Electrostatically tuned DNA adsorption on like-charged colloids and resultant colloidal clustering

Lu Zhang and Yingxi Zhu*
Department of Chemical and Biomolecular Engineering
University of Notre Dame, Notre Dame, Indiana 46556 USA

Supplementary Document (SD)

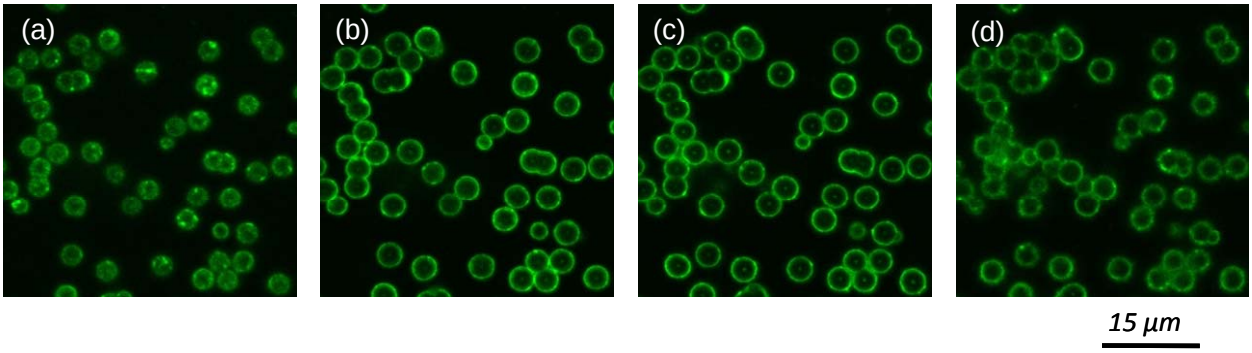
SD Results and Discussion

Estimation of the interaction between DNA and silica particle. We consider that the total interaction, W_{total} between a bare silica particle and a DNA macromolecule mainly come from the contribution of van der Waals (vdW) attraction (W_{vdw}), electrostatic repulsion (W_{EDL}) and hydrophobic attraction (W_H), $W_{total} = W_{VDW} + W_{EDL} + W_H$. According to the DLVO theory, $W_{VDW} = -\frac{A}{6D}\frac{R_1 R_2}{R_1 + R_2}$, where A is the Hamaker constant and is estimated to be 3.48×10^{-21} J, D is the interparticle separation, R_1 is the radius of the silica particle (~1.5 μm) and the R_2 is the radius of the DNA coil (~1 μm), and $W_{EDL} = \left(\frac{128\pi kT\rho_\infty \gamma^2}{\kappa^2}\frac{R_1 R_2}{R_1 + R_2}\right)e^{-\kappa D}$, where κ is the reciprocal of the screening length, $\gamma = \tanh\left(\frac{ze\psi_0}{4kT}\right) \approx \tanh\left[\psi_0(mV)/103\right] \approx -0.503$ where the surface potential, ψ_o is measured ~-57 mV in deionized water. The range and magnitude of hydrophobic attraction remain largely debated over the past decades, we thus tentatively consider the hydrophobic attraction scaling in an exponential decay as $W_H \approx -\frac{84R_1R_2}{R_1 + R_2}e^{-D/D_0} kJ\cdot mol^{-1}$ (Israelachivili et al., Nature, 1982), where D_o ~1 nm, and R_1 and R_2 are ~1.5 μm and ~1 μm for silica particle and DNA, respectively, thus the hydrophobic interaction is estimated as $W_H \approx -8.37\times10^{-17}e^{-D} J$. Therefore, the total interfacial energy is given by $W_{total} = W_{VDW} + W_{EDL} + W_H \approx -3.48\times10^{-19}/D + 1.51\times10^{-17}e^{-D/100} - 8.37\times10^{-17}e^{-D}$, for the silica particles suspended in deionzied water of $1/\kappa$~ 100 nm. Thus, the total interparticle interaction can be attractive (W_{total} <0) at D < 1.743 nm. However, it remains difficult to accurately calculate the DNA-particle interaction as well as the interaction of DNA-adsorbed silica particles due to due to the complexity of the long debated hydrophobic attraction and the effect of DNA adsorption on modifying the colloidal surface charge.

