Electronic Supplementary Material (ESI) for Journal of Materials Chemistry B.

Drug delivery via a 3D electro-swellable conjugated polymer hydrogel

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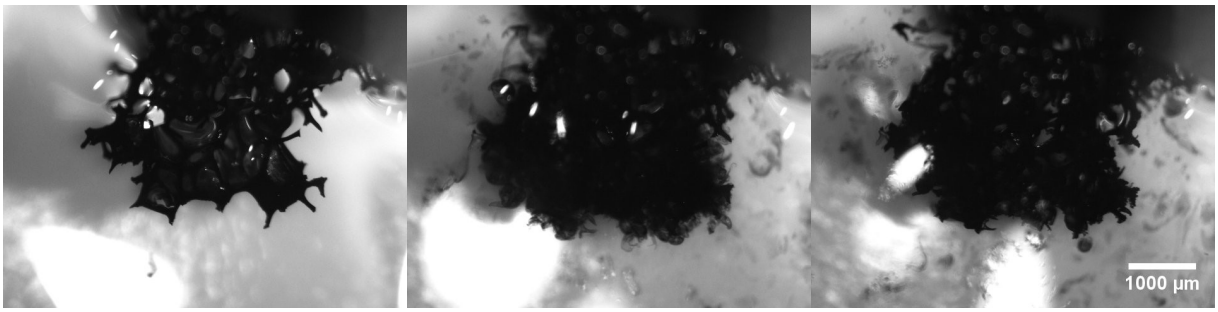

Figure S1 *Representative images of a carbon sponge coated with p(g3T2) in KCl 0.01 M during pristine, expansion and contraction (from left to right, respectively).*

Therapeutic Category	***Charge***	***Drug***	***Molecular weight (g/mol)***	***Typical Dose***	***C_{max}***	***Method of Administration***	***Reference***
Hormone Therapy	*+1*	*Leuprolide*	*1209.5*	*Varies*	*4.6 - 212 ng/mL*	*Subcutaneous or intramuscular injection*	*https://go.drugbank.com/drugs/DB00007*
	+1	*Octreotide*	*1019.24*	*Varies*	*2.5-5.3 ng/mL*	*Subcutaneous or intramuscular injection*	*https://go.drugbank.com/drugs/DB00104*
	+1	*Desmopressin*	*1069.22*	*Varies*	*4-8.1 pg/mL*	*Oral (tablets or nasal solution)*	*https://go.drugbank.com/drugs/DB00035*
Thyroid diseases	*-0.3*	*Thyroxine*	*776.87*	*0.05 – 500 mcg per day*	*Not available*	*Oral tablets*	*https://go.drugbank.com/drugs/DB00451*
Coagulation	*Anionic*	*Heparin*	*3-30k*	*10-100 USPU/mL*	*Not Available*	*Intravenous*	*https://go.drugbank.com/drugs/DB01109*

Table ST1: Typical therapies that require spatio-temporal release of drugs. The table summarizes the drug currently employed for each case, together with the charge, the molecular weight, the typical dose administered with current methods, the maximum concentration (C_{max}) reaching the site of interest and the database where the data were taken.

