

# MULTIFUNCTIONAL HYDROGELS

From Basic Concepts to Advanced Applications

Edited by José García-Torres, Carlos Alemán, and Ram K. Gupta



# Multifunctional Hydrogels

Hydrogels are important polymer-based materials with innate fascinating properties and applications: they are three-dimensional, hydrophilic, polymeric networks that can absorb large amounts of water or aqueous fluids and are biocompatible, mechanically flexible, and soft. The incorporation of functionalities to develop smart and bioactive platforms has led to a myriad of applications. This book offers a comprehensive overview of multifunctional hydrogels, covering fundamentals, properties, and advanced applications in a progressive way. While each chapter can be read stand-alone, together they clearly describe the fundamental concepts of design, synthesis, and fabrication, as well as properties and performances of smart multifunctional hydrogels and their advanced applications in the biomedical, environmental, and robotics fields.

This book:

- Introduces readers to different hydrogel materials and the polymer types used to fabricate them.
- Discusses conducting polymer hydrogels, nanocomposite hydrogels, and self-healing hydrogels.
- Covers synthesis methodologies and fabrication techniques commonly used to confer certain structures and/or architectures.
- Shows how hydrogels can be modified to incorporate new functionalities able to respond to physical and/or chemical changes.
- Examines applications including bioelectronics, sensors and biosensors, tissue engineering, drug delivery, antipathogen applications, cancer theranostics, environmental applications, and soft robotics, with chapters showcasing the main advances achieved up to date in every field.

*Multifunctional Hydrogels: From Basic Concepts to Advanced Applications* serves as a valuable resource for academic and industry researchers from interdisciplinary fields including materials science, chemistry, chemical engineering, bioengineering, physics, and pharmaceutical engineering.



# Multifunctional Hydrogels From Basic Concepts to Advanced Applications

Edited by José García-Torres Carlos Alemán Ram K. Gupta



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# Preface

Hydrogels, a class of soft, water-swollen materials, have been at the forefront of materials science research for decades. Their unique blend of biocompatibility, tunability, and versatility has made them indispensable in a wide range of applications, from biomedicine to environmental remediation. This book, *Multifunctional Hydrogels: From Basic Concepts to Advanced Applications*, represents a comprehensive exploration of the multifaceted world of hydrogels, aiming to provide a definitive resource for researchers, students, and professionals interested in the field.

Hydrogels represent a remarkable type of materials within materials science as they are three-dimensional polymeric networks capable of holding substantial amounts of water while maintaining their structural integrity. Their properties, such as high water content, softness, and resemblance to natural tissues, render them uniquely suited for various applications. This book embarks on a journey through the captivating realm of hydrogels, offering insights into their fundamental principles, synthesis methods, properties, and diverse applications. Our exploration of hydrogels commences with a solid foundation in the fundamental concepts. We delve into the chemistry behind hydrogels, examining the intricacies of polymer structure, followed by their properties (e.g., mechanical, electrical, magnetic), and finally some advanced applications. Thus, readers will gain a deep understanding of main characteristics and how to design hydrogels with tailored properties for specific applications.

The book is composed of 19 chapters in three parts. Part I covers basic concepts of hydrogels, including an introduction to the main characteristics (Chap. 1), the different natural and synthetic hydrogels employed (Chap. 2), and how they can be modified to prepare nanocomposite hydrogels (Chap. 3). Then, it is discussed how they can be synthesized (Chap. 4) and the main fabrication techniques employed (Chap. 5). In Part II, the properties of hydrogels are discussed, covering hydrogels with advanced properties (Chap. 6) as well as chemical (Chap. 7), electrical (Chap. 8), magnetic (Chap. 9), thermal (Chap. 10), and mechanical properties (Chap. 11). Finally, Part III is focused on advanced applications of hydrogels like bioelectronics (Chap. 12), physical and chemical (bio)sensors (Chap. 13), biomedical applications (Chap. 14), drug delivery (Chap. 15), antipathogen applications (Chap. 18), and soft robotics (Chap. 19).

In editing and organizing this book, *Multifunctional Hydrogels: From Basic Concepts to Advanced Applications*, we have made our best efforts to cover the growing field of hydrogels and related technologies. This book will provide basic concepts to more deep insights into the state of the art for new researchers in the field but also for researchers already working in the passionate world of hydrogels. We express our heartfelt gratitude to the numerous scientists and experts who have generously shared their knowledge, insights, and experiences in this book. Their commitment to advancing hydrogel research is evident in the depth and breadth of the content presented here. We would also like to thank Allison Atkins and the rest of the team at CRC/Taylor & Francis for their invaluable help in the publication process.

In conclusion, *Multifunctional Hydrogels: From Basic Concepts to Advanced Applications* is a testament to the extraordinary journey of hydrogels from basic materials to multifunctional wonders with boundless potential. We hope this book serves as both an informative and inspirational resource, fostering further exploration and innovation in the ever-evolving field of hydrogel science and technology.

José García-Torres Carlos Alemán Ram K. Gupta

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Dr. José García-Torres is Serra Húnter Associate Professor in the Department of Materials Science and Engineering at Universitat Politècnica de Catalunya (UPC). Dr. García graduated in chemistry (University of Barcelona (UB)) and engineering of materials (UPC) and received a PhD in chemistry at UB in 2010. He has been a postdoctoral researcher at different internationally renowned universities, research institutes, and companies (University of Surrey, Research Institute for Solid State Physics and Optics, Miquel

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### Prof. Carlos Alemán



Prof. Carlos Alemán graduated in chemistry from the University of Barcelona (Spain). He received his PhD from Universitat Politècnica de Catalunya (UPC) in 1994, where he was promoted to the position of full professor of physical chemistry. He was postdoctoral researcher at the ETH in Zürich (Switzerland) and visiting professor at the Università di Napoli Federico II (Italy; 6 months), University of Twente (Holland; 1 year), and Universidade Federal do Rio Grande do Sul (Brazil; 3 months). Since 2003, he has been the leader of

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### Dr. Ram K. Gupta



Dr. Ram Gupta is an associate vice president for research and support and a professor of chemistry at Pittsburg State University. Gupta has been recently named by Stanford University as being among the top 2% of research scientists worldwide. Before joining Pittsburg State University, he worked as an assistant research professor at Missouri State University, Springfield, MO, and then as a senior research scientist at North Carolina A&T State University, Greensboro, NC. Dr. Gupta's research spans a range of subjects critical to current and future societal needs,

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# 1 Multifunctional Hydrogels An Introduction

