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1 We use hydrophobic effect to solve Flory problem

Hydrophobic effect is an effect which lays in the core of protein folding. It is mostly an entropic effect originating from the disruption of hydrogen bonds between water molecules by the nonpolar solute. [1]. When hydrophobic molecules are placed in the water, water molecules form cage-like structures around them (see fig. 1). When hydrophobes come into contact, water molecules get released; this increases entropy and therefore decreases free energy. This decreases in free energy allows proteins keep a tight hydrophobic core.

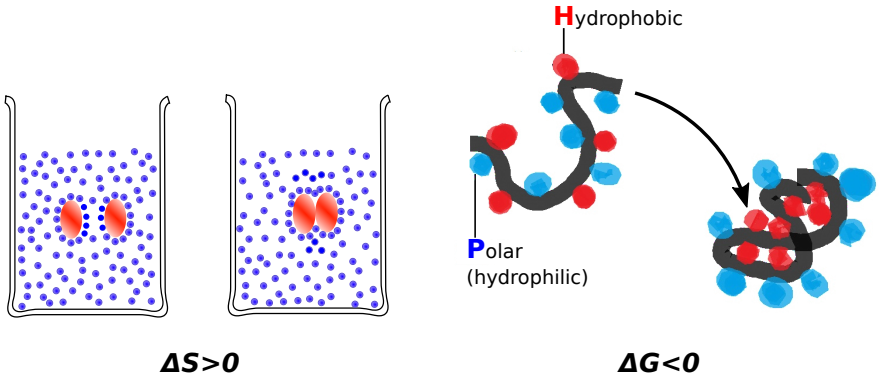

Fig. 1: Hydrophobic effect is an entropic effect originating from the disruption of hydrogen bonds between water molecules by the non-polar solute. When hydrophobic molecules are placed in the water, water molecules form cage-like structures around them. When hydrophobes come into contact, water molecules get released; this increases entropy and therefore decreases free energy.

1.1 We use HP model to represent prebiotic polymerization

To describe effect of hydrophobic interaction on prebiotic polymerization, we adopt the HP model – one of the simplest models of proteins; it's well studied and sequence space is well understood[2–6]. While initially HP model was introduced as a model for proteins, we

are indifferent to exact chemical nature of the prebiotic polymers and consider only principles of spontaneous polymerization.

HP model features:

- It is a two dimensional square lattice model of protein folding
- It has 2 types of monomers: hydrophobic (H) and polar (P).
- HP model has a folding code: presence of hydrophobic interaction makes some conformations of the same chain more energetically favorable than others. Moreover certain chains will have a unique conformation, which delivers free energy minimum. This conformations are called native states, and sequences, which have native state, are considered being capable of folding (see fig. 2).

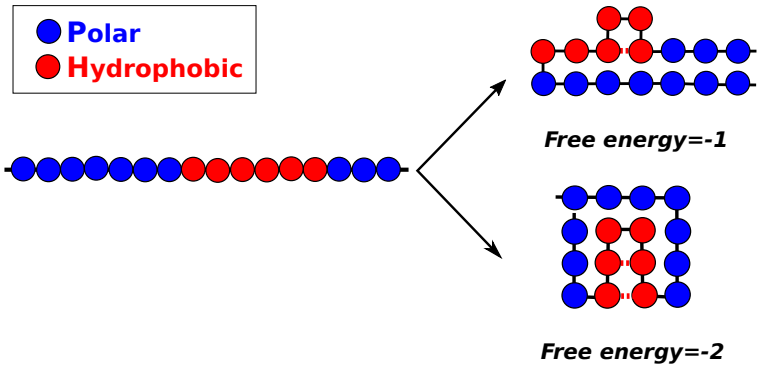

Fig. 2:

Because of the ability to form hydrophobic contacts in water, even hetero-polymers that are as simple as HP-polymers will often fold up, even as short chains. While short HP chains will not necessarily have great stability qualities (they will often be fairly amorphous "oil-drop"-like balls that are ensembles of conformations), some HP sequences will fold more uniquely than others. Latter will spend most of the time in the native state. And, what is important, it has been shown that a relatively large fraction of sequence space will fold to compact structures or compact ensemble structures[2].

