

Dextran-Based Nanoparticles to Formulate pH-Responsive Pickering Emulsions: A Fully Degradable Vector at a Day Scale

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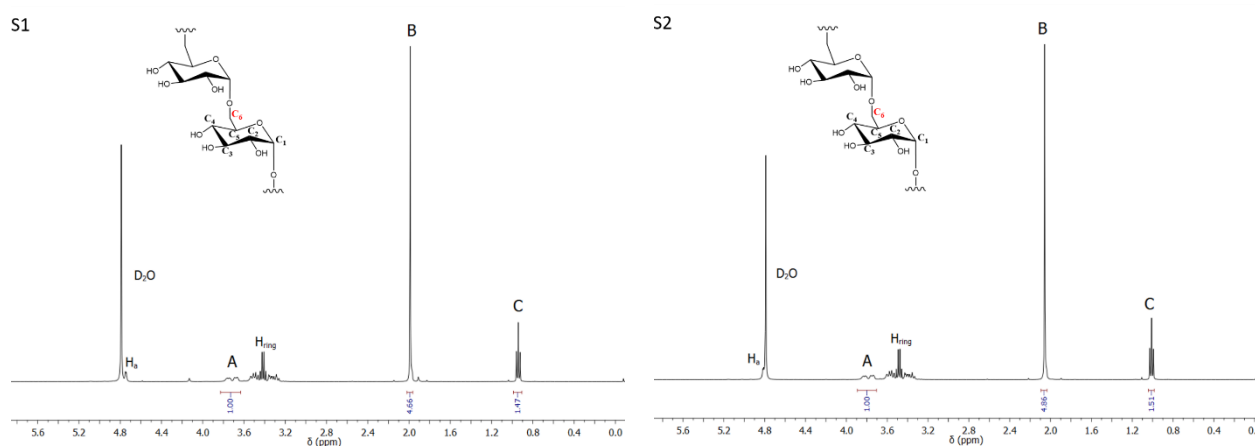


Fig. S1: 400 MHz ¹H NMR spectra of Ace-Dextran from S1 and S2 (left and right respectively) after acidic hydrolysis in D₂SO₄/D₂O. Degradation products are Dextran (A, H_a, H_{ring}), Acetone (B) and Ethanol (C).

Supporting information S2: ¹H NMR analysis to deduce grafting rates

H_a signal corresponds to the anomeric proton bonded to C₁, H_{ring} signals correspond to hydrogens bonded to C₂, C₃, C₄ and C₅ but none of these were used for calculations.

Dextran C₆ hydrogens peaks (A, δ=3.9 ppm, 2H, integration ≡ 1.00); Acetone -CH₃ peaks (B, δ=2.2 ppm, 6H); Ethanol -CH₃ peak (C, δ=1.1 ppm, 3H). Integrations were normalized for each glucosidic unit to calculate modification rates.

Acyclic modification rate was computed as follows:

$$r_{acyclic} = \frac{A_C/3}{A_A/2} \quad (\text{Eq. S1})$$

From these, acyclic modification rate was deduced:

$$r_{cyclic} = \frac{A_B/6}{A_A/2} - r_{acyclic} \quad (\text{Eq. S2})$$

Finally, overall modification rate was computed as follows:

$$r_{overall} = r_{acyclic} + 2 * r_{cyclic} \quad (\text{Eq. S3})$$

Supporting information S3: Multi angle static light scattering definitions

The Guinier representation is defined as follows (eq. S4):

$$\ln\left(\frac{Kc}{\Delta R_\theta}\right) = \ln\left(\frac{1}{M_w}\left(1 + \frac{q^2 R_g^2}{3}\right) + 2A_2c\right) \quad (\text{Eq. S4})$$

where c is the concentration of the diffusing entity, M_w its molar mass, R_{g,z} its radius of gyration and A_{2,z} is the second virial coefficient. K is a constant defined by (eq. S5):

$$K = \frac{4\pi^2 n_{solvent}^2}{\lambda_0^4 N_a} \left(\frac{dn}{dc}\right)^2 \quad (\text{Eq. S5})$$

Where n_{solvent} is the refractive index of the solvent (water), λ₀ is the laser wavelength, N_a is the Avogadro constant and dn/dc is the refractive index increment of the diffusive entities (NPs) in the solvent (water).

