Supporting Information

for *Adv. Healthcare Mater.*, DOI: 10.1002/adhm.201300260

Rapid and extensive collapse from electrically responsive macroporous hydrogels

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Sample preparation for x-ray microtomography imaging: Barium Sulfate ($BaSO_4$) was used as a contrast enhancer for x-ray microtomography (μCT) imaging. After gelation or cryogelation, hydrogels were allowed to swell for 3 days in a 50% wt $BaSO_4$ and deionized water mixture under constant but light stirring. This allowed for the gels to fully swell and remain hydrated while concentrated $BaSO_4$ filled any macropore space that may have been present in the samples. Therefore, when imaged using a X-Tek, HMXST225 μCT x-ray imaging system, macropores appeared as high attenuation "white" spots whereas hydrogel space appeared as low attenuation "dark" space. Inverse images for the 2D and 3D images are provided in Figure 1a, where pore space is represented by black space in 2D renderings and open uncoloured space in 3D renderings.

Sample preparation for scanning electron imaging: For scanning electron microscopy (SEM) images of cryogels before and after electrical exposure, 4% wt AAc, 4% wt AAm, 0.1% wt BA cryogels were used. The "before" cryogel was cryogelated, thawed, allowed to swell overnight, and rinsed three times in deionized water before being cut along its cross-section and flash-frozen by submersion in liquid nitrogen for 2 minutes. The sample was then lyophilized for 3 days and platinum-palladium sputtercoated. The cross-sectional SEM image was obtained using a Zeiss FESEM Supra55VP.

For "after" SEM images, a 4% wt AAc, 4% wt AAm, 0.1% wt BA cryogel was created and collapsed according to the protocols outlined above using 50 V for 10 minutes. The collapsed cryogel was then quickly cut along its cross-section and flash-frozen by submersion in liquid nitrogen for 2 minutes. It was then lyophilized and sputtercoated and imaged similarly to the "before" sample.

The respective roles of electric field, pH changes, and inoic strength on gel collapse: The rapid and extensive volumetric collapse observed from the electrogels required electric field exposure, while pH and ionic strength changes played a less significant, secondary role. Determining the roles of pH and ionic strength was important since it was previously shown that both pH and ionic content affected swelling and deswelling of polyelectrolytic hydrogels.[S1] When initial pH was set at 7, macroporous gels (4% wt AAc, 4% wt AAm, 0.1% wt BA) collapsed rapidly when exposed to 50 V and did not collapse when unstimulated (Figure S2a, i). pH did increase from 7 to10.5 when these gels were exposed to 50 V in deionized water (Figure S2a, ii). Both voltage and gel presence were required to increase the pH, as that was the only condition that allowed for electrical current and therefore electrolysis at the electrode-medium interface. To determine if this increase in pH was responsible for the rapid and extensive gel collapse, the pH was manually increased to 13 at time $t = 0$ through the addition of NaOH and gel collapse was monitored with and without electrical stimulation (Figure S2b). Gels not exposed to electric field did begin to collapse starting at time $t = 0$ (Figure S2b, red curve). However, the rate and degree of collapse was not nearly as fast or extensive as observed under voltage (50 V exposure with initial pH =7, Figure S2a, i, blue curve). We hypothesized that the slight collapse observed in these gels was a result of the sudden introduction of cations to the media and not necessarily the change in pH. A similar experiment was then run where NaCl was introduced at a molar equivalent level, in lieu of NaOH (Figure S2c). Indeed, gels that were not exposed to voltage collapsed at similar rates

and degrees when submerged in 100 mM NaCl instead of NaOH (compare red curves in Figure S2b and c). These data indicate that while pH and ionic strength do play roles in gel collapse, electric fields are the primary driving force behind the observed rapid and extensive collapses.

[S1] P. Calvert, in Electroactive Polymer (EAP) Actuators as Artificial Muscles: Reality, Potential, and Challenges, 2nd Ed. (Ed: Y. Bar-Cohen), SPIE Press, Bellingham, Washington, USA **2004**, Ch. 5.

