Smart Hybrid Graphene Hydrogels: A Study of the Different Responses to Mechanical Stretching Stimulus

Jose M. González-Domínguez,^{†,||} Cristina Martín,^{†,||} Óscar J. Durá,[‡] Sonia Merino,^{†,§} and Ester Vázquez^{*,†,§,||}

[†]Instituto Regional de Investigación Científica Aplicada (IRICA), [‡]Department of Applied Physics, and [§]Facultad de Ciencias y Tecnologías Químicas, Universidad de Castilla-La Mancha, Avenida Camilo José Cela S/N, 13071 Ciudad Real, Spain

ABSTRACT: Polymer-based hydrogels, in particular those containing nanoscale fillers, are currently regarded as promising candidates for a plethora of applications. With respect to graphene, the vast majority of publications concern chemical derivatives, and, as a consequence, knowledge of the potential of pristine graphene within these systems is lacking. In this study, novel graphene-based hydrogels containing nonoxidized graphene have been prepared by a mild aqueous process. The mechanical and electrical properties of these hybrid materials were characterized. In the compositions studied, maximum improvements of Young's modulus, ultimate tensile strength, and toughness of 30, 100, and 70% were obtained, respectively. In addition to obtaining an improved hybrid material in terms of mechanical and electrical properties, the response experienced by these systems on applying mechanical stretching was evaluated and stimuli-response behavior is generated by the presence of graphene. Two different kinds of responses were found. A significant change in electrical resistance was observed and with a strain gauge effect, with an average gauge factor of ~ 9 (for 30% strain). The electromechanical performance of these hybrid hydrogels was tested for a range of mechanical strains and graphene contents, and the stability of these materials was assessed with successive stretching cycles. It was also observed that upon stretching these hybrid hydrogels were able to release the internalized water more efficiently in the presence of graphene, and, as a result, a second possible stimulus response was studied in the form of controlled drug delivery as a proof of concept. The release of a loaded aqueous solution of ibuprofen stimulated by controlled stretching and aided by wet capillary was studied. Much more efficient delivery was achieved in the presence of graphene. These novel systems can be used in the future for sensing or drug-delivery applications.

KEYWORDS: graphene, hydrogel, physical properties, stretching, strain gauge, drug delivery

INTRODUCTION

Several years ago, polymeric hydrogel materials experienced a major breakthrough due to the design of the first examples of systems that were capable of reacting to external stimuli. In certain situations, the so-called “smart” hydrogels may experience structural changes (expansion, shrinkage) upon induced alterations in their environment, thus leading to the release of an internal payload, the self-reparation of cleaved cross-linked parts of the network, or even changing their optical properties (such as transparency, brightness, etc.).¹ Conventional hydrogels have shown enormous potential in regenerative medicine and tissue engineering for decades,^{2,3} but the new synthetic systems with tailored stimuli-response properties are further motivating their study and possible application in medicine.^{4,5} Perhaps the most widely addressed application of smart hydrogels in medicine is drug delivery. As an example, Matsuo and colleagues⁶ fabricated an acrylate hydrogel patch that was capable of overcoming human skin physical barriers and delivering antigenic proteins directly across the stratum corneum tissue, thus revealing the potential

of this hydrogel for an eventual in vivo transdermal drug administration.

In recent years, there has been a growing interest in reinforcing polymeric hydrogels with nanosized fillers to improve and tailor their often poor mechanical consistence. One of the nanostructures that is currently under intense investigation is graphene, which consists of fascinating two-dimensional sp^2 -bonded monoatomic carbon sheets. Indeed, a large number of studies have been carried out on graphene-containing hydrogel hybrids, but most of them are limited to the use of graphene oxide (GO) and reduced graphene oxide (rGO).^{1,7} It is widely reported that GO/rGO-based hydrogels, either in combination with a polymer or not, may present improved mechanical features, self-healing ability, or even a response to thermal stimuli, such as near-infrared (NIR) radiation.^{1,7} Nevertheless, there is an intrinsic physical property that has not been addressed in such systems, namely, the