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# **1.1 INTRODUCTION**

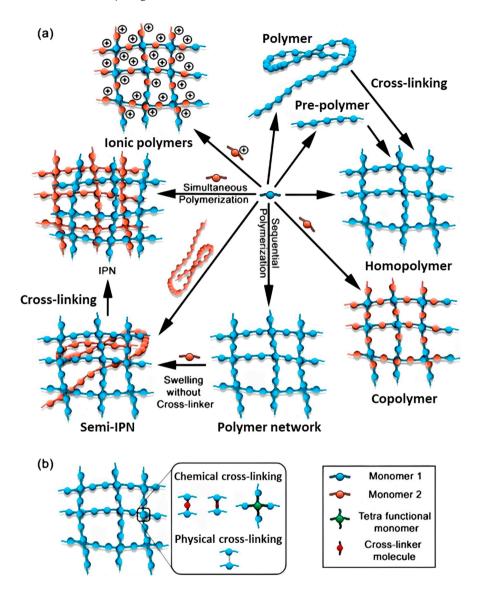
Hydrogels consist of materials with a highly porous 3D-networked structure. Such types of arrangement provide these materials an inherently highly active area as well as interstices that allow the adsorption of components such as water, solvents, electrolytes, biological probes, etc. The capability of properly adsorbing certain species in their structure allows hydrogels to be applicable in many sectors, such as energy storage devices like fuel cells, supercapacitors and batteries, sensors, and biomedical components. This broad range of applications has justified the current investment in these materials. Hydrogels have great potential as components for energy storage devices due to their porous semi-solid phase that eases the permeation of electrolytes, which is a core aspect of the improvement in electrochemical properties. Along with that, hydrogels are inherently flexible materials and allow the flow of ionic species through their networked structure. The combination of high surface area and ionic conductivity along with mechanical stability gives an edge on the use of hydrogels compared to traditional electrode materials, which are usually brittle, may display a relatively lower conductivity, and require specific synthetical approaches to attain high surface area. Furthermore, hydrogels present a distinct swelling behavior, as they can adsorb a relatively large quantity of components such as solvents, ions, and biological probes, among other species while maintaining their networked structure despite the variance in volume. Such a factor is often attributed to the presence of hydrophilic groups, such as -SO<sub>3</sub>H, -CONH<sub>2</sub>, -CONH-, along with others that can adsorb polar solvents and water or retain ionic species. The presence of hydrophilic groups along with the network structure of hydrogels can lead to an intake of water or other polar solvents of more than 20% of its dry weight [1].

Aside from the high adsorption of solvents, another important factor is the reversible stretchability of hydrogels, which allows for cycles of adsorption and desorption of solvents and electrolytes, without noticeable deterioration of mechanical properties. The importance of this factor can be partially associated with electrochemical stability. In the case of supercapacitors, the charging and discharging cycles can eventually cause the electrode material to deteriorate due to the constant insertion and desertion of ions within the network structure. In the case of batteries, a similar charging and discharging process can also lead to the decomposition of the detachment of electroactive materials on the electrode's surface due to phase transformation of the chemical incorporation of ionic species, which applies a considerably high electrochemical strain on the electrode's components. Hence, the fact that hydrogels present a considerable elasticity and can withstand relatively aggressive mechanical deformations without compromising their structure is a highly desired factor for applications in electrochemical devices. Based on these, the type of network and structure of the hydrogel can greatly influence its water and electrolyte uptake, which can be directly related to its electrochemical performance. Figure 1.1 illustrates some of the main types of hydrogel structures that can be obtained based on their cross-linking.

The versatility of hydrogels extends not only to their field of applications but also to their classification, which can be based on different aspects such as the source from which the starting material or polymer is derived, type of cross-linking, type of response when stimulated, and the electrostatic charge on the structure, which are schematized in Figure 1.2. The hydrogels can be synthetic, natural, or a mix of both. Like polymers, hydrogels can be based on a single polymeric structure, a copolymer, a block copolymer, and so on as most of the materials used for the synthesis of hydrogels are polymers. Some examples of the synthetical ones are poly(hydroxyethyl methacrylate) (PHEMA), poly(hydroxypropyl methacrylate) (PHPMA), and poly(glyceryl methacrylate) (PGMA), among many others. Following that, some of the bio-based materials used for the synthesis of hydrogels are polylactic acid (PLA), and polysaccharides that include cellulose, chitosan, chitin, starch, dextran, pectin, alginates, pullulan, and carrageenan, for instance [2]. Cross-linking can take place through several methods, such as free radical polymerization, UV or  $\gamma$  radiation, interpenetrating networks, and solution casting, among others, which can result in either physical cross-linking, which consists of intermolecular interactions such as hydrogen bonding, van der Waals interactions, or physical entanglement between the polymeric chains. On the other hand, chemical cross-linking takes place through the covalent bonding between reactive pending groups in the polymeric chain, such as -COOH, -NH<sub>2</sub>, and -OH. Lastly, the dominant charge on the hydrogel's network is also an important factor that can introduce valuable properties such as ionic conductibility, allowing the hydrogel to be used as a solid-state electrolyte [1,3]. Also, the charges on the hydrogel's structure can present antibacterial properties as well as prevent the adhesion of proteins that can lead to infections [4,5]. Thus, throughout these discussions, this chapter provides some of the main concepts related to hydrogels and their applications in the fields of energy production and storage, sensors, and biomedical, along with some future remarks.

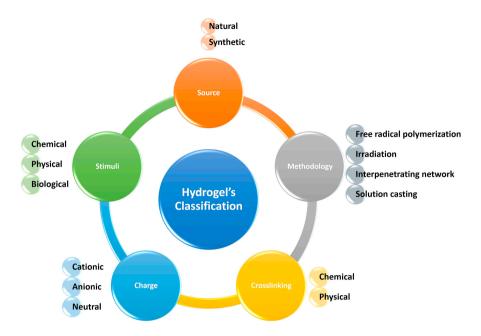
### 1.2 CHEMISTRY AND PROPERTIES OF HYDROGELS

The chemistry and properties of hydrogels are related to their structure and starting materials utilized in their synthesis. One of these factors can be attributed to the presence of hydrophilic groups which, along with the porous and opened networked structure of hydrogels, allow higher water adsorption. Based on that, the mechanical properties of hydrogels drastically change when they achieve their fully swollen



**FIGURE 1.1** (a) Schematics for the different types of hydrogel structures. (b) Scheme displaying the chemical and physical cross-linking. Reproduced with permission [1]. Copyright 2020, John Wiley & Sons.

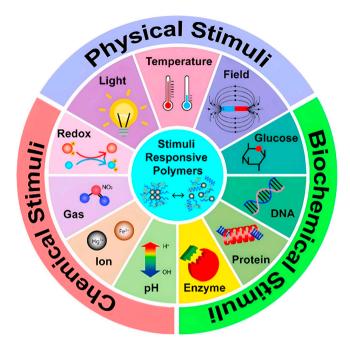
state, as they can have a rubbery, soft, or viscoelastic behavior. Such mechanical behavior is highly desired for biomedical for instance, as their moldability and flexibility allow them to better accommodate the biological system [7]. The hydrophilic nature of hydrogels may increase their interactions with body fluids which may diminish the chances of an allergic reaction and therefore better biocompatibility. For similar reasons, the broad range of mechanical properties



**FIGURE 1.2** Scheme for hydrogel classification. Adapted with permission [6]. Copyright 2020, The authors, Licensee MDPI.

along with the high intake of water or other solvents makes hydrogels attractive for flexible energy storage devices as ions can flow through their networked structure allowing them to be used either in the electrolyte or as an electrode component [8]. Hence, the swelling properties of hydrogels are one of the main aspects that can improve their range of applications. The swelling of hydrogels occurs in three phases. First, water permeates into its network, which is named primary bound water. Second, the polymeric chains become more relaxed due to the arrangement of water in its structure that is named secondary bound water. Third, the hydrogel expands its network and accommodates water that can move more freely in its structure, which is named free water [9]. The swelling property can be influenced by some factors, such as cross-linking degree, type of chemical structure, and a number of hydrophilic groups. If a hydrogel is too densely crosslinked, then it may present a lower swelling ratio. Also, a higher number of hydrophilic groups, along with a chemical structure that can properly expose them, promotes a higher swelling ratio in aqueous media. Such an effect can occur because of their response to pH, as the presence of H<sup>+</sup> can ionize the hydrophilic groups. Through that, charges can be formed within the hydrogel's network, which leads to an increase in volume to accommodate the ions as well as repulsive forces due to charges with the same polarity that cause the hydrogel to expand. This phenomenon causes the hydrogel to change from a glassy, or dry state, to a swollen or rubbery state.

