On/Off Switching on Polymer Conformation

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Summary: The manner of folding transition from elongated coil to compact globule of single polymer chain is discussed. Based on theoretical consideration, it is argued the semi-flexible polymer chain exhibits large discrete transition on the level of individual single chains, whereas the transition looks continuous, or cooperative, on the ensemble of chains. As the experimental verification, in the present article thermodynamic and kinetic aspects of folding transition of single giant DNA molecules are described. It is shown that rich variety of nano-ordered structures are obtained from single DNA molecules through suitable setup of the experimental conditions. The stability of such nano-structures generated from single polymer chain is discussed in relation to the ordered compact structure with large number of chains in semi-dilute and concentrated polymer solutions.

Keyword: coil-globule transition, DNA condensation, nano-ordered structure, polyelectrolyte, single chain observation

Introduction

According to the standard description on texbooks of polymer science, single polymer chain undergoes coil-globule trantion through the so-called θ-state.[1,2] This means that the transition has been regarded as continuous, or cooperative, in general. In contrary to this, recently it has become clear the individual giant DNA molcules exhibit large discrete transition accompanied with the change of the segement density of the order of 10^4-10^5. The common characteristics of the folding transition of single giant DNA molecules are summarized as follows:[3,4]

1) Individual DNA molecules exhibit an all-or-none transition between an elongated coil and a compact globule, irrespective to the chemical nature of condensing chemicals, such as polyvalent cation, hydrophilic polymer, cationic surfactant, etc.
2) There is rather wide parameter area on the coexistence between the unfolded and folded states. The folding transition appears to be steep but continuous for the ensemble average of DNA molecules.
3) The free energy of a single DNA is interpreted with the profile of double minima. The transition is classified as first-order phase-transition under the criterion of Landau.

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4) The negative charge on DNA disappears with the foding transition, except for the surface on the compact state. This means that individual globules, or compact DNAs, behave as soluble colloid.

In the present article, we will argue that the discrete nature of the folding transition is a general property of semi-flexible polymer chains.

ON/OFF Switching of Single Semi-flexible Chain[3-6]

Let us discuss the effect of chain stiffness on the manner of folding transition in a polymer molecule. We consider a polymer chain with the contour length L and Kuhn length λ, corresponding to the length of a segment. Thus, the number of segments is given as $N = L/\lambda$. When a chain is dissolved in a good solvent, the characteristic one-dimensional size R_c (such as end-to-end distance, radius of gyration, hydrodynamic radius) of an elongated polymer chain is represented as in the following relationship.

$$R_c \cong \lambda N^{3/5} \qquad (1)$$

On the other hand, the size of a compact folded chain is given as eq. (2), where s is the cross sectional area of the chain.

$$R_g \cong (\lambda s N)^{1/3} \qquad (2)$$

If the cross section can be represented by a circle of diameter D, the area is represented as $s = \pi D^2/4$, i.e., $D^2 \cong s$. Here, we introduce a parameter on chain stiffness as $\eta = \lambda/D$. When the stiffness paramer is much larger than unity, $\eta \gg 1$, the change in R becomes significant. In the case of DNA, it is known that s = 2nm and λ = 100nm. The contour lenght in natural DNA is rather large; bacterial DNA is on the order of mm and manmalian DNA is above cm. As an example, let us calculate the change of the size on a DNA chain with 30 kilo base pairs, which has the contour lengh of ca. 10 μm and the number of the Kuhn segments N = 100. From eqs.(1) and (2), the diffrence of the density between the globule and coil is obtained as $\rho_g/\rho_c = (R_c/R_g)^3 \cong 10^5$. For comparison, it is to be noted that the change of the density on the transition between liquid water and vapor is only ca. 2000. Now, it has become evident that the density