Received: September 22, 2017

Accepted: December 21, 2017

Published: December 21, 2017

Figure 1. Preparation scheme for a hybrid graphene hydrogel (above) and a picture of representative test samples (below). The BMG contents from left to right are 0.01, 0.025, 0.04, 0.05, and 0.1 wt %. The inset is a representative scanning electron microscopy image showing the porous structure at the maximum swelling degree (see ref 13). Reproduced from ref 13. Copyright 2017, Nature Publishing Group.

electrical conductivity. The electrically insulating nature of GO (and most of the rGO derivatives) seriously hinders the use of graphene-based hydrogels in applications stemming from electrical properties, despite the fact that these nanostructures are easy to prepare and are commonly employed in many laboratories. Given the possibility of obtaining two-dimensional conductive nanoparticles, such as pristine (nonoxidized) graphene, new avenues would be open for hydrogels prepared from this material. For example, stimulus-response properties involving electrical conductivity would justify the greater difficulty in preparing the pristine graphene.

The nanofillers contained in a cross-linked polymer network not only stiffen and toughen the system, but can provide novel features depending on the filler characteristics, e.g., electrical conductivity or a specific absorption profile. Our group has recently reviewed how nanoparticles and hydrogels can exhibit synergistic interactions to provide promising platforms for on-demand drug delivery or self-healable structures, among other applications.⁷ In addition to drug-delivery applications, hybrid hydrogels are increasingly investigated for mechanical actuators. A representative example reported by Tai and co-workers involves a carbon nanotube-alginate hydrogel as a wearable pressure sensor by virtue of the hybrid electrical conductivity and piezoresistive properties.⁸ In general, examples of such hybrid hydrogels for electromechanical applications are still scarce. In contrast, very accurate and sophisticated strain sensors have been demonstrated with other polymer substrates (such as poly(dimethylsiloxane) (PDMS)) combined with nanostructures, and these are based on the principle of piezoresistivity.⁹ Such sensors are promising for the monitoring of bodily motions, blood pressure, or for tactile sensing, but the use of hydrogels instead would be advantageous due to their known unmatched performance in biological interfaces.

The creation of graphene hybrid polymer hydrogels should occur in aqueous suspensions, in which the hydrogel is formed

or assembled, and, as a consequence, aqueous stabilization of pristine graphene sheets is necessary. We have developed in our laboratories a facile graphite exfoliation method that involves ball milling with an affordable laboratory reagent, such as melamine (2,4,6-triaminotriazine).^{10,11} The induced intercalation of melamine molecules into the graphitic interlayer spaces provides few-layer graphene in large amounts, and this material is capable of standing in stable suspension using polar solvents, such as dimethylformamide or water. Taking advantage of this aqueous graphene from the ball-milling process (BMG), our group has recently reported hybrid graphene hydrogels made of poly(methacrylic acid) with controllable drug delivery upon pulsatile electrical stimulation,¹² as well as polyacrylamide (PAAm) hydrogel hybrids as potential scaffolds for neuronal growth.¹³

The purpose of the work described here was to provide new insights into the study of smart hybrid hydrogels based on pristine graphene. In particular, we focused on stimuli based on mechanical stretching, which are still rarely studied in the context of nanocomposite hydrogels. Two different responses were exhibited by these hybrid systems upon stretching, namely, significant changes in electrical resistance (piezoresistivity) and the more efficient release of internalized substances (which is illustrated by a controlled drug-delivery example). Both features are a consequence of a synergistic behavior between BMG and PAAm, and the outcomes may be exploited for different purposes, which are also discussed.

RESULTS AND DISCUSSION

The BMG prepared in this work was obtained by the mechanochemical exfoliation of graphite with melamine (see [Experimental Section](#)), which provides a nanostructure with low levels of defects, as assessed by Raman spectroscopy,¹¹ lateral dimensions with a distribution centered at about 500–600 nm,¹¹ made of few layers (<5),¹⁰ and a negligible content

in oxygen functional groups and melamine (elemental composition: 0.36 wt % nitrogen, 94.3 wt % carbon¹¹).

