

PRECISION NEURAL INTERFACES THROUGH INTRINSICALLY
STRETCHABLE ELECTRONICS

By

Vittorio Mottini

A DISSERTATION

Submitted to
Michigan State University
in partial fulfillment of the requirements
for the degree of

Biomedical Engineering—Doctor of Philosophy

2024

ABSTRACT

The rapid advancement of wearable technology has introduced a new era of human-machine interaction, with soft bioelectronics emerging as a novel field at the intersection of materials science, electrical engineering, and healthcare. Soft bioelectronics offers unprecedented opportunities for seamless integration with the human body, promising to transform personal health monitoring, medical diagnostics, and human-machine interfaces. These flexible and stretchable electronic systems conform to the complex topography of human skin, adapting to its constant motion and deformation while minimizing mechanical stress on tissues. This adaptability enables long-term, comfortable wear for continuous physiological monitoring, advanced prosthetic control, or novel human augmentation, overcoming the limitations of rigid electronic systems. Despite significant progress, challenges persist in developing skin-interfaced electronics that maintain high performance across diverse skin conditions and age groups. This dissertation presents the development and evaluation of "InSkin," an innovative, inclusive skin-interfaced electronic platform designed for high-fidelity, high-density, multi-channel electrophysiological recording. The InSkin technology addresses critical challenges in current skin-interfaced electronics, particularly the variability in signal quality across diverse skin conditions and age groups.

A novel conductive polymer composite, Solution CP-G, was engineered to create a conformal, stretchable interface that adapts to various skin morphologies. This material demonstrated exceptional mechanical properties, maintaining electrical functionality at up to ~1200% strain when supported strain while achieving a 93.18% reduction in electrode-skin impedance compared to commercial electrodes.

Comprehensive characterization studies revealed InSkin's superior performance across different skin types. The device maintained 80.65% of its signal amplitude on wrinkled skin compared to smooth skin and 100% on hairy skin compared to shaved skin. Long-term stability tests showed 75% signal quality retention after 24 hours of continuous wear.

High-density surface electromyography (sEMG) mapping capabilities were demonstrated using a 32-channel array with 12 mm inter-electrode spacing. This enabled detailed visualization of muscle activity patterns, including motor unit action potential propagation and innervation zone identification, showcasing potential applications in neuromuscular research and personalized rehabilitation.

Advanced gesture recognition algorithms integrated with the InSkin platform achieved 97.7% accuracy in classifying ten hand gestures, significantly outperforming commercial electrodes. This performance was consistent across age groups, with only a 4% reduction in accuracy for older participants. The system's efficacy was further validated through successful integration with a prosthetic hand prototype, demonstrating the potential for intuitive, high-precision control.

The dissertation also explores potential applications of InSkin in healthcare monitoring, rehabilitation, and human-machine interfaces. Future research directions include material enhancements, integration with other sensing modalities, and advanced signal-processing techniques.

This work contributes significantly to the field of skin-interfaced electronics by addressing key challenges in adaptability, signal quality, and long-term wearability.

While demonstrating significant advancements, challenges remain in long-term biocompatibility and power management for continuous monitoring applications. This work lays the foundation for a new generation of inclusive bioelectronic devices, with potential impacts spanning from personalized healthcare to advanced human-machine interaction.

Copyright by
VITTORIO MOTTINI
2024

To my family,
whose unwavering support and love
have been the foundation of all my endeavors.

To all those who dare to dream big
and push the boundaries of what's possible.

And to the future generations of scientists and engineers
who will continue to innovate and improve lives through
technology.

ACKNOWLEDGMENTS

First and foremost, I want to express my deepest gratitude to God for blessing me with this life and the opportunities it has presented. My faith has been a constant source of strength and guidance throughout this journey.

Words cannot express my gratitude to my parents for your unconditional love, support, and sacrifices. You have been my pillar of strength, always believing in me even when I doubted myself. Without you, none of this would have been possible. Your unwavering encouragement and wisdom have shaped me into who I am today.

To my siblings, thank you for being my heroes and role models. Your achievements have always inspired me to push harder and reach higher. Your support and guidance have been invaluable, and I am forever grateful for our bond.

To Nadia, thank you for giving my life purpose and meaning beyond academia. Your love, patience, and understanding have been my anchor throughout this challenging journey, and your unwavering belief in me has been a constant source of motivation.

I want to express my sincere appreciation to Elon Musk, whose visionary thinking and relentless pursuit of innovation have been a constant source of inspiration. Your work has shown me the profound impact technology can have on shaping our future, motivating me to strive for excellence in my research.

I am grateful to my advisor, Dr. Jinxing Li, for your mentorship and support throughout my doctoral studies.

I deeply thank my thesis committee members for their input and guidance. Your diverse perspectives and expertise have greatly enriched this work.

To my colleagues and fellow researchers in the lab, thank you for the stimulating discussions, collaborations, and friendships. The countless hours we spent troubleshooting experiments and sharing ideas have been invaluable to this research and my personal growth.

I would like to acknowledge the support of the Department of Biomedical Engineering at Michigan State University for providing the resources and environment conducive to cutting-edge research.

I sincerely thank all the study participants who volunteered their time and effort. Your contributions have been crucial to the success of this project.

This accomplishment is not mine alone but a testament to the collective support, guidance, and inspiration from all of you. Thank you.

TABLE OF CONTENTS

LIST OF FIGURES	ix
LIST OF TABLES.....	xii
LIST OF SYMBOLS	xiii
LIST OF ABBREVIATIONS.....	xiv
Chapter 1: Introduction	1
Chapter 2: Literature Review.....	11
Chapter 3: Materials and Methods.....	41
Chapter 4: Results and Discussion.....	99
Chapter 5: Applications and Future Directions	123
Chapter 6: Conclusion.....	134
BIBLIOGRAPHY	138
APPENDIX A: DETAILED EXPERIMENTAL PROCEDURES	151
APPENDIX B: STATISTICAL ANALYSES.....	158
APPENDIX C: GESTURE RECOGNITION ALGORITHM.....	161
APPENDIX D: ETHICS APPROVAL AND CONSENT FORMS	166

LIST OF FIGURES

Figure 1: Overview of skin-interfaced electronics and their applications in health monitoring and human-machine interfaces.....	2
Figure 2: Illustration of the challenges in electrophysiological recording with traditional rigid electrodes, which cannot intimately conform to the skin's macro (curvature) and micro (wrinkles) features.	4
Figure 3: Comparison of electrode-skin interface for stretchable electrodes and traditional rigid electrodes on wrinkled skin.	5
Figure 4: Thesis structure and chapter interconnections.....	10
Figure 5: Schematic illustration of the InSkin material composition and preparation process. (a) Chemical structures of key components (PEDOT:PSS, WPU, EMIM:ESO ₄ , glycerol, ammonia). (b) 3D render and cross-sectional illustration of the layered structure of the InSkin device. (c) SEM images of the prepared conductive polymer composite film at different magnifications, scale bar: 10 μ m.	44
Figure 6: Fabrication process for the multichannel high-density sEMG array. (i) Preparation of Solution CP-G by mixing PEDOT:PSS, EMIM:ESO ₄ , WPU, ammonia, and Glycerol. (ii) Thin film deposition via drop-casting or spin-coating on PTFE-coated glass. (iii) Vacuum drying overnight. (iv) CO ₂ laser patterning of sensing pads and interconnects. (v) Oxygen plasma treatment for improved adhesion. (vi) Pattern release and (vii-viii) transfer to artificial skin (AS) substrate. (ix) Second plasma treatment for encapsulation preparation. (x-xi) Connection of flat-flexible cables (FFC) with anisotropic tape and (xii) thermal annealing. (xiii) Application of patterned AS encapsulation layer. (ivx) Final thermal annealing. This process yields a flexible, stretchable array for real-time prosthetic control.	56
Figure 7: Overview of characterization instruments for the InSkin device. (left) EIS and CV measurement configuration. (right) Tensile testing setup.	59
Figure 8: Overview of human studies protocol. (a) Electrode placement for the robotic hand control recordings. (d) Photograph of a 16-channel InSkin. (c) Examples of the 10 hand gestures used in the gesture recognition study. (d) Robotic hand prototype used for real-time control demonstration, and the 32-channel sEMG array applied to one of the subject's forearms.	79
Figure 9: Robotic hand control system overview. (a) Block diagram of the entire system from sEMG acquisition to robotic hand movement. (b) Visual illustration of the InSkin application, from material properties to prosthetic control.	98

Figure 10: Mechanical characterization of InSkin. (a) illustration and (b) photo of the effect of the glycerol addition to the conductive composite during stretching: Solution CP (top) presents the formation of cracks along the transverse direction, whereas Solution CP-G (bottom) does not, scale bar: 1 cm. (c) Stress-strain curves, (d) Normalized resistance under strain, (e) Cyclic stress-strain curves for Solution CP, Solution CP-G, artificial skin-supported Solution CP, and artificial skin-supported Solution CP-G, (f) Normalized resistance under cyclic strain, and (g) SEM images showcasing the conformability of Solution CP-G on (left, scale bar 20 μ m) hairs and wrinkles and (right, scale bar 200 μ m) smooth skin. 103

Figure 11: Electrical and electrochemical characterization of InSkin. (a) Normalized resistance vs. strain for Solution CP and the different Solution CP-G formulations, (b) Schematic of the conductive network under strain, (c) Niquist plot for the different materials tested in this study, inset: zoom in the 0 – 1.5k Ω , (d) Bode plot of impedance, (e) Impedance at various frequencies of interest, (f) Equivalent circuit model for electrode-skin impedance, (g) Impedance change under strain, (h) impedance distribution density, (i) Cyclic voltammograms, (j) Normalized enclosed area as function of the elongation..... 107

Figure 12: (a) Illustration of the electrode configurations employed to record sEMG signals, showing their different capability to conform to the skin's surface features. (b) Schematic diagram highlighting the importance of skin-electrode interface for signal attenuation. (c) Raw and processed sEMG signals recorded with CE and InSkin. (d) Impedance measurements for the three electrodes on a smooth, wrinkled, and hairy skin. (e) Signal amplitude for the three electrodes across different skin types. (f) Signal-to-noise ratio (SNR) for the electrodes on smooth, wrinkled, and hairy skin). (** n.s. not significant, **p > 0.05, ***p < 0.005)..... 109

Figure 13: (a) Schematic illustration of the commercial electrode (CE) and solution CP-G 250 electrodes on hairy skin surfaces. (b), (c). Representative sEMG recordings from smooth (blue) and hairy (red) skin using CE (b) and CP-G 250 (c) electrodes. The CP-G 250 electrode demonstrates higher signal fidelity, particularly on hairy skin. (d). SNR comparison between CE and CP-G 250 electrodes on smooth and hairy skin, showing significantly higher SNR for CP-G 250, particularly on hairy skin. (e) Signal amplitude comparison, highlighting enhanced signal capture with CP-G 250 electrodes across both skin types. (f) Electrode-skin impedance measurements, with CP-G 250 showing significantly lower impedance on both skin types, indicating superior skin-electrode interface stability. (g) Illustration of an elderly individual performing activities while equipped with surface electrodes and sEMG signals during motion tests with CE and InSkin electrodes for young and elderly participants. (h) SNR comparison of sEMG signals between commercial and InSkin electrodes during motion for young and elderly participants. (i) User comfort scores for different electrodes during static, dynamic, and long-term wear, with statistical significance noted. (j) Photographs of the 32-channel sEMG array showing flexibility and stretchability under twisting, stretching, and complex

deformation. (k) Photograph of an array made with Solution CP-G on skin, highlighting its conformality with skin's microscale features (scale bar: 5mm). 110

Figure 14: (a) sEMG recordings from a bicep brachii contraction at 1h intervals. (b) SNR evolution over 24 hours. 114

Figure 15: High-density sEMG mapping with InSkin. (a) 32-channel array layout, (b) Photo of the 3D-channel array used for prosthetic hand control, (c) sEMG signal for innervation zone localization, (d) sEMG mapping of the forearm. 116

Figure 16 :(a) Confusion matrix of the DNN model used for gesture recognition showing the prediction accuracy values for each of the ten gestures used to train the model. I, Visual demonstration of hand gestures correlated with their respective sEMG signal patterns, providing a reference for gesture classification. (c) Comparison of gesture prediction heatmaps between younger and elder subjects and between InSkin and CE arrays, highlighting differences in machine learning performance. (d) Graph illustrating the relationship between the number of gestures and classification accuracy for younger and elder subjects with InSkin and CE sEMG arrays. (e) Sequential sEMG signals for different gesture states, displaying the robustness of signal classification over time. (f) An overview of the signal processing pipeline from EMG measurement to machine learning-based prosthetic control. (g) Photo of the prosthetic robotic hand control with the multi-channel HD-sEMG array, (h)Graphical representation of the gesture recognition algorithm. EMG data is segmented into 1-second windows, analyzed for valid gestures (>70% accuracy) or transitions, and processed through a sliding observation window. Recognized gestures are converted to finger angles for prosthetic hand control. 119

LIST OF TABLES

Table 1: Comparison of rigid and semi-rigid electrodes	12
Table 2: Comparison of flexible and stretchable electrodes	15
Table 3: Detailed Summary of Mechanical Properties for Materials Used in Skin- Interfaced Electronics Applications	20
Table 4: Key Parameters of the InSkin Gesture Classification Algorithm	91
Table 5: Key Components and Specifications of the InSkin Robotic Hand Hardware Framework	94
Table 6: Key Components and Implementation Details of the InSkin Software Framework	95
Table 7: Key Stages and Processes in the InSkin Closed-Loop Robotic Hand Control System	96
Table 8: Extensive Summary of Mechanical Properties for Materials in Skin-Interfaced Electronic Devices and Applications	100
Table 9: Comprehensive Comparison of Electrode Performance Across Smooth, Wrinkled, and Hairy Skin Surfaces in Bioelectronic Applications	111
Table B1: Descriptive Statistics for Signal Amplitude, SNR, and Impedance Across Electrode Types and Skin Conditions	159
Table B2: ANOVA Results for Comparison of Electrode Types	159
Table B3: Paired t-Test Results for Skin Condition Comparisons	159
Table B4: Independent Samples t-Test Results for Age Group Comparisons	160
Table B5: Repeated Measures ANOVA Results for Long-Term Stability Analysis	160
Table B6: McNemar's Test Results for Comparing Gesture Recognition Accuracy Across Different Electrode Type	160

LIST OF SYMBOLS

α - Constant phase element (CPE) exponent

ε - Strain

σ - Stress

Ω - Ohm, unit of electrical resistance

μm - Micrometer

mV - Millivolt

Hz - Hertz

k Ω - Kilohm

MPa - Megapascal

R - Resistance

R₀ - Initial resistance

R/R₀ - Normalized resistance

S/cm - Siemens per centimeter, unit of electrical conductivity

V - Volt

wt% - Weight percent

LIST OF ABBREVIATIONS

AI - Artificial Intelligence

AR - Augmented Reality

AS - Artificial Skin

BCI - Brain-Computer Interface

CE - Commercial Electrode

CNT - Carbon Nanotube

COPD - Chronic Obstructive Pulmonary Disease

CPE - Constant Phase Element

CV - Cyclic Voltammetry

CVD - Chemical Vapor Deposition

ECG - Electrocardiography

EEG - Electroencephalography

EGaIn - Eutectic Gallium-Indium

EIS - Electrochemical Impedance Spectroscopy

EMIM:ESO4 - 1-Ethyl-3-methylimidazolium ethyl sulfate

EMG - Electromyography

FDM - Fused Deposition Modeling

HD-EMG - High-Density Electromyography

HiPIMS - High-power Impulse Magnetron Sputtering

HMI - Human-Machine Interface

IL - Ionic Liquid

IMU - Inertial Measurement Unit

IRB - Institutional Review Board

LSTM - Long Short-Term Memory

NIRS - Near-Infrared Spectroscopy

PANI - Polyaniline

PDMS - Polydimethylsiloxane

PEDOT:PSS - Poly(3,4-ethylenedioxythiophene) Polystyrene Sulfonate

PPG - Photoplethysmography

PPy - Polypyrrole

PTFE - Polytetrafluoroethylene

PVD - Physical Vapor Deposition

PWM - Pulse Width Modulation

sEMG - Surface Electromyography

SEM - Scanning Electron Microscopy

SLA - Stereolithography

SNR - Signal-to-Noise Ratio

TENS - Transcutaneous Electrical Nerve Stimulation

UV - Ultraviolet

VR - Virtual Reality

WPU - Waterborne Polyurethane

Chapter 1: Introduction

This chapter introduces the field of skin-interfaced electronics, highlighting its potential for non-invasive health monitoring and human-machine interfaces. It outlines the challenges in electrophysiological recording, particularly for diverse skin conditions and age groups. The chapter presents the objectives and significance of the InSkin project, which aims to develop an adaptive, stretchable electronic interface for high-fidelity, inclusive bioelectronic measurements.

