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Electron transfer through protein-bound water and its bioelectronic application

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ABSTRACT

This article reports that a metastructure of polypeptides with the bound water can have high and stable electron conductivity without classic electron-conducting components. We used gelatin as the model protein since the peptide chains contain numerous sites capable of forming hydrogen bonds with water molecules. The lack of redox sites and the trace amounts of aromatic amino acids also eliminate the possibility that the electron transfer is due to redox reactions or pi-stacking. Our Raman spectroscopy results show that the high electron-conductive metastructure is composed of bound water and unwound gelatin polypeptides. Further removal of bound water from the metastructure dramatically decreases the electron-conductivity, indicating that bound water is crucial to connect the polypeptide chains for the electron-conductivity. In addition, the ability to switch between the low-electron-conductive typical hydrogel state and the high-electron-conductive metastructure state of the gelatin hydrogel allows the gelatin hydrogel to exhibit rewritable nonvolatile resistive memory features. The high ON/OFF current ratio of 10^5 at a low reading voltage of 0.09 V is superior to that of conventional nonvolatile resistive memories by one order of magnitude. The discovered phenomenon of using bound water and flexible polypeptide structure for long-distance electron transfer could provide a new direction for designing highly biocompatible conducting materials or functional devices in bioelectronics.

1. Introduction

Finding ideal materials to bridge electronic devices and biological systems is an important issue for various biomedical applications(Kim et al., 2011; Kumari et al., 2017; Someya et al., 2016; Son et al., 2014). The challenge mainly comes from that electronic devices use electrons for the conduction, but biological systems usually function in an aqueous environment which is thought to hinder effective long-distance electron transfer. Although previous studies have reported that electron can transfer in a protein molecule or a peptide backbone through electron hopping (Morita and Kimura, 2003) or electron tunneling (Antonello et al., 2003; Cordes and Giese, 2009; Gilbert Gatty et al., 2015), the transfer is only limited in a single peptide or self-assembled peptides with supramolecular ordering(Ing et al., 2018; Isied et al., 1992; Watanabe et al., 2005). In this study, we demonstrate that a gelatin hydrogel can become an electron-conductive resistor after the unbound free water is removed and the bound water is maintained.

Gelatin is a protein derived from collagen and contains numerous sites for water-mediated hydrogen bonding(de Wolf, 2003). These sites allow gelatin polypeptides to form hydrogels with the collagen-like triple-helical structure below the gelation temperature. When the gelatin is heated above the gelation temperature, the triple helices unwind into single strands. As a protein, it has been widely used in biomedical applications due to its biocompatibility, biodegradability, commercial availability, and relatively low cost(Choi et al., 1999; Zhang et al., 2005). However, as a protein hydrogel with no redox sites and only trace amounts of aromatic amino acids (de Wolf, 2003), it has not been practically used for electron transfer or any electronic applications.

The switch from a typical hydrogel with low electron-conductivity to a high electron-conductive resistor provides a possibility for the material to have memory applications. Among various types of memories, the resistive-type memories consist of an active layer sandwiched between two electrodes and can be fabricated into a three-dimensional stacking structure to achieve data storage with a high density(Sharma, 2009). Nonvolatile resistive memory devices store and access information by encoding “0” and “1” based on the electrical bistability of the active layer: the high (ON state) and low (OFF state) conductivity response to an applied voltage(Ling et al., 2008; Sharma, 2009). This type of memory demands a mechanism of repeatable switching between different states, and they often rely on voltage or current for the reprogrammability(Heremans et al., 2010; Ling et al., 2008). Previous

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studies have tried to use bio-related materials for constructing memory devices for bioapplications(Hosseini and Lee, 2015; Raeis-Hosseini and Lee, 2016). However, the ON/OFF current ratio (10^2 to 10^3) and passable retention capability ($\approx 10^4$ s) are still low compared with typical memory devices. In addition, the required reading voltage is usually in the order of a few volts, which limits the applications in contacting live creatures directly.

