Electronic Supplementary Material (ESI) for RSC Advances.

Supplementary Information

Fabrication process of the 3D-printed device

The 3D-printed device has a similar fabrication process to the PDMS device except for a few steps. The fabrication process of the 3D-printed device is demonstrated in Figure S1 and summarized here. *Step 1*: Drug reservoir and housing were made with a high precision Freeform Pico 3D printer (Asiga, CA, USA) using PlasClear, a UV curable polymer (Asiga, CA, USA). They were washed with IPA and cured in a UV chamber (Asiga, CA, USA) for 20 minutes. *Step 2*: MB solution was deposited in the reservoir and evaporated until the desired amount of solid MB was reached. *Step 3*: PDMS was spun on a PAA-coated glass slide with the same procedure (500 rpm for 10 s and 1500 rpm for 40 s). Before the PDMS was cured, the magnetic block was placed on the glass slide and the reservoir was subsequently placed so that the magnetic block was located in the center of the reservoir. The PDMS layer was cured at 70 °C for 4 hours. The glass slide was then immersed in water and the reservoir was released with a flat membrane glued to the walls by the adhesive nature of PDMS and a magnetic block at the center of the membrane. *Step 4*: An aperture was created in the center of the membrane similar to the 6th step in the fabrication of the PDMS device. *Step 5*: The housing was aligned with the reservoir and placed on it using a universal flip chip die-bonder (JFP Michrothechnic, Marcoussis, France). After placement, the two ends of the device were glued with two small droplets of PlasClear. The polymer droplets were partially cured with a UV spot cure system (Electro-Lite Corporation, Bethel, CT, USA) for 1 minute and then placed in a UV chamber for 20 minutes for additional curing. Once fabricated, the device was filled with BSA solution with a similar procedure.

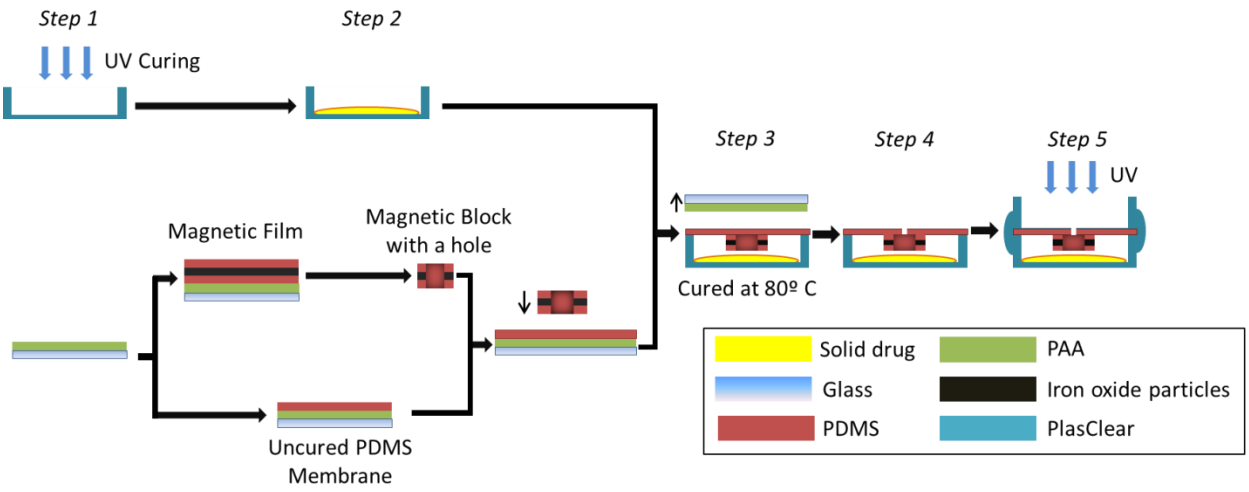

Figure S1 Fabrication steps of the 3D-printed device.

