

**Lectures 7-8:**  
**Statistical Mechanics of Phase Transitions**  
**Order Parameter**  
**Kinetics & Reaction Rates**

**Lecturer:**

*Prof. Brigita Urbanc (brigita@drexel.edu)*

# Fundamentals of Statistical Physics

→ **Why is statistical physics description needed?**

**Many degrees of freedom:**

**secondary structure formation in a 100-residue peptide  
if each residue 2 states**



**$2^{100}$  possible peptide conformations**

→ **Simplifications: statistically averaged structure**

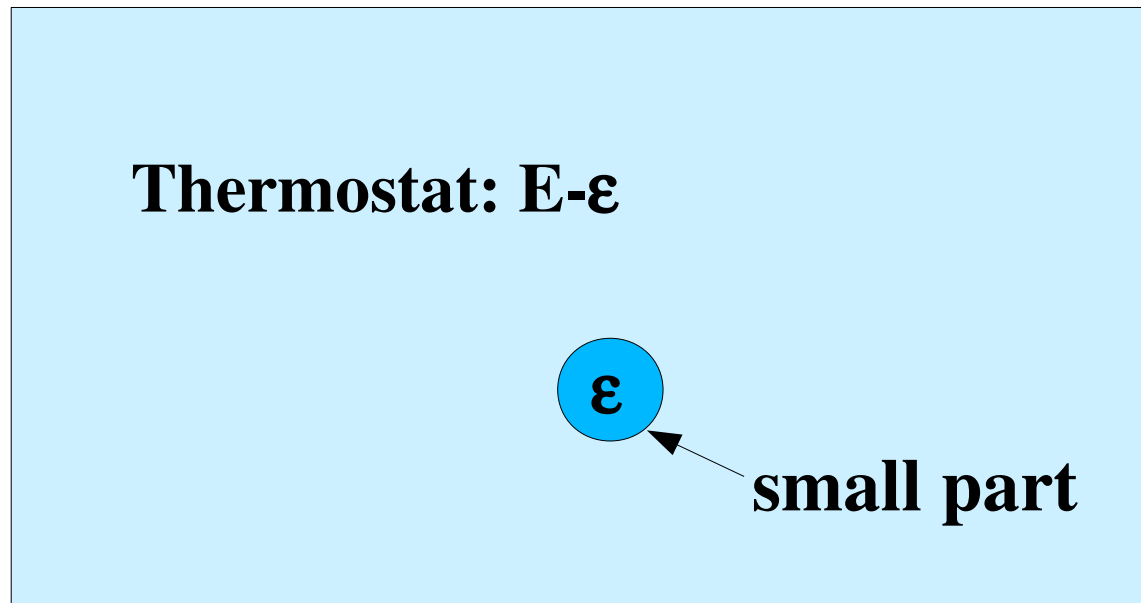
→ **Entropy: how many configurations/microstates correspond  
to the observe macrostate**

→ **Temperature: related to entropy**

**NO numerous states → NO temperature**

# Entropy—Temperature Relationship

- consider a closed system ( $E=\text{const.}$ ): no heat exchange with the environment



- $M_{\text{th}}(E-\epsilon)$  – the number of thermostat microstates
- assumption: no interaction between the small part and the thermostat (e.g. ideal gas)

$S_{\text{th}}(\mathbf{E}-\boldsymbol{\varepsilon})$  – thermostat entropy, by definition:

$$S_{\text{th}}(\mathbf{E}-\boldsymbol{\varepsilon}) = \kappa \ln[M_{\text{th}}(\mathbf{E}-\boldsymbol{\varepsilon})]$$

$M_{\text{th}}(\mathbf{E}-\boldsymbol{\varepsilon})$  – the energy of the small part,  $\boldsymbol{\varepsilon} \ll \mathbf{E}$

$$f(\mathbf{x}+d\mathbf{x}) = f(\mathbf{x}) + df/d\mathbf{x}(\mathbf{x}) d\mathbf{x} + \dots$$

↓

$$S_{\text{th}}(\mathbf{E}-\boldsymbol{\varepsilon}) = S_{\text{th}}(\mathbf{E}) - dS_{\text{th}}/d\mathbf{E} \Big|_{\mathbf{E}} \boldsymbol{\varepsilon}$$

&

$$\begin{aligned} M_{\text{th}}(\mathbf{E}-\boldsymbol{\varepsilon}) &= \exp[S_{\text{th}}(\mathbf{E}-\boldsymbol{\varepsilon})/\kappa] = \\ &= \exp[S_{\text{th}}(\mathbf{E})/\kappa] \times \exp[-\boldsymbol{\varepsilon} dS_{\text{th}}/d\mathbf{E} \Big|_{\mathbf{E}}/\kappa] \\ &= M_{\text{th}}(\mathbf{E}) \times \exp[-\boldsymbol{\varepsilon} dS_{\text{th}}/d\mathbf{E} \Big|_{\mathbf{E}}/\kappa] \end{aligned}$$

**According to the Boltzmann distribution:**

$$\exp[-\epsilon \left. \frac{dS_{\text{th}}}{dE} \right|_E / \kappa] = \exp[-\epsilon / (k_B T)]$$

↓

$$\left. \frac{dS_{\text{th}}}{dE} \right|_E = 1/T \quad \& \quad \kappa = k_B$$

**Thermodynamic definition of temperature:**

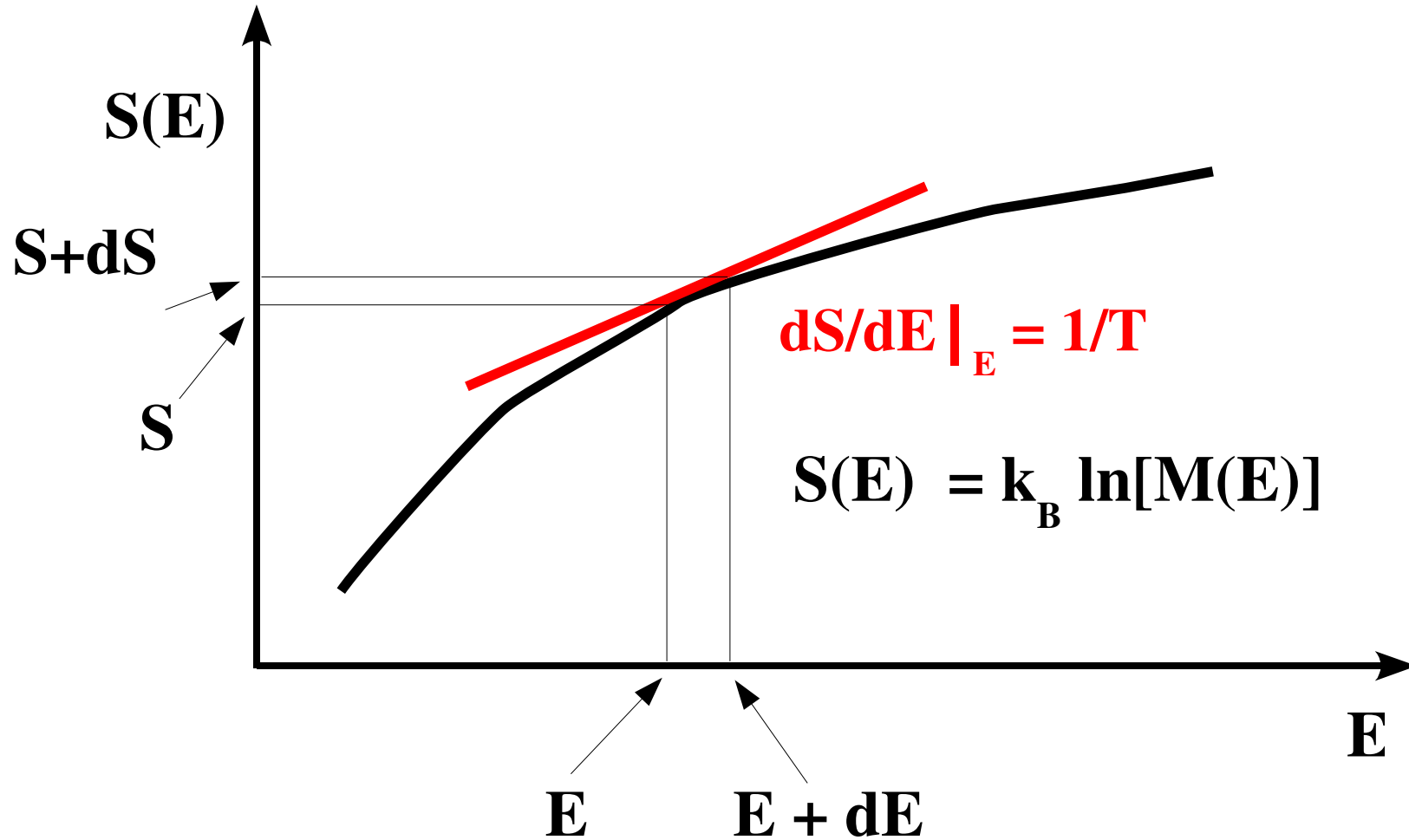
**a reciprocal of the rate of the entropy change with the system energy E**

