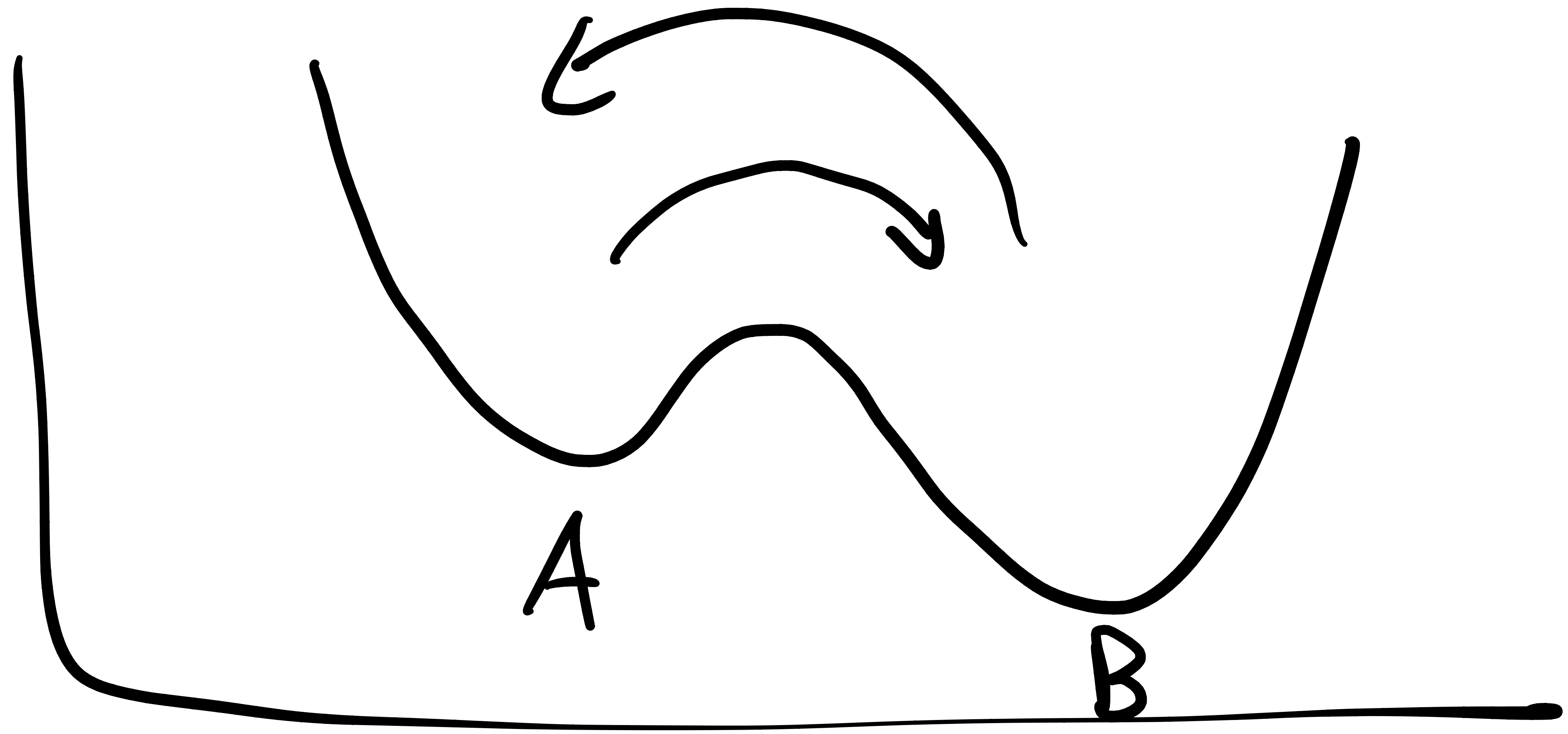
Lecture 16



$$A \rightleftarrows B$$

$$\Delta G^\circ = -RT\ln(K_{eq})$$

$$K_{eq} = \frac{[B]}{[A]}$$

$$K_{eq} = \frac{[B]}{[A]}$$

$$f_A = \frac{[A]}{[A] + [B]}$$

$$[B] = K_{eq}[A]$$

probability (?)

(reactant)

$$f_A = \frac{[A]}{[A] + K_{eq}[A]} = \frac{1}{1 + K_{eq}}$$

$$n_{total} f_A = n_A$$

$$f_A + f_B = 1$$

$f_{product}$

$$f_B = \frac{K_{eq}}{1 + K_{eq}} = \frac{1}{1 + K_{eq}^{-1}}$$

$$f_A = \frac{1}{1 + K_{eq}} \qquad A \rightleftarrows B$$

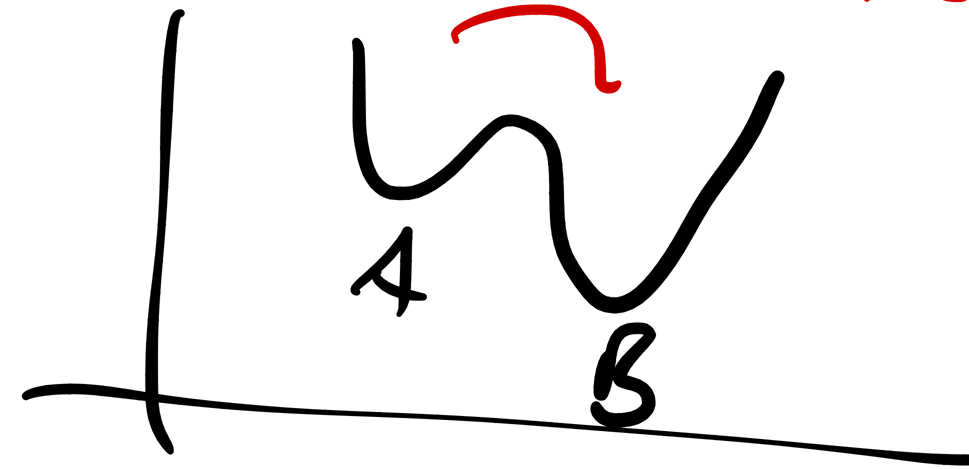
$$f_B = \frac{1}{1 + K_{eq}^{-1}} \qquad K_{eq} = e^{-\Delta G/RT}$$