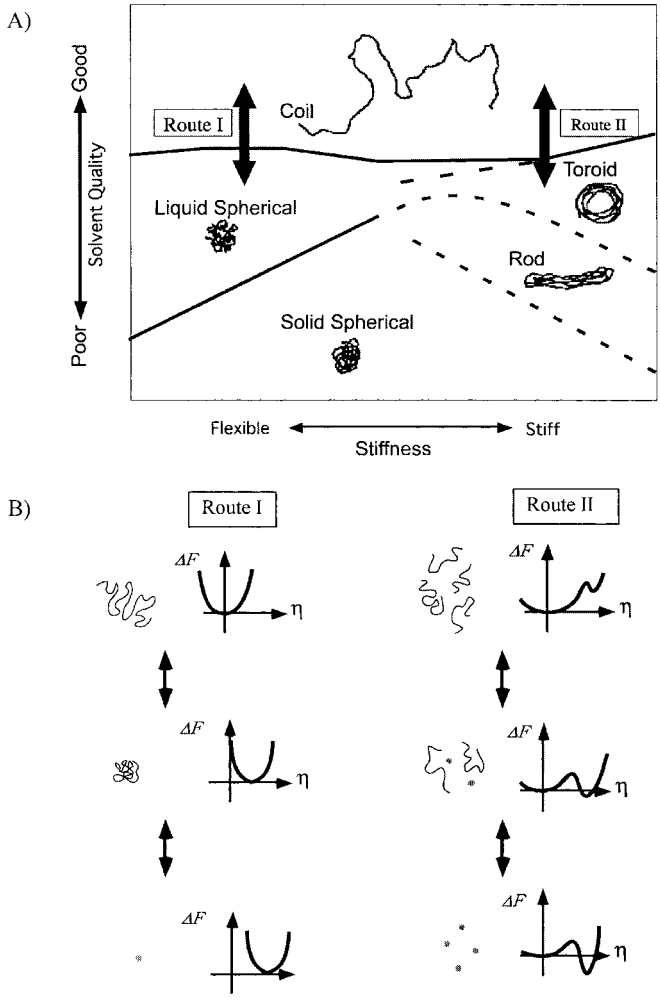

Fig. 1. A) Phase diagram on the conformation of a single polymer chain (modified from the original figure in reference[7]). B) The manner of coil-globule transition is markedly different between the two Routes (see Fig.1 A). The conformational change is schematically represented, together with the corresponding profile of free energy on individual chains. η: density of segments.

difference before and after the folding transition of giant DNA is very significant. Actually, from detailed theoretical considerations it has been established that long stiff plymer, including giant DNA, exhibits large discrete transition, i.e., first-order phase-transition.[7,8]

Phase Diagram in a Single Chain

Figure 1 shows the phase diagram of a single chain with the change of chain stiffness, deduced from a theoretical calculation of Multi-canonical Monte Carlo method.[7] When the stiffness is large enough, the transition from elongated coil into compact state is discrete, i.e., first-order phase-transition. It is noted that depending on the change in the quality of the solvent, or in the pair interaction between the segments, different solid-like states are generated as the most stable conformation, such as toroid, rod and spherical globule. On the other hand, the transition is diffuse or continuous for the molecular chain with lower stiffness, where liquid-like spherical state is generated after the transition. Such continuous nature concides with the current picture of the coil-globule transition in standard textbooks.[1,2] In between the discrete and continuous transitions, a region of the intermediate nature of transition exists. When a polyelectrolyte chain exhibits such intermediate stiffness, intrachain segregated state, or pearling structure, is generated.[9,10]

Nano-ordered Structures from a Single Chain

Figure 2 shows the electron micrograph on variety of structures made from single T4 DNA (165kbp, contour length 57 μm).[3,4] With cationic condensing agents, such as spermidine(3+), spermine(4+), cobalt ion(3+), tightly packed toroids with the diameter of 60-80nm are formed after the coil-globule transition. With the excess of the cationic reagents, the toroids swell into larger size as a result of the weaker attractive interaction between the segments.[11] With a cationic surfactant having multi-cationic head group, lipospermine, spool-like structure is generated.[12] With the addition of PEG-A, amino-pendant polyethelene glycol, partially compact state with the mini-globule(s) is induced.[9] Similar partially segregated structure is generated with polycations having larege number of cationic groups.[13] When DNA is complexed with dicationic surfactant, pearling chain is generated where plural number of mini-toroids are found along a single chain (A. Zinchenko, et. al., unpublished result).

