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Melting transition of directly linked gold nanoparticle DNA assembly

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Abstract

DNA melting and hybridization is a fundamental biological process as well as a crucial step in many modern biotechnology applications. DNA confined on surfaces exhibits a behavior different from that in free solutions. The system of DNA-capped gold nanoparticles exhibits unique phase transitions and represents a new class of complex fluids. Depending on the sequence of the DNA, particles can be linked to each other through direct complementary DNA sequences or via a 'linker' DNA, whose sequence is complementary to the sequence attached to the gold nanoparticles. We observed different melting transitions for these two distinct systems.

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Keywords: DNA phase transition; Gold nanoparticle; DNA melting

1. Introduction

Melting of the DNA duplex is the process by which two DNA strands unbind upon heating. The nature of this transition has been studied for decades [1–3]. For short DNA with fewer than 12–14 base pairs, melting and hybridization can be

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described by a two-state model as an equilibrium between single- and double-stranded DNA [4,5]. For long and heterogeneous DNA, the melting curve exhibits a multi-step behavior consisting of plateaus with different sizes separated by sharp jumps. Although much of the thermodynamic properties of the melting of free DNA are known, DNA melting in a constrained space, such as on surfaces, is still poorly understood [6]. DNA molecules functionalized with gold nanoparticles provide a model system for such study.

The sequence-specific hybridization properties of DNA have been used for self-assembly of nanostructures and for highly sensitive DNA detection [7,8]. Previous work relies on a linker DNA [7–10], and it has been suggested that entropic cooperativity plays an important role in the sharp phase transition of such DNA-linked nanoparticle assembly systems. On the other hand, most simulations do not explicitly incorporate linker DNA [11], and the results cannot be directly compared to experimental data. Here we synthesized a system that eliminated the usage of linker DNA and found that the melting transitions of these direct-linked gold particles exhibit a behavior distinct from those connected via a linker DNA.

2. Experimental procedures

The sample was prepared according to the procedures described in Ref. [8]. Briefly, DNA-capped gold nanoparticles were prepared by conjugating gold colloidal nanoparticles with thiol-modified DNA. The configuration of the DNA used in different experiments is illustrated in Fig. 1. We prepared four sets of samples with different DNA lengths and sequences. In sample I, the gold particles are connected through a 24-base DNA linker; in sample II, the gold particles are directly connected via 12-base complementary DNA on gold particles; in sample III, the gold particles are directly connected via 12- and 18-base DNA; in sample IV, the gold particles are directly connected via 18-base DNA.

The aggregates of DNA-linked gold colloids were allowed to stand at 4 °C for several days for aggregation. Optical spectroscopy was used to study the phase transition of the DNA-linked gold colloids, since DNA bases have strong absorption in the UV region [4,5]. We monitor the thermal melting by measuring the extinction at 260 nm, while slowly heating the solution containing aggregates. The solution was heated from 25 to 75 °C at the rate 0.5 °C/min. All spectra were recorded with a PerkinElmer Lambda 45 spectrophotometer equipped with a peltier temperature controller, magnetic stirrer, and a temperature probe. The recorded temperature of the sample was measured by a temperature probe.

3. Results and discussion

Fig. 2 shows the melting curves of samples I(a) and II(b). The melting curves of corresponding DNA in solution are also shown. The melting temperature of the DNA duplex attached to gold particle surfaces is lower than that of free DNA, and