Another important property of hydrogels is their response to certain changes in the environment, which can be due to physical, chemical, or biological stimuli.



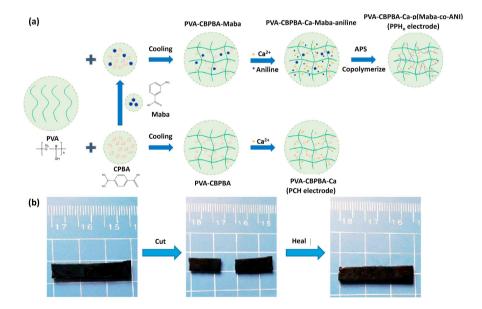
**FIGURE 1.3** Different external environments that can promote a response in hydrogels. Reproduced with permission [10]. Copyright 2021, American Chemical Society.

Physical stimuli are a response that occurs due to an applied mechanical force, light, or temperature, for instance. Chemical stimuli can be observed when there is a change in the concentration of chemical species in the media, such as ions or hydronium, which are related to the ionic strength and pH, respectively. Some of the stimuli responses of hydrogels are illustrated in Figure 1.3.

One example of thermo- and pH-sensitive properties of such materials was presented by Zhou *et al.* [11], who synthesized a chitosan/ $\beta$ -glycerophosphate hydrogel. In their study, it was observed that chitosan solubilizes in acid pH due to the protonation of its amine groups, as this condition can be maintained up to a pH of 6.2. Upon pH values higher than 6.2, a hydrated gel precipitate was formed. Following that, the presence of  $\beta$ -glycerophosphate promoted some important effects, such as adjusting the pH to around 7.0 to 7.4, which is the physiological working range. Also, its solubilization prevents an immediate gelation process which allowed for a tailored gel formation when there was an increase in temperature. Based on these results, the hydrogel could have a transition to a sol state that was influenced by pH, whereas the transition to gel was influenced by temperature.

Hydrogels also display another important set of properties, such as high flexibility, networked, and porous structure, along with self-healing capabilities. By presenting these inherent properties, hydrogels can be used as substrates for the growth of other materials with appreciable electrochemical properties, such as high conductivity and electroactive sites that can be further exposed as it grows on the hydrogel. This concept was explored by Zou *et al.* [12], who fabricated a polyvinyl alcohol (PVA)-based

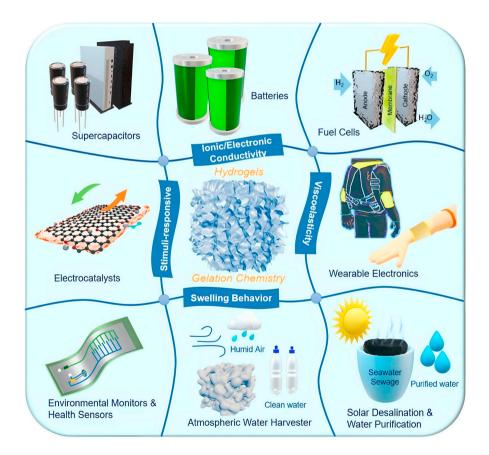
hydrogel supercapacitor. For the electrode, the PVA hydrogel was sandwiched with polyaniline (PANI) through an *in-situ* polymerization process. Alongside that, 3-aminobenzoic acid (Maba) was co-polymerized with aniline because the presence of carboxy groups from Maba can be ionized by Ca<sup>2+</sup> cations that were present on the electrolyte. Following that, for the quasi-solid electrolyte, a PVA hydrogel was physically cross-linked with 4-carboxyphenylboronic acid (CPBA) along with complexation with Ca<sup>2+</sup>. By utilizing the same hydrogel matrix both as an electrode and electrolyte, the supercapacitor could be more flexible, present self-healing properties, and have faster ionic conduction [13,14]. Another important aspect is that utilizing the same material to make the supercapacitor could promote more intimate contact between the electrode/electrolyte interface, reducing some impedance that could arise in the system otherwise. The synthetical diagram for the all-hydrogel supercapacitor is presented in Figure 1.4a. Based on these aspects, the all-hydrogel supercapacitor was assembled by sandwiching two electrodes based on PVA-CPBA-Ca-Maba and PVA-CPBA-Ca in between. Furthermore, the flexible hydrogel-based supercapacitor also presented self-healing properties that were attributed to its network structure that was physically cross-linked, which enabled the reconnection of borate ester bonds along with ionic bonds from the Ca<sup>2+</sup> species by heating the components at 70°C for 4 h. It was proposed that the relatively high temperature allows the PANI chains to move along the PVA and reestablish the severed sessions. The self-healing process of the PVA-CPBA-Ca-p(Maba-co-aniline) is presented in Figure 1.4b.



**FIGURE 1.4** (a) Synthetic scheme for the fabrication of an all-hydrogel based on PVA-CPBA-Ca-p(Maba-co-aniline) as electrode and PVA-CPBA-Ca as electrolyte. (b) Photocopies displaying the self-healing property of PVA-CPBA-Ca-p(Maba-co-aniline) after being exposed to 70°C for 4 h. Reproduced with permission [12]. Copyright 2021, Elsevier.

#### **1.3 APPLICATIONS OF HYDROGELS**

The applications of hydrogels extend to several areas that can go from certain types of foods, such as gelatin, to soft contact lenses and diapers, among others. Yet, these materials are also being applied to energy production, such as fuel cells, and electrocatalysts as well as energy storage such as supercapacitors and batteries, which can be initially attributed to the highly porous network structure that allows it to be embedded with electroactive materials to be used as an electrode or it promotes the flow of ions within its network, which can ensure relatively high conductivity, hence functioning as an electrolyte. Other applications include wearable devices due to their inherent flexibility, sensors due to their response to external stimuli, and water purification systems due to their porous networked structure and swelling behavior. A general schematic displaying the applications of hydrogels is presented in Figure 1.5.

