同行专家业内评价意见书编号：20250854401

附件1

浙江工程师学院（浙江大学工程师学院）
同行专家业内评价意见书

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申报工程师职称专业类别（领域）： 电子信息

浙江工程师学院（浙江大学工程师学院）制

2025年03月21日

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一、个人申报

（一）基本情况【围绕《浙江工程师学院（浙江大学工程师学院）工程类专业学位研究生工程师职称评审参考指标》，结合该专业类别(领域)工程师职称评审相关标准，举例说明】

1.对本专业基础理论知识和专业技术知识掌握情况(不少于200字)

在高校就读期间，我系统掌握了本专业的基础理论知识与专业技术技能。在课程学习中，我深入研习了生物传感技术、医学信号处理、微纳制造与检测等核心专业知识，能够将理论原理与实际应用相结合。在实验与科研过程中，我熟练掌握了柔性电子器件设计、微针阵列制备、信号采集与数据分析等关键技术，具备扎实的实验操作能力和数据处理能力。

在科研实践中，我能够独立进行电化学检测、柔性贴片制备与性能测试等实验，并通过多次在体实验，不断优化监测系统性能，积累了丰富的实践经验。在数据处理与分析方面，我能够利用MATLAB、Python等编程工具进行数据处理与可视化，提升了数据分析的效率与准确性。

2.工程实践的经历(不少于200字)

在科研方面，我曾担任集成式微针传感阵列项目的负责人，负责柔性监测系统的设计、制备与测试，并参与微针电极的制备与动物在体实验测试。在项目中，我熟练掌握了柔性电子器件设计、微针阵列制备、信号采集与数据分析等关键技术，能够独立进行实验方案设计和数据处理，展现出较强的科研能力。

此外，我在浙江大学滨江研究院担任科研助理期间，参与了完整的科研项目，进一步锻炼了实验操作、数据分析和科研写作等专业技能。通过全国大学生生物医学工程竞赛的参赛经历，我强化了在生物医学工程领域的综合实践能力。

综合而言，我在本专业领域内掌握了扎实的基础理论和专业技术知识，并具备将其应用于科研和实践的能力，为未来在工程技术领域的发展打下了坚实的基础。

3.在实际工作中综合运用所学知识解决复杂工程问题的案例（不少于1000字）

在集成式微针阵列多参数离子监测系统的研发过程中，我充分运用了本专业的基础理论知识和专业技术能力，针对电解质动态监测领域中的关键工程问题，展开了系统性研究与技术攻关。在这一过程中，我将材料科学、电化学传感技术、柔性电子器件制造、生物医学工程以及嵌入式系统开发等多学科知识相结合，通过仿真、实验与在体测试，成功解决了微针电极修饰、阵列穿刺效率、系统集成与实时监测等复杂工程难题，最终构建了一套性能稳定、实时可靠的集成式微针阵列多参数离子监测系统。

在项目初期，我聚焦于微针电极的性能优化。由于微针尺寸微小，传统电极修饰方法难以保证膜层的均匀性和附着力，影响了电极的灵敏度与稳定性。针对这一难题，我对比了滴涂法、旋涂法与圈涂法三种修饰方法，经过多轮实验发现，圈涂法能够在微针表面形成连续且均匀的膜层，附着力更强且不易脱落，显著提升了电极的稳定性。同时，我采用等离子体表面重构技术对微针表面进行改性，通过在基底表面引入活性基团，增强了修饰层的结合强度，有效减少了长期监测过程中膜层剥落的风险。优化后的电极在一周内信号漂移率仅为0.9 mV/h，满足了长时间监测的稳定性要求。

在微针阵列的结构设计中，我运用了有限元仿真技术对微针刺入皮肤的力学特性进行模拟分析。通过对比不同微针间距、长度与直径对穿刺效率的影响，我发现增加阵列间距能够有效降低微针之间的相互干扰，从而减少刺入力、提高穿刺效率并减小对皮肤的损伤。基于仿真结果，我设计了间距为600 μm的微针阵列，并在实验中验证了其优越性能。体外测试表明，优化后的阵列穿刺效率提高了21.4%，而皮肤损伤降低了37.6%，有效提升了系统在实际应用中的安全性与可靠性。