The aqueous dispersibility of BMG enabled us to perform *in situ* radical polymerization of acrylic monomers. The general process consisted of dissolving the monomer, cross-linker, and initiator in the BMG suspension and heating the mixture up to induce the polymerization reaction (see [Experimental Section](#)).¹³ The hybrid hydrogels were prepared with different graphene contents, expressed as wt %. This value should be understood as the percentage ratio between the mass of graphene in the aqueous dispersion and the mass of acrylamide monomer, with the amounts of cross-linker and initiator considered negligible. The preparation scheme and a photograph of hydrogel hybrids are displayed in [Figure 1](#). The materials have a smooth aspect and uniform coloration. Some authors have reported that GO and rGO may form a dense “shell” at the outer edges of hydrogel test subjects,¹⁴ but the samples reported here appeared perfectly homogeneous. Full characterization of the BMG/PAAm hybrids microstructure and swelling behavior is reported elsewhere.¹³

Mechanical Properties. The tensile mechanical properties of the PAAm hydrogel matrix and different BMG hybrids are represented in [Figure 2](#). It can be seen that the graphene incorporation approach reported here leads to a significant increase in the maximum stress at failure (i.e., ultimate tensile strength), with improvements of 50 and 100% in relation to the blank matrix with 0.01 and 0.1 wt % BMG, respectively. This finding shows the efficient reinforcement of BMG within

the PAAm matrix. Unexpectedly, the maximum strain exhibited by these hybrids also increases with graphene content, which indicates that BMG enhances the ductility of PAAm hydrogels. A common phenomenon in polymer composites reinforced with nanoscale fillers (such as graphene) is the decrease in the maximum strain with increasing nanofiller content because it restricts the extent of deformation of polymer chains by physical hindrance, sometimes rebounding in the tensile strength.¹⁵ Shen and colleagues reported cross-linked PAAm hydrogels reinforced with GO,¹⁶ and these materials showed a visible reinforcement but with no appreciable increase in ductility at different GO contents. Increases in both strength and elongation are rarely found. In our case, this fact may account for the role of graphene in the final structure. It has already been shown that in our hydrogels graphene is not merely an embedded nanomaterial. In fact, BMG flakes form part of the hydrogel structure and it behaves as a flexible cross-linker.¹³ Further evidence for this may be the improvement in the tensile Young's modulus of PAAm upon incorporation of BMG ([Figure 2](#)), which gives rise to an approximately 30% increase with respect to the blank matrix and leads to stiffening in the hybrid without compromising ductility. As per the tensile toughness (obtained as the area under the stress–strain curve), which accounts for the energy that the material is capable of absorbing until failure, an average value of 217 kPa was obtained for blank PAAm. The inclusion of BMG within the hydrogel matrix resulted in improvements in this parameter of 46% (for 0.01 wt % BMG), 61% (for 0.05 wt % BMG), and 70% (for 0.1 wt % BMG), which provides more evidence for the positive effect of graphene in this system.

Compared to our previous work on this kind of system, in which the compressive mechanical properties were analyzed,¹³ it is clear that tensile and compressive data (although not equal, as expected) are consistent with each other because they are of the same order of magnitude. However, in our previous work, a change in the compressive modulus for a BMG content of 0.1 wt % with respect to the blank PAAm matrix was not observed, and it was only with higher BMG amounts that an increase in compressive modulus was found, with a major effect on the mechanical fatigue not apparent after 100 compressive cycles.¹³ Conversely, in terms of the tensile properties reported here, measurable changes in the tensile elastic moduli of hydrogels were found with lower amounts of BMG, which suggests that these hybrid materials are more sensitive to mechanical stretching than to compression. Furthermore, as will be explained in subsequent sections, a mechanical fatigue was observed on stretching the material due to the release of water from the hydrogel, but this phenomenon was not observed upon compression.