Whereas ΔR_θ is calculated at each angle as follows (eq. S6):

$$\Delta R_\theta = \left(\frac{I_{sample} - I_{solvent}}{I_{toluene}}\right) \left(\frac{n_{solvent}}{n_{toluene}}\right)^2 R_\theta^{toluene} \quad (\text{Eq. S6})$$

where I_{sample} , I_{solvent} and I_{toluene} are the scattered intensities of the sample, the solvent and toluene respectively. n_{toluene} is the refractive index of the toluene and R_0^{toluene} is the Rayleigh constant of toluene at the working wavelength.

The scattering vector q is defined as follows (Eq. S7):

$$q = \frac{4\pi n_{\text{sample}}}{\lambda_0} \sin \frac{\theta}{2} \quad (\text{Eq. S7})$$

Where θ is the angle between the incident light and the detector.

Determination of dn/dc :

SEC (Size Exclusion Chromatography) was used to determine the dn/dc parameter of the nanoparticles. The dn/dc corresponds to the slope of the linear regression of the differential refractive index against the concentration of nanoparticles dispersed in pure water.

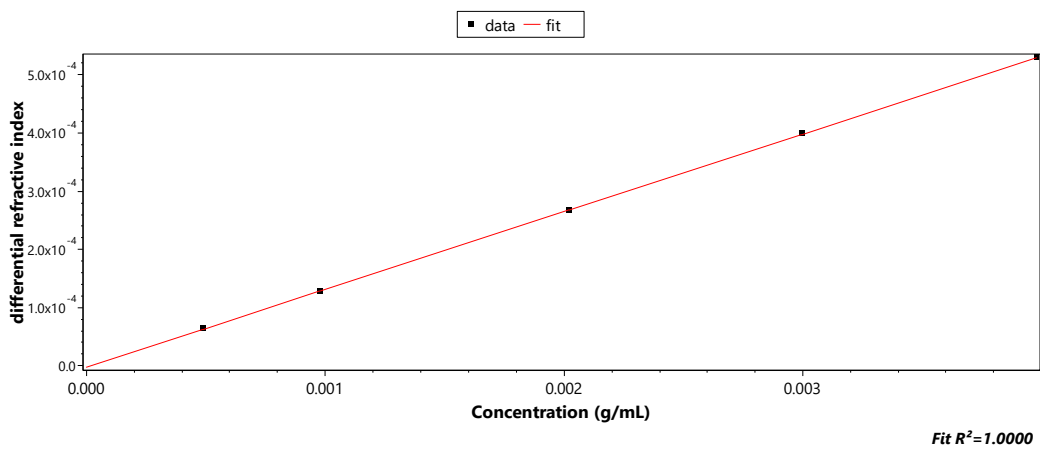


Fig. S4: Determination of dn/dc of the NPs with RI measurement at various concentration.

As a result, dn/dc was equal to 0.1337 ± 0.0005 mL/g.

Supporting information S5: Guinier representation

With the aim to plot the light scattering data by using the Guinier formalism, 6 measurements of 5 s each were proceeded with an angle step of 5° from 50° to 150° using the ALV instrument. The temperature of the toluene bath was kept to 20°C. 5 samples with decreasing concentrations were characterized (from 0.08 g/L to 0.008 g/L). The data is then analyzed using the ALV stat software, giving the Guinier plot (Fig. S6).