在系统集成与开发阶段，我设计了基于STM32单片机的硬件电路平台，负责微针电极信号的实时采集与处理。为了确保信号质量，我在电路中采用了高精度运算放大器与低噪声滤波电路，减少了环境干扰对检测信号的影响。同时，我开发了基于蓝牙BLE协议的无线通信模块，实现了数据的实时传输与显示。在移动端，我自主编写了安卓手机应用程序，能够实时绘制离子浓度变化曲线，并支持历史数据存储与导出，为用户提供了便捷的数据可视化功能。

在系统验证阶段，我通过体外模拟实验和动物在体实验对系统的性能进行了全面评估。在体外实验中，我将微针阵列贴附于模拟皮肤模型，测试其在不同电解质浓度下的响应特性。实验结果显示，系统在1 mM~100 mM范围内线性度良好，R^2均大于0.99，且信号响应快速准确。在动物在体实验中，我选用新西兰兔作为实验模型，将微针阵列贴附于兔皮肤表面进行电解质实时监测。实验结果表明，微针阵列在兔体内的信号稳定性与准确性良好，其监测数据与血液检测结果基本一致，误差在±5%以内，验证了系统的可靠性与临床应用潜力。

在本项目中，我通过多学科知识的综合运用，成功开发了集成式微针阵列多参数离子监测系统，并在系统的性能、稳定性与可靠性上取得了显著优化。该系统能够实时、精准地监测人体电解质水平，在微创医疗诊断与健康监测领域具有广阔的应用前景，并为临床微创多参数动态监测技术的发展提供了重要参考。

（二）取得的业绩（代表作）【限填3项，须提交证明原件（包括发表的论文、出版的著作、专利证书、获奖证书、科技项目立项文件或合同、企业证明等）供核实，并提供复印件一份】					
1. 公开成果代表作【论文发表、专利成果、软件著作权、标准规范与行业工法制定、著作编写、科技成果获奖、学位论文等】					
成果名称	成果类别 [含论文、授权专利（含发明专利申请）、软件著作权、标准、工法、著作、获奖、学位论文等]	发表时间/授权或申请时间等	刊物名称/专利授权或申请号等	本人排名/总人数	备注
Integrated Assembly of Flexible Microneedle Array Patch for Real-time Multi-ion Monitoring	会议论文	2024年09月03日	中国微米纳米技术学会	1/6	
一种自校准多参数微针监测系统	发明专利申请	2024年09月29日	申请号：202411373304.2	2/4	

2.其他代表作【主持或参与的课题研究项目、科技成果应用转化推广、企业技术难题解决方案、自主研发设计的产品或样机、技术报告、设计图纸、软课题研究报告、可行性研究报告、规划设计方案、施工或调试报告、工程实验、技术培训教材、推动行业发展中发挥的作用及取得的经济社会效益等】

无

（三）在校期间课程、专业实践训练及学位论文相关情况	
课程成绩情况	按课程学分核算的平均成绩： 85 分
专业实践训练时间及考核情况(具有三年及以上工作经历的不作要求)	累计时间： 1 年（要求1年及以上） 考核成绩： 87 分
本人承诺	
个人声明：本人上述所填资料均为真实有效，如有虚假，愿承担一切责任，特此声明！ **申报人签名：**马丽坤	

22260304

二、日常表现考核评价及申报材料审核公示结果

日常表现考核评价	非定向生由德育导师考核评价、定向生由所在工作单位考核评价： ☑优秀　　□良好　　□合格　　□不合格 德育导师/定向生所在工作单位分管领导签字（公章）：　　　年　月　日 中共浙江大学工程师学院委员会
申报材料审核公示	根据评审条件，工程师学院已对申报人员进行材料审核（学位课程成绩、专业实践训练时间及考核、学位论文、代表作等情况），并将符合要求的申报材料在学院网站公示不少于5个工作日，具体公示结果如下： □通过　　□不通过（具体原因：　　　　　　） 工程师学院教学管理办公室审核签字（公章）：　　　年　月　日

浙江大学研究生院

攻读硕士学位研究生成绩表

学号：22260304
姓名：马羽坤
性别：女
学院：工程师学院
专业：电子信息
学制：2.5年
毕业时最低应获：24.0学分
已获得：27.0学分
入学年月：2022-09
毕业年月：
学位证书号：
毕业证书号：
授予学位：

