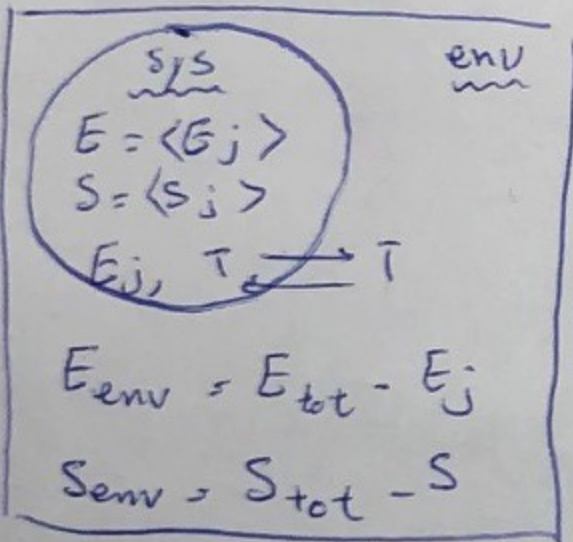


4L25  
 Last time:  $p_j = \frac{1}{W}$  if  $E$  is constant

$$\left. \begin{array}{l} \# \text{ --- } \\ \# + \text{ --- } \\ \vdots \end{array} \right\} p_j \sim e^{-\frac{E_j}{k_B T}} \text{ if } T \text{ is constant?}$$

Proof:



1)  $p_j = \frac{\text{number of ways sys can have energy } E_j}{\text{number of ways sys can have any energy}}$

$$= \frac{W_j(E_j) \cdot W_{env}(E_{tot} - E_j)}{W_{tot}(E_{tot})}$$

$$= W_j \cdot e^{(S_{env} - S_{tot})/k_B}$$

since

$$S = k_B \ln W$$

getting rid of  $S_{env} - S_{tot}$

2) let  $E \equiv \langle E_j \rangle$  and Taylor-expand

$S_{env}$  about  $x = E$ :

$$S_{env}(E_{tot} - E_j) = S_{env}(E_{tot} - E) - \frac{1}{T}(E_j - E) + \dots$$

$$\Rightarrow p_j = W_j e^{(S_{env} - \frac{1}{T}(E_j - E) - S_{tot})/k_B}$$

$$= W_j e^{(-\frac{E_j}{T} + \frac{E}{T} - S)k_B}$$

Today:

\* note that we drop the sys index of

system variables:  $E = E_{sys}; S = S_{sys}; \dots$

(continuing last page's  $p_j$  formula ---)

$$p_j = W_j \frac{e^{-E_j/k_B T}}{Z}, \text{ where } Z = e^{-\frac{E - TS}{k_B T}} = e^{-\frac{F}{k_B T}}$$

wrapping up:

$$*p_j = \frac{1}{W} \text{ if } E = \text{const} : W = \# \text{ of accessible microstates}$$

$$*p_j = \frac{W_j e^{-E_j/k_B T}}{Z} \text{ if } T = \text{const}:$$

$Z = \# \text{ of accessible microstates}$

$$T = \text{const}: \sum p_j = 1 \Rightarrow \sum \frac{W_j e^{-E_j/k_B T}}{Z} =$$

