Electronic Supplementary Information (ESI)

Methacrylate-based polymer foams with controllable connectivity, pore Shape, pore Size and polydispersity

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S1 Biodegradability of poly(1,4-BDDMA) foams

Previously, accelerated degradation studies by Whitely et al. (M. E. Whitely et al., "Prevention of oxygen inhibition of poly-HIPE radical polymerization using a thiol-based cross-linker" *ACS Biomaterials Science & Engineering*, 2017, **3**, 409) demonstrated the hydrolytic degradation of poly(PFDMA-(pentaerythritol tetrakis)) foams with a complete loss of the integrity after 3 weeks in 0.5 M NaOH aqueous solution at 37°C. Poly(PFDMA) foams displayed a reduced rate of hydrolytic degradation with a mass loss of 41.0 ± 1.6 % after 4 weeks. Poly(1,4-BDDMA) foams initially demonstrated negligible levels of mass loss at 0.5 M NaOH in a scouting study. This lack of degradation was attributed to the reduced number of ester groups in the polymer backbone as compared to PFDMA. To determine if poly(1,4-BDDMA) foams are hydrolytically degradable, we carried out a full study at a higher NaOH concentration of 1 M to further accelerate the degradation rate and monitor mass loss over 4 weeks.

The following experiments were conducted on polymer foams fabricated using the protocol as described by Moglia et al. (R. S. Moglia et al., "Injectable polymerized high internal phase emulsions with rapid in situ curing" *Biomacromolecules*, 2014, **15**, 2870). Briefly, the polymer foams were made with 1,4-BDDMA and 10 wt % PGPR 4125 as continuous phase and an aqueous solution of $CaCl_2$ (1 wt%) as dispersed phase. The redox initiators benzyoyl peroxide and trimethylaniline were used at a ratio of 1:1 at 1 wt% of the organic phase emulsion. The gel fraction was quantified to assess the extent of network formation of the poly(1,4-BDDMA) foams. After curing for 24 hours at 37 °C, the samples were sectioned into 25 to 35 mg pieces.

The specimens were vacuumed dried for 48 hours and the initial mass was recorded. The specimens were incubated in dichloromethane at a ratio 10 mg to 1 mL for 48 hours and then vacuum dried until a constant mass was achieved. After correcting the initial weight for the 10 wt% surfactant, the final mass was divided by the initial mass and reported as the gel fraction.

$$gel\ fraction(\%) = 100\% * \frac{final\ mass}{inital\ mass * \frac{0.1}{1.1}} \tag{S1.1}$$

Accelerated degradation testing was performed on poly(1,4-BDDMA) foam specimens that were sectioned using an Isomet® bone saw into 1 mm thick sections. Specimens were dried for 48 hours and dry mass recorded. Specimens were then incubated in 1 M NaOH aqueous solution at a ratio of 1 g to 20 mL solution, secured with Teflon weights, and placed on a shaker table at 37 °C. The solutions were changed every three days with time points every week for four weeks. At each time point, the specimens were washed twice with reverse osmosis (RO) water and then incubated for 1 hour in 1 mL RO water to remove any salts. The specimens were dried under vacuum at 50 °C for 24 hours and were then placed in dichloromethane at a ratio of 10 mg to 1 mL for 24 hours to remove any surfactant or uncured monomer. Finally, the specimens were dried under vacuum at 50 °C for 24 hours and the dry weights were recorded. After correcting the initial weight for 10 wt% surfactant, the percent mass loss was determined by using equation (S1.2). Note that our results (Figure S1) are based on 3 batches of foams fabricated separately ($N = 3$). Each batch of foam provided 3 samples, *i.e.* 9 samples in total ($n = 9$) were observed in the accelerated degradation study. We used the statistical method ANOVA to analyze the differences among group means in a sample. We set our ANOVA tests at a 95% confidence interval ($p < 0.05$). After each comparison between the average mass loss of each week, the p-values were found to be > 0.05. Therefore, there was no significant difference between any two week's average mass loss.

$$mass\ loss(\%) = 100\% * \frac{(intital\ mass * \frac{0.1}{1.1}) - final\ mass}{inital\ mass * \frac{0.1}{1.1}} \tag{S1.2}$$