学习时间	课程名称	备注	学分	成绩	课程性质	学习时间	课程名称	备注	学分	成绩	课程性质
2022-2023学年秋季学期	现代信号处理技术与应用		1.0	84	专业学位课	2022-2023学年冬季学期	产业技术发展前沿		1.5	85	专业学位课
2022-2023学年秋季学期	研究生英语基础技能		1.0	免修	公共学位课	2022-2023学年冬季学期	智能化仪器软硬件系统设计与应用		1.0	85	专业学位课
2022-2023学年秋季学期	研究生英语能力提升		1.0	免修	跨专业课	2022-2023学年春季学期	智能医疗技术应用案例分析		1.0	96	专业学位课
2022-2023学年秋季学期	工程技术创新前沿		1.5	87	专业学位课	2022-2023学年春季学期	自然辩证法概论		1.0	73	专业学位课
2022-2023学年秋季学期	数值计算方法		2.0	93	专业选修课	2022-2023学年春夏学期	微纳传感与检测技术导论		2.0	84	专业选修课
2022-2023学年秋季学期	研究生英语		2.0	免修	专业学位课	2022-2023学年夏季学期	“四史”专题		1.0	88	公共选修课
2022-2023学年冬季学期	生物医学工程方法学		1.0	93	专业学位课	2022-2023学年春夏学期	高阶工程认知实践		3.0	88	专业学位课
2022-2023学年冬季学期	新时代中国特色社会主义理论与实践		2.0	90	专业学位课	2023-2024学年冬季学期	工程伦理		2.0	85	专业学位课
2022-2023学年秋冬学期	研究生论文写作指导		1.0	80	专业选修课		硕士生读书报告		2.0	通过	

说明：1. 研究生课程按三种方法计分：百分制，两级制（通过、不通过），五级制（优、良、中、及格、不及格）。

2. 备注中“*”表示重修课程。

学院成绩校核章：（60）

成绩校核人：张梦依

打印日期：2025-03-20

Integrated assembly of flexible microneedle array patch for real-time multi-ion monitoring

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Abstract. Electrolytes play a critical role in various human physiological processes, including the regulation of muscle functions and the maintenance of acid-base balance. Monitoring electrolyte concentrations is essential for the management of many chronic diseases and during postoperative care. In this context, we have developed a flexible electrolyte monitoring system based on a microneedle array patch. The system is designed for minimally invasive, extra flexible, real-time measurement of potassium (K^+), sodium (Na^+), and calcium (Ca^{2+}) ion concentrations in interstitial fluid. By modifying the microneedle surfaces with multilayer structures and assembling these microneedles into arrays, the sensor achieves high sensitivity and stability for the detection of K^+, Na^+, and Ca^{2+} ions. In vivo test was performed to demonstrate the system's capability to measure multi-ion concentrations subcutaneously.

1. Introduction

Electrolytes are minerals dissolved in bodily fluids that play a crucial role in regulating and maintaining essential physiological functions. Electrolyte imbalances can lead to various clinical symptoms, including arrhythmias, seizures, muscle cramps, and even death [1][2]. In clinical practice, real-time monitoring of electrolytes is essential, particularly for patients in intensive care or undergoing major surgeries, to facilitate timely medical intervention. Currently, electrolyte monitoring in clinical settings primarily relies on blood gas analyzers, which are costly and involve complex procedures. Therefore, the development of rapid, accurate, and real-time electrolyte monitoring systems represents a significant advancement for future clinical applications.

Current systems for monitoring human electrolytes primarily focus on sweat [3] and interstitial fluid. However, sweat-based systems are not ideal for clinical monitoring for the rate of sweating and is susceptible to contamination from skin impurities [4]. Researchers have explored various methods for monitoring interstitial fluid, including laser techniques [5], reverse iontophoresis [6], and microneedle-based approaches. Among these, microneedle-based monitoring systems offer significant advantages for long-term, real-time monitoring [7]. The electrical conductivity of metal microneedles makes them excellent substrates for sensors, meanwhile allowing them to penetrate the skin for subcutaneous electrolyte monitoring with minimal discomfort and rapid wound healing [8]. Many studies have focused on the biomedical applications of microneedles; however, whole-array microneedle manufacturing processes are not well-suited for the monitoring of multiple biochemical parameters. Meanwhile, the small size of microneedles complicates the sensor modification process, affecting the sensor's sensitivity and stability [9]. For sensors contains multiple microneedles [10], it is crucial to assemble the array in a way that minimizes mutual interference and enhances skin adherence.

