Supporting Information

DTX Solubility Equilibration Time

Solid DTX (2 mg) was mixed in 20 ml PBS and samples of solutions were taken at specific time points. The concentration of DTX in the samples was measured using reversed phase high pressure liquid chromatography (HPLC) (Waters HPLC system with millennium software) with a symmetry C18 column (4 mm × 150 mm , Waters Nova-Pak, Milford, MA) at a flow rate of 1 ml/min. The mobile phase was composed of 58% acetonitrile, 37% distilled water, and 5% methanol. Sample injection volumes were 20 µl and detection was performed using UV detection at a wavelength of 232 nm. Before DTX analysis by HPLC, the samples were centrifuged at 14000 ×G for 4 minutes (microfuge® 18 centrifuge Beckman Coulter, Inc., Brea, CA).

The concentration of DTX in PBS was measured at different time points (Figure SI-1). DTX concentration increased to 11.5 µg/ml in the first 6 minutes, decreasing to approximately 5 µg/ml after about 45 min, and remaining constant at that concentration after that time. Therefore, once the filling process of the reservoir is complete (over 24 h) the DTX concentration inside the reservoir may reach an equilibrium state so that is expected that the concentration in the reservoir stays constant at equilibrium as long as there is DTX solid available in the reservoir.

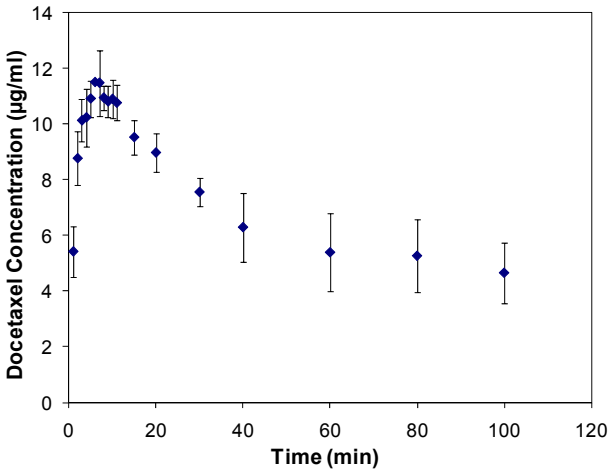

Figure SI-1 Docetaxel solubility equilibration time in PBS. Error bars represent one standard deviation in measured values. The experiment was repeated three times (n=3).

Discharge Time Measurement

TB loaded devices were actuated inside 20 ml glass scintillation vials filled with 4 ml BSA solution while a stereo microscope (Olympus SZ61, Olympus Imaging America, Inc. ,PA, USA) with a CCD

camera was used to take videos (33 frames/second) of TB solution discharge. Video frames were then extracted and the initial discharge velocity was obtained by measuring the TB solution travel distance in the first frame divided by the time taken for its travel (0.03 s). The distance was measured from the membrane surface in the direction perpendicular to the membrane surface using Image J, a general purpose open source image-processing package, and converted to magnetic field values using a characterization curve obtained previously{Pirmoradi, 2011 #95}.

Mixing time

Simulation was performed by considering isotropic diffusion in 2D with the reservoir size of 6 × 0.4 mm^2. The pumped-in fluid represented by a sphere has a radius of 0.1 mm, based on the maximum traveled distance presented in Table 1. The diffusion coefficient value for DTX was assumed to be equal to that of Paclitaxel ($D = 9 \times 10^{-10}$ m^2/s {Lawrence K. Fung, 1998 #13}) due to the similar molecular structures of the drugs. The initial concentration of DTX in the reservoir was set to 5 µg/ml or 0.0068 mol/m^3 (considering DTX molar mass of 807.88 g/mol) based on the DTX equilibrated aqueous solubility (Figure SI-1). The diffusion coefficient of TB was obtained based on extrapolation of the data reported by Inglesby and colleague{Inglesby, 2001 #14} and set to 4.35×10^{-11} m^2/s at 23°C. We set the initial concentration of TB solution in the reservoir to 1 mg/ml or ~1 mol/m^3 as a conservative measure.

