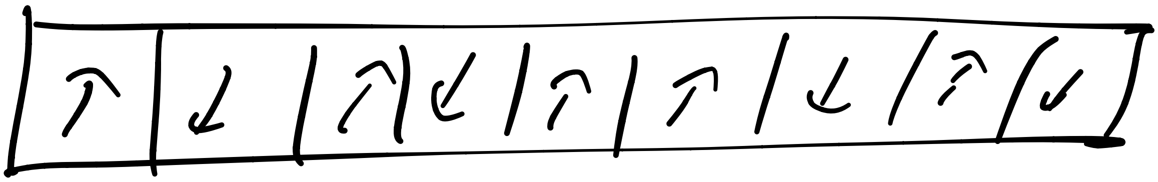
Helix-Coil Model

Previously discussed ising model,
a good model for phase transitions
and many other processes

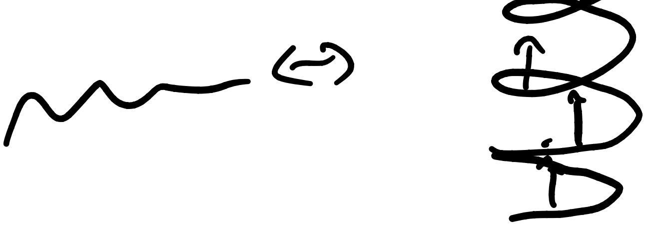


spins $\quad s_i = \pm 1/2$

$$\varepsilon = \sum_{i=1}^{N} \underbrace{-J s_i s_{i+1}}_{\text{neighbor coupling}} \underbrace{- h s_i}_{\text{field, energy}}$$

What is H-C model?

α-Helix is a common SS-element in
proteins



consider each
residue as H or
C conformation

doesn't make much sense for each residue to be independent, but consider for now

Lets say $\varepsilon_{coil} = 0$

$\varepsilon_H = -\varepsilon$ (favorable)

sum over states

for one residue $q = \sum_{n=0}^{1} e^{-\beta \varepsilon_n}$ (2 state model)

$= 1 + e^{+\beta\varepsilon}$

$P_H = \frac{e^{+\beta\varepsilon}}{q}$ $P_c = 1/q$

(think of $\Delta\varepsilon$ as ΔG see book for more details)

$K = P_H/P_c = e^{+\beta\varepsilon}$

$q_{site} = 1 + K$

and $P_H = \frac{K}{1+K}$

$\Delta\varepsilon = h$ ★

Connection to Ising model

$K = \frac{e^{+\beta h/2}}{e^{-\beta h/2}} = e^{\beta h}$ ↑ is H ↓ is C

Now from partition function perspective

$$q = 1 + k$$

N residues: $Q = q^N = (1+k)^N$

Consider short peptide as example

eg 4 sites

$$Q = (1+k)^4 = 1 + 4k + 6k^2 + 4k^3 + k^4$$

coeffs $\binom{N}{m}$ number of HC strings

HHHH CHHH etc CCCC

HCHH

HHCH

HHHC

$$= \sum_{n=0}^{2^n} e^{-\beta E_n} \quad \text{if counted all states}$$

$$= \sum_{E} w(E) e^{-\beta E} \quad E = -n_H \cdot \epsilon$$

$w(E) = \binom{N}{N_H}$ list by energy

$n_H = 0 \to N$

How do we get $\langle f_H \rangle$ from partition func

See that $f_H = \frac{n_H}{N} \left(= \frac{\mathcal{E}_{total}}{N\epsilon} \right)$

if $Q = \sum_{n_H=0}^{N} \binom{N}{n_H} e^{+\beta\epsilon n_H} = \sum_{n_H=0}^{N} \binom{N}{n_H} K^{n_H}$

$$f_H = \left\langle \frac{n_H}{N} \right\rangle = \sum_{n_H=0}^{N} \frac{n_H}{N} P(n_H) = \frac{\sum_{n_H=0}^{N} \binom{N}{n_H} \left(\frac{n_H}{N}\right) K^{n_H}}{Q}$$

$$\frac{\partial \ln Q}{\partial K} = \sum_{n_H=0}^{N} \binom{N}{n_H} n_H K^{n_H - 1} \Big/ Q = \frac{N}{K} f_H$$