$RT \sim 0.6$ kcal/mol or 2.5 kJ/mol
at ~ 300K

$$f_A = \frac{1}{1 + e^{-\Delta G/RT}} \qquad f_B = \frac{e^{-\Delta G/RT}}{1 + e^{-\Delta G/RT}} = \frac{1}{1 + e^{+\Delta G/RT}}$$

$$f_A = \frac{1}{1+e^{-\Delta G/RT}}$$

metastable states



$A \rightleftharpoons B$

$\Delta G < 0$

$\Delta G > 0$ then wat happens

as $1/T$ gets bigger, $f_A \to 1$

$T \to 0$; $f_B \to 0$

$\Delta G < 0$, opposite, $f_A \to 0$

$f_B \to 1$ as $T \to 0$

looks like $P(\text{state}) = e^{-\Delta G/k_B T} \cdot \text{const}$

@ const T

How can we get ΔH & ΔS of folding from an experimental measurement

y_N ← observable for the "native" state

y_D ← observable for "denatured" state

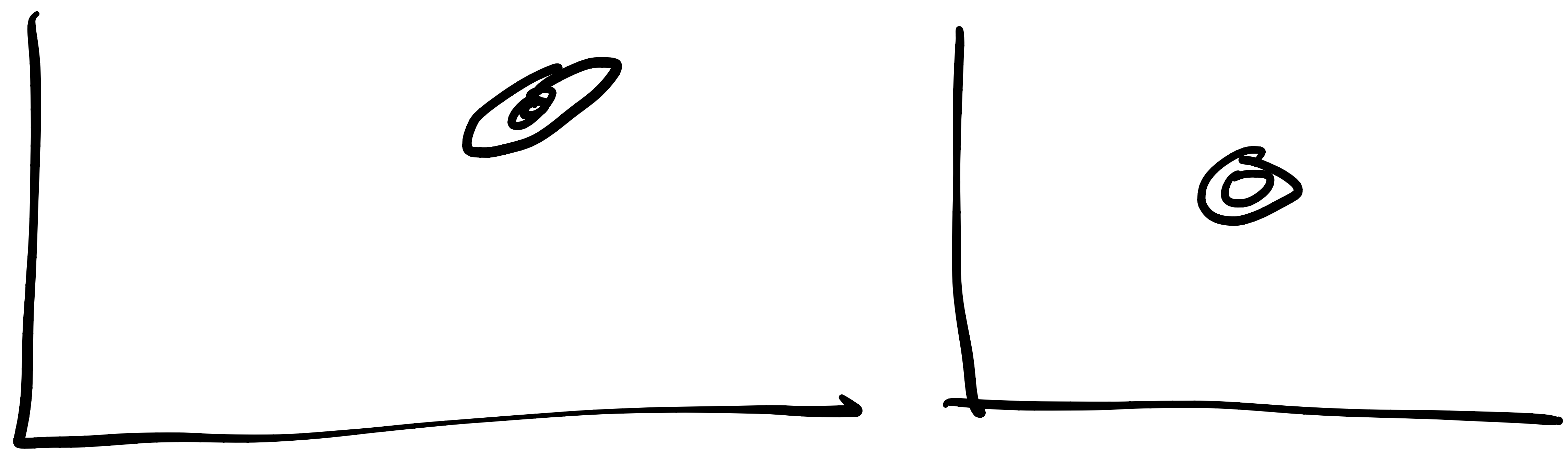
FRET – energy transfer between two dye molecules

resonance energy transfer

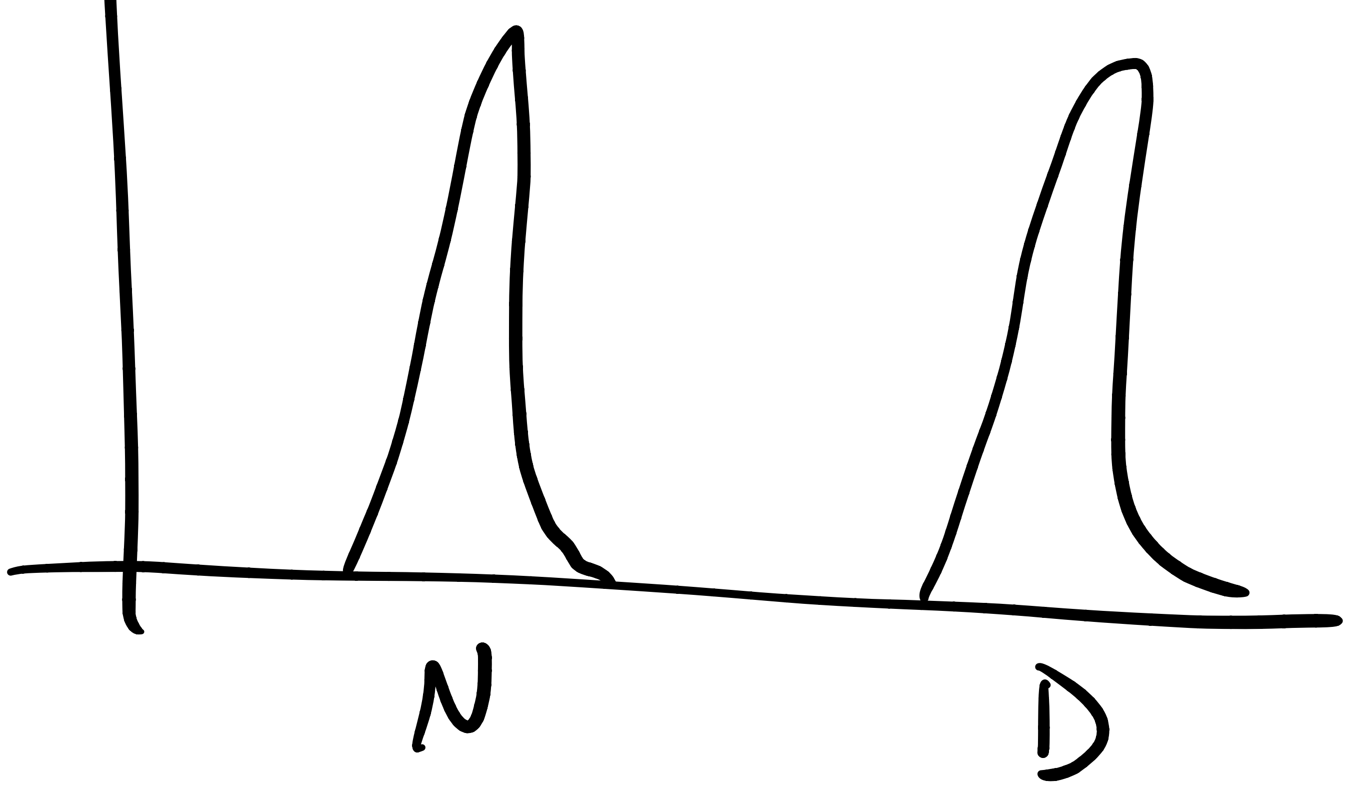
measure fraction of short to long wavelength...