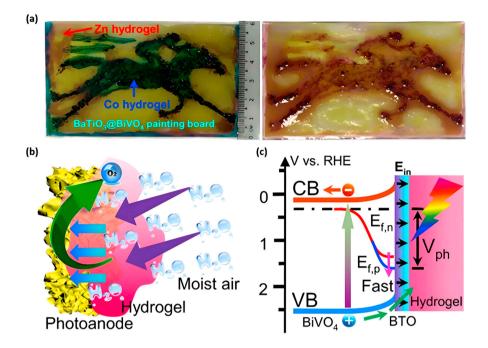


**FIGURE 1.5** Schematic displaying the several applications of hydrogels based on their inherent properties, such as conductivity (electronic and ionic), environmental stimuli, flexibility, and swelling behavior. Reproduced with permission [15]. Copyright 2020, American Chemical Society.

#### 1.3.1 Hydrogels for Energy Production

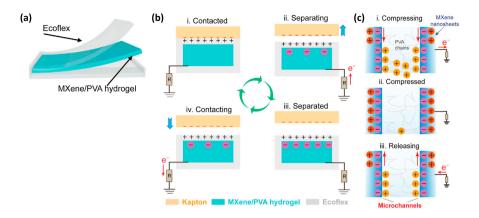
Energy production is one of the most regarded topics due to its pivotal importance for the working of society as it is a resource so intrinsic that became nearly impossible to leave without it. Solar energy is an attractive aspect as it is a highly sustainable, renewable, and zero-carbon emission process. Based on that, Yang et al. [16] proposed the fabrication of a hydrogel composite by using  $BaTiO_3@BiVO_4$ , a ferroelectric-semiconductor that can improve the charge separation as well as the transfer process during the oxidation of H2O. This process can be attributed to some of the properties of BaTiO<sub>3</sub> that can induce the formation of an electric field at the end of the positive polarization. Through that, the photovoltage and the acceleration of holes (h<sup>+</sup>) can be increased, facilitating its transfer to the surface of BiVO<sub>4</sub>. The hydrogel serves as a substrate that can adsorb the moisture from the atmosphere's humidity, which allows the system to be constantly supplied to carry on the  $H_2O$  oxidation process. Highly hygroscopic hydrogels, one based on Zn and the other Co, played the role of carrying H<sub>2</sub>O to the photoanode, which could enhance the mobility of carriers. The photoanode-hydrogel system, along with the solar cells in series, provided a photocurrent of 0.4 mA/cm<sup>2</sup> with a 12% humidity reduction and at an illumination of 10 mW/cm<sup>2</sup>. The application of the ferroelectric-semiconductor hydrogel composite is displayed in Figure 1.6a, which shows a painting board covered with  $BaTiO_3@$ BiVO<sub>4</sub> over a fluorine tin oxide (FTO) substrate. Then, Co and Zn hydrogels were applied over the surface of BaTiO<sub>3</sub>@BiVO<sub>4</sub>. Through that, the composite can adsorb water from the environment under the presence of ambient light. Also, the environment's relative humidity (RH) was associated with the change in color of the hydrogel as the Co-based hydrogel went from green-blue to pink and the Zn-based hydrogel went from transparent to opaque upon adsorption of water. After water adsorption from the hydrogel, the BiVO<sub>4</sub> absorbs a photon, which excites its electron from the valence band (VB) to the conducting band (CB), which leads to a drop of the quasi-Fermi energy of  $h^+$  (E<sub>f,p</sub>) from the electrons (e<sup>-</sup>) quasi-Fermi level (E<sub>f,p</sub>). Such an effect creates a photovoltage  $(V_{ph})$  at which the larger the  $V_{ph}$  the better the H<sub>2</sub>O oxidation process, as it leads to a lower energy barrier for the  $h^+$  transfer process. Also, according to the authors, the electric field generated by  $BaTiO_3$  (E<sub>in</sub>) due to the positive polarization could have facilitated the h<sup>+</sup> transfer process to the composite's surface; meanwhile, the  $e^{-}$  would be driven towards the bulk [17]. Based on the mechanistic process, it could be inferred that the hydrogel could provide a constant supply of H<sub>2</sub>O, whereas the BaTiO<sub>3</sub>@BiVO<sub>4</sub> could carry out the charge transfer process to promote the photoelectrochemical splitting of H<sub>2</sub>O. The scheme for the mechanism and the energy diagram of this process are presented in Figure 1.6b-c.

Hydrogels can be included in the fabrication of triboelectric nanogenerators (TENGs), which are composed of a junction of materials that can convert mechanical energy into electricity. However, the initial hindrance to this technology is that traditional supercapacitors and batteries tend to be rigid. Yet, the introduction of hydrogels can lead to advantageous processes as they can be highly flexible and stretchable, conducting, and self-healing. Through that, hydrogels may provide an alternative for the development of triboelectric devices [18]. Despite that, other components are required to further optimize their properties to make them suitable



**FIGURE 1.6** (a) Photo of the ferroelectric-semiconductor hydrogel composite at which  $BaTiO_3@BiVO_4$  was applied over the FTO substrate, whereas the Co and Zn hydrogels were placed. (b) Mechanism of  $H_2O$  adsorption by the hydrogel as the  $H_2O$  is transferred to the photoanode to undergo the splitting process, realizing  $O_2$ . (c) The energy diagram displays the enhancement of the  $e^- - h^+$  charge separation and transfer. The occurrence of the photochemical process was attributed to an electric field generated by  $BaTiO_3$ , along with the upward bending of  $BiVO_4$  to the generation and transfer of  $h^+$  to the composite's surface where the  $H_2O$  oxidation process occurs. Reproduced with permission [16]. Copyright 2019, Elsevier.

for flexible energy generation devices. Based on these aspects, MXenes can serve as an addition to the hydrogels, as these 2D transition metal carbide-based nanomaterials present relatively higher conductivity, high surface area, hydrophilic nature, and satisfactory mechanical properties. Luo *et al.* [19] fabricated a composite composed of PVA hydrogel and MX nanosheets (MH-TENG). Furthermore, a Si rubber (Ecoflex) was used as a triboelectric layer to avoid the loss of water from the hydrogel. The tests revealed that the MH-TENG could harvest vibrational energy, showing potential uses as a wearable energy harvesting device as well as a wearable sensor (Figure 1.7a). For that, the MXene/PVA hydrogel functioned as the electrode. Also, in the Si rubber, ion transport could occur for electrostatic screening of triboelectric charges. This process occurred in several steps, as shown in Figure 1.7b. Step i: first, a Kapton film is placed in contact with the Ecoflex, which is sandwiched with the MH-TENG through mechanical force. This induces the formation of the same amount of positive and negative charges on the surface of Ecoflex and Kapton, respectively, which is known as the triboelectric effect. Step ii:



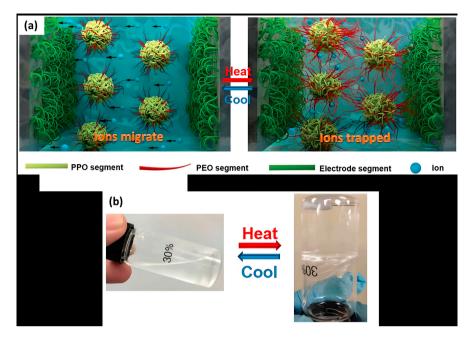
**FIGURE 1.7** (a) Scheme of the MH-TENG electrode. (b) Working principle scheme for the single-electrode system of MH-TENG. (c) A triboelectric mechanism consisting of the presence of microchannels of the MXene/PVA hydrogel composite. Adapted with permission [19]. Copyright, 2021, John Wiley & Sons.

