Supporting Information.

Monodisperse protein-polymer biohybrid nanoparticles.

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General

All organic solvents were of analytical quality or distilled before use. Buffers were prepared from milliQ® grade water. FPLC(SEC) was performed using a Superose 6 analytical column (Amersham biosciences) on a Amersham Ettan system, fitted with a fractionating device. Buffers for FPLC were filtered with a Millipore 0.2 μm filter before use. GPC was taken on a Polymer Labs PLgel 5 μm column with chloroform as the eluent on a Shimadzu 10A LC system and was calibrated with monodisperse polystyrene samples obtained from Polymer Labs. NMR was taken on a Bruker DMX 300 MHz or on a Varian DPX 400 MHz machine with TMS as the internal standard. TEM grids (Formvar-Carbon) were exposed to an electron discharge treatment, after which 1 μL of sample was put on the grids. After about 1 min. the sample was carefully dried using filter paper. Subsequently, 1 μL of ammonium molybdate (5% w/v) was added and the drying procedure was repeated. Dynamic Light scattering was performed using a ALV/SP-86 goniometer and a ALV5000 correlator equipped with a Spectra Physics 2000 Argon Ion laser, with λ= 514.5 nm at 200 mW power output.

SDS-PAGE was carried out following standard protocols in 12% acryl amide gel and protein bands were visualized by staining with Coomassie brilliant blue.

Experimental

*Ethyl styrene sulfonate (**3**)*

To a solution of sodium styrene sulfonate (20.6 g, 0.1 mol), in water (150 mL) at 0^{o}C, a solution of $AgNO_3$ (18.7 g, 0.11 mol) in water (50 ml) was added dropwise over a 15 min period. Considerable efforts were taken to exclude light from the mixtures and all further manipulations of the product. After complete addition the mixture was stirred for 2 hrs after which the precipitate was filtered off and washed with water (3 x) and with Et_2O (3 x). The solid was then redissolved in CH_3CN, filtered, and evaporated under reduced pressure. The product was then co evaporated with 1,4-dioxane (2 x).

The dry styrene sulfonate silver salt was then dissolved in acetonitrile (250 ml) and ethyl bromide was added (20 ml, 0.34 mol). The flask was equipped with a cooler and the mixture was heated to 70^{o} C overnight. The mixture was then filtered with Hyflo and evaporated under reduced pressure. The resulting greenish oil was dissolved in toluene and filtered over Hyflo again.Yield: 14 g., 67 mmol, 67%. ^{1}H NMR ($CDCl_3$): δ 1.31, (t, 3H, *J*=6.9 Hz, CH_3 Et); 4.14 (q, 2H, *J*= 7.2 Hz, O-CH_2); 5.48 (d, 2H, *J*= 11.1 Hz, CH_2 vinyl); 5.93 (d, 2H, *J*=17.7 Hz, CH_2 vinyl); 6.81 (dd, 1H, CH vinyl); 7.57 (d, 2H, *J*=8.4 Hz, CH arom); 7.88 (d, 2H, *J*=8.4 Hz, CH arom.) ^{13}C NMR ($CDCl_3$): δ 14.96 (CH_3); 66.99 (CH_2) 117.83 (CH Ph) 126.59 (CH arom) 127.99 (CH arom) 134.82 (CH vinyl) 134.96 (CH vinyl) 142.57 (Cq) ESI-MS: 213 (M+H).

N-*(3-aminopropyl)-5-(dimethylamino)naphthalene-1-sulfonamide (**1**)*

To a vigorously stirred solution of 1,3-propyldiamine (2.8 ml, 33 mmol) in DCM (150 ml) at 0°C, a solution of dansyl chloride (0.88 gr, 3.3 mmol) in DCM (100 ml) was added dropwise. The reaction was stirred at 0°C for 4 hrs., after which 50 ml of aqueous 1N NaOH was added, and the layers were separated. After extraction of the organic layer with water (2x100 ml) the organic layer was dried over Na_2SO_4 and evaporated under reduced pressure. The obtained oil was then co-evaporated with DMF (3x) to yield the product as a yellow oil. (1.07 g, 100%) ^{1}H NMR ($CDCl_3$): δ 1.46 (dt, 2H, *J*=6 Hz, CH_2 alkyl); 2.64 (m, 2H, $C\underline{H}_2$-NH_2); 2.87 (s, 6H, NMe_2, dansyl); 2.99 (t, 2H, *J*=6 Hz, CH_2-NH); 7.14 (d, 1H, *J*=7.5 Hz, CH arom.); 7.50 (dd, 2H, CH arom.); 8.22 (d, 1H, *J*=7.2 Hz, CH arom) 8.31 (d, 1H, *J*=8.7 Hz, CH arom) 8.52 (d, 1H, *J*=7.2 Hz, CH arom).

