Q's / recap / correction

$$\ln\left(\frac{K_2}{K_1}\right) = -\frac{\Delta \bar{H}^\circ}{R}\left(\frac{1}{T_2} - \frac{1}{T_1}\right)$$

$$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$$

usually ΔS isn't const

constant heat capacity

$$aA + bB \rightleftarrows cC$$

for chemical reactions ΔH is constan't w/ T

$$aA + bB \rightleftarrows cC + dD$$

ν_A (→ a), ν_B (→ b), ν_C (→ c), ν_D (→ d)

~~$\nu_A \xi = \nu_B \xi = \dots$~~

$$2A + 3B \rightleftarrows 5C$$

$$dN_A = -\nu_A \, d\xi$$

$$dN_C = \nu_C \, d\xi$$

etc

$$dG = \mu_A dN_A + \mu_B dN_B + \dots$$

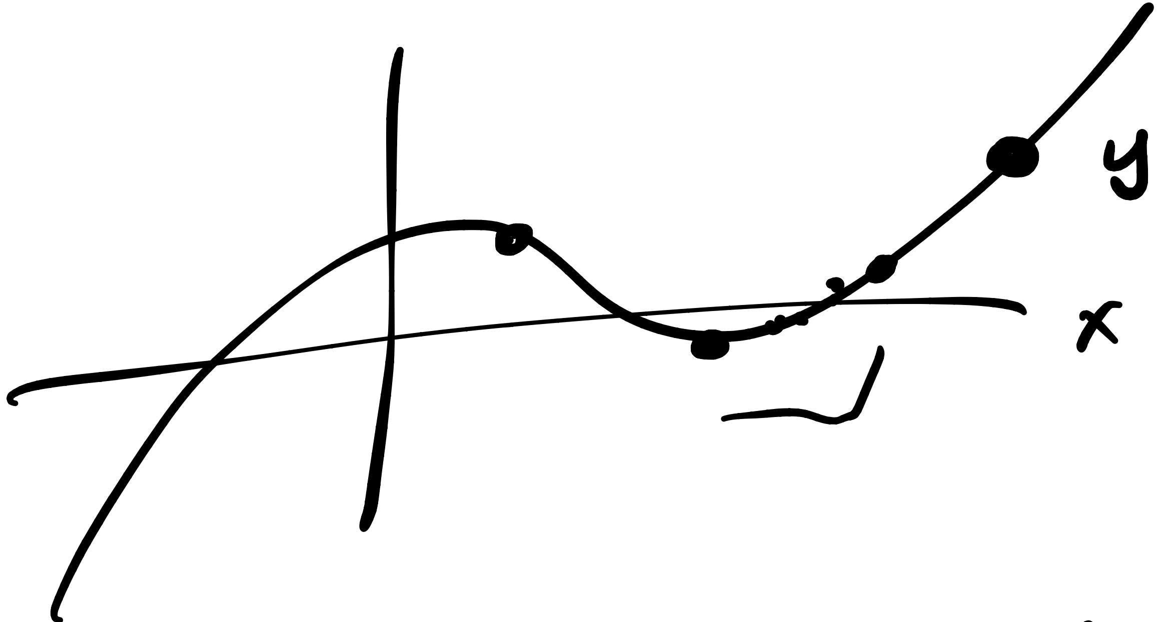
$$aA + bB \rightleftharpoons cC$$

$$Q = \frac{[C]^c}{[A]^a [B]^b}$$

$$aA + bB \rightleftharpoons cC$$

1 molar   1 molar B   0.5 C

$(1M - a\xi)$ $(1M - b\xi)$ $(0.5M + c\xi)$



$$\Delta G = -RT \ln Q(\xi)$$

~~$\Delta G + RT \ln Q(\xi)$~~ $= 0$

$$e^{-\Delta G/RT} = Q(\xi)$$

$$e^{-\Delta G/RT} - Q(\xi) = 0$$

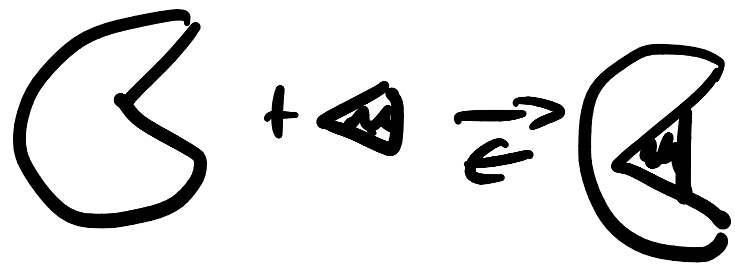
Conformational Equilibrium

① "folding"