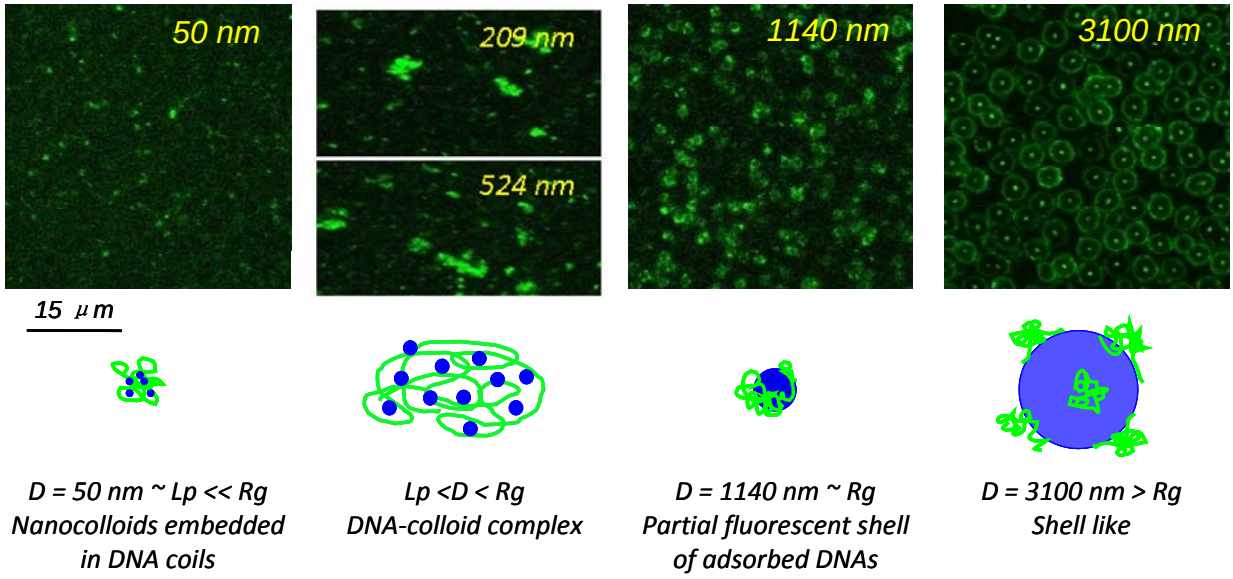
Discussion of the preferable formation of doublet and triplet clusters in DNA-colloidal aqueous suspensions. To further elucidate the formation of colloidal clusters containing 2-3 particles, we have tentatively sought the possible answer based on the diffusion controlled collision of DNA adsorbed colloidal particles in suspensions to form stable colloidal clusters in specific sizes. Briefly, we assume that only N_1 singlets exist in the suspension of constant volume (V), giving the number density of n_1=N_1/V at the initial state, and the collision frequency, Z_{11} (unit: the number of collision between two singlets per unit time) of colloidal

