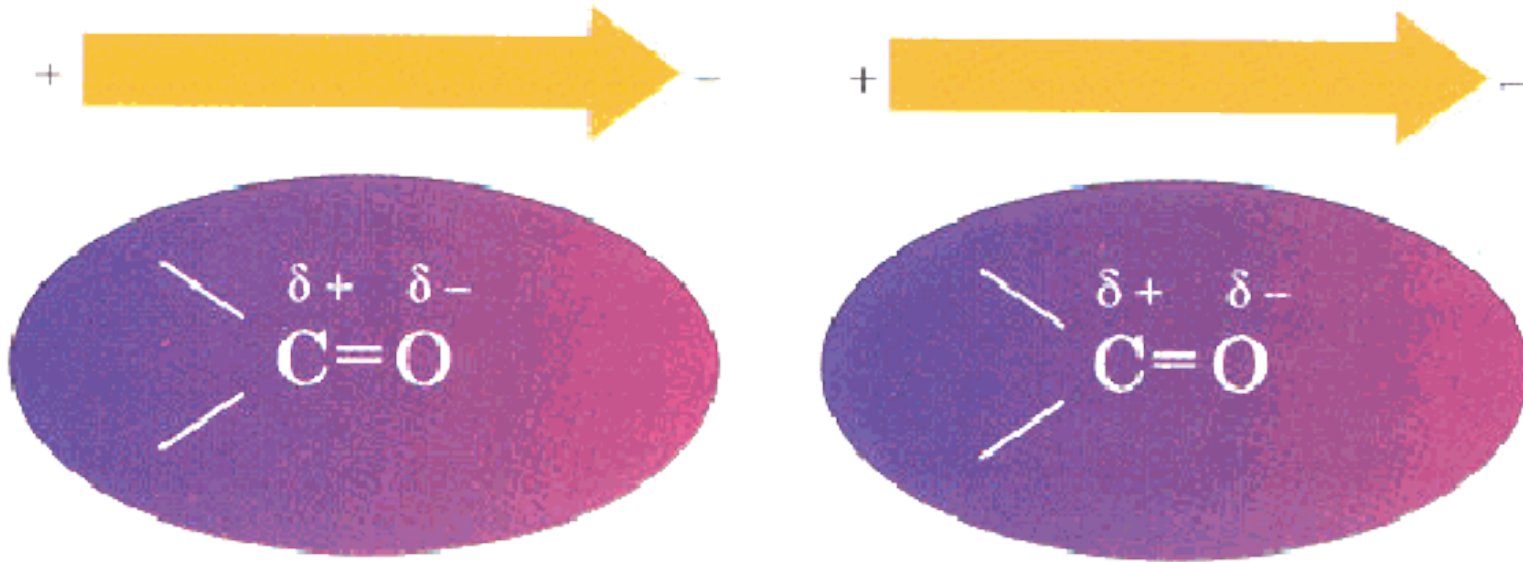


# Protein Folding

Protein folding is similar to DNA hybridization in that they both have a “melt temperature”. For DNA the melt temperature refers to the temperature at which proteins unfold and DNA becomes single-stranded. For proteins it refers to the temperature at which the protein is 50% unfolded. In both cases  $\Delta G^\circ$  is Temperature dependent and the melt temperature Corresponds to the conditions  $\Delta G^\circ = 0$ .

We next consider the interactions that stabilize folded proteins.