after that, Kapton and MH-TENG are slowly separated, which leads to a polarization of negative and positive charges on the surface of MXene/PVA hydrogel and Ecoflex, respectively. Because of that, e<sup>-</sup> from the connected wire flows toward the hydrogel. Step iii: once the Kapton is far enough, the system stops generating charges because of the complete screening of the positive and negative charges from the Ecoflex and MXene/PVA hydrogel, respectively. Step iv: upon approaching Kapton and Ecoflex, a decrease of potential difference occurs between the two, which is because of an increment in the electrostatic shielding. That effect leads to the repulsion of the negative ions from the upper surface of the MXene/ PVA hydrogel, leading to an excess of e<sup>-</sup> flow out of the system. Upon contacting Kapton and Ecoflex, the system returns to step i. Furthermore, it is also worth describing the mechanism that takes place on the MXene/PVA hydrogel, known as streaming vibrational potential (SVP), which is described in Figure 1.7c. In step i there is a formation of hydrogen bonds between the PVA and the MXene nanosheets. This interaction leads to the formation of microchannels in the MXene, which can be filled with PVA chains and water. Upon the interaction between water and MXenes, polarization happens in a way that positive and negative charges are generated in the former and latter, respectively. This process leads to an electric double layer, which can generate a non-Faradaic current. When the MH-TENG is pressurized, water can flow out of the positive ions while maintaining the negative charges on the MXene's surface. That process leads e<sup>-</sup> from the external circuit to be repelled out of the system, whereas positive charges are induced onto the MXene. Step ii, when maximum compression is applied, most of the positive ions present in the microchannel are expelled to the outside microchannels, which causes the MXene's positive and negative charges to be in equilibrium; hence, no external current passes through the system. Step iii, upon release of pressure, the water can flow back, which leads to the buildup of the electric double layer and therefore a reversed external current.

#### **1.3.2 Hydrogels for Energy Storage**

There has been a plethora of materials that have been employed in the fabrication of energy storage devices, such as transition metal derivatives that include oxides, sulfides, and bimetallics, along with conducting polymers, metal-organic frameworks, and covalent organic frameworks, among many others. Yet, hydrogels can also be incorporated into supercapacitors and batteries, given their highly porous networked structure, conductibility, and stimuli response to external gradients, which may add a novel factor to energy storage devices derived from them. Some electrochemical devices may undergo an increase in temperature that can lead to fires or explosions due to overcharging, aggressive use, or inappropriate environments [20,21]. Because of that, introducing active ways to prevent thermal runaway is an important factor to avoid failure of the device, along with longer cycle life and electrochemical stability. Some examples of polymers that can perform phase separation or sol-gel transitions at high temperatures have been used as electrolyte matrices in Li-ion batteries [22,23]. This feature provides a safety step in case of overheating, as the reversible sol-gel transition can protect the device by temporarily stopping the charging or discharging process until the temperature is back to the safe working range. One of the polymers that have been used for this end is poly(N-isopropylacrylamide) (PNIPAM) [21,23]. Yet, a broader transition temperature range along with more feasible synthetical approaches are desired. Shi et al. [24] utilized a block polymer composed of poly (propylene oxide) in between poly(ethylene oxide) (PEO-PPO-PEO), which was employed as a smart electrolyte that could shift to the gel state based on the temperature. Based on that, it was observed that at low temperatures the polymer was in the solution state, which allowed the ions to move freely within its structure. Yet, with the increase in temperature, the PEO-PPO-PEO transitioned to the gel state, which hindered the ionic flow, causing the device to cease working. This type of feature provides some advantages, such as a reversible self-protection mechanism. Also, the trigger temperature for the gel to the formed as well as the capacity loss can be tuned based on the molecular weight. Lastly, the polymers employed to make the electrolyte matrix are commonly used, along with their proper interaction with different electrode materials may present some potential for larger-scale applications. The schematics for the representation of ionic motion and the physical aspect of the PEO-PPO-PEO in its solution and gel state are presented in Figure 1.8.

The versatility of hydrogels can go beyond the types of polymers that can be employed to synthesize them. Aside from it, hydrogels can be mixed with several nanomaterials to enhance their properties and perform the transport of different ionic species. Also, hydrogels can function as a core component for the development of flexible energy storage devices, which have attracted some attention from the scientific community due to the novel products that can be obtained, such as smart watches, e-skins, portable devices, and so on [25–27]. Chen *et al.* [28] studied the effect of different electrolytes on a composite electrolyte based on graphene thin films and PVA gels as the schematics for the device are presented in Figure 1.9a. Several electrolytes, such as NaCl, KCl, NaOH, KOH, H<sub>2</sub>SO<sub>4</sub>, and H<sub>3</sub>PO<sub>4</sub>, were studied. After performing the cyclic voltammetry (CV), it was observed that H<sub>3</sub>PO<sub>4</sub> had the best overall performance by presenting a typical

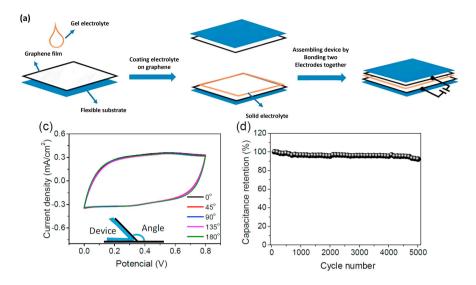


**FIGURE 1.8** (a) Illustration of the hydrogel thermal response upon an increase in temperature that leads to the formation of a gel system that hinders the movement of the ions in the electrolyte preventing the storage device from overheating. (b) PEO-PPO-PEO in the solution state at cooler temperatures and in the gel state at higher temperatures. Adapted with permission [24]. Copyright 2016, John Wiley & Sons.

electric double-layer capacitance mechanism based on the squared shape of the CV plot. The authors proposed that the higher capacitance of  $H_3PO_4$  was attributed to the higher ionic strength of the acid when compared to the other electrolytes. Also, the H<sup>+</sup> could diffuse more easily through the PVA-graphene structure when compared to relatively larger Na<sup>+</sup> and K<sup>+</sup>. Alongside that, the lower amount of H<sup>+</sup> derived from the  $H_2SO_4$  when compared with  $H_3PO_4$  for the same concentration led to a decrease in the capacitance of  $H_2SO_4$ . In addition, the presence of flexible PVA gels allowed the device to perform at several bending angles with virtually no decrease in performance, along with satisfactory electrochemical stability after 5,000 CV, which is demonstrated in Figure 1.9b-c.

