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SUPPORTING INFORMATION

CONTROLLING THE RESOLUTION AND DURATION OF PULSATILE RELEASE FROM INJECTABLE MAGNETIC 'PLUM-PUDDING' NANOCOMPOSITE HYDROGELS

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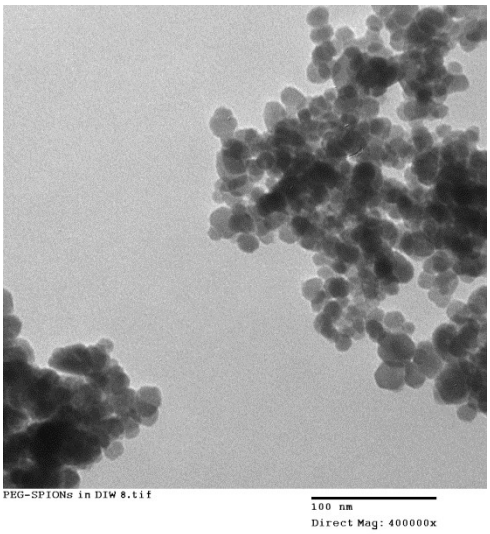

Figure S1: TEM image of PEG-functionalized SPIONS. The particle clustering on the copper grids, occurring during sample preparation for TEM, is typical of hydrophilic nanoparticles.

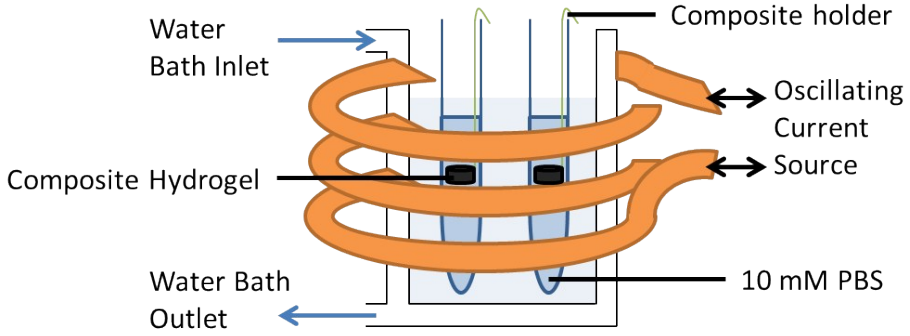

Figure S2: Schematic of the set up for AMF-mediated pulsatile release from nanocomposites capable of keeping the nanocomposites at a 37°C baseline temperature.

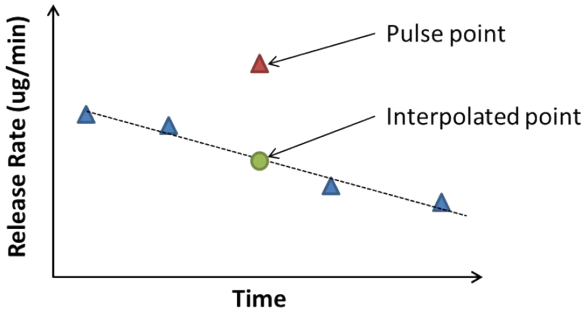

Figure S3: Representation of how the increase in the rate of the release is determined. From the rate of release results, the expected release rate is estimated by interpolating between the rates observed at the two (non-pulsed) time points prior to and two time points after pulsatile induction. The ratio between actual rate of release immediately after the AMF pulsed application (the pulse point) and the interpolated expected release point is taken as a percentage and is the increase in the rate of release at each given pulse time point (which there are 4-6 of per day).

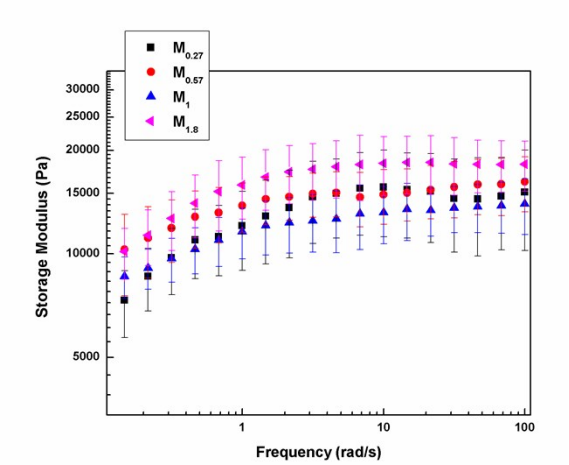

Figure S4: Storage modulus of nanocomposites prepared with differing PNIPMAM:PNIPAM contents with 8 wt% PNIPAM-Hzd/Dex-Ald precursor polymers.