Circular Dichroism - Circularly polarized light
reports on SS in proteins
eg 220 nm

NMR -

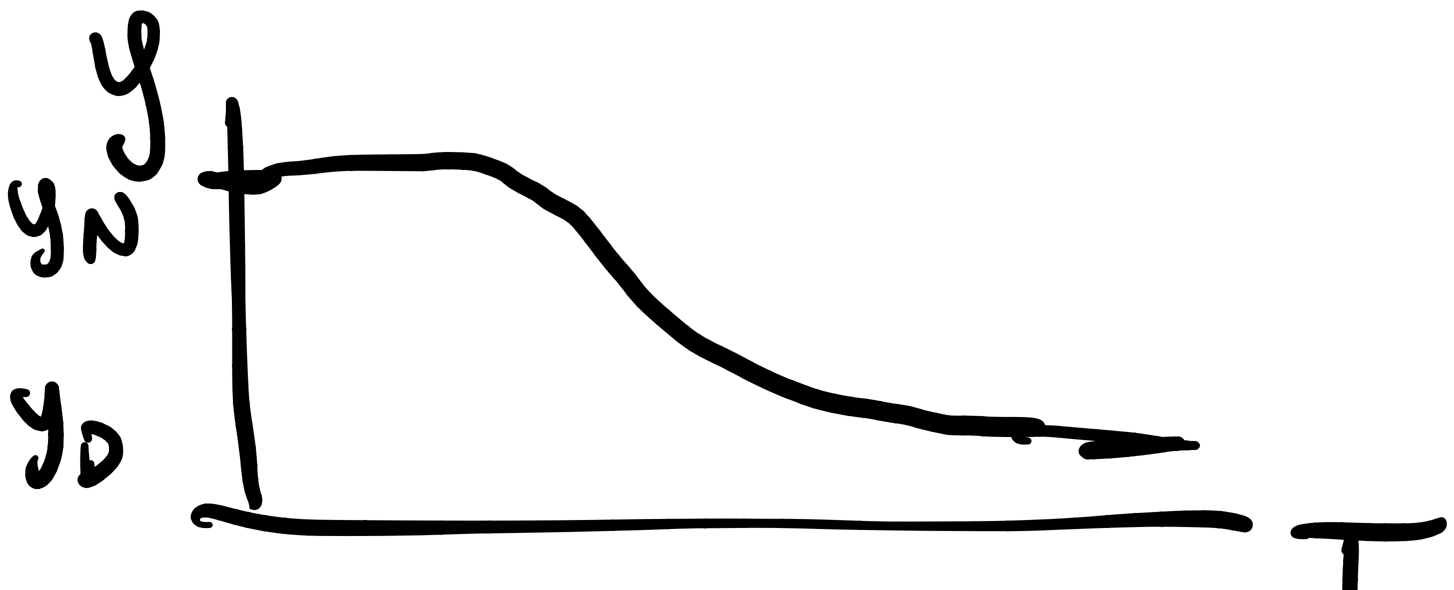


50/50



look like 100% N

question is what is $f_N = \frac{1}{1+e^{\Delta G/RT}}$



$$\langle y \rangle = \sum_i y_i \, P(i)$$

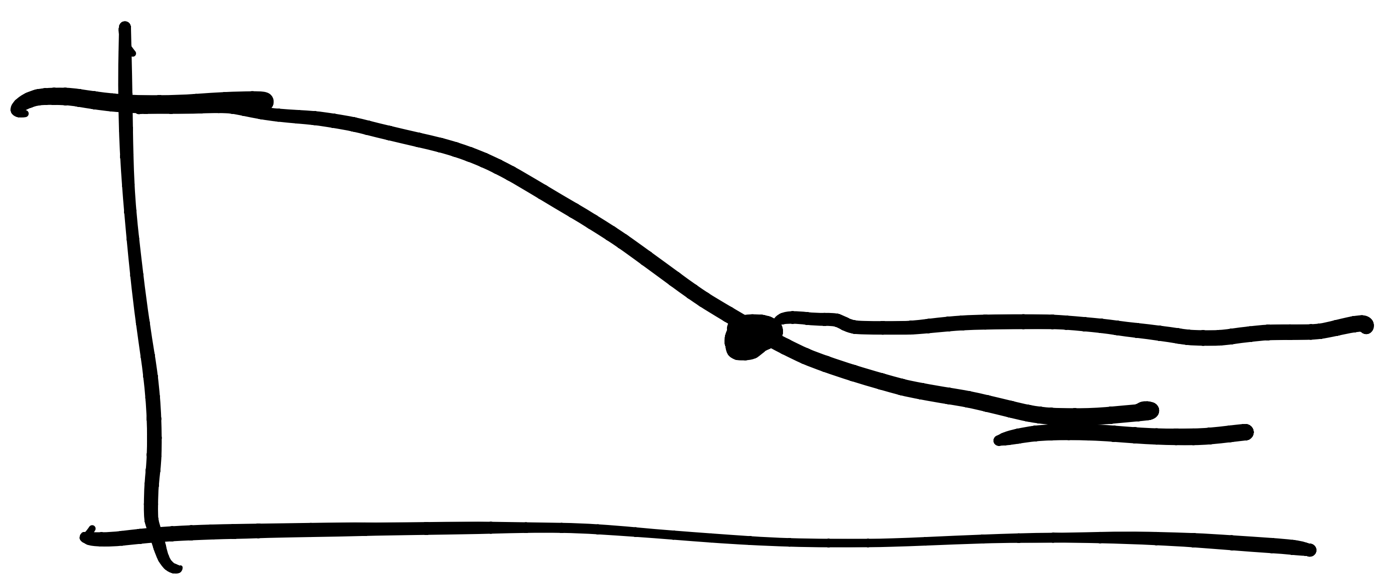
discrete states

$$= y_N \frac{1}{1+e^{\Delta G/RT}} + y_D \frac{1}{1+e^{-\Delta G/RT}}$$

$$f_D = \frac{1}{1+\underbrace{e^{-\Delta G/RT}}_{K}}$$

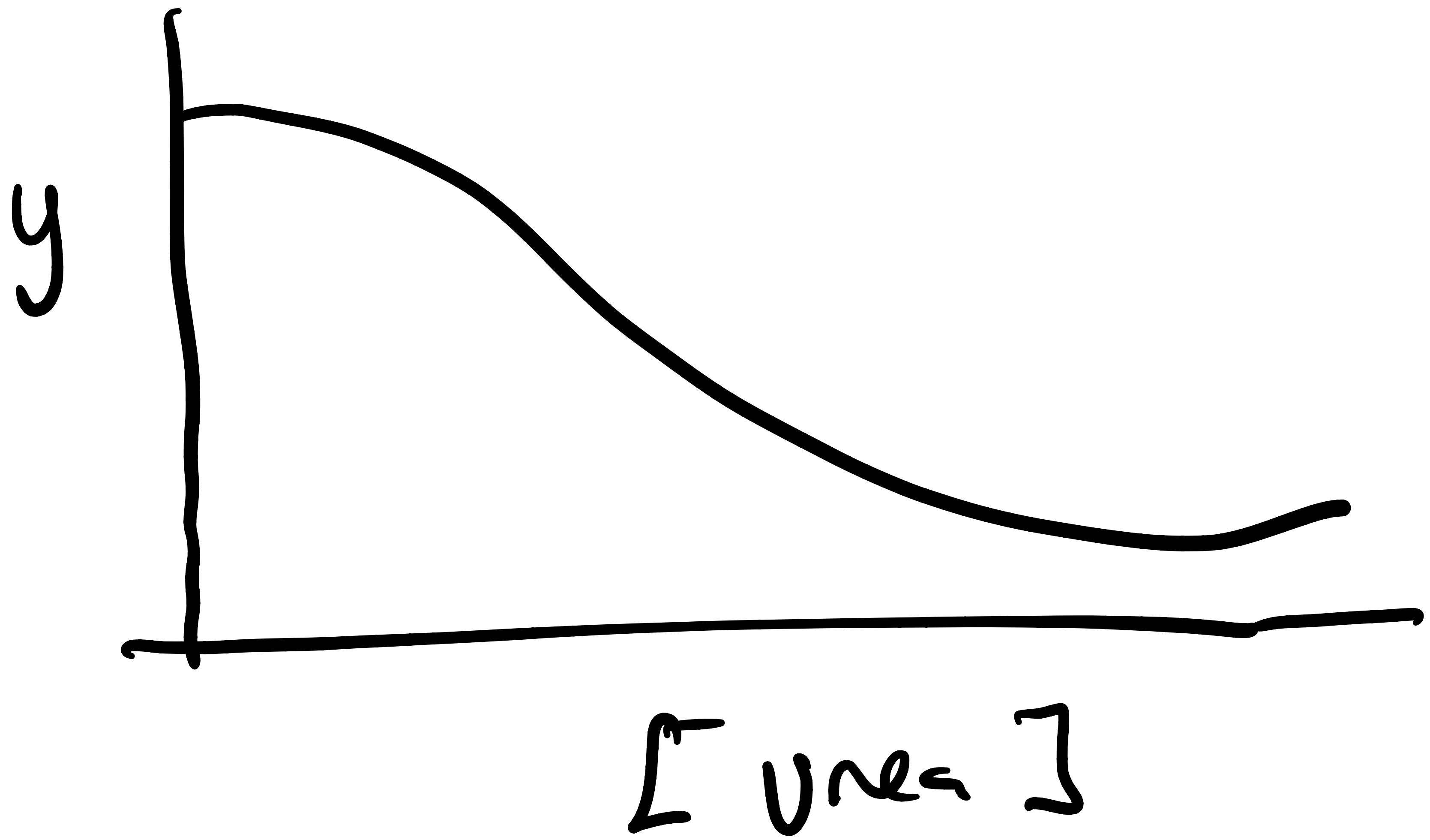
$$f_N = \frac{K}{1+K} = \frac{e^{-\Delta G/RT}}{1+e^{-\Delta G/RT}}$$