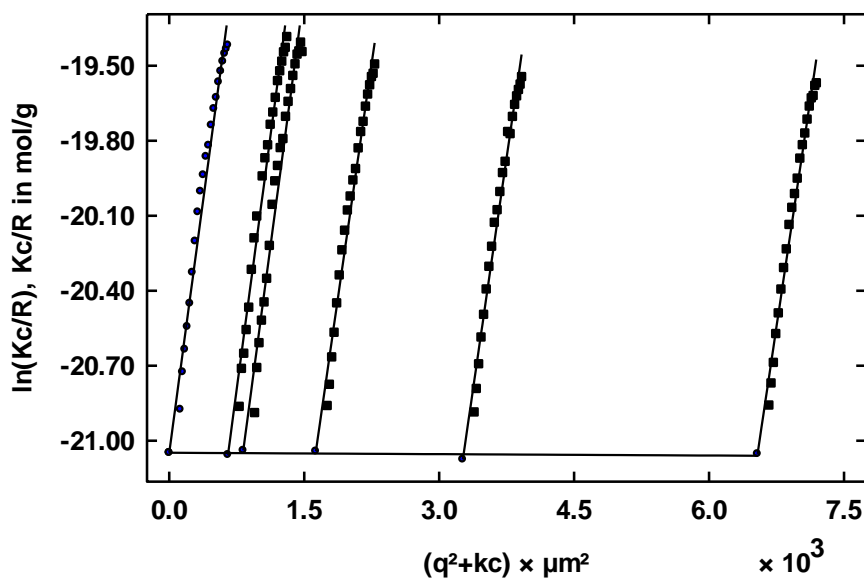


Fig. S6: Static light scattering results represented with a Guinier plot

From this, a double extrapolation ($c \rightarrow 0$; $q \rightarrow 0$) is performed to determine M_w and $\langle S^2 \rangle_z$ (which is the z-average of the square of the radius of gyration) and finally R_g . With Guinier assumption, $q \cdot R_g \ll 1$, (eq. S4) can be simplified further. The results obtained are summarized in Fig. S7.

Sample	Conc/(g/dm ³)	$M_w(\text{app})$ /(g/mol)	$\langle S^2 \rangle_z(\text{app})/\mu\text{m}^2$	$R_g(\text{app})/\text{nm}$
Conc.=0	0.0000	1.384e9	8.036e-3	89.644
S1	0.0764	1.390e9	7.250e-3	85.144
S2	0.0381	1.421e9	7.444e-3	86.276
S3	0.0190	1.375e9	7.506e-3	86.640
S4	0.0096	1.371e9	8.109e-3	90.051
S5	0.0076	1.395e9	8.102e-3	90.012

Fig. S7: Results obtained from the Guinier plot using concentration extrapolation to zero

In the following, M_w and $\langle S^2 \rangle_z$ values used will be $1.384 \cdot 10^9$ g/mol and $8.036 \cdot 10^{-3} \mu\text{m}^2$ respectively. M_w found with q extrapolation to zero was the same. The relative standard deviations calculated by the software for M_w and R_g are 1.08% and 1.9% respectively.

Supporting information S8: Average structural polymer density of the NP calculation

M_w can be then used to calculate the average polymer density ρ of the NP as described by Dautzenberg in (eq. S8) ¹:

$$M_w = \frac{4\pi}{3} \rho N_a a_m^3 \quad (\text{Eq. S8})$$

Where a_m is the geometrical radius of the NP. It is related to the z-average of the square of the radius of gyration as follows (eq. S9) ¹:

$$\langle S^2 \rangle_z = \frac{3}{5} a_m^2 e^{-5\sigma_a^2} \quad (\text{Eq. S9})$$

Where σ_a is the relative standard deviation of the NPs population. As it is squared, we assume that it is equivalent to the so-called polydispersity index (PDI) derived from the fitting of the autocorrelation function by the cumulants approach which is routinely used in dynamic light scattering (eq. 2). We used the PDI obtained with DLS 90° (equal to 0.088 at the time of the measurements (Fig. S3)). The standard deviation for PDI was calculated with two measurements and was equal to 0.02.