$$D \rightleftharpoons N$$

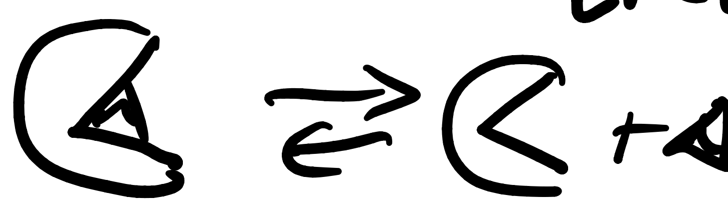
$$Q_{folding} = \frac{[N]}{[D]}$$

② "binding"

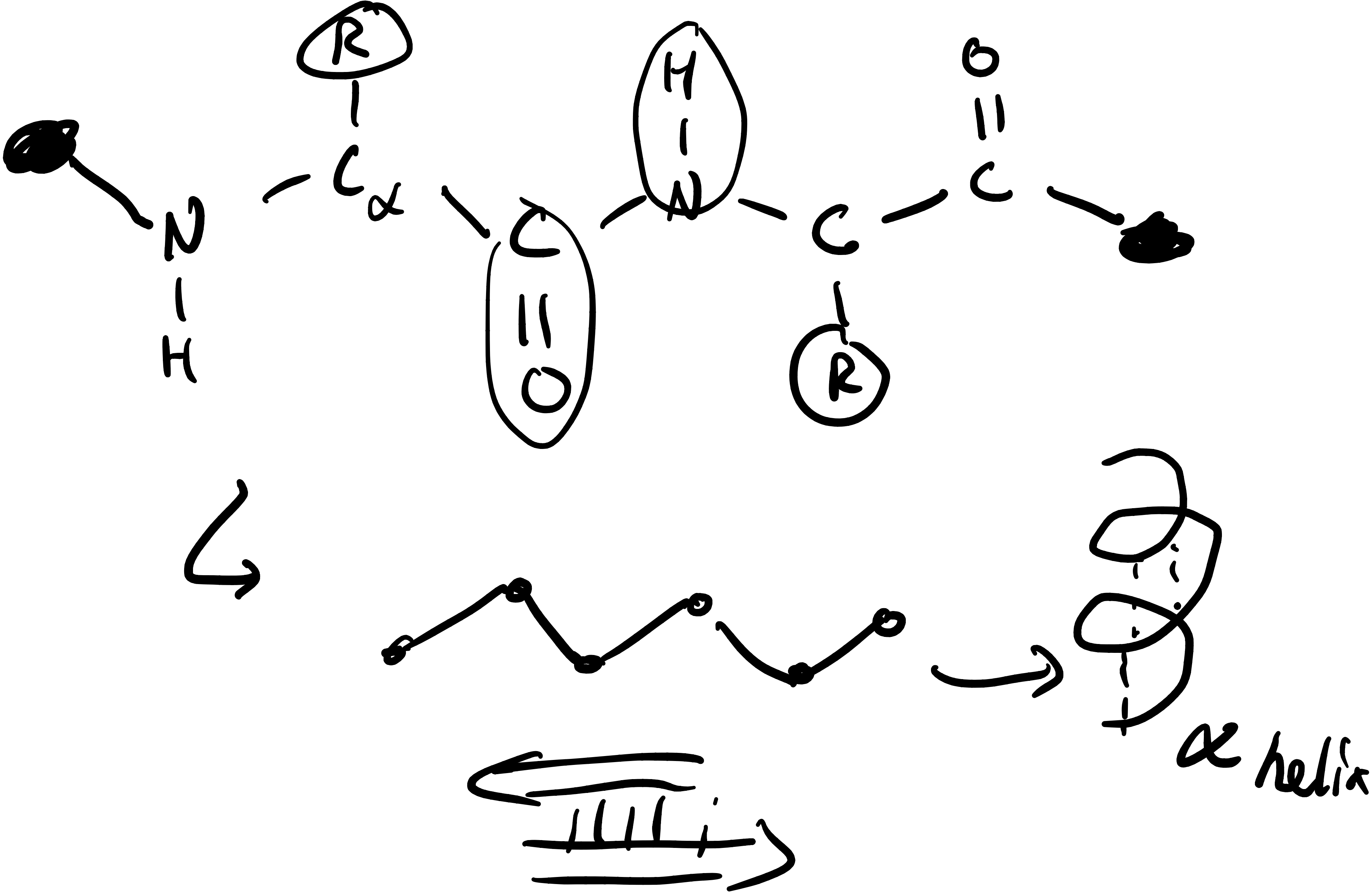


$$R + L \rightleftharpoons RL$$

$$Q_{bind} = \frac{[RL]}{[R][L]}$$



$$K_D = \frac{[R]_{eq}[L]_{eq}}{[RL]_{eq}}$$



