

A Miniaturized Electrochemical Biosensor for Real-Time In Vivo Potassium Monitoring in the Inner Ear

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Abstract:

This work presents a novel miniaturized potassium-selective biosensor with an integrated solid-state reference electrode (RE), designed for real-time, in vivo monitoring of potassium ion (K^+) dynamics in the cochlea. K^+ is essential for auditory transduction and mechano-electrical signal conversion in the inner ear, where sensory hair cells depend on potassium-rich endolymph. Disruptions in K^+ homeostasis are linked to disorders such as Ménière's disease (1). Despite its importance, current diagnostic methods cannot provide real-time, in vivo monitoring of K^+ in the inner ear, limiting our understanding of the ionic mechanisms involved in auditory function and disease progression (2). Unlike prior studies that focused on K^+ monitoring in interstitial fluid, transdermal applications, or the brain (3, 4), this system addresses a critical need for real-time monitoring of K^+ fluctuations, providing valuable insights into both physiological and pathological changes within the inner ear.

A 50 μm copper wire was used as the substrate for both the working electrode (WE) and RE. For the WE, a palladium layer was deposited to enhance surface roughness, followed by electrochemical polymerization of PEDOT/PSS1, which served as an ion-to-electron transducer. A potassium-selective membrane was then applied to enable ion selectivity toward K^+ . To fabricate the RE, the copper wire was coated with a silver layer and further chlorinated using HCl/KCl solution to make Ag/AgCl RE. A reference membrane was then applied to ensure stable performance across varying ionic environments (Fig.1a). The final sensor assembly consisted of two miniaturized electrodes (WE and RE) designed to fit within the confined structure of the cochlea.

After surface characterization, extensive benchtop validation confirmed the performance of the sensor (Fig.1b-f), demonstrating high sensitivity (~ 52.8 mV/dec), a broad linear range (10^{-5} – 10^{-1} mol/L), a limit of detection of $10^{-5.16}$ mol/L, strong selectivity coefficients (-2.62 for Na^+ , -4.10 for Mg^{2+} , and -3.85 for Ca^{2+}) (Table1), and excellent stability over two months. Additional experiments using artificial perilymph validated the device's selectivity under physiologically relevant ionic conditions, confirming minimal interference from interfering ions.

To evaluate in vivo functionality, the biosensor was implanted in the guinea pig's cochlea from dorsal and ventral approaches. Following the application of 500 mM KCl at the cochlear base, the sensor detected a rapid increase in potential, indicating elevated K^+ levels. This response plateaued for approximately 15 minutes before gradually returning to baseline within 28 minutes, likely due to cerebrospinal fluid influx via the cochlear aqueduct after cochlear perforation, confirming the sensor's responsiveness and ability to dynamically track ionic changes in vivo.

¹ 3,4-ethylenedioxythiophene / poly (4-styrenesulfonic acid) solution

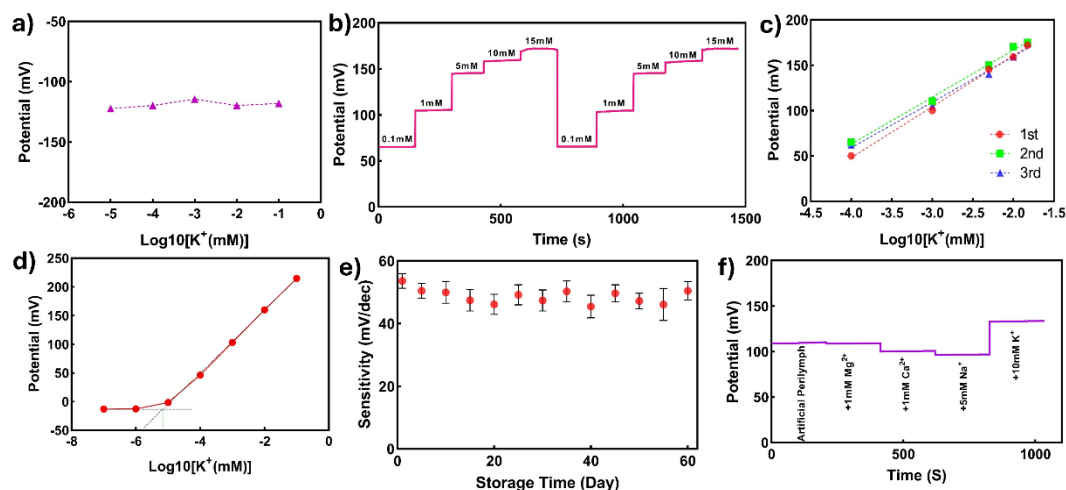


Figure 1: a) Potential stability of the RE. Characterization of the WE: b) Repeatability, c) Sensitivity, d) Linear detection range, e) Long-term stability, and f) Selectivity against interfering ions.

Ion	Log of selectivity coefficient
Na ⁺	-2.62±0.1
Mg ²⁺	-4.10±0.03
Ca ²⁺	-3.85±0.06

Table1: Selectivity coefficients of the proposed potassium sensor determined using the fixed interference method.

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