Combining (eq. S8) and (eq. S9) allows representing ρ as a function of $\langle S^2 \rangle_z$, M_w and σ_a (eq. S10):

$$\rho = \frac{3M_w}{4\pi N_a} * \frac{1}{\left(\frac{5}{3}\langle S^2 \rangle_z e^{-5\sigma_a^2}\right)^{\frac{3}{2}}} \quad (\text{Eq. S10})$$

We finally obtain the following results:

Average structural polymer density ρ (g/mL)	0.685 (\pm 15%)
Geometrical radius a_m (nm)	92.87 (\pm 5%)

The PDI used for the calculation has a strong influence on the calculated average polymer density. The influence of the standard deviation of M_w could be then neglected.

Supporting information S9: Surface coverage (C) calculation

From (eq. 6) the surface coverage can be calculated with the slope of Fig. S10 graph (eq. S11):

$$C = \frac{1}{4 * \rho_p * d_p * slope} \quad (\text{Eq. S11})$$

Where ρ_p is the particle density (g/m^3) (here the average polymer density in the nanoparticle) and d_p the geometric diameter of the nanoparticles (186 nm). Slope is here equal to $2.097 \text{ m}^2\text{g}^{-1}$ ($2.097 \cdot 10^{-3} \text{ mL}\cdot\mu\text{m}^{-1}\text{mg}^{-1}$).

Finally, we obtain $C = 0.94 \pm 0.14$. Standard deviation was computed by taking into account the one of the average polymer density in the nanoparticle.

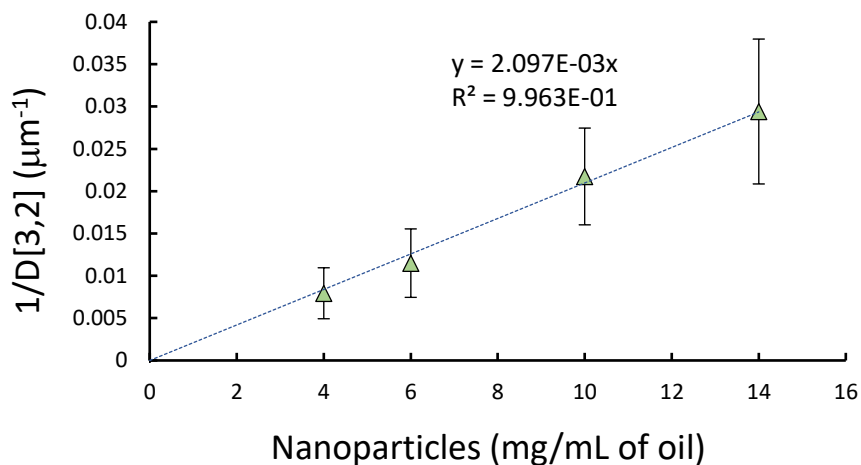


Fig. S10: Limited coalescence domain of dodecane in water droplets stabilized by NPD1 nanoparticles

