Supplementary Information for:

Building Reversible Nano-raspberries

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Materials and Methods

Synthesis of silica nanoparticles

100 mg L-lysine (Fluka) was dissolved in 100 ml pure water in a 250 ml three-neck flask by magnetically stirring (270 rpm) at 60 °C. Thereafter, the formation of the SiO₂ NPs was initiated by adding 6 ml tetraethyl orthosilicate (TEOS) to the reaction solution and the reaction vessel was closed off by a rubber septum with a small needle inserted as a vent. The reaction was left meanwhile stirring for 1 day.

Surface modification of silica nanoparticles

Silica nanoparticles need to be surface modified to provide them with the proper charge density and as a result, having a controllable interaction for building block assembly for the following step. To modify the surface of silica nanoparticles, 1 wt% (3-Aminopropyl) triethoxysilane (APTES) (Sigma-Aldrich) solution in water (pH ∼11) was slowly added to the as-prepared silica suspension while stirring vigorously (~700 rpm). The initial amount of APTES and colloidal silica used had a silane:silica weight ratio of 1:50, above which the particles rapidly coagulated. The silane-silica mixture was then washed by repeated centrifugation and replacement of the supernatant for at least five times.

Size measurements of silica and polystyrene latex nanoparticles

Size distributions were determined by manually measuring the short and long axes of individual silica nanoparticles (SiO₂ NPs) in cryoTEM images using an in-house made MATLAB script. The average radius of a SiO₂ NP was taken to be a quarter of the sum of the long and short axes of the SiO₂ NP and the size is reported as: mean ± standard deviation of the mean (262 SiO₂ NPs were used to calculate the size distribution and the size was found to be 28.8 ± 0.4 nm). The results can be seen in Figure SI1.
Figure SI1. The size distribution of the SiO$_2$ NPs determined from a-b) cryoTEM images using an in-house made MATLAB script, c) Histogram showing the size distribution of silica nanoparticles obtained from image b, and d) The number distribution of the size of the silica nanoparticles before and after surface modification determined by DLS.

Figure SI2. The size distribution of the PSL NPs determined from DLS.
**Supplementary Results**

**DLS measurements of silica, polystyrene latex, and mixtures at different pH values**

Dynamic light scattering (DLS) is a technique that depends on the interaction of the light with the nanoparticles of interest in a given solution. It measures the diameter of the particles $D$ under Brownian motion by calculating the time-dependent fluctuations of the intensity of the scattered light. The output of DLS is the intensity weighted distribution, which is proportional to $D^6$, while imaging results in the number distribution proportional to $D^9$. Considering the fact that in our system, there is approximately a 3.5 fold difference for the diameter of the SiO$_2$ and PSL NPs, a factor 3.5$^6$ difference in scattering power in the Rayleigh region results. Therefore, the signal coming from 100 nm PSL NPs overshadows the signal which is coming from 30 nm SiO$_2$ NPs in the intensity weighted distribution.

![Figure SI3](image)

**Figure SI3.** Results obtained from dynamic light scattering analysis by using individual polystyrene latex, silica nanoparticles and mixture at pH 2. a) The autocorrelation function $g$ of individual nanoparticles and the mixture of polystyrene latex and silica nanoparticles mixed after 2 minutes at pH 2, b) The autocorrelation function $g$ of the mixture at pH 2 over time, c) Intensity weighted, and d) Number weighted dynamic light scattering results of the mixture at pH 2 showing the size distribution of mixture depending on the time after which reaction is initiated.
Figure SI4. The autocorrelation function $g$ of mixtures of polystyrene latex and silica nanoparticles as a function of time. Dynamic light scattering measurements obtained mixing after; a) 2 minutes, b) 30 minutes, c) 1 hour, d) 1.5 hours, e) 6 hours, and f) 1 month.

Figure SI5. a) Zeta potential and b) electrophoretic mobility for PSL NPs and SiO$_2$ NPs mixtures as a function of pH.
Pseudo-reversibility of nano-raspberries

The pseudo-reversibility of nano-raspberry assembly and disassembly was evaluated by changing the pH of the solution repeatedly. Figure SI6 shows the cryoTEM and DLS results of the mixture after the 5th time of pH change and the results indicate that after a critical point, SiO2 NPs and PSL NPs cannot form well-defined nano-raspberries anymore due to the increased salt concentration.

Figure SI6. CryoTEM image corresponds to the point marked with the yellow arrow which is cycle #5.

Theoretical Considerations

Derjaguin-Landau-Verwey-Overbeek (DLVO) theory was employed to investigate the colloidal stability of the individual silica and polystyrene latex nanoparticles, and the nano-raspberries as DLVO theory provides a quantitative theoretical understanding of the interaction potential between two charged particles interacting in a liquid medium. According to DLVO theory, the net interaction between two nanoparticles ($V_{DLVO}$) is the sum of the repulsive electrostatic double-layer or Coulomb interactions ($V_{Coul}$) and the attractive van der Waals ($V_{vdW}$) interaction potential, so that

$$V_{DLVO} = V_{vdW} + V_{Coul}$$

The electrostatic interactions between two spherical objects of equal surface potential and equal size is calculated using Poisson-Boltzmann formulation. The classical DLVO theory is based on the linearized Poisson-Boltzmann equation for which an analytical solution exists, but various approximate expressions have been proposed. Here we used the expression as given by Sader et al. in order to calculate the electrostatic interaction potential between two spherical objects at the constant surface potential for any distance regardless of the particle size:
\[ V_{\text{Coul}} = 64\pi \left( \frac{R^2}{2R + h} \right) \varepsilon \varepsilon_0 \left( \frac{k_B T}{ze} \right)^2 Y^2 \ln \left( 1 + \exp(-\kappa h) \right) \]

where \( Y = \exp(\kappa h/2) \tan^{-1} h \left( \exp(-\kappa h/2) \tan(h \psi_0/4) \right) \)

and where \( \varepsilon \) is the relative dielectric constant of the solvent, \( h \) is the closest separation between the nanoparticles’ surfaces, \( \psi \) is the surface potential of the particle of interest (which can be an individual nanoparticle system or nano-raspberries), and \( \kappa \) is the Debye length, which is described in the main text. Above mentioned equations are good approximations for the numerical calculations of the full Poisson-Boltzmann equation at constant surface potential\(^6\).

