Materials Horizons

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Journal:	*Materials Horizons*
Manuscript ID	MH-COM-07-2019-001115.R1
Article Type:	Communication
Date Submitted by the Author:	15-Oct-2019
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MODULATING AND ADDRESSING COLLOIDAL INTERACTIONS USING LIGHT

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New concepts

We demonstrate a new method to modulate interactions between colloidal particles on millisecond timescales. Simulations and theory have shown that rapid control over interparticle binding is necessary for controlled non-equilibrium self-assembly in colloids. Until now, that rapid control has been experimentally infeasible. In current systems, the rate at which binding can be modulated is limited by the rate at which the temperature of the entire suspension can be changed. We overcome this limitation by coupling light absorption to localized heating of individual particles. This local heating has the added benefit of allowing for independent tuning of the interactions between different species of particles in solution. Compared to other light-driven modulations schemes involving photochemistry—using, for example, azobenzene groups to modify the DNA strands—our method requires no chemical modification of the system. The underlying concept that we present is that converting light to heat (photothermal modulation, as opposed to photochemical or purely thermal modulation) is a simple and effective way to rapidly modulate colloidal interactions. This concept may lead to new non-equilibrium and sequential self-assembly schemes.

Journal Name

ARTICLE TYPE

Cite this: DOI: 00.0000/xxxxxxxxxx

Modulating and addressing interactions in polymer colloids using light†

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Received Date
Accepted Date

DOI: 00.0000/xxxxxxxxxx

DNA-mediated linkages between colloidal particles enable controlled assembly and, by virtue of the sharp thermal binding-unbinding transition, provide a mechanism to create switchable structures. However, bulk thermal heating limits switching times to tens of seconds or more. We show that the timescale can be reduced to milliseconds by using light to dynamically control interactions among DNA-coated colloidal particles. We dye particles, such that when they are uniformly illuminated with unfocused light with a wavelength in the absorption band of the dye, they locally heat. We show that the interactions can be reversibly switched by modulating the light intensity. By using multiple dyes and different wavelengths of light, we independently address interactions between different sets of particles. Calculations show that light-driven heating produces local temperature gradients around the constituent particles that build up and dissipate on timescales of milliseconds, and experiments show that particle interactions can be modulated on timescales of 50 ms or less. This light-driven control is straightforward to implement in existing DNA-coated colloidal systems and opens the door to sequential and non-equilibrium assembly schemes.

Materials that exhibit controlled responses to external cues are needed for a wide variety of applications, ranging from biomedical devices to physical sensing.[1,2] In materials made from colloidal particles, light is a useful stimulus, because the particles can interact strongly with optical fields[3,4], and optical illumination can be controlled rapidly and precisely.

Another useful stimulus for colloidal materials is temperature. Temperature-responsive colloidal materials can be made by grafting DNA strands to colloidal particles. Particles grafted with complementary strands interact through a thermally-reversible DNA-mediated attraction.[5–14] As a result, it is possible to design and experimentally realize complex phase transitions for colloidal materials, including transitions between different crystal structures,[15,16] gelation of two-component colloidal mixtures,[17] crystallization upon heating,[18] solid-fluid-solid-fluid transitions,[19] and crystallization over wide temperature ranges.[20] Many of these schemes rely on thermal equilibration.

Here we describe a way to couple light to local heating of DNA-grafted colloids, and thereby to combine the speed and precision of light as a stimulus with the versatility of DNA-mediated interactions. The goal is to modulate the DNA-mediated colloidal interactions on very short timescales (milliseconds or smaller). Such short timescales could enable materials to be assembled by a wide variety of non-equilibrium methods that have been proposed in recent theoretical and computational studies[21–27]. These methods require modulating the interactions on timescales smaller than the characteristic diffusion time of the particles. However, it is not possible to achieve such timescales by directly heating suspensions of DNA-grafted colloids. Relying on bulk heating also limits the breadth of applications, because it does not allow independent control of interactions between different types of particles in the same suspension.

