Monodisperse hydrogel microspheres by forced droplet formation in aqueous two-phase systems

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Supporting information

Materials and methods

Dextran solution 20 % w/w (av. molar mass 110 kg/mol from Leuconostoc ssp., Fluka) and polyethylene glycol solution 10 % w/w (av. molar mass 35 kg/mol, Fluka) were prepared by dissolving the powders in water using ultrasonication. Phase separation of the two solutions occured 5 minutes after mixing them in a test tube.

The interfacial tension between the phase-separated liquids was 0.10 ± 0.05 mN/m, as measured by the pendant drop method (Kruss, EasyDrop). The values represent the statistical average and standard deviation of the interfacial tension of sixteen independently measured droplets. The contrast of the pendant droplet in the liquid environment was enhanced manually to allow for automatic detection and fitting. The viscosity of the solutions was measured using a rheometer with couette geometry (TA Instruments AR-G2) at a temperature of 25 °C. The average viscosity for the shear rate in the range $1 - 100\ s^{-1}$ was 58.1 ± 0.2 mPas and 22 ± 0.1 mPas for dextran and PEG solution respectively.

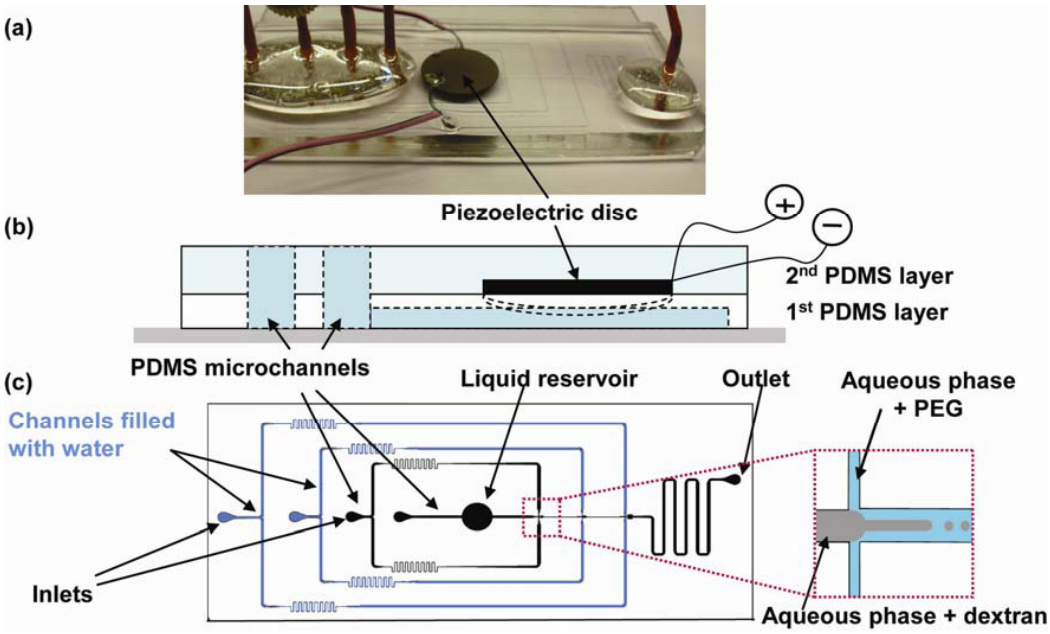

Figure 1S (a) Microfluidic device including a flow-focusing junction and a piezoelectric bending disc actuator (b) lateral view of the piezo-electric actuation device, (c) scheme of the microfluidic network.

In our droplet experiments, we used the device as shown in Fig. 1S. It consists of a flow focusing junction where one of the two immiscible liquids was injected as a thin jet inside the other liquid. The inner liquid was the dextran solution, fed at a flow rate of 6 µl/h, and the outer liquid was the PEG solution fed at a rate between 60 and 84 µl/h. Syringe pumps (Harvard Apparatus PicoPlus) were used to drive our solutions into the microfluidic device. The coflowing liquids subsequently entered the main channel (width 100 ± 5 µm, height 85 ± 5 µm) and, further downstream, a meandering 300 µm wide channel, which

was connected to outflow. The remaining channels shown in Fig. 1S were filled with water and closed. They have no function in our experiment.

Fabrication of our microfluidic device was done using soft lithography. In brief, a 4-inch silicon wafer was patterned by exposing a layer of photo-resist (SU8-2050, Micro Resist Technology GmbH, Germany) to UV light (EVG-620, total energy: 250 mJ/cm^2) through an optical transparency containing the design of the microchannel network. After development of the resist, the patterned wafer was used as a master to replicate the structure in poly(dimethylsiloxane) (PDMS). Our devices were constructed from two layers of PDMS. After curing the first 1 mm thin layer, a piezoelectric bending disc (diameter: 12.7 mm, max. displacement 19.1 µm at 180 V) was placed on top of the center the fluid reservoir, and covered with a second thicker layer of PDMS. In this way, the piezo disc was embedded in the PDMS chip and separated from the fluid reservoir by a 1 mm thin PDMS membrane. Both the first and second layer of PDMS were prepared using a 10:1 prepolymer/curing agent mixture (Sylgard 184, Dow Corning). After curing the second layer at 68 °C for 2 hours, the PDMS structure was removed from the patterned wafer, cut to size, and provided with holes for the fluid connections. The channels were closed by irreversibly bonding a glass slide to the PDMS structure using an oxygen plasma treatment (Harrick PDC-002).

Visualization of the measurements was performed using an inverted microscope (Zeiss, Axiovert 100M) equipped with a black and white camera (AxioCam). In our experiments, the jet was destabilized by applying a sinusoidal voltage, generated by a function generator (33120A , Hewlett Packard) and amplified using a linear amplifier (Trek 50/750).

The derivatized dextran was synthesized as follows. Dextran T500 (MW=500000 g/mol, Fluka) (5 g) was dissolved in dimethyl sulfoxide (DMSO, 45 mL) in a stoppered 250 mL round-bottom flask under nitrogen atmosphere. After dissolution of 1.0 g 4-(N,N-Dimethylamino)pyridine (DMAP, MW=122.17 g/mol, 81.85 mmol), 0.876 g of hydroxyethyl methacrylate (HEMA, MW=130 g/mol, 67.4 mmol) was added. The solution was stirred at room temperature for 48 h. Reaction was stopped by adding (an equimolar amount) of 4M HCL (2.046 mL, 8.185 mmol) to neutralize the DMAP. The reaction mixture was transferred to a dialysis tube and extensively dialyzed for 10 days against demineralized water at RT. Water was removed by evaporation and by freeze-drying. White product (3.4359 g) was obtained. From NMR (and eq provided in ref1) we calculated degree of substitution DS=15.