1.1. Background on Skin-Interfaced Electronic

Skin-interfaced electronics represent a rapidly evolving field at the intersection of materials science, electrical engineering, and biomedical engineering. These devices aim to bridge the gap between human physiology and external technology by creating seamless, non-invasive interfaces with the skin. Beyond its primary role as a protective barrier, human skin is a dynamic conduit between our inner physiology and the external environment, offering a unique platform for monitoring health and facilitating communication with technological systems ¹⁻³.

The skin interface allows for monitoring various physiological events and signals, broadly categorized into molecular, biochemical, and electrical phenomena ^{4,5}. This diversity in detectable signals makes skin-interfaced electronics a versatile tool for comprehensive health monitoring and human-machine interaction (Figure 1.1).

The development of skin-interfaced electronics has been driven by the need for continuous, non-invasive monitoring of physiological signals and the desire to create more intuitive human-machine interfaces ⁴. These devices can record various electrophysiological activities through the epidermis, enabling the diagnosis of conditions such as arrhythmia and epilepsy and providing control inputs for prosthetic devices or machines in both real-world and virtual reality (VR) environments ⁶⁻⁸.

This work has focused on the noninvasive detection of biopotentials, specifically surface electromyography (sEMG), with additional demonstrations in electroencephalography (EEG) and electrocardiography (ECG). These electrophysiological signals provide crucial

information about muscle activity, brain function, and cardiac performance, respectively ⁹⁻¹¹.

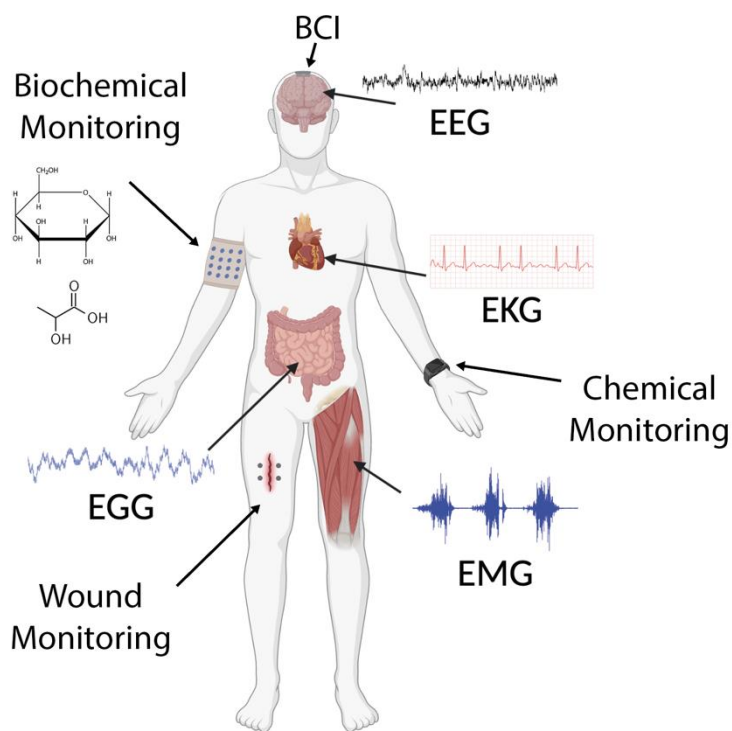


Figure 1: Overview of skin-interfaced electronics and their applications in health monitoring and human-machine interfaces.

Recent advances in flexible electronics and sensing technologies have created skin-like and skin-interfaced biomolecular sensors, often called electronic skin or e-skin ¹². These innovations allow for continuous, non-invasive screening of metabolic analytes such as glucose and lactate through sweat analysis ¹³. Beyond metabolic monitoring, electronic skins have shown remarkable versatility, including thermal sensing ¹⁴, pressure and tactile sensing ¹⁵, hydration monitoring ¹⁶, electrocardiography (ECG) ¹⁷, respiratory monitoring ¹⁸, chemical and gas sensing ¹⁹, electromyography (EMG) ²⁰, UV radiation monitoring ²¹, moisture and sweat detection ²², and wound healing monitoring ²³.

The potential impact of these technologies is significant, as they can enhance health monitoring, enable early disease prediction, and contribute to human augmentation,

ultimately leading to more scalable and ubiquitous healthcare solutions for precision medicine ²⁴.

However, the development of effective skin-interfaced electronics faces several challenges. One of the primary obstacles is the variability in skin surface properties across individuals and over time. Factors such as age, hydration, and environmental conditions can significantly affect the mechanical and electrical properties of the skin, impacting the performance and reliability of skin-interfaced devices ^{25,26}. These challenges are particularly pronounced in biopotential detection, where maintaining consistent electrode-skin contact and minimizing signal artifacts are crucial for accurate measurements ²⁷.

Given these challenges, it is crucial to understand the specific issues faced in electrophysiological recording, which forms the core focus of the InSkin project.

The InSkin project builds upon these advancements by introducing a novel conductive polymer composite combining high stretchability and excellent electrical properties. This approach addresses the critical challenge of maintaining consistent performance across diverse skin types and conditions, a key limitation of current technologies. By focusing on inclusivity and adaptability, InSkin aims to expand the applicability of skin-interfaced electronics to broader populations, including elderly users who have been historically underserved by existing solutions.

1.2. Challenges in Electrophysiological Recording

Electrophysiological recording through skin-interfaced electronics, particularly surface electromyography (sEMG), faces several critical challenges that impact these technologies' reliability, consistency, and inclusivity. These challenges stem from the inherent variability in skin properties across individuals and the dynamic nature of the skin-electrode interface, as well as the unmet need for conformal interfaces that can adapt to the moving and irregular surface of the skin ^{28,29}.

One of the primary challenges is the variation in skin properties across different populations, especially in seniors. As individuals age, their skin undergoes significant changes: it becomes thinner, develops wrinkles and age spots, and experiences reduced strength and elasticity. Furthermore, the activity of sebaceous and sweat glands diminishes,

leading to drier and more fragile skin ³⁰. These age-related changes alter the skin's impedance and conductance, making it difficult to obtain precise and consistent signal recordings ³¹. The impact of these changes on electrophysiological recordings is further compounded by the fact that skin properties can vary significantly even within the same individual, depending on factors such as body location, hydration status, and environmental conditions ³².

Current sEMG interfaces, which typically use large dry conductors or electrolytic gel electrodes, struggle to maintain consistent performance across diverse skin conditions. These electrodes can dry out quickly, causing rigid electrodes to lose conformal contact with wrinkled and irregular skin surfaces during use and motion ^{33,34}. This issue is particularly pronounced for seniors with wrinkled or dry skin, resulting in large interface impedance, motion artifacts, signal drift, source dislocation, and potential skin irritation. The limitations of current electrode technologies are further exacerbated by the dynamic nature of human movement, which can cause continuous changes in the skin-electrode interface ³⁵ (Figure 1.2).

Another significant challenge is the need for high-density, high-fidelity, high-stability, and high-comfort biodata acquisition, especially for seniors with degraded motor neuron

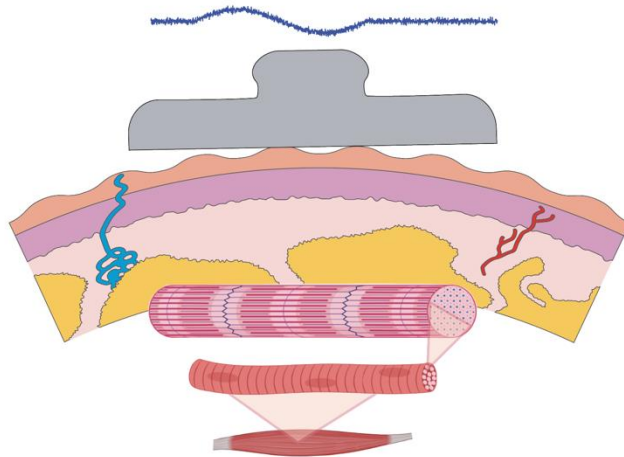


Figure 2: Illustration of the challenges in electrophysiological recording with traditional rigid electrodes, which cannot intimately conform to the skin's macro (curvature) and micro (wrinkles) features.

activities ²⁸. Traditional electrode systems often fail to provide the necessary spatial resolution and signal quality to capture the subtle electrophysiological changes associated with aging or neuromuscular disorders. This limitation is particularly critical in applications such as precise gesture recognition or detecting early signs of neurodegenerative diseases, where subtle changes in muscle activation patterns can indicate underlying conditions ³⁶.

The mechanical mismatch between rigid electrodes and human skin's soft, dynamic nature further complicates electrophysiological recording. This mismatch can lead to poor adhesion, increased motion artifacts, and inconsistent signal quality, particularly during long-term monitoring or when the subject is in motion ³⁷. The challenge of creating electrodes that can maintain intimate contact with the skin while allowing for natural movement and comfort is a key area of research in the field of skin-interfaced electronics ^{38,39} (Figure 1.3).

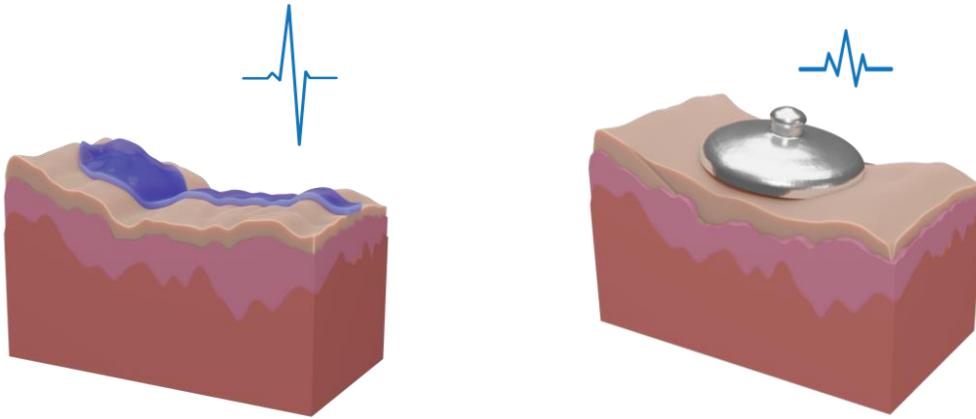


Figure 3: Comparison of electrode-skin interface for stretchable electrodes and traditional rigid electrodes on wrinkled skin.

Moreover, the challenge extends beyond mere signal acquisition to the realm of data interpretation and machine learning⁴⁰. The variability in signal quality and characteristics across different skin types and conditions can significantly impact the accuracy and reliability of gesture recognition algorithms and other analytical tools used in prosthetic control and human-machine interfaces ^{39,41,42}. This variability necessitates the development

of robust algorithms that can adapt to individual differences and changing conditions, a task that becomes increasingly complex as the applications of skin-interfaced electronics expand ^{43,44}.

The environmental factors affecting skin-interfaced electronics also present significant challenges. Factors such as temperature, humidity, and physical stress can all impact the performance of these devices. For instance, sweating during physical activity can alter the electrical properties of the skin-electrode interface, potentially leading to signal degradation ^{45,46}. Similarly, prolonged wear of electrodes can lead to skin irritation or changes in the local skin environment, further complicating long-term monitoring applications ^{47,48}.

Addressing these challenges requires a paradigm shift in designing and fabricating skin-interfaced electronics. The InSkin project addresses these challenges through a multifaceted approach. By developing a novel conductive polymer composite (Solution CP-G), we aim to create a material that combines high stretchability with excellent electrical properties, enabling consistent performance across diverse skin conditions.

1.3. Research Objectives and Significance

This thesis argues that developing a highly stretchable, conductive polymer composite with adaptive properties makes it possible to create a skin-interfaced bioelectronic platform that maintains consistent performance across diverse skin conditions and age groups. The InSkin technology aims to demonstrate superior signal quality, reduced motion artifacts, and improved long-term stability compared to existing commercial electrodes, potentially revolutionizing applications in healthcare monitoring and human-machine interfaces.

The InSkin project addresses the critical challenges in skin-interfaced electronics and electrophysiological recording by developing an innovative, inclusive, and adaptive bioelectronic platform. The primary objectives of this research are:

1. To develop a skin-mimicking, stretchable polymeric electronic interface that adapts to various skin properties, ensuring high-fidelity, high-density electrophysiological recording across diverse populations.

2. To create a conductive polymer composite that reduces the modulus and forms a gel-like interface with the skin, thereby improving conformality and signal quality.
3. To design and fabricate scalable, large-area electrode arrays for reliable sEMG mapping, with reduced motion artifacts and capability for long-term monitoring.
4. To evaluate the performance of the InSkin platform across different age groups and skin conditions, with a particular focus on senior populations.
5. To demonstrate the application of the InSkin platform in gesture recognition and prosthetic control, leveraging machine learning techniques.

The significance of this research lies in its potential to revolutionize and accelerate the field of skin-interfaced electronics and advance the inclusivity of human-machine interfaces. By addressing the limitations of current technologies, the InSkin project has far-reaching implications:

1. **Enhanced Inclusivity:** By developing a platform that performs consistently across various skin types and ages, this research promotes more equitable access to advanced bioelectronic technologies. This is particularly significant for senior populations whose existing skin-interfaced electronics have historically been underserved.
2. **Improved Healthcare Monitoring:** The InSkin platform's high-fidelity, long-term monitoring capabilities could enable more accurate and comprehensive health assessment, potentially leading to earlier detection of health issues and more personalized treatment strategies.
3. **Advanced Prosthetics and Rehabilitation:** InSkin's improved signal quality and gesture recognition accuracy could significantly enhance the control and functionality of prosthetic devices, improving the quality of life for individuals with limb loss or mobility impairments.
4. **Expanded Applications in Human-Machine Interfaces:** The InSkin platform's adaptability and performance open up new possibilities in fields such as virtual and augmented reality, remote robotic control, and other areas requiring precise and reliable bioelectronic interfaces.

5. Material Science Advancements: Developing novel conductive polymer composites contributes to the broader field of materials science, potentially inspiring new approaches in flexible and stretchable electronics beyond biomedical applications.

6. Data Quality for Machine Learning: By providing more consistent and high-quality electrophysiological data across diverse populations, the InSkin platform could significantly improve the training and performance of machine learning models in biomedical applications.

This research addresses a critical gap in existing sEMG technology by offering improved signal quality and adaptability, advancing the inclusivity of human-machine interfaces. As global populations age, the demand for such equitable, personalized bioelectronic solutions will continue to rise, positioning the InSkin platform as a pioneering, impactful innovation poised to revolutionize human-machine interfacing and improve accessibility for all.

1.4. Thesis Structure and Overview

This thesis is structured to comprehensively explore the InSkin project, from its theoretical foundations to its practical applications and future implications. The organization of the chapters is as follows:

Chapter 1: Introduction

This chapter provides the background on skin-interfaced electronics, outlines the challenges in electrophysiological recording, and presents the research objectives and significance of the InSkin project.

Chapter 2: Literature Review

A comprehensive review of existing skin-interfaced bioelectronics, including rigid and semi-flexible electrodes and flexible and stretchable electronics, is presented. This chapter also discusses the challenges in current technologies, materials for stretchable electronics, fabrication techniques, and applications in healthcare and human-machine interfaces. The review concludes by identifying gaps in research and potential areas for improvement.

Chapter 3: Materials and Methods

This chapter details the materials selection and preparation process for the InSkin platform, including the development of the conductive polymer composite. It describes the device

fabrication process, characterization techniques, and the protocols for human studies. The chapter also outlines the setup for biopotential recording and the robotic hand control system used in the project.