# Dipole-Dipole Interactions

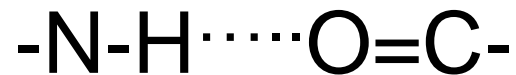


Dipoles often line up in this manner.  
Example:  $\alpha$ -helix

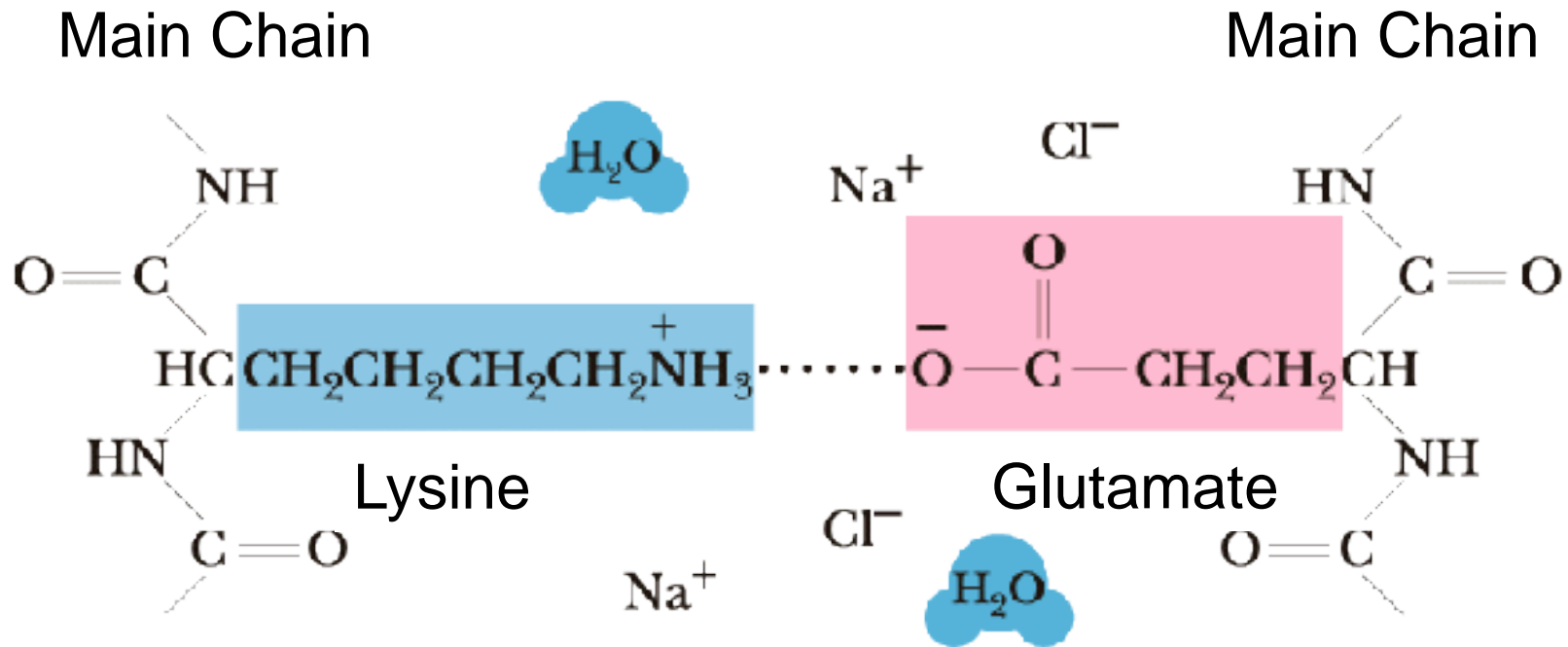
