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Polyion Detection via All-Solid-Contact Paper-Based Polyion-Sensitive Polymeric Membrane Electrodes

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Abstract

The first all-solid-contact paper-based single-use polyion-sensitive ion-selective electrodes (ISEs) are described. These polyion-sensitive ISEs are fabricated using cellulose filter paper coated with a carbon ink conductive layer. A polyanion sensing membrane is cast on a section of the coated paper and the sensor is insulated, resulting in a disposable, single-use device. Various polyanions are shown to yield large negative potentiometric responses when using these disposable devices for direct polyanion detection. These new sensors are further demonstrated to be useful in indirect polycation detection when polycations (i.e., polyquaterniums (PQs)) are titrated with polyanionic dextran sulfate (DS). Titrations monitored using these paper-based, all-solid contact devices yield endpoints proportional to the given PQ concentration present in the test sample.

Keywords: ion-selective electrodes, polyion sensors, paper-based devices, titration, polyquaternium species

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Polyion sensing technologies have grown into a well-established field in which a wide variety of electrochemical and optical sensing methods have been reported. The bulk of research and development for these sensing technologies has largely been focused on detecting biomedically relevant polyions (e.g., protamine [1,2], heparin [3,4], etc.). Although biomedical polyions are quite important, there is a large number of other types of polyionic species that have found widespread use in various industrial and cosmetic applications/products [5-10]. Therefore, the expansion of polyion sensing technology to the detection of these polyions in a variety of matrices, such as personal care product formulations or water treatment processes, can assist in developing new applications of polyion sensors as well as spark the development of new types of polyion sensing methodologies for fundamental and/or applied studies.

New configurations of polyion sensors targeted toward biomedical polyion measurements has been an active area of investigation. Some of these configurations have included coated wire electrode heparin sensors,[11] fully reversible all-solid-contact pulsed galvanostatic

protamine sensors,[12,13] and solid contact silicon chip-based heparin sensors [14]. Sensors directed toward measuring more industrial/cosmetic polyions (i.e., polyquaterniums (PQs)) have, to date, not undergone the same rate of targeted sensor development and application. To our knowledge, sensor configurations directed toward PQ analysis has only recently become an area of active exploration [15]. Continuing to expand on new advancements in sensor configurations will allow analysts to choose the configuration for PQ analysis that best fits the desired application.

All-solid-contact polyion-sensitive ISEs represent an important area of development for polyion analysis and characterization. More specifically, paper-based sensing devices have seen an increase in development over recent years, as paper has a wide number of beneficial properties (e.g., affordability, flexibility, biocompatibility, etc.) [16]. Indeed, paper-based polyion-sensitive optical devices for PQ measurements have already been reported by our group [15]. Hence, paper-based electrochemical devices are a logical next progression.