Magnetic field strength of the NdFeB permanent magnet

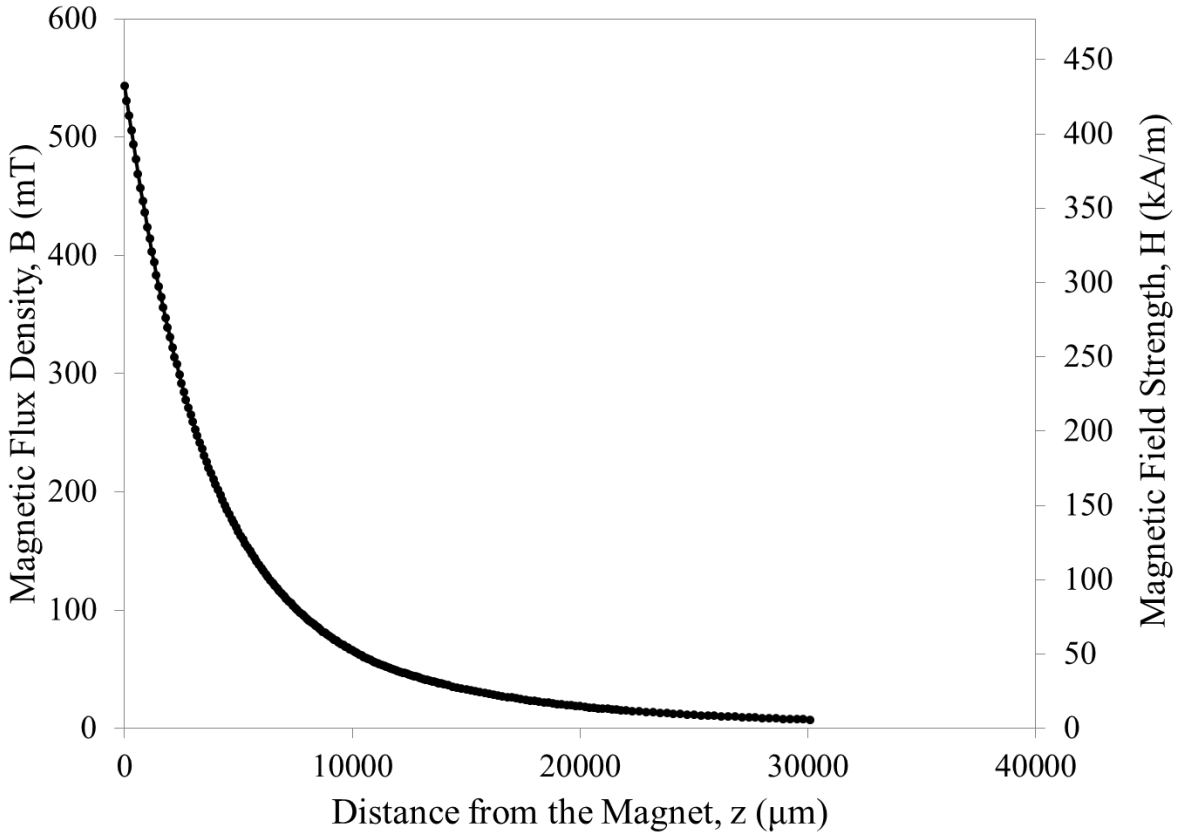

Figure S2 Magnetic flux density and magnetic field strength of the NdFeB permanent magnet as a function of distance from the surface of the magnet.