↓

$$\begin{aligned} \ln[M(E + k_B T)] &= S(E + k_B T) / k_B = [S(E) + 1/T k_B T] / k_B \\ &= S(E) / k_B + 1 = \ln[M(E)] + 1 \end{aligned}$$

**Energy increase by  $k_B T$  results in an increase of the number of microstates by a factor of  $e=2.72$ .**

# Graphical representation of temperature:



$M(E)$  – energy spectrum density,  $M(E) \gg 1$

**Consider a small system in a thermostat at fixed T & V**

**→ probability  $w_i$  of being in the state  $i$  with the energy  $\epsilon_i$ :**

$$w_i = \exp(-\epsilon_i/k_B T) / Z(T)$$

$$Z(T) = \sum_i \exp(-\epsilon_i/k_B T)$$

**Z(T) – partition function**

**If Z(T) is known, all thermodynamic quantities can be calculated (see the derivation below):**

$$E(T) = \sum_i w_i \epsilon_i$$

$$S(T) = k_B \sum_i w_i \ln(1/w_i)$$

→ consider  $N$  systems, each of them can be in states  $\{1, 2, \dots, J\}$  with probabilities  $\{w_1, w_2, \dots, w_J\}$

$$N_i \text{ (of all } N \text{ systems will be in state } i) = w_i N$$

$$N = \sum_i w_i N = \sum_i N_i$$

→ In how many ways can these  $N$  systems be distributed over the  $J$  states? (definition of the entropy)

- select  $n_1$  systems (out of  $N$ ):  $N! / n_1! (N-n_1)!$

- select  $n_2$  systems (out of  $N-n_1$ ):  $(N-n_1)! / n_2! (N-n_1-n_2)!$

- total:  $[N! / n_1! (N-n_1)!] \times [(N-n_1)! / n_2! (N-n_1-n_2)!]$   
 $= N! / n_1! n_2! (N-n_1-n_2)!$

- for all  $J$  states:  $N! / n_1! n_2! \dots n_J!$



→ Stirling's approximation:  $n! \sim (n/e)^n$

$$\begin{aligned} \rightarrow N! / n_1! n_2! \dots n_J! &\sim (N/e)^N (e/n_1)^{n_1} (e/n_2)^{n_2} \dots (e/n_J)^{n_J} \\ &= (N/n_1)^{n_1} (N/n_2)^{n_2} \dots (N/n_J)^{n_J} \\ &= (1/w_1)^{Nw_1} (1/w_2)^{Nw_2} \dots (1/w_J)^{Nw_J} \\ &= [(1/w_1)^{w_1} (1/w_2)^{w_2} \dots (1/w_J)^{w_J}]^N \\ &= [\text{the number of distributions of each system}]^N \end{aligned}$$

↓

$$S(T)/k_B = \ln [(1/w_1)^{w_1} (1/w_2)^{w_2} \dots (1/w_J)^{w_J}]$$

**Helmholtz Free Energy  $F$  ( $V, T = \text{const.}$ ):**

$$\begin{aligned} F(T) = E(T) - T S(T) &= \sum_i w_i \{ \epsilon_i - T[-k_B \ln(w_i)] \} \\ &= -k_B T \ln[Z(T)] \end{aligned}$$