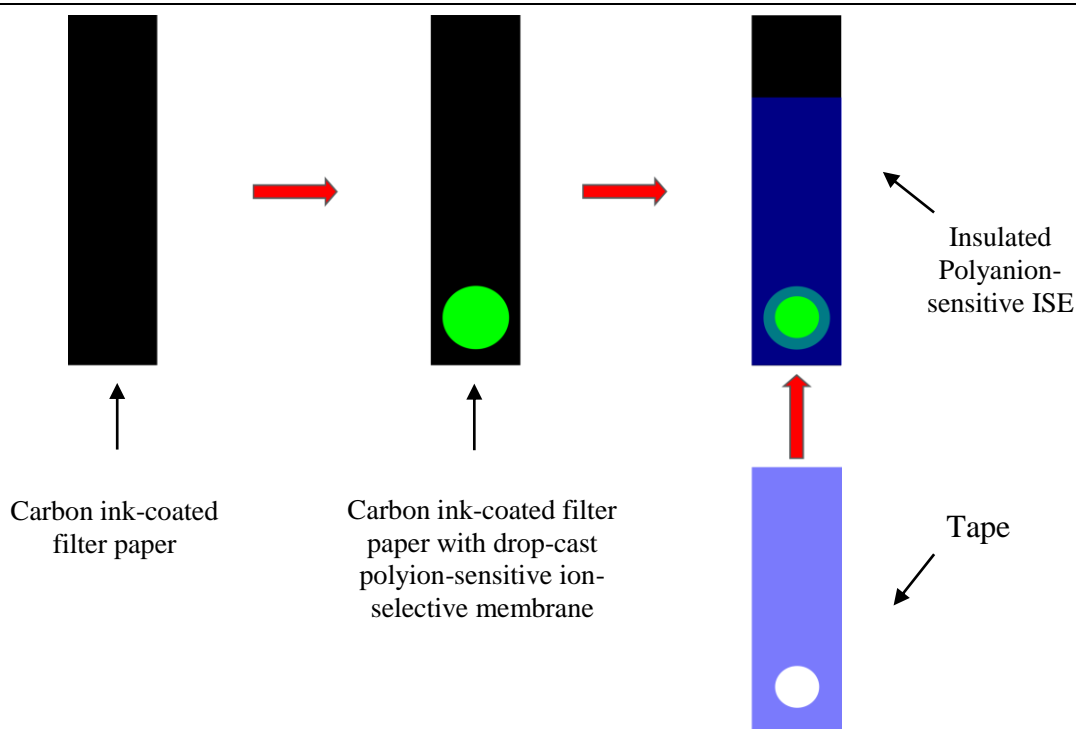


Figure 1. Fabrication process of paper-based all-solid-contact polyanion-sensitive ISEs.

In this communication the fabrication and application of the first all-solid-contact paper-based single-use polyanion-sensitive membrane electrodes are described. These all-solid-contact devices are constructed from cellulose filter paper and do not require an inner filling solution in contact with an internal Ag/AgCl reference electrode (RE) to act as an ion-to-electron transducer. Indeed, single-walled carbon nanotubes (SWCNTs) are used in place of the inner filling solution and Ag/AgCl RE. This approach was first explored by Crespo et al.[17] for potentiometric devices in the development of an all-solid-contact ISE for K^+ determinations. The proposed sensors described herein are capable of detecting a variety of polyanions in a simple buffered background electrolyte. These sensors are also demonstrated to be capable of indirectly detecting various PQ species *via* potentiometric titrations using dextran sulfate (DS) as the polyanionic titrant, with the PQs being detected in the

ppm range.

Parent base sensors were batch fabricated by first cutting approximately 9.0 cm x 15.5 cm rectangles from a sheet of Whatman™ qualitative filter paper (grade 5; diameter: 240 mm; thickness: 200 μm) (Fisher Scientific, Waltham, MA). These paper rectangles were coated with one layer of SWCNT conductive aqueous ink (Sigma-Aldrich, St. Louis, MO) on each side using a conventional paint brush. Each coated rectangle was allowed to air dry for 10 min, followed by oven drying for 10 min at ca. 60 °C. The electrical resistance of three coated rectangles was measured using a handheld multimeter (Hewlett Packard, Palo Alto, CA). The process of coating each side of the rectangle and air/oven drying was repeated an additional 5 times for a total of 6 coats; paper resistance was measured after each oven drying process. Once dried, individual base sensors were cut from each coated rectangle (approximately 1.0 cm x 4.5 cm).

Sensing membrane cocktails were prepared by mixing 66% poly(vinyl chloride) (PVC) (Sigma-Aldrich, St. Louis, MO), 32.5% bis(2-ethylhexyl) sebacate (DOS) (Sigma-Aldrich, St. Louis, MO), and 1.5% tridodecylmethylammonium chloride (TDMAC) (Polysciences, Warrington, PA) (w/w) in 8 mL of anhydrous THF (Sigma-Aldrich, St. Louis, MO) and allowed to completely dissolve overnight. Once dissolved, 30 μL aliquots of the membrane cocktail were drop-cast directly onto one end of one side of each individual paper-based sensor. The THF was allowed to evaporate for no less than 5 min. Additional single

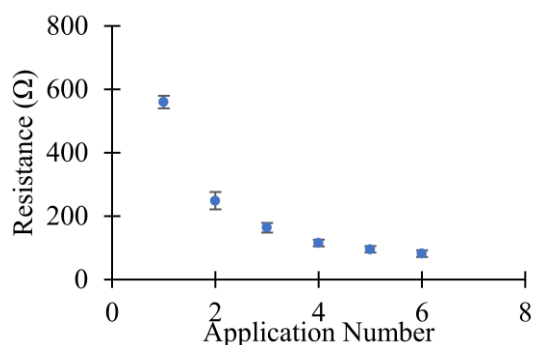


Figure 2. Resistivity of cellulose paper after successive applications of carbon ink. Each data point represents the average resistivity (\pm s.d.) of three different rectangles of cellulose paper coated in carbon ink.