Chapter 4: Results and Discussion

The results of the InSkin project are presented and discussed in this chapter. It covers the mechanical properties of InSkin, its electrical and electrochemical characterization, and its performance in sEMG recording across different skin conditions. The chapter also presents findings on high-density sEMG mapping and the platform's application in gesture recognition and prosthetic control.

Chapter 5: Applications and Future Directions

This chapter explores the potential applications of the InSkin platform in healthcare and human-machine interfaces. It discusses the limitations of the current work and proposes areas for future research and development, including material enhancements, integration with other sensing modalities, and advancements in machine learning integration.

Chapter 6: Conclusion

The final chapter summarizes the key findings of the research, reiterates its significance and impact, and provides concluding remarks on the future of skin-interfaced electronics and the role of InSkin in advancing this field.

Each chapter builds upon the previous ones, providing a logical progression from the theoretical background to the practical implementation and future implications of the InSkin project. Throughout the thesis, emphasis is placed on the inclusive nature of the technology and its potential to address the needs of diverse populations, particularly seniors.

This structure allows for a comprehensive examination of the InSkin project, providing readers with a clear understanding of its development, capabilities, and potential impact on the field of skin-interfaced electronics and beyond (Figure 1.4).

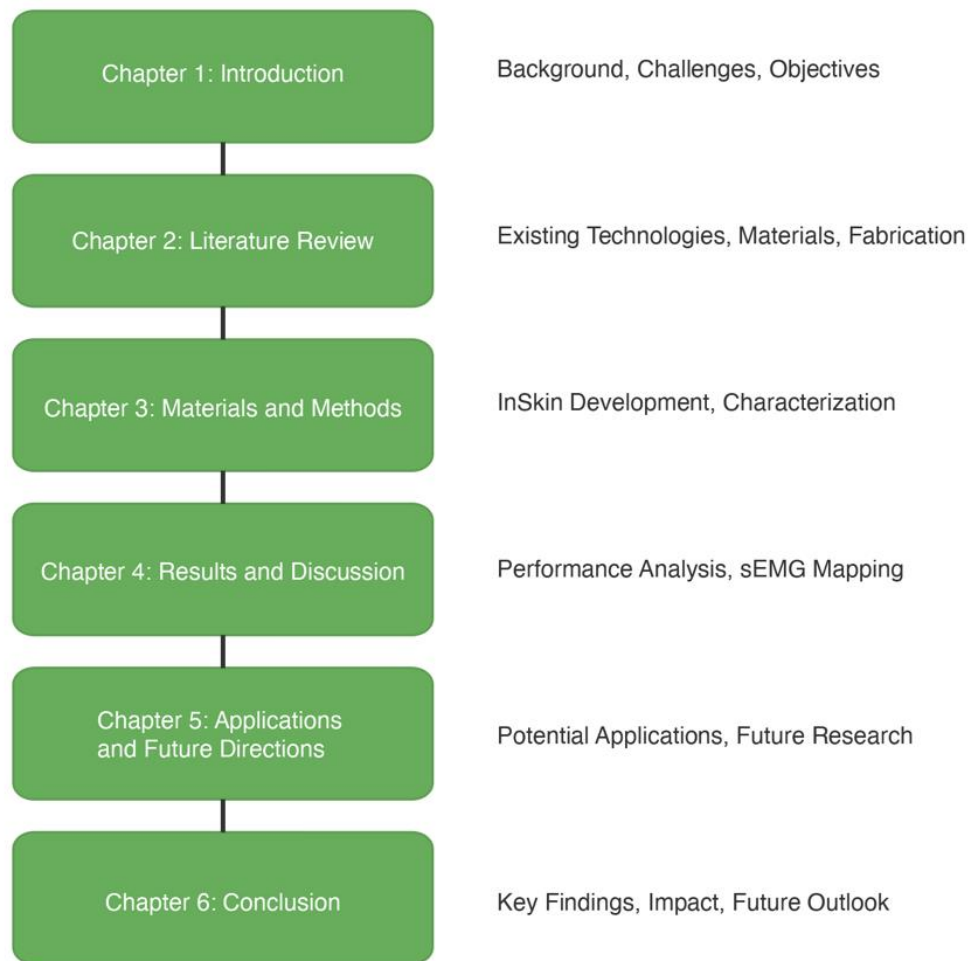


Figure 4: Thesis structure and chapter interconnections.

Chapter 2: Literature Review

This chapter provides a comprehensive review of existing skin-interfaced bioelectronics, from rigid electrodes to flexible and stretchable systems. It explores current challenges, materials, and fabrication techniques in the field. The chapter discusses applications in healthcare and human-machine interfaces and identifies key research gaps. It sets the stage for the InSkin project's innovations in addressing these challenges, particularly in creating an inclusive platform for diverse skin types and conditions.

2.1. Existing Skin-Interfaced Bioelectronics

The field of skin-interfaced bioelectronics has undergone rapid evolution in recent years, driven by the growing demand for non-invasive, continuous health monitoring and seamless human-machine interfaces ⁴⁹. This section provides a comprehensive overview of existing technologies, categorized into three main types: rigid, semi-flexible, and flexible/stretchable electronics, highlighting the progression that has led to the need for more advanced solutions like InSkin.

2.1.1. Rigid and Semi-Flexible Electrodes

Traditionally, skin-interfaced bioelectronics have relied on rigid or semi-flexible electrode systems, as summarized in Table 1. Among these, Silver/Silver Chloride (Ag/AgCl) electrodes have long been considered the gold standard in clinical settings for ECG and EMG recordings, owing to their good signal quality ⁵⁰. These electrodes employ electrolytic gels and adhesives for skin contact, providing good ionic conductivity. However, their dependence on wet interfaces presents significant drawbacks. The electrolyte gels tend to dry out over time, leading to signal degradation and limiting their efficacy for short-term use only. Moreover, prolonged contact with gels and adhesives can cause discomfort and allergic reactions in some users. These issues render Ag/AgCl electrodes unsuitable for extended wear, typically restricting their use to no more than twenty minutes ⁵¹.

In response to the gel-related challenges of Ag/AgCl electrodes, dry electrodes were developed. Typically crafted from metals or conductive polymers ⁵², these electrodes

eliminate the need for electrolytic gels. However, they introduce their own set of challenges. (i) The absence of an electrolyte layer results in higher skin-electrode impedance, potentially compromising signal quality. (ii) Dry electrodes are particularly susceptible to motion artifacts, especially on hairy or irregular skin surfaces, leading to signal distortions. (iii) The harder materials used in their construction can cause discomfort during long-term wear.

Textile-based electrodes represent a step towards more wearable bioelectronics by integrating conductive materials into fabrics⁵³. While offering improved comfort for long-term wear, these electrodes face unique challenges. Sweat accumulation and movement can lead to changes in the electrode-skin interface, affecting signal quality over time. Despite their flexibility, these electrodes may not conform well to complex body contours and skin's topological micro features, resulting in inconsistent contact and variable signal quality. Furthermore, the integration of electronics with textiles raises concerns about long-term durability and maintenance, particularly in terms of washability.

Each of these electrode types represents a progression in the field of skin-interfaced bioelectronics, with each iteration attempting to address the limitations of its predecessors. However, as the field continues to evolve, researchers are increasingly focusing on developing more advanced, flexible, and stretchable electronics that can better adapt to the dynamic nature of human skin and movement, as will be discussed in subsequent sections.

Table 1: Comparison of rigid and semi-rigid electrodes

Electrode Type	Advantages	Challenges
Silver/Silver Chloride (Ag/AgCl) Electrodes	- Good signal quality	- Short-term efficacy: Gel dries out, leading to signal degradation
	- Widely used in clinical settings	- Skin irritation from prolonged gel and adhesive contact
		- Unsuitable for long-term monitoring (limited to <20 minutes)

Table 1 (cont'd)

Dry Electrodes	- No need for electrolytic gels	- High skin-electrode impedance due to lack of electrolyte layer, compromising signal quality
		- Motion artifacts, especially on hairy/irregular skin surfaces
		- Comfort issues due to harder materials
Textile-Based Electrodes	- Improved comfort for long-term wear	- Signal degradation due to sweat accumulation and movement
	- Flexible	- Conformability issues with complex body contours
		- Washability and durability concerns

2.1.2. Flexible and Stretchable Electronics

Recent advancements in materials science and fabrication techniques have led to the development of flexible and stretchable electronics, as summarized in Table 2. These technologies aim to overcome the limitations of rigid systems and represent the cutting edge of skin-interfaced bioelectronics. Thin-film electronics, utilizing flexible materials like polyimide or parylene as substrate and encapsulating elements, can conform to macro- and meso-scale skin contours, representing a significant improvement over rigid systems⁵⁴. For example, Moin et al. developed a wearable biosensing system with in-sensor adaptive machine learning for hand gesture recognition, demonstrating improved signal quality and user comfort⁵⁵. Elastomeric electronics employ intrinsically stretchable materials or engineered structures and composites to achieve conductive materials with both flexibility and stretchability. Liu et al. demonstrated morphing electronics that can accommodate tissue growth, opening new possibilities for long-term bio-integrated systems⁵⁶. Recent advancements in conductive polymers have focused on enhancing their biocompatibility and long-term stability. For instance, Wang et al. (2023) developed a self-healing

conductive polymer that maintains its electrical properties even after mechanical damage, addressing concerns about the longevity of skin-interfaced devices ⁵⁷. Hydrogel-based interfaces offer a unique combination of mechanical compliance and ionic conductivity, addressing key limitations of traditional electrode systems. Pan et al. developed a compliant ionic adhesive electrode with ultralow bioelectronic impedance, promising long-term, stable recordings. These hydrogels exhibit mechanical similarity to biological tissues and are highly biocompatible, with some variants capable of stretching up to 1000% ^{59–61}. Nanocomposite materials, integrating nanomaterials into polymer matrices, have yielded electrodes with both high conductivity and stretchability. Zou et al. created high-fidelity sEMG electrodes based on silver nanowires, demonstrating improved signal quality for hand gesture classification ⁶². Composite nanomaterials, such as silver nanowires in PDMS, can achieve stretchability up to 500% while maintaining moderate biocompatibility ^{63–65}. E-tattoos represent ultrathin, skin-like electronic devices that conform intimately to skin texture, offering unprecedented integration with the human body. Tian et al. developed hairy-skin-adaptive viscoelastic dry electrodes for long-term electrophysiological monitoring, addressing the challenge of recording from hairy skin ⁶⁶. These devices represent the closest analog to InSkin's vision. Liquid conductors, such as eutectic gallium indium (EGaIn), possess infinite stretchability and high conductivity due to their fluidic nature. Typically embedded in microfluidic channels or printed on elastic substrates, they create flexible and stretchable conductors ^{67–69}. Finally, innovative structural designs, including ultrathin materials, wavy/wrinkled layouts, serpentine interconnects, and mesh networks, can achieve high stretchability and conformability even when using rigid electronic components ^{70–75}. These structure engineering approaches further expand the possibilities for creating highly adaptable skin-interfaced electronics.

These flexible and stretchable technologies represent significant advancements in skin-interfaced bioelectronics, offering improved conformality, reduced motion artifacts, and enhanced long-term stability. However, challenges remain regarding scalable fabrication, consistent performance across diverse skin types, and integration with data processing and transmission systems.

The development of the InSkin platform builds upon these advancements, aiming to address the remaining challenges and push the boundaries of what's possible in skin-interfaced bioelectronics.

Table 2: Comparison of flexible and stretchable electrodes

Material/System Type	Advantages	Challenges
Thin-Film Electronics	- Conforms to macro- and meso-scale skin contours	- Limited to flexible but not stretchable applications
	- Improved signal quality and user comfort	
Elastomeric Electronics	- Stretchable and flexible	- Longevity and biocompatibility concerns, though improving with new materials like self-healing polymers
	- Accommodates tissue growth for long-term use	
Hydrogel-Based Interfaces	- High mechanical compliance and ionic conductivity	- Variability in biocompatibility and mechanical properties depending on formulation
	- Biocompatible and stretchable	
Nanocomposite Materials	- High conductivity and stretchability	- Moderate biocompatibility; complex manufacturing process
	- Enhanced signal quality for specific applications	

Table 2 (cont'd)

E-Tattoos	- Ultrathin and skin-like, offering close integration with the skin	- Challenges in long-term stability and durability, especially for hairy skin areas
Liquid Conductors	- Infinite stretchability with high conductivity	- Requires careful embedding or printing within substrates to maintain structure and functionality
Structure Engineering	- Innovative designs enable stretchability even with rigid components	- Complexity in design and fabrication, potentially higher production costs

2.2. Challenges in Current Technologies

Despite significant advancements in skin-interfaced bioelectronics, several challenges persist that limit these technologies' widespread adoption and effectiveness. This section outlines the key challenges faced by current skin-interfaced electronic systems.

2.2.1. Mechanical Mismatch

One of the primary challenges in skin-interfaced bioelectronics is the mechanical mismatch between rigid or semi-flexible electronic components and the soft, dynamic nature of human skin. This mismatch manifests in several critical areas. Conformability is a significant issue, as rigid electrodes often fail to maintain consistent contact with skin, especially on curved or irregularly shaped body parts. This problem is particularly pronounced in areas with complex topography, such as the face or hands ⁷⁶. The inability to conform to skin contours can lead to gaps between the electrode and skin, resulting in poor signal quality and unreliable measurements.

Strain accommodation presents another crucial challenge. Human skin possesses remarkable elasticity, capable of stretching up to 30-40% during normal movement ⁷⁷. This natural flexibility poses a significant hurdle for electronic systems, which typically struggle to accommodate such levels of deformation without compromising their electrical

performance or mechanical integrity. The development of stretchable electronics that can match the skin's elasticity while maintaining functionality is an active area of research.

The mismatch in mechanical properties between rigid electronics and soft tissue can lead to interfacial stress, causing discomfort and potentially damaging the skin during prolonged use

^{78,79}. To address this issue, researchers are focusing on developing devices that mimic the low Young's modulus of the skin ^{65,80,81}. This approach aims to create electronics that move and flex in harmony with the body's natural movements, reducing interfacial stress and improving user comfort. Innovative materials and structural designs are being explored to achieve this biomechanical compatibility.

2.2.2. Signal Quality and Stability

Maintaining high-quality, stable signals over extended periods is a significant challenge for current skin-interfaced bioelectronics. Motion artifacts present a persistent problem, as the subject's movement can cause relative motion between the electrode and the skin, leading to signal distortions. This issue is particularly problematic for applications requiring precise signal detection, such as EMG-based prosthetic control ^{82,83}. The dynamic nature of human activity necessitates innovative approaches to electrode design and signal processing to mitigate these motion-induced artifacts.

Impedance variations pose another hurdle to signal stability. Changes in skin properties due to factors like hydration, sweating, or hair growth can cause fluctuations in electrode-skin impedance, affecting signal quality and consistency ⁸⁴. These variations can be particularly challenging in long-term monitoring scenarios, where environmental and physiological changes can significantly impact the electrode-skin interface over time. Developing adaptive electrode systems that can compensate for these impedance fluctuations is crucial for maintaining signal quality across diverse conditions.

Long-term stability remains a significant challenge, as many current systems suffer from signal degradation over time due to factors such as electrode drying, skin irritation, or changes in skin-electrode interface properties ^{85,86}. This degradation can compromise the reliability of long-term monitoring applications. Research into novel materials and

interface designs that can maintain stable electrical properties over extended periods is ongoing, with the goal of creating systems suitable for continuous, long-term physiological monitoring.

2.2.3. Long-Term Biocompatibility

For continuous monitoring applications, long-term biocompatibility is crucial yet challenging to achieve. Skin irritation is a primary concern, as prolonged contact between electrodes and skin can lead to irritation, allergic reactions, or other adverse effects, especially with the use of adhesives or electrolytic gels ⁸⁶. This not only causes discomfort for the user but can also compromise the integrity of the recorded signals. Developing materials and adhesives that are gentle on the skin while maintaining good electrical contact is an ongoing area of research.

Breathability is another critical factor in long-term biocompatibility. Many current electrode systems impede the skin's natural processes of perspiration and gas exchange, potentially leading to skin maceration or other dermatological issues ^{86,87}. Creating breathable, permeable electrode systems that allow for normal skin function while maintaining electrical performance is essential for long-term wear.