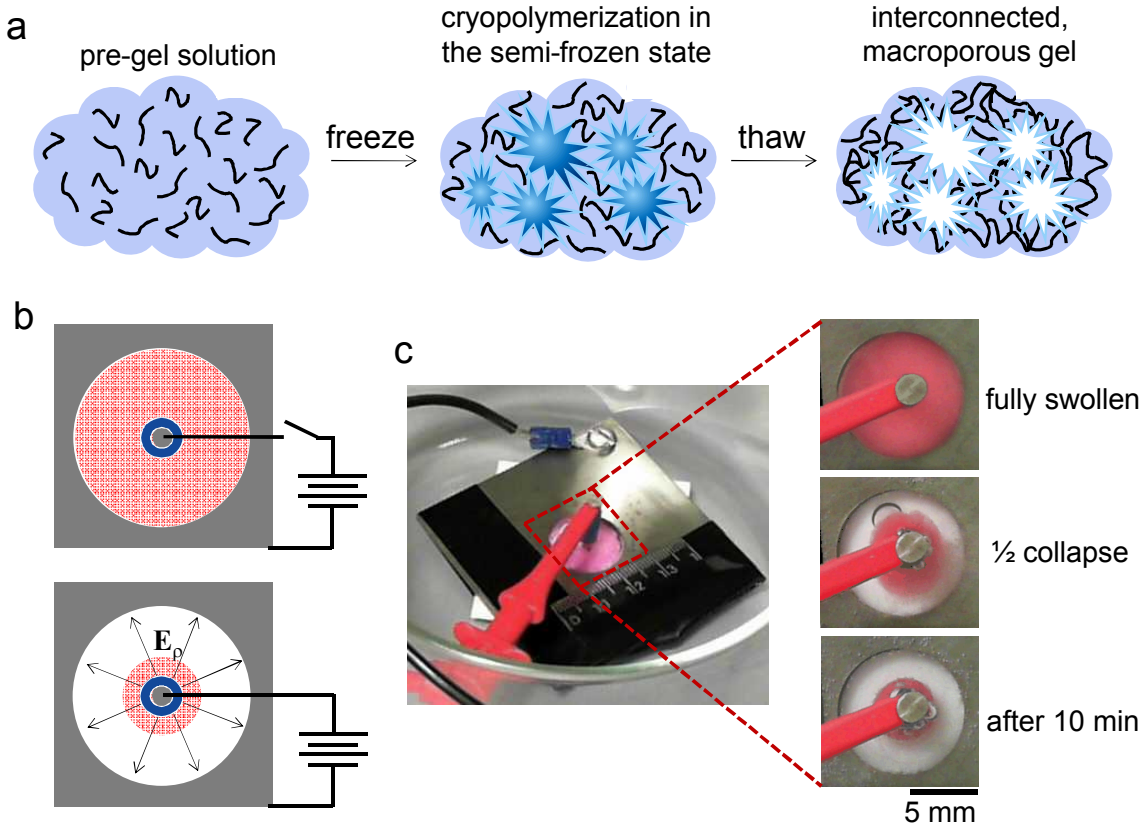

Figure S1. The polyanionic, macroporous gels used in this study are made with a cryopolymerization approach and can be monitored in an experimental apparatus capable of collapsing polyanionic gels inward by generating an outward, radial electric field. a) A pre-gel solution is prepared by mixing monomers and/or polymers, freezing that solution during the polymerization process to generate ice crystals, and thawing the gel after polymerization, leaving interconnected voids (or pores) where the ice crystals once existed. b) A schematic of the experimental apparatus is shown to illustrate placement of the gel (top; pink), the directionality of the electric field used to stimulate the gels and the direction of expected gel collapse (bottom). c) A photograph of the experimental apparatus (left) and snapshots of a gel, colored with encapsulated polystyrene beads, collapsing under electrical stimulation (right from top to bottom). Electrical responsivity tests can take place with gels submerged in different solutions.