Magnetization of the magnetic film

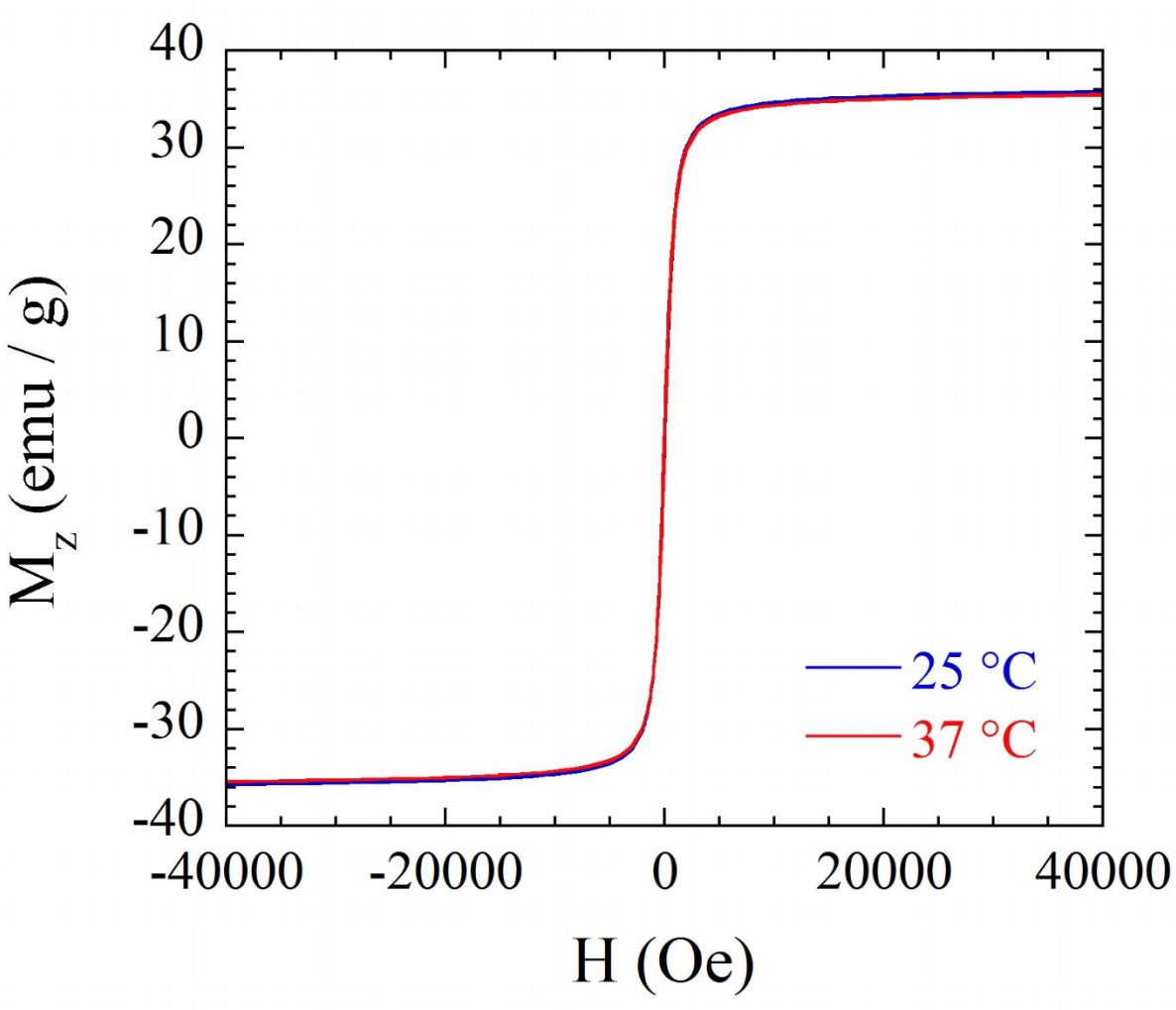

Figure S3 Magnetization curve of the magnetic film versus the applied magnetic field.

Release time

In order to release sufficient drug, the device may require actuation many times. This is due to the small displaced volume created by the movement of the membrane and the low solubility of DTX in water. In order to release repeated doses of drug in consecutive actuation cycles, the membrane should be given time to achieve maximum deflection. This way, we can ensure the volume of the released drug solution in each actuation cycle is constant and equal to the maximum displaced volume of the device. If the release time is too short, then the amount of released drug would be less than the maximum displaced volume. Therefore, drug release time is the minimum time required for the release of the maximum achievable volume of the discharged solution (equal to the maximum displaced volume, see Figure S4) under a specific magnetic field in a single actuation. In order to estimate drug release time, the velocity of the discharging solution from the aperture was measured.

An MB-loaded PDMS device was placed in a petri dish. The petri dish was then filled with 1% w/v BSA/PBS solution and placed on a stage. A stereo microscope (Olympus, MA, USA) was aligned horizontally and focused on the membrane. Drug release was recorded at 20 frames per second with a camera attached to the end of the microscope (Basler vision technologies, Ahrensburg, Germany). Therefore each frame follows a 50 ms interval.

Figure S5 shows the maximum travelled distance of the discharged MB in three different magnetic fields. As the magnetic field gradient becomes stronger, it exerts more force on the magnetic block, leading to an increase in the acceleration of the block. This causes the membrane to deflect faster and discharge the MB solution with a higher velocity.

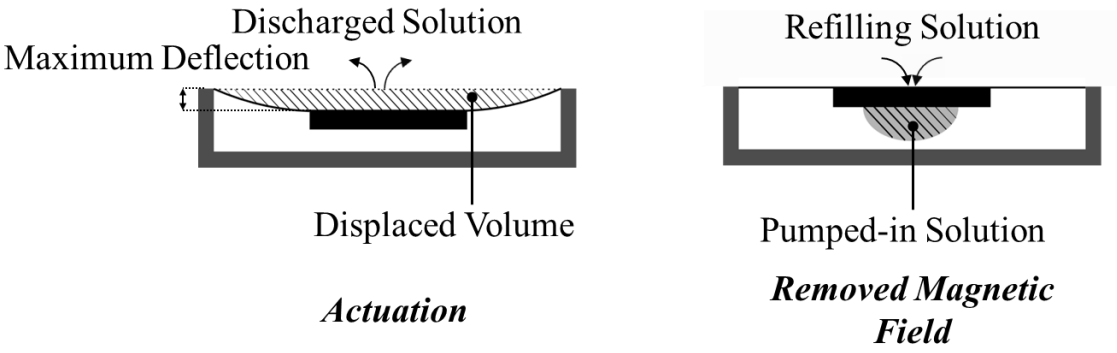

Figure S4 Displaced volume under actuation and pumped-in solution after removing the magnetic field.