The concepts of self-healing and biodegradability are gaining importance in the field. The ability to self-repair damage from repetitive deformation or accidental punctures is desirable for enhancing device durability and longevity. For implantable or temporary devices, biodegradability is critical for minimizing foreign body response and eliminating the need for surgical removal ⁸⁸⁻⁹⁰. These advanced material properties could significantly extend the usable life of skin-interfaced devices and improve their safety profile.

2.2.4. Adaptability to Diverse Skin Properties

Skin properties vary significantly across individuals and even across different body locations on the same individual, posing challenges for consistent device performance. Age-related variations in skin, including decreased elasticity, increased dryness, and altered electrical properties, can significantly affect the performance of bioelectronic devices ^{91,92}. These changes necessitate the development of adaptive technologies that can maintain consistent performance across a wide range of skin conditions and age groups.

Skin type diversity further complicates the design of universally effective skin-interfaced electronics. Variations in skin thickness, hair density, and sebum production across different ethnicities and body locations can impact electrode-skin contact and signal quality^{93,94}. Devices must be designed to accommodate these variations while maintaining consistent performance. This challenge requires innovative approaches in electrode design and material selection to ensure reliable operation across diverse skin types.

Dynamic changes in skin properties pose additional challenges. Skin properties can change rapidly due to factors like physical activity, emotional state, or environmental conditions⁹⁵. These dynamic changes require adaptive technologies capable of real-time adjustment to maintain consistent performance under varying conditions. Developing sensors and algorithms that can detect and compensate for these rapid changes in skin properties is an active area of research, aimed at creating more robust and reliable skin-interfaced bioelectronic systems.

Addressing these multifaceted challenges requires interdisciplinary approaches, combining advances in materials science, electrical engineering, and biomedical engineering. The development of new materials with tunable mechanical and electrical properties, innovative electrode designs that can adapt to skin variations, and advanced signal processing algorithms to compensate for environmental and physiological changes are all critical components in the evolution of skin-interfaced bioelectronics.

Table 3 summarizes the key mechanical properties of various materials and designs used in skin-interfaced electronics, highlighting their suitability for different applications and the trade-offs involved in their selection.

Table 3: Detailed Summary of Mechanical Properties for Materials Used in Skin-Interfaced Electronics Applications

Material/Design	Young's Modulus (kPa)	Stretchability (%)	Biocompatibility	Self-Healing	Biodegradability	References
EGaIn	≈ 2	>1000	Good	Excellent	Limited	67–69
Hydrogels	10–1000	Up to 1000	Excellent	Good (physical crosslinking)	Good (natural polymers)	59–61
PEDOT:PSS	≈ 100	Up to 300	Good	Good (modified)	Limited	88–90
AgNWs/PDMS	≈ 100	Up to 500	Moderate	Moderate	Limited	63,64,96
Ultrathin Plastic	≈ 10	>100	Good	Limited	Good (biodegradable plastics)	65,80,81
Serpentine	Tunable	Up to 800	Dependent on substrate	Dependent on substrate	Dependent on substrate	70–72
Mesh	Dependent on structure	Up to 1600	Dependent on materials	Dependent on materials	Dependent on materials	73–75

2.2.5. Integration and Scalability

Integrating multiple functionalities and scaling up production while maintaining performance presents significant challenges in the field of skin-interfaced bioelectronics. One of the primary hurdles is achieving multifunctionality, where combining sensing, data

processing, and wireless communication capabilities in a single, compact, skin-interfaced device remains a complex task ^{97,98}. This integration requires careful consideration of component compatibility, power requirements, and spatial constraints, all while ensuring that each function performs optimally without interfering with others.

Power management is another critical challenge in the development of skin-interfaced bioelectronics. The creation of efficient, long-lasting power sources that are compatible with flexible, stretchable electronics is an ongoing area of research ^{99,100}. This challenge is multifaceted, involving the development of novel energy storage materials, innovative energy harvesting techniques, and ultra-low-power circuit designs. The power source must not only be flexible and stretchable but also safe for long-term skin contact, adding another layer of complexity to the design process.

Scalable manufacturing poses a significant obstacle in bringing cutting-edge skin-interfaced electronics from laboratory prototypes to widespread commercial availability. Many of these advanced devices rely on complex, laboratory-scale fabrication processes that are difficult to scale up for mass production ^{5,99}. This challenge involves not only adapting fabrication techniques for large-scale production but also ensuring consistency in device performance, developing quality control measures, and optimizing costs. The transition from small-scale, highly controlled laboratory environments to industrial-scale production often requires significant re-engineering of fabrication processes.

Addressing these challenges is crucial for the advancement of skin-interfaced bioelectronics. The InSkin project aims to tackle these issues through innovative materials design and fabrication techniques, which will be discussed in subsequent chapters. By focusing on these key areas, the project seeks to bridge the gap between laboratory innovations and practical, widely accessible skin-interfaced electronic devices.

2.3. Materials for Stretchable Electronics

The development of stretchable electronics for skin-interfaced applications relies heavily on innovative materials that can maintain electrical functionality under mechanical deformation. This field has seen rapid advancements in recent years, with various material classes and approaches being explored to create systems that can seamlessly integrate with

the human body. This section explores the key materials and approaches used in creating stretchable electronic systems, focusing on their relevance to the InSkin project.

2.3.1. Conductive Polymers

Conductive polymers offer a unique combination of electrical conductivity and mechanical flexibility, making them ideal candidates for stretchable electronics. Poly(3,4-ethylenedioxythiophene) polystyrene sulfonate (PEDOT:PSS) is widely used due to its high conductivity, transparency, and solution processability. While conductivities exceeding 4000 S/cm have been reported, these are typically achieved with specific formulations and processing techniques. More commonly, PEDOT:PSS can achieve high conductivity (hundreds to thousands of S/cm) while maintaining low stretchability (up to 10 percent)¹⁰¹. Other conductive polymers like Polyaniline (PANI) and Polypyrrole (PPy) offer good environmental stability and can be easily synthesized. Recent studies have shown that PANI nanofiber networks can achieve conductivities of up to 350 S/cm with stretchability of up to 200% under specific conditions¹⁰². Incorporating ionic liquids into polymer matrices can enhance both ionic and electronic conductivity while maintaining flexibility. For example, ionic liquid-modified PEDOT:PSS has demonstrated conductivities of up to 2000 S/cm with improved stability in aqueous environments¹⁰³.

2.3.2. Elastomers and Hydrogels

Elastomers and hydrogels provide the stretchable substrate or matrix for many skin-interfaced electronic systems. Silicone elastomers like polydimethylsiloxane (PDMS) are widely used due to their biocompatibility, transparency, and ability to be easily molded. Specialized formulations have achieved PDMS with stretchability up to 1000% while maintaining biocompatibility^{104,105}. Thermoplastic polyurethanes offer good elasticity and can be engineered with varying degrees of hardness, making them versatile for different applications. Recent research has developed polyurethane-based materials with self-healing properties and stretchability up to 600%¹⁰⁶. Hydrogels, water-based polymer networks, can offer tissue-like mechanical properties and ionic conductivity. They are particularly promising for interfaces requiring mechanical and electrochemical coupling

with biological tissues. Advanced hydrogels have demonstrated stretchability up to 2000% and self-healing capabilities ¹⁰⁷.

2.3.3. Nanocomposites

Nanocomposites combine the stretchability of polymer matrices with the electrical properties of conductive nanomaterials. Metal nanowire composites, such as silver nanowires embedded in elastomeric matrices, can create highly conductive and stretchable materials. These composites can maintain conductivity even at high strains due to the formation of percolation networks. Recent work has achieved up to 8700 S/cm conductivities at 50% strain ¹⁰⁸. Carbon nanotube (CNT) composites can form conductive networks within elastomeric matrices, offering both high conductivity and stretchability. Their high aspect ratio allows for conductivity at relatively low loading percentages, with recent advances producing CNT composites with conductivities up to 1000 S/cm at 100% strain ¹⁰⁹. Graphene-based composites, incorporating graphene and its derivatives into polymer matrices, can provide excellent electrical and mechanical properties. These materials often offer additional functionalities such as high thermal conductivity. Recent research has developed graphene-based composites with conductivities up to 1500 S/cm and stretchability of 800% ^{110,111}.

2.3.4. Liquid Metal Alloys

Liquid metals, particularly gallium-based alloys, have gained attention for their unique combination of high electrical conductivity and fluidic nature. Eutectic Gallium-Indium (EGaIn), a room-temperature liquid metal alloy, can be encapsulated in elastomeric microchannels to create stretchable conductors. It maintains conductivity even under extreme deformations, with recent work demonstrating EGaIn-based conductors with negligible resistance change up to 700% strain ^{112,113}. Gallium-based particles can be dispersed in elastomers to create soft, conductive composites that can self-heal after mechanical damage. Recent developments have achieved composites with conductivities up to 1.6×10^4 S/cm and stretchability of 350% ¹¹⁴, though high particle loading may affect mechanical properties.

2.3.5. Engineered Structures

Beyond material composition, the structural design of stretchable electronics plays a crucial role in their performance. Serpentine and kirigami structures allow rigid electronic components to be made stretchable by arranging them in serpentine patterns or using kirigami-inspired cut patterns. These designs enable macroscopic stretching through structural deformation, with recent work achieving stretchability up to 300% using optimized serpentine designs ¹¹⁵. Textile-based structures leverage the inherent stretchability of fabric constructions by weaving or knitting conductive materials into textile structures. Advanced textile electronics have demonstrated stretchability up to 500% while maintaining functionality ^{116,117}. Advanced 3D printing techniques allow for the creation of complex, hierarchical structures that can enhance the overall stretchability and functionality of electronic systems. Recent developments in 4D printing have produced structures with programmable shape-changing capabilities and stretchability up to 400% ^{118,119}.

The InSkin project builds upon these material advances, particularly focusing on developing novel conductive polymer composites that combine the stretchability of elastomers with the electrical properties of conductive polymers and nanomaterials. By integrating the most promising aspects of these materials and structures, InSkin aims to create a highly stretchable, conductive, and biocompatible platform for next-generation skin-interfaced electronics. This approach not only addresses the current limitations in the field but also opens up new possibilities for advanced, multifunctional skin-interfaced devices that can seamlessly integrate with the human body for a wide range of applications in healthcare, human-machine interfaces, and beyond.

2.4. Fabrication Techniques for Skin-Interfaced Devices

The development of effective skin-interfaced devices, such as InSkin, relies on advanced materials and innovative fabrication techniques. These techniques must enable the creation of devices that are thin, flexible, and conformable to the skin while maintaining electrical functionality. This section explores the key fabrication methods used in the field of skin-interfaced bioelectronics, with a focus on their relevance to the InSkin project.

2.4.1. Thin-Film Deposition

Thin-film deposition techniques are fundamental in creating the conductive and functional layers of skin-interfaced devices. These methods have evolved significantly to meet the unique challenges posed by flexible and stretchable electronics.

Physical Vapor Deposition (PVD) methods, such as sputtering and thermal evaporation, are primarily used for depositing thin metal films. These techniques can create highly conductive layers with thicknesses down to a few nanometers, offering precise control over film composition and structure. However, they often require additional patterning steps and can be challenging to apply to highly stretchable substrates. Recent advancements in high-power impulse magnetron sputtering (HiPIMS) have enabled the deposition of dense, highly adhesive metal films on polymer substrates with improved stretchability¹²⁰. This breakthrough has expanded the range of materials that can be effectively used in flexible electronics.

Chemical Vapor Deposition (CVD) has proven particularly useful for depositing high-quality graphene and carbon nanotube films. This method allows for the direct growth of these materials on flexible substrates, ensuring good adhesion and electrical contact. Recent progress in plasma-enhanced CVD has enabled low-temperature deposition of graphene on polymer substrates, preserving their flexibility¹²¹. This development is crucial for incorporating high-performance carbon-based materials into flexible electronic devices without compromising the mechanical properties of the substrate.

Solution processing methods, including spin-coating, dip-coating, drop-casting, and spray-coating, are widely used for depositing conductive polymer and nanocomposite layers. These techniques offer several advantages for skin-interfaced electronics, including compatibility with large-area fabrication and roll-to-roll processing, making them highly scalable. Recent developments in ultrasonic spray coating have achieved uniform deposition of PEDOT:PSS films with conductivities up to 4600 S/cm on flexible substrates^{100,122,123}. This advancement represents a significant improvement in the performance of solution-processed conductive polymers, bridging the gap between solution-processed and vacuum-deposited conductive films.

In the InSkin project, solution processing serves as the primary method for depositing the conductive polymer composite layers. This approach enables precise control over thickness and composition, allowing for the creation of highly customizable and functional layers essential for the performance of skin-interfaced bioelectronic devices. The versatility of solution processing also facilitates the incorporation of various functional materials, such as nanoparticles or biomolecules, into the conductive matrix, expanding the potential functionalities of the resulting devices.

2.4.2. Patterning Techniques

Precise patterning of conductive and functional materials is crucial for creating complex electrode designs and circuitry in skin-interfaced devices. The field has seen significant advancements in adapting traditional patterning methods to flexible and stretchable substrates, as well as the development of novel techniques specifically suited for soft electronics.

Photolithography, traditionally used for rigid electronics, has been adapted for flexible substrates. It offers high resolution, down to sub-micron features, making it valuable for creating intricate electrode patterns and fine interconnects. However, applying photolithography to highly stretchable systems has been challenging due to issues such as resist cracking and delamination during processing. Recent progress in the development of stretchable photoresists and hybrid lithography techniques has enabled patterning on substrates with up to 100% strain ^{117,124}. These advancements have opened up new possibilities for creating high-resolution patterns on highly deformable substrates, crucial for next-generation skin-interfaced devices.

Screen printing has emerged as a widely used technique for depositing and patterning conductive inks and pastes in flexible electronics. Its suitability for large-area fabrication and compatibility with roll-to-roll processing make it an attractive option for scalable production of skin-interfaced devices. Recent advancements have led to the development of highly stretchable, self-healing conductive inks, enabling screen-printed electrodes with stretchability up to 700% ^{125,126}. This breakthrough significantly expands the potential applications of screen-printed electronics in wearable and implantable devices. In the

InSkin project, screen printing is employed for depositing larger area electrode patterns and interconnects, particularly in the more stretchable layers, leveraging its ability to create robust and flexible conductive structures.

Inkjet printing offers a digital and maskless approach to patterning, allowing for precise deposition of functional inks. This technique is particularly valuable for prototyping and customizable designs, offering minimal material waste and the ability to rapidly iterate designs. Recent innovations in multi-material inkjet printing systems have enabled the fabrication of complete stretchable electronic devices in a single process^{127,128}. This capability is especially relevant for creating complex, multi-layered devices with integrated sensing and actuation capabilities, potentially streamlining the fabrication process for advanced skin-interfaced electronics.

Laser patterning, particularly using CO₂ laser engraving, has emerged as a powerful tool for patterning conductive materials with high precision. This technique allows for complex electrode designs and interconnects without the need for masks or resists, offering flexibility in design and rapid prototyping capabilities. Recent developments in femtosecond laser patterning have achieved sub-micron resolution on polymer substrates without thermal damage^{111,129}, pushing the boundaries of what's possible in terms of feature size and pattern complexity on flexible substrates. In the InSkin project, laser patterning plays a critical role, serving as the primary method for creating the high-density electrode array and intricate interconnect patterns. This technique enables the unique stretchable design of the device, allowing for the creation of complex, meandering patterns that can accommodate large strains while maintaining electrical functionality.

2.4.3. Transfer Techniques

Transfer techniques are crucial for integrating rigid electronic components with stretchable substrates, a key aspect of the InSkin design. These methods allow for the combination of high-performance electronic materials with soft, biocompatible substrates, enabling the creation of hybrid systems that leverage the advantages of both rigid and flexible electronics.

Transfer printing is a process that involves patterning materials or devices on a donor substrate and then transferring them onto a target stretchable substrate. This technique enables the integration of high-performance silicon-based electronics with soft, biocompatible materials, bridging the gap between conventional rigid electronics and soft, skin-interfaced devices. Recent advancements in this field have led to the development of programmable adhesion surfaces, enabling selective, multi-material transfer with micron-scale precision ¹³⁰. This capability allows for the precise placement of various functional components on a single flexible substrate, facilitating the creation of complex, multi-functional skin-interfaced devices.