# **1.3.3 Hydrogels for Sensors**

The external stimuli response of hydrogels is one of their unique properties that allow their use in the fabrication of varied sensors, such as for the identification of humidity, pressure, temperature, ionic strength, and biomolecules, among many others. Several synthetic polymers can be used in the development of sensors, such as PVA, poly(ethylene glycol) (PEG), poly(vinylpyrrolidone) (PVP), poly(vinyl imidazole) (PVI), and poly(acrylamide) (PAM), among others [29]. Based on that,



**FIGURE 1.9** (a) Scheme for the fabrication of the composite PVA-graphene hydrogelbased electrode. (b) CV plot for the PVA-graphene hydrogel with  $H_3PO_4$  as an electrolyte at different bending degrees. (c) Electrochemical stability test performed up to 5,000 cycles. Adapted with permission [28]. Copyright 2014, Royal Society of Chemistry.

it is possible that these hydrogels can convert some type of mechanical deformation, such as compression or strain, into an appreciable electrical signal, making them applicable as sensors. However, one of the recurrent challenges lies in providing an external energy source that allows the generation of detectable and stable signals [30–32]. Under this line, it is deemed necessary to develop hydrogel-based sensors that can function without the need for a power supply, as this can expand their applications as sensors. In a previous study, hydrogel-based sensors for the generation of electricity through moisture were developed [33].

In another work, a TENG capable of converting applied mechanical energy into electricity was fabricated [34]. In this case, the device was self-powered and could effectively perform as a strain sensor. Another work based on the use of hydrogels for the development of sensors was performed by Wang et al. [35], who used a PVA hydrogel with malic acid (MA). It is worth noting that MA has a relatively high acidity, which leads to an increase in output voltage. Alongside that, when compared to other organic acids, such as acrylic acid, citric acid, and tannic acid, for instance, MA displays the highest redox potential, ionizability, and conductivity, making it a feasible candidate as an electrolyte. Also, Ca<sup>2+</sup>, in the form of CaCl<sub>2</sub>, was introduced to improve conductivity, enhance the self-powering properties, and prevent the hydrogel from drying and freezing. Through that, the MA-CA-PVA could deliver a voltage of around 0.55 V along with a conductivity of around 5.3 S/m. Also, the hydrogel could provide strain-related signals based on the changes in the output current without an external supply for power. In addition, the hydrogel could monitor human motion at temperatures as low as -20°C. Based on that, the scheme for the fabrication of the MA-Ca-PVA hydrogel is presented in Figure 1.10.

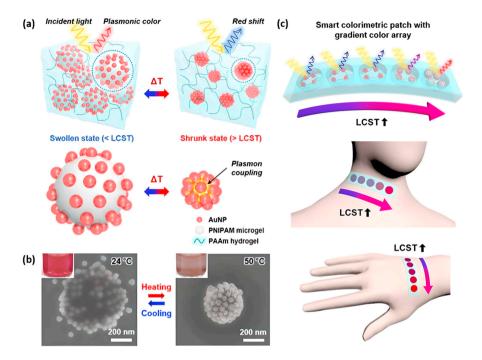


**FIGURE 1.10** Scheme for the synthesis process of MA–CA–PVA (MCP) hydrogel. Adapted with permission [35]. Copyright 2020, Royal Society of Chemistry.

There is a need for the development of a fast responsive sensor that can be obtained on a large scale. One of the fields that has a higher demand for this technology is biomedical, for accurate and fast diagnosis, for instance. Based on these aspects, Choe et al. [36] fabricated a PNIPAM microgel that was decorated with Au nanoparticles (AuNP) over a flexible PAA hydrogel matrix. The composite hydrogel presented a thermosensing color gradient that presented a resolution of temperature sensing of around 0.2°C. The device was fabricated using the composite hydrogel that functioned as a color-based thermometer. The color change properties were attributed to the localized surface plasmon resonance (LSPR), which is the phenomenon by which a collection of oscillatory conducting electrons become excited by the incidence of light in a metallic nanoparticle [37,38]. The LSPR is the main principle of operation for the PNIPAM AuNP-hydrogel, as at around 24°C, the microgel has a loose structure, whereas at temperatures of around 50°C, the structure shrinks. Through that, the system presents an uncoupled/couple plasmon or swollen/shrink mode around 24 and 50°C, respectively (Figure 1.11a). The scanning electron microscopy (SEM) of the plasmonic microgel at 24 and 50°C shows the swelling/shrinking effect in the function of temperature that leads to a variety of colors, which is shown in Figure 1.11b. Based on this property, the thermo-sensitive hydrogel can be incorporated into an array of sensors that can provide a broader range of temperatures, leading to a more accurate measurement of the temperature, as shown in Figure 1.11c. Such a type of device can find several fields of applications, aside from biomedical, yet it shows a convenient and effective way to analyze the temperature based on a thermo response of a hydrogel decorated with nanoparticles.

#### 1.3.4 HYDROGELS FOR BIOMEDICALS

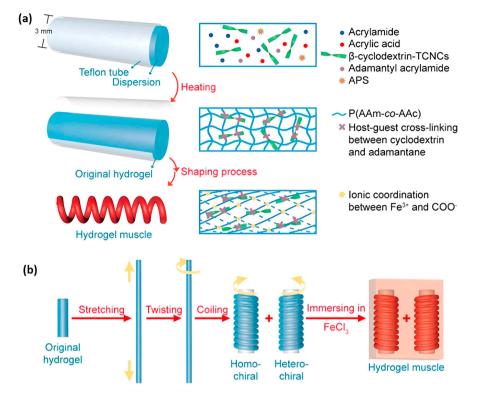
Hydrogels present a vast range of applications within the biomedical field, as they can function as drug delivery systems, scaffolds for tissue regeneration and engineering, antibacterial agents, and biosensors for the identification of biomolecules, along with presenting good biodegradability and biocompatibility. The combination of such properties makes it an attractive component for the design of medical products [39–41]. Cui *et al.* [42] fabricated a hydrogel reinforced with tunicate cellulose nanocrystals (TCNCs) that presented a tendril shape that could potentially function as an artificial muscle. The hydrogel was obtained through the polymerization of acrylic acid, acrylamide, and adamantly acrylamide in the



**FIGURE 1.11** (a) Scheme of the temperature response of the PNIPAM microgel decorated with AuNP at a PAAM hydrogel substrate that is based on the LCST phenomenon. (b) SEM images showing the swollen and shrunk state of the plasmonic microgel and the inlet photocopy displaying the color based on the temperature of 24 and 50°C, respectively. (c) Schematic for the sensor array that can be placed on human skin for temperature measurement. Reproduced with permission [36]. Copyright 2018, The authors, Licensee NPG Asia Materials.

presence of TCNC modified with  $\beta$ -cyclodextrin ( $\beta$ -CD-TCNCs). Furthermore, the tendril shape was obtained by submersing the hydrogel into a FeCl<sub>3</sub> solution that would promote Fe<sup>3+</sup>/-COO<sup>-</sup> ionic coordination bonds in the structure. During the shaping process, the chirality of twisting and coiling were controlled which yield artificial muscles with both homo- and heterochiral. Because of that, the hydrogels could respond to the presence of solvents by contracting or expanding, allowing the hydrogel to function as a muscle. The full schematic for the synthetic process of the hydrogel artificial muscle is provided in Figure 1.12.