$$= \frac{1}{1+K^{-1}} = \frac{1}{1+e^{\Delta G/RT}}$$

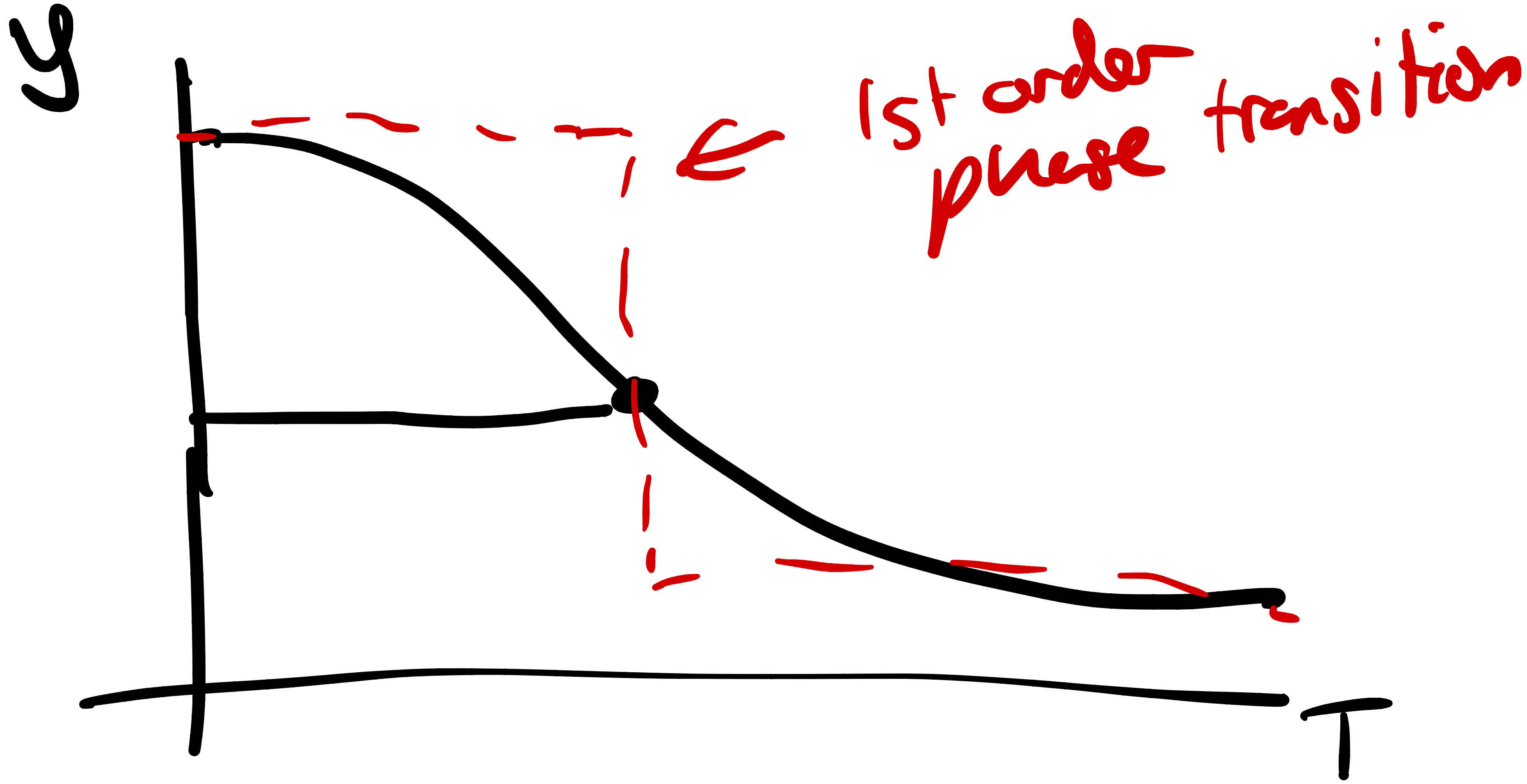


f_N or f_D

$$f_N = \frac{y - y_D}{y_N - y_D}$$



chemical
denaturation



$$f_N \cdot y_N + f_D \cdot y_D$$

" ?