Conductive Behavior. Electrical conductivity (σ), or its inverse (resistivity, ρ), is an intrinsic property of materials, and it depends on their natural ability to allow transit of charge carriers within their structure. Physically, one can obtain σ or ρ from direct current (DC) electrical resistance (R), where a weighting factor related to the material dimensions is necessary. The geometrical correction accounts for the charge pathways and relates the extensive magnitude (R , in Ω) with the intensive magnitude (σ , in S/cm).¹⁷ Conversion of an insulating or poorly conductive material into a conducting or semiconducting material is easily achievable by the addition of conductive particles, as reported here. It was observed that the formation of the hybrid graphene gel results in an increase in the electrical conductivity of the blank hydrogel. The electrical

Figure 2. (a) Representative stress–strain curves for PAAm and some hybrid graphene hydrogels; (b) average values of Young's modulus and ultimate tensile strength of samples. Note that the BMG content (wt %) is defined as the percentage mass ratio between graphene and the acrylamide monomer.

Figure 3. Linear electrical behavior of PAAm and different hybrid graphene hydrogels.

Figure 4. Relative change in resistance (dR/R_0) with a 30% stretching ratio ($dl/l_0 = 0.3$) for sequential stretching cycles in a hybrid graphene hydrogel containing 0.01 wt % BMG.

mechanical sensitivity of our composites was quantified through the gauge factor (G_F , see [Experimental Section](#)).

The study described here focused on samples with a low BMG content as a conductivity increase was already observed at these low contents ([Figure 3](#)). The average G_F values for different hydrogel hybrids are represented in [Figure 5a](#). Two main conclusions can be drawn:

- (1) The strain gauge effect is exclusively the result of the BMG as the neat matrix did not show any piezoresistive response, despite its appreciable electrical conductivity. To validate this finding, the developed expression for G_F was considered¹⁹

$$G_F = \frac{dR/R_0}{\varepsilon_1} = \frac{d\rho/\rho_0}{\varepsilon_1} + 1 + 2\nu$$

where ν stands for Poisson's ratio and ε_1 refers to the relative strain ($\Delta l/l_0$). It can be seen that each G_F has a resistivity-related term, also known as the intrinsic piezoresistive effect $[(d\rho/\rho)/\varepsilon_1]$, and a geometrical effect ($1 + 2\nu$). According to literature data, a PAAm gel with the AAm/ N,N' -methylenebis(acrylamide) (MBA)/water ratio of the material discussed here should have $\nu \sim 0.45$.^{20,21} The geometrical term becomes ~ 1.9 , and this means that the major contribution to the G_F relies on the intrinsic effect provided by the BMG conductive network, and this changes R with mechanical deformation.

- (2) The studied range has a close coincidence with the average G_F values, and these do not appear to be dependent on the BMG content in the studied range, with a G_F of ~ 9 . The standard deviation for each average G_F value increases as the BMG content increases, which is indicative of a departure between the initial and final G_F values within the whole set of stretching cycles. This in turn indicates a higher fatigue effect with higher graphene content, as discussed below.

It is interesting to note that the average G_F values obtained are within the range found for similar high-performance elastic composite strain gauges, such as that for a liquid-phase-exfoliated graphene infused into natural rubber,²² lithographically imprinted Ag nanowires in a poly-(dimethylsiloxane) (PDMS) elastomer,²³ or graphene thin films directly prepared from spray coating over plastic

Figure 5. (a) Relationship between the gauge factor and BMG content for PAAm and hybrid graphene hydrogels cyclically stretched to 30% (average of 11 cycles). (b, c) Evolution of gauge factor with the number of cycles for the same samples stretched to 30% in the “load” and “unload” displacements.