Coupling light to heat has previously been explored in metallic nanoparticles, which have surface plasmon resonances that can be excited optically.[28–31] However, these methods are limited since they require nanoparticles whose sizes, shapes, and compositions are precisely tuned. Also, although these methods can melt DNA bonds near the surface of the particles,[32–37] there are trade-offs between the reversibility of the melting and its speed and yield. An alternative approach to modulating DNA-mediated colloidal interactions is photochemical methods relying on azobenzene modifications,[38,39] but these methods require chemically modifying the DNA.

We introduce a broadly applicable approach to using light to reversibly and independently control interactions between differ-

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† Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 00.0000/00000000.
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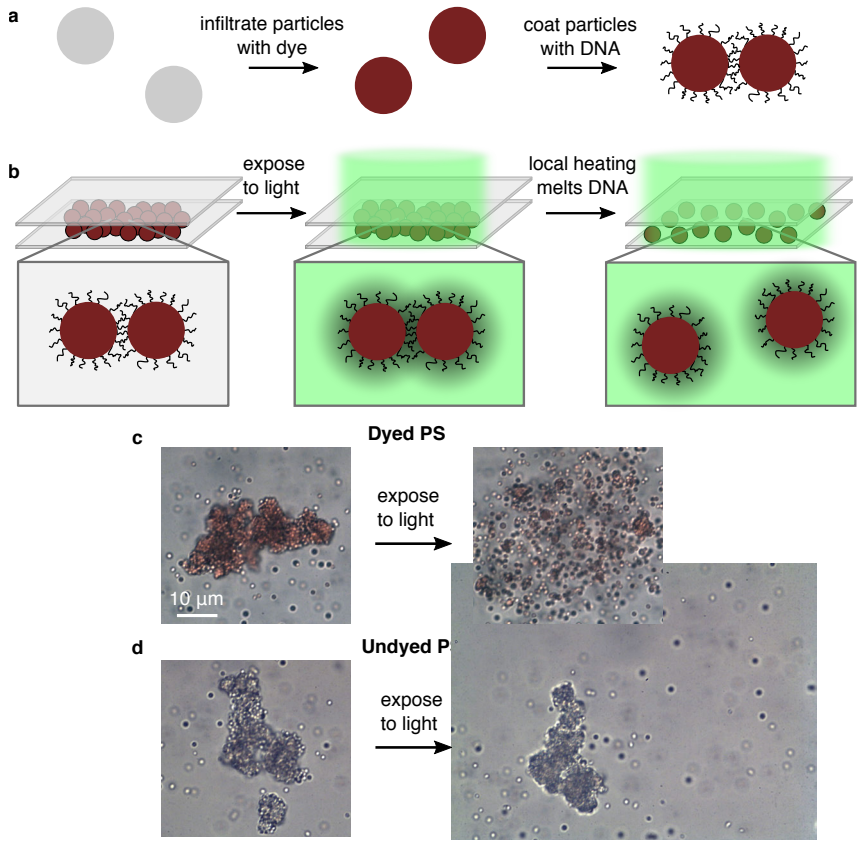

Fig. 1 Overview of light-driven modulation. a) We begin with undyed 1 μm polystyrene particles (shown schematically in gray), which we infiltrate with non-fluorescent dye (here shown as red). b) When coated with complementary strands of single-stranded DNA (ssDNA), the particles aggregate at temperatures below their melting temperature. When exposed to light (here shown as green) the particles heat up, as illustrated by the dark gray corona around the particles, and the aggregates fall apart. c, d) Optical micrographs of dyed and undyed particles coated in identical sequences of DNA, held 1 °C below their melting temperatures, and exposed to green light. The undyed particles remain aggregated while the dyed particles melt. The area of illumination in (c) and (d) is 100 × 100 μm.