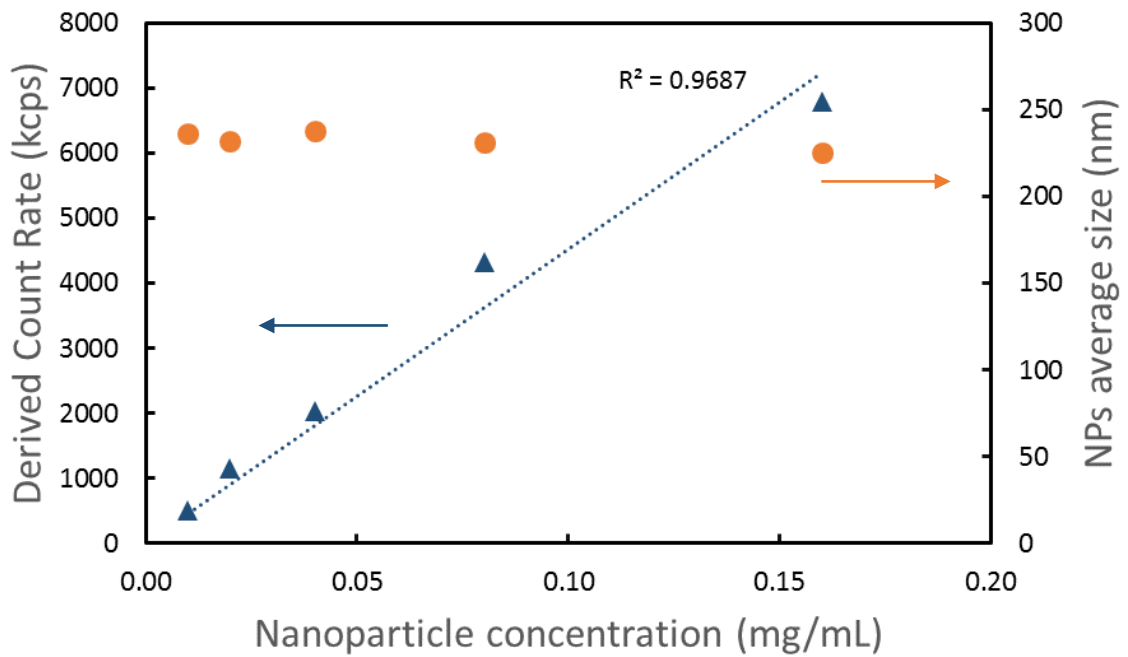


Fig. S11: Calibration curve of DCR with different concentrations of nanoparticles from NPD2 (blue) and their average size obtained by DLS (orange)

There is a satisfying linear relationship between the DCR and the nanoparticle concentration with a small variation of the measured average size by DLS. DCR is linked to the concentration of the nanoparticles and their radius. Consequently, no variation of the radius means that DCR value only depends on the concentration of nanoparticles.

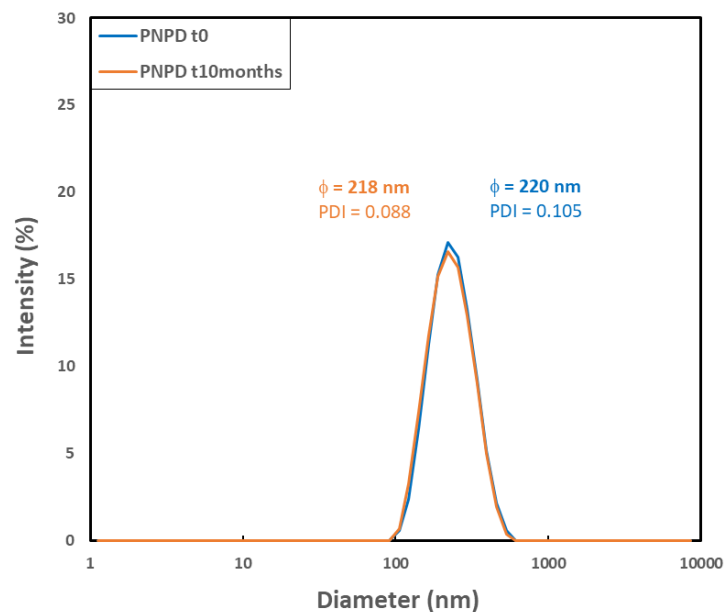


Fig. S12. Size distributions of NPD1 at t_0 and after 10 months of storage.

Nanoparticles (mg/mL of oil)	D[3,2] (μm)
4	126 \pm 50
6	90 \pm 19
10	46 \pm 15
14	34 \pm 14
16	35 \pm 11
18	37 \pm 12
20	30 \pm 6

Fig. S13: Size measurements of Pickering emulsions stabilized by NPD1 nanoparticles

Reference:

- (1) Dautzenberg, H. Light Scattering Studies on Polyelectrolyte Complexes. *Macromol. Symp.* **2000**, *162* (1), 1–22.