Supporting Information for

Block Copolymer Membranes for Efficient Capture of a Chemotherapy Drug

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This file includes: experimental information on the synthesis and characterization of polymers, membrane fabrication and sulfonation, determination of ion content, water uptake measurements, small angle X-ray scattering (SAXS) and cryogenic scanning transmission electron microscopy (cryo-STEM) experiments, and in vitro doxorubicin absorption kinetics experiments.

Synthesis and characterization of polymers: Homopolymer polystyrene (hPS) was synthesized by anionic polymerization using sec-butyl lithium as the initiator. Polystyrene-*b*-polybutadiene diblock copolymer was synthesized by sequential anionic polymerization of styrene and butadiene and the living diblock copolymer was coupled to yield polystyrene-*b*-polybutadiene-*b*-polystyrene (SBS) triblock copolymer using dibromoethane as the coupling agent.

The molecular weight of hPS was determined by gel permeation chromatography (GPC) experiments on a Viscotek GPC Max VE-2001 equipped with a TDA 302 triple-detector system, calibrated using polystyrene standards with tetrahydrofuran (THF) as the eluent. The molecular weight of the polystyrene block of the SBS triblock copolymer was determined by obtaining an aliquot of the reaction mixture after completion of polymerization of styrene, before the addition of butadiene, terminating the living anions in the aliquot with methanol in an air-free environment, and conducting GPC experiments at the same conditions described above. The molecular weight of the polybutadiene (PB) block of the SBS copolymer was determined using ^{1}H nuclear magnetic resonance (NMR) spectroscopy ($CDCl_3$, 25 °C). Using cyclohexane as the solvent for polymerization

resulted in 93 mol% of 1,4-addition of the PB block, determined by ^{1}H NMR. The coupling reaction yielded a ratio of triblock copolymer to diblock copolymer of 82% to 18%, based on GPC results. High temperature NMR (toluene-d_8, 90 °C) was used to ensure complete hydrogenation of the polybutadiene block to yield SES. The dispersities of hPS and SBS were 1.06 and 1.02, based on polystyrene standards. The characteristics of hPS and SES are given in Table S1.

Table S1 Physical characteristics of polymers used in this work.

Polymer	**PS M_n (kg/mol)**	**PE M_n (kg/mol)**	**PS volume fraction**
hPS	5.9	-	1
SES	13.2	65.7	0.26

Membrane preparation and sulfonation: Membranes containing mixtures of hPS and SES were prepared by dissolving hPS and SES of predetermined ratios in *o*-xylene at 100 °C and casting the solutions on an ultraclean aluminum foil using a custom-build solvent caster equipped with a doctor blade. The solvent caster was heated to 80 °C. The concentration of the solution and the height of the doctor blade were adjusted to obtain membranes with thicknesses of 50 ± 10 μm. The membranes were dried on the solvent caster for 1h and under vacuum at 80 °C for 24 h. After drying, the membrane was gently peeled off from the aluminum foil by immersing it in methanol. The resulting free-standing membrane was washed with deionized water several times and dried under vacuum at room temperature for 16 hours.

Homopolymer polystyrene in the hPS/SES blend membranes was selectively dissolved by washing the membranes in tetrahydrofuran, followed by a methanol rinse. This was repeated three times. After the washing procedure, the membranes were dried in vacuum at room temperature for 24 hours. The weight of the membranes before and after the washing procedure was measured to calculate the amount of hPS extracted from the membrane. For all the membranes used in the study, the weight of hPS originally blended into SES was equal to the weight extracted. We define ϕ_v as the volume fraction of hPS that was blended with SES and subsequently extracted. Pristine nonporous SES membranes were prepared following the same steps described above for systematic comparison.

After the washing and drying steps, SES membranes were sulfonated in one piece in a custom-designed three-neck reactor where the membranes were fixed in place above the stir bar by a custom-designed Teflon clamp. The sulfonation reaction took place in the course of 4 hours in 1,2-dibloroethane with the presence of acetic sulfate. After sulfonation, membranes were washed with methanol and deionized water several times and soaked in deionized water with changing water every day for 7 days. The sulfonated membranes (S-SES) were stored in deionized water prior to measurements. The membrane fabrication process was reported in detail in ref. S1.

