Article

A Solid-Contact Reference Electrode Based on Silver/Silver Organic Insoluble Salt for Potentiometric Ion Sensing

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ABSTRACT: Solid-contact ion-selective electrodes are a type of ion measurement devices that have been focused in wearable biotechnology based on the features of miniaturization and integration. However, the solid-contact reference electrodes (SC-REs) remain relatively less focused compared with numerous working (or indicator) electrodes. Most SC-REs in wearable sensors rely on Ag/AgCl reference electrodes with solid electrolytes, for example, the hydrophilic electrolyte salts in polymer matrix, but face the risk of electrolyte leakage. Herein, we report a type of SC-REs based on the silver/silver tetraphenylborate (Ag/AgTPB) organic insoluble electrode. The SC-RE consists of a Ag substrate, a solid contact (AgTPB), and a plasticized poly(vinyl chloride) (PVC) membrane containing the hydrophobic organic salt of tetrabutylammonium tetraphenylborate (TBATPB). The potentiometric measurements demonstrated that the SC-RE of Ag/AgTPB/PVC-TBATPB showed a reproducible standard

potential in various electrolytes and disclosed high long-term stability. This SC-RE was further fabricated on a flexible substrate and integrated into all-solid-state wearable potentiometric ion sensor for sweat Cl⁻ monitoring.

KEYWORDS: reference electrode, solid-contact, potentiometric sensing, ion-selective electrodes, wearable sensors
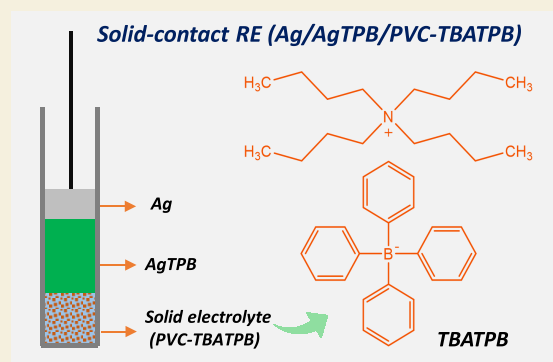
1. INTRODUCTION

Solid-contact ion-selective electrodes (SC-ISEs) are a type of miniaturized potentiometric analytical devices for ion and biochemical analysis and monitoring in complex environments.[1−5] For example, environmental trace heavy metal analysis remains a significant issue hitherto.[6] Recently focused wearable sensors have also accelerated the development of SC-ISEs due to the requirements of ion monitoring in human biological fluids,[7−12] typically like sweat. Since the rudiment of SC-ISEs (coated wire electrodes)[13] was proposed in 1971, intensive research has focused on improving the performances, particularly for the potential stability through development of advanced solid contacts.[2,4,14] In addition to the working (or indicator) electrodes, the solid-contact reference electrodes (SC-REs) as an indispensable part of integrated SC-ISEs are of the same significance and even more challenging. A reliable SC-RE is a prerequisite for the development of highly reproducible[15] and even calibration-free[16] solid-contact potentiometric sensors. Traditional liquid-junction REs consist of a reference element and a salt bridge filled with concentrated aqueous salt solution (internal reference solution). The liquid-junction REs have a stable and fixed potential because of the inner solution with a constant concentration and ionic composition that determines the phase

boundary potential, typically like the interface between the metal/metal insoluble salt and inner electrolyte solution.