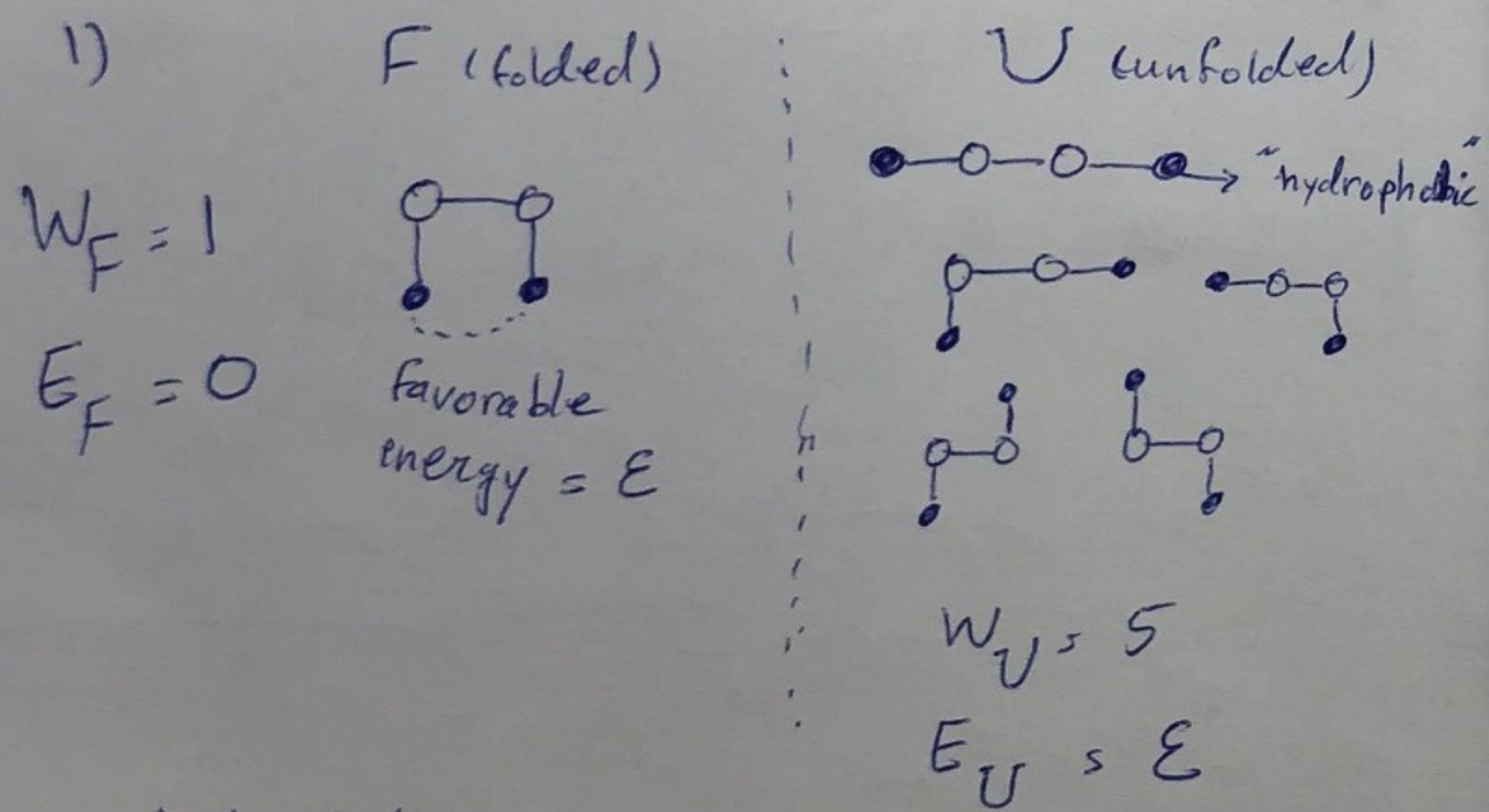
$$\frac{1}{Z} \sum W_j e^{-E_j/k_B T} = 1 \Rightarrow Z = \sum W_j e^{-E_j/k_B T} = e^{-\frac{F}{k_B T}}$$



\* by relating  $E_j$  and  $F$  using the formula for  $Z$  one can obtain  $F$  from the energies ( $E_j$ s) of system, e.g. derived from QM calculations.