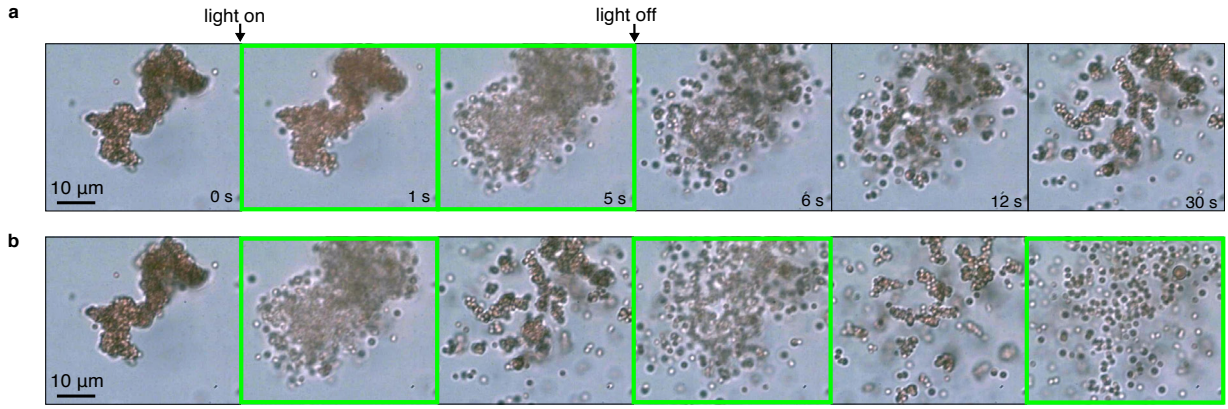

Fig. 2 Optical micrographs of light-driven melting. When a stable aggregate (leftmost micrograph) is exposed to light (denoted by a green frame) the aggregate melts. When the light is turned off, the aggregate re-forms. a) This light-induced aggregate melting is shown in the second and third micrograph as a function of the time that the cluster has been exposed to green light. When the light is subsequently turned off, the particles reaggregate, as seen in the last three micrographs. b) This melting-reaggregation process can be repeated many times.

ent particle species on millisecond timescales. To demonstrate this control, we infiltrate 1 μm polystyrene particles with non-fluorescent dyes by swelling the particles with a dye solution while functionalizing them with ssDNA (Figure 1a). The dyes absorb certain wavelengths of light and convert that energy to heat, resulting in a rapid, local change in temperature and, consequently, interaction strength (Figure 1b). Our method is straightforward to implement, requires no additional chemical modification to the DNA, and should be applicable to any size of particle that can be infiltrated with sufficient quantities of dye. The method used to dye and functionalize the particles has previously been shown to work in other types of polymeric particles,[40] so the applications are not limited to polystyrene colloids. We directly observe and quantify the behavior of our system, providing evidence for the reversibility of the process and the high rates at which the interactions can be modulated.

We first demonstrate that light can melt aggregates of dye-infiltrated, DNA-grafted particles. We allow ssDNA-functionalized particles to aggregate at a temperature below the melting transition. The particles are dyed with Oil Red O dye (Sigma-Aldrich), which has an absorption peak at 520 nm. When we illuminate the particles with a wide-field beam at 560 nm, which is close to the absorption peak (see Figure 5), the aggregates melt (Figure 1c). Aggregates of undyed particles grafted with identical ssDNA do not melt under the same illumination (Figure 1d). Aggregates of dyed particles illuminated with a wavelength (648 nm) far removed from the absorption peak also do not melt. Finally, aggregates outside of the area of illumination do not melt. We can therefore conclude that the melting is caused by absorption of light by the dye.

The response of the system to light is fast. As shown in Figure 2a, aggregates begin to melt within the first second of illumination and then spread outward by approximately 5 μm over the next 5 s. The 5-μm displacement is consistent with the expected mean-squared displacement for non-interacting particles,[41] which we calculate to be 4.8 μm over 5 s. When we turn the light off after 5 s, the particles immediately start to bind to one another, and within 25 s they re-form large aggregates. We estimate that the time to form aggregates of this size for a diffusion-limited process is approximately 21 s (see Section S6), in good agreement with the measurements. Thus, the effect of the light is to modulate the short-ranged interparticle attractions.

To demonstrate reversibility, we hold a sample of particles dyed with Oil Red O dye at 45 °C, which we term the "background" temperature of the water and which is 3 °C below the particle melting temperature T_m. We then cycle the illumination multiple times (Figure 2b). The aggregates melt each time the light is on and re-form when the light is off. The reversibility requires an oxygen scavenging system: we add glucose oxidase and catalase to the sample. Without the scavenging system, reversible aggregation and melting is limited to a few cycles. The irreversibility in the absence of an oxygen scavenger likely occurs because free oxygen radicals that damage the DNA are generated when the dye is excited.[42] With the oxygen scavenging system, we find that we can modulate the system for at least 1 h, and possibly much longer.