strain was evaluated (Figure 5b,c). The load and unload processes were distinguished in the stretching motion from the zero position at 15 mm/min rate up to 30% strain and the reverse path at -15 mm/min rate, respectively. As illustrated in Figure 5b,c, there is virtually no difference between the G_F values calculated for the two processes, nor in their evolution with cycles. This finding indicates the full reversibility of the process in each single cycle at this strain. However, there was a significant variation in behavior for the different BMG contents. From 0.01 to 0.025 wt %, there was a nearly constant G_F value, and this gave rise to an average with low deviation. In the range 0.04–0.1 wt % BMG, there were larger deviations. In these latter samples, the initial G_F increased with the wt % of BMG, but rapidly decreased as the number of cycles increased. According to the aforementioned typical variable G_F in strain gauges, the sensitivity of the conductive network becomes lower as the content of the conductive filler increases. This would mean a higher sensitivity as a strain sensor in the initial cycles but lower stability over time and thus lower life expectancy. It is also important to consider the variability within each individual cycle (deviation from the average in a few repeated experiments on different specimens) as this seems to be detrimentally affected by these possible irreversible effects on the conductive network while cyclically stretching the hybrids. According to the previously discussed tensile data, the higher ductility of samples with higher BMG content might impede the full reconstitution of the network upon stretching-induced disruption.²⁵ Additionally, during the course of this work, it was observed empirically that PAAm was able to release small amounts of water when stretched, and this phenomenon was also observed in the presence of graphene. Furthermore, the higher the BMG content, the easier the hydrogel was able to release the water upon mechanical stretching. This behavior could have interesting implications (as will be shown later) because graphene may impart a slightly higher hydrophobic character to the system, which could also explain the mechanical fatigue observed on increasing the number of stretching cycles at higher BMG contents.

The discussion so far has concerned 30% strain, but it was of interest to explore further the strain gauge characteristics of our hybrid graphene hydrogel under different strains. Bearing in mind that tensile linear ranges were observed up to 55–60% strain, a level of 50% strain was selected as the maximum permissible to use these hydrogels in a strain sensor with fairly reversible properties. Strain levels of 5 and 15% were employed with the same wt % BMG as for the 30% strain case. The results obtained were mapped and are displayed in Figure 6. The maximum G_F values were obtained for 30% strain, whereas at strains above and below this level, the numbers decreased for all graphene ratios. In general terms, the sensitivity of these strain gauges is better at low strains, with an empirical maximum reached at 30%, after which the proximity to the nonelastic deformation of the hydrogel worsens the piezoresistive performance. However, another general trend was observed in the standard deviation of G_F at different strains (Figure 6), considering the averages shown in Figure 5, because this mainly seems to be related to the BMG content. Beyond 0.05 wt %, the deviation of G_F increased markedly (therefore lowering the durability of a strain sensor made from these hybrids). In brief, we have successfully manufactured graphene-based hybrid hydrogels that show a clear strain gauge effect. The average G_F values can be ranked alongside the good-to-best values in the literature for similar

substrates.²⁴ In the examples described here, similar G_F values were obtained with very low amounts of graphene, and, interestingly, simplicity is the key, as we prepared hybrid systems in “one-pot” without multiple sandwiching stages or delicate deposition processes. Regarding the data dispersion, it is commonly accepted in the electromechanical field that piezoresistive materials are challenging as they inherently suffer from hysteresis and variable G_F values, which are highly dependent on the mechanical stability of the system.²⁵ This is mainly due to the conductive network changes that occur with mechanical fatigue. It was observed that there was less deviation in G_F at 30% strain with lower BMG contents, and markedly higher deviation occurred as the concentration increased. In an attempt to understand this finding, the evolution of G_F with the succession of stretching cycles at 30%

Figure 6. (a) Mapping of average gauge factors for PAAm and hybrid graphene hydrogels with different contents of BMG and different strains. (b) Standard deviation of the average values within the same region.

Figure 7. Conceptual approach for the stretch-triggered release of ibuprofen from drug-loaded hybrid hydrogels.

and Di et al.²⁷ may be the most representative in the literature of stretch-induced delivery of drugs from hydrogels, but these authors needed to mount the hydrogel vector into an elastomer thin film, as the former could not experience large deformations without failure. It was therefore very interesting to obtain a system that could respond to a natural or spontaneous stretching motion to release a local amount of a drug.