Determination of Ion Content: Ion exchange capacity (IEC) is defined as the milliequivalents of sulfonic acid groups per dry gram of polymer (mmol/g). IEC was determined using an ion exchange procedure described in ref. S2. A piece of hydrated membrane was cut out and immersed in 0.1 M NaCl solution. The membrane-containing solution was gently stirred for 16 hours to allow complete exchange of H^+ ions in the

membrane with Na^+ ions in the solution. The membrane was removed from the solution and the pH of the solution was determined by titrating with a standard 0.01 M NaOH solution to the phenolphthalein endpoint. The membrane was soaked in 0.1 M HCl for 2 hours to return it to the acid form, followed by washing with deionized water several times and soaking in deionized water for 16 hours. Finally the membrane was dried under vacuum at room temperature for 24 hours and then at 80 °C for two hours. Dry weight of the membrane, W_{dry}, was measured after membrane was cooled down in the vacuum oven through constant purging of dry nitrogen. IEC is calculated using equation S1.

$$\text{IEC (mmol/g)} = \frac{\text{volume of NaOH solution (mL)} \times \text{concentration of NaOH solution (M)}}{W_{\text{dry}}\ \text{(g)}} \qquad \text{(S1)}$$

The sulfonation level (SL) of S-SES, defined by equation S2, was calculated from IEC and the weight fraction of PS block in SES.

$$\text{SL} = \frac{\text{mol SSA}}{\text{mol S} + \text{mol SSA}} \qquad \text{(S2)}$$

where SSA is styrene sulfonic acid and S is styrene.

Water uptake measurements: Water uptake, WU, of the membranes is defined by equation S3,

$$\text{WU} = \frac{W_{\text{wet}} - W_{\text{dry}}}{W_{\text{dry}}} \times 100\% \qquad \text{(S3)}$$

where W_{wet} is the wet weight of the membrane and W_{dry} is the dry weight of the membrane. To obtain W_{wet}, a piece of hydrated membrane was cut out and the surface water was removed by gently dabbing the membrane with Kimwipe. The weight of the membrane was then quickly measured on a balance. Membrane was subsequently dried in vacuum at room temperature for 24 hours and then at 80 °C for two hours. It was allowed to cool down in the oven in a dry nitrogen purge before W_{dry} was measured.

Small angle X-ray scattering (SAXS) measurements: Hydrated samples were prepared by sealing a small piece of hydrated membrane in a Teflon washer. The Teflon washer was sandwiched between two pieces of Kapton films and filled with deionized water before sealing with heat resistant sealant. SAXS experiments were performed at beamline 7.3.3 of the Advanced Light Source (ALS) at Lawrence Berkeley National Laboratory (LBNL) as well as beamline 1-5 of the Stanford Synchrotron Radiation Lightsource (SSRL) at SLAC National Accelerator Laboratory. The original two-dimensional scattering images were azimuthally averaged to generate one-dimensional scattering intensity profiles, *I(q)*. The scattering wave vector $q = 4\pi \sin(\theta/2)/\lambda$, where θ is scattering angle and λ is the wavelength of the incident beam.

Cryogenic scanning transmission electron microscopy (Cryo-STEM): To prepare dry STEM samples, thin sections with thickness about 70 nm were obtained by cryomicrotoming dry S-SES membranes at −140 °C using a Leica EM FC6 cryomicrotome. The thin sections were placed onto a lacey carbon supported copper grid (Electron Microscopy Sciences). Hydrated samples were obtained by annealing the microtomed thin sections in 6 µL of deionized water for 15 min, dabbing off surface water with filter paper and plunging into liquid ethane using an FEI vitrobot (Mark IV).

Dark field STEM images were acquired on a Tecnai F20 UT FEG using a high angle annular dark field (HAADF) detector with 200 kV acceleration voltage. Dry samples were imaged at room temperature. Hydrated samples were imaged at −184 °C, using a Gatan 914 high tilt cryo-stage.

***In vitro* doxorubicin absorption kinetics experiments**: A volume of 48.75 mL of phosphate buffered saline (PBS) solution that simulates physiologic serum electrolyte composition and pH (GE Healthcare Life Sciences) was transferred into a glass jar and warmed to 37 °C. 1.25 mL of Doxorubicin HCl injection, USP with 2 mg/mL concentration (Pfizer) was added into the PBS solution, resulting in 50 mL of Doxorubicin solution with an initial concentration of 0.05 mg/mL. An aliquot of 200 µL was drawn from the solution before adding drug capture membranes. To prepare drug capture membranes, a piece of fully hydrated membrane with an area of 22.5 cm^2 (1 side) was punched out and soaked in fresh deionized water for 16 hours prior to measurement. The membrane was added to the doxorubicin solution under strong stirring and a timer was started at the same time. The glass jar was sealed with a Teflon cap. Aliquots of 200 µL were drawn at a series of predetermined time intervals over a course of 4 hours. The concentrations of the aliquots were determined by measuring the fluorescence of the aliquots using a fluorospectroscopy and comparing it with a standard calibration curve. The fluorescence was measured at an emission wave length of 550 nm with an excitation wavelength of 480 nm.

References

S1. Chen, X. C.; Kortright, J. B.; Balsara, N. P. *Macromolecules* **2015**, *48*, 5648-5655.
S2. Peckham, T. J.; Schmeisser, J.; Rodgers, M.; Holdcroft, S. *J. Mater. Chem.* **2007**, *17*, 3255-3268.