Poly(1,4-BDDMA) foams displayed a gel fraction of 94.5 ± 0.9% after removal of unreacted monomer. Unlike the previous poly(PFDMA) foam degradation studies, the percent mass loss did not change over the 4 week accelerated degradation testing ranging from an average of 3.9 ± 1.7% to 5.1 ± 1.7% (Figure S1). Given that this mass loss is comparable to the measured sol fraction for these poly-HIPE foams, we attribute the mass loss to the removal of unreacted

monomer rather than to degradation. These results indicate that poly(1,4-BDDMA) did not display degradation under the selected conditions and suggest a much slower hydrolytic degradation than the previously studied PFDMA-based foams. Therefore, PFDMA-(pentaerythritol tetrakis) will be used in future experiments to fabricate biodegradable polymer foams.

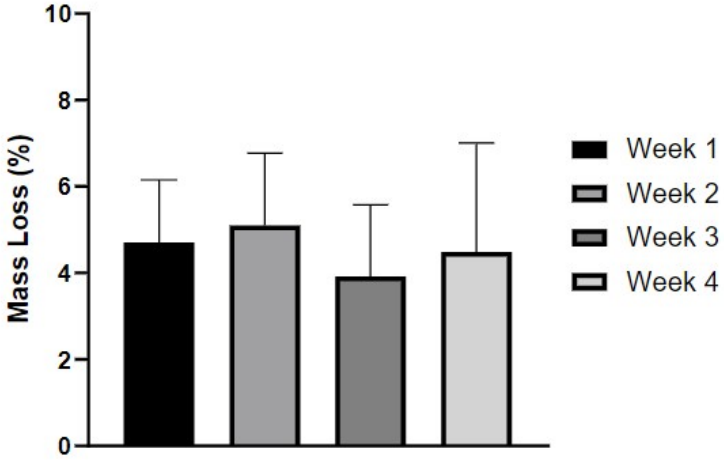

Figure S1: Accelerated degradation analysis of poly(1,4-BDDMA) foams in 1 M NaOH. Data is presented as a mean with SD error bar (N = 3, n = 9). No significant difference across all groups determined with multiple comparison ANOVA, $p < 0.05$.

S2 Emulsion generation and polymer foam synthesis

First experiments were made with 1,4-BDDMA and 10 wt% PGPR 4125 (calculated with respect to the mass of 1,4-BDDMA) as continuous phase and pure water as dispersed phase. As initiators we used the same as in Robinson et al. (J. L. Robinson et al., *Tissue Engineering: Part A*, 2016, **22**, 403) but at a lower concentration. Robinson et al. obtained an interconnected pore structure if the monomer-soluble initiator BPO was used and a closed-cell pore structure if the water-soluble initiator APS was used. To find out whether we can also control the connectivity of monodisperse polymer foams simply by changing the type of initiator we generated monodisperse emulsion templates containing either 2 mol% BPO in the continuous phase or 2 mol% APS in the dispersed phase via microfluidics. The initiator concentrations were calculated with respect to the amount of 1,4-BDDMA. These templates were then thermically polymerized for 24 h at 70 °C, washed, and dried. We obtained a low-porous polymer with a closed-cell structure if we used BPO for the polymerization (Figure S2.1, left) and a very inhomogeneous, polydisperse porous polymer with particles inside the pores with APS (Figure S2.1, right). The low porosity of the BPO initiated polymer is due to the fact that the density of water is lower (ρ = 0.997 g ml^{-1} at 25 °C) than that of the monomer 1,4-BDDMA (ρ = 1.023 g ml^{-1} at 25 °C). This prevents droplet sedimentation and therefore the creation of a

closed-packed structure. The phase density problem was solved by adding 5 wt% NaCl to the dispersed phase (ρ = 1.032 g ml^{-1} at 25 °C). The mass of salt was calculated with respect to the mass of water. In case of APS initiated samples, however, the main problem seemed to be a destabilisation of the emulsion template due to a too slow polymerisation rate rather than the missing density difference. The polymerisation rate was increased by adding 5 mol% APS (without NaCl) to the dispersed phase (Figure S2.2). However, due to unknown reasons the presence of APS in the dispersed phase did not allow us to generate monodisperse templates with one pressure setting. Therefore, APS was substituted by KPS for all follow-up studies. Note that for all further experiments, UV-polymerization was used instead of thermal polymerization because the polymerization via UV-light is "softer", especially for the polymerization of emulsion templates with large droplets.