folding $\Delta G_{fold} = \Delta H_{fold} - T\Delta S_{fold}$

folding

$[A \rightleftarrows B]$

$\Delta H_{folding} < 0$ ← more favorable

in general $\Delta S_{folding} < 0$ ← "more order"

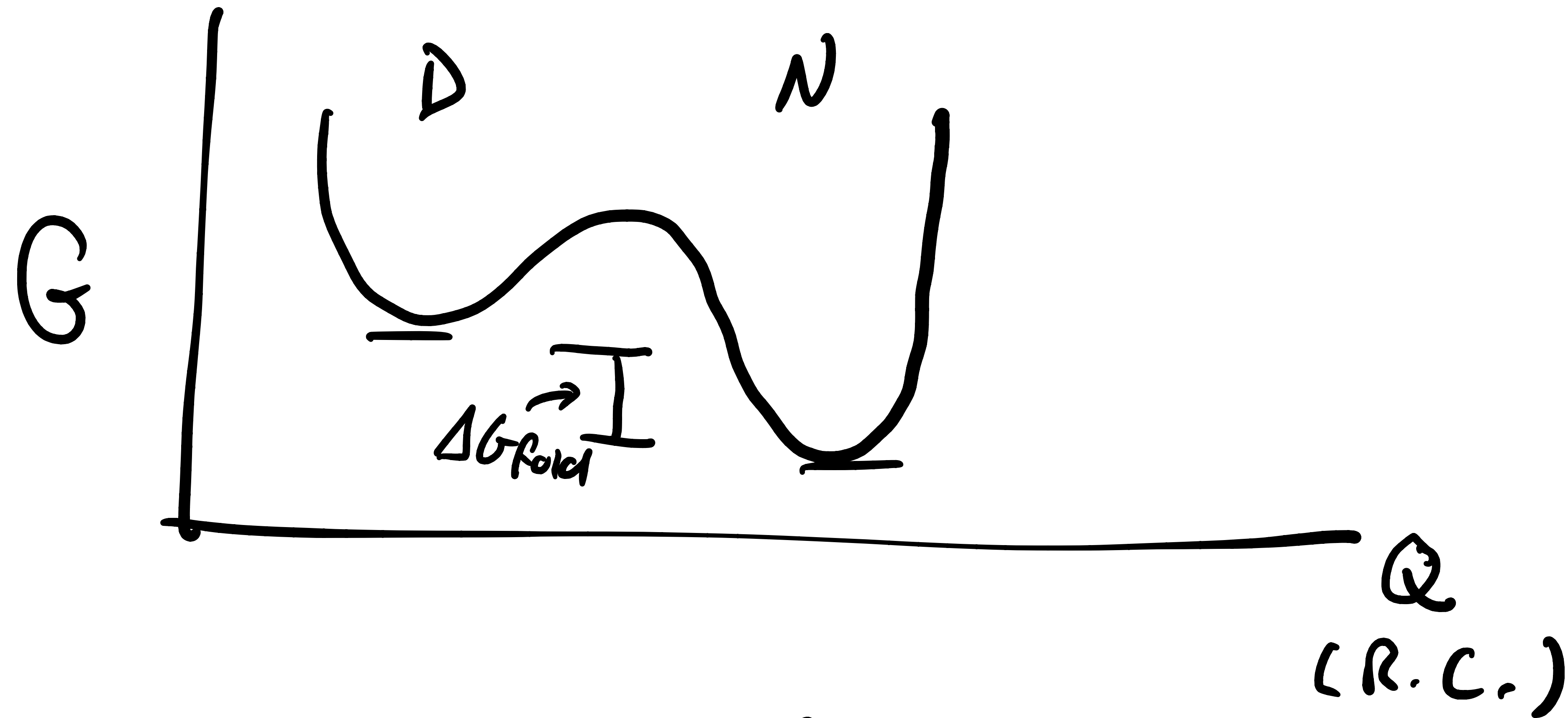
(also consider solvent ...)