In this study, we found that protein-bound water can facilitate long-distance electron transfer, and used the discovery to generate a non-volatile memory. We used gelatin as the protein in this study since it contains numerous sites capable of forming hydrogen bonds with water molecules (de Wolf, 2003). Since previous studies have reported that hydrogen bonds can transfer electrons (Meidanshahi et al., 2015; Nishino et al., 2013), it is possible that the bound-water-mediated hydrogen bonds can transfer electron across different polypeptide chains. In addition, since the electron transfer in biology is often attributed to the existence of abundant aromatic amino acids, redox centers, or metal ion complexes (Cordes and Giese, 2009; Isied et al., 1992), the lack of these factors in gelatin also eliminates the possibility that the electron transfer is due to pi-stacking or redox reactions. Our electrical characteristic and Raman spectroscopy results show that the existence of the bound water between the unwound gelatin polypeptide chains is crucial for the effective electron transfer across the entire gel. In a typical wet gel below the gelation temperature, bound water is primarily inside the gelatin triple helices and cannot help connect different helices. The dynamic free bulk water between different helices could also hinder the electron transfer and therefore causes the low electron-conductivity. The switch of the electron-conductivity based on the controllable structural change and bound water connection allows us to operate a gelatin memory device with a fundamentally different mechanism from the existing resistive memories. In addition, the required reading voltage is much lower than the one required by conventional nonvolatile resistive memory devices, making it suitable for bio-applications requiring low voltage operations.

2. Methods

2.1. Fabrication of a gelatin hydrogel device

A 10 wt% gelatin solution was obtained by dissolving an appropriate amount of Type B gelatin powder (Sigma-Aldrich) in 100 mM NaCl solution (pH 5.8) under gentle stirring for 2 h at 60 °C to generate a homogeneous solution. The gelatin solution was spin-coated on an indium tin oxide (ITO)-coated glass (7 Ω, Ruilong-glass Co., Ltd.) with the speed of 2000 rpm for 20 s. The ITO-coated glass was pretreated with argon plasma (Harrick Plasma, Ithaca, NY) for 10 min (Medium) before the spin-coating. Gelatin thin films were then dried at 4 °C for 30 min, followed by soaking in 100 mM NaCl solution (pH 5.8) for 30 min. To fabricate a gelatin hydrogel device for electrical measurements, two gelatin-coated ITO glasses as working electrodes ($2 \times 2.5\ cm^2$ in size) were sandwiched and fixed with clips (see Fig. 1(d)).

2.2. Electrical performance measurements

A Keithley 2636B sourcemeter from TEKTRONIX, Inc. (Beaverton, OR) was used to conduct all the electrical property measurements. The steady current-voltage (I–V) characteristics were recorded as the corresponding steady current under each fixed reading voltage bias from −0.09 V to +0.09 V. Capacitor and resistor behaviors were recorded as the instantaneous current under a voltage sweep rate of 0.36 V/s. The stability performance of the gelatin memory device was tested at the reading voltage of +0.09 V. The devices were heated at 60 °C for 30 min in the heating process for writing and were cooled to ambient temperature before performing the reading measurements. The erasing process was completed by immersing the devices in 100 mM NaCl solution (pH 5.8) for 30 min. All the measurements were conducted under the environmental condition with a relative humidity of 40%. For the control experiment with “no water loss,” parafilm was used to seal the device to prevent water evaporation. For the control experiment with “no temp. increase,” the device was kept at room temperature during the water evaporation.

2.3. Raman spectroscopy study of water state and gelatin structure

The Raman spectroscopic measurements were carried out using an inVia™ confocal Raman microscope (Renishaw, UK) equipped with a He—Ne laser for 633 nm excitation. The average laser power was 14.1 mW, and the intensities were kept low to avoid any laser-induced damage. Raman data were retrieved using Renishaw WiRE 5.0 software. All spectra were smoothed, and the baselines were subtracted to remove the background. The Raman spectra including gelatin and the water OH-stretch region were normalized to attain the same intensity for the CH-stretch band at 2950 cm^{-1}, representing the gelatin amount in the samples. The spectra including the amide band were normalized to obtain the same intensity for the CH deformation band at 1450 cm^{-1}.

3. Results and discussion

3.1. Electrical characteristics of a gelatin hydrogel

A typical wet gelatin hydrogel contains mobile electrolytes in the liquid part and therefore acts as a capacitor after a voltage is applied. Here, we discovered that a gelatin thin film switches from a capacitor to a resistor with high conductivity when the water content of the gel is reduced at a temperature above the gelation temperature (T_{gel}). Fig. 1(a) shows the current response when we applied a voltage sweep rate at 0.36 V/s between −0.09 V and +0.09 V. The voltage-sweep current-voltage curve of a typical wet gelatin film (OFF state) demonstrates a nearly ideal capacitor characteristic with a capacitance of 30.2 μF, which is similar to the behavior of pure liquid with no gelatin (0.1 M NaCl). On the other hand, the current measured after the water content of the gel is reduced above T_{gel} (ON state) is proportional to the instantaneous voltage, and the device acts as a resistor with a high electron-conductivity of 6.8 ± 1.3 μS/cm (n = 3 independent samples), which is in the range of the conductivity of a semiconductor or electrically conductive polymers (Kaur et al., 2015).