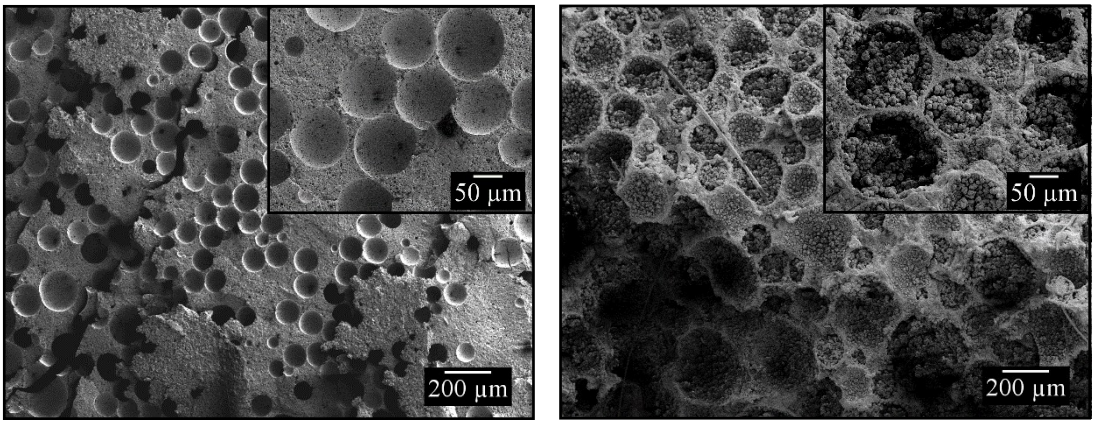

Figure S2.1: SEM pictures of an organic phase initiated poly(1,4-BDDMA) foam containing 2 mol% BPO (left) and an interfacial initiated poly(1,4-BDDMA) foam containing 2 mol% APS (right). The continuous phase consisted of 1,4-BDDMA containing 10 wt% PGPR 4125, the dispersed phase was water (left) or an aqueous phase containing 2 mol% APS.

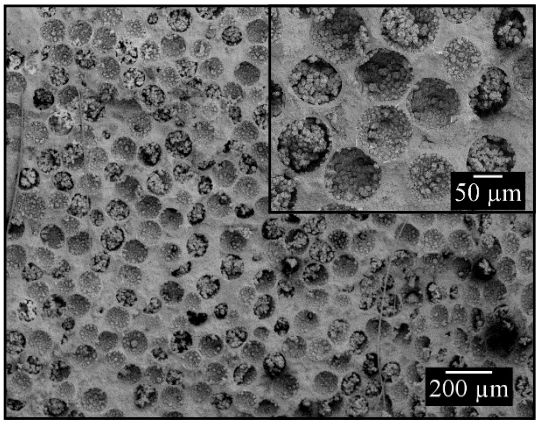

Figure S2.2: SEM pictures of an interfacial initiated poly(1,4-BDDMA) foam containing 5 mol% APS. The continuous phase consisted of 1,4-BDDMA containing 10 wt% PGPR 4125, the dispersed phase was an aqueous phase containing 5 mol% APS.