# Electrostatic Interactions

Coulomb's Law:  $V = q_1q_2/\epsilon r$

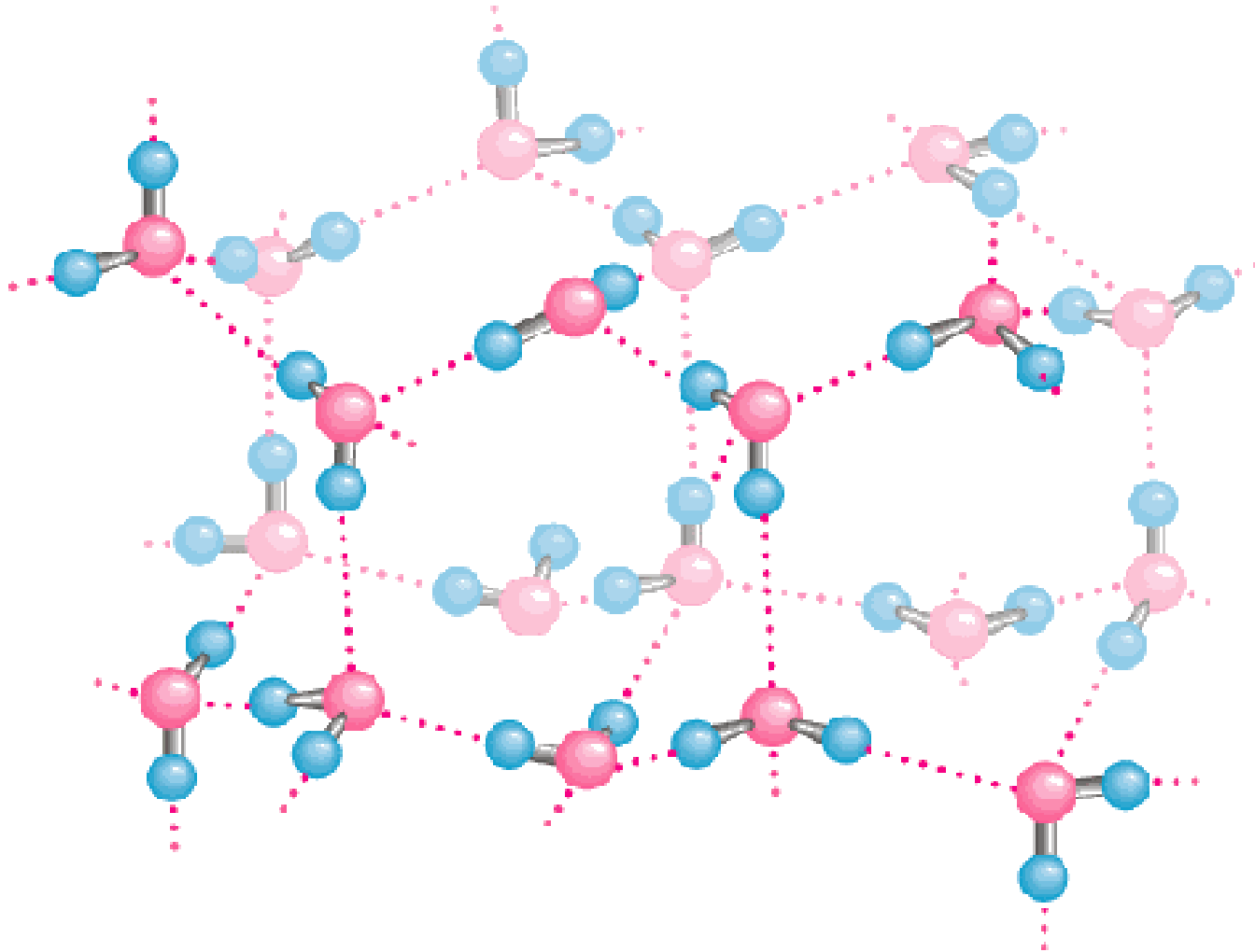
Example of a hydrogen bond



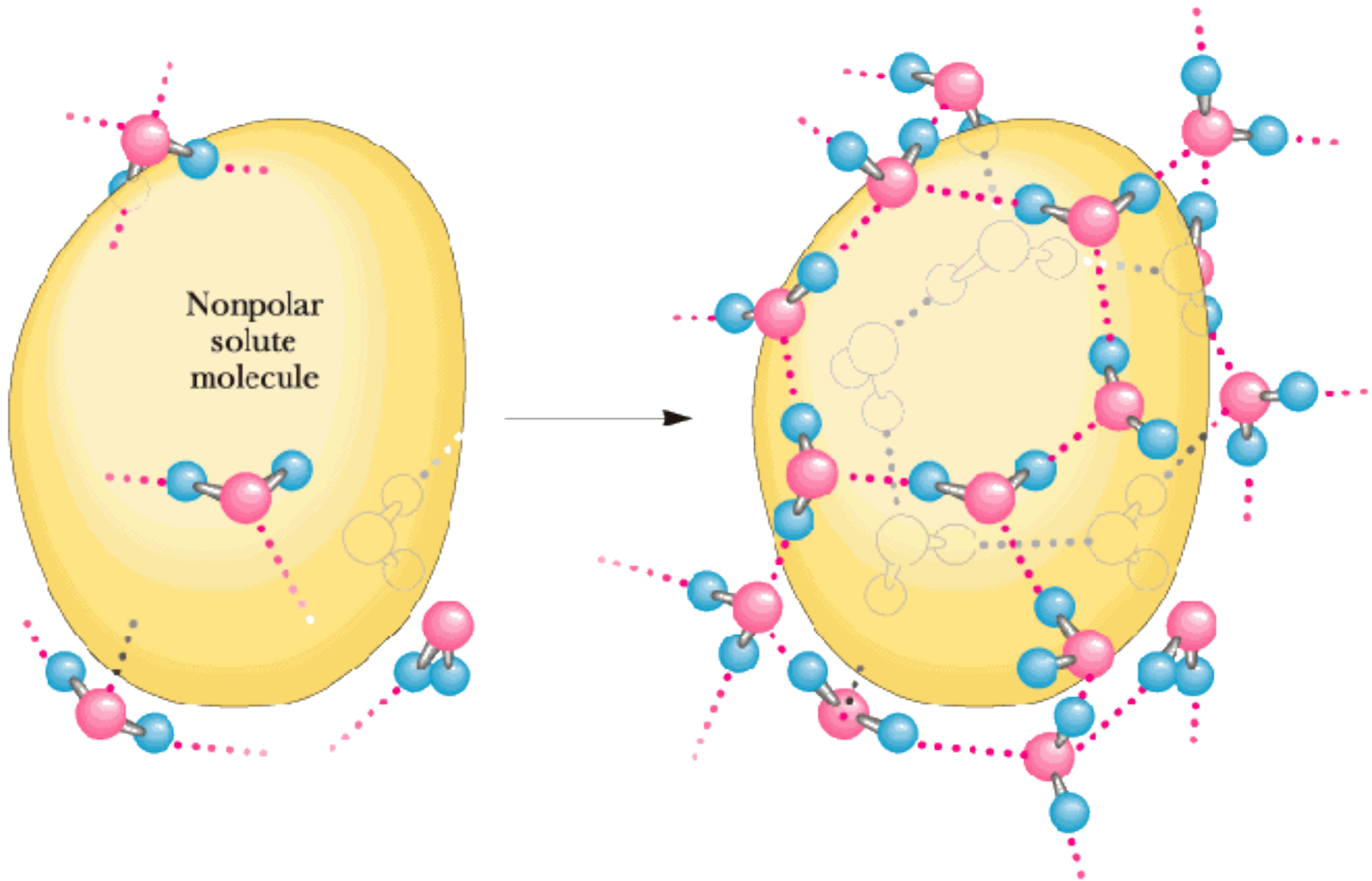
Example of a Salt Bridge