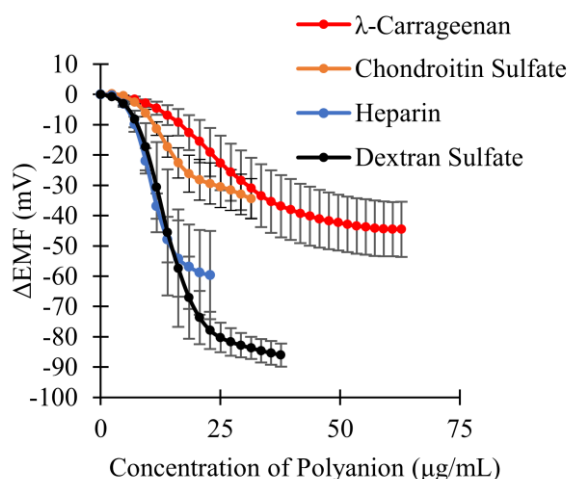


Figure 3. Dose-response curves of four different polyanions. Each data point represents the ΔEMF (\pm s.d.) per concentration of polyanion from three different polyanion sensors placed in the same solution.

aliquots of 30 μL each of the membrane cocktail were drop-cast on top of the previous layers and the THF was allowed to evaporate for no less than 10 min. A single piece of semiconductor wafer tape (Semiconductor

Equipment Corporation, Moorpark, CA) was placed on the side of the paper-based polyanion-sensitive ISE that did not contain the sensing membrane; the top portion of the sensor was left exposed to facilitate electrical contact between the voltmeter and the sensor using a standard alligator clip. A hole of approximately 1 mm in diameter was punched into another piece of semiconductor wafer tape. This piece of tape was used to cover the remaining side of the paper-based polyanion sensing device; the hole was oriented directly over the center of the cast membrane. Fig. 1 shows the overall sensor construction process.

All-solid-contact polyion-sensitive ISEs have a number of benefits for both in-field analyses and point-of-care diagnostic testing. In their construction, paper is a notable target as an inexpensive and robust mechanical support material. This requires the mechanical support to be electrically conductive. As cellulose paper does not exhibit inherent electrical conductivity, it is necessary to impart conductivity by the application of a conductive material (i.e., carbon ink). Figure 2 shows how the resistivity of the cellulose paper decreases with each successive application of the carbon ink layers. The resistivity of the cellulose paper begins to plateau after the fourth application; additional coats after the fourth