$$Z(T) \rightarrow F(T) \rightarrow E(T): \quad S(T) = -(dF/dT)$$

$$E(T) = F(T) + T S(T) = F(T) - T (dF/dT)$$



**Knowing  $Z(T)$ , we can get a complete TD description of the system!**

**Additional notes:**

→ **internal temperature of the small system =  $T$**

→ **total energy = kinetic + **potential****

**-kinetic – depends on speeds**

**-potential – depends on coordinates**

**-speeds & coordinates separate  
degrees of freedom**

**Only potential energy contributes to conformational changes!**

**Conformational changes:**

**→ gradual**

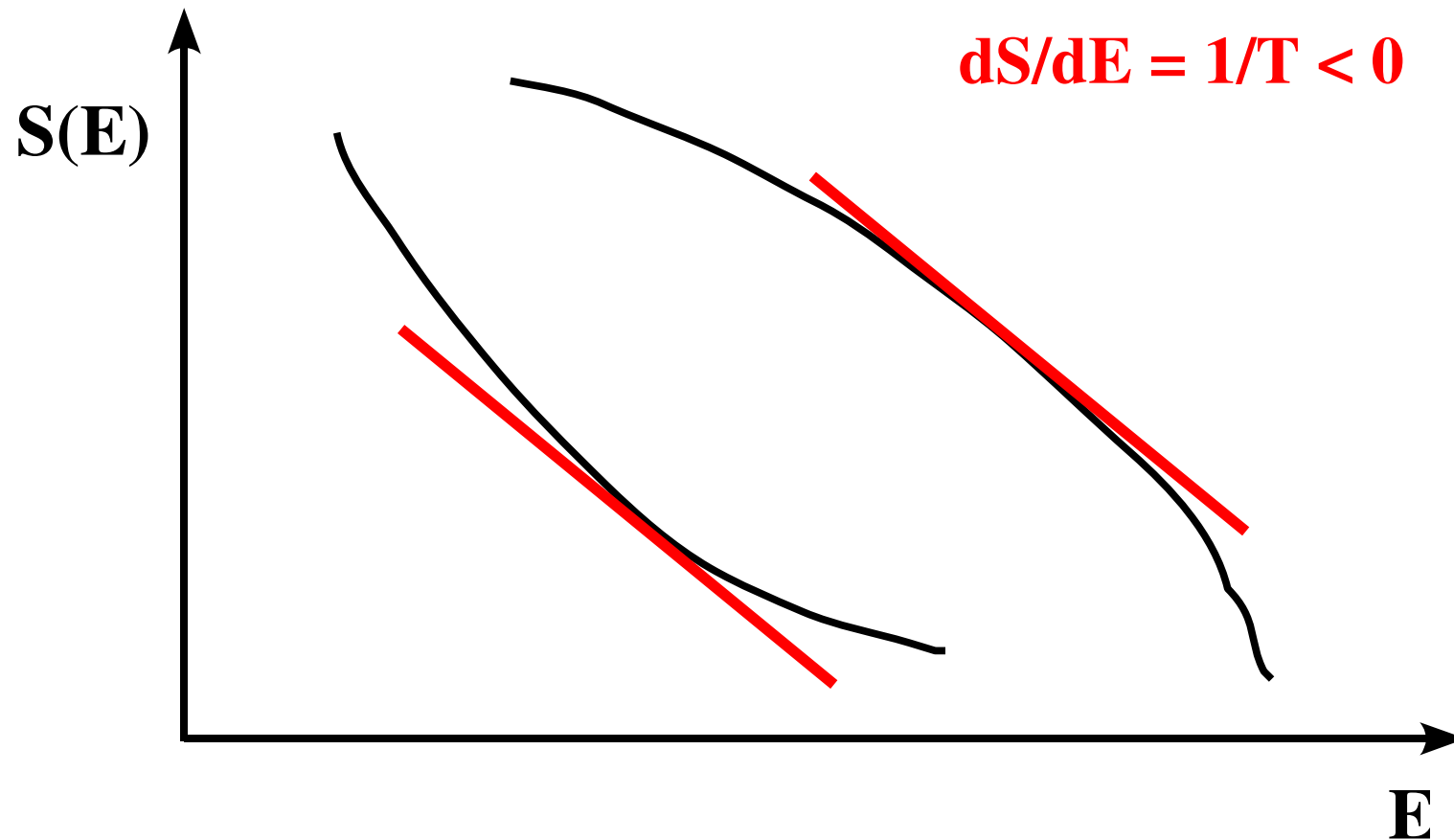
**→ sharp (phase transitions)**

**How to identify stable states at a given T, given the energy spectrum density M(E)?**

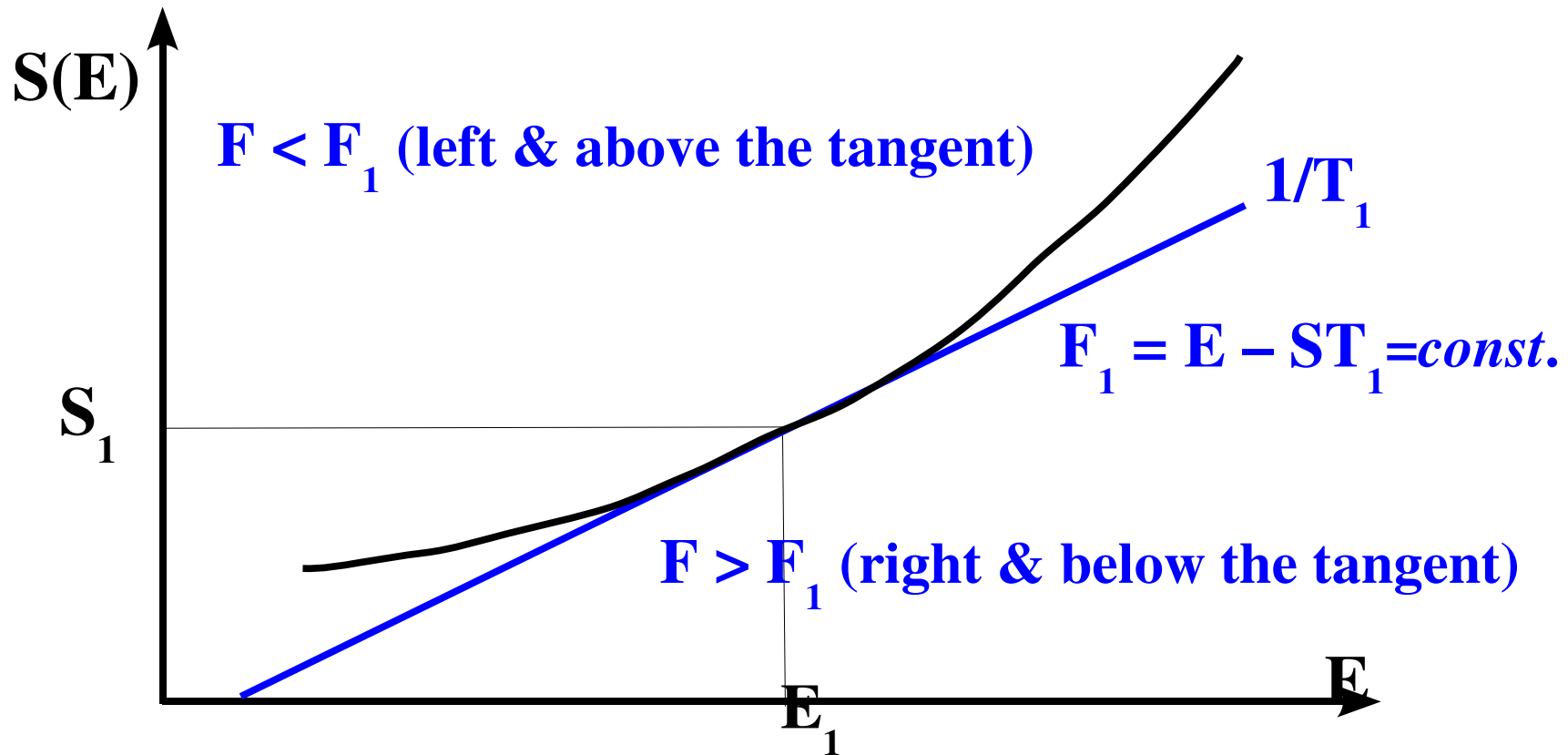
**$S(E) = k_B \ln[M(E)]$  – find a stable state at  $T=T_1$**

**Consider:  $1/T_1 = dS/dE$**

**Entropy  $S(E)$  cannot be a decreasing function of energy  $E$   
→ negative temperature**

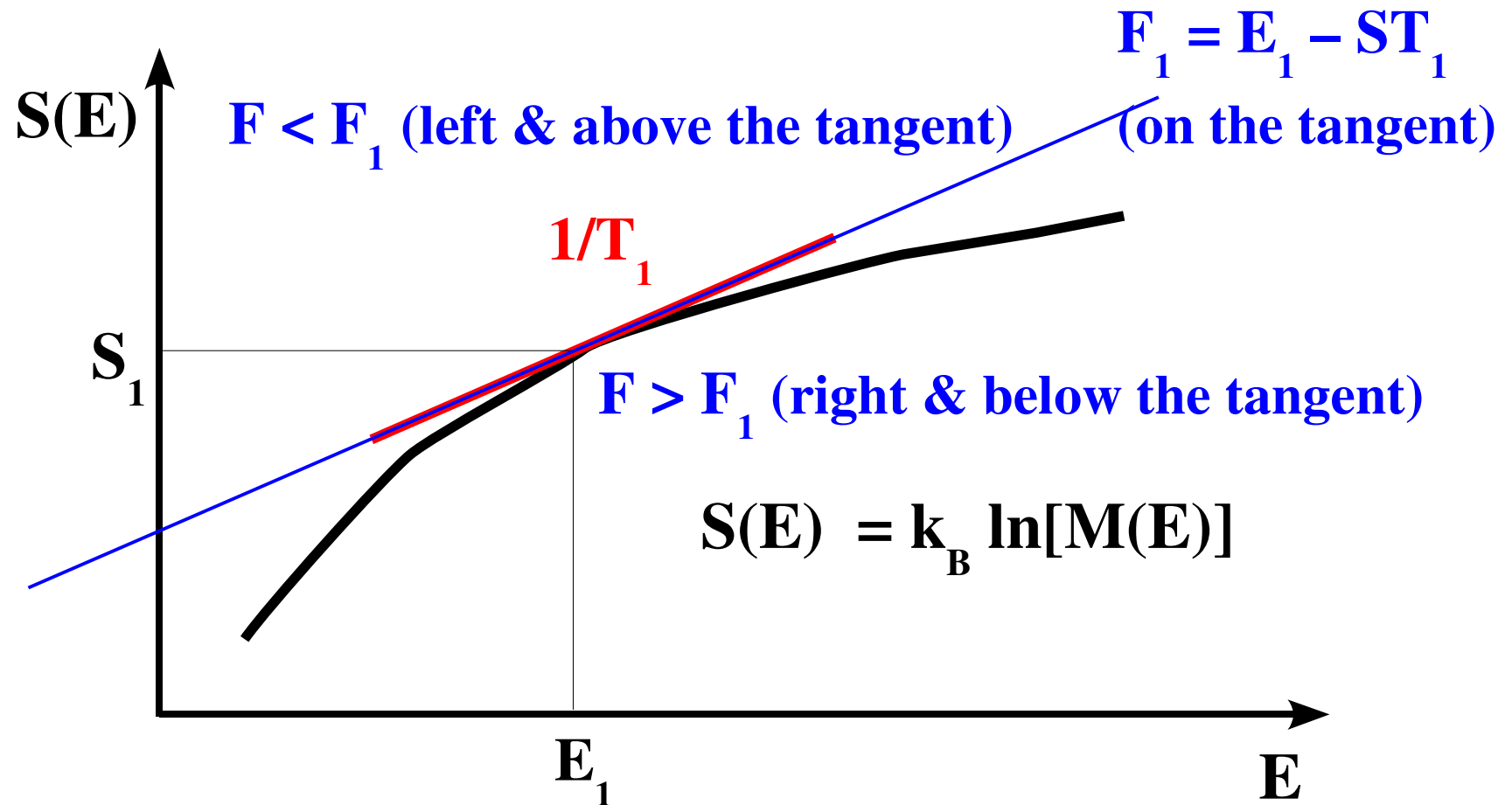


**A concave shape of  $S(E)$  does NOT correspond to a stable state.**



**Why?** The system can decrease  $F$  by moving along  $S(E)$ !

$S(E)$  needs to have a **convex** (not concave) shape:



# Introducton to Phase Transitions

→ **What is a phase transition:**

**an abrupt change in TD behavior associated with a discontinuity in some TD function**

→ **A more mathematical definition:**

**at  $p=const.$ , a phase transition occurs at  $T_0$ , at which the Gibbs free energy  $G(P,T)$  is singular**

→  **$G(P,T)$  is continuous at  $T_0$ , some derivative is discontinuous at  $T_0$ :**

**$1^{st}$  derivative discontinuous →  $1^{st}$  order phase transition**

**$2^{nd}$  derivative discontinuous →  $2^{nd}$  order phase transition**

## First-Order Phase Transitions

→ **Examples: boiling and freezing of water  $\Delta V$  and  $\Delta S$  at  $T_0$ :**

$$V = (\partial G / \partial P)_{T_0} \quad \& \quad S = -(\partial G / \partial T)_{T_0}$$

→ **Latent Heat:  $L_0 = T_0 (s_2 - s_1)$**

$s_i$  – **specific entropy (per particle**

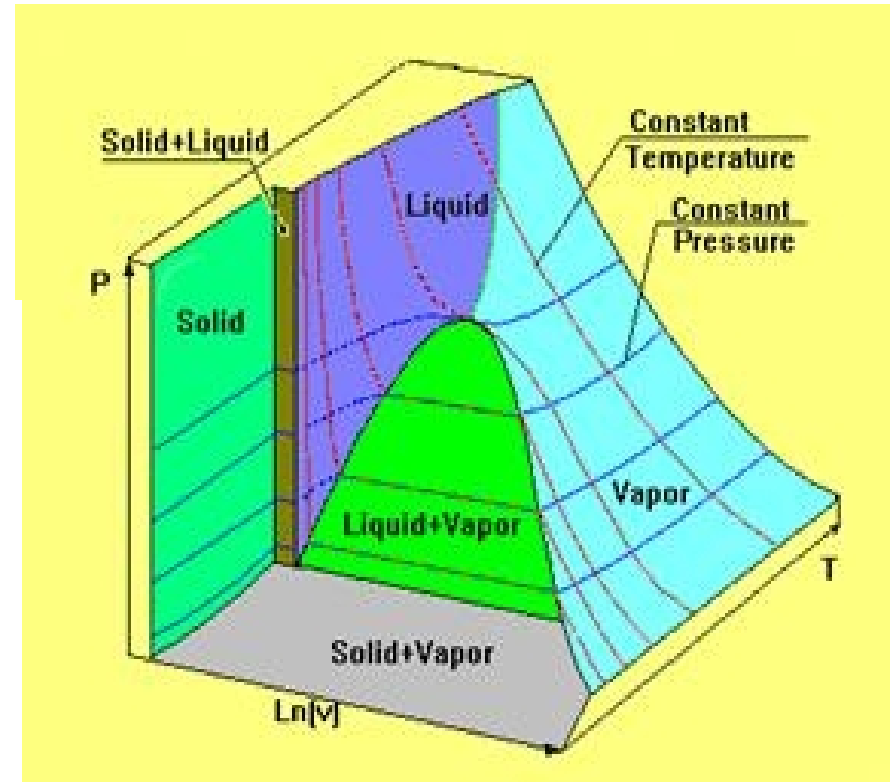
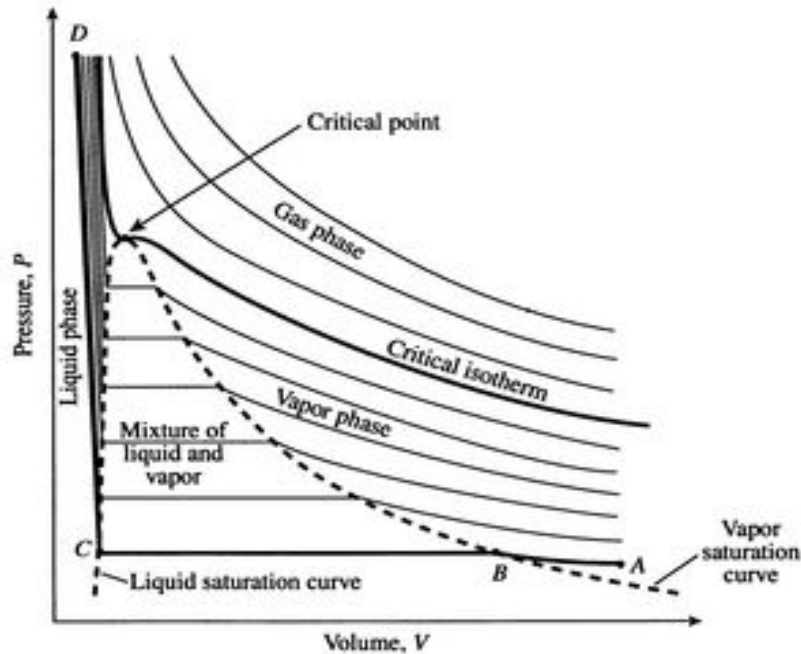
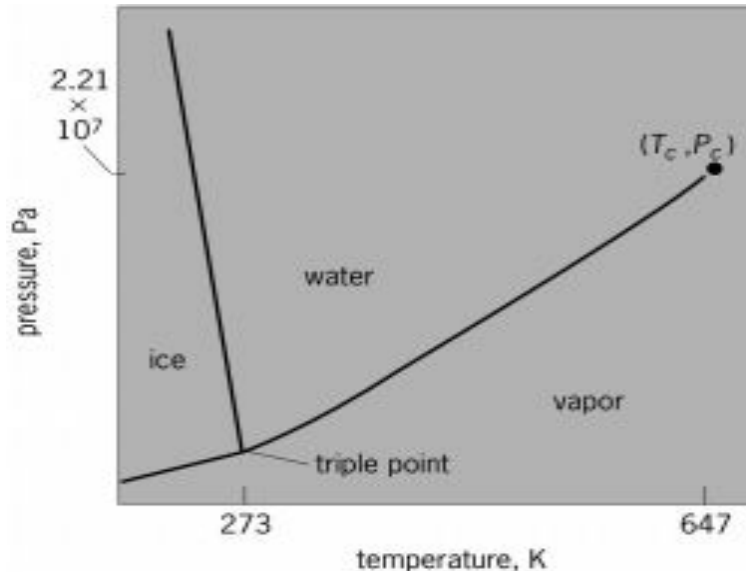
**per mol,**

**per unit mass, or**

**per unit volume)**



# Phase Diagrams of the Liquid-Gas (L-G) Transition



## Second-Order Phase Transitions

- **Example: at the critical point of L-G transition**  
**L & G → same densities & specific entropies**
- **Heat Capacity (2<sup>nd</sup> derivative of G) is singular at the transition temperature  $T_c$ :**  
$$C_p = - T d^2G/dT^2 = C_0 |t|^{-\alpha},$$
  
where **t is reduced temperature:  $t = T - T_c / T_c$ .**
- **Exponent  $\alpha$  (critical exponent) is the same for  $T < T_c$  and  $T > T_c$ , but the constant  $C_0$  is not. NO latent heat!**

## **Other examples of the 2<sup>nd</sup> order phase transition:**

- ferromagnetic transition in magnetic materials**
- order-disorder transition in metallic alloys**
- conductor → superconductor transition**
- fluid → superfluid transition**

## **Order Parameter:**

- the low-temperature state typically more ordered than the high-temperature state**