# Hydrogen bonding in water



# Hydrophobic interactions

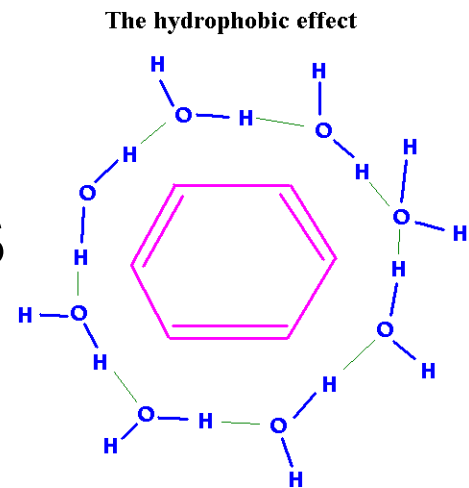


# Protein Folding

## Non-covalent forces in proteins

### What holds them together?

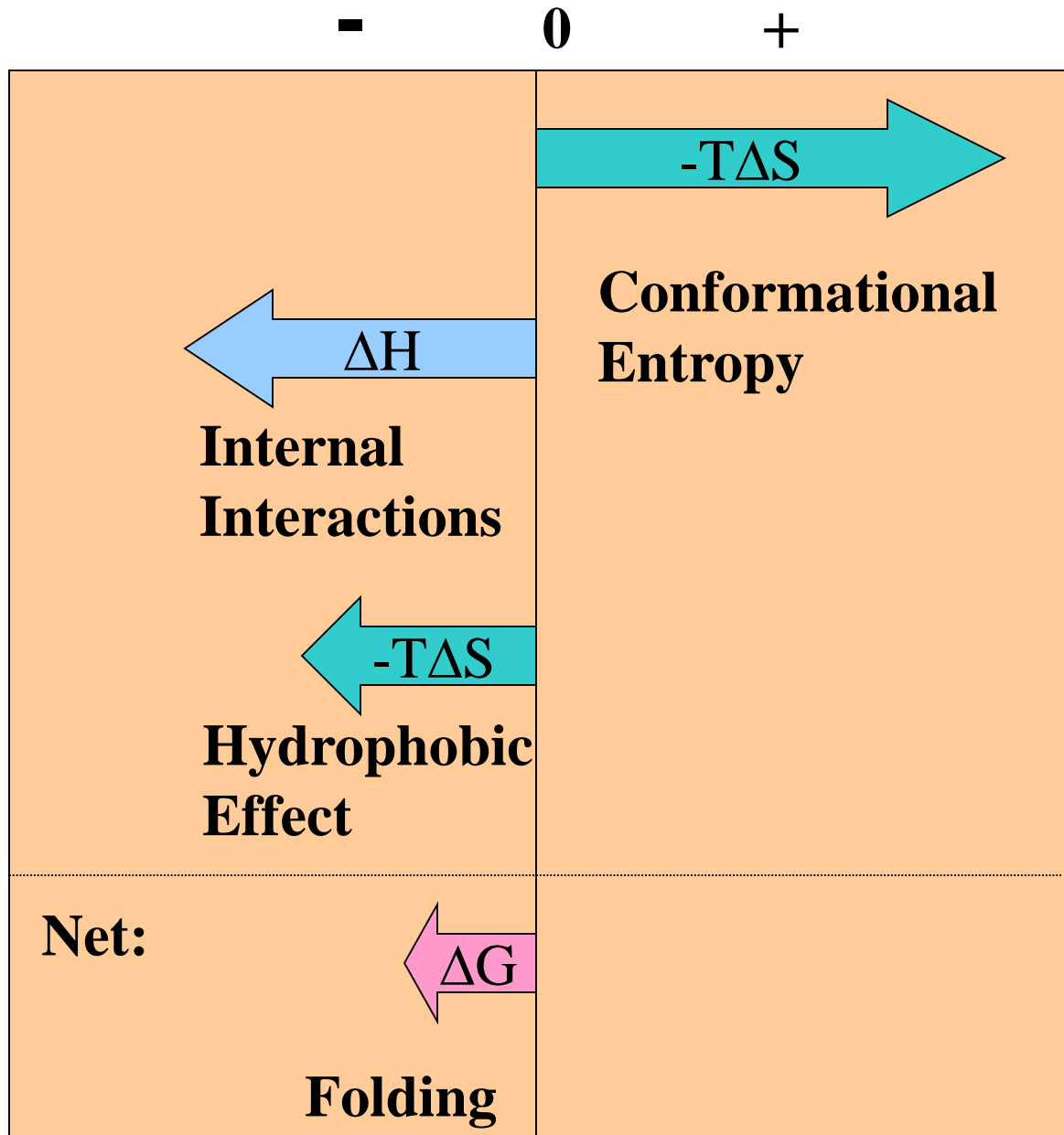