Tissue engineering technologies have the main goal of promoting the growth of healthy tissue. Yet, such a process is inherently challenging, as there are several factors that one must consider before introducing certain types of material within a physiological system. Some of these aspects include introducing a material that can imitate the natural extracellular matrix (ECM), to serve as a substrate at which the cells can grow without triggering an inflammatory reaction. Also, it is desired that the material used as a scaffold for the growth of cells or as tissue recovery can slowly degrade as the healthy tissue is regenerated. Also, during its *in-vivo* decomposition



**FIGURE 1.12** (a) Schematics for the synthesis of hydrogel-based artificial muscle. (b) The approach adopted to shape the hydrogel artificial muscle to obtain homo- and heterochiral materials. Reproduced with permission [42]. Copyright, 2021. American Chemical Society.

process, there should be the formation of non-toxic compounds of fragments to provide a safer excretion from the body [43,44]. Another important aspect of tissue recovery lies in the controlled dosage of growth factors or drugs that are associated with delivery system technology. Based on that, the material must release the drug in concentrations that are within the therapeutic range to prevent the drug from becoming poisonous. One reported example is the case of nerve growth factor, which has been shown to have an optimal dosage of 800 pg/µL in rats to promote the growth of neurites. However, at higher concentrations, it hinders its growth [45,46]. Hydrogels are feasible components for the development of scaffolds, tissue recovery, and drug delivery systems due to their porous structure that can enable the growth of cells and tissue recovery. Also, the high porosity enables the adsorption of drugs that can be released in a target region in the body. Alongside that, the versatile chemical nature of hydrogels permits the use of materials that can be biocompatible as well as biodegradable. Despite that, there are several that must be considered for the development of an ideal tissue engineering material. In this sense, mimicking the cellular structure includes presenting similar mechanical, structural, and chemical properties of the cell. Also, if the hydrogel carries a drug for cell growth or treatment, it should present a controlled release.

Yan *et al.* [47] fabricated a  $\beta$ -hairpin peptide hydrogel that could be potentially employed as an injectable solid. The main feature of this material was based on its reversible mechanical properties, as under an applied shear, the hydrogel network was disrupted into domains that allowed it to flow. However, once the shear force was removed, these domains could promptly recover to their initial state. Such a process occurred due to the physically cross-linked structure of fibrillar branching and entanglements [48,49]. Hydrogels with such behavior can potentially find applications in the biomedical field. Yet, several factors must be considered, such as biocompatibility, biodegradability, and capability of the hydrogel to either host cells for their growth if used for tissue engineering or recovery. Also, if the aim is focused on drug delivery systems, the hydrogel should be able to adsorb the drug and release it in the targeted area.

### 1.4 CONCLUSION

Hydrogels have been growing within research due to the vast number of commonly known compounds that can be used for their synthesis, which expands their classification in terms of materials used, types of cross-linking, type of bonding, type of stimulus, and surface charge, among others. Aside from the chemical and synthetical versatility, their most attractive point is their properties that arise from their networked structure that promotes a swelling behavior. Along with that, hydrogels present a distinct property of sense that can take place through different stimuli such as physical, chemical, or biological. The combination of all these factors made hydrogels attractive to the scientific community in several areas of research, such as energy generation and storage, sensors, biosensors, and biomedical to name a few. Hydrogels are applicable in energy generation, such as fuel cells due to their high porosity, which allows the diffusion of water to properly perform its redox process. Also, by presenting a chemically stable and open morphology, electroactive materials can be easily grown in their structure to obtain a composite. Similarly, hydrogels can be used in energy storage devices, such as supercapacitors and batteries, as their porous structure enables the permeation of electrolytes to promote the charging process in supercapacitors. Also, in the case of batteries, hydrogels can be particularly useful because of their swelling properties, as they can withstand chemical as well as physical strain after the incorporation of metal atoms, which could lead to an improvement in electrochemical stability. Yet, further research is required to optimize this process as there is a relatively smaller number of studies in this specific area. Hydrogels can respond to different external factors such as temperature, pH, mechanical forces, specific chemical compounds, and so on. This unique property is highly desired for the application of sensors. Lastly, hydrogels have been widely used in the biomedical field as tissue engineering and drug delivery systems. Their networked structure functions as nucleation sites for the growth of cells, along with the possibility of carrying growth factors or drugs to expedite this process. Also, hydrogels can be obtained from biocompatible and biodegradable materials, which allows for them to be inserted into a biological system and released without harming the body. Despite the vast realm of applications of hydrogels, there is still the need to further tailor their properties to optimize their uses.

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# 2 Hydrogels Based on Natural and/or Synthetic Polymers

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# 2.1 INTRODUCTION

Hydrogels are mixtures of cross-linked polymeric chains with a three-dimensional structure, which are capable of absorbing and retaining a considerable amount of water inside due to their hydrophilic nature. Hydrogels can contain polar groups such as

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-COOH, -OH, -NH<sub>2</sub>, -CONH, -CONH<sub>2</sub>, and -SO<sub>3</sub>H. These functional groups provide the polymeric network with the characteristic appearance of hydrogels on a microscopic and macroscopic scale [1,2]. Depending on the source of origin, the polymer network can be synthesized by various standardized methods that are generally reproducible without difficulty. Cross-linking is a key step that can be accomplished by strategies involving covalent bonding or by non-covalent interactions, such as ionic bonding or hydrogen bonding [3,4]. Whether by the selected method of synthesis or polymers (hence, the functional groups present in the hydrogel) will result in the characteristics of the hydrogel, in other words, water retention capacity; the percentages of cross-linking; and usefulness at a determined pH [5–7], temperature [8], or ionic strength [9].

There are several types of hydrogels and are classified according to the origin of components, which means natural or synthetic; another way to classify them is by the synthesis method, which can involve physical or chemical cross-linking. The characterization of hydrogels is performed through various physical parameters, such as pore size, elastic modulus, degree of swelling, degradation rate, and biocompatibility degree [10]. Currently, research has focused on hydrogels prepared from biological materials of protein origin, such as collagen or elastin, and polysaccharide polymers such as glycosaminoglycans, chitosan, and alginate, among others. Synthetic polymer-based hydrogels are obtained from polymers such as poly(acrylic acid) (PAAc) [11], poly(*N*-isopropylacrylamide) (PNIPAm) [12], poly(ethylene glycol) (PEG) [13], poly(*N*-vinyl caprolactam) (PNVCL) [14], or poly(2-hydroxyethylmethacrylate) (HEMA) [15], which are obtained using techniques of addition polymerizations, and may have stimuli-responsive properties such as pH, temperature, magnetic, and/or ionic strength [16].