**⇒**

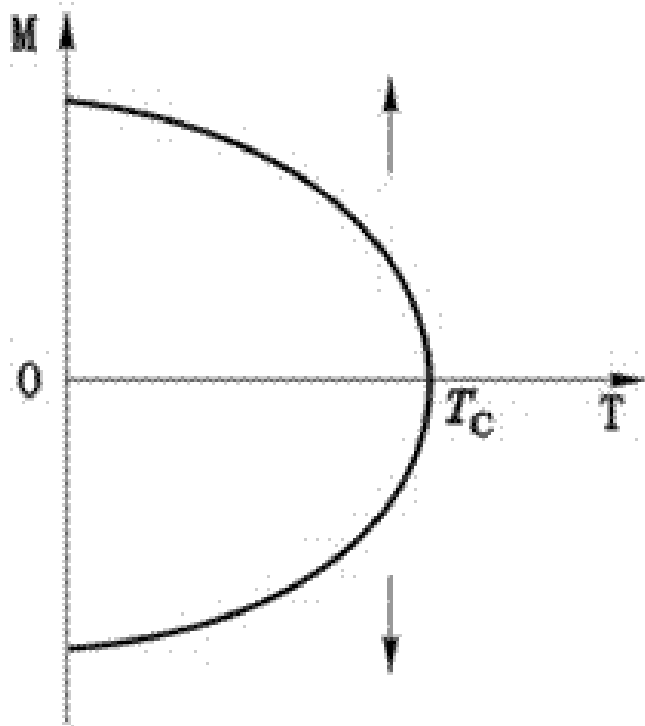
- ∃ order parameter (=0 in the high-temperature state):**

$$\text{e.g. magnetization: } M \sim m_0 |t|^\beta,$$

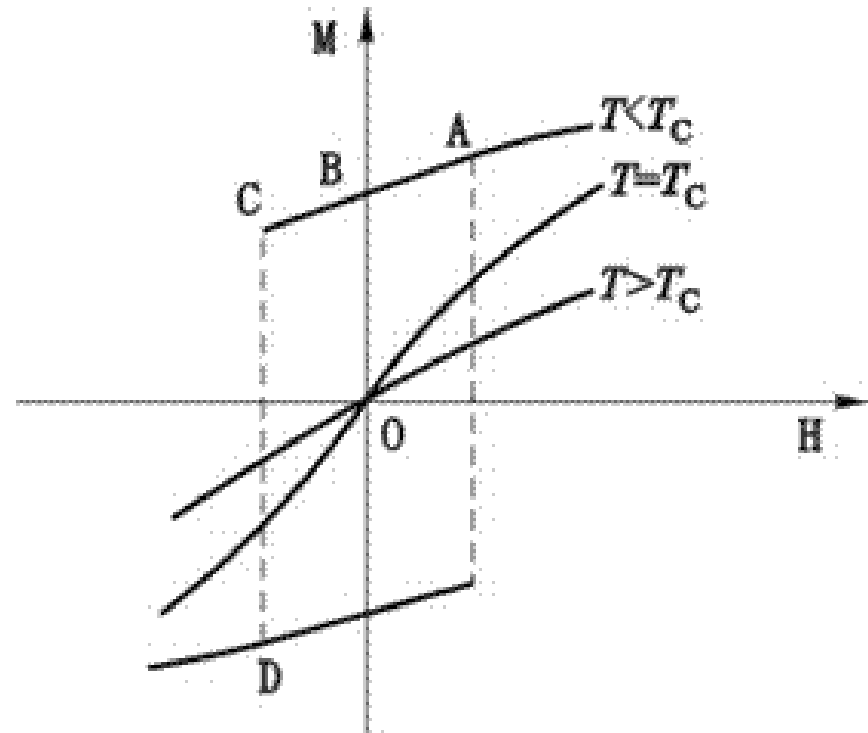
- critical exponent  $\beta$  (associated with the order parameter)**

At zero magnetic field ( $H=0$ ), 2<sup>nd</sup> order transition, at  $H>0$ ,  
1<sup>st</sup> order transition

Order Parameter (M) vs T



Phase Diagram M vs H



## **The Most Important Critical Exponents:**

- $\alpha$  (heat capacity/specific heat,  $C_p \sim |t|^{-\alpha}$  diverges)**
- $\beta$  (order parameter, e.g. magnetization  $M \sim |t|^\beta$  goes to 0)**
- $\gamma$  (susceptibility  $\chi$ :  $M = \chi H$ ,  $\chi \sim |t|^{-\gamma}$  diverges)**
- $\nu$  (correlation length  $\xi$ :  $\xi \sim |t|^{-\nu}$  diverges)**

**⇒**

**Critical exponents, characteristic of the 2<sup>nd</sup> order phase transitions, indicate power-law behavior of key TD quantities ⇒ no characteristic length scale at  $T_c$ !**

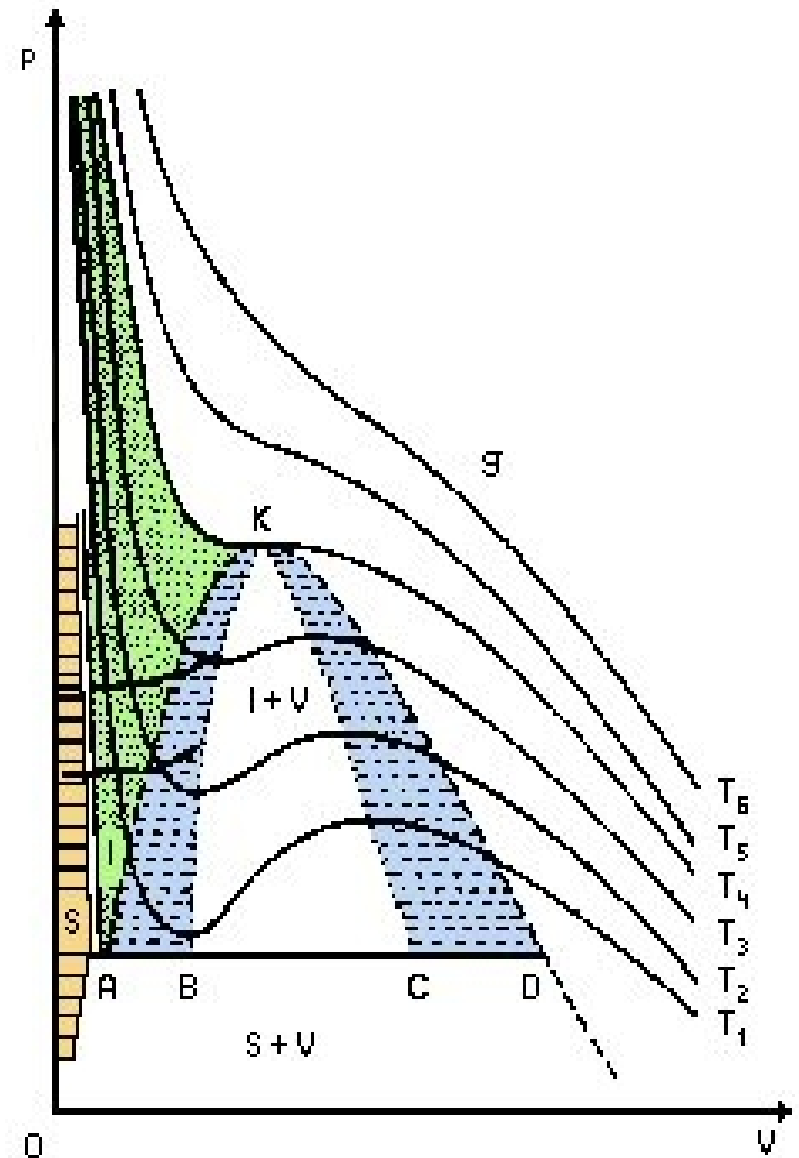
**Divergent correlation length ⇒ details are not important**