- Hydrogen bonds
- Salt-bridges
- Dipole-dipole interactions
- Hydrophobic effect
- Van der Waals forces



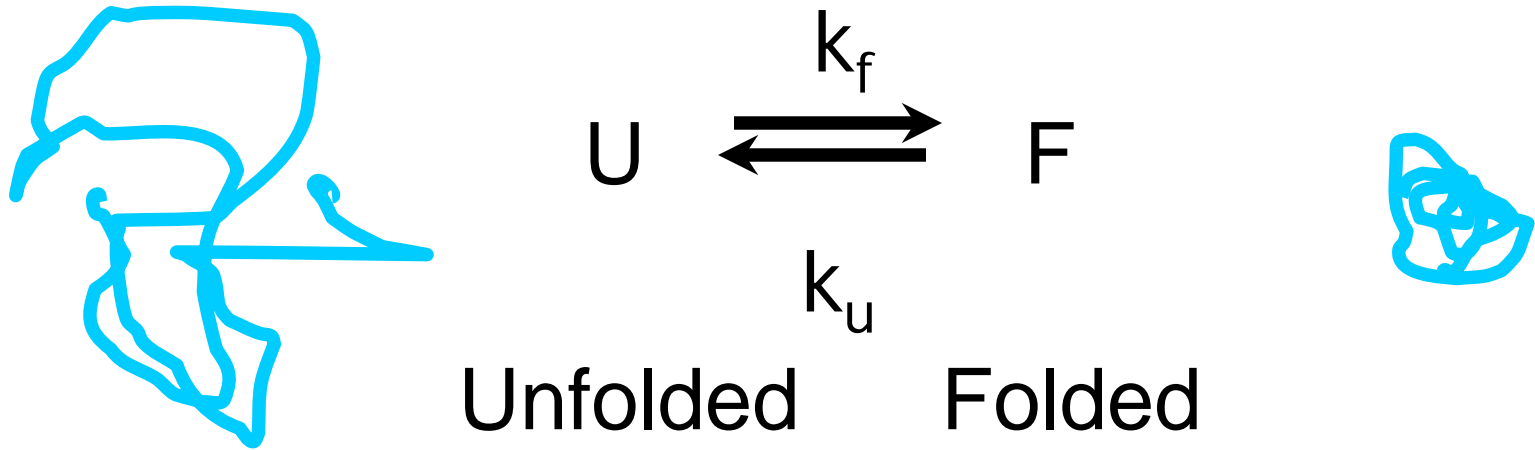
### What pulls them apart?