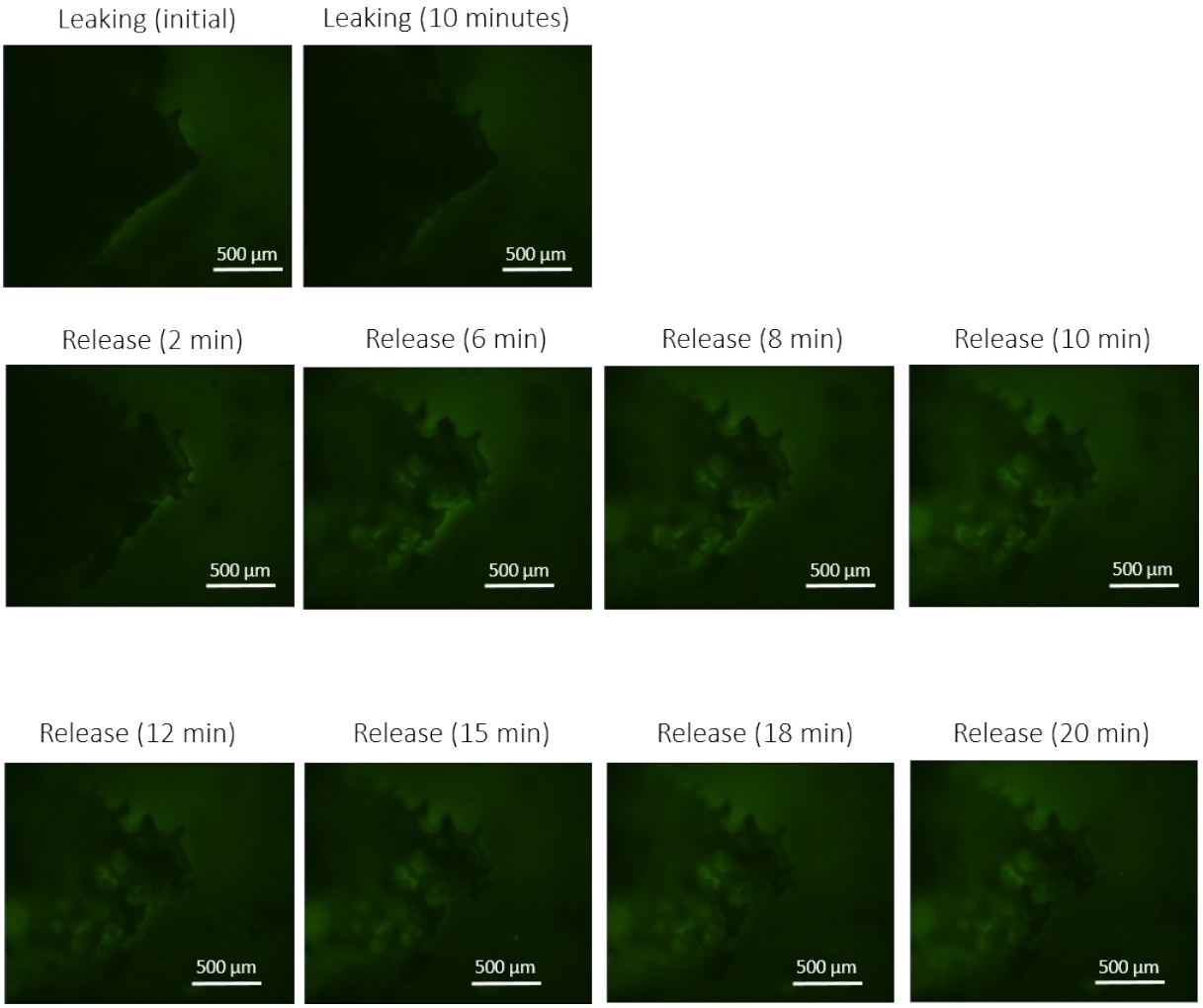

Figure S2 *Representative microscopy images of p(g3T2)-coated sponge loaded with Insulin-FITC at selected time points for the leaking and the active release conditions. A fluorescent corona can be appreciated around the sponge perimeter during the whole leaking duration, indicating that the Insulin-FITC was successfully loaded. During the first minutes of release, the polymer contracts and the labelled protein diffuses in the electrolyte.*