Fig. 1(b) further shows the steady current-voltage (*I–V*) characteristics. Each point in Fig. 1(b) indicates the corresponding steady current performance under the voltage bias from −0.09 V to +0.09 V. At +0.09 V, the wet gelatin hydrogel (OFF state) has a low current value of 4.28×10^{-9} A. After the heating/water loss process (ON state), the current increases to 5.30×10^{-4} A. The large current difference allows it to become a memory device with an ON/OFF current ratio of 1.24×10^5. Different from the conventional memory devices requiring at least several volts to write or erase (Heremans et al., 2010; Tan et al., 2015), the writing process is completed through heating/water loss process, and the erasing process is completed through the addition of water, suggesting a unique way for data recording.

Note that the mobile electrolytes in the typical gelatin hydrogel can cause the gel to have a large transient current due to the capacitor effect at the beginning when we change the applied voltage (Fig. 1(c)). The measured currents in Fig. 1(b) are not the beginning transient currents caused by the capacitor effect but the steady currents, which are typically reached in 0.02 s every time when we change the applied voltage (Fig. 1(c)). The steady current of the typical gelatin hydrogel is at nA level, indicating very few electrons can move across the hydrogel layer. In the ON state, a high steady current was observed from the beginning, and no capacitor effect was observed, supporting that it acts as a resistor.

Fig. 1(d) illustrates that the gelatin device is composed of a gelatin hydrogel film with two ITO-coated substrates on the sides as the

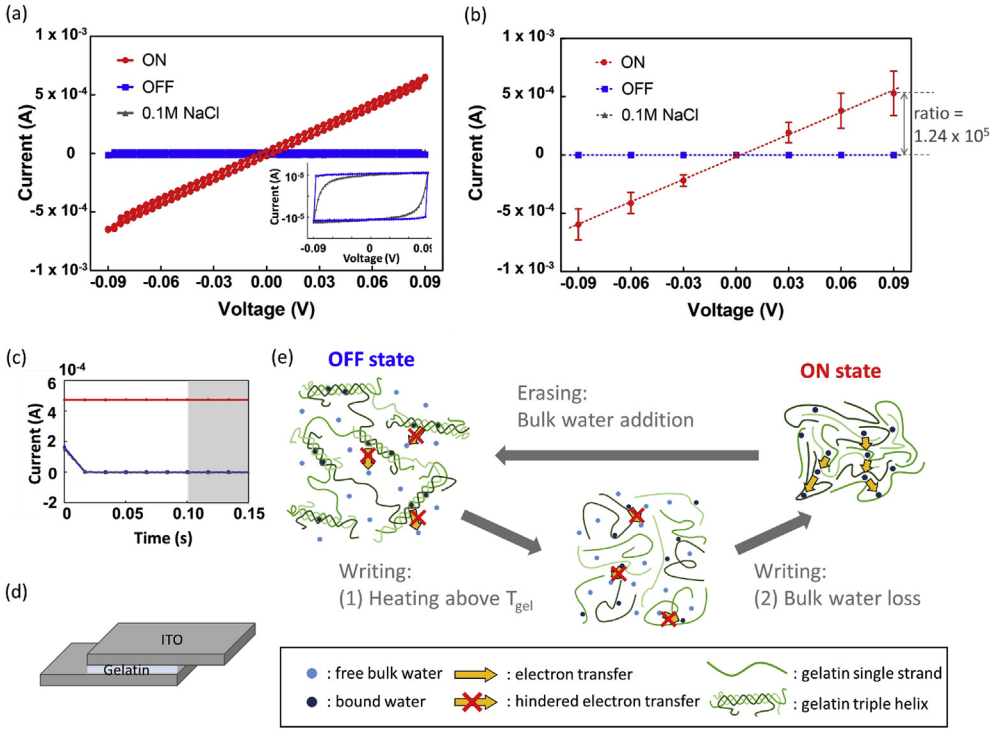

Fig. 1. (a) Voltage sweep to show the capacitor behavior at the OFF state and the resistor behavior at the ON state of the gelatin film. The voltage sweep rate is at 0.36 V/s. Inset: close-up of the capacitor behavior at the OFF state and the comparison with the capacitor behavior of the used solution (0.1 M NaCl) without gelatin. (b) The current-voltage (I–V) characteristic of the gelatin film, where the writing process is conducted through heating/water loss. (n = 3) (c) The current vs. time under a +0.09 V reading voltage of the OFF and ON states. The steady current versus the applied voltage can be used to plot the steady current-voltage characteristics in (b). (d) Measurement setup. Two ITO electrodes spin-coated with gelatin thin films are sandwiched together. (e) Proposed mechanism for the writing and erasing processes of the gelatin device. Free bulk water (light blue dots) between the ploypeptide chains could hinder the inter-chain electron transfer. When the free bulk water is removed above T_{gel}, the polypeptide strands could compact together, and the bound water (dark blue dots) on a polypeptide could form stable hydrogen bonds with neighboring polypeptide chains and could help the inter-chain electron transfer (yellow arrows).