1.2 HP-foldamers can work as prebiotic catalysts

Our central premise is that the same promiscuous hydrophobic interactions that can cause random HP heteropolymers to collapse into compact, folded, structures. However hydrophobic interaction will also cause polymer-polymer attraction and binding between molecules. In some cases, a folded HP-polymers can provide a hydrophobic "landing site" for another HP polymer and/or another H monomer (see fig. 3).

When a folded chain has exposed hydrophobic monomers on its surface it can attract another chain with hydrophobes as well as activated hydrophobic monomer. Interaction

between 3 of them localizes growing chain and next monomer (fig.3(a)). In addition to that, hydrophobic interaction also lowers activation barrier of the polymerization reaction, accelerating reaction this way.

One hydrophobic interaction is about $1-2kT$. Given that rate of catalysis is proportional to an exponent of the activation barrier, 3-4 hydrophobic interactions are enough to increase polymerization rate ≈ 100 times (fig.3(b)). Of course, this is not a good rate enhancement, compared to $2 \cdot 10^7$-fold rate enhancement brought about by modern ribosomes[7]. However the very first catalysts don't have to be very efficient: their purpose is to create a driving force of evolution.

HP-catalysis drives addition of hydrophobes to hydrophobes. A seemingly logical conclusion would be that one will end up with purely hydrophobic polymers. However this is not true. Sequences capable of catalysis must have a relatively stable structure. Purely hydrophobic sequences don't have this property: they have very many conformational states with the same low free energy. Therefore they will spend a lot of time jumping between those states and their bonds will be affected by hydrolysis. They also will not be able serve as catalysts. Sequences with $50-80\%$ of hydrophobes, on the other hand, will have the most stable structures; they will be protected from hydrolysis and will be able to localize growing chain with the next added monomer.

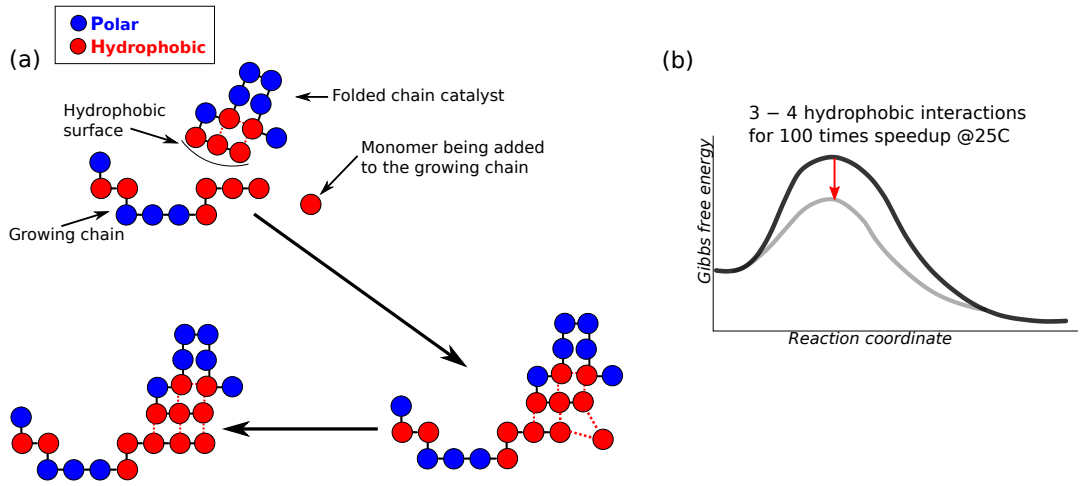

Fig. 3: Catalyst catalyzes a growing of an unfolded hp-polymer. Having just 3-4 hydrophobic contacts is enough to lower an activation barrier for $\propto 100$ times at room temperature.

References

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