$f_H = \frac{K}{N} \frac{\partial \ln Q}{\partial K}$ but $Q = (1+K)^N$

$= K/_{1+K}$ as before for one site

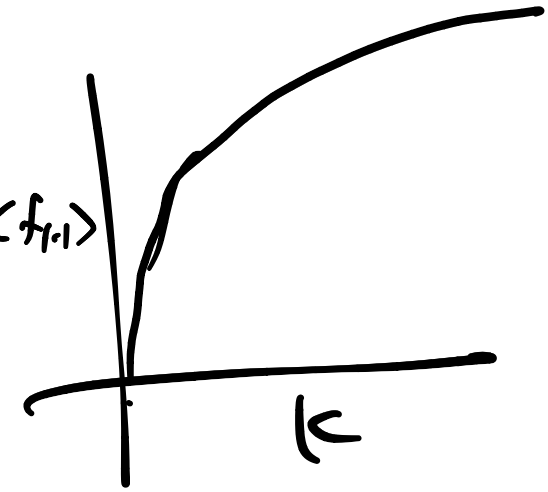
How does this connect to energy description

$\langle \mathcal{E}_{tot} \rangle = -\langle n_H \rangle \epsilon$

and $\langle \mathcal{E} \rangle = -\dfrac{\partial \ln Q}{\partial \beta} = -\dfrac{\partial \ln Q}{\partial K} \cdot \dfrac{\partial K}{\partial \beta}$

if $K = e^{+\beta\epsilon}$

$\dfrac{\partial K}{\partial \beta} = +\epsilon e^{+\beta\epsilon} = +\epsilon K$



so $\langle \mathcal{E}_{tot} \rangle = -\epsilon K \dfrac{\partial \ln Q}{\partial K}$

so $f_H = \langle n_H / N \rangle = -\dfrac{\langle \mathcal{E}_{tot} \rangle}{N\epsilon} = \dfrac{K}{N} \dfrac{\partial \ln Q}{\partial K}$ ✓

Heteropolymers:

proteins are chains of AA with different identities - 20 natural AA's

Each site could be different, and at this independent level, different K's

So $k_\alpha, k_\beta \ldots$

$$q_i = (1 + k_i)$$

and $$Q_N = \prod_{i=1}^{N} q_i$$

eg $(1+k_A)^{N_A}(1+k_B)^{N_B}$ for two types

Interacting model

Should really depend on neighbors

right now CHCHHC

$$BF = (1)(k)(1)(k)(k)(1) = k^3$$

But can add coupling τ for neighboring H

$$BF = (1)(k)(1)(k\tau)(k)C = k^3\tau$$

adding $\tau > 1$ makes stretches of helices

CF ising model τ is like J

but only 0's & 1's

final prob - exact analogy

<u>Zipper model</u>

Can solve in 1d exact partition function - first physical approx

Suppose τ very large so

eg a chain w/ 3 helices much more likely to have CCC HHH than HCCHCH eg

Contiguous

$\# = N - n_H + 1$ for $n_H = 1 \to N$

$(0, \# = 1)$

So $Q = 1 + \sum_{n_H=1}^{N} (N - n_H + 1) K^{n_H} \tau^{n_H - 1}$

c^N

$$= 1 + \frac{1}{\tau} \sum_{n_H=1}^{N} (N - n_H + 1)(K\tau)^{n_H}$$ Skip

$$= 1 + \frac{1}{\tau}\left[(N+1)\sum (K\tau)^{n_H} - \sum n_H (K\tau)^{n_H}\right]$$