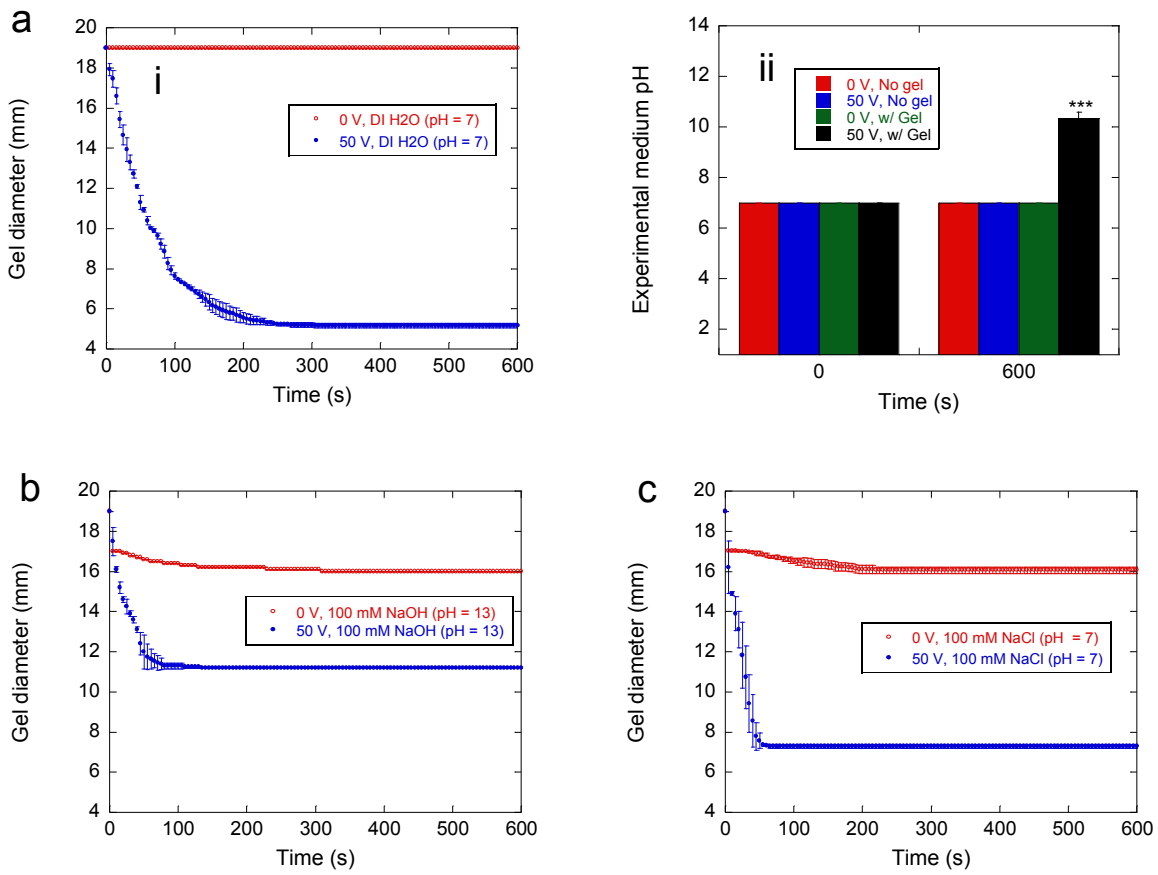

Figure S2. Electric field exposure is required for rapid and extensive gel collapse while the pH and ionic strength of the experimental media play a secondary role. a) (i) Comparison of the collapse of 4% wt AAc, 4% wt AAm, 0.1% wt BA gels when exposed (blue) and not exposed (red) to 50 V. (ii) pH was measured before (t = 0 s) and after (t = 600 s) experiments where 0 or 50 V was used, with and without gels present. b) Collapse over time for gels exposed to 50 V (blue) or 0 V (red) when pH was changed from 7 to 13 at time t = 0 through the addition of NaOH. c) Collapse over time for gels exposed to 50 V (blue) or 0 V (red) when the solution was changed to 100 mM NaCl at time t = 0 through the addition of NaCl. In (a) through (c), gel diameter vs time values represent mean and standard deviation (N = 3). In (a), part ii, N = 4 and statistical significance was calculated comparing data at 600 s to data at 0 s. *** indicates $p \leq 0.001$.