Table 1
Electron-conductivity of the gelatin memory device with different writing conditions.

Writing condition	Conductivity ($S \cdot cm^{-1}$)
No temp. increase & No water loss (OFF)	$5.6 \times 10^{-11} \pm 0.7 \times 10^{-11}$ (n = 3)
Temp. increase & Water loss (ON)	$6.8 \times 10^{-6} \pm 1.3 \times 10^{-6}$ (n = 3)
No temp. increase & Water loss	4.5×10^{-11}
Temp. increase & No water loss	5.2×10^{-11}

electrodes. In this study, the wet gelatin film has a thickness of 152 μm and the dried gelatin film after the water loss has a thickness of 100 μm. To examine whether the writing process through heating requires both temperature increase and water loss as the two key factors for the switching behavior of the memory device, we performed experiments with temperature increase/no water loss, and water loss/no temperature increase. Neither case can cause the high electron-conductivity, as shown in Table 1 (details in Supplementary material), suggesting that both factors are important for the high electron-conductivity.

Fig. 1(e) illustrates our proposed mechanism of the memory characteristic based on controlling the temperature and water content in gelatin hydrogels. When the gelatin is heated above the gelation temperature, the triple helices unwind into single strands. The free bulk water can be easily removed while the water molecules bound to the polypeptides are more difficult to be removed (Unal et al., 2014). When the free bulk water (light blue dots) is removed, the single strands could compact together, and the bound water (dark blue dots) on a polypeptide could form hydrogen bonds with neighboring polypeptide chains. The water-mediated hydrogen bonds could help the inter-chain electron transfer (yellow arrows), and the device switches to an ON state with high electron-conductivity. Even if the temperature goes back to a temperature below the gelation temperature, the situation does not go back to the triple-helical state because the chain mobility is low when the free bulk water content is low. Adding water at room temperature (RT) can be an erasing step because the free bulk water content is rebuilt and the mobility of polypeptide chains recovers. The mobile polypeptide chains can quickly reform the preferred triple-helix structure below the gelation temperature, switching the device back to the OFF state with low electron-conductivity. More details will be discussed in the following section.

To investigate further the stability and durability of the gelatin devices, we obtained the retention time and WRER

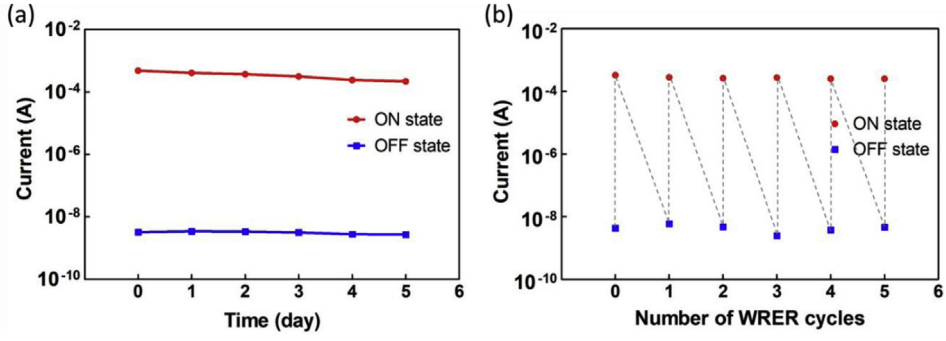

Fig. 2. The memory characteristics of the gelatin memory device. (a) The retention time curves. (b) The switching stability.

(write–read–erase–reread) cycles as shown in Fig. 2. At +0.09 V, no obvious current change is observed in both the ON and OFF state for at least 5 days. Fig. 2(b) shows the currents in the ON and OFF states as a function of the number of WRER cycles. Through the erasing process, the memory device can be reset to the initial OFF state, and they can be rewritten again into the ON state. No obvious current change is observed in 5 WRER cycles. Unlike conventional organic resistor-type memories (Heremans et al., 2010; Qian et al., 2016), the gelatin memory device can retain the ON state for a long time, up to 5 days, without providing any power supply. In addition, instead of applying a voltage sweep, the erasing process is completed by increasing the water content.