We selected ibuprofen as a suitable model to illustrate our premise. Ibuprofen is probably the best-known member of the nonsteroidal anti-inflammatory drug family. Ibuprofen is widely used for the treatment of different forms of arthritis, pain and fever symptoms,^{28–30} but its oral administration has detrimental effects on health (such as gastric damage). The use of hydrogels combined with ibuprofen has been proposed in the literature,^{28,30} but to our knowledge, none of these approaches are based on a three-dimensional cross-linked network.

In the system described here, the viability of a wide variety of strains and different graphene contents had been demonstrated. For the proof of concept, we selected the conditions that gave the best G_F value (0.05 wt % BMG, 30 % strain) with a PAAm/graphene hybrid hydrogel containing ibuprofen in its bulk. Consecutive stretching cycles were carried out, and the amounts of drug released by the wet capillary effect of ibuprofen were evaluated in each cycle (see [Experimental Section](#) for details). The results are displayed in [Figure 8](#). For comparative purposes, control samples were included and these consisted of nonstretched specimens that underwent identical characterization (also clamped in the tensile device) but without any applied stress. It was confirmed that the stretching motion itself promoted the release of internalized substances from the hydrogel bulk, but there was a significant difference between materials with graphene or not

systems, and the nature of the variability makes it necessary to prioritize either sensitivity or duration without critical consequences in any envisioned application.

Mechanically Induced Drug Delivery. The kinds of responses that the hybrid hydrogels may present to a stimulus based on mechanical stretching were investigated. As commented earlier, it was observed that stretching of these hydrogels led to the release of water and that this phenomenon was enhanced by the presence of graphene. It was therefore of interest to evaluate whether this release of water could cause the concomitant release of internalized substances, for which a proof of principle was carried out in the form of a controlled drug-delivery experiment.

Given the mechanical stimulus-responsive nature of our PAAm/graphene hybrids, we were encouraged to test them beyond the electromechanical effects and to ascertain whether they might be able to achieve drug delivery by mechanical means (depicted in [Figure 7](#)). In fact, reports of mechanically triggered drug release in three-dimensional (3D) soft polymer networks is very rare in the literature, and examples mostly concern compression rather than stretching. Tensile motions occur naturally in the human body at every moment and they are also effortlessly applied at will. As a consequence, it is very appealing to exploit such motions as a means to achieve on-demand drug delivery. The examples reported by Hyun et al.²⁶

Figure 8. (a) Release profile of ibuprofen from stretched and nonstretched hydrogels. (b) Cumulative values, both relative to the initial amount of ibuprofen.

in the system. Hybrid hydrogels containing BMG showed a markedly higher release ability than neat PAAm upon stretching. Consequently, the differences observed in the stretch-triggered drug delivery of ibuprofen could be ascribed to the mechanical features that graphene imparts on the PAAm. In other words, an unprecedented effect of graphene in a hydrogel matrix was observed in this experiment. Even if the BMG did not generate the drug-releasing effect in PAAm, it did make the delivery of a hydrophobic drug occur more efficient.

CONCLUSIONS

In the present work, graphene-based hybrid hydrogels were prepared by a mild aqueous route that provides pristine few-layer graphene. It was shown that cross-linked PAAm-graphene hybrids not only have improved characteristics, but also exhibit mechanically triggered responsiveness, such as a strain gauge effect or more efficient drug release induced by stretching. These two different properties can be exploited in different applications. For instance, these graphene-based hydrogels would be perfect candidates for smart materials in the medical field. We envisage their potential in naturally occurring stretch motions that require a therapeutic response in a wet environment, such as inflammation of open wounds. These hydrogels could “sense” the inflammation by co-stretching with the surrounding tissue and counteract it with the local delivery of an amount of a drug. On the other hand,

the electromechanical response upon stretching is a valuable asset as the mechanical performance of the hydrogels could be electrically monitored or used for motion sensing. The uniqueness of the hybrids described in this work opens up new possibilities for electromechanical sensing, where the hydrogel nature is of capital relevance, such as in 3D printing or in water-based (bio)interfaces.