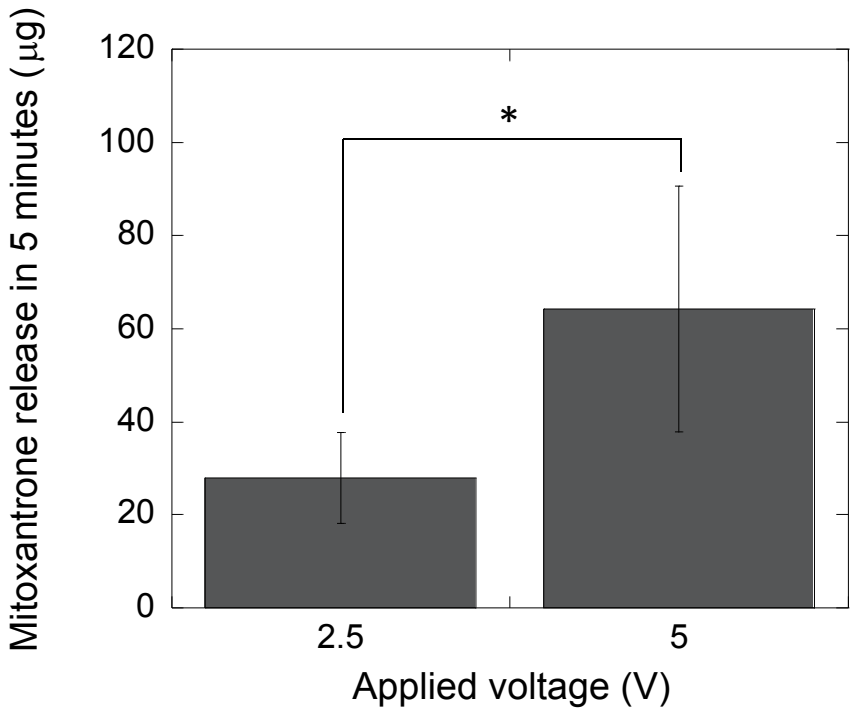

Figure S3. Drug release is regulated by applied voltage. The cumulative amounts of mitoxantrone released during 5 minutes of electrical stimulation in PBS as a function of applied voltage. Values represent mean and standard deviation (N = 4). * indicates $p \leq 0.05$.

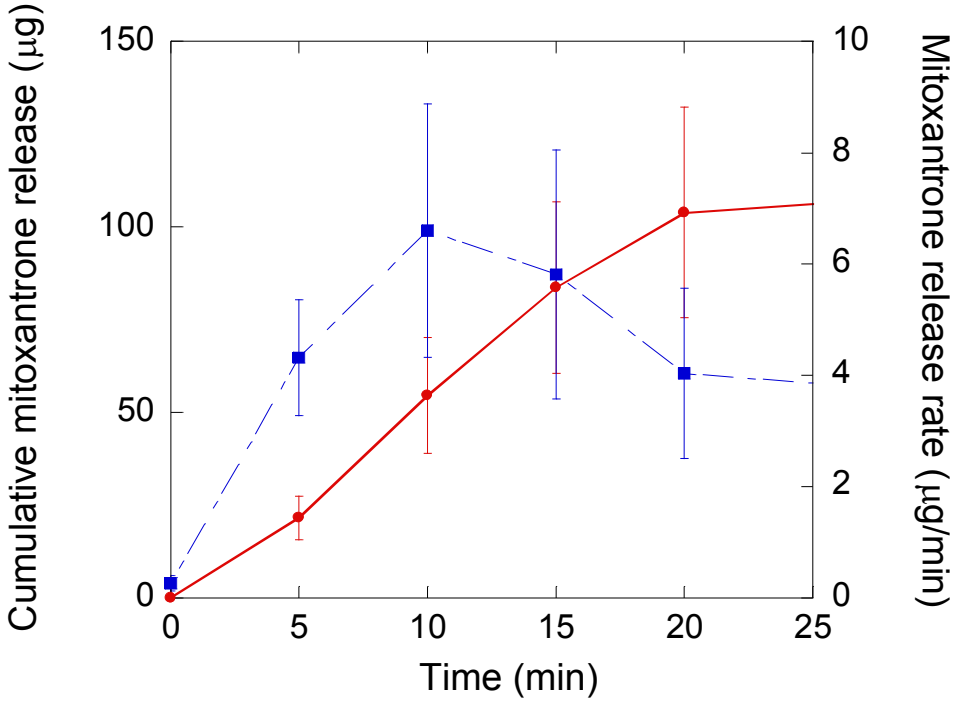

Figure S4. Cumulative drug release can be increased by extending voltage exposure, though release rate is not constant. 9% wt AAc cryogels crosslinked with 1% wt PEG-DM were loaded with mitoxantrone and exposed to 2.5 V for 25 minutes in PBS. Cumulative mitoxantrone release (red curve, left *y*-axis) and release rate (blue dashed curve, right *y*-axis) are plotted over time. Values represent mean and standard deviation (N = 4).