The van der Waals attraction between two particles of equal size is calculated according to the Hamaker formulation of intermolecular forces assuming pairwise additivity\(^2\). Although this still is an approximation, it nevertheless describes the physical origin of the interaction\(^1\). The expression for the van der Waals interaction potential is given by:

\[ V_{\text{vdW}} = -\frac{A_H}{6} \left[ \frac{2R^2}{h^2 + 4Rh} + \frac{2R^2}{h^2 + 4Rh + R^2} + \ln \left( \frac{h^2 + 4Rh + 4R^2}{h^2 + 4Rh} \right) \right] \]

where \( R \) is the radius of the particle, \( h \) is the closest separation between the nanoparticles’ surfaces, and \( A_H \) is the Hamaker constant, which quantifies the properties of the material\(^7\). For the calculation we consider one single nano-raspberry as a particle composed of a spherical polystyrene latex core and silica nanoparticles attached to the curved surface. The radius of silica nanoparticles used was \( R_{\text{SiO}_2} \approx 15 \) nm while polystyrene latex core radius was \( R_{\text{PS}} \approx 50 \) nm which totals to a nano-raspberry nanoparticle diameter of \( D = 160 \) nm. For silica and polystyrene \( A_H \) values as given by Bergström\(^8\), \( A_H = 4.6 \times 10^{-21} \) J, and by Tsaur\(^9\) and Fowkes\(^10\), \( A_H = 5.0 \times 10^{-21} \) J, were used. For nano-raspberries covered with SiO\(_2\) nanoparticles, the value of for silica, \( A_H = 4.6 \times 10^{-21} \) J, was used\(^8\).

The stability of individual PSL NPs, SiO\(_2\) NPs, and nano-raspberries as calculated is shown in Figure SI7. The results indicate that the Si NPs have an energy barrier of about \( 3.3 kT \) as compared to the PSL NPs with about \( 50 kT \). The calculations for the DLVO potential energy diagrams in Figure SI7b were made by considering the fact that PSL NPs and SiO\(_2\) NPs formed nano-raspberries in the medium at certain pH values. For example, at pH 2, we consider the supraparticle for the DLVO calculations to be a single particle with a radius of 80 nm. As can be seen from the results, at pH 2 supraparticles have an energy barrier of about \( 1.5 kT \), indicating that nano-raspberries cannot stay separated from each other for a longer period of time, as also shown via cryoTEM in the manuscript (Figure 2n–2p). Moreover, the DLVO potential curves
calculated for the nano-raspberries and individual nanoparticle systems show numerical values in good agreement with calculations made on similar systems\textsuperscript{11}, strongly indicating the applicability of our system to different sizes of nanoparticle mixtures.

Figure SI7. The total interaction potential of a) two SiO\textsubscript{2} NPs and two PSL NPs as a function of separation distance, and b) nano-raspberries at different pH values.

Obviously, the calculations given above do not describe the formation process of the nano-raspberries. To model that formation process, several aspects should be considered.

- The mixing entropy of the dispersion is changing as the counter-ions are decorating the particles. The effect is expected to be not too large, but a calculation will require the surface density of charged sites on the surface of the particles.

- The assumption of a constant dielectric permittivity as normally used is unlikely to be valid close to the nano-raspberries, which renders the decay not exponential as in the original DLVO theory. Instead, it becomes close to arithmetic, like electrostatics close to a bilayer, as shown, for example, in a Monte Carlo simulation\textsuperscript{12}.

- Various options exist to model the van der Waals contribution\textsuperscript{13}. This refers not only to the expression used for the van der Waals attraction, but also to the assumed structure of the interacting parts involved.

- For really small particles (5-10 nm) the hydration forces are relevant\textsuperscript{14,15}. Even if modeled by an exponential function, this requires information about two more parameters.

- As there are positively and negatively charged particles, there is a coupling between the various equilibria involved\textsuperscript{16} upon mixing the particles, which should be considered.

- Finally, the SiO\textsubscript{2} NPs can be considered as a polyion for which the equilibrium also should be taken into account\textsuperscript{17,18}.

All these aspects will have to be incorporated to realistically model nano-raspberry formation, but this inevitably will result in a complex model.
**Supplementary Tables**

**Table S1.** Composition of pH buffers used in this study

| Target pH | Measured pH | Ingredient A | Concentration of A (M) | Volume of A (ml) | Ingredient B | Concentration of B (M) | Volume of B (ml) | Ionic Strength (mM) |
|-----------|-------------|--------------|------------------------|------------------|--------------|------------------------|------------------|---------------------|
| 2         | 1.6         | KCl          | 0.1                    | 50               | HCl          | 0.1                    | 13               | 79.4                |
| 4         | 3.9         | Acetic acid  | 0.1                    | 164              | CH₃COONa     | 0.1                    | 36               | 72                  |
| 6         | 5.9         | KH₂PO₄       | 0.1                    | 100              | NaOH         | 0.1                    | 11.6             | 89.6                |
| 12        | 12.4        | KCl          | 0.1                    | 50               | NaOH         | 0.1                    | 12               | 80.6                |

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