**⇒**

**Universal Behavior → ∃ Universality Classes  
(defined by specific values of critical exponents)**

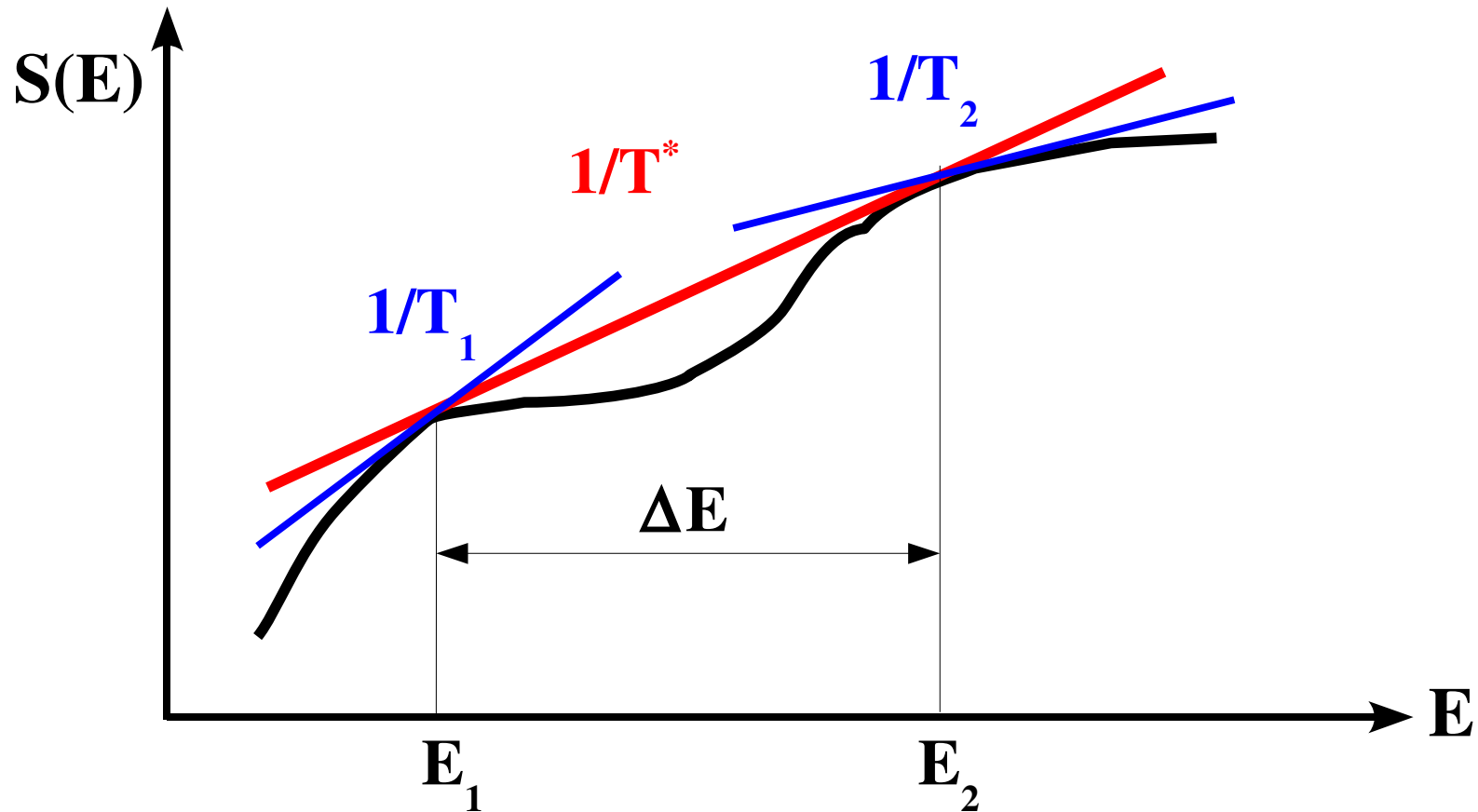
# Spinodal Decomposition/Nucleation

- **AKD: coexistence curve**  
(equilibrium transition)  
L&G co-exist below AKD
- **BKC: spinodal curve**  
(separates states with  
positive compressibility  
from non-physical  
negative compressibility)
- **inside spinodal: spontaneous  
phase separation occurs**
- **between AKD and BKC (blue):  
nucleation (metastable states)**



## First – Order (“All-Or-None”) Transition:

$\exists$  of an unstable concave region on the  $S(E)$  curve  $\in [E_1, E_2]$



Transition occurs within **the coexistence region**  $T \in [T_1, T_2]$

## How do we get a complete thermodynamic description?

→  $S(E)$  known

→  $1/T = dS(E)/dE \rightarrow T=T(E) \rightarrow E=E(T)$

→ calculate  $F(T) = E(T) - T S(E(T))$

→ calculate probability of having energy  $E$  at temperature  $T$ :