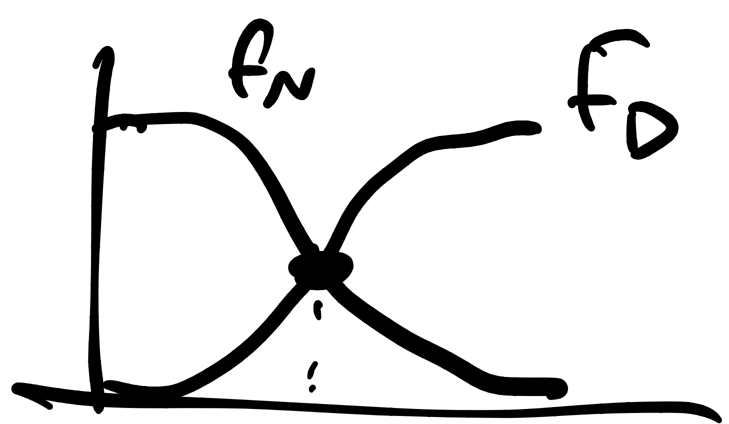
$\frac{1}{2}$

$$f_N \ \& \ f_D = \frac{1}{2}$$

$$\frac{y^* - y_D}{y_N - y_D} = 0.5$$

$$f_N = \frac{1}{1+e^{+\Delta G/RT}} \qquad f_D = \frac{1}{1+e^{-\Delta G/RT}}$$

$$\Delta G = 0$$



$@\ T = T_{melt}$

@ T_m $\quad \Delta G = 0 = \Delta H - T_m \Delta S$

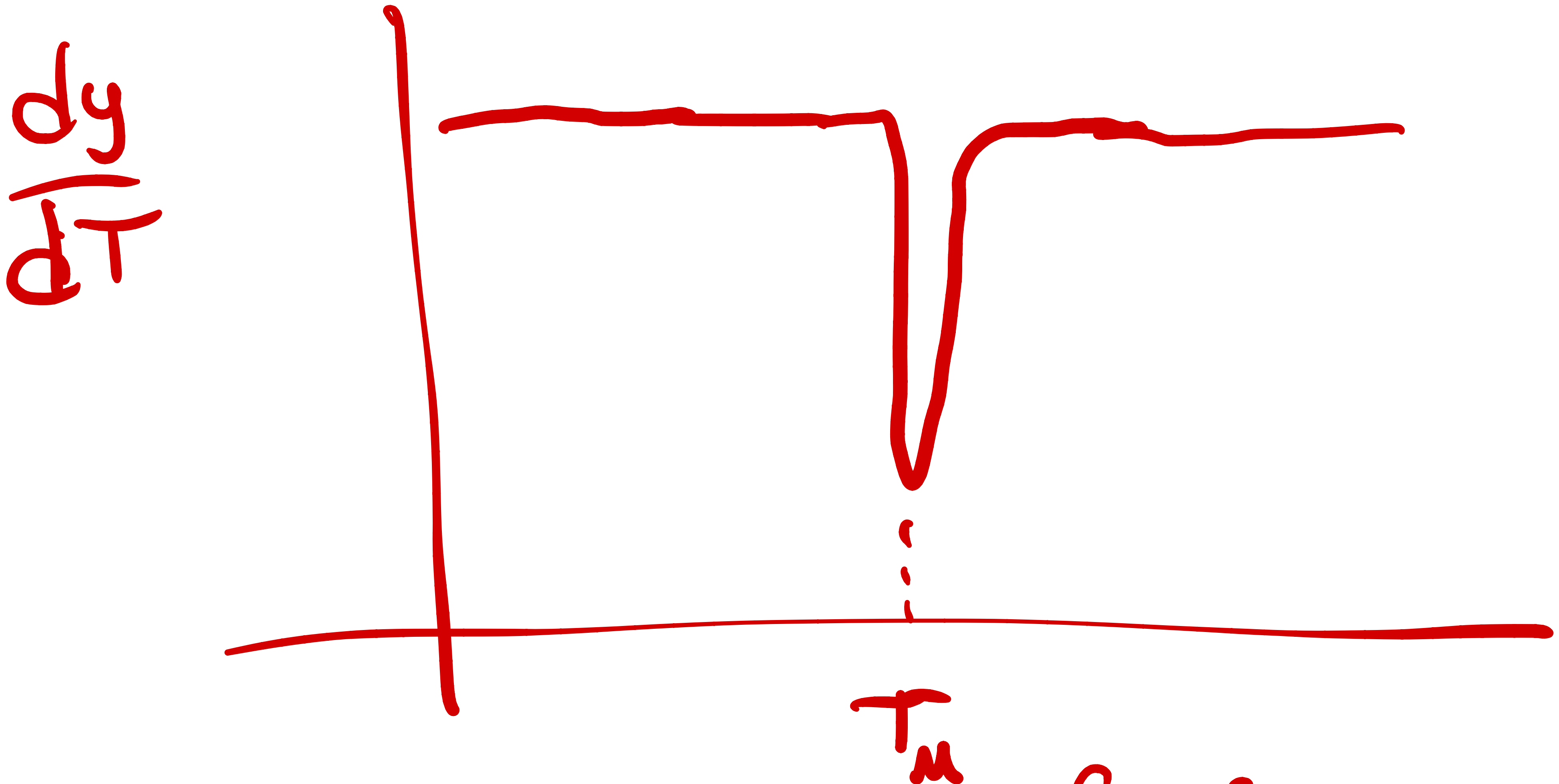
$$T_m = \Delta H / \Delta S$$

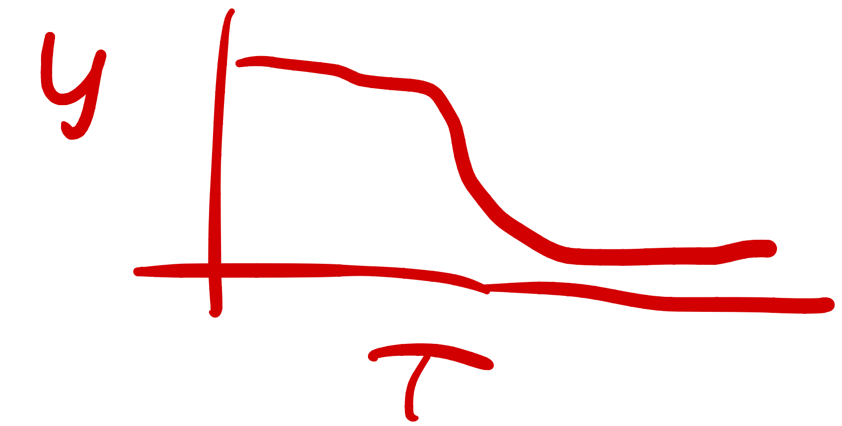