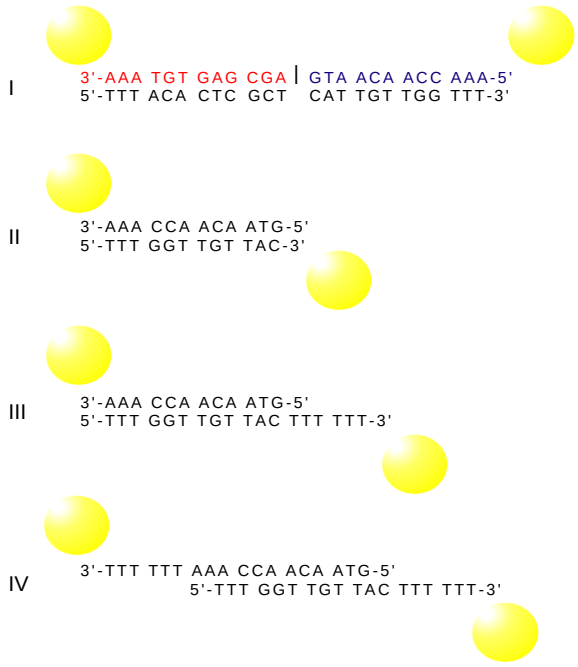

Fig. 1. DNA sequences used to form DNA-linked gold nanoparticles. Sample I is connected through a linker DNA. The line between bases A and G in the probe DNA sequences indicates that there is no chemical bond between these two bases. Samples II–IV are directly connected through surface-attached DNA with spacings of 12, 18, and 24 DNA bases between particles.

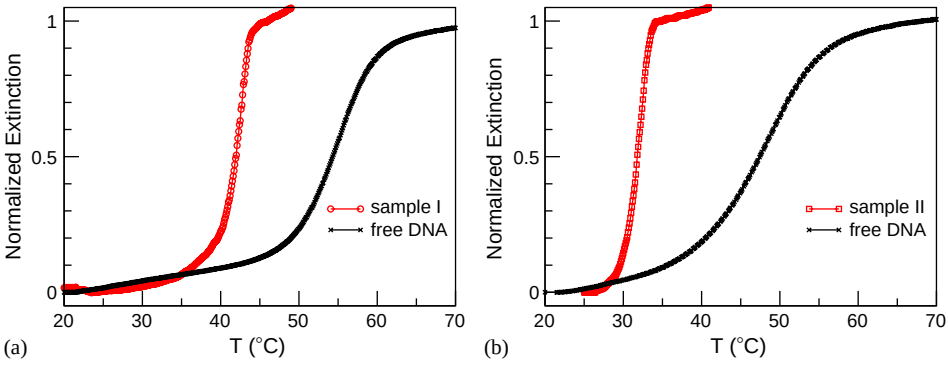

Fig. 2. Melting curves of gold nanoparticles connected (a) with a DNA linker (sample I), and (b) via direct hybridization of complementary surface-attached DNA (sample II). The corresponding free DNA melting curves are also shown.

the melting transition is much sharper. However, direct comparison of melting temperatures between these two systems is difficult, since the DNA compositions are different for these two systems. The system without linker appears to have a lower

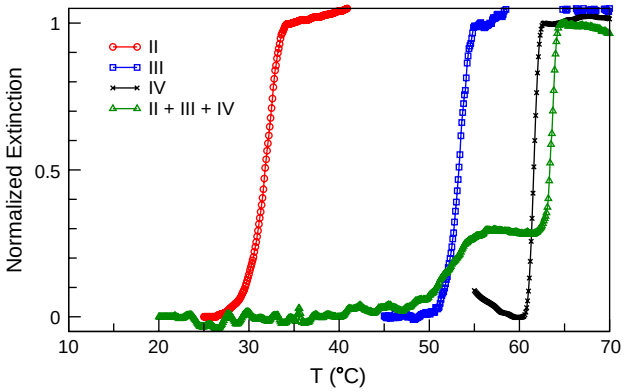

Fig. 3. Melting curves of 12/12 (sample II), 12/18 (sample III), 18/18 (sample IV), and a combination of 12/12, 12/18, and 18/18 (Sample II + III + IV). The mixed system shows multi-step melting at temperatures corresponding to T_m's, within the experimental uncertainty, for samples II and III.

melting temperature, perhaps due to the short distance between gold particles (12 base versus 24 base).

To study how the melting depends on the spacing between gold particles, we prepared gold particles capped with 18-base DNA (Sample III), which is composed of sequence identical to the 12-base DNA in Sample II plus a 6-base DNA spacer (see Fig. 1). The difference between samples II and III is the spacer DNA length, which alters the spacing between gold particles. The melting temperature is 62 °C for sample IV versus 32 °C for sample II (see Fig. 3), which suggests that increased particle spacing leads to higher melting temperature of the assemblies.