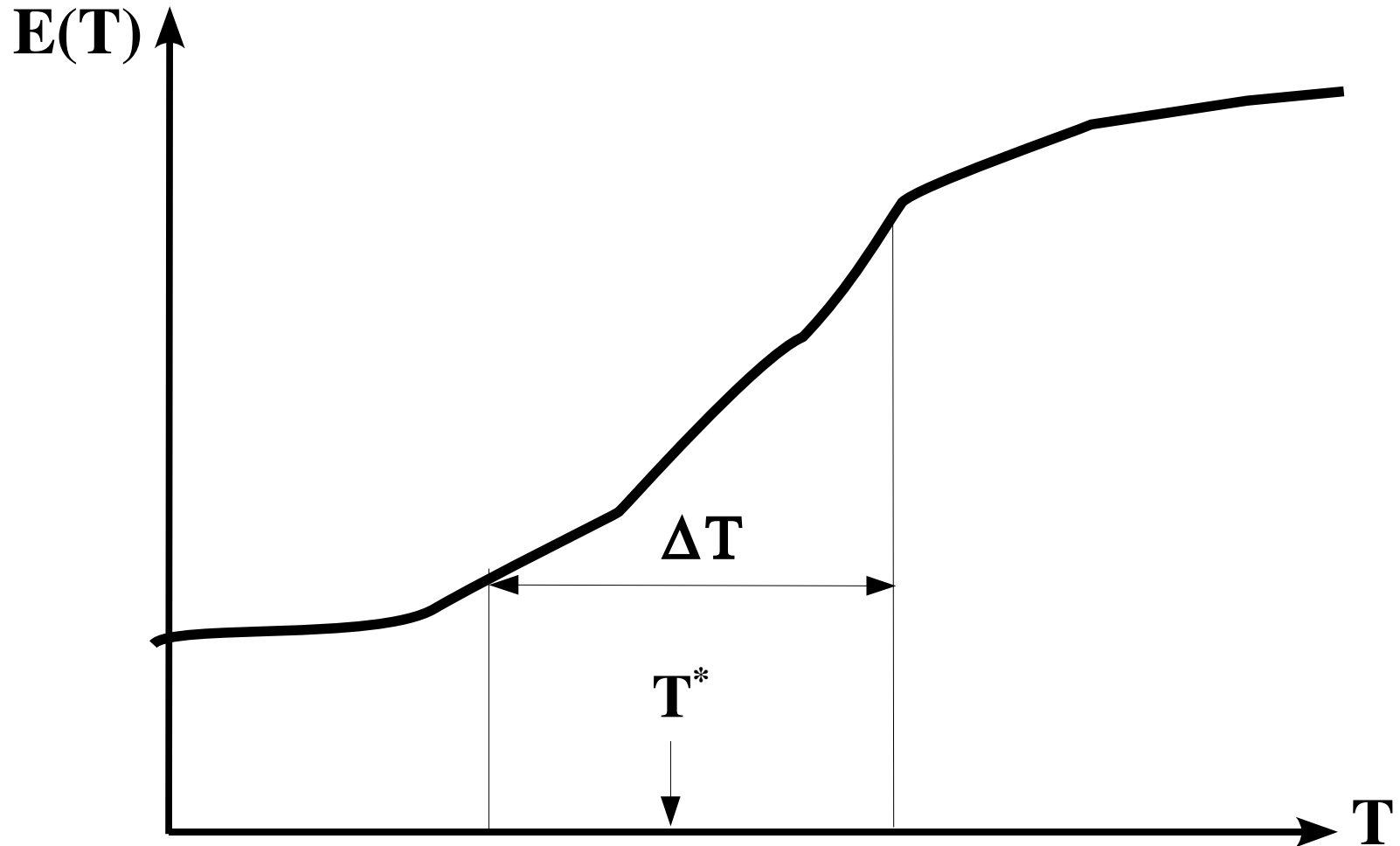
$$w(E) \propto \exp[-(E-TS(E))/k_B T]$$



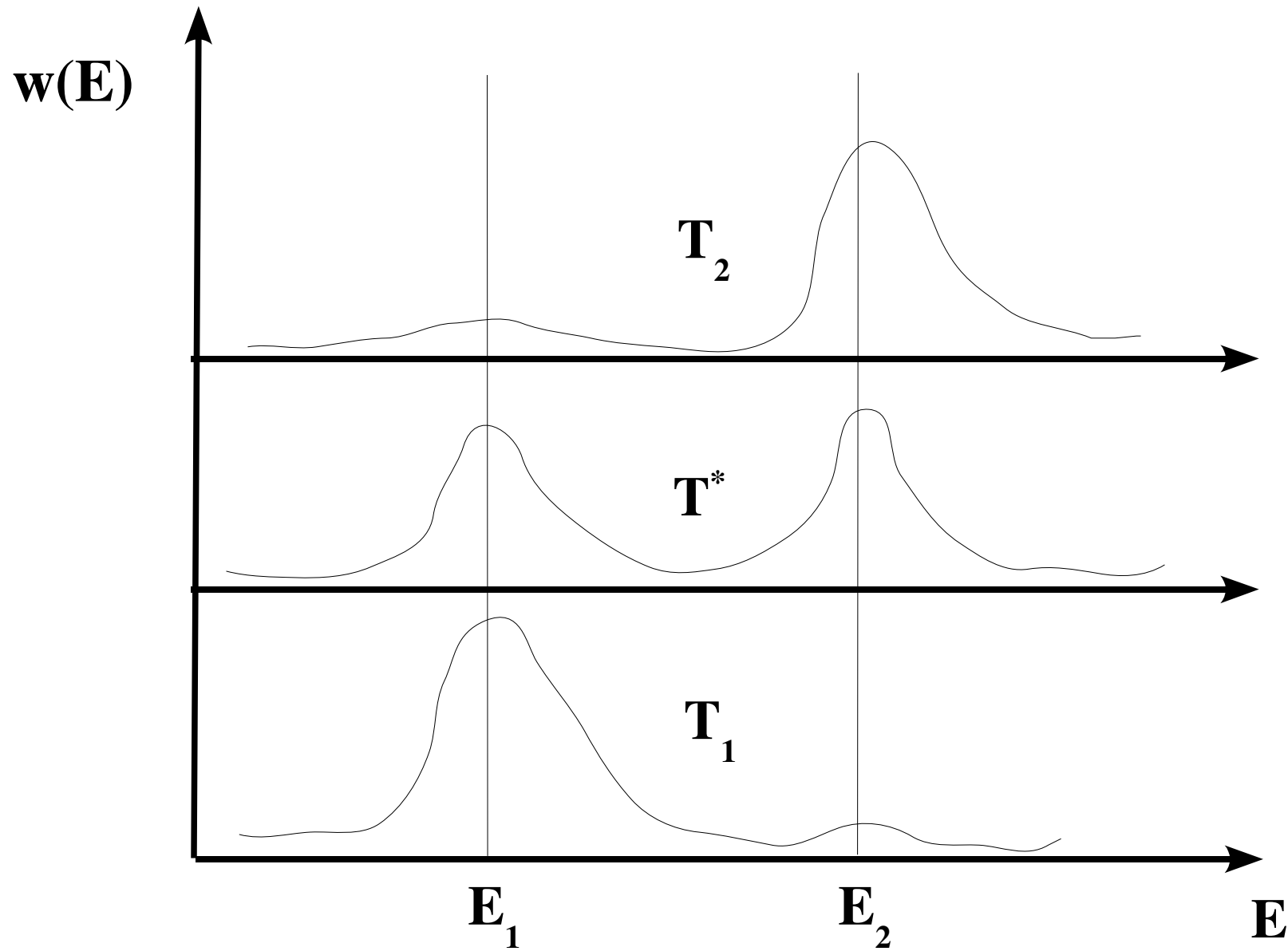
# Energy versus Temperature

$\Delta T$  – coexistence of low and high energy states

$T^*$  – transition temperature



# Probability Distribution $w(E)$ at Different Temperatures



How about states with intermediate energies  $E \in (E_1, E_2)$ ?

→ because they lie below the tangent of  $1/T^*$ , these intermediate states have a higher free energy  $F$

⇒

→ the two stable states are separated by **a free energy barrier  $\Delta F$**

→ in proteins, a transition at  $T^*$  occurs as a jump over  $\Delta F$   
(takes time to occur)

⇒

→ Hysteresis (with respect to  $T^*$ ):

- slight overcooling (when freezing)
- slight overheating (when melting)



metastable  
states -  
nucleation

## Estimation of the temperature interval $\Delta T$ (the coexistence region):

→ at transition temperature :  $F_1(T^*) = F_2(T^*)$

$$F_1(T^*) = E_1 - T^* S_1$$

$$F_2(T^*) = E_2 - T^* S_2$$

⇒

$$E_2 - E_1 = T^*(S_1 - S_2)$$

→  $\delta F = F_1(T^* + \delta T) - F_2(T^* + \delta T) =$

$$F_1(T^*) + (\delta F_1/\delta T) \delta T - F_2(T^*) - (\delta F_2/\delta T) \delta T =$$

$$F_1(T^*) - F_2(T^*) + [(\delta F_1/\delta T) - (\delta F_2/\delta T)] \delta T =$$

$$0 + [-S_1 + S_2] \delta T = (S_2 - S_1) \delta T$$

→ the phases coexist when:  $\exp(-\delta F/k_B T^*) \in [0.1, 10]$

(factor that determines the probabilities)

→  $\ln(10) \sim 2$  &  $\ln(0.1) \sim -2 \Rightarrow \delta F/k_B T^* \in [-2, 2]$

→  $\Delta T (S_2 - S_1)/k_B T^* = 2 - (-2) = 4 \Rightarrow \Delta T = 4 k_B T^*/(S_2 - S_1)$

→  $\Delta T = 4 k_B T^{*2}/(E_2 - E_1)$

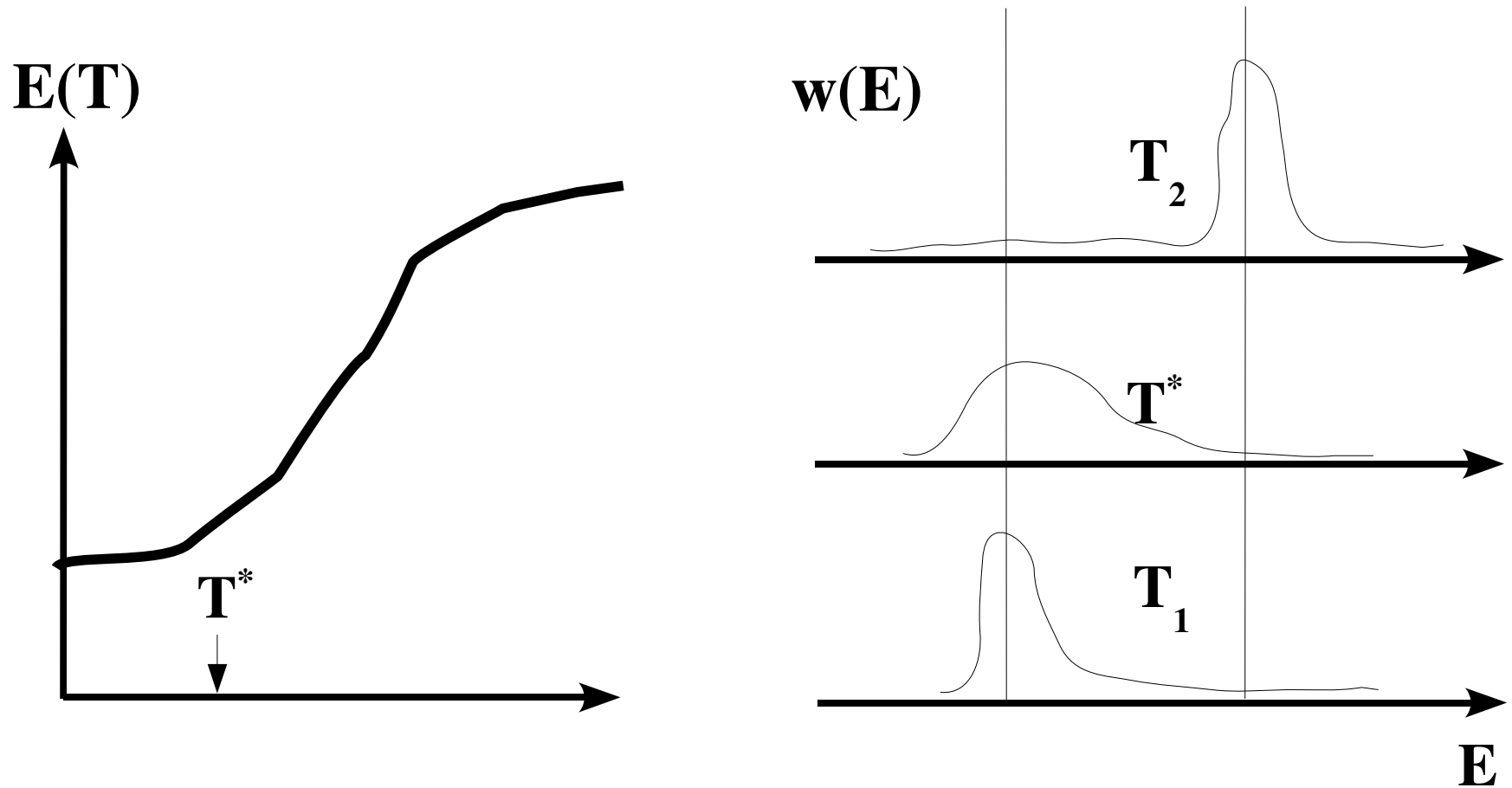
→ estimate  $\Delta T$ :