Based on a similar strategy for traditional salt bridges, a few approaches of constructing SC-REs have been proposed.[17−19] The popular RE element is the Ag/AgCl electrode due to its simple fabrication and biocompatibility. The crucial point is the solid electrolyte compositions. The often-used method is mixing concentrated electrolytes into hydrophobic polymeric membranes, such as, hydrophilic and lipophilic salts.[20−24] For example, most SC-REs in wearable sensors are based on Ag/AgCl with polymer mixed electrolytes (KCl or NaCl).[25−29] However, there is a risk that the electrolytes could continuously and slowly leak into the sample solution. The other representative SC-REs are the ionic-liquid-based reference electrodes.[30−34] A stable potential could be formed between ionic liquid and aqueous phases by the distribution equilibrium. However, the ionic liquids still exhibit a certain solubility in an aqueous solution.[35] Conducting polymers[36]
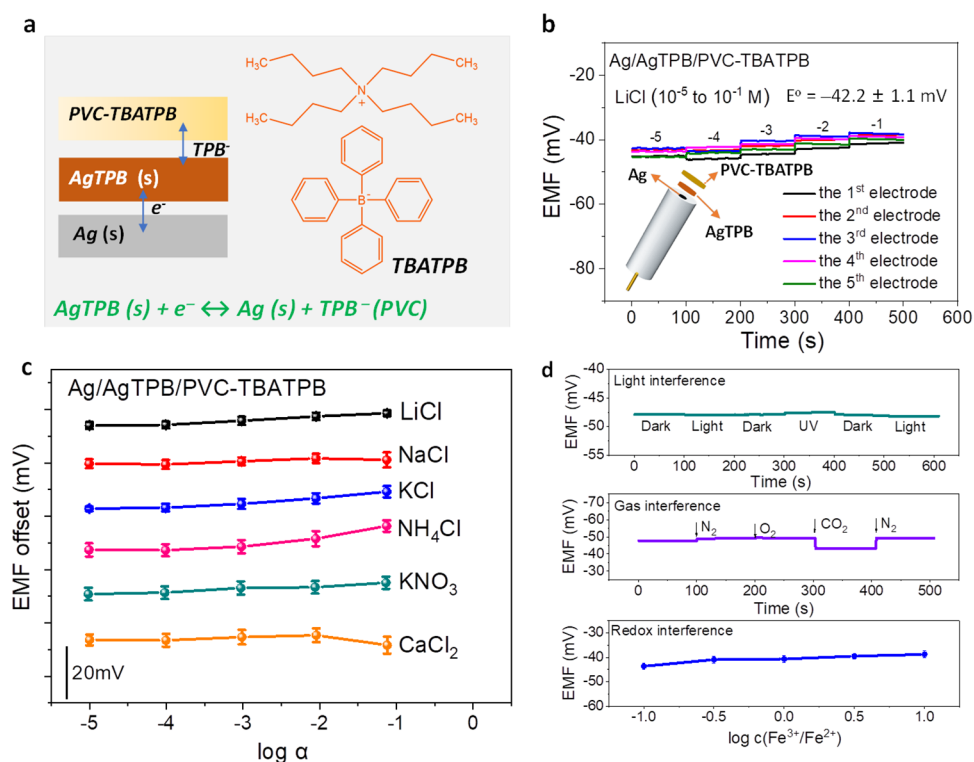
Figure 1. Principle and performances for the SC-RE of Ag/AgTPB/PVC-TBATPB electrodes. (a) Basic structure and response principle. (b) Potentiometric measurements for the Ag/AgTPB/PVC-TBATPB electrodes ($n = 5$) in a LiCl electrolyte under the concentration range of 10^{-5} to 10^{-1} M as an example. The numbers on the curves represent the logarithms of the electrolyte concentrations. The inset shows the schematic of fabricated SC-RE. (c) The potential responses for the SC-RE in different electrolytes. The EMF is shown in an offset model along the y-axis. (d) Interferences tests of light, gas, and redox couples. The potential measurements for gas and light were carried out in 0.1 M NaCl.

and carbon materials[37−39] have been also used as SC materials for the fabrication of SC-REs but face the same challenges of solid electrolyte leaking. Recently reported Ag/AgI SC-RE has identified a truly all-solid-state RE without a solid electrolyte layer.[40] The electrolyte (I^-) was in situ produced by a current pulse (self-referencing pulstrode). This Ag/AgI SC-RE has been demonstrated for feasibility in sample analysis. However, the local I^- concentration should be enough to maintain the potential stability and avoid interferences from sulfide containing species. In addition, the current pulse might be a relatively complex method in the application of wearable sensors.

In this work, we proposed a type of SC-RE based on a silver/silver tetraphenylborate organic insoluble salt (Ag/AgTPB) electrode containing tetrabutylammonium tetraphenylborate (TBATPB) as a solid electrolyte (Figure 1a). The TBATPB is a hydrophobic electrolyte that has very low solubility in water ($\sim0.26\ \mu$M),[41] which could overcome the issue of leaking. We investigated the potential stability of Ag/AgTPB SC-RE in various electrolyte solutions with examinations of concentration, light/gas, and redox interferences. This SC-RE even shows long-term stability in deionized water. Moreover, the Ag/AgTPB SC-RE was fabricated on a flexible substrate and integrated with a Cl^--SC-ISE for on-body sweat analysis.