- Conformational Entropy

# Contributions to $\Delta G$



# Protein folding example: Two state model



$$K = [F]/[U]$$

$$K = ff/(1-ff)$$

Fraction folded  $ff$  Fraction unfolded  $1-ff$



# Thermodynamic model

$$ff = K/(1+K)$$

$$K = e^{-\Delta G^0/RT}$$

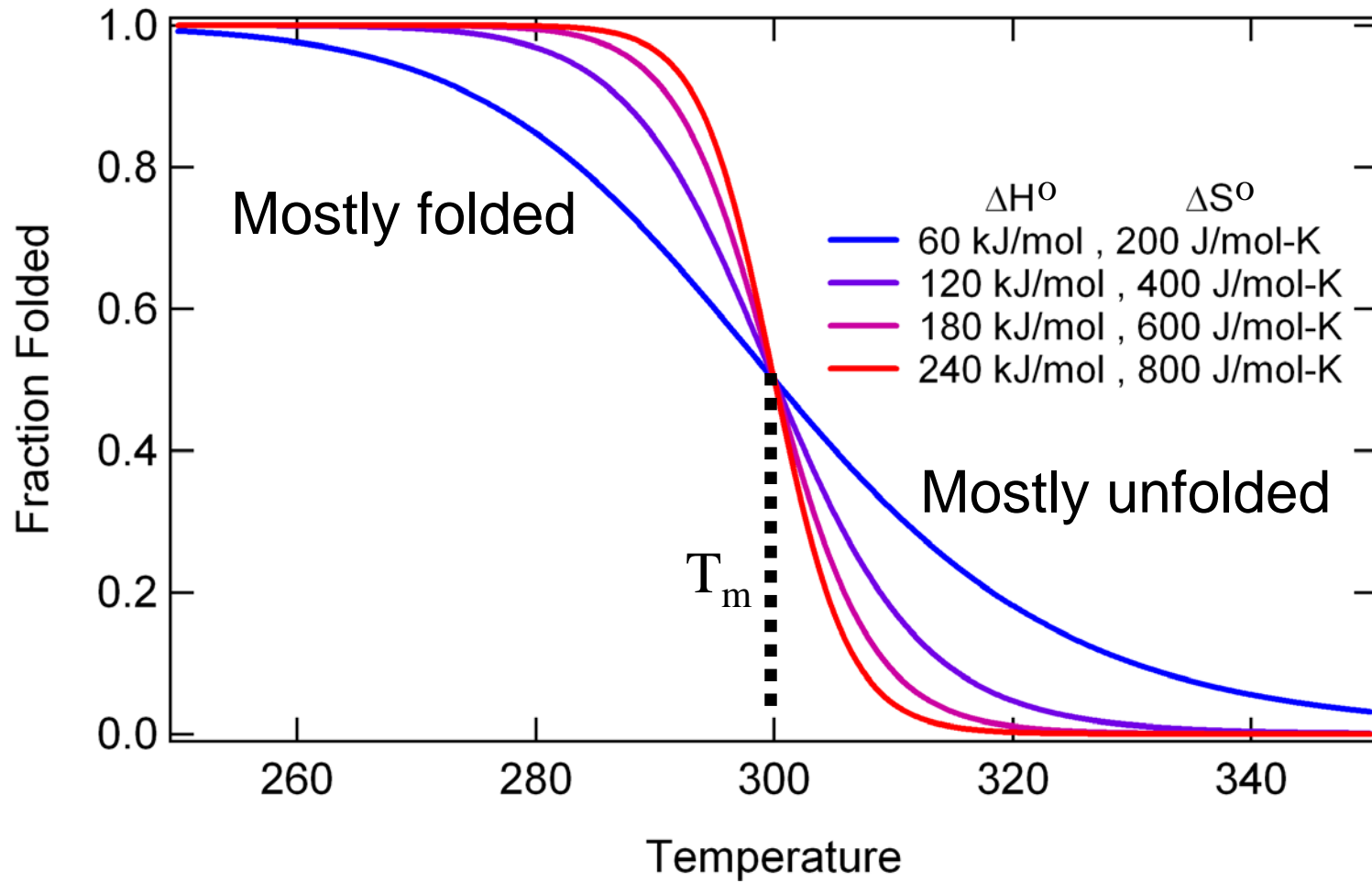
$$ff = 1/(1 + e^{\Delta G^0/RT})$$

$$ff = 1/(1 + e^{\Delta H^0/RT} e^{-\Delta S^0/R})$$