folding is a competition between
enthalpy & entropy

go folded to unfolded by increasing T

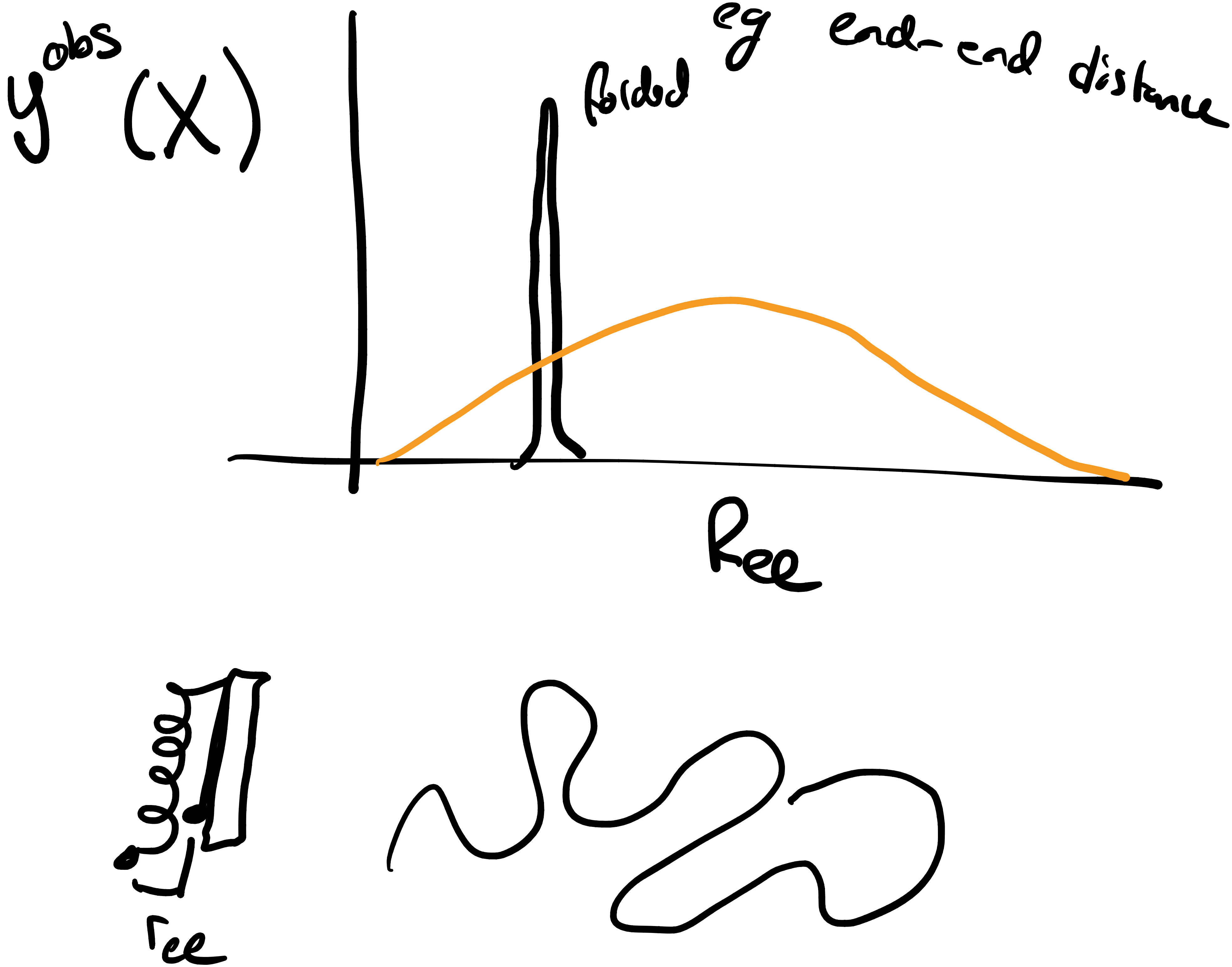
$\Delta G_{folding} \sim -10$ kcal/mol

Free energy landscape

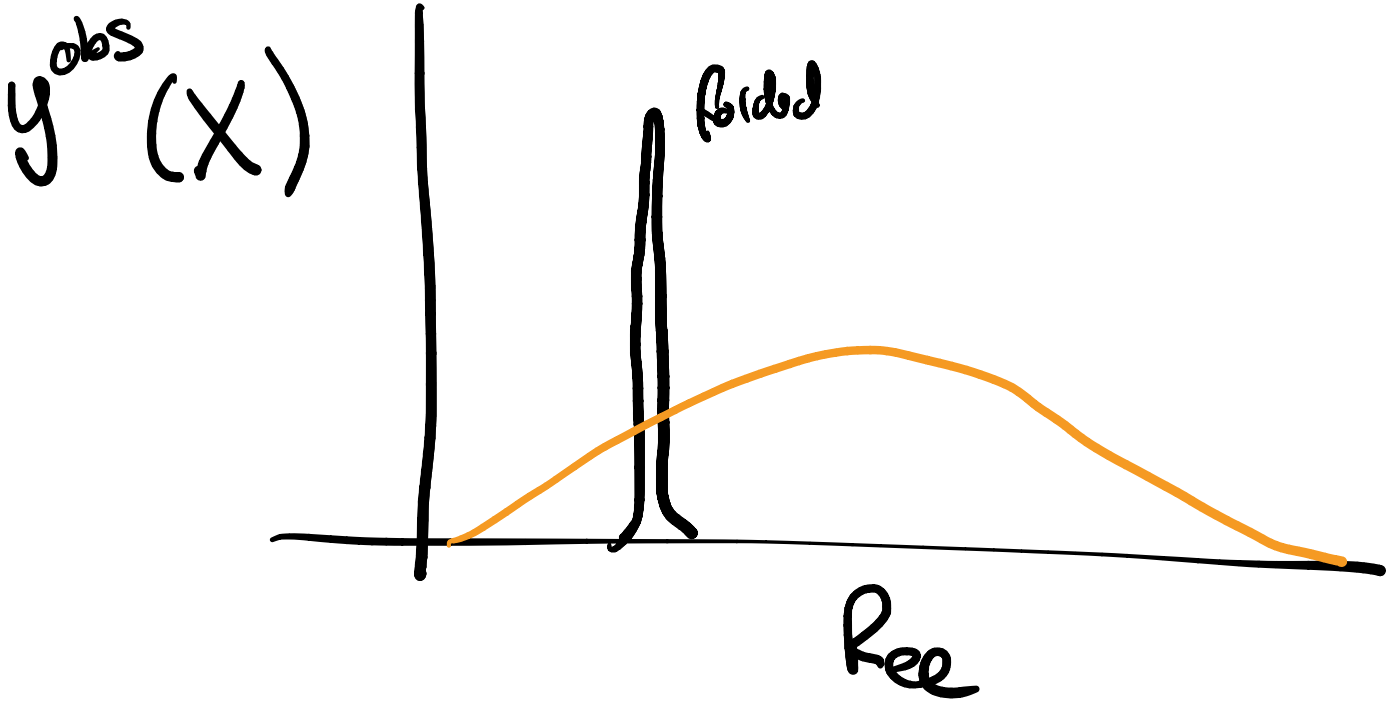


$$K_{eq} = \frac{[N]_{eq}}{[D]_{eq}}$$

$$\Delta \bar{G}^{\circ}_{folding} = -RT \ln K_{eq}$$

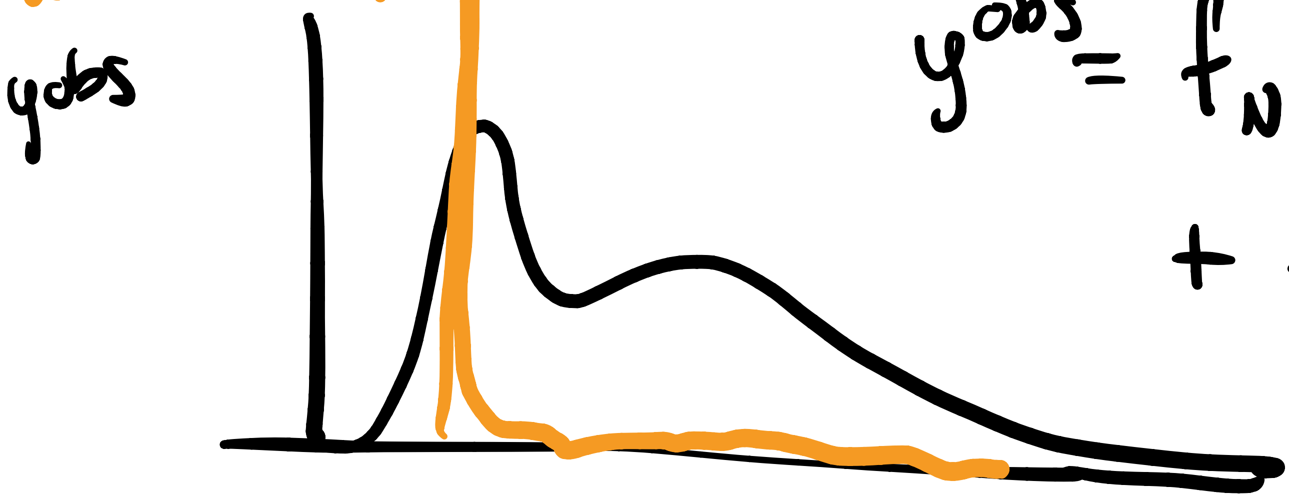


y^obs (X)
folded
eg end-end distance
Ree
ree



if 50/50 D to N, K = 1

what if $f_N = 0.98$



$$y^{obs} = f_N\, y_N(x) + f_D\, y_D(x)$$