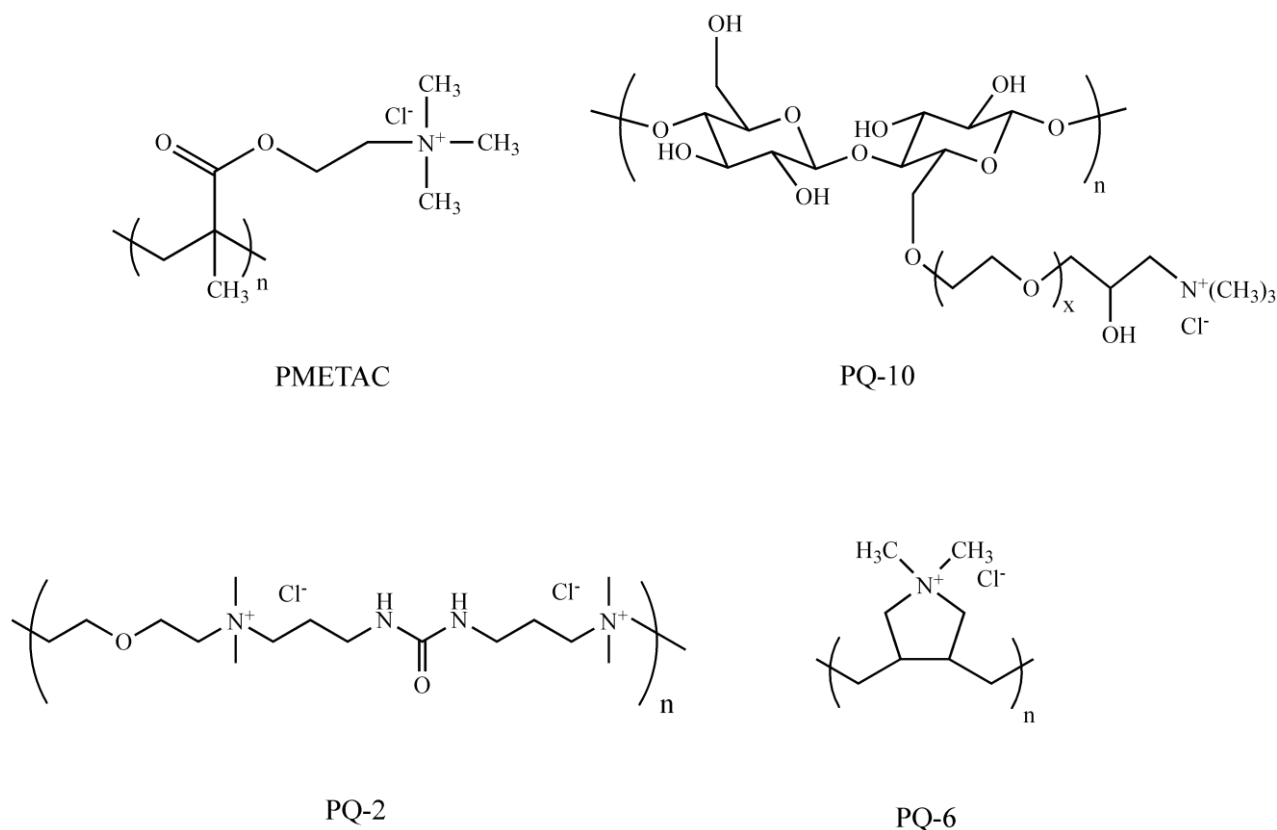


Figure 4. Chemical structures of four different PQ species indirectly detected using all-solid-contact paper-based polyanion-sensitive ISEs.

application did not decrease the resistivity significantly.

Once the sixth coat of the carbon ink was completely dried, the addition of the polyanion-sensitive membrane and the subsequent insulation of the sensor with tape was performed. The polyanion-sensitive membrane used for the preparation of these sensors is designed for single-use polyanion detection applications. The sensors were used in conjunction with a gel-filled double junction RE to obtain their dose-response toward four different polyanions.

Direct polyanion detection was performed using DS, heparin, chondroitin sulfate, and λ -carrageenan as representative polyanions. The measurements were performed by first aliquoting 50 mL of 10 mM PBS solution within a glass beaker. This same buffer was also used as a diluent for all experiments and was prepared by diluting a 100 mM phosphate buffer, pH 7.4, containing 100 mM NaCl solution (unless otherwise noted). A gel-filled double junction RE (Sigma-Aldrich, St. Louis, MO) was placed into the 10 mM PBS solution with three paper-based polyanion-sensitive ISEs connected to a high impedance voltmeter using an alligator clip. The inner compartment of the double junction RE contained a gel composed of 3 M KCl and the outer compartment was composed of 10% KNO_3 solution. Prior to the addition of a polyanion for a dose-response experiment, a stable baseline for each sensor was allowed to develop over 5 min when the EMF of each paper-based polyanion-sensitive ISE was measured against the double junction RE. Once stable baselines were established, each polyanion was injected into the 10 mM PBS sample solution using a dual-syringe infusion/withdrawal pump (Cole-Parmer, Vernon Hills, IL) at a flow rate of 239 $\mu\text{L}/\text{min}$. Each ΔEMF value was calculated by averaging the last 10 pseudo-equilibrium values (sampled every 5 s) of each 1 min interval after pump initiation for each sensor and subtracting this value from the average EMF baseline potential value of the same sensor. The concentration of the polyanion corresponding to each ΔEMF value was calculated based on the pump flow rate and the time at which each average EMF value was recorded. Figure 3 shows the resulting response curves toward each polyanion. Each polyanion generates a super-Nernstian response where each data point represents the average ΔEMF for the corresponding concentration of added polyanion (average signals \pm s.d. from $n = 3$ sensors).

