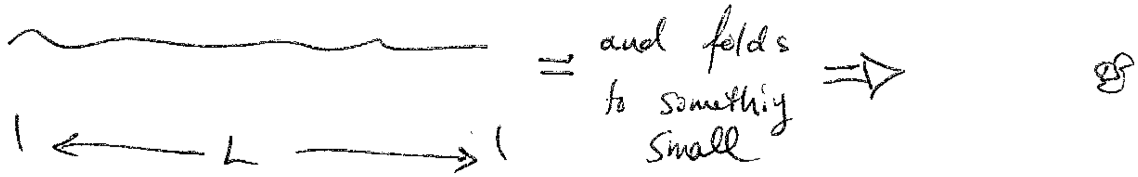
$\beta = 2.36\ \sqrt{nm}$. Putting this into 8. gives

$T_R = 27{,}300\ \sqrt{N_{bp}}\ s$ for $\Delta L = 1\ bp$

w/ $N_{bp} = 1000$, $T_R = 240\ h$ and $x = 590\ cm$

Villin

8. Somewhere in the paper the authors state they start folding from an "extended" conformation. Assuming this means "stretched out", the initial state looks like



The rmsd (treating the folded state as v. small) is

$$R_i \simeq \left[\frac{\sum_i (r_i - 0)^2}{N}\right]^{\frac{1}{2}}$$

position of i^{th} residue, relative to midpoint of segment

N residues in segment

For a $C_\alpha - C_\alpha$ distance of $\sim 4\text{Å}$ $\quad r_i \sim i \cdot 4\text{Å}$ with the midpoint $r_{\frac{N}{2}}$ mapping to zero ie.

$$R \simeq \left[\frac{\sum_i \left(i\,(4\text{Å}) - \frac{N}{2}(4\text{Å})\right)^2}{N}\right]^{\frac{1}{2}} \simeq 4\text{Å} \cdot \left[\frac{\sum_{-N/2}^{N/2} (i)^2}{N}\right]^{\frac{1}{2}}$$

for $N \sim 18$ residues (in each segment) $\quad \sum_{-\frac{N}{2}}^{N/2} i^2 \simeq 570$, so

$$R \sim 4\text{Å} \cdot \sqrt{\frac{570}{18}} = 22\text{Å}$$

So the starting point was around $(20, 20)\text{Å}$: way off scale on their plot.

HP model
(partial solution).

4a. See attached graphs. Sequence 2 is convex b/t 2 and 4. Near this region the relevant transition temperatures correspond to $T_{4\to3}$, $T_{3\to2}$ and $T_{4\to2}$:

$$T_{4\to3} = 0.346\ \varepsilon/k_B$$

$$T_{3\to2} = 0.289\ \varepsilon/k_B$$

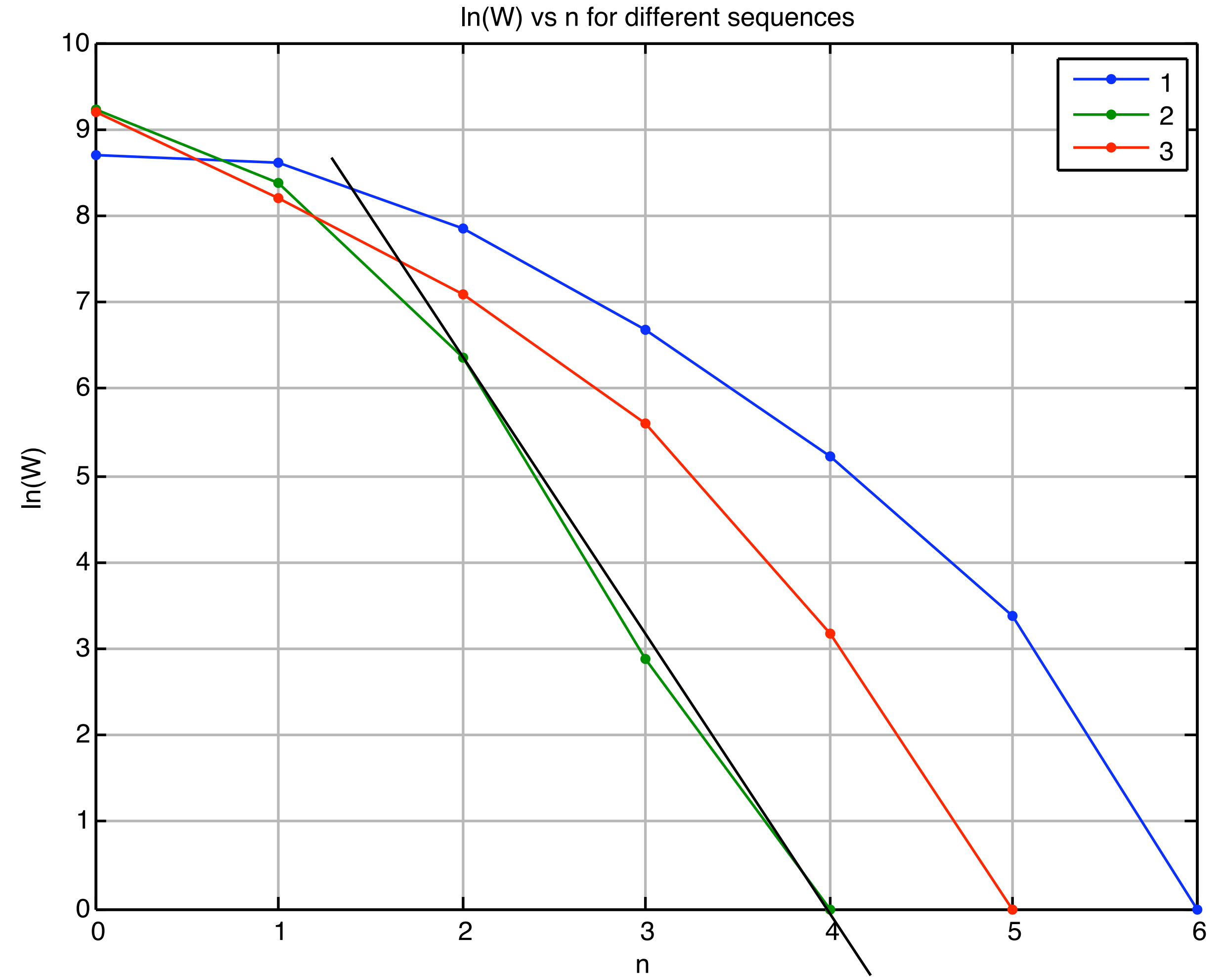
$$T_{4\to2} = 0.315\ \varepsilon/k_B.$$

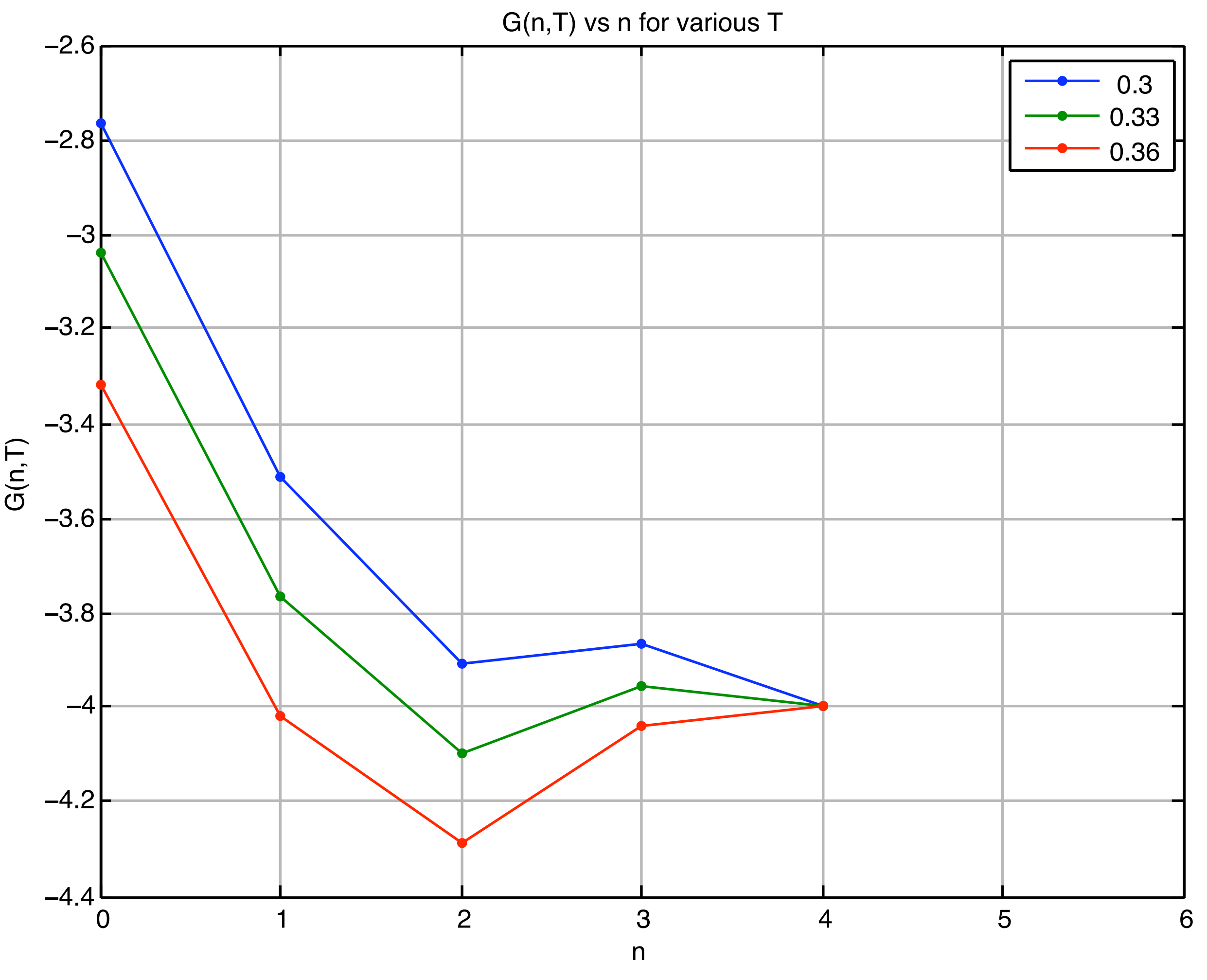
As temperature rises, first 3 becomes unstable towards 2 (though 3 isn't populated, so this doesn't matter), then 4 becomes unstable towards 2 (though it would have to pass through 3 first) and finally 4 becomes unstable with respect to 2.

This last condition ($T_{4\to3}$) is the end of metastability. Above $T_{4\to2}$ the ground state is <u>not</u> the global minimum but it is a local minimum. I.e.

$$0.315\frac{\varepsilon}{k_B} < T_{\text{metastable}} < 0.346\frac{\varepsilon}{k_B}$$

I've plotted $G(n,T)$ for $T = 0.30, 0.33, 0.36$


ln(W) vs n for different sequences
ln(W)
n
1
2
3
0
1
2
3
4
5
6
7
8
9
10
0
1
2
3
4
5
6


G(n,T) vs n for various T
G(n,T)
n
0.3
0.33
0.36
−2.6
−2.8
−3
−3.2
−3.4
−3.6
−3.8
−4
−4.2
−4.4
0
1
2
3
4
5
6