Water transfer printing has emerged as another valuable technique in this domain. It allows for the transfer of thin, pre-patterned films onto complex 3D surfaces, including textured or curved substrates. This method is particularly suited for creating conformal electronic devices that can adapt to the topography of the human body. Recent progress in this area has resulted in the development of stretchable electronic "temporary tattoos" using water transfer printing, achieving intimate contact with the skin ¹³¹. This approach offers a promising route for creating ultra-thin, skin-like electronic devices that can conform to the micro-scale features of the skin surface.

These advancements in transfer techniques have significantly expanded the possibilities for creating highly integrated, stretchable electronic devices that can seamlessly interface with the human body. By enabling the combination of high-performance electronic components with soft, stretchable substrates, these methods pave the way for skin-interfaced devices that offer both advanced functionality and excellent mechanical compatibility with biological tissues.

2.4.4. 3D Fabrication Methods

Three-dimensional fabrication methods enable the creation of complex, hierarchical structures that can enhance device functionality and stretchability. These techniques offer new possibilities for designing skin-interfaced electronics with improved mechanical properties and novel form factors.

3D printing techniques, such as fused deposition modeling (FDM) and stereolithography (SLA), have emerged as powerful tools for creating complex 3D structures in flexible electronics. These methods are particularly useful for creating structures with embedded channels for liquid metals or conductive composites, enabling the integration of stretchable conductors within a 3D-printed matrix. Recent innovations in multi-material 3D printing have enabled the fabrication of complete stretchable electronic devices with integrated sensing and actuation capabilities^{132,133}. This advancement allows for the creation of monolithic devices that combine structural, mechanical, and electronic functionalities in a single fabrication process, potentially simplifying the manufacturing of complex skin-interfaced devices.

Electrospinning is another valuable 3D fabrication method that creates fibrous structures with high surface area and porosity. This technique is particularly useful for creating breathable and conformable electrode interfaces, addressing the need for gas-permeable electronic skins that allow for normal skin function. Recent advancements in coaxial electrospinning have produced conductive fiber networks with core-shell structures, enhancing both electrical and mechanical properties¹³⁴. These structures offer unique advantages for skin-interfaced electronics, combining high conductivity with the ability to conform to skin topography and allow for moisture and gas exchange.

The InSkin project leverages a combination of these advanced fabrication techniques to create a highly integrated, stretchable, and skin-conformable device. By utilizing laser patterning for high-precision electrode designs, solution processing for depositing conductive polymer composites, and transfer printing for integrating rigid components, InSkin achieves a unique balance of high performance and stretchability. This multifaceted approach allows for the creation of devices that can adapt to the complex mechanical environment of the skin while maintaining reliable electrical functionality.

The integration of these diverse fabrication techniques represents a significant advance in the field of skin-interfaced electronics. It enables the creation of devices that combine the high performance of traditional electronics with the mechanical properties required for seamless integration with the human body. As these fabrication methods continue to

evolve, they promise to unlock new possibilities in wearable and implantable bioelectronics, paving the way for more advanced, comfortable, and reliable skin-interfaced devices.

2.5. Applications in Healthcare and Human-Machine Interfaces

Skin-interfaced bioelectronics, including technologies like InSkin, have a wide range of applications in healthcare and human-machine interfaces. These applications leverage the unique capabilities of these devices to provide continuous, non-invasive monitoring and intuitive control interfaces.

2.5.1. Healthcare Monitoring

Continuous physiological monitoring enabled by skin-interfaced bioelectronics represents a significant advancement in healthcare. These technologies allow for real-time, long-term tracking of vital signs such as heart rate, respiratory rate, and body temperature, offering unprecedented insights into patient health.

Liu et al. (2020) demonstrated the potential of morphing electronics that can accommodate tissue growth, enabling long-term monitoring in pediatric patients¹³⁵. This breakthrough addresses the challenge of maintaining consistent sensor contact during growth, a critical factor in pediatric care. The InSkin project builds upon this concept, offering enhanced conformability and signal stability across diverse skin types. By maintaining reliable contact and consistent performance on various skin conditions, InSkin enables more accurate and dependable long-term monitoring, potentially improving patient outcomes and reducing healthcare costs.

Electromyography (EMG) applications have been revolutionized by high-density surface EMG arrays, providing detailed maps of muscle activity. These systems are invaluable for diagnosing and monitoring neuromuscular disorders and in rehabilitation settings. Farina et al. (2014) developed advanced decomposition techniques for high-density EMG signals, enabling detailed motor unit analysis¹³⁶. The InSkin technology advances this field by offering higher spatial resolution and improved signal quality, particularly on challenging

surfaces like elderly or scarred skin. This capability could lead to more precise diagnoses and personalized treatment plans for neuromuscular conditions.

In the field of electrocardiography (ECG), continuous cardiac monitoring without the discomfort of traditional rigid electrodes has become a reality. Yang et al. (2022) created ultra-thin, breathable ECG electrodes for long-term wear ¹³⁷. InSkin innovates further by integrating ECG monitoring with other modalities in a single, comfortable platform. This multi-modal approach could provide a more comprehensive view of cardiovascular health, potentially leading to earlier detection of cardiac issues and more effective management of heart conditions.

For electroencephalography (EEG), long-term brain activity monitoring is crucial for epilepsy management and sleep studies. Kim et al. (2022) developed miniaturized, wireless EEG sensors for home monitoring ¹³⁸. The InSkin project shows potential in exploring behind-the-ear and forehead EEG monitoring with improved comfort and signal quality. This advancement could make long-term EEG monitoring more feasible and comfortable for patients, potentially improving the diagnosis and management of neurological disorders.

Sweat analysis applications have emerged as a non-invasive method for monitoring various physiological parameters. Pour et al. (2024) created a multi-analyte sweat sensor with integrated microfluidics ¹³⁹, representing a recent breakthrough in this field. These sensors provide real-time analysis of sweat composition, offering insights into hydration, electrolyte balance, and glucose levels. The integration of such capabilities with the InSkin platform could create a comprehensive health monitoring system, combining electrophysiological measurements with biochemical analysis for a more complete picture of an individual's health status.

2.5.2. Rehabilitation and Physical Therapy

In the field of rehabilitation and physical therapy, skin-interfaced bioelectronics offer several key applications that can significantly enhance treatment efficacy and patient outcomes.

Movement assessment is a critical component of rehabilitation programs. High-density EMG arrays provide detailed muscle activation pattern analysis, enabling progress assessment and the development of tailored rehabilitation programs. Merletti et al. (2016) developed protocols for using high-density EMG in clinical movement analysis ¹⁴⁰.

InSkin enhances this approach by providing more comprehensive muscle mapping. The InSkin project enhances this approach by providing more comprehensive muscle mapping. This increased detail could lead to more precise tracking of rehabilitation progress and allow for finer adjustments to treatment plans.

Biofeedback systems have long been recognized as valuable tools in rehabilitation. These systems utilize real-time feedback on muscle activity or body posture to improve movement patterns during rehabilitation. Historically, Crow et al. (1989) pioneered EMG biofeedback for stroke rehabilitation ¹⁴¹. The InSkin technology has the potential to advance this field by providing more accurate and detailed feedback, potentially accelerating the rehabilitation process and improving outcomes.

Prosthetic control has seen significant advancements in recent years, with intuitive and precise control of prosthetic limbs using advanced EMG interfaces. Moin et al. (2020) developed an in-sensor computing system for low-latency prosthetic control ⁵⁵. The InSkin project contributes to this field by offering enhanced pattern recognition capabilities, potentially enabling more natural, multi-degree-of-freedom prosthetic control. This advancement could significantly improve the quality of life for individuals using prosthetic limbs, allowing for more intuitive and functional control.

2.5.3. Human-Machine Interfaces

The field of human-machine interfaces has been revolutionized by skin-interfaced bioelectronics, enabling more intuitive and seamless interactions between humans and technology.

Gesture recognition has emerged as a powerful tool for controlling electronic devices and interacting with virtual environments. López et al. (2023) achieved high-accuracy gesture recognition using a hybrid CNN-LSTM network ¹⁴². The InSkin project advances this technology with improved accuracy in gesture differentiation, which is particularly

beneficial for elderly users with less distinct muscle signals. This enhancement could make gesture-based interfaces more accessible and reliable for a broader range of users.

Virtual and augmented reality applications benefit significantly from haptic feedback and gesture control, enhancing immersion and interaction. Kim et al. (2024) created a skin-integrated VR system with haptic and thermal feedback ¹⁴³. InSkin shows potential for integrating multi-modal sensing and feedback in a single, unobtrusive device, potentially enabling more immersive and realistic VR/AR experiences. This could have applications in fields ranging from entertainment to medical training and therapy.

Teleoperation applications enable intuitive control of remote robotic systems, with significant implications for telesurgery and operations in hazardous environments. Xia et al. (2024) demonstrated a wearable EMG-based system for intuitive robot arm control ¹⁴⁴. The InSkin technology has the potential to enhance precision and reduce latency in teleoperation through advanced signal processing. This could lead to more accurate and responsive remote-control systems, improving safety and efficiency in various industries.

2.5.4. Assistive Technologies

Skin-interfaced bioelectronics offer innovative solutions in the field of assistive technologies, particularly for individuals with severe motor impairments.

Communication aids provide alternative channels for individuals who cannot use traditional communication methods. Kaur et al. (2022) reviewed EMG-based communication systems for paralyzed individuals ¹⁴⁵. The InSkin project offers more reliable signal acquisition, potentially improving communication accuracy, especially for users with limited muscle control. This advancement could significantly enhance the quality of life for individuals with severe motor impairments by providing them with more effective means of communication.

Smart home control applications leverage EMG-based gesture recognition to enable control of various devices, enhancing independence for individuals with mobility impairments. Vasylykiv et al. (2019) developed a wearable EMG system for intuitive smart home control ¹⁴⁶. The integration of InSkin technology in such systems could provide more

reliable and diverse control options, potentially increasing the autonomy of individuals with mobility limitations.

2.5.5. Performance Monitoring and Enhancement

In the realm of performance monitoring and enhancement, skin-interfaced bioelectronics offer valuable tools for optimizing physical performance and preventing injuries.

Sports performance applications provide detailed insights into muscle activation patterns, enabling training optimization and injury prevention. Sun (2012) reviewed applications of EMG in sports science and rehabilitation ¹⁴⁷. The InSkin project shows potential for integration with motion capture and other biometric data, enabling comprehensive performance analysis. This could lead to more effective training regimens and reduced injury risk for athletes at all levels.

Ergonomics applications use wearable sensors to assess and improve workplace conditions through muscle fatigue and activation pattern monitoring. Sabino et al. (2024) used wearable EMG sensors to evaluate workplace ergonomics ¹⁴⁸. InSkin advances this field by offering long-term, comfortable monitoring for extended studies. This could lead to more accurate assessments of workplace ergonomics and the development of more effective interventions to reduce work-related musculoskeletal disorders.

2.5.6. Personalized Medicine

The field of personalized medicine stands to benefit greatly from advancements in skin-interfaced bioelectronics, enabling more tailored and proactive healthcare approaches.

Treatment monitoring through continuous physiological monitoring allows for tracking the effectiveness of interventions over time. Vaghasiya et al. (2023) reviewed personalized health management systems based on wearable sensors ¹⁴⁹. The InSkin technology could contribute to this field by providing more reliable and comprehensive physiological data, potentially enabling more accurate assessment of treatment efficacy and facilitating timely adjustments to treatment plans.

Early disease detection applications aim to identify subtle physiological changes indicative of disease onset before clinical symptoms appear. Hughes et al. (2023) demonstrated the potential of wearable bioelectronics for early detection of cardiovascular diseases ¹⁵⁰. The

high-fidelity, multi-modal sensing capabilities of InSkin could enhance these early detection systems, potentially enabling earlier interventions and improved health outcomes.

The InSkin project, with its focus on creating an inclusive and adaptive bioelectronic platform, has the potential to significantly enhance many of these applications. By providing more reliable and consistent performance across diverse populations, particularly addressing the needs of elderly users, InSkin could broaden the accessibility and effectiveness of these technologies in healthcare and human-machine interface applications. As research in this field continues to advance, we can expect to see even more innovative applications emerge, further revolutionizing healthcare, human-machine interaction, and personalized medicine.

2.6. Gaps in Research and Potential Improvements

Despite significant advancements in skin-interfaced bioelectronics, several key areas require further research and development. This section identifies the primary gaps in current research and potential avenues for improvement, which the InSkin project aims to address.

2.6.1. Adaptability to Diverse Skin Conditions

One of the most critical challenges is adaptability to diverse skin conditions. Current technologies often struggle to maintain consistent performance across different age groups, particularly in elderly populations with more fragile and wrinkled skin. This issue is compounded by the fact that skin properties change not only with age but also with various environmental and physiological factors, making it difficult for existing devices to provide reliable, long-term monitoring.

Many existing studies focus on a limited range of skin types, neglecting the diversity in human populations^{23,151}. This gap in research has led to devices that may perform well in laboratory settings but fail to deliver consistent results across a broader demographic. The variability in skin thickness, hydration levels, and elasticity across different ethnicities and age groups poses a significant challenge for creating truly universal skin-interfaced electronics. Furthermore, even within individual users, skin properties can vary

dramatically across different body locations, adding another layer of complexity to device design and optimization.

2.6.2. Long-Term Stability and Comfort

Additionally, few current systems can adapt in real time to changes in skin properties due to factors like hydration, temperature, or physical activity. This lack of dynamic adaptability limits the long-term efficacy of skin-interfaced devices in real-world conditions. For instance, during physical exertion, increased perspiration can alter the electrical properties of the skin-electrode interface, potentially leading to signal degradation or increased motion artifacts. Similarly, changes in ambient temperature and humidity can affect skin hydration levels, further impacting device performance .

The InSkin project addresses these challenges through a multi-faceted approach. First, it focuses on developing adaptive electrode designs that can conform to varying skin textures and elasticities. This involves exploring novel materials and structures that can maintain intimate contact with the skin surface despite variations in topography or mechanical properties. Second, the project emphasizes comprehensive testing and optimization across various skin types and conditions. This includes conducting extensive studies with diverse participant groups representing a wide range of ages and skin conditions to ensure the technology performs consistently across different populations.

By focusing on these areas, InSkin aims to create a more inclusive and reliable platform for skin-interfaced bioelectronics that can serve diverse populations and maintain performance under changing environmental and physiological conditions. The goal is to develop a technology that not only performs well in controlled laboratory settings but also translates effectively to real-world applications, accommodating the wide variability in human skin properties and conditions. This approach has the potential to significantly expand the accessibility and efficacy of skin-interfaced electronics, opening up new possibilities in personalized healthcare, advanced prosthetics, and human-machine interaction across diverse user groups.

2.6.3. High-Density, Multi-Modal Sensing

The field of skin-interfaced bioelectronics is rapidly advancing towards high-density, multi-modal sensing capabilities, presenting both exciting opportunities and significant challenges. Improving spatial resolution is a primary focus, with researchers developing systems that provide detailed data over large areas without compromising flexibility or comfort. This is crucial for applications requiring precise mapping of physiological signals across broad body regions.

Multi-modal integration, combining various sensing modalities in a single platform, is another key area of development. This integration is challenging due to the diverse nature of sensing technologies and the need to minimize interference. Recent advancements have shown promising results, but further research is needed to make these technologies practical for everyday use.

Managing crosstalk between closely spaced electrodes in high-density arrays remains a significant technical hurdle. As electrode density increases, so does the risk of signal interference, potentially compromising data quality. The InSkin project addresses this through novel electrode designs and machine learning-based signal separation algorithms. These advancements could enable more detailed health assessments, improve human-machine interfaces, and open new possibilities in personalized medicine and advanced prosthetics. However, challenges remain in miniaturization, power management, and data analysis for these complex systems.

2.6.4. Power Management and Wireless Communication

The development of energy-efficient skin-interfaced bioelectronic devices is a critical challenge in the field. As these devices become more sophisticated, their power requirements increase substantially, necessitating ultra-low-power systems that can operate for extended periods without frequent charging. Researchers are exploring efficient power management circuits and energy harvesting techniques to maximize operational lifespan while minimizing device size and weight, crucial factors for user comfort and long-term adoption.