Having shown that light-driven melting is caused by the dye and is both rapid and reversible, we examine two hypotheses for its origin: either the light triggers a thermally reversible photochemical change in the DNA, or the light is converted to heat, which modulates the interactions between particles. To determine which effect occurs, we examine the melting of aggregates of different sizes. We find that the larger the aggregate, the lower the background temperature from which light-induced melting occurs (Figure 3), under constant illumination conditions. We are not aware of any photochemical process that would account for such a relationship. However, as described below, our observations *are* consistent with the hypothesis that the light heats the dyed particles, leading to melting of the DNA bonds bridging the particles together.

If the heating hypothesis is correct, the effect should depend on four factors: the rate of heat dissipation into the medium, the illumination time, the illumination intensity, and the absorption of the light by the dye. We model the effects of these factors by solving the time-dependent thermal diffusion equation for a sphere of radius a exposed to light in an infinite medium of wa-

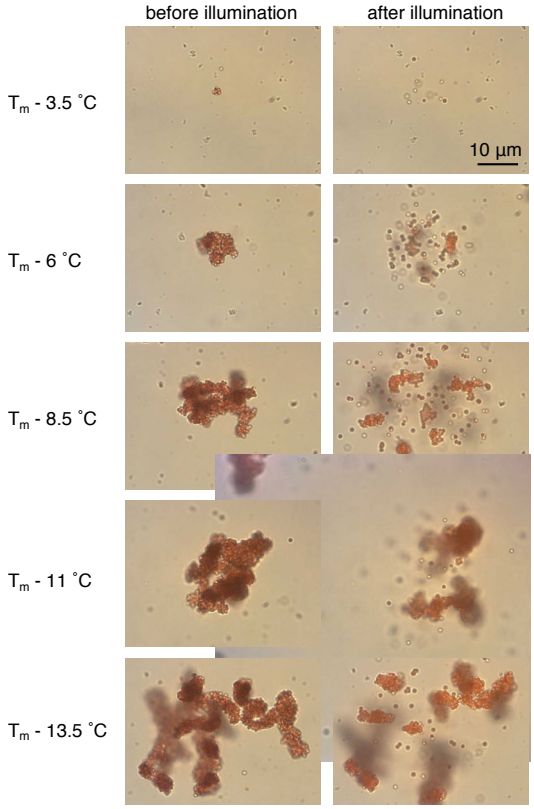

Fig. 3 Optical micrographs showing melting of clusters of different sizes under illumination. For each temperature, we show the smallest cluster that begins to melt within the first minute of illumination. Larger clusters melt entirely, while smaller clusters remain stably aggregated.

ter. The sphere can represent either a single dyed particle or an aggregate of particles, which we approximate as a single sphere of larger radius. We solve the following set of equations[43] for the change in temperature of the sphere (T_s) and water (T_w) from the background temperature:

$$\begin{aligned} \frac{1}{k_s}\frac{\partial T_s}{\partial t} &= \frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial T_s}{\partial r}\right)+\frac{A}{K_s} \quad \text{for } 0 \le r \le a \\ \frac{1}{k_w}\frac{\partial T_w}{\partial t} &= \frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial T_w}{\partial r}\right) \quad \text{for } r > a, \end{aligned} \tag{1}$$

where A is the (constant) rate of heat produced by the sphere per unit volume per unit time, k is the thermal conductivity, K is the thermal diffusivity, t is the time since the start of illumination, and the subscripts s and w refer to the sphere and to the water. The boundary conditions are

$$\begin{aligned} T_s = T_w = 0 \quad & \text{at } t = 0 \\ T_s = T_w \quad & \text{at } r = a \\ K_s\frac{\partial T_s}{\partial r} = K_w\frac{\partial T_w}{\partial r} \quad & \text{at } r = a. \end{aligned} \tag{2}$$

T_s must remain finite as $r \to 0$, and T_w must remain finite as $r \to \infty$.