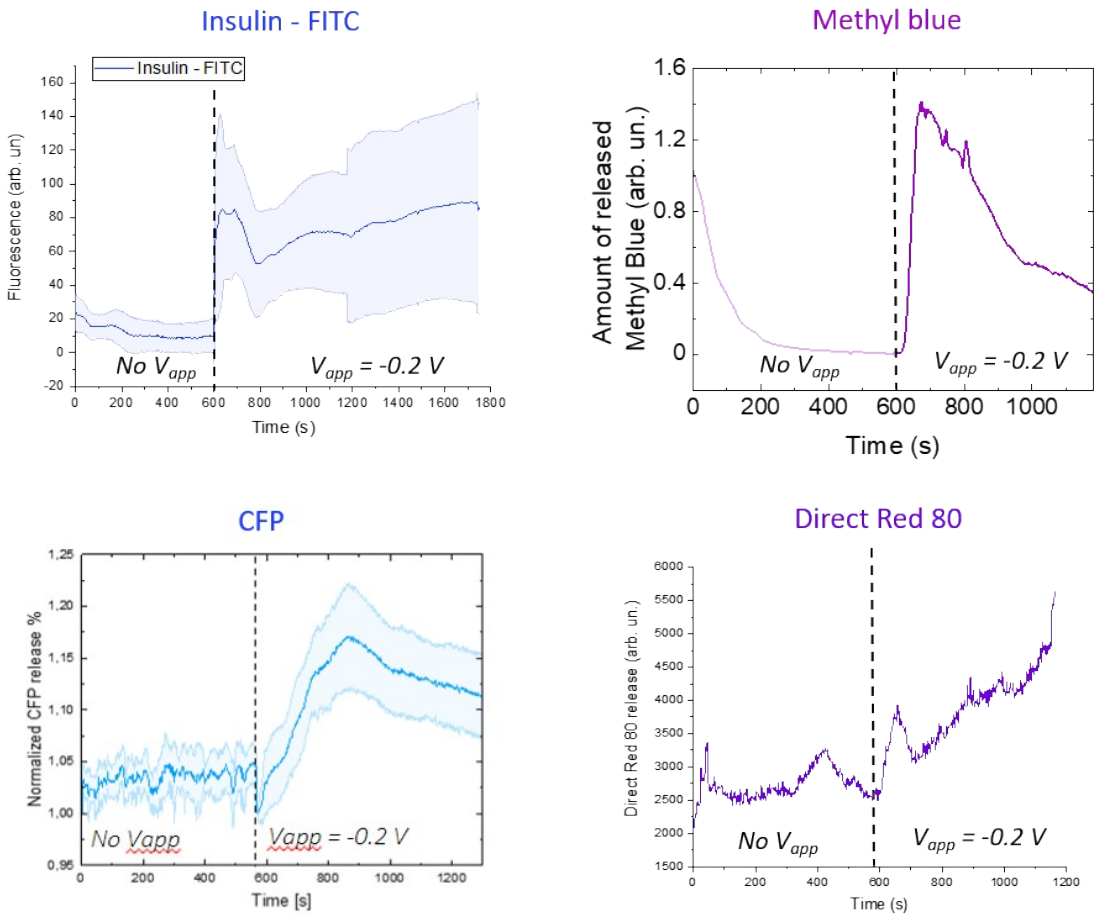

Figure S3 *Representative dynamics of Insulin – FITC, Methyl Blue (reported from Figure 2), CFP and Direct Red 80 during leaking (No Vapp) and release (Vapp = -0.2 V).*

Released Insulin

Negative control
(KCl 0.01 M)

Positive controls

5 ug/L

1.7 ug/L

Figure S4 *Representative images of the reaction occurring during the ELISA insulin test. The insulin released from the polymer binds to the insulin-specific antibody, generating a blue colour due to the reaction with the detector antibody. The negative control, KCl with no insulin, does not induce any colour change as expected. As a positive control we tested solutions of insulin of known concentration. For both concentrations the reaction with the antibodies occurs resulting in the blue color.*

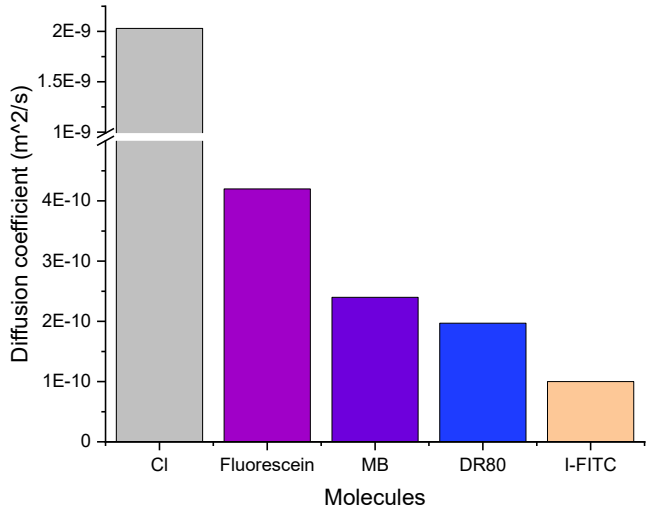

Figure S5 *Diffusion coefficient in water for the different molecules compared to the Cl anions, reported from: Cl* [1], *Fluorescein* [2], *MB* [3], *DR80* [4], *I-FITC* [5].

Supporting Note 1*: We define the release efficiency as*

$eff = mol_{released}/mol_{loaded,}$

where

$mol_{loaded} = C_{loaded} * V_{swollen\_polymer}$,

$mol_{\_released} = C_{\_released} * V_{\_chamber}$,

$mol_{\_after\_loading} = C_{\_after\_loading} * V_{\_chamber\_after\ loading}$

$V_{\_chamber\_after\ loading} = V_{\_chamber} - V_{swollen\_polymer}$

and

$C_{\_loaded} = C_{loading\_sol} - C_{after\_loading}$.