3.2. Switching mechanism through the gelatin polypeptide structural change and the free bulk water content

Unlike traditional organic resistor-type memories, which store data based on the switching of the high- and low-conductivity resistor states (Duggal and Sun, 1998; Henisch and Smith, 1974; Kevorkian et al., 1971; Ma et al., 2000; Szymanski et al., 1969), the gelatin thin film switches between a capacitor state and a resistor state (Fig. 1(a)). The OFF state is a typical wet hydrogel in which the electrolytes in the liquid part can move when a voltage is applied, and the hydrogel acts as a capacitor; the ON state appears when most of the free bulk water is removed after the hydrogel is heated above the gelation temperature, and the hot-dried gel acts as a resistor with high electron-conductivity.

As shown on the right side of Fig. 3(a), the typical wet gelatin (OFF state; RT-wet gelatin) adopts a triple-helix structure where the major repeating amino acids (Gly–Pro–HyPro) have abundant sites to form hydrogen bonds to maintain the triplets (Brodsky and Ramshaw, 1997; Thakur et al., 2017). Although electrons could be transferred in a polypeptide chain (Cordes and Giese, 2009; Isied et al., 1992), the free bulk water molecules surrounding the triple helices act as an electron insulator and prevent the electron transfer between different triple helices, as shown in Fig. 3(d).

The triple-helix structure cannot be sustained when the gelatin is heated over 30 °C and the triple helices unwind to single strands (Gorgieva and Kokol, 2011; Te Nijenhuis, 1997). When free bulk water loss occurs at the single-stranded state, the single strands become close to each other and could form direct hydrogen bonding with each other through the abundant glycine residues or form water-mediated hydrogen bonding through abundant proline/hydroxyproline residues[30], as illustrated in Fig. 3(b) (ON state; hot-dried gelatin). Because previous studies have suggested that electrons can transfer across hydrogen bonds (Meidanshahi et al., 2015; Nishino et al., 2013), the electrons could transfer between the neighboring polypeptide chains through the hydrogen bonds. Under an applied voltage for the reading process, electrons could be conducted not only intramolecularly in a single polypeptide chain but also intermolecularly between different polypeptide chains through the hydrogen bonds. Therefore, the bounded metastructure could act as a resistor in which electrons can continuously transfer under an applied DC voltage.

In contrast, if free bulk water is maintained when the temperature is above the gelation temperature (Fig. 3(c); hot-wet gelatin), the distance between the polypeptide chains is far, and the dynamic free water between the chains hinders the electron transfer, resulting in poor electron-conductivity (Figure S1, cyan trace).

For the gelatin film that is dried under room temperature, the gelatin remains in its triple-helix structure (Fig. 3(e); RT-dried gelatin). Although there is a lack of free water molecules, the performance reveals that the device did not switch to the high electron-conductivity state (Figure S1, gray trace). The reason could be that the hydrogen-bonding sites of gelatin polypeptides are used to form hydrogen bonds within the helical structure. Few sites were left for the hydrogen bonds between the triple helices to assist the inter-helix electron transfer and therefore hindered the long-distance electron transfer across the entire gel.