$\langle y \rangle$

$$= y_{obs} = \frac{y_D + y_N e^{-\Delta G/RT}}{1 + e^{-\Delta G/RT}}$$

what does this look like near T_m

how steep is the transition





$$\frac{dy}{dT} = (y_N - y_D)\overbrace{\frac{K}{(1+K)^2}}^{f_N \cdot f_D}\frac{\Delta H}{RT^2}$$

$$K = e^{-\Delta G/RT}$$

@ T_m

$K = 1$

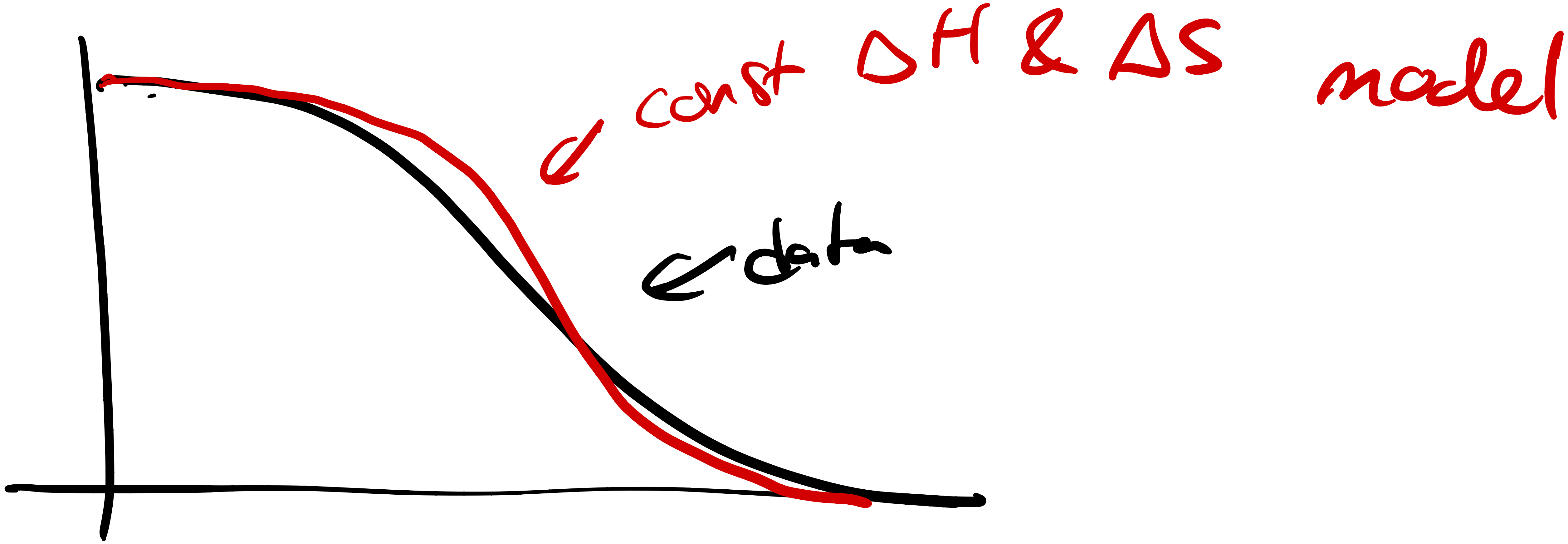
$$\left.\frac{dy}{dT}\right|_{T_m} = \frac{(y_N - y_D)}{4} \frac{\Delta H}{R T_m^2}$$