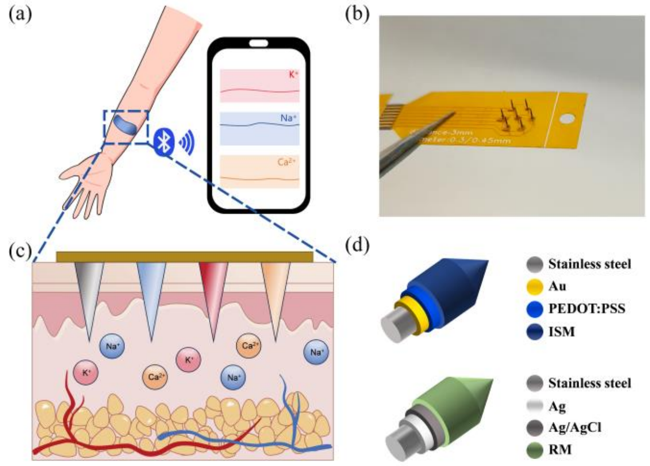

Figure 1. (a) A real-time multi-ion monitoring system with a flexible microneedle array patch. (b) Microneedle array patch with ion selective electrode and reference electrode. (c) Microneedle sensor for transdermal ion monitor. (d) Schematic for ion selective electrode (top) and reference electrode (bottom).

In this work, we investigated a multi-ion monitoring system based on an all-solid-state ion-selective microneedle array patch. A multilayer structure is applied to stainless steel microneedles to create reference electrodes and all-solid-state microneedle electrodes sensitive to K^+, Na^+, and Ca^{2+} ions. These different microneedle electrodes are then fixed onto a flexible circuit board as shown in Fig.1(b), allowing for better adhesion to the skin and establishing electrical connections with the detection circuit. As shown in Fig.1(a) and Fig.1(c), during use, the microneedle array patch was inserted and secured onto skin, allowing real-time monitoring of various ion concentrations within the body, thereby providing feedback on the individual's health status.

As shown in Fig.1(d), The ion-selective electrodes consist of four layers: stainless steel needle, sputtered gold substrate, Poly(3,4-ethylenedioxythiophene) polystyrene sulfonate (PEDOT:PSS) layer, and an ion-selective membrane (ISM) layer. The stainless-steel needle and gold substrate provide the electrodes with excellent penetration hardness and conductivity. The PEDOT:PSS layer, which possesses both electronic and ionic conductivity, is finely deposited on the microneedle electrode surface via electropolymerization, serving as an effective ion-electron transduction material [11]. The reference electrode is coated with a reference membrane (RM) to improve its stability and minimize interference from other salt ions. The sensors developed cover the physiological concentration ranges of human ions. They exhibit sensitivities of 58.80 mV/decade for potassium, 53.61 mV/decade for sodium, and 23.32 mV/decade for calcium, meantime with good linearity.

2. Experimental

2.1. Materials

Microneedles with a diameter of 250 μm, 3,4-ethyldiothiophene (EDOT), valinomycin, calcium ionophore IV were purchased from Aladdin Co., Ltd. Poly(Sodium 4-styrene sulfonate) (NaPSS), potassium tetrakis(4-chlorophenyl)borate (KTClPB), dioctyl sebacate (DOS), tetrahydrofuran (THF) were purchased from Macklin Co., Ltd. Sodium ionophore X, sodium tetrakis[3,5 bis(trifluoromethyl)phenyl]borate (NaTFPB), were purchased from Sigma Aldrich Co., Ltd. Conductive silver paste was purchased from Ted Pella, Inc.

2.2. Fabrication of microneedle electrodes

Preparation of ion selective membrane (ISM) solution: selective membrane solution is composed of ionophore, ion changer, plasticizer, polymer and organic solvents. Here, we used THF as organic solvents. The components and contents of different ion-selective membranes in 1ml THF solvent are shown in Table 1. All ISM solution were sealed and stored at 4°C.

Preparation of reference membrane solution: dissolve 79.1 mg of PVB completely in 1 ml of methanol and store the solution for future use. Then, dissolve 50 mg of NaCl and 50 mg of $AgNO_3$ into the prepared PVB solution. Stir the mixture for 30 minutes. The resulting mixture is an opalescent liquid, where the milky appearance is due to AgCl precipitate, which is surrounded by PVB.