singlets is given by $Z_{11} = \sqrt{2} \cdot \pi \cdot n_1 \cdot d_{11}^{\ 2} \cdot \bar{u}_1$, where d_{11} is the center-to-center distance between the two singlets upon collision, and $\bar{u}_1$ is the mean travelling speed of the colloidal singlet. Thus, the number of doublets formed per unit time, N_2 can be considered as $N_2 = f_{11} \cdot Z_{11} \cdot N_1 / 2 = f_{11} \cdot \pi \cdot n_1 \cdot d_{11}^{\ 2} \cdot \bar{u}_1 \cdot N_1 / \sqrt{2}$, where the unitless f_{11} (≤ 1) represents the probability of two singlets to form a stable doublet after collision and can be affected by the strength of DNA bridging across particles. For the formation of colloidal triplets, we consider two pathways to form a triplet by the collision of either three individual singlets or one singlet with a doublet; thus the number of triplets formed per unit time, N_3 is given by $N_3 = f_{111} \cdot Z_{111} \cdot N_1^{'} / 3 + f_{12} \cdot Z_{12} \cdot N_1^{'}$, where f_{111} represents the probability of three collided singlets to form a triplet, Z_{111} is the collision frequency of three individual singlets and can be considered nearly zero in our work due to the very dilute particle concentration in the suspension, $N_1^{'} (= N_1 - 2N_2)$ is the number of remaining singlets in the suspension, f_{12} represents the probability of one singlet and one doublet to form a triplet after collision and Z_{12} is the collision frequency of a singlet with a doublet and can be estimated as $Z_{12} = \sqrt{2} \cdot \pi \cdot n_2 \cdot d_{12}^{\ 2} \cdot \bar{u}_1$ in a similar way as the estimation of Z_{11}. Therefore, we can obtain $N_3 = f_{12} \cdot Z_{12} \cdot N_1^{'} = \sqrt{2} \cdot f_{12} \cdot \pi \cdot n_2 \cdot d_{12}^{\ 2} \cdot \bar{u}_1 \cdot N_1^{'}$. Similarly, we can also calculate the number of clusters (N>3) formed per unit time per unit volume in the suspension. Apparently, the number of colloidal clusters decreases considerably when the clusters become larger by containing more particles in a cluster. With the difficulty in obtaining the probability, f_{11} and f_{12}, here we just tentatively compare the number ratio of the remaining doublets, $N_2^{'}$ to the triplets, N_3 in the suspension $N_2^{'} / N_3 = (N_2 - N_3) / N_3 \sim f_{11} N_1^{\ 2} d_{11}^{\ 2} / 2 f_{12} (N_1 - 2N_2) N_2 d_{12}^2 - 1$. If we assume that there is 100 colloidal singlets (N_1 = 100) in the suspension of constant DNA and salt concentration at the initial state and according to the volume fraction of the doublets and triplets is experimentally measured as ~30-40% and ~9-19%, respectively, the number of the doublets N_2 is experimentally analyzed ~ 18-26 (N_2' is ~15-20 and $N_2 = N_2' + N_3$=(15~20) +(3~6)=18~26) and thus $N_1^{'}$ for the remaining singlets is ~48-64. Considering the geometry of doublet and triplets, we estimate d_{11} is ~ 3 μm and d_{12} is ~ 2.6-4.5 μm for colloidal particle of ~3 μm in diameter. If we assume $f_{11} \approx f_{12}$, we can thus obtain $N_2^{'} / N_3$ in the range of 1.86 to 2.10. We also roughly estimate that $N_2^{'} / N_4$ could be greater than 10, and thus the volume fraction for the cluster of N≥4 is experimentally immeasurable. That is why we mainly observe the stable colloidal cluster containing 2-3 particles, though larger clusters could also exist in the suspension. It should be cautiously noted that the ratio f_{11} / f_{12} could be greater than 1, as one could consider a lower probability of DNA bridging with doublets that have fewer available hydrophobic patches than singlets. Thus, we could expect that $f_{11} > f_{12} > f_{22}, f_{13}$ and so on, also leading to the less probability of larger colloidal clusters, i.e. N≥4. It should be noted that the above rough estimation is based on the simplest diffusion controlled process for particle collision among singlets and doublets to form doublet and triplet clusters, yet a rigorous theoretical and/or simulation prediction would be highly desired to further provide the insight into the mechanism for the formation of stable colloidal clusters with certain selected particle numbers.