$$-K \sum \tau^{n_H} \frac{d}{dK} K^{n_H}$$

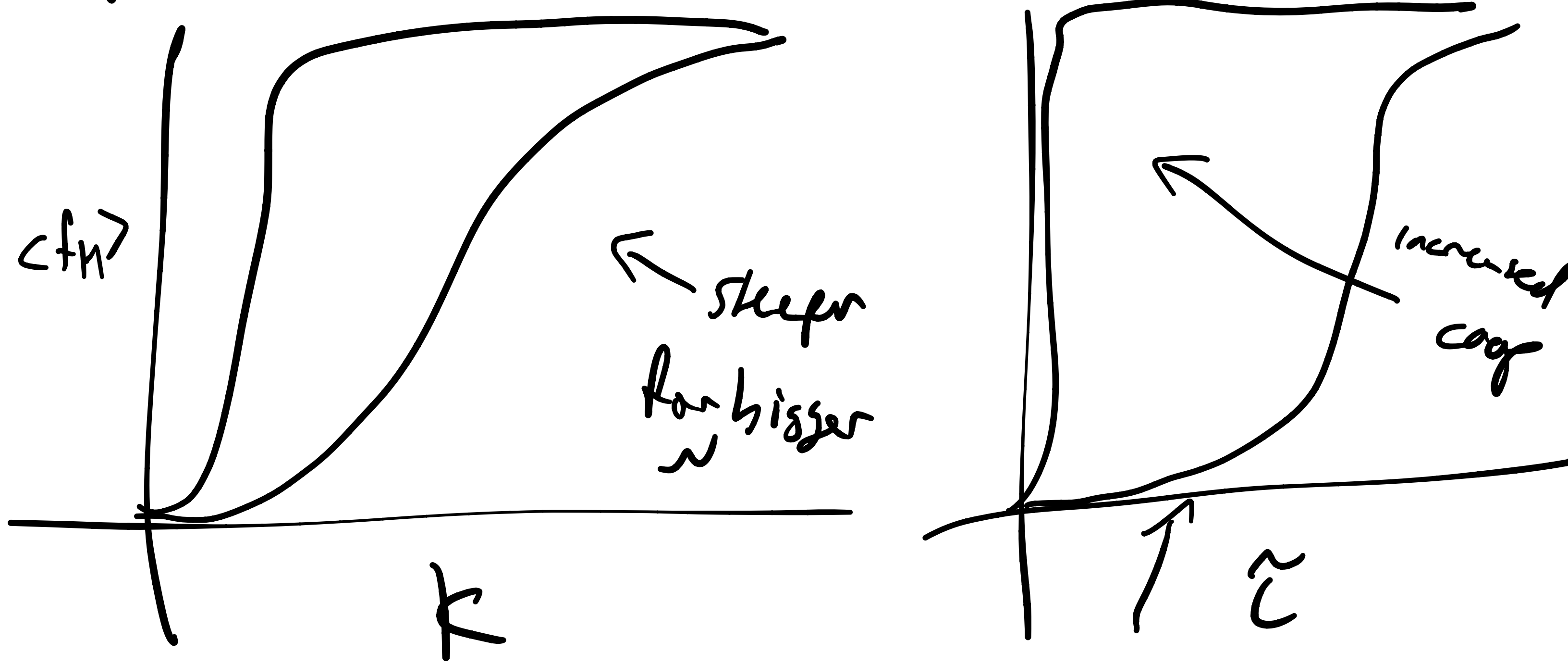
$$"$$

$$-K \frac{\partial}{\partial K}\left(\sum \left(\tau^{n_H} K^{n_H}\right)\right)$$

$$\sum_{n=1}^{N} x^n = \frac{(x^N - 1)x}{x - 1}$$

then can get f_H as $\frac{K}{N} \frac{\partial \ln Q}{\partial K}$ still complicated formula!

physically



$\tilde{\tau} = 1$ curve is wrong

we're in high $\tilde{\tau}$ limit for solution

How do we solve exactly?

Method called <u>transfer matrices</u>

partition function has 2^n terms

$$Q = \sum_{x_1=0,1} \sum_{x_2=0,1} \cdots \sum_{x_N=0,1} \prod_{i=1}^{N} k^{x_i} \tau^{x_i x_{i+1}}$$

2^N terms

$$x_i = \begin{cases} 0 & \text{helix} \\ 1 & \text{coil} \end{cases}$$

matrix mult $\begin{pmatrix} a & b \\ c & d \end{pmatrix} \begin{pmatrix} w & x \\ y & z \end{pmatrix}$

$$= \begin{pmatrix} aw+bx & ax+bz \\ cw+dy & cx+dz \end{pmatrix}$$ creates sums

transfer matrix represents possibilites for neighbors

$i-1 \backslash i$	h_i	c_i
h_{i-1}	$k\tau$	1
c_{i-1}	k	1

value at pos i

$$w = \begin{pmatrix} k\tau & 1 \\ k & 1 \end{pmatrix}$$

Every time we multiply W we get sums of terms representing Q if first pos is a helix or coil