2. EXPERIMENTAL SECTION

2.1. Reagents

Tetrabutylammonium chloride (TBACl), sodium tetraphenylborate (NaTPB), and acetonitrile were purchased from Innochem. High

molecular weight poly(vinyl chloride) (PVC), 2-nitrophenyl octyl ether (NPOE), tetrahydrofuran (THF), and sodium nitrate were obtained from Sigma-Aldrich. Other inorganic salts were used at least in analytical grade. All the reagents were used by ultrapure water (>18.2 MΩ·cm) to prepare aqueous solutions without further treatment.

2.2. Preparation of Solid-Contact Reference Electrodes (SC-REs)

The silver disk electrodes (3 mm diameter) were polished with 1 and 0.3 μm alumina powder and then ultrasonically cleaned with water−ethanol−water successively. The silver electrodes were then placed in a 0.01 M NaTPB-0.067 M $NaNO_3$ mixture solution. The electrodeposition was carried out through a constant current of 5 μA for 2800 s by a Gamry electrochemical workstation (reference 600 plus). A thin layer of silver tetraphenylborate (AgTPB) was deposited on the Ag electrode (Ag/AgTPB). The Ag/AgTPB was further covered by dropping 30 μL of PVC-based reference electrolyte membrane solution and dried at ambient temperature overnight. The reference electrolyte membrane solution was obtained by dissolving 200 mg of the membrane cocktail in 2 mL of THF: 28.5 wt % PVC and 56.9 wt % NPOE and 14.6 wt % tetrabutylammonium tetraphenylborate (TBATPB). The TBATPB was prepared by the precipitation reaction between NaTPB and TBACl in a molar ratio of 1:1 in aqueous solution and was recrystallized in acetone. The final SC-RE is described as Ag/AgTPB/PVC-TBATPB. Before the test, the SC-RE was conditioned in 10^{-5} M NaCl solution overnight.

2.3. Electrochemical Characterizations

All potentiometric measurements of the SC-REs of Ag/AgTPB/PVC-TBATPB electrodes were recorded by a multi-channel potentiometer EMF6 (Lawson Lab, Inc). The potential response tests were measured in various electrolyte solutions with the concentration range from 10^{-5} to 10^{-1} M. The potentiometric tests were also performed through other two modes including different electrolytes
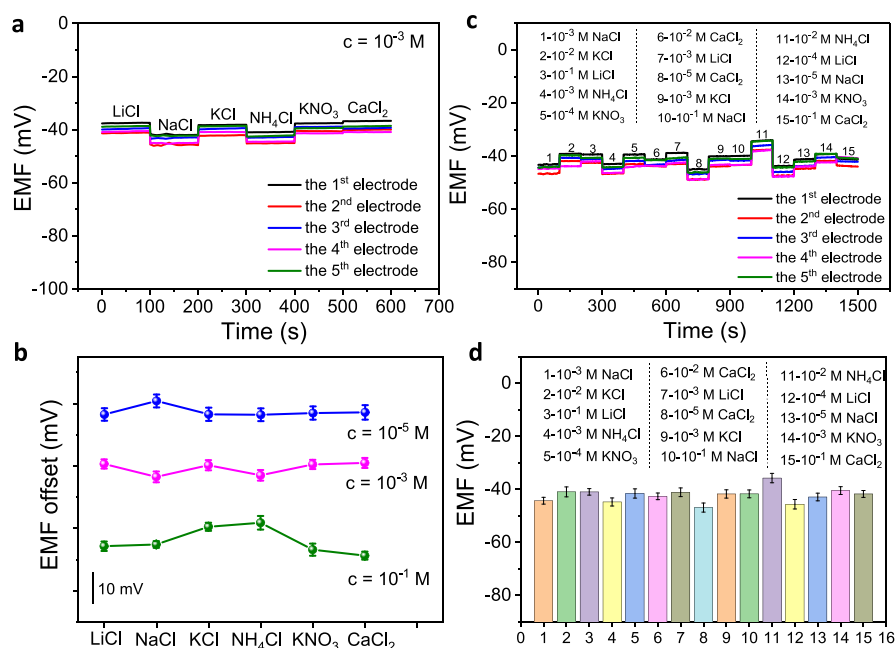
Figure 2. Potential responses for the Ag/AgTPB/PVC-TBATPB electrodes (n = 5) in (a, b) different electrolytes with the same concentration and (c, d) in randomly selected types and concentrations of electrolytes. The EMF in (b) is shown in an offset model along the y-axis.

under the same concentration and random electrolytes with random concentrations. The anti-interference experiments toward light, gas, and redox were performed. The water-layer tests for the Ag/AgTPB/PVC-TBATPB electrodes were carried out through varied solutions of 0.1 M NaCl/ 0.1 M LiCl/0.1 M NaCl. The long-term stability was examined in both 0.1 M NaCl and deionized (DI) water. A commercial Hg/Hg$_2$Cl$_2$/ saturated KCl/1 M LiOAc (SCE) was used as a reference electrode. The ion activities were calculated using the Debye−Hückel equation.