Figure SI-2 shows the simulation results after 200 s from the time fluid was pumped into the reservoirs for both DTX and TB solutions. The average concentration of the pumped-in fluid over time can serve as a measure for determining the required mixing time (t_w) before each actuation cycle. This measure is presented in Figure 3 as the average concentration in the sphere domain over the average concentration in the entire reservoir for both DTX and TB solutions in the reservoirs. According to the data in Figure 3, if 200 s is allowed before each actuation, the average concentration of DTX and TB in the pumped-in fluid reaches 95% and 70% of that of the reservoir. Based on the simulation results, in all the experiments with DTX and TB, t_w was set to 200 s. Although, due to the lower diffusion coefficient of TB compared to DTX, a longer equilibration time is required for TB solution, similar wait times for both solutions were used for comparison purposes.

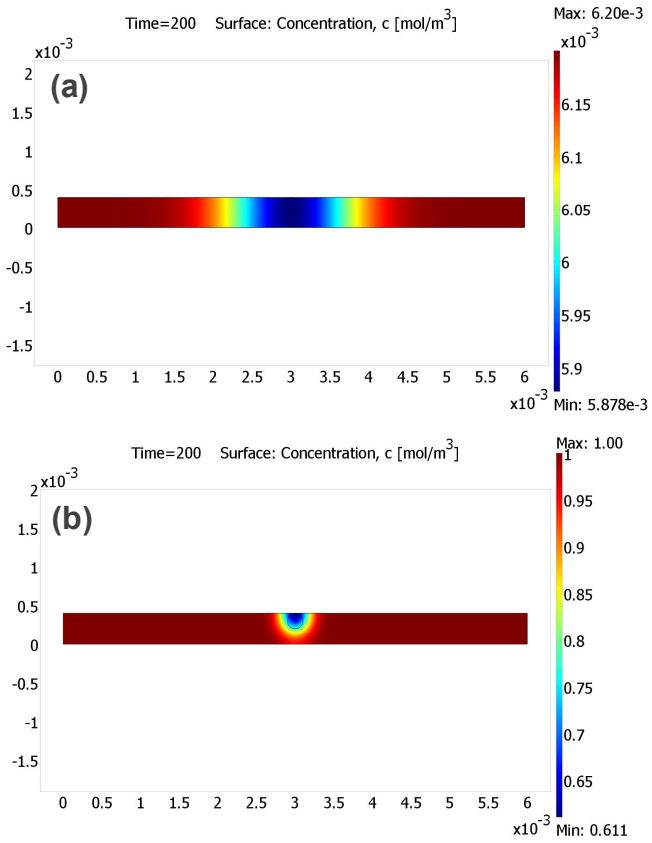

Figure SI-2 Diffusion transport of pumped-in fluid inside the reservoir filled with (a) DTX, and (b) TB, after 200s.

Membrane Deflection with Magnetic Field

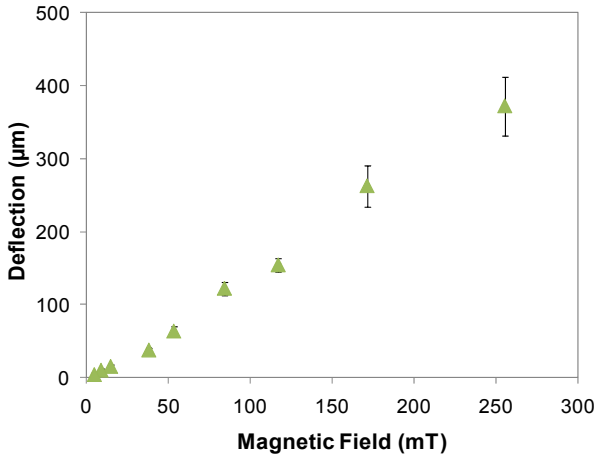

Figure SI-3 Membrane deflections obtained from released amounts of DTX in each actuation cycle under various magnetic fields.