With $C_{loading\_sol}$ *(known concentration) before loading the sponge;* $C_{after\_loading}$ *being the concentration of the solution in the well after the loading (extracted from the calibration curve). The loaded concentration,* $C_{\_loaded}$ *can be calculated as the difference between the two. As it is not possible to directly measure or to extract the* $V_{\_swollen\_polymer}$ *or the* $V_{\_chamber\_after\ loading}$ *since the sponge has a complex geometry and the expansion is inhomogeneous in such a 3D structure, we estimated the efficiency by combining the information of the current and the measured released amount using absorption or fluorescence.*

Assuming that for every hole injected or extracted from the polymer, one anion will be expelled or injected accordingly, we extracted the moles of released anions as

$$Q = \int Idt$$

$mol_{\_current} = Q/(nF)$ *(where F is the Faraday constant in C/mol and n is the net charge)*

However, the solution contains both Cl anions and the negatively charged dye, so we calculated the fraction of dye that contributes to the current by comparing the moles calculated by the current and the moles calculated from the absorption of the dye when released.

We define the dye fraction $X_{\_dye}$ *as*

$X_{\_dye} = mol_{\_rel\_abs} / mol_{\_current}$

Then we assumed that the fraction of the current is the same for release and loading and therefore calculated the loaded amount from the moles calculated from the loading current ($mol_{\_loaded\_current}$*) as:*

$mol_{\_loaded} = mol_{\_loaded\_current} * X_{\_dye}$

Hence the efficiency as:

$Eff = mol_{\_rel\_abs} / mol_{\_loaded}$

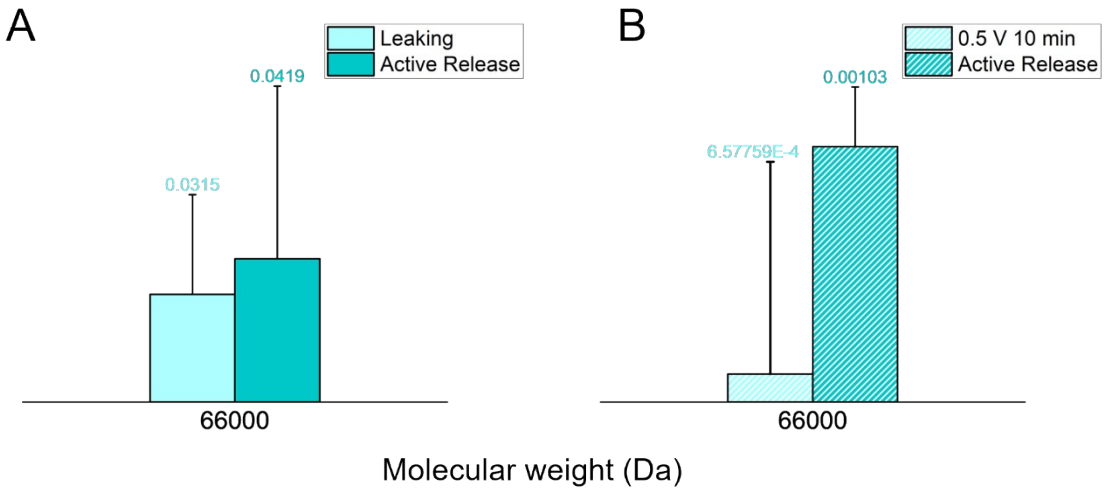

Figure S6 *Release of FITC conjugated Bovine Serum Albumin after leaking (A) and holding (B) conditions. The data represent the average + SD. The labels reported on each bar show the concentration (mg/ml) recorded at the end of each condition. There is no significant difference between the leaking or the holding and the active release.*

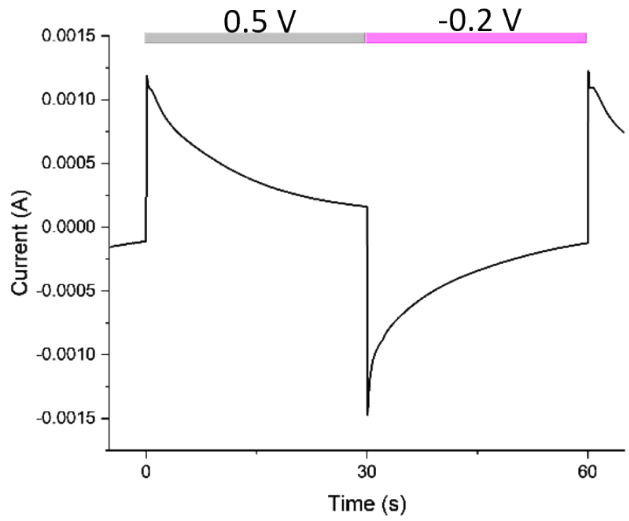

Figure S7 *Charging and discharging behaviour of the p(g3t2)-coated sponge recorded in KCl 0.01 M.*