Wireless power transfer represents another key innovation area for skin-interfaced bioelectronics. The ability to power these devices wirelessly would eliminate the need for bulky batteries or frequent recharging, significantly enhancing their usability. Recent progress has demonstrated promising results in flexible wireless power transfer systems designed for wearable electronics, focusing on both efficiency and safety to ensure compatibility with long-term use on human skin

Efficient and secure data transmission is equally crucial for high-density, skin-interfaced sensor arrays. As these devices collect large volumes of sensitive physiological data, there is a need for low-power wireless communication methods that can transmit information reliably and securely. The InSkin project is investigating advanced compression algorithms and low-power communication protocols to balance data fidelity, transmission speed, and energy efficiency. These developments are essential for realizing the full potential of skin-interfaced bioelectronics in real-world applications, from continuous health monitoring to advanced human-machine interfaces.

2.6.5. Signal Processing and Interpretation

The advancement of skin-interfaced bioelectronics is increasingly focused on real-time processing, machine learning integration, and personalization. Many current systems rely on offline processing, limiting their applications. There's a growing need for algorithms capable of real-time signal processing and interpretation, especially for complex, high-density data. The InSkin project is addressing this by developing edge computing solutions for on-device processing, aiming to reduce latency and enable more responsive systems.

Machine learning integration presents both opportunities and challenges. The variability in skin-interfaced recordings necessitates robust, adaptable algorithms. Recent advancements have shown promise, with self-adaptive models improving accuracy in real-world scenarios. However, developing algorithms that can generalize across diverse populations while maintaining performance under varying conditions remains a challenge.

Personalization is another significant hurdle. Current systems often require extensive calibration for individual users, which can be impractical for everyday use. Researchers are exploring methods for rapid calibration and personalized signal interpretation, aiming

to create systems that can quickly adapt to new users and continuously adjust to physiological changes over time. This level of seamless personalization is crucial for developing user-friendly and effective bioelectronic systems that can cater to diverse populations and use cases.

2.6.6. Scalable Manufacturing

The scalability of skin-interfaced bioelectronics presents significant challenges in fabrication, cost-effectiveness, and quality control. Large-area fabrication is a key hurdle, as scaling up production while maintaining device performance is complex. Recent advancements in roll-to-roll processing for flexible electronics show promise, and the InSkin project is adapting industrial laser techniques for high-throughput production of stretchable electronics.

Cost-effective production is crucial for widespread adoption, especially in healthcare applications. Recent studies have analyzed cost factors in wearable sensor production, proposing optimization strategies to reduce expenses without compromising quality. This is essential for making advanced bioelectronic devices accessible to a broader population. Quality control in large-scale production of flexible, stretchable electronics poses unique challenges due to the materials' properties and complex fabrication processes. Recent advances include AI-driven quality control systems for flexible electronics manufacturing, which could significantly improve efficiency and reliability in production. These innovations in fabrication, cost reduction, and quality assurance are vital for transitioning skin-interfaced bioelectronics from laboratory prototypes to widely available commercial products.

The InSkin project aims to address several of these gaps, particularly focusing on developing an adaptive, inclusive interface that performs consistently across diverse skin conditions and age groups. By tackling these challenges, InSkin and similar technologies have the potential to significantly advance the field of skin-interfaced bioelectronics, enabling more widespread adoption and opening up new applications in healthcare and human-machine interfaces.

The review of existing technologies, materials, and fabrication techniques in skin-interfaced bioelectronics reveals significant advancements but also highlights persistent challenges. These include adapting to diverse skin conditions, ensuring long-term stability and comfort, achieving high-density multi-channel sensing and stretchability, and developing scalable manufacturing processes. The InSkin project aims to address these gaps by developing a novel conductive polymer composite that offers enhanced stretchability, conductivity, and high conformality. By focusing on creating an adaptive, inclusive interface, InSkin has the potential to significantly advance the field of skin-interfaced bioelectronics, enabling more widespread adoption and opening up new applications in healthcare and human-machine interfaces. The subsequent chapters will detail the specific materials, methods, and results of the InSkin project, demonstrating how it tackles these challenges and pushes the boundaries of skin-interfaced electronic systems. The InSkin project aims to address these challenges by developing a novel conductive polymer composite that combines high stretchability with excellent electrical properties. By focusing on creating an adaptive, inclusive interface, InSkin has the potential to significantly advance the field, enabling more reliable and consistent performance across diverse populations and dynamic conditions. The subsequent chapters will detail the specific materials, methods, and results of the InSkin project, demonstrating how it tackles these challenges and pushes the boundaries of skin-interfaced electronic systems.

Chapter 3: Materials and Methods

This chapter details the innovative materials and methods employed in the development of the InSkin platform, a skin-interfaced electronic system designed for high-fidelity, high-density electrophysiological recording. The chapter is structured around six key areas:

Materials Selection and Preparation: We introduce a novel, water-soluble, and solution-processable conductive polymer composite, combining PEDOT:PSS, waterborne polyurethane, ionic liquids, and glycerol. This unique formulation enables both high electrical conductivity and mechanical stretchability.

Device Fabrication Process: A scalable fabrication technique is presented, integrating solution processing, laser patterning, and transfer methods to produce large-area, high-density electrode arrays.

Characterization Techniques: Comprehensive mechanical, electrical, electrochemical, and morphological analyses are outlined, providing a holistic understanding of the InSkin device's capabilities.

Human Studies: Rigorous protocols for evaluating the InSkin device across diverse populations and skin conditions are described, including sEMG recording, gesture recognition, and long-term wearability assessments.

Biopotential Recording Setup: Detailed configurations for recording various physiological signals (sEMG, ECG, EEG) are presented, showcasing the versatility of the InSkin platform.

Robotic Hand Control System: An integrated system demonstrating the practical application of InSkin in advanced prosthetic control is described, combining high-density sEMG recordings with machine learning algorithms.

This chapter lays the foundation for understanding the unique properties and capabilities of the InSkin device, setting the stage for the results and discussion that follow in subsequent chapters.

A detailed protocol for the InSkin interface preparation is presented in Appendix A.

3.1. Materials Selection and Preparation

Developing the InSkin platform required careful selection and preparation of materials to achieve the desired stretchability properties, conductivity, and conformality. A key innovation in this project is the creation of a water-soluble and solution-processable conductive polymer composite, enabling facile fabrication and potential for scalable manufacturing. The selection of materials for the InSkin device was guided by the need to balance high electrical conductivity with exceptional mechanical properties. The novel conductive polymer composite, Solution CP-G, was developed through an iterative process of formulation and testing. Key considerations in the material design included stretchability, conductivity under strain, biocompatibility, and ease of fabrication. The following subsections detail the specific components and their roles in achieving the desired properties of the InSkin platform.

3.1.1. Conductive Polymer Composite

The InSkin platform is built upon a novel conductive polymer composite that forms its core. This composite is designed to provide a unique combination of high electrical conductivity and mechanical stretchability, addressing the fundamental challenges in creating flexible and stretchable bioelectronics. A key innovation of this composite lies in its entirely water-soluble and solution-processable nature, offering significant advantages in terms of ease of fabrication, scalability, and environmental friendliness. The carefully selected components of this composite work synergistically to achieve the desired properties (Figure 3.1a).

The primary conductive component of the composite is Poly(3,4-ethylenedioxythiophene) polystyrene sulfonate (PEDOT:PSS), sourced from Heraeus Clevios™ PH1000. This material, with a solid content of approximately 1.1–1.3 wt% and a PEDOT to PSS weight ratio of about 1:2.5, serves as the main contributor to the composite's electrical conductivity. PEDOT:PSS was selected for its high conductivity, solution processability, and stability. Its ability to form a continuous conductive network when properly formulated is crucial for maintaining conductivity under strain, a key requirement for stretchable

electronics ¹⁵². The acidic nature of PEDOT:PSS (pH ~2) necessitates careful consideration in formulation to ensure compatibility with other components.

To provide the necessary stretchability and form the matrix of the composite, Waterborne Polyurethane (WPU) from Alberdingk Boley (ALBERDINGK® U4101) is incorporated. This material, with a solid content of 39–41 wt% and an impressive elongation at break of approximately 1400%, offers excellent elasticity and compatibility with water-based processing. The high elongation at break of WPU ensures the stretchability of the final composite, allowing it to conform to the dynamic nature of human skin ¹⁵³. The neutral pH range (7.0–8.5) of WPU also helps balance the acidity of PEDOT:PSS in the final mixture. An ionic liquid, specifically 1-Ethyl-3-methylimidazolium ethyl sulfate (EMIM:ESO₄) sourced from Sigma-Aldrich, is incorporated to enhance the conductivity and plasticity of the PEDOT:PSS. This component serves a dual function as both a plasticizer and a conductivity enhancer, improving the overall performance of the composite. The ionic liquid's compatibility with water-based systems maintains the solution-processability of the mixture, which is crucial for the fabrication process ¹⁵⁴.

Glycerol, also sourced from Sigma-Aldrich, plays a multifaceted role in the composite. It improves stretchability, enhances resistance stability under stretching, contributes to conductivity, and improves the conformality of the composite. Acting as a secondary plasticizer, glycerol further enhances the mechanical properties of the composite while contributing to its ability to conform to the skin's microfeatures ¹⁵⁵. This conformability is essential for maintaining consistent contact with the skin, a critical factor in reliable bioelectronic measurements.

To address the pH incompatibility between PEDOT:PSS and WPU, a 25% ammonia solution from Sigma-Aldrich is utilized. The ammonia helps to neutralize the acidic PEDOT:PSS, ensuring better miscibility with the WPU and enhancing the stability of the final composite ¹⁵⁶. This pH adjustment is crucial for achieving a homogeneous mixture and preventing phase separation during processing and use.

The water-soluble nature of all components allows for a homogeneous mixture to be achieved through simple solution-based processing techniques. This characteristic not only

simplifies the fabrication process but also enables fine-tuning of the composite properties by adjusting component ratios. The resulting composite demonstrates remarkable versatility in terms of deposition methods, being compatible with various solution-processing techniques such as drop-casting, spin-coating, spray-coating, screen-printing, and inkjet printing. This flexibility in fabrication methods offers significant advantages in terms of scalability and adaptability to different device designs and applications.

In summary, the careful selection and integration of these components result in a composite material that combines high electrical conductivity, excellent mechanical stretchability, and ease of processing. These characteristics make it ideally suited for the creation of skin-interfaced bioelectronic devices, capable of conforming to the complex topography of human skin while maintaining reliable electrical performance. The following sections will delve into the detailed fabrication process and characterization of this innovative material,

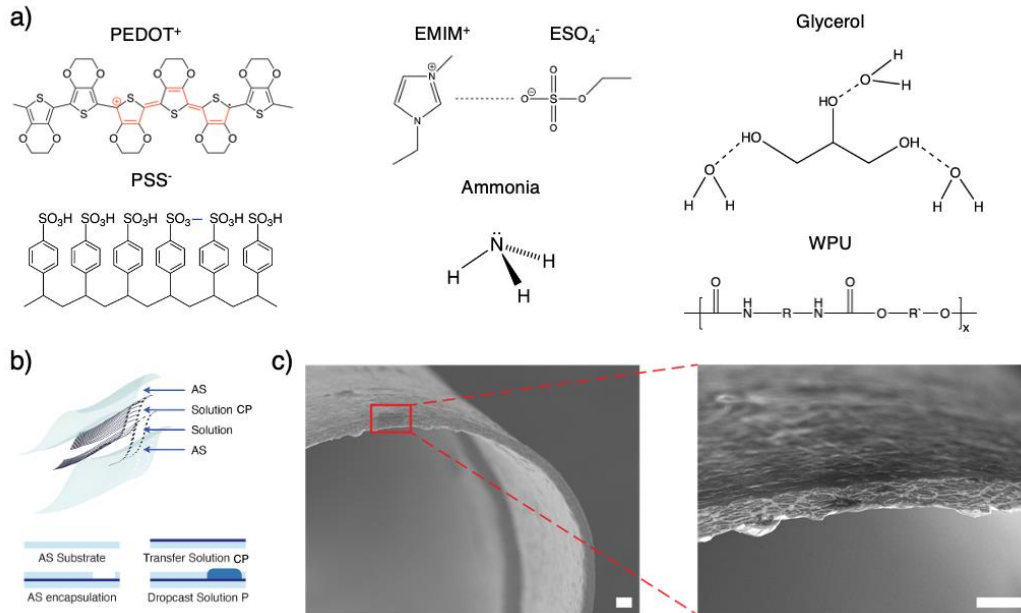


Figure 5: Schematic illustration of the InSkin material composition and preparation process. (a) Chemical structures of key components (PEDOT:PSS, WPU, EMIM:ESO₄, glycerol, ammonia). (b) 3D render and cross-sectional illustration of the layered structure of the InSkin device. (c) SEM images of the prepared conductive polymer composite film at different magnifications, scale bar: 10 μm.

demonstrating its potential to revolutionize the field of wearable and implantable bioelectronics.

3.1.2. Substrate and Encapsulation Materials

The design of the substrate and encapsulation layers for the InSkin platform was crucial to ensure mechanical support, protection, skin compatibility, and breathability. These layers play a vital role in the overall performance and user comfort of the device.

The key material selected for both the substrate and encapsulation layer is a specialized artificial skin (AS) material:

Artificial Skin (AS):

- Type: Polyurethane membrane with acrylic adhesive
- Source: 3M™ Tegaderm™
- Function: Serves as both substrate and encapsulation layer, providing a biocompatible interface with the skin while allowing for perspiration and prolonged device use during sweating
- Rationale: Tegaderm™ was chosen for its proven biocompatibility, breathability, thinness, and ability to conform to skin contours. Its transparency also allows for visual inspection of the skin underneath during long-term wear.

The selection of Tegaderm™ as the artificial skin material was based on its unique combination of properties that align closely with the requirements of skin-interfaced bioelectronics. The polyurethane membrane provides a flexible and durable base, while the acrylic adhesive ensures secure attachment to the skin. The material's breathability is crucial for maintaining skin health during extended wear, allowing for normal perspiration and preventing moisture buildup that could lead to skin irritation or compromise device performance.

The thinness of Tegaderm™ contributes to the overall low profile of the InSkin device, enhancing its conformability to skin contours and reducing user awareness of the device during wear. This conformability is essential for maintaining consistent contact between the electrodes and the skin, which is critical for reliable signal acquisition.

Furthermore, the transparency of Tegaderm™ offers an additional advantage in clinical and research settings. It allows for visual inspection of the underlying skin without removing the device, enabling monitoring of skin condition during long-term wear and facilitating early detection of any potential irritation or adverse reactions.

The combination of the water-soluble, solution-processable conductive composite with the breathable, biocompatible artificial skin substrate creates a unique platform that balances electrical performance, mechanical properties, and user comfort. This innovative material system forms the foundation of the InSkin device's capabilities, as illustrated in Figure 3.1b. The synergy between these components allows for a device that not only provides high-quality electrophysiological measurements but also adapts to the dynamic nature of human skin and movement.

3.1.3. Material Preparation

The preparation of the conductive polymer composite, which forms the core of the InSkin platform, was carried out through a series of carefully optimized steps. The base composite, named "Solution CP," was prepared as follows:

1. PEDOT:PSS and Ionic Liquid Mixture:

- The ionic liquid (EMIM:ESO4) was first diluted to 1.48 wt% with deionized water to ensure uniform distribution.
- This diluted Solution was then added dropwise to the PEDOT:PSS dispersion in a precise ratio of 15:25.
- The mixture was subjected to thorough stirring at 400 rpm for 12 hours, ensuring complete and homogeneous incorporation of the ionic liquid into the PEDOT:PSS matrix.

2. pH adjustment:

- To address the inherent acidity of PEDOT:PSS and improve its compatibility with other components, 0.15 wt% of ammonia solution was added to the dispersion. This step is crucial for achieving a stable and homogeneous final composite.

3. WPU Addition:

- Waterborne Polyurethane (WPU) was incorporated into the mixture to achieve a final ratio of 25:15:85 PEDOT:PSS:IL:WPU.
- This mixture was stirred for 2 hours to ensure homogeneous dispersion of all components, creating a uniform composite material.