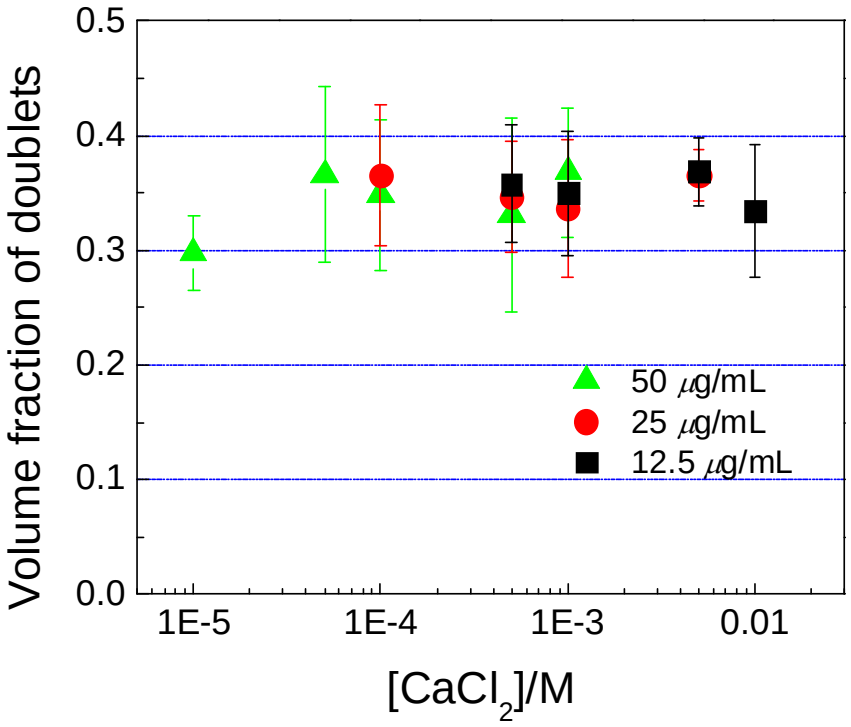
Supplementary Figure 1. (a-d) Representative fluorescent micrographs taken from a Z-stack profile indicate that DNAs are not necessarily centered in the COOH-silica particles but rather randomly located on the particle surfaces. The spacing separation between each two micrographs (panel a-d) is 0.9 μm, while the entire Z-stack profile was acquired by confocal laser scanning microscopy at a 0.3 μm increment along Z across the suspension from the coverslip surface.



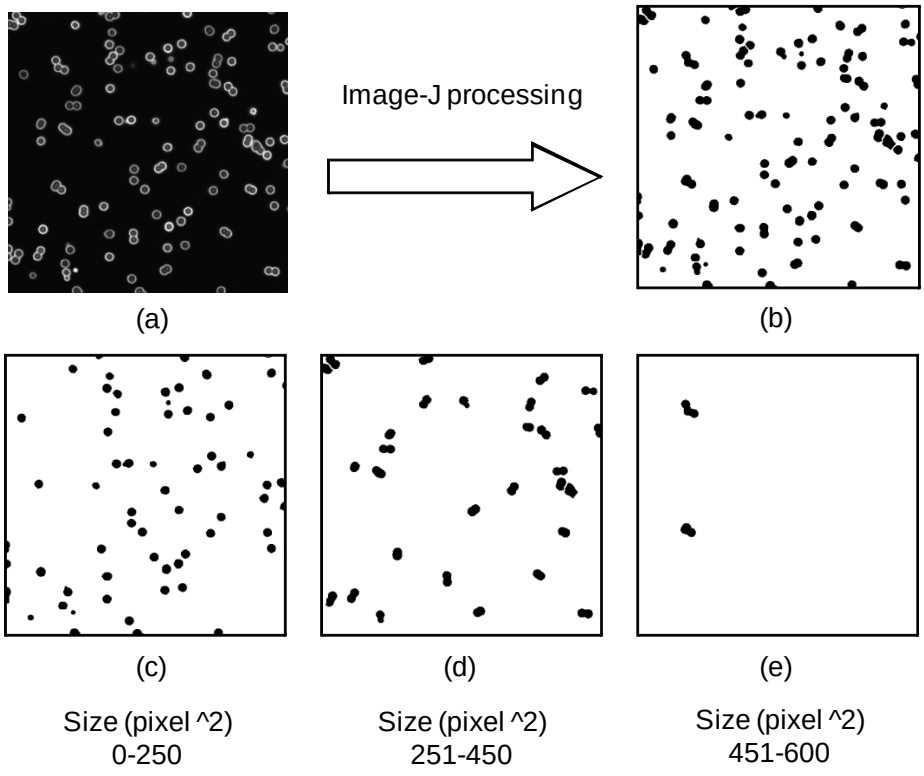
Supplementary Figure 2. Varied DNA-colloidal complex structures formed from the suspensions of mixed DNA and COOH-silica particles of varied particle diameter ranging from 50 nm to 3100 nm.



Supplementary Figure 3. Measured volume fractions of doublet colloid clusters that are induced by adsorbed DNAs on COOH-silica particles at varied DNA concentrations and salt concentrations.