2.4. Preparation of Flexible Sensor

A polyethylene terephthalate (PET) substrate (7 × 7 cm) was cleaned by water−acetone−isopropanol successively followed by O$_2$ plasma etching for 2 min. Then, a 300 nm silver layer was deposited on the PET using ultra-high vacuum sputtering technology (AJA Orion 5) through a silver target. The sputtering parameters include the sputtering speed of 2.5 A/s, the sputtering power of 60 W and the sputtering time of 1200 s. A polydimethylsiloxane (PDMS) insulating layer was further coated except for the regions of the working and reference electrodes (d = 5 mm). The electrode was then dried at 90 °C for 50 min. The flexible SC-RE was further obtained by an oxidizing sputtered silver electrode in acetonitrile solution containing 0.01 M NaTPB under a constant current of 5 μA for 30 min (Ag/AgTPB), and then, 20 μL of reference electrolyte membrane solution was dropped and dried at room temperature (Ag/AgTPB/PVC-TBATPB). The flexible SC-RE was finally conditioned in 10^{-5} M NaCl solution overnight before use. For the working electrode of Cl$^-$-SC-ISEs, the process is similar to a previous work.[42] The sputtered Ag electrode was further oxidized in 0.05 M FeCl$_3$ for 10 s to obtain the flexible Ag/AgCl electrode for sweat Cl$^-$ detection. Three Cl$^-$-SC-ISEs were fabricated in parallel, which could simultaneously measure the concentration of sweat Cl$^-$.

2.5. Sweat Analysis

A commercial sweat guide band was used to fix the prepared flexible electrode. Combining with a multi-channel mini-potentiometer (MEK1000, Guangdong Dynechem Electronic Technology Co., Ltd.) and wireless data transmission mode, the variation trend of chloride ion concentration in the sweat produced by the volunteer during exercising was analyzed. Three Cl$^-$ sensors were worn by the volunteer and measured at the same time. Before starting the exercise, the volunteer's forehead was wiped with medical alcohol and

deionized water in turn. Then, the volunteer exercised for a period to produce sweat. The concentration of chloride ion in sweat was recorded by the flexible wearable sensor. The sweat sample was collected and diluted for ex situ analysis by ion chromatography (CIC-D120, Qingdao Shenghan, Co., Ltd). It should be noted that the volunteer agrees with this test of wearable sensor for sweat analysis.

3. RESULTS AND DISCUSSION

3.1. Characterizations of the SC-RE of Ag/AgTPB/PVC-TBATPB

The SC-RE was prepared by the electrodeposition of AgTPB on polished clean Ag electrodes in a NaTPB-NaNO$_3$ electrolyte solution (see the Experimental Section for details). After electrodeposition for 2800 s at a constant current of 5 μA, a thin layer of AgTPB was covered on the Ag electrode. Further, the solid polymeric electrolyte containing PVC, NPOE, and TBATPB electrolytes was drop-casted on the surface of AgTPB to form final SC-RE of Ag/AgTPB/PVC-TBATPB (Figure 1a). The PVC-TBATPB is a hydrophobic membrane (∼113° water contact angle, Figure S1), and the TBATPB electrolyte has very low solubility in water (∼0.26 μM).[41] In addition, the AgTPB should be either insoluble in organic NPOE since it has been used as an organic interface electrode in the early studies of liquid/liquid interface electrochemistry.[43,44] The basic principle is like the case of Ag/AgCl-based SC-REs. An electron-coupled ion transfer reaction mechanism occurs at Ag/AgTPB and AgTPB/PVC-TBATPB interfaces, which can be described by AgTPB (s) + e$^-$ ↔ Ag(s) + TPB$^-$(PVC) (Figure 1a). A reliable SC-RE should not respond to a broad concentration range of any electrolyte solutions. To verify this point, the potential responses to a series of salt solutions were evaluated in a concentration range from 10^{-5} to 10^{-1} M against a commercial double-junction SCE. For example, the potential response curves in a LiCl electrolyte under a four magnitude concentration are shown in Figure 1b. The Ag/AgTPB/PVC-TBATPB electrodes show small potential variation even