To introduce disorder, we mixed the 12- and 18-base DNA-capped gold particles in one solution. Thus, the 12-base DNA is allowed to hybridize with either 12- or 18-base DNA, and the 18-base to 18- or 12-base DNA. This combination allows three possible duplex formations: 12/12 (sample I), 12/18 (sample II), and 18/18 (sample III) hybridization in one solution and possibly in one aggregate. Note that in all three base pairing, only 12 bases are complementary, and the only variable is the non-pairing DNA spacer length, which controls the interparticle distance. Since the duplexes with higher melting temperatures are more stable, we expect to see more of those duplexes forming. Indeed, Fig. 3 shows that the most abundant duplex is the 18/18 combination, followed by the 12/18, with almost no 12/12 duplex formed.

The multi-step melting is an unusual phenomenon in DNA-capped gold particle assembly. For the system connected by either 24- or 30-base DNA linker, where the 30-base linker differs from the 24-base one by an extra 6-base spacer in the middle of the linker, heating the assembly results in a single melting temperature T_m. The T_m of the system with spacer is higher (37 °C) than that without spacer (33 °C). When equal amounts of linkers with and without spacer are present in the solution, the system has a T_m in between the high T_m (37 °C) and low T_m (33 °C) systems. The T_m of the mixed system (36.5 °C) is much closer to the more stable system (37 °C), as illustrated in Fig. 4(a). However, free DNA with the same sequences exhibits

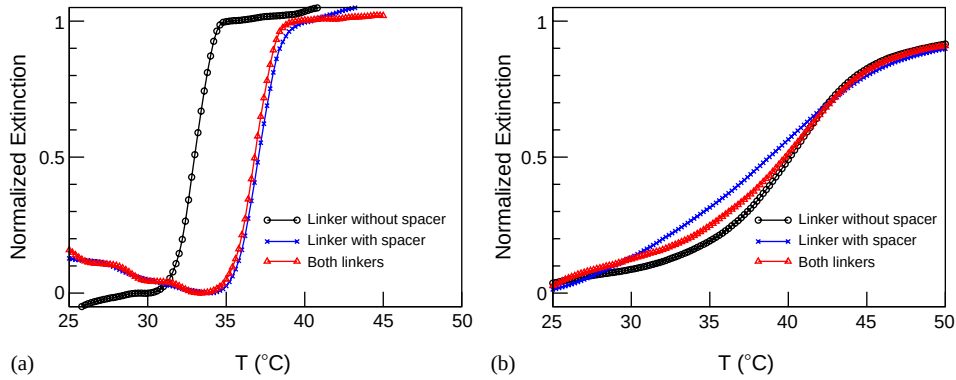

Fig. 4. Melting curves of DNA duplex containing spacer for (a) nanoparticle assembly and (b) free DNA.

different trend in T_m (see Fig. 4(b)), where a linker with spacer results in lower melting temperature than that without spacer. The finding suggests that interparticle distance plays an important role in determining the T_m in the nanoparticle system. On the other hand, the multi-step melting in the system without linker DNA suggests that most clusters are composed of either 12/18 connections or 18/18 connections and few with both connections in the same cluster, unlike the systems with linker DNA. The abundance of clusters of a given connection is related to its stability. We speculate that once the clusters nucleate with a certain type of connection (defined here by the DNA length, hence the interparticle spacing), only the same type of connection is allowed to grow. Further studies are needed to determine whether this phenomenon is kinetics or thermodynamics driven.

4. Summary

In summary, we have studied the thermal denaturation of DNA strands attached to gold nanoparticle surfaces. In the DNA-capped gold nanoparticle systems, the interactions are complex, involving DNA–DNA interactions and particle–particle interactions. The DNA are constrained to a gold particle surface and often exhibit interesting behaviors not seen by DNA in free solution. The multi-step melting of systems with different spacers is unique to systems directly linked with DNA that are attached to gold nanoparticles.

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