Table 1. Compositions of ISMs

ISM	Compositions(mg)						
	Ionophore			Ion changer		Plasticizer	Polymer
	K^+	Na^+	Ca^{2+}	NaTFPB	KTClPB	DOS	PU
K^+	2.00	/	/	/	0.55	66	33
Na^+	/	1.00	/	0.55	/	66	33
Ca^{2+}	/	/	1.00	0.90	/	66	33

Preparation of ion selective sensor: PEDOT:PSS film was deposited on the surface of the microneedle by electrochemical polymerization (ECP). The ECP solution was obtained by dissolving 0.01M EDOT and 0.1M NaPSS in DI water. Using the microneedle as the working electrode, the polymerization current of 14uA was applied for 700s in a three-electrode system. Then, use a copper wire ring to dip into ISM membrane solution, and pass the microneedle through the ring to make the membrane solution attached to the tip. Let dry for ten minutes and repeat the process three times.

Preparation of reference electrode: The microneedle with silver layer was modified by coating a silver/silver chloride (Ag/AgCl) paste. Then the reference membrane is applied via dip-coating, with 2 μL of the solution dispensed and dried for 10 minutes per application, repeated three times. The microneedle was then dried for 4 hours.

2.3. Fabrication of microneedle patch

The microneedle array is mounted on a flexible circuit board featuring gold fingers, pads, and leads. Using UV adhesive, the modified microneedle electrodes are vertically fixed onto the pads of the flexible circuit board. The modified microneedle electrodes are vertically fixed onto the pads of the flexible circuit board, with only the 1 mm needle tips exposed. The excess portions of the microneedles are then trimmed off. The spacing between each microneedle is 3 mm. Conductive silver paste is then applied to cover both the microneedle and copper pad surfaces, establishing electrical connections between the microneedles and the circuit.

3. Result and discussion

3.1. Performance of ion selective electrode

The physiological concentration ranges of various ions in the human body are as follows: 3.2-5.7 mmol/L for K^+, 133-146 mmol/L for Na^+, and 1.84-2.72 mmol/L for Ca^{2+}. During the performance testing of ion-selective electrodes, the test concentration ranges were chosen to cover these physiological levels to ensure the effective application of electrodes. The test ranges were 2-32 mmol/L for K^+, 16-256 mmol/L for Na^+, and 1-16 mmol/L for Ca^{2+}. The open circuit potential (OCP) between the ion-selective electrode and a standard reference electrode was measured at various concentrations.