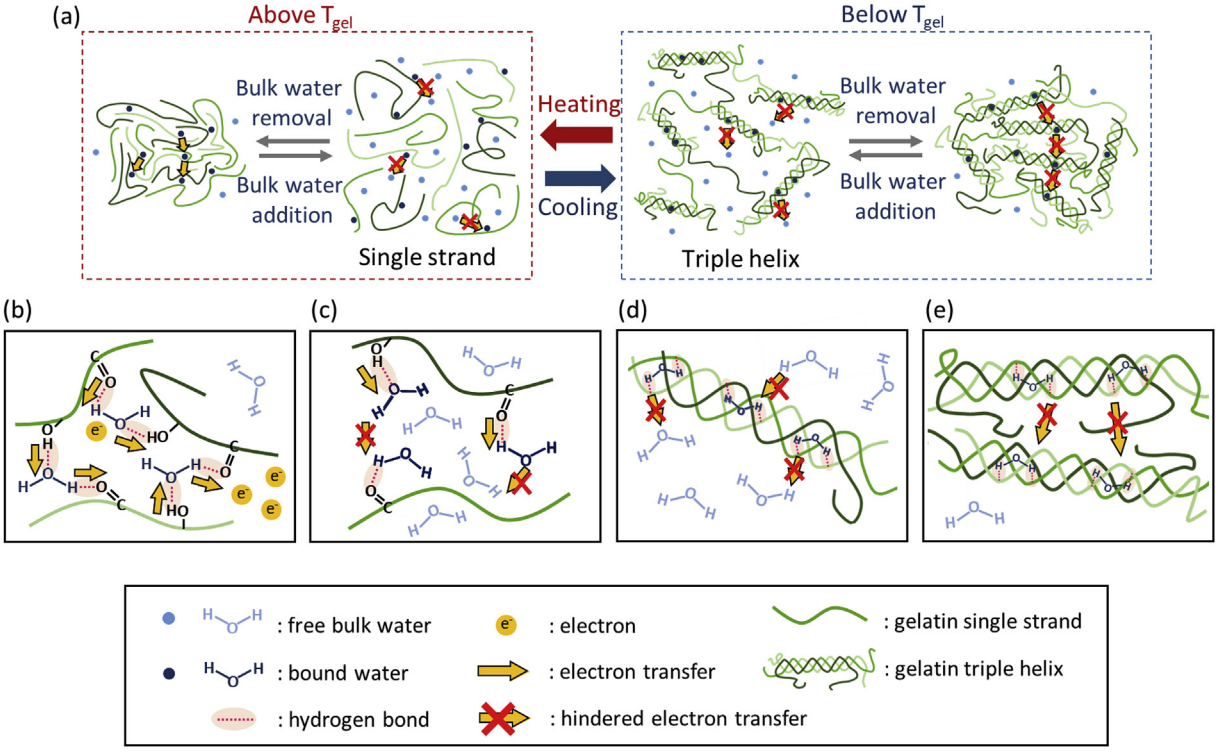

Fig. 3. (a) Proposed gelatin structural change with temperature and free bulk water content. The triple helices form below the gelation temperature and unwind when heated above the gelation temperature (T_{gel}). The single chains or helices condense as free bulk water contents reduce. Insets of the above four different states: (b) hot-dried state; (c) hot-wet state; (d) RT-wet state; and (d) RT-dried state.

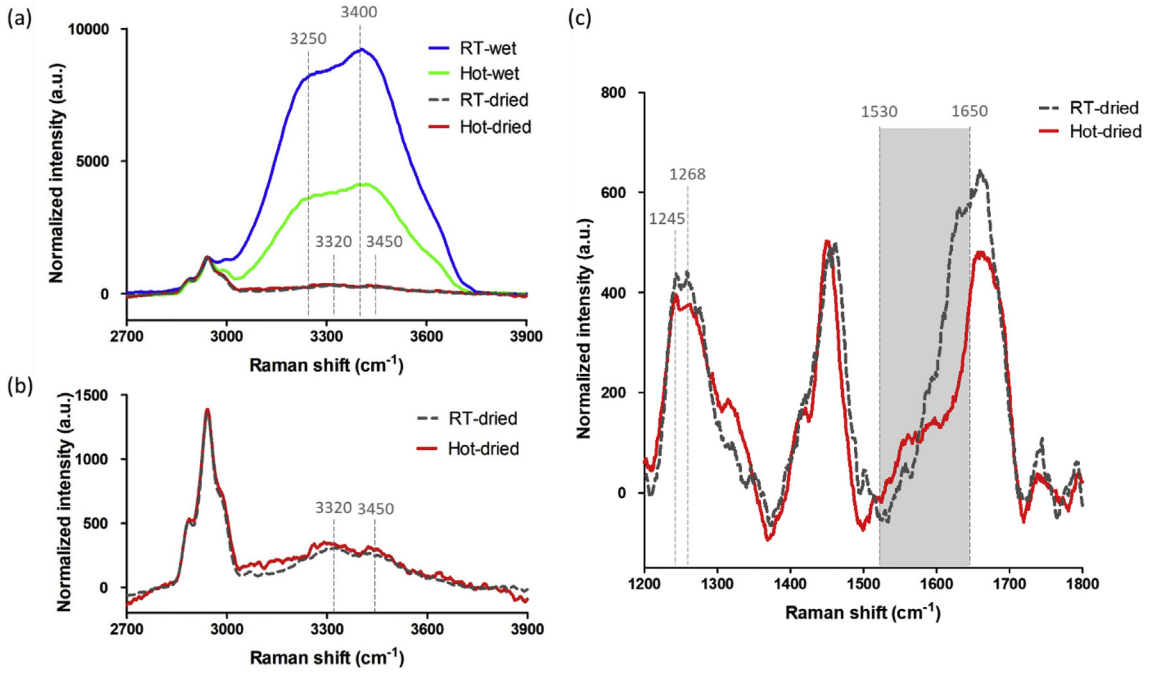

Fig. 4. (a) Raman spectra of gelatin films in four different states covering gelatin and water OH-stretch regions, where the data were normalized based on the gelatin CH-stretch intensity at 2950 cm^{-1}. (b) Enlarged spectra of (a) to show the bound water peaks of RT-dried gelatin and hot-dried gelatin. (c) Raman spectra of RT-dried gelatin and hot-dried gelatin in the Amide III and Amide I regions to reveal the secondary structure situations.