Supplementary Figure 4. (a) The exported raw data (TIF image) obtained by confocal microscopy; (b) the *Image-J* image analysis software is used to process the image shown in panel (a), where all objects in the images are in solid black and are ready for particle analysis; (c-e) the colloidal clusters distinguished based on size, where (c) represents singlets and the size ranges from 0-250 pixel^2, (d) represents doublets and the size ranges from 251-450 pixel^2, (e) represents triplets and the size ranges from 451-600 pixel^2. For all the clusters containing N>3 colloidal particles, the size is measured in the range of 600–∞ pixel^2 and the number of clusters (N>3) = 0 for this specific image.



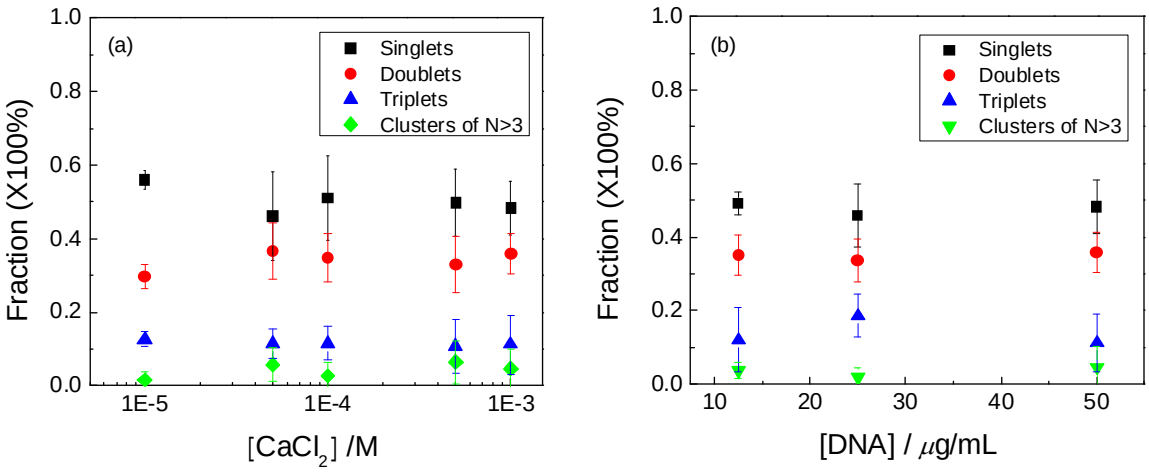
The number of singlets: $N_1 = 64$
The number of doublets: $N_2 = 29$
The number of triplets: $N_3 = 2$
The number of clusters of N > 3: $N_{N>3} = 0$

$N_{total} = N_1 + 2 \times N_2 + 3 \times N_3 + \ldots = 128$

⇨

The fraction of singlets: $N_1 / N_{total} = 0.5$
The fraction of doublets: $2 \times N_2 / N_{total} = 0.453$
The fraction of triplets: $3 \times N_3 / N_{total} = 0.047$
… …

Supplementary Figure 5. (a) The volume fraction of singlets, doublets, triplets and clusters of N>3 as a functional of $CaCl_2$ concentration, [$CaCl_2$]. All the data points represent the average of 5 separate experiments and image analysis at the constant DNA concentration, [DNA]=50 μg/ml and COOH-particle concentration, [COOH-particle]=1.25 mg/ml; (b) The volume fractions of singlets, doublets, triplets and clusters of N>3 as a functional of [DNA]. All the data points represent the average of 5 separate experiments and image analysis at the constant salt concentration, [$CaCl_2$] = 1 mM and COOH-particle concentration, [COOH-particle]=1.25 mg/ml.



Supplementary Figure 6. (a) The confocal image of a two-week old DNA-colloidal suspension after sonication: small colloidal clusters, such as doublets and triplets, remain in the suspension; (b) the confocal image of a diluted DNA-colloidal suspension: the [DNA] = 50 μg/ml and [COOH-particle] = 1.25 mg/ml in the original suspension, and the [DNA] = 0.8 μg/ml after the suspension is diluted in deionized water, where similar colloidal clusters, such as doublets and triplets, are observed.