Heat capacity of a folding hairpin (RNA, protein)

- 1) specify system
- 2) postulates 1 & 2  $\Rightarrow$  formula for system



\* hydrophobic residues are more stable if bound together, hence, folded state has a favorable hydrophobic interaction

$$Z = W_F \cdot e^{\frac{-0}{kBT}} + W_U \cdot e^{\frac{-E}{kBT}}$$

Joules molecule<sup>-1</sup>

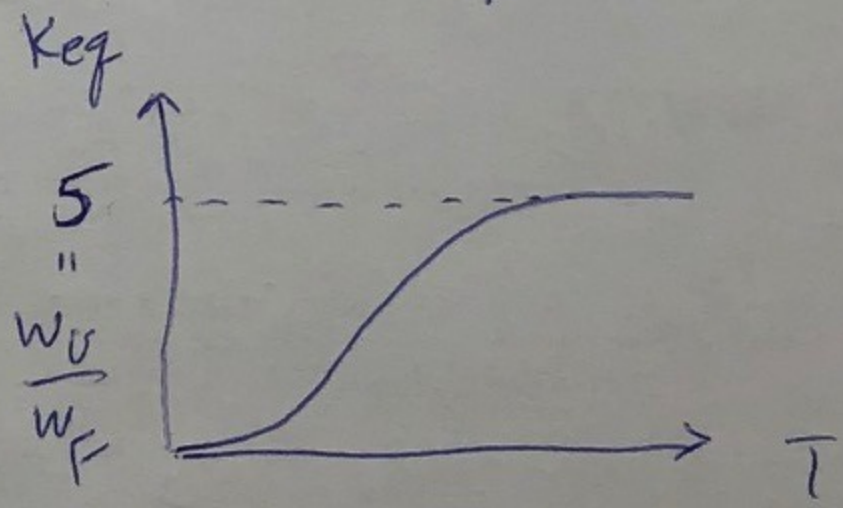
$$= W_F + W_U \cdot e^{\frac{-E}{RT}}$$

Joules mole<sup>-1</sup>

Also,  $P_F = \frac{W_F}{Z}$  ;  $P_U = \frac{W_U e^{-E/RT}}{Z}$

$$\frac{P_U}{P_F} = \frac{[U]}{[F]} = K_{eq} = U \rightleftharpoons F$$

$$= \frac{W_U e^{-E/RT}}{W_F} = 5 e^{-\frac{E}{RT}}$$





now, let's find the average energy:

$$E = \sum P_j E_j = P_F E_F + P_U E_U =$$

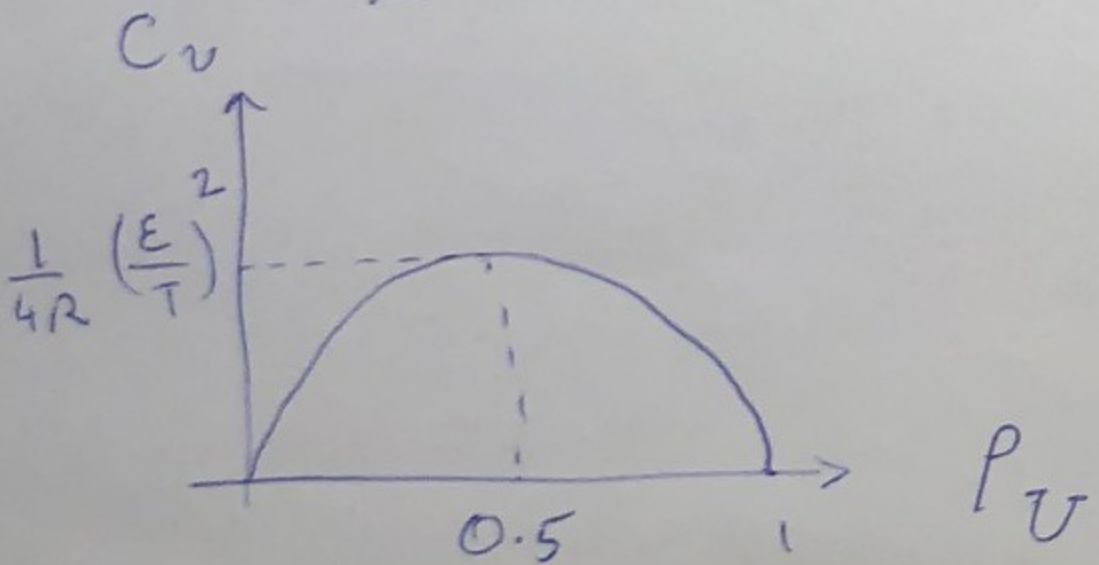
$$0 + \frac{W_U e^{-\frac{E}{RT}}}{Z} \cdot E = \frac{W_U E e^{-\frac{E}{RT}}}{Z}$$