4. Glycerol Incorporation:

- To optimize the mechanical and electrical properties of the composite, various concentrations of glycerol were systematically tested. The ratios ranged from 1:1 to 1:300 (glycerol to Solution CP).
- After extensive performance tests, balancing conductivity and stretchability, the optimal ratio was determined to be 1:250. This formulation, designated as Solution CP-G 250, exhibited the best overall performance characteristics.

5. Film Formation:

- The prepared solutions were then processed into thin films using either spin-coating or drop-casting techniques. These methods were applied to bare glass slides or PTFE-coated glass slides, depending on the specific requirements of subsequent fabrication steps.
- To ensure complete solvent evaporation and optimal film formation, the samples were dried in a vacuum desiccator at room temperature overnight. This step is critical for achieving consistent film properties and is illustrated in Figure 3.1c.

This preparation process, entirely based on water-soluble components and aqueous processing, demonstrates not only the simplicity of the InSkin material system but also its potential for scalable manufacturing. The ability to fine-tune the composite properties by adjusting component ratios offers a versatile platform for optimizing device performance for a wide range of applications.

3.1.4. Material Characterization

To fully understand and optimize the properties of the InSkin materials, a comprehensive initial characterization was conducted. This characterization encompassed mechanical, electrical, and morphological analyses:

1. Mechanical Testing:

- Stretchability and elastic modulus measurements were performed using a CellScale UniVert equipped with a 20-N loading cell.
- Sample dimensions were standardized at $30 \times 10 \times 0.1 \text{ mm}^3$ (length $\times$ width $\times$ thickness) to ensure consistency across tests.
- A stretching rate of 1%/s was applied to simulate realistic deformation scenarios.
- These tests provided crucial insights into the mechanical behavior of the composite under various strain conditions, informing the design of stretchable electrode patterns and predicting device performance during skin deformation.

2. Electrical Characterization:

- Resistance measurements during stretching were conducted using a high-resolution potentiostat (PalmSens4, PalmSens). This allowed for real-time monitoring of electrical properties under mechanical stress.
- Electrochemical Impedance Spectroscopy (EIS) was performed in PBS buffer solution (pH 7.4) over a frequency range from 10 MHz to 10 Hz. This technique provided valuable information about the electrode-electrolyte interface properties, crucial for understanding signal transduction in bioelectronic applications.
- These measurements were instrumental in assessing the composite's electrical properties and their stability under deformation, a critical factor for maintaining signal quality during device use.

3. Morphological Analysis:

- Scanning Electron Microscopy (SEM) was carried out using a JEOL 6610LV SEM operated at 15 kV. This high-resolution imaging technique allowed for detailed examination of the composite's microstructure.
- SEM analysis provided invaluable insights into the distribution of conductive components within the composite matrix. This information was crucial for understanding the mechanism of conductivity under strain and optimizing the material composition for improved performance.

The careful selection, preparation, and characterization of these materials form the foundation of the InSkin platform, enabling its unique combination of stretchability, conductivity, and stability. The water-soluble, solution-processable nature of the composite not only simplifies fabrication but also opens up possibilities for scalable manufacturing and potential customization for specific applications.

The subsequent sections will detail how these carefully characterized materials were utilized in the fabrication of the InSkin devices, and their performance in various application scenarios. This comprehensive approach to material development and characterization sets the stage for the creation of highly effective, adaptable skin-interfaced bioelectronic devices with the potential to revolutionize fields ranging from healthcare monitoring to human-machine interfaces.

3.2. Device Fabrication Process

The fabrication of the InSkin device leverages the water-soluble and solution-processable nature of the conductive polymer composite, combining it with advanced patterning and transfer techniques. This process enables the scalable production of large-area, high-density electrode arrays. The fabrication process consists of several key steps, each optimized for performance and scalability (Figure 3.2):

3.2.1. Solution Preparation

The preparation of Solution CP, as detailed in Section 3.1.3, forms the foundation of the fabrication process. The optimized Solution CP-G 250 was used for all subsequent steps. The water-based nature of this solution allows for easy handling, mixing, and deposition,

significantly simplifying the fabrication process compared to organic solvent-based systems.

3.2.2. Film Deposition

The fabrication process of the InSkin device begins with the careful preparation and deposition of the conductive polymer composite film. This critical stage sets the foundation for the device's electrical and mechanical properties.

Substrate Preparation: The initial step involves preparing a suitable substrate for film deposition. Glass slides (Fisherbrand™ Superfrost™ Plus Microscope Slides) are coated with a chemically resistant polytetrafluoroethylene (PTFE) film (McMaster-Carr Chemical-Resistant Slippery Film Made from Teflon® PTFE). This hydrophobic PTFE coating serves a dual purpose: it ensures easy release of the patterned film in subsequent steps, which is crucial for successful transfer printing, and it enables the creation of free-standing films. The use of this chemically inert layer affords greater flexibility in device design and application, allowing for the fabrication of complex, multi-layered structures.

Solution CP-G Deposition: The prepared Solution CP-G, our novel conductive polymer composite, is then deposited onto the PTFE-coated glass slides using a drop-casting method. This technique was chosen for its simplicity and ability to create uniform films over large areas. The solvent (water) is allowed to evaporate overnight in a controlled environment, resulting in a uniform and smooth thin film. Precise control over the deposition process enables the achievement of a final film thickness of 7.5 μm , a dimension that balances conductivity with flexibility and stretchability.

The solution-based nature of this deposition process offers significant advantages in terms of scalability. It is compatible with various coating techniques, such as spin-coating or spray-coating, which are amenable to industrial-scale production. This versatility in deposition methods positions the InSkin fabrication process well for future scaling and commercialization efforts.

Surface Treatment: Following deposition and drying, the Surface of the Solution CP-G film undergoes a critical treatment step. The film is cleaned and subjected to oxygen plasma

treatment (Plasma Etch Inc. Model PE-50, 120 VAC 60Hz, 200 mTorr) for 5 minutes. This plasma treatment serves multiple purposes:

1. It improves the conductivity of the film surface, enhancing the overall electrical performance of the device.
2. It increases adhesion between the film and the Artificial Skin (AS) substrate in subsequent steps, crucial for device integrity.
3. The treatment enhances the hydrophilicity of the surface, which is vital for maintaining good contact with skin during device operation. This improved wettability ensures better conformity to skin microstructures and enhances signal acquisition.

The plasma treatment process was optimized through extensive experimentation to achieve the optimal balance between surface modification and preservation of the bulk material properties.

3.2.3. Patterning and Transfer

The patterning and transfer stages are critical in transforming the uniform conductive film into a functional electrode array and integrating it with the flexible substrate.

Laser Patterning: A Universal Laser System™ VLS6.75 equipped with a CO₂ laser and High-Power Density Focusing Optics (HPDFO) is employed for precise patterning of the Solution CP-G film. The laser parameters were meticulously optimized: a power of 1.5 W, speed at 11% of maximum, and a focal point of 25.4 μm. These settings allow for the creation of intricate electrode and interconnect patterns with high precision.

The choice of laser patterning offers several advantages:

- High precision in feature creation, allowing for complex electrode geometries.
- Flexibility in design, enabling rapid prototyping and easy customization of electrode layouts.
- Non-contact processing, minimizing potential contamination or mechanical damage to the film.

Pattern Release and Transfer: Following laser patterning, the excess film is carefully removed from the substrate, leveraging the release properties of the PTFE-coated surface. This step results in a clean, patterned electrode array ready for transfer.

The transfer process to the Artificial Skin (AS) substrate is a critical step:

1. A pre-cut rectangle of AS is prepared by removing the protective coating from its adhesive layer.
2. Precise alignment between the patterned Solution CP-G and the AS is crucial for maintaining the integrity of the electrode layout.
3. The patterned array is then carefully transferred onto the AS substrate.

This transfer printing approach allows for the seamless integration of the high-performance conductive composite with the flexible, biocompatible AS substrate. It combines the electrical properties of the Solution CP-G with the mechanical and biocompatible properties of the AS, creating a unique hybrid structure.

Post-Transfer Treatment: After transfer, the array undergoes a second oxygen plasma treatment. This additional treatment serves multiple purposes:

- It further improves adhesion with the encapsulation layer.
- It enhances the electrode-skin interface properties.
- It improves the electrical connection with the flat flexible cable (FFC) used for device output.

This second plasma treatment is crucial for optimizing the performance of the transferred electrodes, particularly in terms of skin adhesion and signal quality. The parameters for this treatment were carefully optimized to enhance surface properties without damaging the underlying structures.

The combination of precise laser patterning and carefully controlled transfer processes results in a high-resolution, stretchable electrode array intimately integrated with a flexible, biocompatible substrate. This approach overcomes many of the challenges associated with traditional fabrication methods for skin-interfaced electronics, paving the way for devices that can truly conform to the complex topography of human skin while maintaining high-fidelity electrophysiological recording capabilities.

3.2.4. Encapsulation and Functionalization

The final stages of the InSkin device fabrication involve crucial steps of electrical connection, encapsulation, and electrode functionalization. These processes are essential for creating a robust, functional, and biocompatible device.

Electrical Connection: To establish reliable connectivity between the electrode array and external electronics, flat-flexible cables (FFC) are attached using anisotropic conductive tape. This approach ensures low-resistance electrical pathways while maintaining the device's overall flexibility. The assembly then undergoes a carefully optimized annealing process at 80°C for 15 minutes. This thermal treatment enhances the electrical connection by promoting better contact between the conductive particles in the tape and the electrode surfaces, resulting in improved signal transmission and reduced noise.

Encapsulation: A second layer of Artificial Skin (AS) is employed for encapsulation, crucial for protecting the device's internal components while maintaining its flexibility and biocompatibility. This layer is precisely patterned using laser ablation to create openings that correspond to the electrode pads on the array. The patterned AS is then meticulously aligned and applied to the connected array. This strategic encapsulation serves a dual purpose: it isolates the interconnects, protecting them from environmental factors and potential short circuits, while leaving the sensing pads exposed for direct skin contact. This design enables both protection and functionality, a critical balance in skin-interfaced electronics.

Electrode Functionalization: To optimize the electrode-skin interface, a novel functionalization step is implemented. A solution of PEDOT:PSS and Glycerol in a 1:1 ratio, designated as Solution P, is prepared. This solution is carefully drop-cast onto each sensing electrode, creating a softer, more conformal interface with the skin. This functionalization significantly enhances the InSkin's electrical performance by:

1. Reducing the electrode-skin impedance, crucial for high-quality signal acquisition.
2. Improving signal quality by enhancing the ionic and electronic conductivity at the interface.

3. Increasing the mechanical compliance of the electrode surface, allowing better conformation to skin microstructures.

Final Annealing: The fabrication process concludes with a final annealing step at 60°C for 10 minutes. This low-temperature annealing serves multiple purposes:

1. It ensures proper drying of Solution P, optimizing its electrical and mechanical properties.
2. It enhances the overall stability of the device structure.
3. The carefully chosen temperature is compatible with the thermal stability of the AS substrate, preserving its integrity while optimizing the properties of the functionalized electrodes.

3.2.5. Quality Control

Rigorous quality control measures are implemented throughout the fabrication process to ensure the consistency and reliability of the produced devices:

Optical Microscopy: High-resolution optical microscopy is employed to inspect the uniformity of the Solution CP-G film and the precision of laser patterning. This technique allows for the confirmation of feature resolution down to 50 μm in the laser-patterned structures. Such meticulous inspection ensures the fidelity of the electrode array design and enables the identification of any potential defects in the patterning process, crucial for maintaining the device's performance and reliability.

Impedance Testing: Each electrode in the array undergoes individual impedance testing to ensure uniformity across the device. A narrow impedance distribution is targeted, critical for maintaining consistent signal quality across the entire electrode array. This comprehensive testing approach enables the identification and potential rectification of any outliers, ensuring that each device meets stringent performance criteria.

Mechanical Testing: Random sampling of fabricated devices is conducted for stretch tests to confirm the maintenance of conductivity under deformation. This crucial step verifies both the stretchability and electrical stability of the produced devices, ensuring they meet the rigorous design specifications required for skin-interfaced electronics. The tests

simulate real-world usage conditions, providing valuable data on the device's performance under various strain scenarios.

The fabrication process described leverages the unique properties of the water-soluble, solution-processable conductive polymer composite to create highly stretchable, skin-conformable electrode arrays with high spatial resolution. The synergistic combination of solution processing, precise laser patterning, and careful transfer and encapsulation techniques results in a device capable of adapting to various skin properties while maintaining high-fidelity electrophysiological recording capabilities.

This innovative process offers several significant advantages for the production of skin-interfaced electronics:

1. **Scalability:** The solution-based processing and laser patterning techniques are inherently amenable to scaling up for larger production volumes. This scalability potentially enables cost-effective manufacturing of these advanced bioelectronic devices, a crucial factor for widespread adoption and commercialization.
2. **Flexibility in Design:** The laser patterning approach provides unparalleled flexibility, allowing for rapid prototyping and easy customization of electrode layouts. This adaptability is invaluable for optimizing designs for specific applications or anatomical locations, enabling tailored solutions for diverse biomedical needs.
3. **Environmental Friendliness:** The predominantly water-based nature of the primary materials and processes significantly reduces the use of organic solvents. This aligns with green chemistry principles and potentially simplifies regulatory compliance, an important consideration for medical devices.
4. **Compatibility with Existing Manufacturing Infrastructure:** Many of the techniques employed, such as solution coating and laser processing, are already well-established in various industries. This compatibility potentially facilitates the adoption and scaling of this technology, reducing barriers to entry and accelerating commercialization.

5. Potential for Roll-to-Roll Processing: The planar nature of the device structure and the solution-based material system are inherently compatible with roll-to-roll manufacturing processes. This compatibility opens up exciting possibilities for high-volume production in the future, potentially revolutionizing the manufacturing of skin-interfaced electronics.

In conclusion, the fabrication process developed for the InSkin device represents a significant advancement in the field of skin-interfaced bioelectronics. By combining novel materials with innovative processing techniques, this approach addresses many of the key challenges in creating flexible, stretchable, and high-performance bioelectronic devices. The rigorous quality control measures ensure the reliability and consistency of the produced devices, setting a new standard for skin-interfaced electronics. As this technology continues to evolve, it holds the promise of enabling a new generation of wearable and implantable bioelectronic devices with unprecedented capabilities in healthcare monitoring, human-machine interfaces, and beyond. The successful implementation of this fabrication process demonstrates the potential of the InSkin platform for creating next-

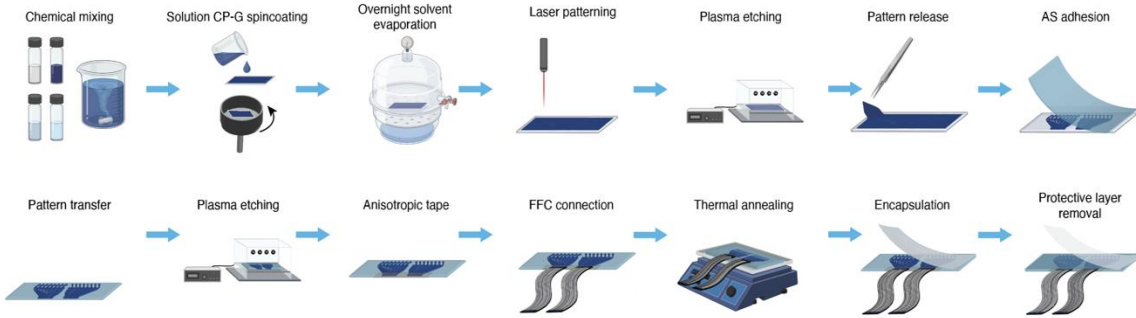


Figure 6: Fabrication process for the multichannel high-density sEMG array. (i) Preparation of Solution CP-G by mixing PEDOT:PSS, EMIM:ESO₄, WPU, ammonia, and Glycerol. (ii) Thin film deposition via drop-casting or spin-coating on PTFE-coated glass. (iii) Vacuum drying overnight. (iv) CO₂ laser patterning of sensing pads and interconnects. (v) Oxygen plasma treatment for improved adhesion. (vi) Pattern release and (vii-viii) transfer to artificial skin (AS) substrate. (ix) Second plasma treatment for encapsulation preparation. (x-xi) Connection of flat-flexible cables (FFC) with anisotropic tape and (xii) thermal annealing. (xiii) Application of patterned AS encapsulation layer. (ivx) Final thermal annealing. This process yields a flexible, stretchable array for real-time prosthetic control.

generation skin-interfaced electronic systems. The ability to produce high-performance, stretchable electrode arrays using scalable techniques represents a significant step towards the widespread adoption of advanced bioelectronic devices in healthcare, human-machine interfaces, and beyond.

