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

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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
67 electrical conductivity. The electrically insulating nature of GO
68 (and most of the rGO derivatives) seriously hinders the use of
69 graphene-based hydrogels in applications stemming from
70 electrical properties, despite the fact that these nanostructures
71 are easy to prepare and are commonly employed in many
72 laboratories. Given the possibility of obtaining two-dimen-
73 sional conductive nanoparticles, such as pristine (nonoxidized)
74 graphene, new avenues would be open for hydrogels prepared
75 from this material. For example, stimulus-response properties
76 involving electrical conductivity would justify the greater
77 difficulty in preparing the pristine graphene.
78 The nano-
79 fillers contained in a cross-linked polymer network
80 not only sti-
81 ffen and toughen the system, but can provide novel
82 features depending on the filler characteristics, e.g., electrical
83 conductivity or a specific absorption profile. Our group has
84 recently reviewed how nanoparticles and hydrogels can exhibit
85 synergistic interactions to provide promising platforms for on-
86 demand drug delivery or self-healable structures, among other
87 applications. In addition to drug-delivery applications, hybrid
88 hydrogels are increasingly investigated for mechanical
89 actuators. A representative example reported by Tai and co-
90 workers involves a carbon nanotube-alginate hydrogel as a
91 wearable pressure sensor by virtue of the hybrid electrical
92 conductivity and piezoresistive properties. In general, examples of such hybrid hydrogels for electromechanical
93 applications are still scarce. In contrast, very accurate and
94 sophisticated strain sensors have been demonstrated with other
95 polymer substrates (such as poly(dimethylsiloxane) (PDMS))
96 combined with nanostructures, and these are based on the
97 principle of piezoresistivity. Such sensors are promising for
98 the monitoring of bodily motions, blood pressure, or for tactile
99 sensing, but the use of hydrogels instead would be advantage-
100 ous due to their known unmatched performance in
101 biological interfaces.
102 The creation of graphene hybrid polymer hydrogels should
103 occur in aqueous suspensions, in which the hydrogel is formed
104 or assembled, and, as a consequence, aqueous stabilization of
105 pristine graphene sheets is necessary. We have developed in
106 our laboratories a facile graphite exfoliation method that
107 involves ball milling with an affordable laboratory reagent, such
108 as melamine (2,4,6-triaminotriazine). The induced inter-
109 calation of melamine molecules into the graphitic interlayer
110 spaces provides few-layer graphene in large amounts, and this
111 material is capable of standing in stable suspension using polar
112 solvents, such as dimethylformamide or water. Taking
113 advantage of this aqueous graphene from the ball-milling
114 process (BMG), our group has recently reported hybrid
115 graphene hydrogels made of poly(methacrylic acid) with
116 controllable drug delivery upon pulsatile electrical stimula-
117 tion, as well as polyacrylamide (PAAm) hydrogel hybrids as
118 potential scaffolds for neuronal growth.
119
120 The purpose of the work described here was to provide new
121 insights into the study of smart hybrid hydrogels based on
122 pristine graphene. In particular, we focused on stimuli based on
123 mechanical stretching, which are still rarely studied in the
124 context of nanocomposite hydrogels. Two different responses
125 were exhibited by these hybrid systems upon stretching,
126 namely, significant changes in electrical resistance (piezo-
127 resistivity) and the more efficient release of internalized
128 substances (which is illustrated by a controlled drug-delivery
129 example). Both features are a consequence of a synergistic
130 behavior between BMG and PAAm, and the outcomes may be
131 exploited for different purposes, which are also discussed.

■ RESULTS AND DISCUSSION

The BMG prepared in this work was obtained by the
132 mecanochemical exfoliation of graphite with melamine (see
133 Experimental Section), which provides a nanostructure with
134 low levels of defects, as assessed by Raman spectroscopy, and
135 lateral dimensions with a distribution centered at about 500–
136 600 nm, made of few layers (<5), and a negligible content
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). The hybrid hydrogels were prepared with different graphene contents, expressed as wt %. This value should be understood as the percentage ratio between graphene and PAAm hydrogel matrix, 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, but the samples reported here appeared perfectly homogeneous. Full characterization of the BMG/PAAm hybrids microstructure and swelling behavior is reported elsewhere.