These end up in bottom row, easiest to see w/ example

$$W = \begin{pmatrix} k\tau & 1 \\ k & 1 \end{pmatrix} \qquad Q = q = 1 + k$$

first is coil

first is helix

Chain of 2:

CC		CH	HC		HH
1	$+$	k	k	$+$	τk^2

$$W^2 = \begin{pmatrix} k\tau & 1 \\ k & 1 \end{pmatrix}\begin{pmatrix} k\tau & 1 \\ k & 1 \end{pmatrix}$$

$$= \begin{pmatrix} - & - \\ k^2\tau + k & k + 1 \end{pmatrix}$$

And this continues. To get bottom row sum

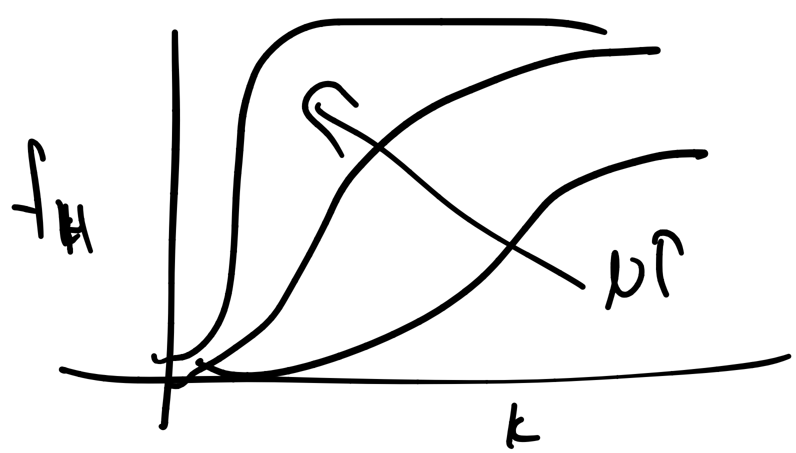
$$(0\ \ 1)\begin{pmatrix} a & b \\ c & d \end{pmatrix} = (0+c \quad 0+d) = (c\ \ d)$$

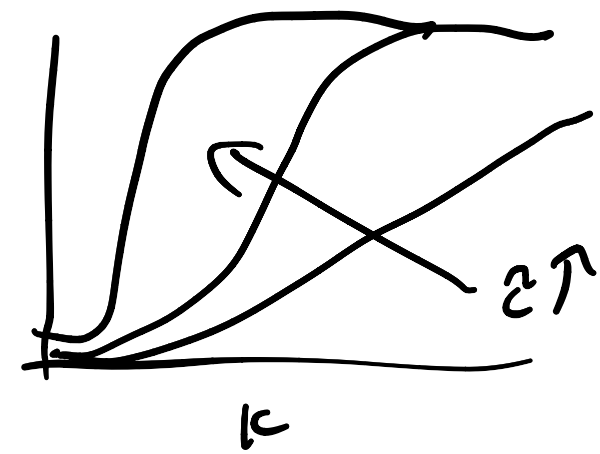
$$(c\ \ d)\begin{pmatrix} 1 \\ 1 \end{pmatrix} = c + d$$

$$Q = (0\ \ 1)\ W^N \begin{pmatrix} 1 \\ 1 \end{pmatrix}$$

can generate on computer

and get $f_H = \dfrac{K}{N} \dfrac{\partial \ln Q}{\partial K}$





Other versions / extensions
eg Zimm-Bragg

$$CCCCC \underset{\sigma}{\rightleftharpoons} CHCCC \underset{s}{\rightleftharpoons} CHHCC$$

$\sigma << 1 < s$

σ is cost of lone helix
s is bonus for adjacent H

$$w = \begin{pmatrix} k\tau & 1 \\ k & 1 \end{pmatrix}$$

$$w - I\lambda = \begin{pmatrix} k\tau - \lambda & 1 \\ k & 1-\lambda \end{pmatrix}$$

$$| \ | = (k\tau - \lambda)(1-\lambda) - k$$

$$= \lambda^2 - \lambda(k\tau + 1) + k(\tau - 1)$$

$$\lambda = \frac{(k\tau+1) \pm \sqrt{(k\tau+1)^2 - 4k(\tau-1)}}{2}$$