when exposed to different ionic activities of electrolyte solutions. The $E°$ value was determined to be -42.2 ± 1.1 mV. For other electrolytes, the potential response curves are presented in Figure 1c and Figure S2. The potentials basically disclose small variations for the whole concentrations. Relatively apparent potential fluctuations are observed for NH_4^+ and Ca^{2+} at a high concentration of 0.1 M, which is possibly ascribed to cation interaction with the TPB^- anion. However, there is no apparent effect under concentration of less than 10 mM. At least, it should work for sweat analysis since their concentration levels in sweat are relatively low.[7] The $E°$ is between -38.5 and -44.9 mV, and the maximum standard derivation (STD) is ~ 2.5 mV for these electrolytes (Figure S2). The reproducibility for $E°$ in these six types of electrolytes is determined to -41.7 ± 2.3 mV (Figure S2f). This performance is comparable to state-of-the-art Ag/AgCl-based SC-REs with STD of ~ 2 mV for $E°$ (Table S1).

The anti-interference abilities of the SC-RE of Ag/AgTPB/PVC-TBATPB toward light, gas, and redox were further evaluated. As shown in Figure 1d, the SC-RE is almost unaffected by the light (< 0.5 mV). For the gas interference, the SC-RE shows a stable potential under N_2 and O_2, while a minor potential variation (~ 5 mV) resulted for CO_2. It should be noted that the concentration of CO_2 in the solution herein is close to a saturated state by purging CO_2 gas in the solution. However, for most of systems, the low concentration of CO_2 could have less effect on the potential fluctuation. For the redox sensitivity, the SC-RE was measured in five different concentration ratios of $K_3[Fe(CN)_6]/K_4[Fe(CN)_6]$ (log $C_{Fe^{3+}/Fe^{2+}} = -1$ to 1). The SC-RE does not either show considerable sensitivity to redox species. The total potential variation is about 5 mV when the concentration is changed by two magnitudes.

The potential responses for the Ag/AgTPB/PVC-TBATPB electrodes were further examined in randomly selected types and concentrations of electrolytes according to analytical quality protocol for solid-state reference electrodes.[45,46] Under different electrolytes with the same concentration of 1 mM (Figure 2a), the potential variation is determined to 4.6 ± 0.9 mV. For the other two concentrations of 10^{-5} and 10^{-1} M (Figure 2b and Figure S3), the electrodes show the potential variations of 4.6 ± 0.8 and 10.6 ± 1.8 mV, respectively. It is reasonable that the high ionic strength has a relatively significant effect since the phase boundary potential between PVC-TBATPB and water interfaces is affected due to ion distribution in the two immiscible phases. Further harsh examinations were tested in randomly selected electrolytes (Figure 2c,d). The potential variation is around 11.1 ± 0.4 mV. This result is comparable and even better than representative Ag/AgCl-based SC-REs based on lipophilic salts[23] (~ 11.7 mV) and ionic liquids-based SC-REs[30] (15$-$25 mV).

For the proposed SC-RE of Ag/AgTPB/PVC-TBATPB, there are in fact three phase boundary interfaces, including Ag/AgTPB, AgTPB/PVC-TBATPB, and PVC-TBATPB/solution interfaces. The phase boundary potentials at first two interfaces are determined by the Nernst equation of Ag and AgTPB redox couple. The phase boundary potential at the PVC-TBATPB/solution interface is dependent on the ion distribution between the hydrophobic membrane phase of PVC-TBATPB and the sample aqueous solution. According to the early studies of ion transfers at the liquid/liquid interface,[47] the phase boundary potential is determined to by their standard Gibbs transfer energies of TBA^+ and TPB^- ions (see

the supplementary discussion in the Supporting Information). The phase boundary potential could keep a constant value. This might be the reason that the potential of the proposed SC-RE could be basically stable even though the type or concentration of ions changes.