**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. Shen and colleagues reported cross-linked PAAm hydrogels reinforced with GO, 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. 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, 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. 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 ($\sigma$), or its inverse (resistivity, $\rho$), 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 $\sigma$ or $\rho$ from direct current (DC) electrical resistance ($R$), where $R$ is 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 $\Omega$) with the intensive magnitude ($\sigma$, in S/cm). 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...
behavior of various samples is represented in Figure 3. The current–voltage (I–V) linear behavior following Ohm’s law allowed the electrical conductivity of these hydrogels to be calculated with a linear slope by normalization with the specimen’s dimensions. In our case, it was found that neat PAAm had a value of $3.2 \times 10^{-5}$ S/cm, whereas the incorporation of graphene at low loadings (0.01 and 0.05 wt %) led to an increase in the conductivity to $3.88 \times 10^{-5}$ and $5.4 \times 10^{-5}$ S/cm, respectively. An example of a PAAm hybrid with a much higher BMG content (1 wt %) still had a higher conductivity than neat PAAm, with a value of $7.5 \times 10^{-5}$ S/cm.

The procedure was carried out on the same tensile stretching (at a constant rate) up to 30% strain in different hybrid 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 considered:

$$G_F = \frac{dR/R_0}{\epsilon_1} = \frac{d\rho/\rho_0}{\epsilon_1} + 1 + 2\nu$$

where $\nu$ stands for Poisson’s ratio and $\epsilon_1$ 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 $(d\rho/\rho)/\epsilon_1$, 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 $\nu \sim 0.45$. 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 $\sim 9$. 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 composite strain gauges, such as that for a liquid-phase-exfoliated graphene infused into natural rubber, or graphically imprinted Ag nanowires in a poly(dimethylsiloxane) (PDMS) elastomer, 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.

substrates. 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. 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% 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. 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 systems, leading to the hypothesis that graphene-based hybrid hydrogels offer a promising platform for the development of stretchable strain sensors with high sensitivity and durability under cyclic mechanical loading.
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. and Di et al. 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, 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, 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.
the local delivery of an amount of a drug. On the other hand, stretching with the surrounding tissue and counteract it with these hydrogels could in a wet environment, such as in occurring stretch motions that require a therapeutic response the medical hydrogels would be perfect candidates for smart materials in different applications. For instance, these graphene-based hybrids could “sense” the inflammation by co-stretching with the surrounding tissue and counteract it with the local delivery 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 (p = 1–3 × 10⁻⁵ Ω cm, ref #735825).

**Preparation of BMG Aqueous Suspensions.** The exfoliation of graphite was carried out using a ball-milling procedure developed by our group. 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 the melamine was no longer detected in the permeate. The resulting suspension was used 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 concentration 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 at 0.05 wt% cross-linker, 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 cycles. 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 redispersed 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 control the native swelling degree. These hydrogels could “sense” the inflammation by co-stretching with the surrounding tissue and counteract it with the local delivery of a drug. On the other hand, the linear electrical behavior was confirmed on representative selected samples. I–V curves were measured using a standard four-probe technique. The results were compared with the reference hydrogel nature is of capital relevance, such as in 3D printing or in water-based (bio)interfaces.

**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 prepared by a mild aqueous route that provides pristine few-layer graphene. It was shown that cross-linked PAAm prepared by a mild aqueous route that provides pristine few-layer graphene. In the present work, graphene-based hybrid 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 cycles. 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 redispersed with sufficient ultrapure water to reach the native swelling degree. Unless otherwise stated, all hydrogel tests are referred to the native swollen state.

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In order to measure the electrical behavior of the hydrogel, a Keithley 2400 source-meter instrument was used. The gauge factor ($G_F$) was calculated according to the expression

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

where $R$ denotes the specimen’s electrical resistance and $l$ is the length in the initial position (zero) and the difference between this and the stretched state ($\Delta l$). The term $\Delta l/l_0$ (strain) is often abbreviated as $\epsilon$. Three repetitions of each experiment were performed, and the results are averages with their corresponding standard deviation.

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

**REFERENCES**