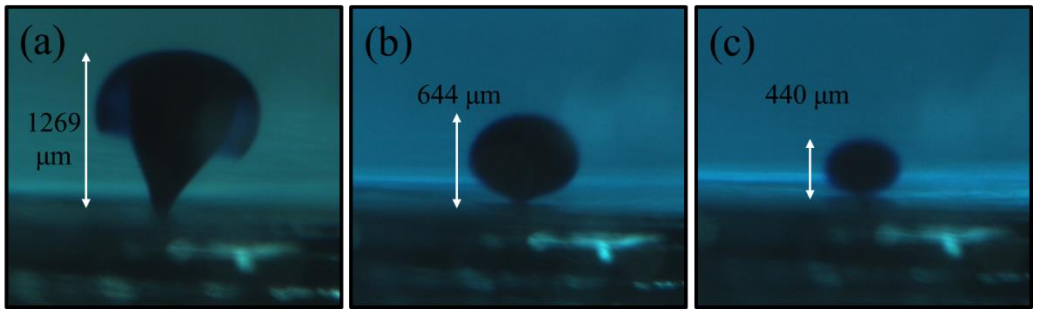

Figure S5 Maximum travelled distance of the discharged solution in (a) 135.7 mT, (b) 65.8 mT and (c) 32.9 mT magnetic fields.

Since the low concentrations of DTX, MB or BSA are unlikely to affect the viscosity of the water, the measured velocity of the released MB solution is assumed to be equal with the velocity of the discharged DTX solution. It is assumed that the velocity of the discharged solution is constant during the release time and equal to the initial velocity of the discharging solution. However, this is a simplifying assumption as the velocity of the released solution would probably decrease over time. Still, this simplified discharge velocity could be used for estimation purposes. Therefore, drug release time can be calculated from the following equation:

$$t_d = \frac{\Delta V}{A.v} \quad (1)$$

In which t_d is the time of release in seconds, ΔV is the stroke volume calculated from the simulated COMSOL model, A is the aperture area and v is the measured velocity of the released solution obtained from the first four frames of the recorded MB release videos. Drug release times in three different magnetic fields are demonstrated in Table S1.

Distance from Magnet (mm)	Magnetic Field (mT)	Maximum Travelled Distance (µm)	Initial Velocity (mm/s)	Displaced Volume (µl)	Release Time (s)
6	135.7	1269±74	4.4±0.5	1.5	34.1
10	65.8	644±25	1.4±0.2	0.6	42.9
15	32.9	440±28	0.6±0.1	0.2	33.3

Table S1 Estimated release time in different magnetic fields.

Mixing Time

Another important time constant required for continuous actuation of the device is the mixing time. Mixing time is the minimum time required for the concentration of the pumped-in solution to return to its saturation limit after the magnetic field is removed (see Figure S4). To obtain this time constant, Pirmoradi et al. solved the mass balance equation for transport using COMSOL Multiphysics software.[1] This equation is defined as follows:

$$\frac{\partial c}{\partial t} + u.\nabla c = \nabla.(D\nabla c) \quad (2)$$

Where c is the concentration, D is the diffusion coefficient and u is the velocity vector. The term $u.\nabla c$ on the left is the convective transport and the term on the right-hand side of the equation is the diffusive transport. In (2), the velocity field inside the reservoir was neglected since the mixing time required by the diffusion was longer than that of convection because of the low Péclet number (1 < Pe < 1000). Moreover, it was stated that the velocity field only existed for 0.1% of the total mixing time inside the reservoir which facilitates the mixing. So by ignoring the velocity field, an over-estimated value for the required mixing time inside the reservoir was obtained. Equation 2 was reduced to Fick's law for diffusive transport and solved in a 2D space with the assumption of isotropic diffusion. The mixing time for DTX with the diffusion coefficient of 9×10^{-10} m^2/s was calculated at t_m = 200 seconds. This is the time required for the pumped-in solution to reach 95% of the initial reservoir concentration.

Since our device has a smaller stroke volume in the same magnetic field compared to the device in reference [1] (for instance, 2.3 µl compared to 2.8 µl in a 230 mT magnetic field) the volume of the pumped-in solution after removing the magnetic field is smaller. Therefore the required mixing time for our device is smaller than 200 seconds. However, we use 200s mixing time for the in-vitro release studies. This over-estimated mixing time ensures consistent release rates of DTX per actuation.

References

1 F. N. Pirmoradi, J. K. Jackson, H. M. Burt and M. Chiao, *Lab Chip*, 2011, **11**, 3072-3080.