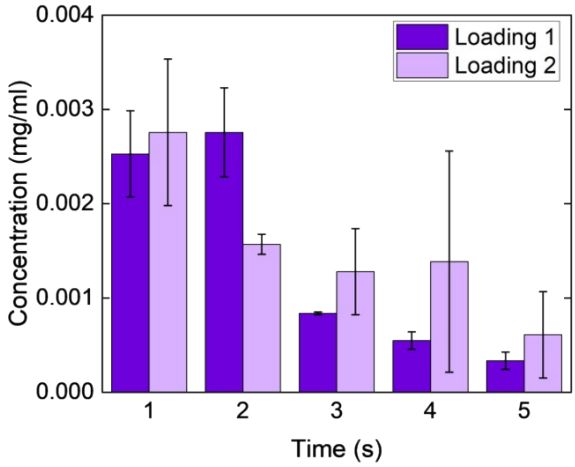

Figure S8 *Concentration of Direct Red 80 released at each pulse after two consecutive loadings of the p(g3t2)-coated sponge.*

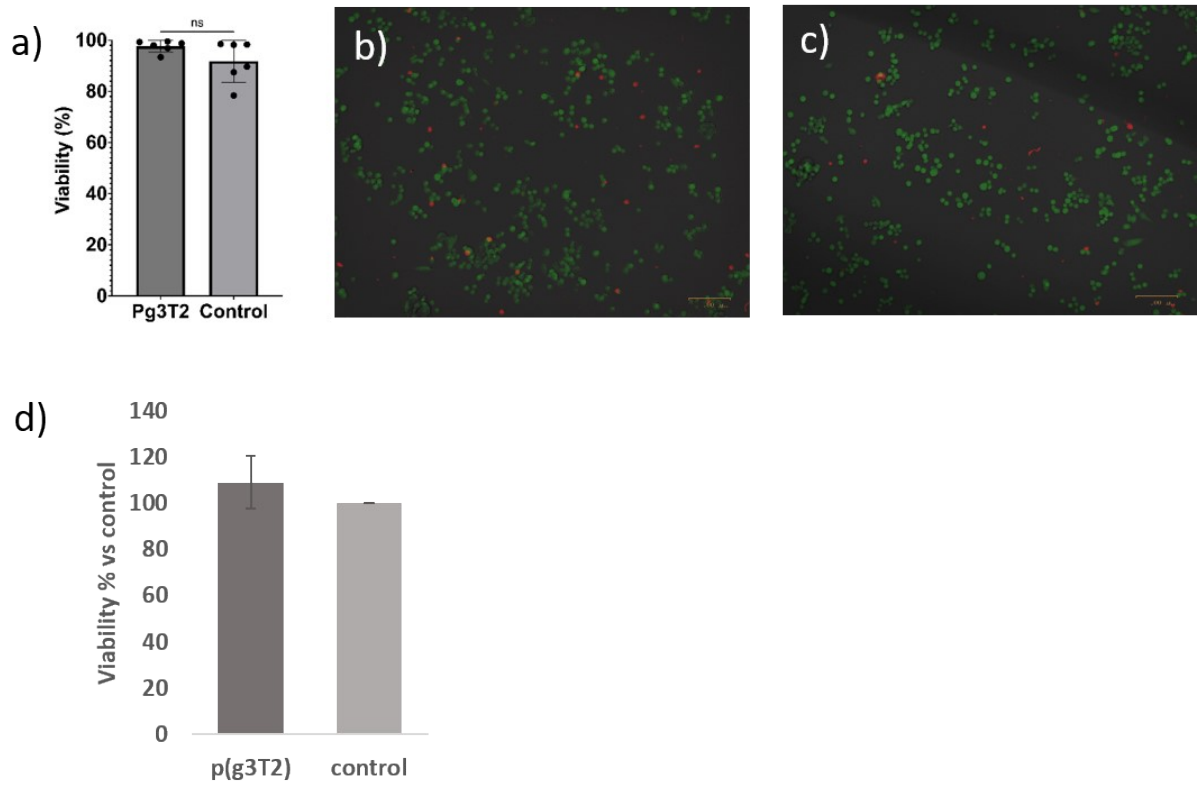

Figure S9 *Biocompatibility of p(g3T2) with Live/dead staining. a) Live/Dead staining average values after cells were incubated on top of p(g3T2) for 24 hours. Data are presented as mean +/- SD. Mann-Whitney test was used to significance. (n=6 replicates per group) (b,c) Representative images of (b) control sample and (c) p(g3T2) treated labware with living cells depicted in green and dead cells in red. Biocomptability of p(g3T2) with Alamar Blue test (d). The results are reported as mean +/- SD.*

References

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