4-(1-Bromoethyl)-N-*(3-(5-(dimethylamino)naphthalene-1-sulfonamido)propyl)benzamide (**2**)*

To a solution of **1** (0.34 g, 1.1 mmol) in DMF (20 ml), DIPEA (N,N,N-diisopropylethylamine) (1.3 mmol, 0,23 ml) was added, as well as 1-bromo-1-ethyl benzoic acid (0.28 g, 1.21 g) and EDC (0.25 g, 1.3 mmol). The reaction was stirred at room temperature for 3 hrs, after which the solvent was evaporated. Silica gel column chromatography (eluent: toluene/acetone 0/100 to 20/80, v/v) yielded pure **2** (0.22 g, 46 %) ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.63 (dt, 2H, *J*=6 Hz, CH_2 alkyl); 1.96 (d, 3H, *J*=7.04 Hz, CH_3 ethyl); 2.93 (m, 2H, $C\underline{H}_2$-NH-SO_2); 3.44 (m, 2H, $C\underline{H}_2$-NH-CO); 5.14 (q, 1H, *J*= 7 Hz, CH-Br); 6.27 (t, 1H, *J* =6.4 Hz, NH); 7.00 (t, 1H, *J*= 6.1 Hz, NH); 7.14 (d, 1H,

J=7.5 Hz, CH arom.); 7.35 (d, 2H, *J*=8.4 Hz, CH arom phenyl); 7.50 (dd, 2H, CH arom.); 7.67 (d, 2H, *J*= 8.3 Hz, CH arom phenyl); 8.17 (d, 1H, *J*=7.2 Hz, CH arom); 8.33 (d, 1H, *J*=8.7 Hz, CH arom); 8.51 (d, 1H, *J*=7.2 Hz, CH arom.) LCMS (eluent: CH_3CN/10 mM $NH_4OH(H_2O)$ 50/50 to 95/5, column Zorbax extent C18) M 518 (M+H ^{79}Br), M 520 (M+H ^{81}Br). Calculated: 517.10