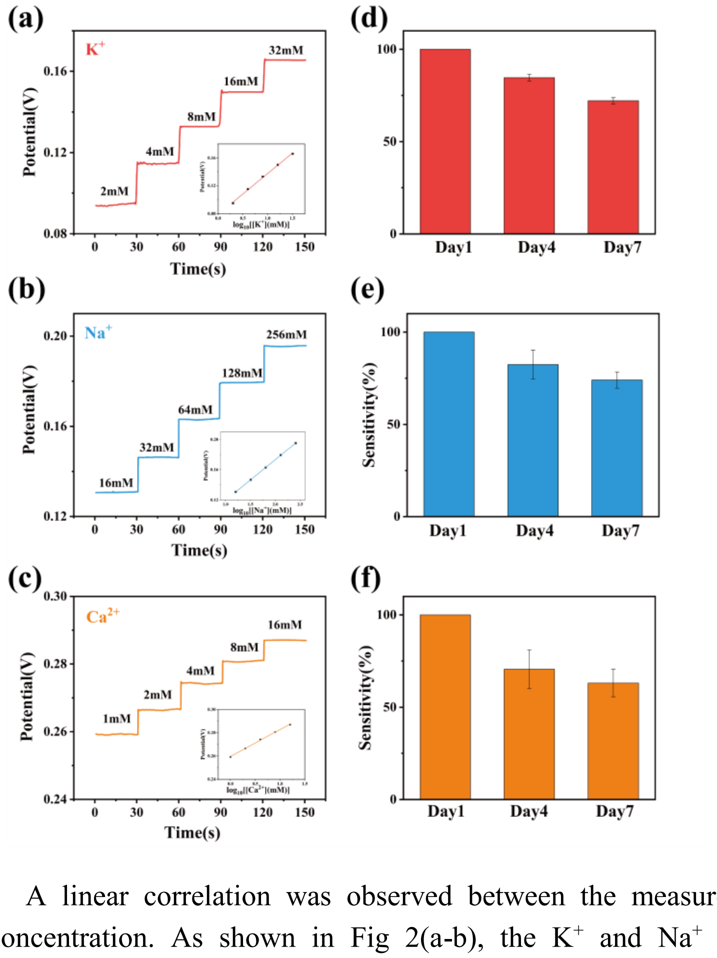

Figure 2. (a-c) Potential responses and corresponding calibration curve of K^+ (red), Na^+ (blue), Ca^{2+} (orange) selective electrode. (d-f) Stability of K^+ (red), Na^+ (blue), Ca^{2+} (orange) selective electrode over seven days.

A linear correlation was observed between the measured OCP and the logarithm of the ion concentration. As shown in Fig 2(a-b), the K^+ and Na^+ microneedle electrodes exhibited good sensitivities of 58.80 mV/decade and 53.61 mV/decade, respectively, which are close to the theoretical value of 59.2 mV/decade predicted by the Nernst equation. The voltage signals showed a strong linear relationship with ion concentrations, with R^2 of 0.998 and 0.999. The Ca^{2+} microneedle electrode also demonstrated a good linear relationship between voltage signal and ion concentration, with a sensitivity of 23.32 mV/decade (R^2=0.998) as shown in Fig 2(c).

The stability of the electrodes was also tested over a seven-day period. Sensitivity measurements were taken every two days, while the electrodes were stored in corresponding high-concentration ion solutions on the intervening days. The tests revealed that the sensitivities of the K^+ and Na^+ ion-selective electrodes remained above 70% of their initial values throughout the seven days as shown in Fig.2(d-e). In contrast, the sensitivity of the Ca^{2+} ion-selective electrode stayed above 70% of its initial value for the first four days, but decreased to 63% by the sixth day as shown in Fig.2(f). These results highlight the importance of regular calibration of ion-selective electrodes for long-term monitoring.

3.2. Performance of microneedle array patch

Due to the detection method of open-circuit potential in ion-selective electrodes, the stability of the microneedle reference electrode (RE) is crucial in developing. The potential of conventional Ag/AgCl paste-coated reference electrodes varies with chloride ion concentration as shown in Fig.3(a). The results in the figure were obtained by gradually adding a specific concentration of NaCl to the solution. Changes in chloride ion concentration led to a potential shift of -51 mV/decade for RE coated with Ag/AgCl paste. By covering the electrode with a reference membrane (RM), this effect is mitigated, resulting in a stable microneedle reference electrode.

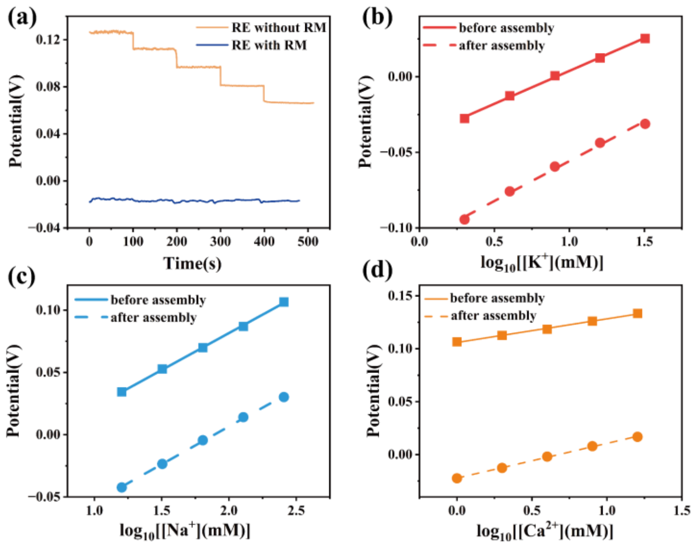

Figure 3. (a) Potential of microneedle reference electrode without RM (orange) and reference electrode with RM (blue). (b) Corresponding calibration curve of K^+ before assembly (solid) and after assembly (dashed). (c) Corresponding calibration curve of Na^+ before assembly (solid) and after assembly (dashed). (d) Corresponding calibration curve of Ca^{2+} before assembly (solid) and after assembly (dashed).