3.2. Water-Layer Test and Potential Stability

Another significant basis for the SC-REs is the potential stability. We first performed the water-layer tests for the Ag/AgTPB/PVC-TBATPB electrode since it consists of a PVC-based solid electrolyte membrane. The water layer might exist at the interface between the AgTPB and PVC membrane. According to a general protocol,[48] the electrode was tested in two types of solutions, first in 0.1 M NaCl, then in 0.1 M LiCl, and back to 0.1 M NaCl (Figure 3a). When the solution was
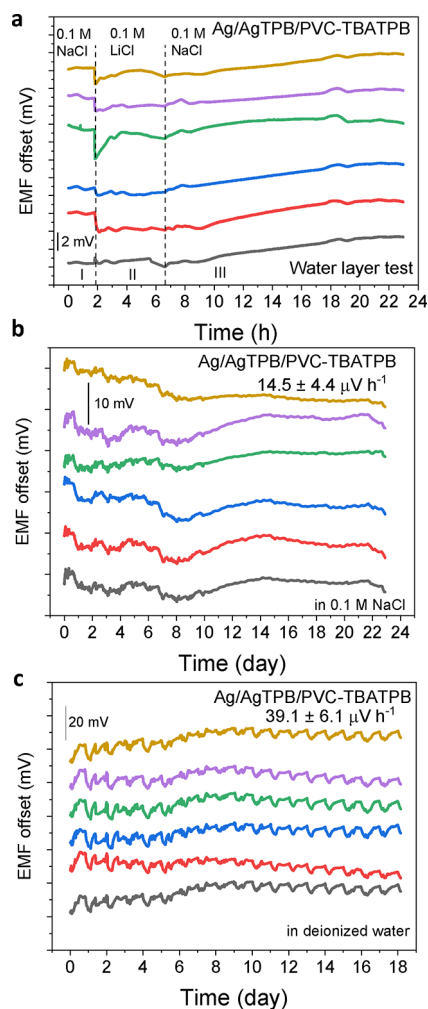

Figure 3. Water-layer and stability measurements. (a) Water-layer tests for the Ag/AgTPB/PVC-TBATPB electrodes ($n = 6$). (b, c) The long-term stability was examined in both 0.1 M NaCl and deionized (DI) water. The EMF is shown in an offset model along the y-axis. The EMF in the general non-offset model is shown in Figure S4.