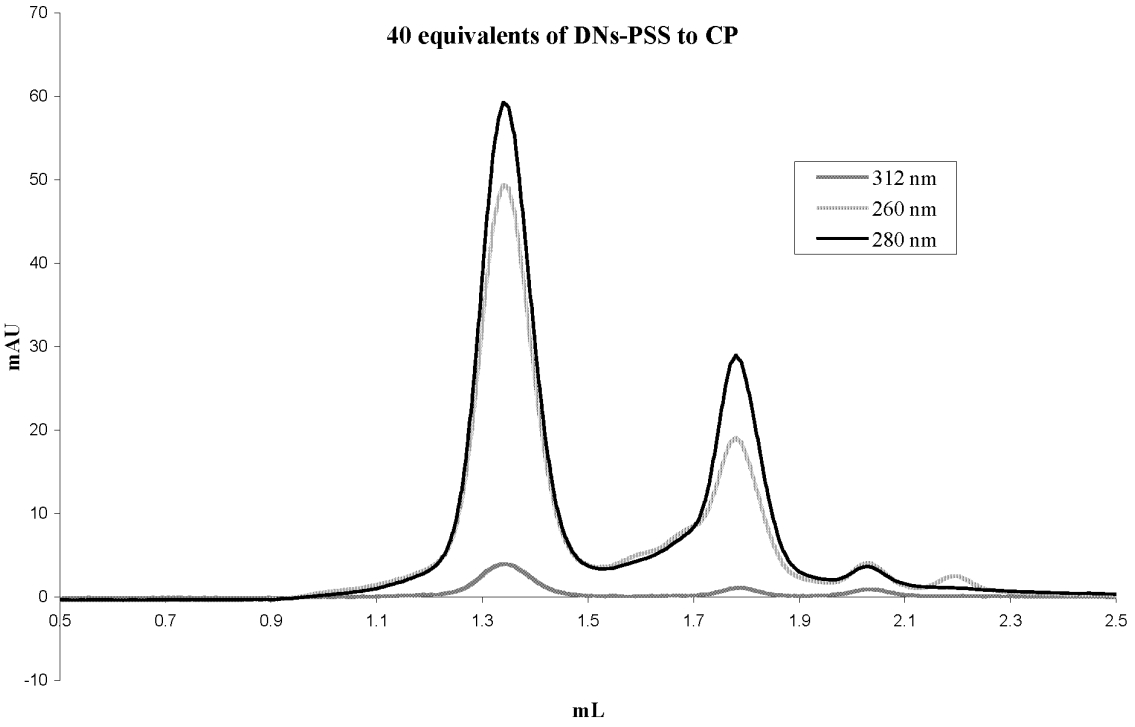
ATRP of ethyl styrene sulfonate

A degassed and dry Schlenk vessel was charged with CuBr (18 mg, 0.12 mmol), 2,2'-bipyridine (20 mg, 0.12 mmol), anisole (3 ml) and ethyl styrene sulfonate (2 ml, 9.4 mmol). The mixture was degassed by three vacuum/argon cycles and immersed in an ice bath. Initiator (**2**) (32 mg, 0.063 mmol) was added and the degassing cycle was repeated. The vessel was then placed in a thermostatted oil bath at 80^o C and samples were taken at regular intervals to determine conversion by ^1H NMR. A semi-logarithmic plot of conversion versus time showed a straight line, confirming first order kinetics. After the desired conversion was reached (~ 5 hrs.) the polymerization was stopped by exposing the catalyst to air. The resulting slurry was taken up in a large volume of $CHCl_3$ (300 ml) and extracted with EDTA solution (100ml, 10g/l, 2x), and water (1x). After drying the solution over $MgSO_4$ all solvents were evaporated under reduced pressure. The resulting glass was taken up in a minimal amount of $CHCl_3$ and precipitated in heptane. The resulting milky suspension was allowed to settle, decanted, the remaining suspension evaporated and this procedure was repeated, although it did not fully remove the monomer. The polymer was obtained by evaporation of the solvent under reduced pressure and isolated as a yellow-green glass (1.1 g., ~50 %) GPC-SEC($CHCl_3$):

Mp=9920, PDI 1.12. ^{1}H NMR ($CDCl_3$): δ 1.34 (br., CH_3 Et); 1.53 (br., CH_2 backbone); 4.15 (br., O-CH_2); 6.70 (br., 2H, CH arom.); 7.65 (br., 2H, CH arom).

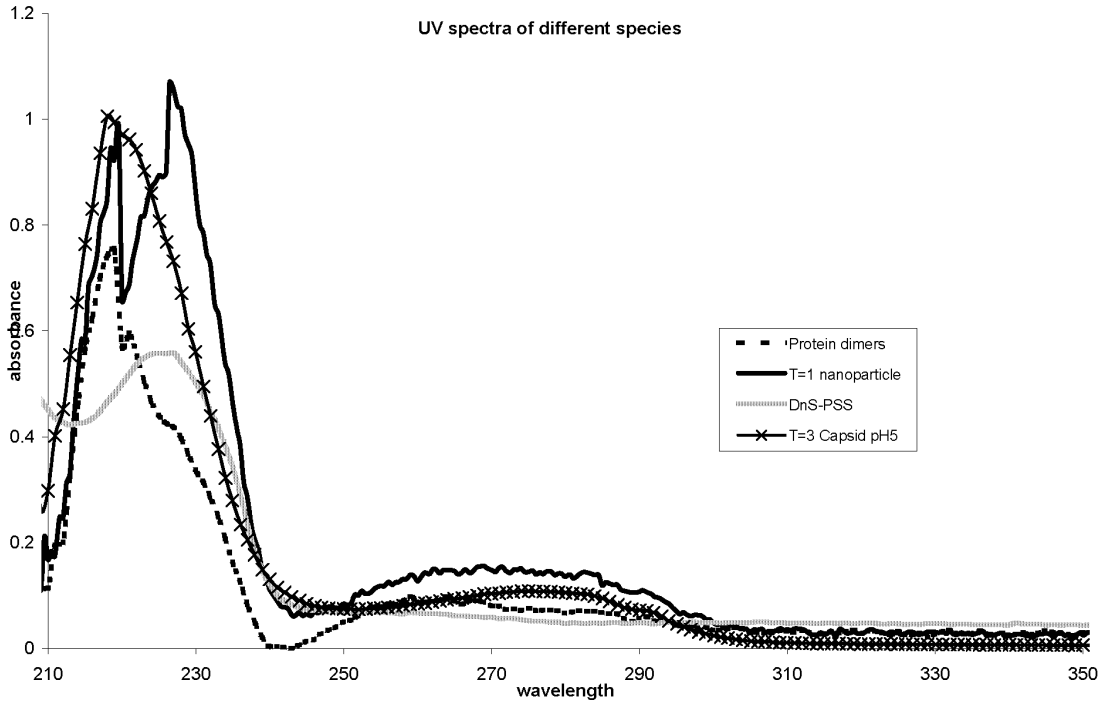
*Dansyl functionalized Polystyrene sulfonate (**4**)*

Dansyl functionalised polystyrene sulfonate ethyl ester was dissolved in DMF/H_2O (90/10, 50 ml) and NaN_3 (1.9 g, 30 mmol) was added. The mixture was heated at 50^{o}C overnight, after which the DMF was evaporated under reduced pressure. The resulting solid was dissolved in water (~ 5 ml) and dialysed in a continuous setup overnight against demineralized water. The solution was then evaporated yielding a off-white solid. TLC analysis (Rf=0 in any solvent) revealed fluorescence under UV (365 nm), indicating the presence of a fluorescent group. ^{1}H NMR (D2O): δ 1.5 (br., CH, CH_2 backbone); 6.7 (br., CH-arom.); 7.6, (br., CH arom.).