$k_B T^* = 0.6$  kcal/mol (at  $T^* = 300$ K)

$E_2 - E_1 = 50$  kcal/mol (typical of protein melting)

$\Delta T \sim 10$ K (as opposed to 50 kcal/system  
for a piece of ice  $\Delta T \sim 10^{-23}$ K)

## Second order phase transitions (NO coexistence of states):



## Kinetics of Conformational Changes:

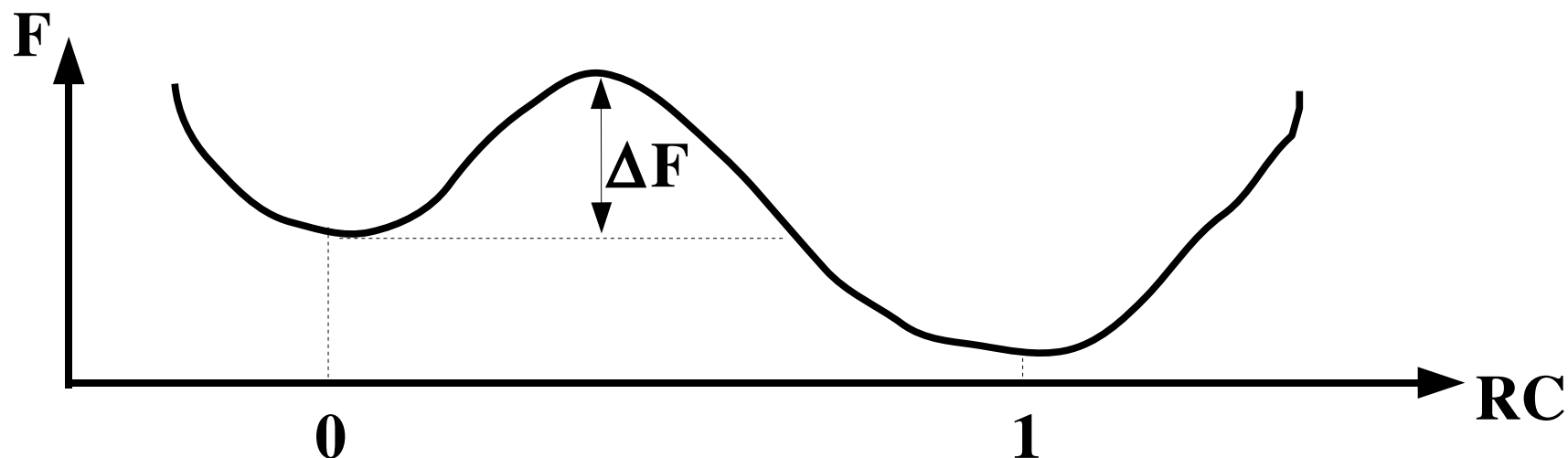
→ the time scale of an elementary process  $\tau$

(e.g.  $\tau \sim 1\text{ns}$  for each residue to adopt a secondary structure)

→ the time scale of the process within the entire peptide of  $N$  residues **NOT**  $N \times \tau$  but much **LONGER**

(e.g.  $N=100$ , process takes not  $N \times \tau = 100\text{ ns}$  but  $1\text{s}$ )

→ reason for a **SLOW** rate: a free energy barrier  $\Delta F$



## Classical Theory of Transition States:

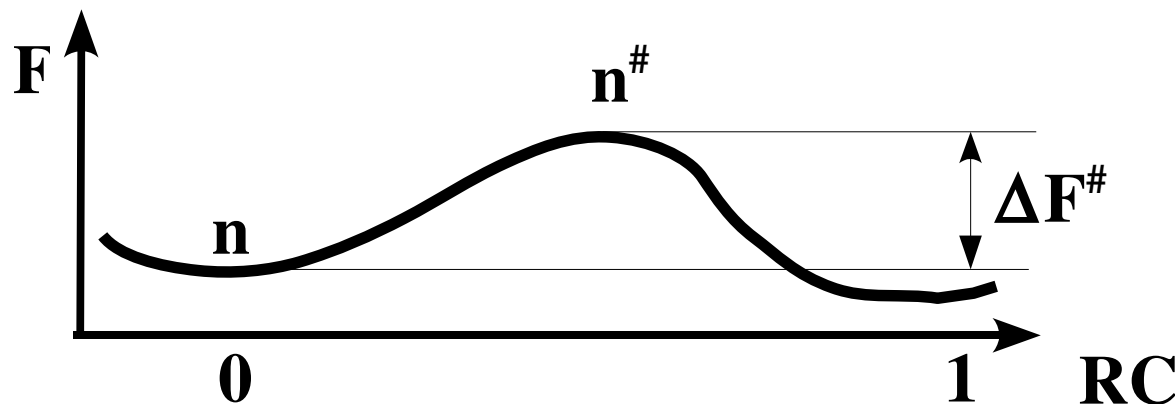
→ a system going from state 0 → state 1 with one barrier #  
(no traps)

→ process rate determined by:

(a) the population of the transition states  
(states ON TOP of the barrier #)

(b) the transition rate from the top of the  
barrier to state 1 (post-transition state)

→ free energy (F) versus **reaction coordinate (RC)**:



$$\tau - \text{time of one reaction step } \# \rightarrow 1$$
$$t_{0 \rightarrow 1} = \tau (n/n^\#) = \tau \exp(+\Delta F^\# / k_B T)$$



**Transition rate 0→1 definition:  $k_{0\rightarrow 1} = 1/t_{0\rightarrow 1}$**

$$k_{0\rightarrow 1} = \tau^{-1} \exp(-\Delta F^\# / k_B T)$$

**How does  $\exists$  of a trap X affect the 0→1 transition rate?**

**→ sequential barriers, 0→X and X→1, on the transition path result in a sum of transition times:**

$$t_{0\rightarrow 1} = t_{0\rightarrow X} + t_{X\rightarrow 1}$$

**→ parallel transition paths: 0→1 through barrier #1**

**0→1 through barrier #2 ...**

**result in a sum of transition rates:**

$$k_{0\rightarrow 1} = k_{0\rightarrow X} + k_{X\rightarrow 1}$$

**Sequential barriers slow down the transition, parallel transition pathways speed up the transition.**

**For only a few barriers or transition pathways:**

- the barrier with the largest  $\Delta F^\ddagger$  determines the overall transition rate**
- the transition pathway with the smallest  $\Delta F^\ddagger$  determines the overall transition rate**

## **Kinetic Energy Dissipation and Diffusion**

- time needed for a molecule to dissipate its kinetic energy (because of the friction against a viscous fluid):  $\sim 10^{-12}$  s**
- diffusion time:  $\sim 10^{-9}$  s**
- folding time typically  $10^{-6}$  to  $10^{-3}$  s  $\gg$  diffusion time**  
**↓**  
**indication of the free energy barrier**

**Free energy barrier is typically a consequence of entropy loss upon bringing different parts of the chain together.**