fit to get ΔH, get ΔS from ΔH & T_m

$$\Delta G = \Delta H - T\Delta S = \Delta H - T\,\Delta H / T_m$$

$$= \frac{\Delta H (T_m - T)}{T_m}$$

$$K = e^{\frac{\Delta H (T - T_m)}{RT \cdot T_m}}$$



more sophisticated model: constant heat capacity model

C_p for N & D is const

$$d\bar{H}_N = \bar{C}_p^N \, dT$$

$$d\bar{S}_N = \frac{\bar{C}_p^N}{T} \, dT$$

$$f_N = \frac{1}{1+e^{\Delta G/RT}}$$

$\Delta G = \Delta\bar{H}_N - T\Delta\bar{S}^N$

for T close to T_m

$$\begin{cases} \Delta\bar{H}_N = \bar{C}_p^N (T - T_m) \\ \Delta\bar{S}_N = \bar{C}_p^N \ln(T/T_m) \end{cases}$$

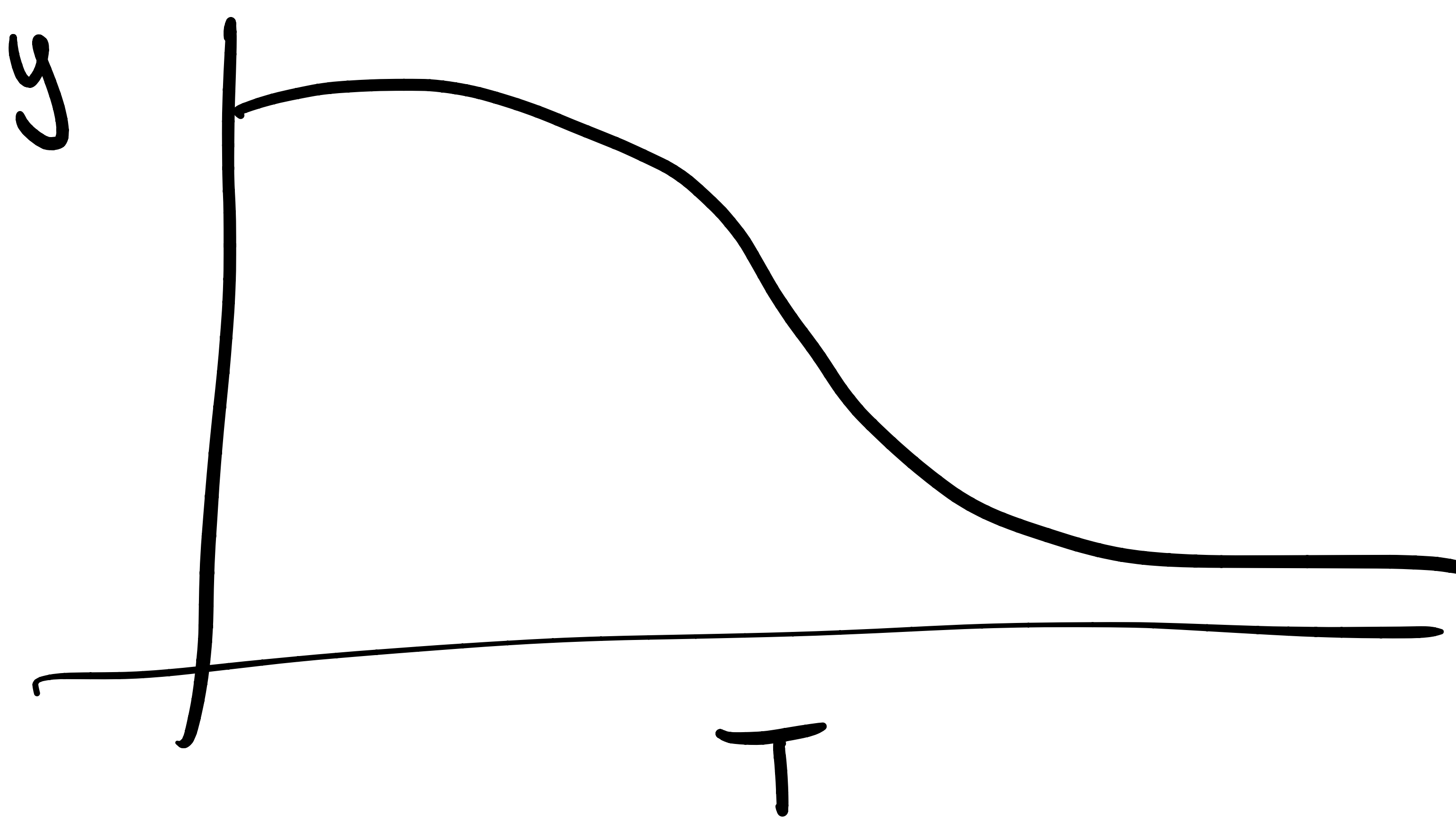
same thing for $\Delta\bar{H}_D$

Preview

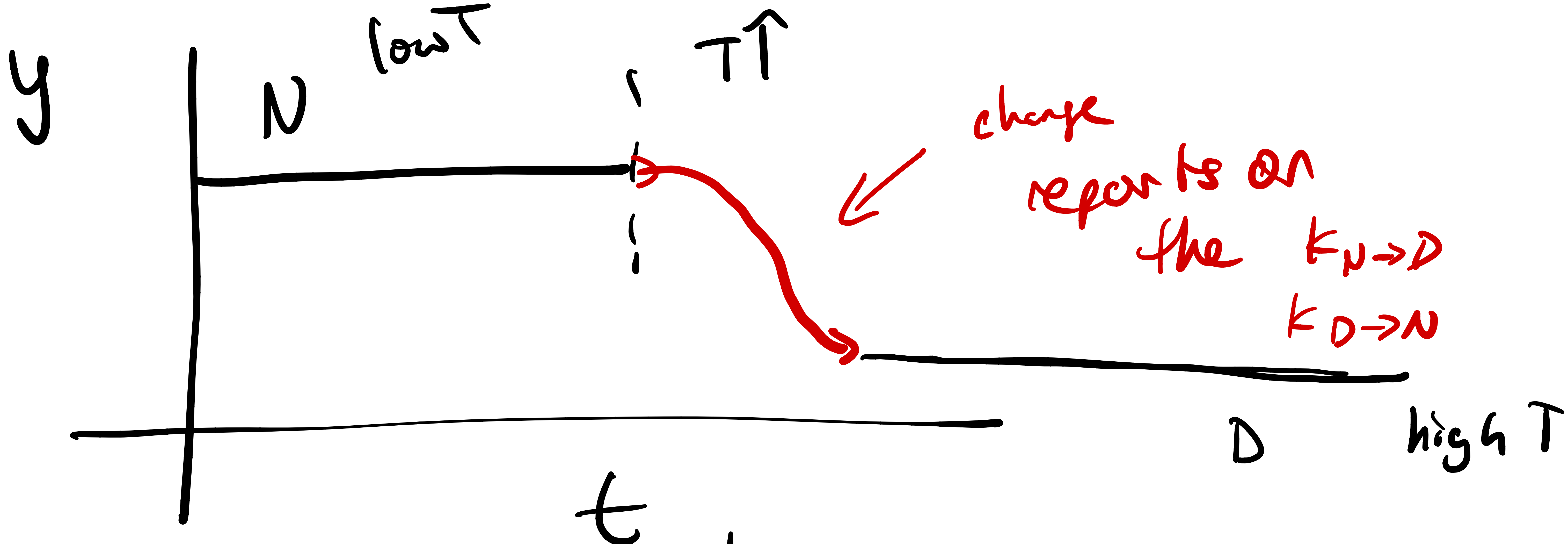
We will see

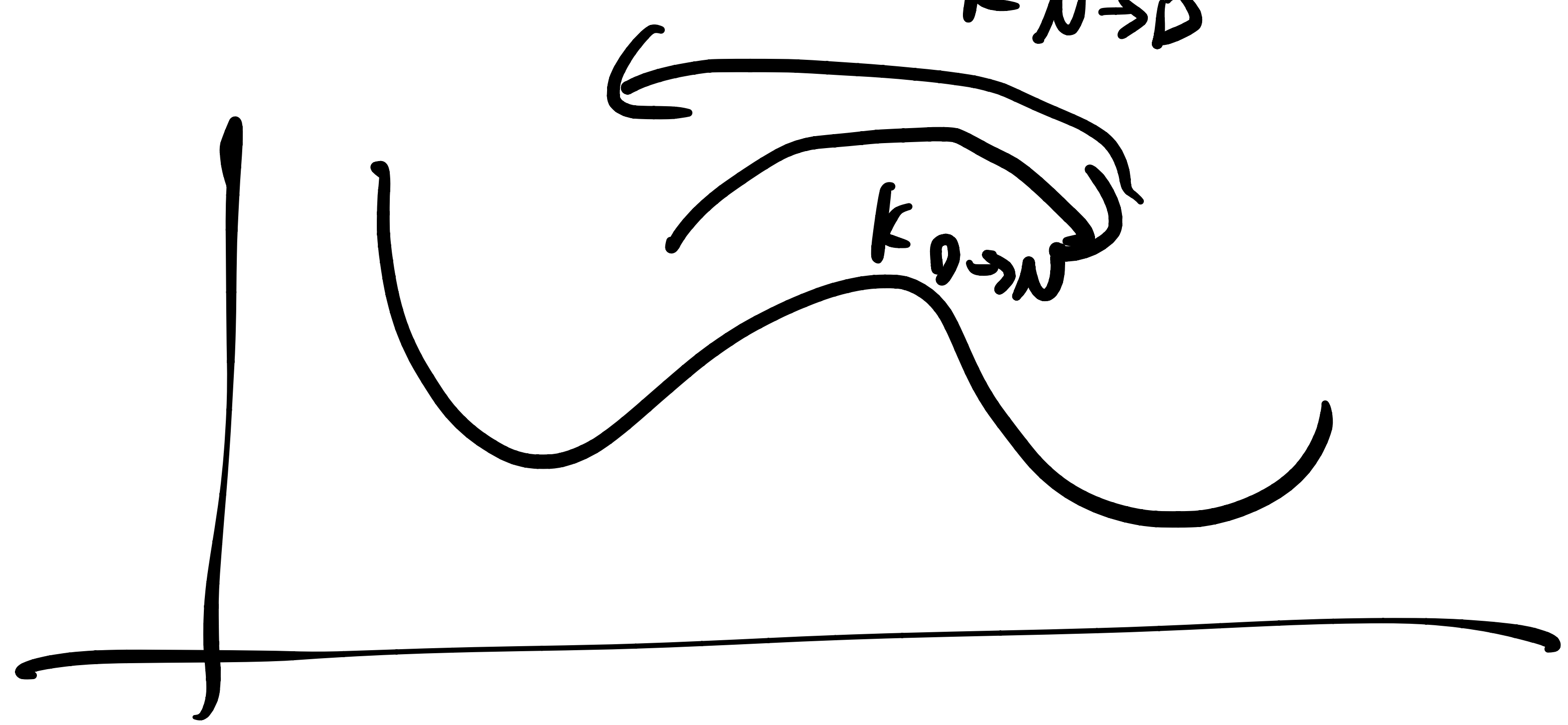
$$C \propto \mathrm{Var}(\mathcal{E})$$

Preview



What happens if you change T quickly?


y
N
low T
T↑
change
reports on
the $k_{N\to D}$
$k_{D\to N}$
D
high T
t


$k_{N\to D}$
$k_{D\to N}$