The temperature at which the protein is 50% folded can be defined as  $T_m$  the melt temperature.

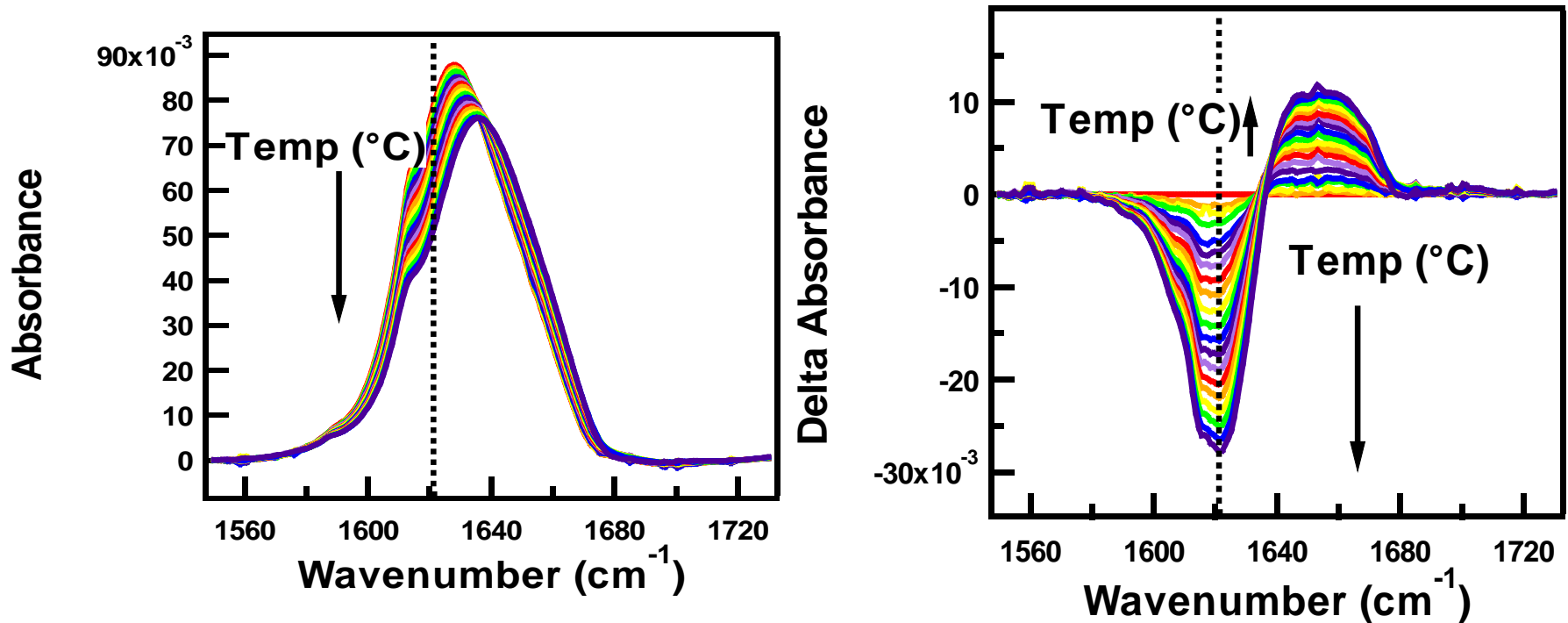
At  $T_m$  ,  $\Delta G^0 = 0$  or  $T_m = \Delta H^0/\Delta S^0$ .

# Equilibrium melt curves



In this case:  $T_m = 300 \text{ K} = \Delta H^\circ / \Delta S^\circ$

# Thermal melt data



Infrared absorption spectra in the amide I region of the peptide. This is a probe of degree of folding.