↳  $E(T)$  is good enough to calculate the heat capacity of the protein

as  $C_V = \frac{\partial E}{\partial T}$

$$C_V = \frac{1}{R} \left(\frac{E}{T}\right)^2 P_U P_F$$

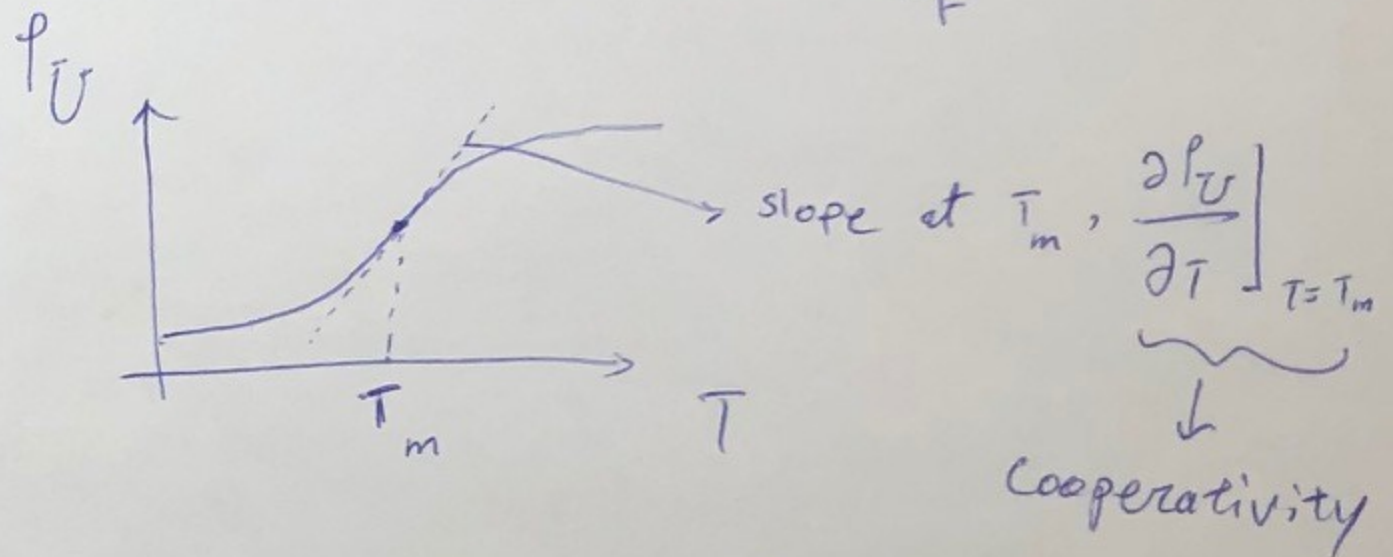
$$= \frac{1}{R} \left(\frac{E}{T}\right)^2 P_U (1 - P_U)$$



therefore, measuring heat capacity can give us the energy of folding ( $E$ ) using the plot on the previous page.

Now, plotting  $P_U$  (fraction of unfolded):

$$P_U = 1 - P_F = \frac{\frac{W_U}{W_F} e^{-\frac{E}{RT}}}{1 + \frac{W_U}{W_F} e^{-\frac{E}{RT}}}$$



\* by calculating  $\frac{\partial P_U}{\partial T} \Big|_{T=T_m}$  it can be shown that this slope (cooperativity) is proportional to  $\frac{W_U}{W_F}$ . In the extreme case,  $W_U \gg W_F$  and the plot becomes a step function, same as ~~ice~~ ice melting.