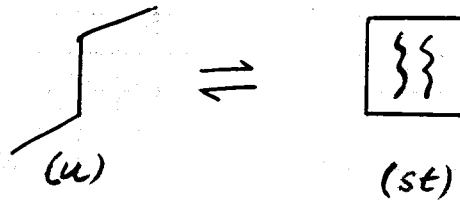


Stacking of dimers. - in dinucleotide phosphates:



This process can be followed:

- Absorption (hypochromism of stacked form).
- NMR (chemical shift of base protons)
- CD (due to helical structure upon stacking).

A two-state model appears sufficient:



$$K = \frac{(st)}{(u)} ; \quad \Delta G^\circ = -RT \ln K$$

$$-RT \ln K = \Delta H^\circ - T \Delta S^\circ$$

Since $\Delta H^\circ \neq 0$; $\Delta H^\circ < 0$, K is a function of the temperature. There exist a temperature for which $(st) = (u)$ and $K = 1$. In this case 50% of the bases are stacked and 50% unstacked. This temperature is called the melting point or T_m :

$$0 = \Delta H^\circ - T_m \Delta S^\circ$$

T_m is a direct measure of how much larger is the stab. ΔH over the destabil. ΔS .

$$T_m = \frac{\Delta H^\circ}{\Delta S^\circ}$$

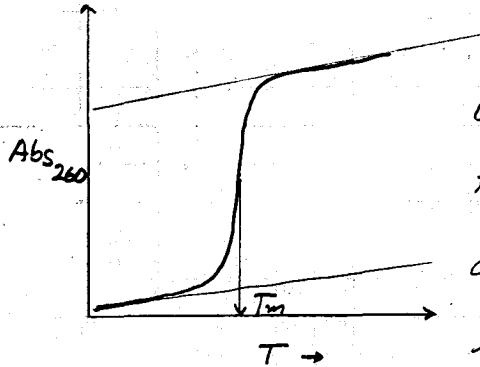
{ the existence of a melting point is the result that this process is accompanied by both ΔH° and $\Delta S^\circ < 0$

Denaturation and Renaturation of DNA.

If a soln of DNA is heated up \rightarrow molecules lose their native conformation above $T \cong T_m$.

can be followed:

- Optically: (As $T \uparrow$, $Abs_{260} \uparrow$; hyperchromism)



Occurs on a narrow T range \Rightarrow it is a highly cooperative phenomenon.

The uncoiling of one part of the structure destabilizes the other.

- Viscosity of DNA decrease suddenly at $T \cong T_m$

Properties of the melting process:

- It's reversible \rightarrow "renaturation" process. When the chains are totally separated at $T > T_m$, these can get back together by lowering the temperature. A process called "annealing" \rightarrow usually $T < T_m$.
- The stability of the DNA molecule and thus its T_m depends on ionic strength and pH.
- The DNA stability depends on the molecule sequence. But for random sequences it depends more on the base content.

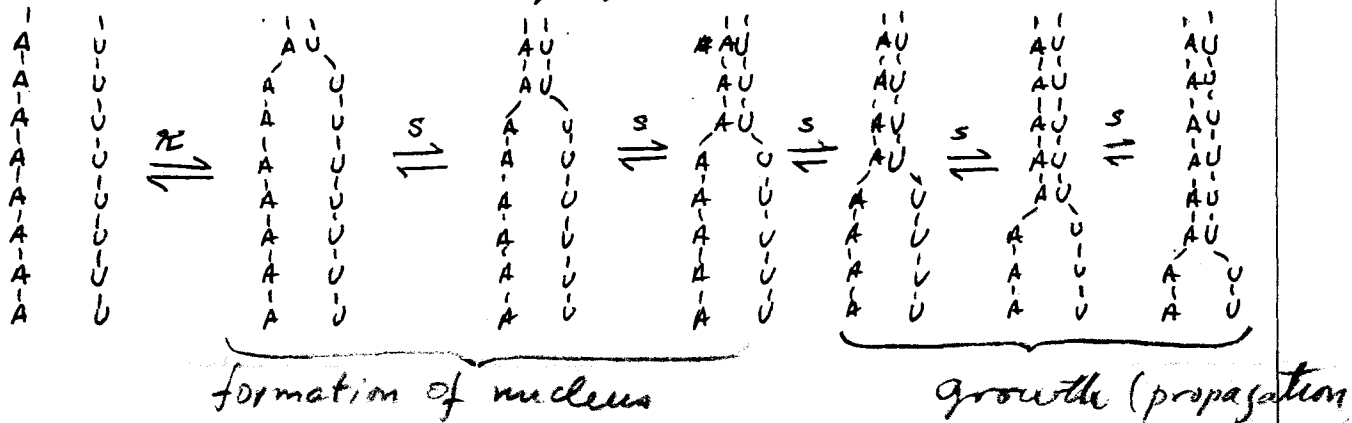
Formation and Breakdown of a double helix:-

A double helix with a well-defined pitch resembles a crystalline lattice.