Indirect detection of four different PQs was performed using potentiometric titrations. Samples containing increasing concentrations of poly(2-methacryloxyethyltrimethylammonium) chloride (PMETAC), PQ-10, PQ-6, and PQ-2 (see Fig. 4 for structures) were prepared in 10 mM PBS at final volumes of 50 mL. The same gel-filled double junction RE used in direct detection experiments was immersed in each sample and three paper-based polyanion-sensitive ISEs

were also placed within each sample. Stable baselines for each sensor were allowed to develop over a 5 min period and then the EMF of each paper-based polyanion-sensitive ISE was measured vs. the RE. Each sample was then titrated with DS delivered by the same syringe pump

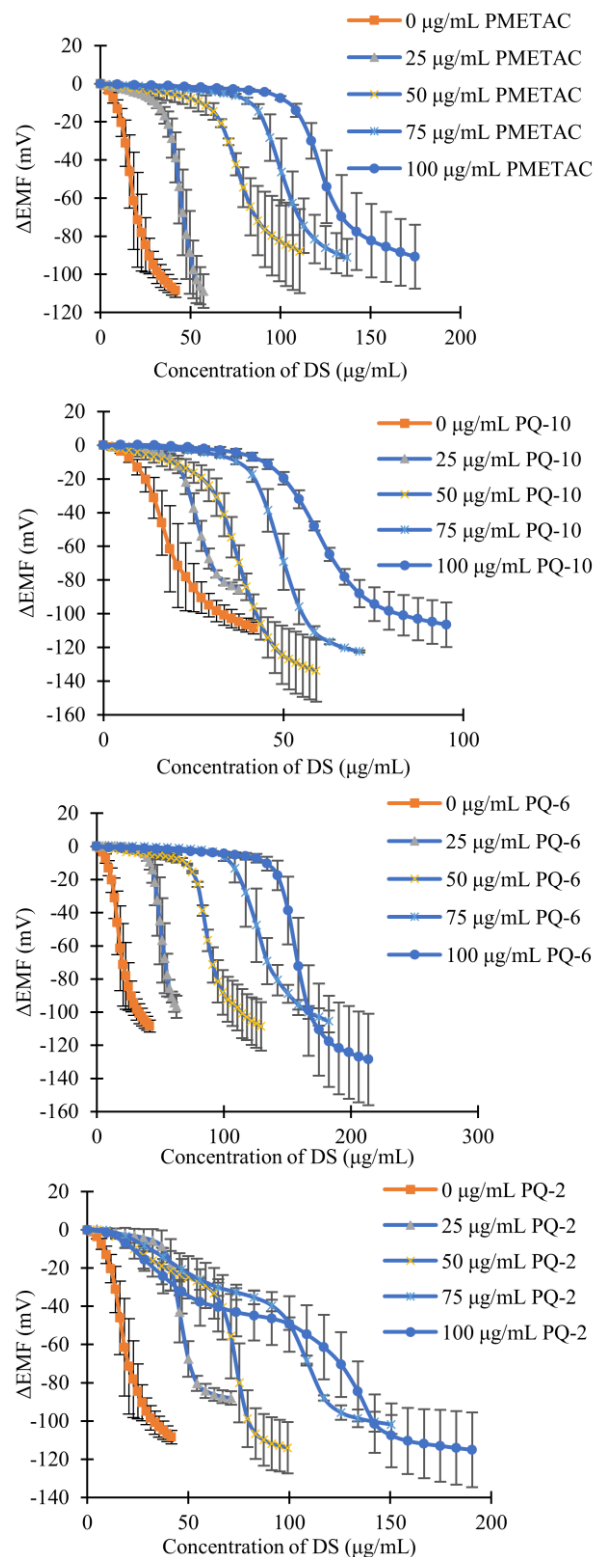


Figure 5. Titration curves of four PQ species titrated with DS. Each data point represents the average of three ΔEMF (\pm s.d.) units per unit concentration of free DS in the sample phase. Each data point represents the average ΔEMF per unit concentration of polyanion from three different polyanion sensors placed in the same solution.

used in direct detection experiments at a flow rate of 239 $\mu\text{L}/\text{min}$.