EXPERIMENTAL SECTION

Materials and Reagents. Melamine, acrylamide (AAM), N,N' -methylenebis(acrylamide) (MBA), potassium peroxydisulfate (KPS), and ibuprofen were purchased from Sigma-Aldrich as reagent-grade materials. Graphite powder was acquired from Bay Carbon Inc. (SP-1 reference; www.baycarbon.com). Silver paint was obtained from Sigma-Aldrich ($\rho = 1-3 \times 10^{-5} \Omega \text{ cm}$, ref #735825).

Preparation of BMG Aqueous Suspensions. The exfoliation of graphite was carried out using a ball-milling procedure developed by our group.^{10,11} In a typical experiment, 30 mg of a graphite/melamine mixture (1:3) was ball-milled at 100 rpm for 30 min. The resulting solid mixture was dispersed in 20 mL of water to produce a dark suspension. The process was repeated as much as necessary and then the liquid was placed in dialysis sacks (Spectrum Labs, ref #132655, 6–8 kDa molecular weight cut-off) and dialyzed against water at 70 °C with frequent replacements and mild sonication cycles until melamine was no longer detected in the permeate. The resulting suspension was left to settle for 5 days and some precipitate (mainly pure or poorly exfoliated graphite) segregated from the liquid. The liquid fraction with stable sheets in suspension (few-layer graphene) was carefully extracted. The final BMG aqueous suspensions were freeze-dried (Telstar LyoQuest device, –80 °C and 0.05 mbar) and redispersed in water at the desired concentration¹¹ to control the filler ratio within the hydrogel matrix.

Preparation of PAAm Hydrogels and PAAm/BMG Hydrogel Hybrids. Pure PAAm hydrogels were prepared using AAM, MBA as cross-linker, and KPS as initiator. AAM was initially dissolved in ultrapure Milli-Q water (200 mg/mL) together with the MBA (0.2 mg/mL). The solution was homogenized by stirring and mild sonication. KPS was then added (at a final concentration of 0.4 mg/mL) and the system was allowed to polymerize at 75 °C over a period of 1 h. Only on using Teflon molds was the system preheated for 1 h at 75 °C before the intended thermal polymerization. In the case of the hybrid BMG–PAAm hydrogels, an identical process was followed, except for the use of BMG aqueous dispersions instead of plain water, with the necessary concentration to achieve the desired wt % graphene within the hydrogel matrix. The BMG content varied between 0.01 and 1 wt %, expressed on a dry weight basis. Hydrogels were washed by immersion in an excess of ultrapure water, with frequent water replacements over several days. The samples were fully dried under ambient conditions and reswelled with sufficient ultrapure water to reach the native swelling degree. Unless otherwise stated, all hydrogel tests are referred to the native swollen state.

In the case of ibuprofen-loaded hydrogels, the same cylindrical specimens used for electrical measurements (vide infra) were employed and these were washed as mentioned above. After drying, samples were reswelled with sufficient aqueous solution of ibuprofen (0.0157 mg/mL, 76 μM) to reach the native swelling degree.

Characterization Techniques. Mechanical tests were performed on hydrogels under ambient conditions (26.2 ± 0.6 °C and 30% relative humidity) with a Mecmesin MultiTest 2.5-i dynamic mechanical analyzer. The extent of the deformation was measured in terms of strain. For such tensile tests, hydrogel samples were molded in a dog-bone shape following the UNE-EN ISO 37 standard dimensions by use of carved Teflon molds. Specimens were uniaxially stretched at a rate of 15 mm/min until breakage, and tensile Young's modulus was obtained as the slope of the linear elastic section in the initial stages (typically up to 55–60% strain in our case). The obtained values are in agreement with literature data.²¹

The linear electrical behavior was confirmed on representative selected samples. I – V curves were measured using a standard four-

541 point probe method with a Keithley 2400 source-meter instrument,
542 where the copper wires were attached to the samples by silver paste to
543 cylindrical specimens of ~5 mm diameter and 10–20 mm length. At
544 least six measurements were performed for each sample by contacting
545 crocodile-type electrodes to the ends of the specimen. Electrical
546 conductivity (σ) was calculated as the inverse of resistivity (ρ), which
547 in turn was obtained from its relationship with R

$$R = \rho \frac{l}{s}$$

548 where l and s are the specimen's length and sectional area,
549 respectively. The linear electrical behavior was confirmed on
550 representative selected samples by measuring I – V curves using a
551 standard four-point probe method with a Keithley 2400 source-meter
552 instrument.