Crystals form by seeding (nucleation) and growth (propagation)

Moreover, crystals display phase transitions, viz. melting. These are sudden, highly cooperative processes. The association (or dissociation) of 2 single strands to form a double helix has similar characteristics. This process can be treated at various levels of complexity.

We will follow the model of Applegquist and Danle « the staggering zipper model ». This is mostly useful to describe macropolymer complexation.



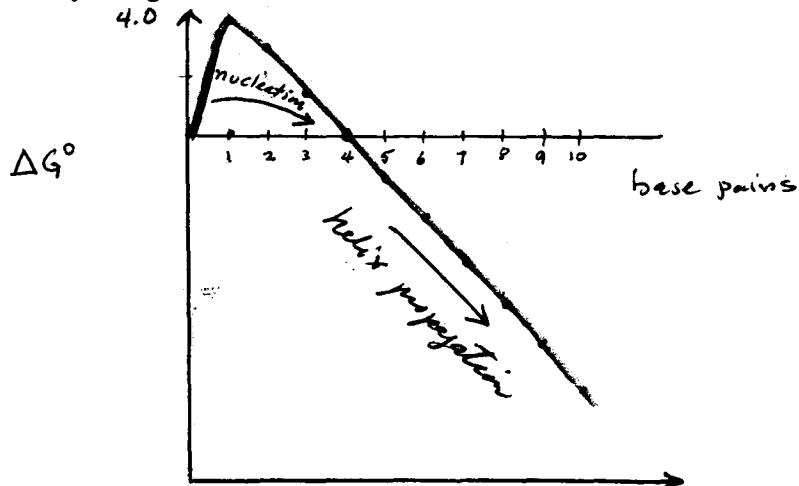
i.e.

The first step involves bringing together the two chains and creating the first base pair. The equil. constant responsible for this, $K_{0,1}$, can be written as the product of a nucleation parameter, β , and a chain growth parameter, s .

4?

In the case of poly A poly U, $\beta \approx 10^{-3} M^{-1}$ and $s \approx 10$ at $0^\circ C$. $s = 1$ at T_m . (Values obtained from relaxation kinetics).

The first step is unstable due to the influence of β , but the addition of a second neighbor stacked base pair follows with stability constant s , (not diminished by β). A third base pair can then form, again with stability s and now, the overall stability constant of this 3 base pair initial stack is now 1. This initial 3-base pair stack constitutes a nucleus. From here onward, growth of the double helix in a zipper-like manner is thermodynamically favorable.



Enthalpy and entropy contributions to nucleation and growth:-

Nucleation:-

Hydrogen bonding, the only major interaction in nucleation has probably negligible enthalpy in water, thus:

$$\Delta H_{nuc} = 0 \quad \text{and} \quad \Delta G_{nuc} = -T\Delta S_{nuc}$$

i.e. all the contribution to the free energy of nucleation is entropic; $\Delta S < 0$ to bring the two strands together and $\Delta G_{nuc} > 0$.

Growth:-

< 0 $\left\{ \Delta H_{growth} = \right.$ stacking enthalpies, including nearest neighbor interactions and contributions.

< 0 $\left\{ \Delta S_{growth} = \right.$ unstacked to stacked.

		ΔH° (kcal)	ΔS° (kcal/deg)	ΔG° (kcal at 25°C)
	$\begin{array}{c} -A-A' \\ \cdot \\ -U-U' \end{array} \rightarrow \begin{array}{c} -A-A' \\ \cdot \\ -U-U' \end{array}$	- 8.2	- 0.0235	- 1.2
	$\begin{array}{c} -A-U' \\ \cdot \\ -U-A \end{array} \rightarrow \begin{array}{c} -A-U' \\ \cdot \\ -U-A \end{array}$	- 6.5	- 0.0164	- 1.6
	$\begin{array}{c} -C-A \\ \cdot \\ -G-U \end{array} \rightarrow \begin{array}{c} -C-A' \\ \cdot \\ -G-U \end{array}$	- 5.9	- 0.0127	- 2.1
	$\begin{array}{c} -C-G' \\ \cdot \\ -G-C \end{array} \rightarrow \begin{array}{c} -C-G' \\ \cdot \\ -G-C \end{array}$	- 13.0	- 0.0335	- 3.0
	$\begin{array}{c} -C-C' \\ \cdot \\ -G-G \end{array} \rightarrow \begin{array}{c} -C-C' \\ \cdot \\ -G-G \end{array}$	- 13.7	- 0.0298	- 4.8