S3 Generation of monodisperse water-in-1,4-BDDMA emulsion templates

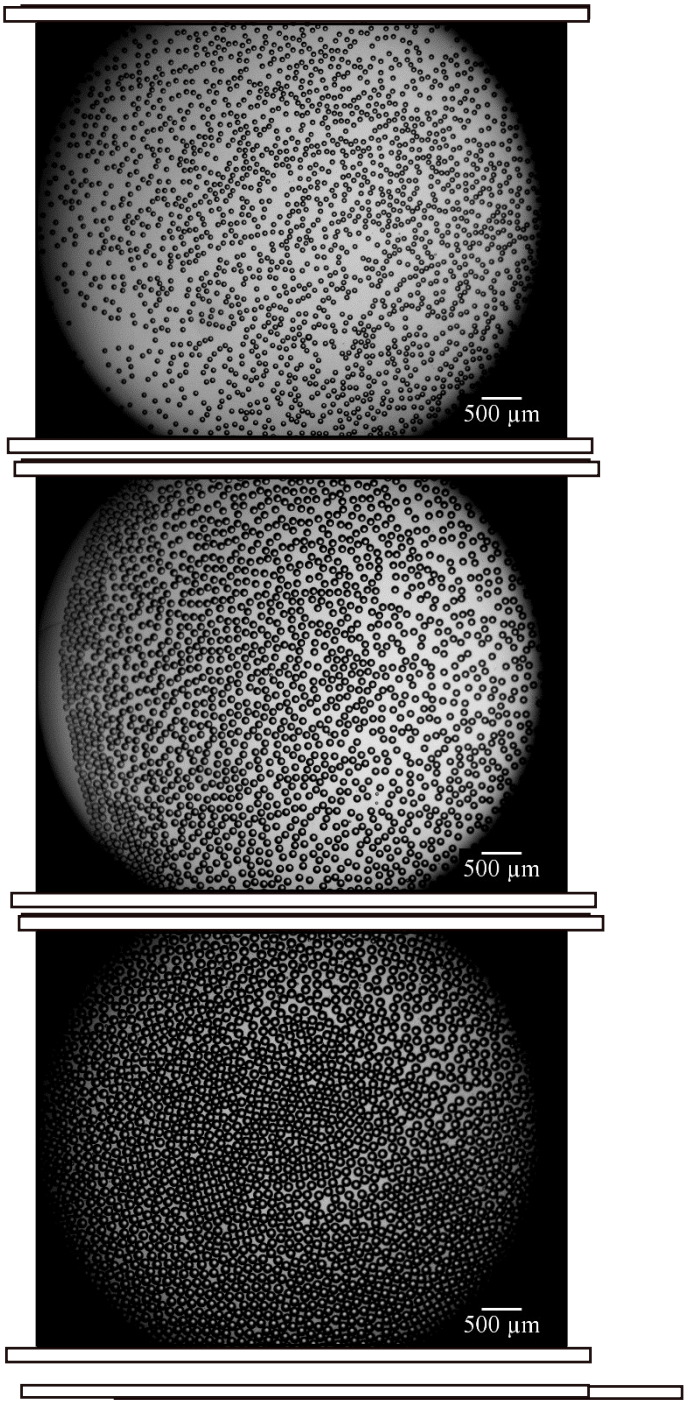

Figure S3: Microscope pictures of monodisperse monolayers with droplet diameters of around 70 µm (top), 100 µm (middle) and 120 µm (bottom) for samples containing KPS in the dispersed phase. The continuous phase of the emulsion templates consisted of 1,4-BDDMA containing 10 wt% PGPR 4125, the dispersed phase was an aqueous phase containing 5 wt% NaCl.

S4 Poly(1,4-BDDMA) foams with controllable polydispersity

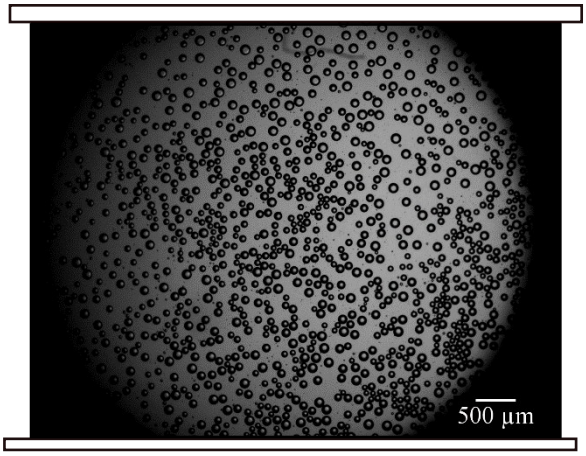

Figure S4: Microscope picture of the resulting liquid monolayer for a sample containing KPS in the dispersed phase. The continuous phase of the emulsion template consisted of 1,4-BDDMA containing 10 wt% PGPR 4125, the dispersed phase was an aqueous phase containing 5 wt% NaCl.