changed from NaCl to LiCl, the potential variation was 1.2 ± 1.2 mV. Upon going back to NaCl from LiCl, the response reaches equilibrium rapidly with a potential variation of only 0.3 ± 0.2 mV. This result indicates no existence of a water layer. Subsequently, we examined the long-term stability (23 days) of the electrodes in 0.1 M NaCl aqueous solution. As shown in Figure 3b, the potential fluctuation (ΔE) is
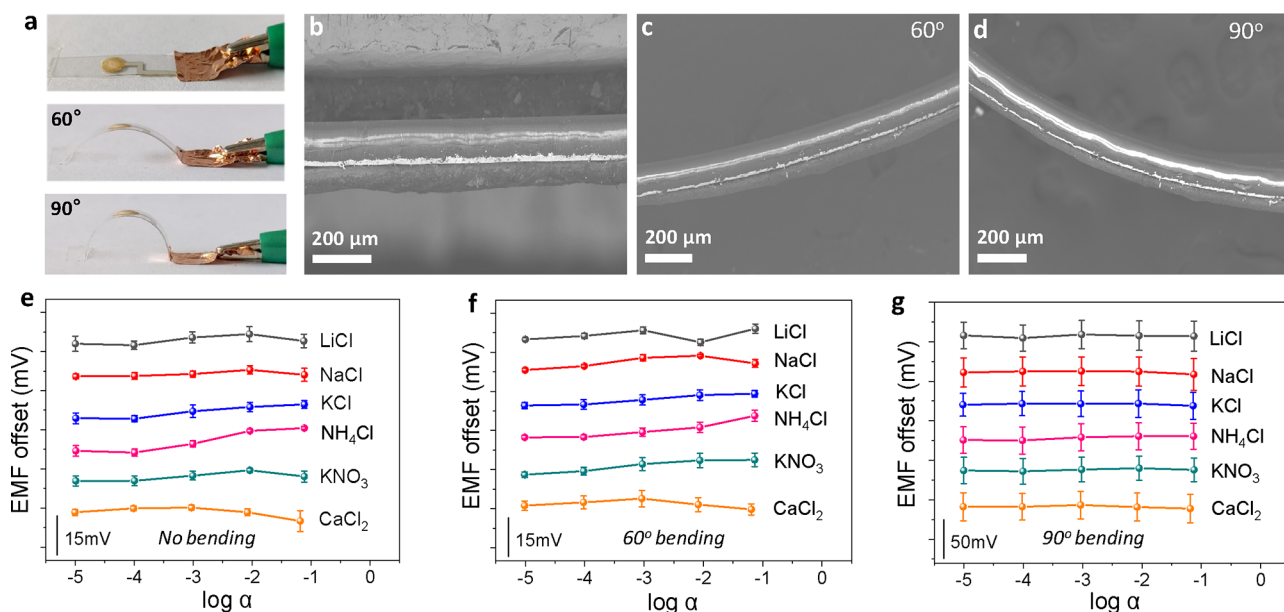
Figure 4. Potentiometric measurements of flexibility Ag/AgTPB SC-RE. (a) Photo image of Ag/AgTPB/PVC-TBATPB under no bending and 60 and 90° bending. (b–d) Scanning electronic microscopy (SEM) images of Ag/AgTPB/PVC-TBATPB under different bendings. (e–g) Potentiometric measurements in different electrolytes under different bendings ($n = 3$). The EMF is shown in an offset model along the y-axis.
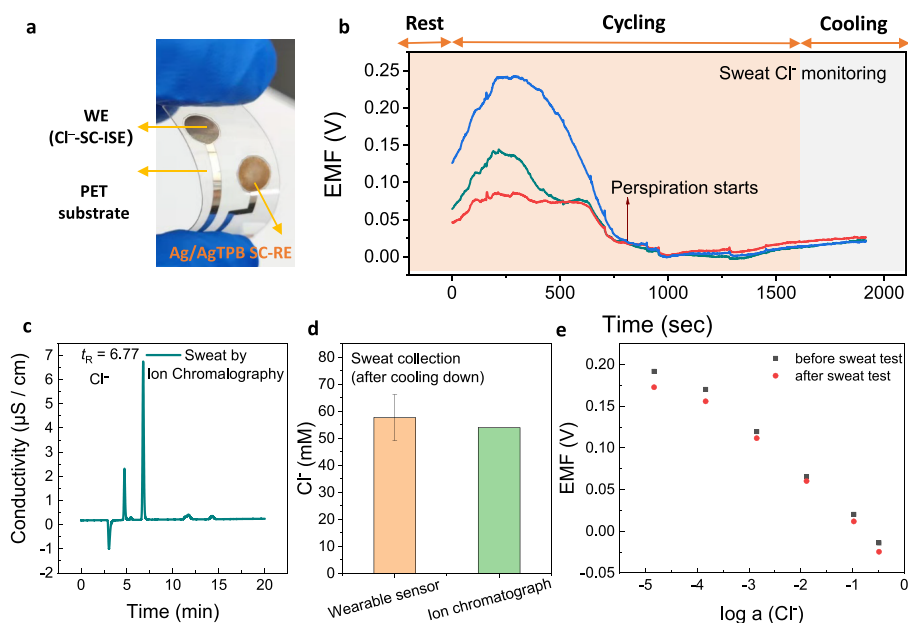
Figure 5. Wearable potentiometric Cl⁻ sensing. (a) Photo image of the potentiometric Cl⁻ sensor chip integrated with a Cl⁻ indicator electrode of a bare Ag/AgCl electrode and SC-RE of Ag/AgTPB/PVC-TBATPB. (b) On-body sweat Cl⁻ measurements ($n = 3$). (c) Ex situ analysis for sweat Cl⁻ by ion chromatography. The sweat was collected after cooling down. (d) Comparison of testing results between the wearable sensor and ion chromatograph. (e) Potentiometric calibration curves for the Cl⁻ sensor before and after sweat measurements.

determined around ∼14.5 ± 4.4 μV h⁻¹. It should be noted that the fluctuation was determined from the difference between the maximum and minimum potentials. The SC-RE is generally relatively stable in electrolyte solution, for example, the quasi-reference electrode, typically a bare silver wire, which could keep somewhat stable in an electrolyte solution at a constant concentration. Thus, a harsh examination was performed in deionized (DI) water. As shown in Figure 3c, the SC-RE maintains relatively stable (∼39.1 ± 6.1 μV h⁻¹) near 18 days although there is a potential oscillation possibly due to the high resistance. We have compared the stability with

representative Ag/AgCl-based reference electrodes (Table S1). The stability is comparable or even better than those electrodes.