553 The strain gauge effect was evaluated by combining the
554 aforementioned mechanical and electrical characterization techniques,
555 using the Mecmesin MultiTest 2.5-i dynamic mechanical analyzer
556 mentioned previously and a digital multimeter (working in DC) with
557 a maximum resolution of 0.1 μ A and a basic accuracy of $\pm 1.0\%$.
558 Copper wire electrodes were used for the measurements. Cylindrical
559 specimens of 5 mm diameter (and several centimeters long) were
560 clamped at both ends and situated in a “zero” position with the
561 minimum possible tension. Two small Ag spots were painted
562 approximately at 1/3 and 2/3 of the specimen length between
563 clamps, in opposite sides. Stretching recovery cycles were applied at
564 specific ratios (namely, 5, 15, 30, or 50% strain) with 15 and –15
565 mm/min stretching rates, respectively, through 11 cycles. Electrical
566 resistance was measured in each stretched and recovered position for
567 every cycle with the multimeter in a two-point probe configuration.
568 The gauge factor (G_F) was calculated according to the expression

$$G_F = \frac{\Delta R/R_0}{\Delta l/l_0}$$

569 where R denotes the specimen's electrical resistance and l is the length
570 in the initial position (zero) and the difference between this and the
571 stretched state (Δ). The term $\Delta l/l_0$ (strain) is often abbreviated as ϵ_l .
572 Three repetitions of each experiment were performed, and the
573 reported values are averages with their corresponding standard
574 deviation.

575 The strain-induced release of ibuprofen from PAAm hydrogels was
576 tested as follows. A piece of the ibuprofen-loaded cylindrical specimen
577 (a few centimeters long) was clamped to both ends in the uniaxial
578 tensile device and cyclically stretched according to the following
579 program: 15 mm/min ramp up to 30% strain, held for 30 s in the
580 stretch position, and recovery at –15 mm/min to the initial rest
581 position. During the whole time, a rectangular strip of high-quality
582 chromatographic paper (Whatman), previously humidified with Milli-
583 Q water, was stuck to the hydrogel specimen to cover its entire outer
584 surface. The paper was removed after each cycle and a new one was
585 put in place. Upon removal, each piece of paper was immersed in 3
586 mL of Milli-Q water and left soaking overnight. The released amount
587 of ibuprofen was assessed from the UV absorbance (Cary 5000 UV–
588 vis–NIR spectrophotometer) of the aqueous aliquots using an
589 extinction coefficient of 1.4614 $\text{cm}^{-1} \text{mg}^{-1} \text{mL}$ ($\lambda = 264 \text{ nm}$),
590 which was empirically obtained by ourselves. Blank tests were run to
591 ensure that the chromatographic paper did not leach out any
592 interfering substance into the water.

593 AUTHOR INFORMATION

594 Corresponding Author

595 *E-mail: ester.vazquez@uclm.es.

596 ORCID

597 Jose M. González-Domínguez: 0000-0002-0701-7695

598 Ester Vázquez: 0000-0003-3223-8024

Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Author Contributions

J.M.G.-D. and C.M. have contributed equally.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

The authors acknowledge financial support from the EU Graphene-based disruptive technologies, Flagship project (no. 696656), and Spanish Ministry of Economy and Competitiveness (MINECO) under project grant CTQ2014-53600-R. Dr. J.M.G.-D. greatly acknowledges MINECO for his researcher grant (Formación Postdoctoral).

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