(true if dilute)

Keq quantity

$$\text{fraction}\ N = \frac{[N]_{eq}}{[N]_{eq} + [D]_{eq}}$$

$$\chi_N$$

$$K_{eq}^{fold} = [N]_{eq}/[D]_{eq} \equiv K$$

$$= \frac{K[D]}{K[D]+[D]} = \frac{K}{1+K}$$

$$\text{fraction}\ D = \frac{1}{1+K}$$

What can you measure?

NMR - different patterns of peaks for different states

CD - ex. absorption @ 220nm

how much secondary structure

FRET - measuring distances @ molecular level ~nm scale

Argue that can distinguish your states if $10\% < f_N < 90\%$

$$0.1 < f < 0.9$$

$\uparrow$

$K/K+1$

$$\frac{1}{9} < K < 9$$ can distinguish

$\downarrow$

$$-\ln 9 < \ln K < \ln 9 \Rightarrow -2.2 < \ln K < 2.2$$

$-2.2 < \ln K < 2.2$

$$\Delta \bar{G}^\circ = -RT \ln K$$

(RT) ≈ 0.6 kcal/mol

$\Rightarrow 1.3 \geq \Delta \bar{G}^\circ_{fold} \geq -1.3$ kcal/mol

$$K_{eq} = e^{-\Delta \bar{G}^\circ / RT}$$

Boltzmann distribution

$e^{2.3} \approx 10 \rightarrow \Delta G^\circ = -1.4$ kcal/mol typical protein @ room temperature

$K_{fold} > 10^3$

Key is to denature the protein