We analytically solve Equation (1) subject to the boundary conditions to obtain both the steady-state and time-dependent temperature profiles. At steady state, the temperature falls off quadratically with distance from the particle center within the particle, and as $1/r$ outside the particle (Figure S3). From the time-dependent solution, we find that the relaxation time of the temperature gradient is only 5 ms (Section S5). Because the timescale for the temperature gradient to develop is smaller than the timescale for particles to diffuse a distance equal to their diameter (approximately 1 s), we can view heating and diffusion as separate, sequential processes. Hence the calculations explain why the melting and re-aggregation processes are diffusion-limited.

The model also explains the observation that, at constant illumination conditions, larger aggregates melt at lower background temperatures. For a single particle, the temperature gradient outside the particle decays by a fraction of a degree Centigrade over a distance comparable to the ssDNA length (Figure S3). Because the interaction strength is a steep function of temperature, as shown by the theoretical singlet fraction in Figure S1, even this small change in temperature can cause a small aggregate to melt, if it is close to the melting temperature. However, for a 10-μm spherical aggregate of particles, the temperature can increase by nearly 11 °C at the center and 6 °C near the edge. Such an aggregate can melt even when the solution temperature is many degrees below the melting temperature. Interestingly, while the model predicts that it takes longer for these 10 μm clusters to reach steady state, it also shows that the surface temperature reaches the melting temperature of the DNA three orders of magnitude more quickly than for a solitary 1 μm particle (Section S5).

Finally, the model predicts that heating should be rapid—on the order of a few milliseconds, as discussed above. To test this prediction, we use optical tweezers to construct particle dimers composed of 2-μm particles infiltrated with Oil Blue N dye (Sigma-Aldrich) and expose them to pulses of 560 nm light with a controlled duration. We track the positions of the particles for the next 1 s to see whether the dimer separates. We repeat this experiment many times and for pulses of different durations. We then use a Bayesian statistical model to infer the probability of the dimer breaking apart, $\hat{P}_b$, during or after the pulse as a function of the pulse duration (see Section S7). As shown in Figure 4, the duration at which $\hat{P}_b$ is significantly higher than the baseline provides an estimate of the timescale over which the interaction changes. We find that the timescale is between 20 and 50 ms, comparable to the calculated timescale for the temperature gradient to develop. This timescale is three to four orders of magnitude smaller than that required to change the interaction potential by directly heating the sample.

Having shown that light causes rapid and reversible changes in interaction potential between DNA-grafted particles, we now show that it can be used to address different species of particles (Figure 5). We infiltrate two batches of particles with different dyes: Oil Red O, which absorbs in the blue, and Oil Blue N, which absorbs in the red (see absorption spectra in Figure 5). We coat these particles, as well as undyed particles, with identical ssDNA. We bring a sample of each species to 1 °C below the melting temperature and expose each to 485-nm and 648-nm light. The undyed particles remain aggregated under exposure to both

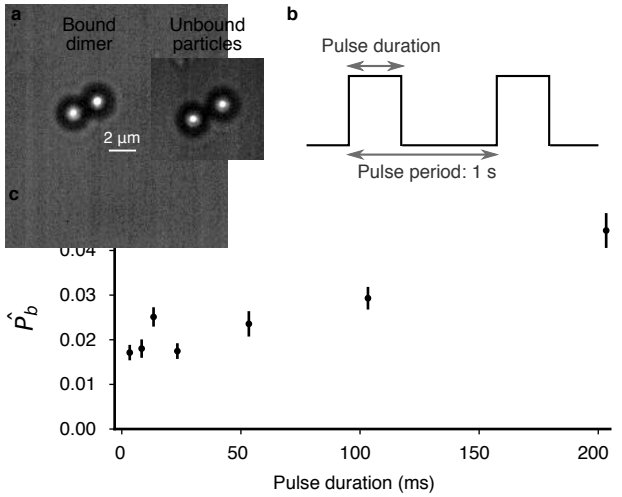

Fig. 4 Results of experiments on melting dimers under pulsed illumination. a) Optical micrograph of a particle dimer and a pair of unbound particles. We use a cutoff distance of 2.21 μm to determine when two particles are no longer bound to one another. b) Schematic of light intensity as a function of time for the experiment. c) Mean probability that a dimer separates within 1 s of the beginning of a light pulse, as a function of the duration of the pulse. Error bars correspond to a 1-σ credible interval, as described in Section S7. See Figure S5 for results at different cutoff distances.