Using the microneedle reference electrode instead of the standard reference electrode, the ion-selective electrodes were assembled and tested as previously described, and the results were compared with those obtained before assembly. As shown in Fig 3(b-d), the results showed that, compared to the standard reference electrode, the calibration curves of the microneedle array exhibited a shift in intercept. This shift is attributed to the voltage difference between the microneedle reference electrode and the standard reference. In terms of sensitivity, the results were consistent with those obtained before assembly, indicating that this assembly method does not adversely affect the microneedle electrodes and is a reliable and efficient array assembly method.

3.3. *In vivo test*

To validate the performance of the microneedle array patch monitoring system subcutaneously, in vivo testing was conducted using anesthetized New Zealand rabbits. The sensitivity of the ion-selective electrodes was measured in standard solutions and simulated body fluid (SBF) to establish linear calibration curves. The electrode patch was then applied and secured to the rabbit's skin, and the potential changes of the electrodes were measured over a period. Fig.4 shows that the test results indicate the ion concentration fluctuates steadily within a certain range. Upon removal of the patch, the rabbit's skin showed minimal visible damage, with no signs of redness or inflammation. The ion electrodes were also calibrated in a modified simulated body fluid (SBF) after removal. This approach aims to conduct secondary calibration to account for the effects introduced by the puncture process.

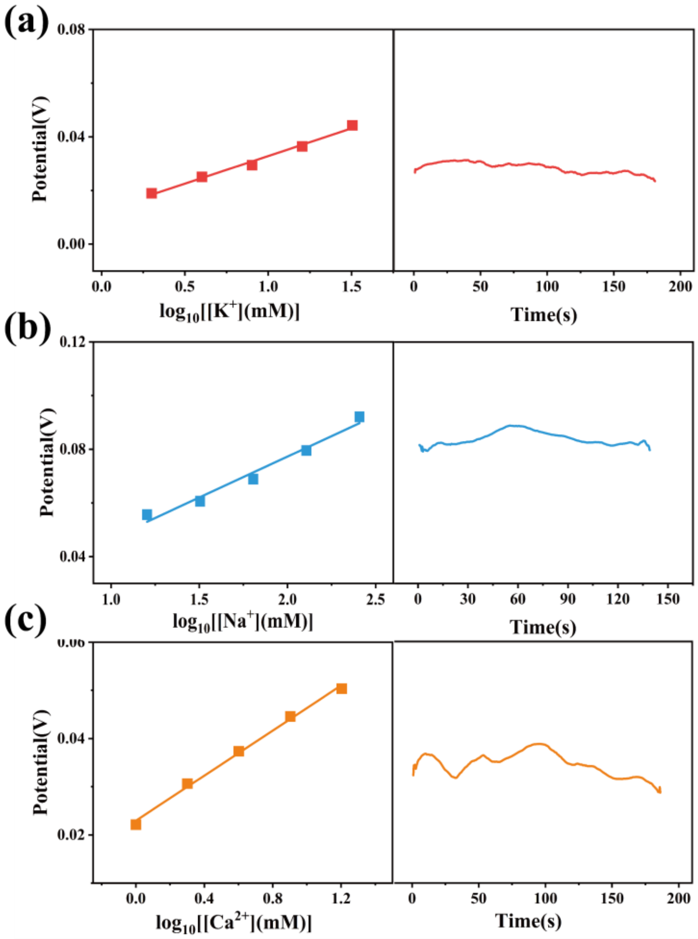

Figure 4. In vivo test result in anesthetized New Zealand rabbits: (a) The calibration curve of K^+ selective electrode (left) and its real-time potentials in vivo test (right). (b) The calibration curve of Na^+ selective electrode (left) and its real-time potentials in vivo test (right). (c) The calibration curve of Ca^{2+} selective electrode (left) and its real-time potentials in vivo test (right).

4. Conclusion

In this study, we developed a flexible microneedle array patch and its monitoring system for real-time subcutaneous ion concentration measurement. By applying a multilayer structure on the microneedle surface, we created ion-selective and reference electrodes with excellent sensitivity and stability. A highly efficient and rapid assembly method was used to construct the microneedle array patch, ensuring the original performance of the microneedles was maintained without mutual interference. In vivo testing of the microneedle array patch confirmed its ability to successfully penetrate the skin and monitor ion concentrations subcutaneously. This assembly method overcomes the challenges associated with the fine modification of microneedles. It paves the way for the future integration of various functional microneedle sensors. This advancement could significantly expand the applications and usage scenarios of microneedles in diverse fields.

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