3.3. Raman spectroscopy to show abundant bound water and unwound structure in the ON state

To support our proposed mechanism, we used Raman spectroscopy to obtain structural information of the four different states of the gelatin gel. Previous studies have used OH-stretch bands to study bound water content in collagen (Cavatorta et al., 1976; Leikin et al., 1997; Unal et al., 2014). Fig. 4(a) shows the Raman spectra covering the gelatin characteristic peaks and water OH-stretch peaks, where the spectral range of 2800–3000 cm^{-1} represents CH stretching in gelatin and the range of 3200–3700 cm^{-1} represents OH stretching in water. All spectra are scaled to obtain the same intensity of the CH-stretch band so that the intensities of the OH-stretch band are normalized by the gelatin amount. The two peaks at 3250 cm^{-1} and 3400 cm^{-1} in RT-wet gelatin and hot-wet gelatin are associated with in-phase OH-stretch and OH-stretch that lose the phase relationship (Sun, 2009). The intensities of these two peaks decrease significantly in RT-dried gelatin and hot-dried gelatin, indicating the loss of free bulk water after the dehydration process. In the RT-dried gelatin and hot-dried gelatin, we observed two peaks at 3320 cm^{-1} and 3450 cm^{-1} instead, which are considered as the existence of tightly bound water (Cavatorta et al., 1976; Leikin et al., 1997; Unal et al., 2014). This bound water could be the water molecules that form hydrogen bonds with gelatin polypeptides. For the RT-dried gelatin, the bound water could be the hydrogen-bonded water molecules inside the triple helices. As shown in Fig. 4(b), the similar intensities of the bound water peaks for the hot-dried gelatin compared with those of the RT-dried gelatin suggest that similar amount of bound water still exists after the triple helices unwind and many unwound single strands could “connect” with each other through the bound water.

To discriminate further the protein secondary structure of the RT-dried and hot-dried states, we collected the Raman spectra covering the protein amide region as shown in Fig. 4(c). In the Amide I spectrum region (1500-1750 cm^{-1}), the RT-dried gelatin has characteristic peaks associated with both ordered and disordered secondary structures (Devitt et al., 2018; Gullekson et al., 2011). On the other hand, the peaks associated with the ordered secondary structure (1530-1650 cm^{-1}) (Devitt et al., 2018; Gullekson et al., 2011; Lefèvre et al., 2007) disappear in the hot-dried gelatin. In addition, in the Amide III spectrum region, the decreased intensity at 1268 cm^{-1} and the increased intensity at 1245 cm^{-1} of the hot-dried gel compared with those of the RT-dried gel also indicate the loss of triple-helix structure (Dehring et al., 2006; Dong et al., 2004) in the hot-dried gelatin. These results support that the hot-dried gelatin is in the single-stranded state and bound water could “connect” the single strands to form a metastructure to allow the long-distance electron transfer.

3.4. The importance of bound water for the inter-chain connection

Since gelatin contains no redox sites and the trace amounts of aromatic amino acids, which eliminate the possibility that the electron transfer is due to redox reactions or pi-stacking, we believe that the long-distance electron transfer is through hydrogen bonding which electron transfer ability has been supported by many previous studies (Meidanshahi et al., 2015; Nishino et al., 2013). The gelatin polypeptide chains could form hydrogen bonds with each other directly through the abundant glycine residues or could form water-mediated hydrogen bonds through abundant proline/hydroxyproline residues[30], as illustrated in Fig. 3(b) (ON state; hot-dried gelatin). We think that the hydrogen bonding mediated by the bound water could be the main route for the electron transfer. The reason is that the direct hydrogen bonding requires the glycine residues on the neighboring chains to be close enough for a hydrogen bond to form (around 0.3 nm) (Jeffrey, 1997), and therefore there is less chance for the direct hydrogen bonding between disordered polypeptide chains. Bound water molecules could provide more flexibility in the distance and orientation for the neighboring chains to be connected through hydrogen bonds.

To further demonstrate that bound water is crucial for connecting the polypeptide chains for the electron transfer, we placed the ON-state device under vacuum to further reduce the bound water content. Fig. 5 shows that the reduction of bound water content dramatically decreased the electron-conductivity, indicating that bound water is