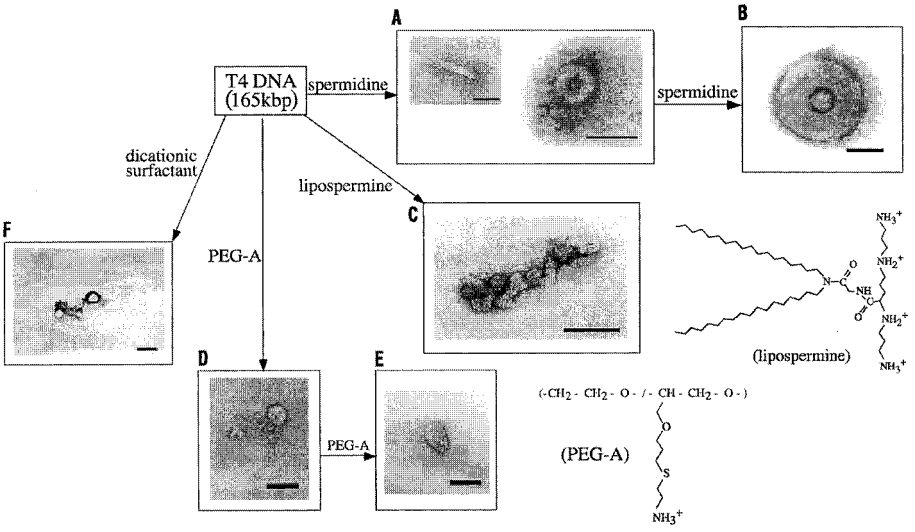

Fig. 2. Electron microscopic images of compact states generated from single T4 DNA molecules. The bars indicate 0.1μm. (The original references are A:[14], B:[11], C:[12], D and E:[9], F: Zinchenko, et. al., unpublished).

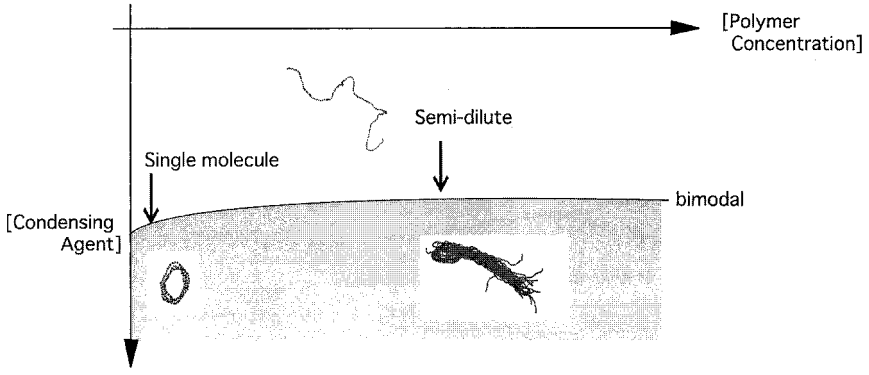

Fig. 3. Diagram of transition of stiff polymer. With the increase of polymer concentration, bundle with multiple chains is generated. (T. Sakaue, et. al., unpublished).

Competition Between the Events of Single Chain and Multiple Chains

With the increase of the polymer concentration in stiff chains, assembly of multiple chains becomes to be generated as is schematically shown in Figure 3. Interesting to say, it has been found, form the experiments on giant DNA, that the necessary concentration to cause the compaction of single chain at low polymer concentrations and also the condensation of multiple chains at high polymer concentrations are essentially the same (T. Iwataki, et. al., unpublished result). It is of scientific value to extend further the experimental and theoretical studies on the conformational change of polymers by comparing single and multiple-chain processes.

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