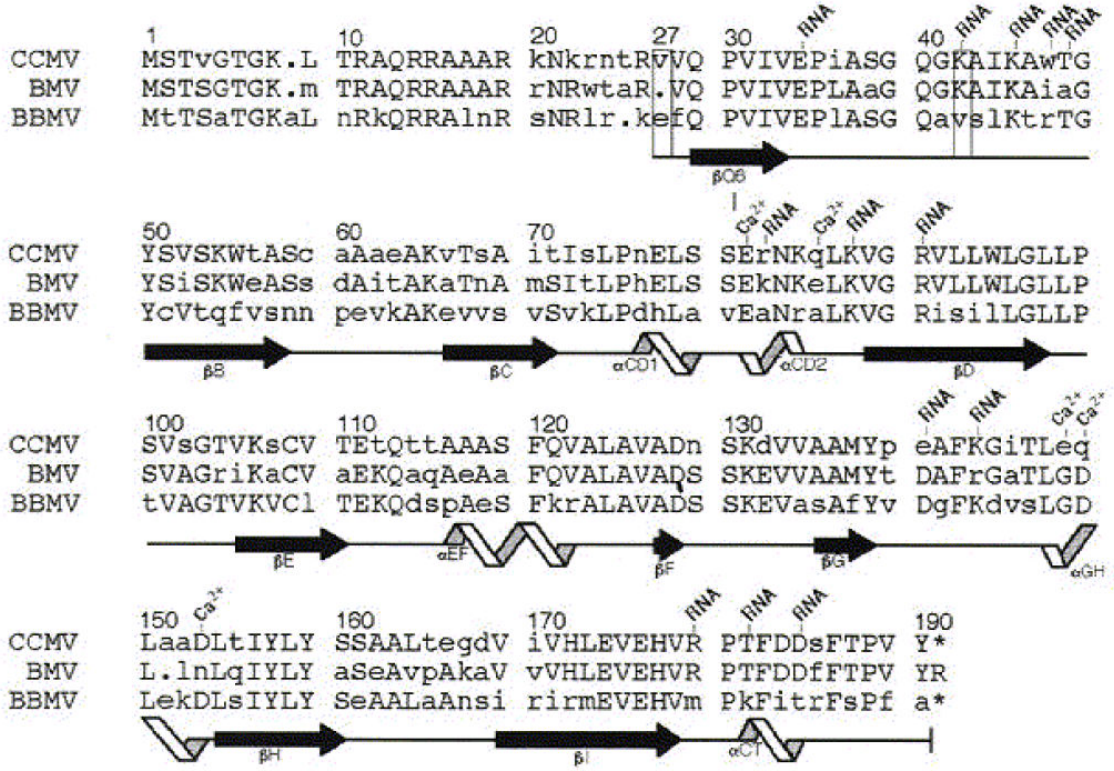


Fast performance Liquid Chromatograph of T=1 nanoparticle formed at 40 equivalents of DNs-PSS to CP. The ratio of the areas under the curves for λ = 260 nm (predominantly protein adsorption) and λ = 312 nm (predominantly polymer adsorption) were determined for each signal at a different retention volume.

The following results were obtained: for the peak at 1.34 mL a value of A_{260}/A_{312} = 13 was obtained and for the peak at 1.78 mL a value of A_{260}/A_{312} = 30 was obtained, indicating a strong increase of adsorption at λ = 312 nm for the former signal corresponding to the T=1 nanoparticle relative to free CP. This in turn indicates inclusion of polymer with the dansyl group.



Normalized UV spectra of various species. Although, the indivual adsorption of the dansyl group is hardly visible at this concentration, the adsorption of the main polymer chain is clearly noticed at λ = 225 nm. The T=3 capsid pH 5 trace does not show any additional adsorption in this region, whereas the T=1 nanoparticle does, confirming, the encapsulation of the polymer.



Amino acid sequence of the capsid protein (CCMV) and labeling of the RNA binding residues. Taken from Speir *et al. Structure* **1995**, *3*, 63078