3.3. Flexibility of Ag/AgTPB/PVC-TBATPB

The above measurements have confirmed the feasibility of the Ag/AgTPB SC-RE. It should be noted that all electrochemical characterizations are based on solid Ag column electrodes. In this section, we fabricate a flexible Ag/AgTPB SC-RE to examine the possibility in wearable sensing. The electrode was prepared by sputtering an Ag layer on a flexible PET substrate and followed by running the same procedure as the Ag column

electrode. As shown in Figure 4a, the flexible Ag/AgTPB/PVC-TBATPB could undergo bending at 60 and 90° angles. Cross-section SEM images disclose that the thickness of the flexible Ag/AgTPB/PVC-TBATPB including the polyethylene terephthalate (PET) substrate was ∼200 μm (Figure 4b). The solid electrolyte layer does not separate or fall off under 60 and 90° bending (Figure 4c,d). Subsequently, potentiometric measurements for the flexible Ag/AgTPB/PVC-TBATPB were characterized. Under no bending state, the potentiometric responses in various electrolytes exhibit similar results like the Ag column electrode (Figure 4e and Figure S5). Under 60 and 90° bending, the electrodes still maintain relatively stable potentials (Figure 4f−g and Figures S6 and S7). However, it should be noted that the electrode-to-electrode reproducibility under 90° is less than that at 60°, possibly due to the decreased interfacial adhesion under high strength bending. We also examined the reproducibility of a single Ag/AgTPB/PVC-TBATPB electrode at 90° bending (Figure S8). It is found that the potential fluctuation for three tests is around 1−5 mV, which indicates a good reproducibility for a single electrode. Overall, the endurability under 60−90° bending should meet the requirements for the wearable sweat sensors.

3.4. Wearable Cl⁻ Sensor for Sweat Analysis

Sweat not only contains a variety of electrolytes and metabolites that can provide healthy information but also has non-invasive characteristic of sampling and analysis.[7] As the main anion in extracellular fluid, the chloride ion (Cl⁻) plays an important role in maintaining acid−base balance, osmotic pressure distribution, and muscular activity.[49] Herein, we integrate a working electrode of Cl⁻-SC-ISE and a SC-RE of Ag/AgTPB/PVC-TBATPB on a flexible PET substrate for on-body sweat Cl⁻ analysis (Figure 5a). The Cl⁻-SC-ISE was based on the bare Ag/AgCl electrode. The detailed preparation is presented in the Experimental Section. The integrated wearable Cl⁻ sensor was worn on the volunteer's forehead in combination with a mini-potentiometer and a mobile battery. While the volunteer exercised on a spinning bike, the sensor performs a real-time analysis of sweat Cl⁻. At the same time, the potential signal is displayed wirelessly transmitted in a customized mobile application program that matches the above mini-potentiometer.

As shown in Figure 5b, after ∼13 min exercise, the perspiration starts, and the potential response shows a relatively stable result. With the amount of sweat further increasing, the concentration of Cl⁻ increases gradually to a stable value of ∼57.7 ± 8.5 mM. After cooling down, a microtube was used to collect the sweat dripping. After dilution, the sweat sample was analyzed by the ion chromatograph for comparison (Figure 5c). The Cl⁻ concentration was determined 54 mM by ex situ analysis. The test results demonstrate that the wearable sensor has a high accuracy with a relative error of 7.0% compared with the ion chromatograph (Figure 5d). Subsequently, the sensor was taken off and measured again for the calibration curve (Figure 5e). The sensor maintains a Nernst response toward Cl⁻ after sweat tests. The calibration curves show the potential difference ∼10−20 mV for the low concentrations (10⁻⁵ and 10⁻⁴ M) but nearly overlap over 1 mM (Figure 5e). Since the Cl⁻ in sweat is around 50 mM, which demonstrates the accuracy of test result. Overall, the flexible wearable sensor integrated with

Ag/AgTPB/PVC-TBATPB has shown relatively high reliability for on-line sweat analysis.

4. CONCLUSIONS

SC-REs remain a daunting challenge in the solid potentiometric ion sensing. In this work, we have developed an Ag/AgTPB/PVC-TBATPB organic insoluble salt electrode as an SC-RE. Compared with the state-of-the-art Ag/AgCl-based SC-REs, the Ag/AgTPB/PVC-TBATPB has demonstrated high potential stability, particularly under the rigorous examination in deionized water. Additionally, the SC-RE exhibited flexibility and could maintain potential stability under a certain mechanical bending strength. A proof-of-concept application of sweat Cl⁻ monitoring finally demonstrated that this SC-RE could be used for wearable sensors.

■ ASSOCIATED CONTENT

ⓈⒾ Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsmeasuresciau.2c00036.

> Supplementary figures for the hydrophobicity of membrane (Figure S1) and potentiometric responses of SC-REs (Figures S2−S8) and a comparison of analytical performances (Table S1) (PDF)

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Notes

The authors declare no competing financial interest.

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