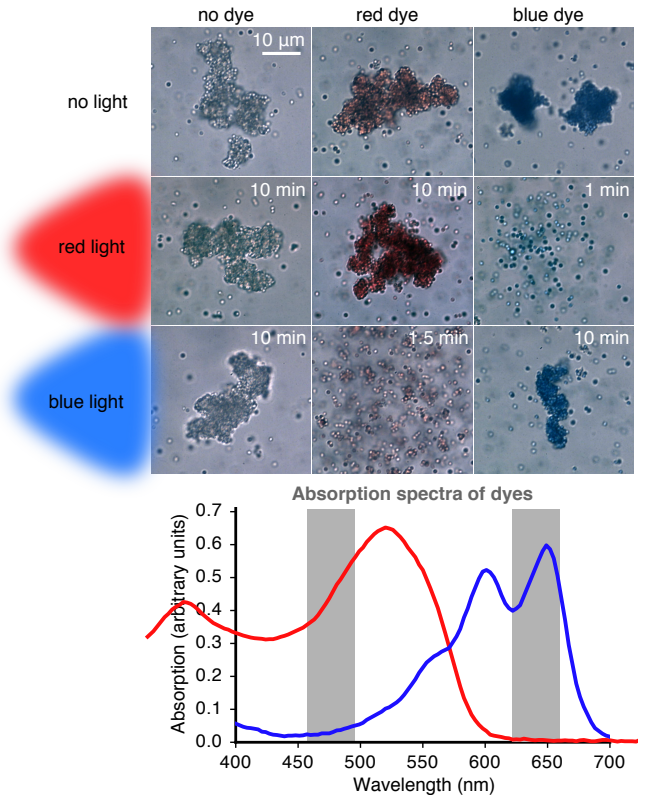

Fig. 5 Optical micrographs of aggregates of undyed, red, and blue particles each coated in the same sequence of DNA and held 1 °C below their melting temperature. The response of these aggregates to exposure of different wavelengths of light is shown (the amount of time that they were exposed is noted in the top right corner of each micrograph). The absorption spectra of the dyes are shown below with the regions of illumination shaded in gray.

wavelengths of light. The Oil Red O-dyed particles remain aggregated under exposure to 648-nm light, where the dye does not absorb, and melt under exposure to 485-nm light, where the dye absorbs strongly. Conversely, the Oil Blue N-dyed particles remain aggregated under exposure to 485-nm light, and melt under exposure to 648-nm light. Hence, light-driven heating can be used to address interactions between different species of particles with independent triggers.

In conclusion, we have demonstrated a simple method to rapidly modulate and address interactions between colloidal particles. Compared to direct heating, our method decreases the timescale for changing the temperature, and therefore the interparticle interaction strength, by three to four orders of magnitude. In addition, our method provides a way to independently change the interactions between multiple species in the same solution, which is not possible with direct heating. The method is simple to implement: it requires only adding dyes to the particles and an oxygen scavenging system to the solution. No chemical modification of the DNA is necessary.

This new method could be used in concert with self-assembly to make materials with tunable responses to external stimuli, a longstanding goal in soft matter.[44,45] For example, it can enable sequential self-assembly schemes, since the interactions between different species can be modified independently. Furthermore, it can be used to explore non-equilibrium self-assembly, because the interparticle interactions can be modulated on timescales shorter than the characteristic diffusion time. It might also be used to controllably trigger release of DNA into solution upon exposure to light.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

We thank Colm Kelleher, Agnese Curatolo, and Michael Brenner for helpful discussion. The work was funded by the National Science Foundation through grant no. DMR-1435964, by the Harvard MRSEC through grant no. DMR-1420570, and by the Army Research Office through the MURI program under award no. W911NF-13-1-0383.

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