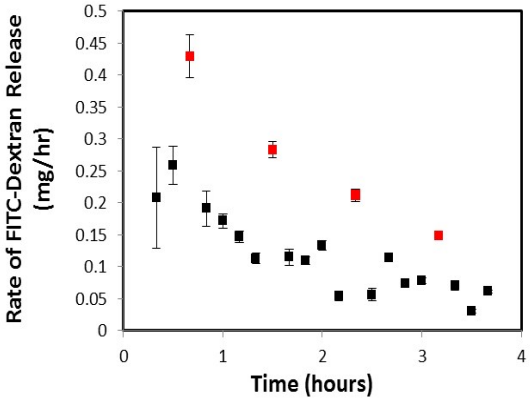

Figure S5: Representative release profile (expressed as rate of drug release) of 4 kDa FITC-Dex during the first day of a pulsatile release test: 8 wt% hydrogel, 8 wt% microgel, 5 wt% PEG-SPIONs, and 1 wt% 4 kDa FITC-Dex. The composite was incubated at 37°C. The red dots indicate the rate of release for the measured time point immediately after applying the AMF on the sample, showing the increase in the rate of release due to an AMF pulse, and the release rates that were compared to the points around them to determine the increase in the rate of release.

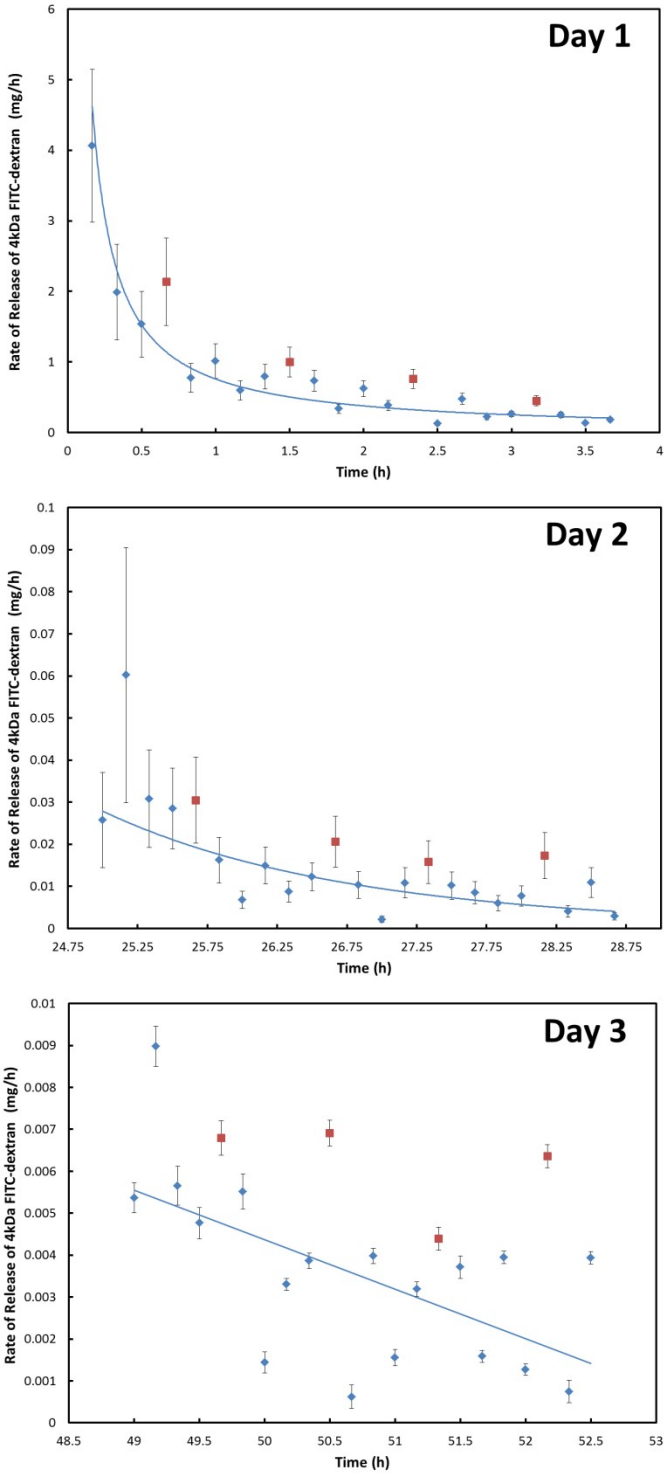

Figure S6: Representative rates of release plots over multiple days (1-3), with the point immediately following the pulse shown in red and the baseline release points and curve shown in blue dots and the blue trend line, respectively. There is a decrease in the release rate throughout this entire period as the amount of drug remaining in the nanocomposites decreases over time. This particular example is the experimental data for the 8 wt% $M_{1.8}$ microgel nanocomposite.