The characteristics of polymers present in a hydrogel should include high biocompatibility, biodegradability, and low cytotoxicity. Fortunately, these positive properties are shared by many natural and synthetic hydrogels. Certain characteristics, such as the chemical reactivity of the hydrogel, can be manipulated by adding, removing, or blocking specific functional groups. The chemical formula, in turn, affects the physical rheology in a solution; so, it is important to control the swelling degree, network size, or viscosity, to control the capacity of the hydrogel to diffuse and trap molecules [17], and/or cells within its network [11]. These properties allow hydrogels to be applied in multiple industrial, pharmaceutical, and biomedical fields [18], due to the great similarity and acceptance of hydrogels with soft tissue [19]. All hydrogels, both natural and synthetic, have qualities, limitations, and disadvantages; for example, some hydrogels that contain only natural polymers in their structure have limitations, such as poor mechanical properties or rapid degradation [19]. For this reason, natural polymers are often combined with synthetic polymers to create composite hydrogels. In general, composite polymers contain in their structure at least one polymer matrix that is reinforced by fillers, which produces an improvement in overall performance; therefore, their possible applications are increased [20], since synthetic polymer hydrogels can be designed to obtain customized mechanical properties, which otherwise, by themselves, do not usually have an inherent bioactivity. Therefore, adapting the hydrogels based on a potential application is the most useful tool in the engineering of hydrogels [21].

Hydrogels are widely studied in most of the materials science disciplines due to the number of possibilities for synthesis and their possible uses and applications [18]; it is common to find hydrogel materials for heavy-duty use but also in biomedical microdevices [22]. Many hydrogel systems have already been successfully tested in biomedical applications [23], including drug delivery systems [10], three-dimensional (3D) cell cultures [24], tissue implants [25], tissue regeneration [26], contact lenses [27], and other personal hygiene products [28]. Each type of hydrogel can be adapted according to the application for which it is designed. This also includes choosing of a specific method and technique to achieve the product of interest with the chemical and physical properties required.

Although it has already been said that hydrogels may have their special characteristics depending on the final use, certain general parameters are expected to be mostly covered, such as desirable characteristics all around their high water absorption or a well-known water retention capacity under a controlled time [29].

#### 2.2 NATURAL HYDROGELS

Natural hydrogels are made up of polymers extracted from plants, animals, or microorganisms [30]. The most used natural polymers for the synthesis of hydrogels are macromolecules such as carbohydrates and proteins, which are essential components of organisms, and therefore their properties can be transferred to the biomedical device with a specific physicochemical characteristic or resistance [31]. In addition, natural polymers exhibit high biocompatibility, biodegradability, accessibility, stability, lack of toxicity, and low cost [32]. The inherent advantages of these materials are evident once they are used and the life cycle is complete since the residues are reincorporated into the environment in a more harmonious way to be used later as all organic matter [33]. There are several types of natural polymers, of which the most representative are proteins, polysaccharides, polynucleotides, polyisoprenes, and lignin. Protein and polysaccharide polymers are inexpensive compared to other natural polymers and are highly available, biodegradable, and biocompatible [33]. Therefore, these polymers are recommended for applications in tissue scaffolds [34] and regenerative medicine because hydrogels can easily reach this functionality, given that they can replicate an extracellular matrix, which is a common property among natural raw materials available in the market [35].

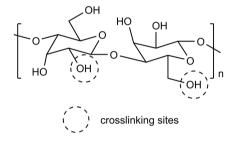
#### 2.2.1 CELLULOSE AND STARCH

Cellulose is the most abundant polysaccharide in plants, consisting of a linear chain of  $\beta$  (1 $\rightarrow$ 4) linked D-glucose units. The first use of cellulose as a material is in the paper industry, where the main sources are bamboo, cotton, linen, and practically every fiber from plants. Cellulose can interact well with water but it is insoluble in it, which is a limitation [36]. Nonetheless, cellulose is an interesting biopolymer because it is biodegradable and biocompatible. For these reasons, it is a sturdy candidate as a biomaterial for medical devices or sanitary disposables. The potential of cellulose-based hydrogels is big, despite the problems related to chemical modifications needed before the formation of the hydrogel, which is essential because cellulose is a stable macromolecule. Therefore, cellulose derivatives are prepared as precursors of hydrogels. The list includes, for example, methylcellulose, hydroxyethyl cellulose,

hydroxypropyl cellulose, and carboxymethyl cellulose sodium [37]. These previous modifications aim to provide the hydrophilic groups to make the reaction easier with the cross-linking agents that improve the hydrophilicity eventually. Methods employed are also vast and comprise of gamma radiation, chemical cross-linking, photocross-linking, freeze-thaw, etc. [38]. These changes enhance the absorption of water and swelling without dissolving the material. Using cellulose as a hydrogel matrix is only the first example of a natural matrix because other natural polymers attain superior performance and other capabilities, as we see with starch below.

Starch and cellulose are the most known carbohydrates. Starch is present in plants and is one of the main sources of food for human consumption, so our body can easily recognize it. Starch is found abundantly in plants in green leaf chloroplasts and in seed amyloplasts [39]. Starch has in its structure two types of glucose units. These are the parts of the polymer chain and are covalently bound through glycosidic bonds, mainly with linear and helical amylose (containing D-glucose monomers bound to  $\alpha$ -1,4) in a ratio ranging 20–25% and by amylopectin (which contains  $\alpha$ -D-(1,6) bonds, located each 25–30 linear units of glucose) in a percentage of 75 to 80% (Figure 2.1). The exact

Cellulose





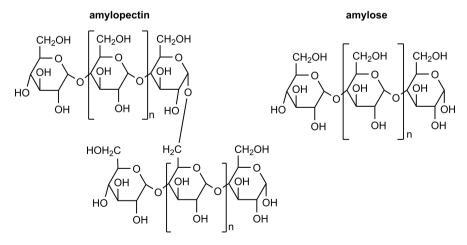


FIGURE 2.1 Structure of polysaccharides cellulose (up) and starch (down).

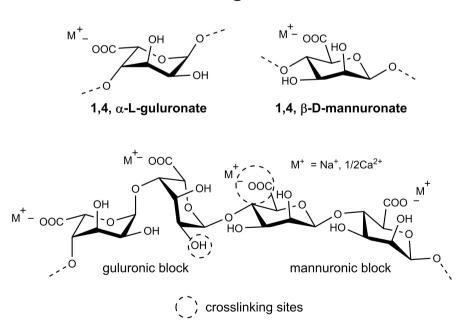
composition varies depending on the starch source, but the microstructure of the starch remains identical, regardless of the source. These two types of starch components also have different physical properties because amylose is a semicrystalline biopolymer soluble in hot water, while amylopectin is crystalline and almost insoluble in hot water [40].

Assets of starch-based hydrogels lie in their hydrophilicity; this property is translated as high swelling and hydration capacity since these hydrogels are characterized by absorbing a large volume of water. In fact, starch chains can retain water through two mechanisms, besides direct hydrogen bonding with hydrophilic groups; starch hydrogels can also retain water through hydrophobic groups and cross-linking chains, which increases the total retention capacity [41].

Starch-based hydrogels are suitable for the load and controlled release of many drugs. For example, quercetin, a low molecular weight polycyclic molecule, mainly contains aromatic -OH groups, that form hydrogen bonds with the starch in an aqueous medium [42].

### 2.2.2 ALGINATES

Alginate is a highly hydrophilic linear chain polysaccharide that contains two types of monosaccharide units in the backbone. These are  $1,4-\alpha$ -L-guluronic acid and  $1,4-\beta$ -D-mannuronic acid, which allows the mannuronic and guluronic blocks (Figure 2.2). Alginate hydrogels can absorb huge amounts of water up to 20 times its weight.



Alginates