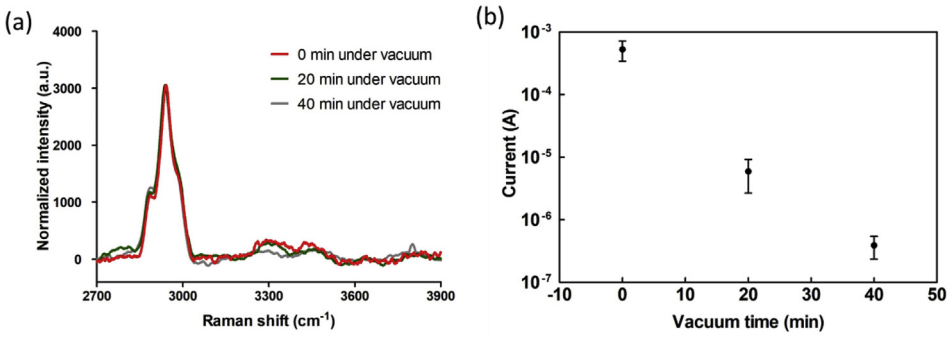

Fig. 5. The characteristics of the gelatin memory device after the ON-state device was further placed under vacuum to remove bound water. (a) Raman spectra to show the bound water content in the device with different time durations under vacuum. (b) The corresponding steady-state currents measured at 0.09 V (the reading voltage in this study).

crucial for the electron conduction.

3.5. Perspective of long-distance electron transfer in biological systems

Electron transfer through or between proteins plays important roles in biology (Marcus and Sutin, 1985). However, the mechanisms are still unclear, and the occurrence is often attributed to the existence of aromatic amino acids, redox centers, or metal ion complexes (Cordes and Giese, 2009; Isied et al., 1992). In this study, we showed the occurrence of electron transfer through water-mediated hydrogen bonds instead of those classic electron-conducting components. Previous studies have shown intramolecular electron transfer through hydrogen bonds in the secondary structure of a protein or a polypeptide (Antonello et al., 2003; del Mercato et al., 2007; Głowacki et al., 2013; Ing et al., 2018; Morita and Kimura, 2003; Nadav, 2015) and intramolecular electron transfer through the hydrogen bonds in DNA or some organic molecules (Huang et al., 2010; Lin et al., 2005; Nishino et al., 2013). These reports support that electron transfer can occur through hydrogen bonds. The new perspective of this study is that biomolecules could also use the hydrogen bonds mediated by bound water to transfer electrons. Bridging the electron transfer by bound water could further facilitate effective electron transfer between donor-acceptor pairs that are not close to each other in biomolecules or biomolecular complexes.

Note that although the conduction through proteins or hydrogen bonds has been sometimes attributed to proton transfer (Chaplin, 2006; Głowacki et al., 2013), our electrical characteristics of the ON state do not show proton transfer characteristics. In the absence of redox reactions to consume or generate protons at the electrodes, proton transfer should cause the accumulation of proton toward the cathode. If proton accumulates with time in our system, capacitor characteristics should be observed in the voltage-sweep I-V curve, and the I-t curve should decrease with time. However, we obtained a resistor-type voltage-sweep I-V curve and a steady current in the I-t curve (Fig. 1(a)(c)), indicating that electron transfer is the major cause for the high conductivity in our case.

The electron transfer over hundreds of microns has been rarely reported in aqueous biological systems probably because the electron transfer could be confined in a certain structured biomolecular assembly where hydrogen bonds or pi stacking can form. Free bulk water between different structured biomolecular assemblies may hinder the electron transfer between them. Although free bulk water can also form hydrogen bonds with each other, the hydrogen bonds of dynamic free water can rapidly rearrange in response to the changing conditions and would not be suitable for steady electron transfer. In this study, we removed free bulk water and therefore the stable bound water could connect the polypeptide chains for the electron transfer across the entire gel.

4. Conclusion

We discovered that gelatin polypeptides and the bound water can form a metastructure with high electron-conductivity. We demonstrated that a gelatin hydrogel which typically acts as a capacitor can be switched to the high electron-conductive metastructure state if the free bulk water content is reduced above its gelation temperature. The bistable electrical switching characteristics with an ON/OFF current ratio of 10^5 can be reached at a reading voltage of 0.09 V, which performance is superior to that of conventional nonvolatile resistive memories by one order of magnitude. Our Raman spectra data suggest that the bound water connects unwound gelatin polypeptide chains to allow the inter-chain electron transfer in the metastructure state. The discovered phenomenon of using bound water for electron transfer and the structural change of polypeptides for switchable and reprogrammable conductivity provides a new direction for designing conducting materials to bridge the interface of biology and electronics.

Associated content

Supplementary material. Data to show that both temperature increase and water loss are required for switching the device to the ON state.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

U-Ting Chiu: Methodology, Software, Validation, Formal analysis, Investigation, Data curation, Writing - original draft, Visualization. **Ling Chao:** Conceptualization, Methodology, Resources, Writing - review & editing, Visualization, Supervision, Project administration, Funding acquisition.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bios.2019.04.012.

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