Table S1: Excess 4 kDa FITC-Dex released over the duration of the magnetic pulse for composites made with microgels with different formulations

	Extra Drug Released During Pulses (µg)			
Test Name	Day 1	Day 2	Day 3	Day 5
$M_{1.8}$	21 ± 5	0.42 ± 0.07	0.13 ± 0.04	0.02 ± 0.01
M_{1}	18 ± 2	0.35 ± 0.02	0.10 ± 0.01	0.02 ± 0.01
$M_{0.56}$	20 ± 2	0.10 ± 0.02	0.02 ± 0.01	-0.03 ± 0.03
$M_{0.27}$	14 ± 5	0.07 ± 0.04	0.00 ± 0.01	-0.04 ± 0.05

Table S2: The volume fraction of the nanocomposite corresponding to microgel, the volume fraction of the gel that becomes free volume at 37°C and 43°C due to heating, and the resulting increase in free volume fraction due to AMF activation (i.e. magnetic heating to 43°C from a 37°C baseline temperature).

Wt% Microgel	$10M_{1.8}$	$8M_{1.8}$	$6M_{1.8}$	$4M_{1.8}$	$0M_{1.8}$
Vol % Microgel	7.02	5.62	4.21	2.81	0
Vol% Pore Network at 37°C (change between 25°C and 37°C)	5.61	4.49	3.37	2.24	0
Vol% Pore Network at 43°C (change between 25°C and 43°C)	6.95	5.56	4.17	2.78	0
Change in Vol% Pore Network Between 37°C and 43°C	1.34	1.07	0.80	0.54	0

Table S3: Average excess 4kDa FITC-Dex released over the duration of an AMF pulse for composites made with different microgel contents.

	Extra Drug Released During Pulses (µg)			
Microgel Content	Day 1	Day 2	Day 3	Day 5
10 $M_{1.8}$	25 ± 6	0.71 ± 0.07	0.12 ± 0.03	0.02 ± 0.01
8 $M_{1.8}$	21 ± 5	0.42 ± 0.07	0.13 ± 0.05	0.02 ± 0.03
6 $M_{1.8}$	27 ± 3	0.28 ± 0.04	0.12 ± 0.04	0.03 ± 0.01
4 $M_{1.8}$	21 ± 3	0.22 ± 0.08	0.01 ± 0.04	-0.01 ± 0.02
0 $M_{1.8}$	16 ± 3	0.01 ± 0.09	0.01 ± 0.08	NA

Table S4: Average excess 4 kDa FITC-Dex released over the duration of an AMF pulse for composites with different swelling behaviours.

% CMC (remainder Dex)	Extra Drug Released During Pulses (µg)			
	Day 1	Day 2	Day 3	Day 5
100 CMC	15 ± 1	0.29 ± 0.08	0.05 ± 0.01	-0.04 ± 0.07
75 CMC	15 ± 4	0.28 ± 0.11	0.03 ±0.01	-0.02 ± 0.05
50 CMC	15 ± 2	0.58 ± 0.09	0.16 ±0.02	0.07 ± 0.02
25 CMC	41 ± 5	0.57 ± 0.12	0.19 ±0.02	0.10± 0.02
0 CMC	36 ± 9	0.38 ± 0.10	0.04 ±0.01	0.03 ± 0.01

Table S5: Average excess 4 kDa FITC-Dex released over the duration of an AMF pulse for 8wt% $M_{1.8}$ composites exposed to different durations of applied AMF pulses.

Pulse Time	Extra Drug Released During Pulses (µg)			
	Day 1	Day 2	Day 3	Day 5
10 min	21 ± 5	0.42 ± 0.07	0.13 ± 0.05	0.02 ± 0.03
20 min	23 ± 2	0.47 ± 0.03	0.12 ± 0.06	0.02 ± 0.02

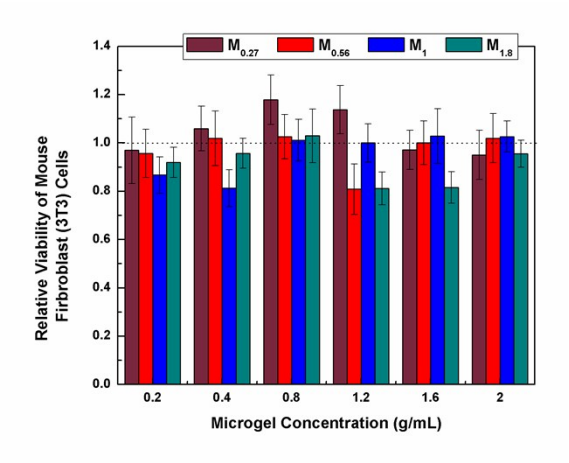

Figure S7: Relative viability of 3T3 mouse fibroblast cells after a 24 hour exposure to various microgel compositions in an MTT assay.