Single-use conventional polyanion-sensitive ISEs constructed using liquid contact macroelectrodes (Oesch Sensor Technology, Sargans, Switzerland) have already been shown to be useful in the indirect detection of a variety of cosmetic/industrial polycations (i.e., PQs) [18,19]. These prior studies demonstrated that analytically useful potentiometric titration data for each PQ species can be obtained when PQs are titrated with a polyanion and the concentration of free polyanion is monitored by a single-use polyanion-sensitive ISE. These new all-solid-contact paper-based polyanion-sensitive ISEs should also be able to generate analogous data with similar limits of detection. Figure 5 shows potentiometric titration data obtained by titrating various PQ species with DS using these new paper-based sensors as single-use detectors. Each generated titration curve shifts to the right as the concentration of the PQ species increases. Figure 6 shows the calibration curves for each PQ species generated by plotting the first derivative of each titration curve to estimate the equivalence point. These data demonstrate that PQ quantification is possible using indirect titration methods with limits of detection (3σ) for PMETAC, PQ-10, PQ-6, and PQ-2 being 17.66, 38.08, 12.17, and 14.56 $\mu\text{g}/\text{mL}$, respectively. Further, the slope values of the calibration curves for PMETAC, PQ-10, PQ-6, and PQ-2 generated using the proposed paper-based polyanion sensors are all in excellent agreement with the slope values generated using conventional single-use macroelectrode-type polyanion-sensitive ISEs [18]. The slope values of each calibration curve generated using the

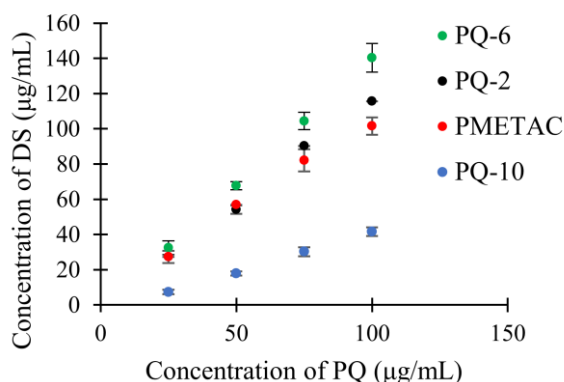


Figure 6. Calibration curves of four different PQs. These data are calculated based on the titration curves found in figure 5.

all-solid-contact polyanion-sensitive ISEs also retain the same descending order with respect to the magnitude of the slope. This suggests that these sensors yield the same relative charge density information as found in earlier potentiometric studies [18,20]. Lastly, PQ-2 titration curves yield the same shape as can be seen in earlier

titration experiments, originating from the decreased equilibrium constant between PQ-2 and DS [18].

In summary, the all-solid-contact paper-based polyanion-sensitive membrane electrodes described herein have been shown to be useful in the direct detection of polyanions and the indirect detection of polycations (i.e., PQs). These sensors are completely disposable, single-use devices that can be employed as electrochemical polyanion detectors in the same fashion as their liquid contact macroelectrode counterparts.^{18,19} These paper-based polyanion sensors have a variety of advantages including not requiring an inner filling solution in contact with an internal Ag/AgCl RE, their potential ability to be batch-fabricated in large quantities using screen printing technology, and their low cost of fabrication. Further optimization and experimentation are required to determine the limits of these new sensors and how changing various parameters (e.g., number of coats of carbon ink, polyanion-sensitive membrane application number, polyanion-sensitive membrane volume per aliquot, etc.) might impact sensitivity and/or detection limits of the proposed all-solid-contact polyanion-sensitive ISEs.

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