3.3. Characterization Techniques

To thoroughly evaluate the properties and performance of the InSkin device, a comprehensive set of characterization techniques was employed. These methods span mechanical, electrical, electrochemical, and morphological analyses, providing a holistic understanding of the device's capabilities. The multi-faceted characterization approach is crucial for validating the performance of the InSkin platform across various conditions relevant to skin-interfaced electronics.

3.3.1. Mechanical Property Characterization

Understanding the mechanical behavior of the InSkin device is indeed crucial for ensuring its ability to conform to skin and maintain functionality during body movements. The comprehensive mechanical characterization employed in this study provides valuable insights into the device's performance under various conditions. Let's elaborate on the techniques used and their significance:

Tensile Testing: The tensile testing protocol was designed to evaluate the fundamental mechanical properties of the InSkin material. Using a CellScale UniVert system equipped with both 20-N and 50-N loading cells (Figure 3.3), this setup allows for precise force measurements across a wide range of applied strains.

Sample preparation was standardized to ensure reproducibility and comparability of results. Rectangular strips measuring $30 \times 10 \times 0.1 \text{ mm}^3$ (length $\times$ width $\times$ thickness) were carefully prepared, with particular attention paid to maintaining uniform thickness across samples.

The testing parameters were chosen to simulate real-world conditions while also pushing the material to its limits:

- A stretching rate of 1%/s was selected to mimic the typical rates of skin deformation during normal body movements.

- The maximum elongation of up to 1500% far exceeds the typical strains experienced by human skin (around 30-40%), providing a substantial safety margin and insights into the material's behavior under extreme conditions.

Key measurements obtained from these tests include:

- Stress-strain curves: These provide a comprehensive view of the material's behavior under load, from initial elastic deformation through to plastic deformation and failure.
- Young's modulus: This quantifies the material's stiffness in the elastic region, crucial for matching the mechanical properties of human skin.
- Ultimate tensile strength: This indicates the maximum stress the material can withstand before failure, important for ensuring device integrity under extreme conditions.
- Elongation at break: This measure of ductility is critical for understanding the material's ability to conform to complex skin topographies without failure.

The significance of these tests cannot be overstated. They provide crucial information about the stretchability and mechanical strength of the InSkin material, ensuring it can withstand the deformations experienced during skin interfacing. This data is essential for predicting device performance and longevity in real-world applications.

Cyclic Strain Testing: While tensile testing provides information about the material's response to a single stretching event, cyclic strain testing simulates the repeated deformations the device might experience during long-term wear. This testing is crucial for understanding the material's fatigue resistance and durability.

Using the same CellScale UniVert system, samples were subjected to repeated stretching cycles at various strain levels:

- Strain levels of 50%, 100%, and 200% were chosen to represent a range of potential deformations, from moderate to extreme.
- Up to 100 cycles were performed at each strain level to simulate extended use scenarios.

The key measurements from these tests include changes in mechanical properties over repeated stretching cycles, such as:

- Changes in elastic modulus
- Stress softening effects (Mullins effect)
- Permanent deformation or set
- Changes in maximum stress at a given strain

The significance of cyclic testing lies in its ability to predict long-term performance. It provides insights into the device's durability and fatigue resistance, crucial factors for any wearable technology intended for continuous use. By understanding how the material's properties change over repeated deformations, we can better predict its behavior during extended wear and design devices that maintain their performance over time.

These mechanical characterization techniques, when combined, provide a comprehensive understanding of the InSkin material's behavior under various mechanical stresses. This knowledge is fundamental to designing devices that can reliably conform to the dynamic nature of human skin while maintaining their functional integrity. The data obtained from these tests not only validates the material's suitability for skin-interfaced electronics but also informs future iterations and optimizations of the InSkin technology.

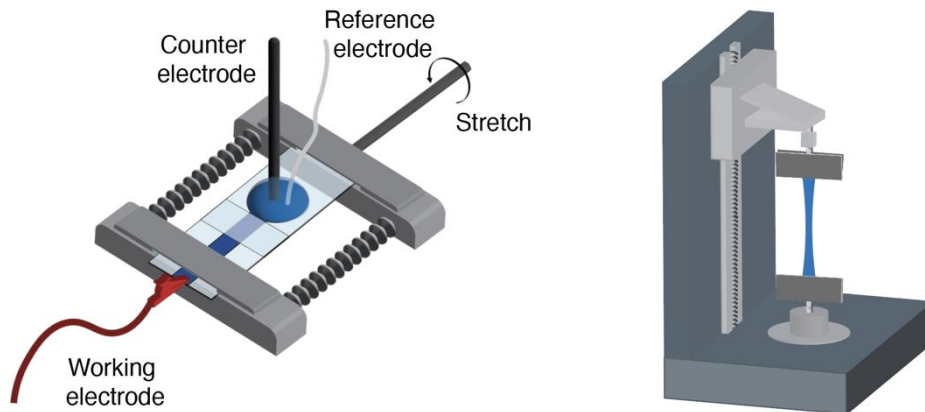


Figure 7: Overview of characterization instruments for the InSkin device. (left) EIS and CV measurement configuration. (right) Tensile testing setup.

3.3.2. Electrical and Electrochemical Characterization

The electrical and electrochemical properties of the InSkin device are paramount to its function as a high-fidelity biopotential recording system. To comprehensively assess these properties, we employed a range of sophisticated techniques, each providing unique insights into the device's performance under various conditions. This section details the methods used and their significance in evaluating the InSkin platform.

Resistance Measurements

To evaluate the device's ability to maintain electrical conductivity under strain—a crucial factor for its performance during body movements—we conducted resistance measurements using a high-resolution potentiostat (PalmSens4, PalmSens) paired with a CellScale UniVert equipped with a 20-N loading cell. The experimental protocol involved chronoamperometry with a 0.5V bias applied during tensile testing. This setup allowed us to measure resistance changes as the device was stretched to the point of failure.

The significance of this technique lies in its ability to simulate real-world conditions where the device would be subjected to various degrees of stretching when applied to the skin. By quantifying the relationship between mechanical strain and electrical resistance, we could assess the robustness of the conductive pathways within the device. This information is critical for optimizing the material composition and structural design to ensure consistent electrical performance across a range of body movements and postures.

Electrochemical Impedance Spectroscopy (EIS)

Electrochemical Impedance Spectroscopy was performed using a PalmSens4 potentiostat to gain insights into the electrode-electrolyte interface properties. We conducted measurements over a broad frequency range from 10 MHz to 10 Hz, using a PBS buffer solution (pH 7.4) as the electrolyte to mimic physiological conditions. The key parameters measured were impedance magnitude and phase angle as functions of frequency.

EIS is particularly valuable in understanding the signal transduction mechanisms at the electrode-skin interface. The impedance characteristics across different frequencies provide crucial information about the electrode's ability to detect and transmit biopotential signals. Low-frequency impedance is especially important for capturing slow-changing

biosignals, while high-frequency behavior informs on the electrode's capacity for rapid signal transmission. By analyzing these data, we could optimize the electrode design for low-impedance recordings, thereby enhancing the overall signal quality and reducing noise in the biopotential measurements.

Cyclic Voltammetry (CV)

We employed Cyclic Voltammetry to assess the electrochemical stability and charge storage capacity of the electrodes. Using the PalmSens4 potentiostat, we performed CV scans over a voltage range of -0.5V to +0.5V at a scan rate of 0.1V/s. To ensure reproducibility and account for any initial stabilization effects, we averaged the results of 10 consecutive scans. The enclosed area of the CV curves was computed to quantify changes under elongation, providing a measure of the electrode's electroactive surface area and its stability under mechanical stress.

The significance of CV in our study is multifaceted. Firstly, it allows us to characterize the electrochemical reactions occurring at the electrode surface, which is crucial for understanding the long-term stability of the electrode-electrolyte interface. Secondly, by analyzing the CV curves under different elongation conditions, we can assess how mechanical strain affects the electrochemical properties of the electrodes. This information is vital for predicting and optimizing the long-term recording stability of the InSkin device, especially in dynamic, real-world applications where the device is subjected to continuous movement and deformation.

Motion Artifact Analysis

To quantify the device's susceptibility to motion artifacts—a common challenge in wearable bioelectronics—we conducted controlled motion tests with simultaneous EMG recording. We used an INTAN RHD recording controller with a 32-channel amplifier for data acquisition. The primary metric of interest was the variation in signal-to-noise ratio (SNR) between static and dynamic conditions.

This analysis is crucial for optimizing the design of the InSkin device for stable recordings during movement. By systematically introducing controlled motions and measuring their impact on signal quality, we could identify specific design elements or material properties

that contribute to motion artifact reduction. This information guided iterative improvements in the device architecture, electrode-skin interface design, and signal processing algorithms to minimize the influence of motion on the recorded biopotential signals.

Long-term Stability Testing

To evaluate the InSkin device's suitability for continuous monitoring applications, we conducted long-term stability testing over a 24-hour period. This involved continuous EMG recording with measurements taken at 1-hour intervals. We analyzed signal amplitude and quality over time to assess factors such as electrode degradation and signal drift.

The significance of this testing cannot be overstated for wearable bioelectronics intended for extended use. Long-term stability is crucial for applications requiring continuous monitoring, such as in clinical settings or for tracking physiological parameters over extended periods. By characterizing how signal quality evolves over time, we could identify potential limitations in the current design and develop strategies to mitigate issues such as electrode fouling, material degradation, or changes in the electrode-skin interface properties over prolonged use.

In conclusion, this comprehensive suite of electrical and electrochemical characterizations provides a multifaceted understanding of the InSkin device's performance as an electrophysiological recording system. By systematically evaluating aspects such as conductivity under strain, electrode-electrolyte interface properties, electrochemical stability, motion artifact susceptibility, and long-term recording stability, we have established a robust foundation for assessing and optimizing the device's capability to provide high-quality, stable signals across various conditions. The insights gained from these characterizations not only validate the current design but also inform future iterations and improvements of the InSkin platform.

3.3.3. Morphological Characterization

Morphological analysis plays a pivotal role in elucidating the structure and composition of the InSkin materials. This characterization is fundamental to understanding the intricate relationships between material properties and device performance. In this study, we employed two complementary imaging techniques: Scanning Electron Microscopy (SEM) and Optical Microscopy. Each method provides unique insights into the material structure at different scales, contributing to a comprehensive understanding of the InSkin device's physical properties.

Scanning Electron Microscopy (SEM)

Scanning Electron Microscopy was utilized to investigate the microstructure of the InSkin materials at high resolution. We employed a JEOL 6610LV SEM, operating at an accelerating voltage of 15 kV. To enhance imaging quality and prevent charging effects, samples were prepared by sputter coating with a thin layer of gold (10 nm thickness). This preparation technique ensures optimal conductivity for high-quality imaging without significantly altering the surface morphology of the samples.

The SEM analysis focused on three key aspects:

1. **Surface Morphology:** High-resolution imaging of the material surface revealed intricate details of the topography, including surface roughness, porosity, and the distribution of conductive elements within the composite matrix.
2. **Cross-sectional Structure:** By examining cross-sections of the InSkin device, we gained insights into the layered architecture, interface quality between different materials, and the depth distribution of conductive components.
3. **Material Distribution Analysis:** SEM imaging allowed us to assess the homogeneity of the conductive composite, identifying any potential aggregations or non-uniformities in the distribution of conductive particles.

The significance of SEM in our study extends beyond mere visualization. By revealing the microstructure of the conductive composite, SEM imaging provides crucial information for understanding the formation of conductive networks within the material. These networks are fundamental to the electrical properties of the device, influencing aspects such

as conductivity, resistance to strain, and long-term stability. Moreover, the cross-sectional analysis offers insights into the integration of different layers, which is critical for assessing the device's mechanical properties and potential failure modes under stress.

The high-resolution capabilities of SEM also allow for the examination of the electrode-substrate interface, a crucial area for signal transduction. By analyzing this interface, we can optimize the adhesion between layers and ensure efficient electrical contact, both of which are essential for high-fidelity biopotential recordings.

Optical Microscopy

While SEM provides high-resolution imaging at the microscale, optical microscopy offers a complementary perspective by allowing large-area morphological analysis. We utilized an Olympus BX51 microscope equipped with a digital camera for this purpose. The optical microscopy analysis focused on two primary aspects:

1. **Large-area Morphology:** By examining larger sections of the InSkin device, we could assess overall structural uniformity, identify any macroscale defects or inconsistencies, and evaluate the quality of the fabrication process across the entire device area.
2. **Uniformity of Electrode Patterns:** Optical microscopy is particularly useful for examining the geometry and spatial distribution of the electrode patterns. This analysis is crucial for ensuring consistency in electrode size, shape, and spacing - factors that directly influence the spatial resolution and coverage of biopotential recordings.

The significance of optical microscopy in our characterization process lies in its ability to bridge the gap between microscale features observed in SEM and the macroscale properties of the entire device. This technique is invaluable for quality control, allowing us to identify and address any large-scale manufacturing inconsistencies that might affect device performance.

Furthermore, optical microscopy plays a crucial role in the iterative process of formulation selection and optimization. By providing rapid feedback on how different material

compositions and fabrication parameters affect the overall structure and uniformity of the device, optical microscopy guides the refinement of our manufacturing processes.

The combination of SEM and optical microscopy provides a multi-scale view of the InSkin device's morphology. This comprehensive approach to morphological characterization yields valuable insights into the structure-property relationships of the InSkin materials. Understanding these relationships is crucial for several reasons:

1. **Performance Optimization:** By correlating morphological features with electrical and mechanical properties, we can identify structural characteristics that enhance or limit device performance. This knowledge guides the optimization of material composition and fabrication processes to achieve desired performance metrics.
2. **Quality Assurance:** Morphological analysis serves as a powerful tool for quality control, allowing us to establish standards for structural uniformity and detect potential defects that could compromise device functionality.
3. **Durability and Reliability:** Examining the microstructure and overall morphology helps predict how the device will behave under various conditions, including mechanical stress and prolonged use. This information is crucial for enhancing the durability and reliability of the InSkin platform.
4. **Interfacial Properties:** Detailed morphological analysis of the electrode-substrate and electrode-skin interfaces provides insights into signal transduction mechanisms and guides the development of strategies to enhance signal quality and reduce noise.

In conclusion, the morphological characterization of the InSkin device, combining high-resolution SEM imaging with large-area optical microscopy, provides a comprehensive understanding of the material structure across multiple scales. This multi-faceted approach not only elucidates the current properties of the device but also informs future iterations, guiding the development of advanced skin-interfaced electronics with enhanced performance, reliability, and user comfort.

3.3.4. Biocompatibility and Skin Interaction Studies

Ensuring the safety and comfort of the InSkin device for long-term skin contact is crucial for its practical application. To assess these aspects, we conducted skin irritation studies focusing on the device's interaction with human skin during extended wear periods.

Skin Irritation Studies

To evaluate the potential for adverse skin reactions and ensure user comfort, we implemented a human wear test protocol. This study was designed to assess the skin's response to the InSkin device over different durations, providing insights into both short-term and extended wear scenarios

Methodology

1. Study Design:

- Participants: A group of healthy volunteers
- Wear Durations: Two distinct testing periods were implemented: a) 2-hour continuous wear for acute and dynamic testing b) 24-hour continuous wear for chronic testing

2. Data Collection:

- Visual Analysis: Examination of the skin was conducted at baseline and after device removal, focusing on identifying any signs of irritation or other visible skin changes.
- Participant Comfort Rating: Subjects provided subjective comfort ratings using a standardized scale.

Significance

These studies are crucial for several reasons:

1. Safety Assessment: By monitoring for signs of skin irritation or allergic reactions, we can evaluate the safety profile of the InSkin device for extended skin contact.
2. User Comfort: Participant comfort ratings provide valuable insights into the wearability of the device over prolonged periods, a critical factor for user acceptance and compliance in real-world applications.

3. **Optimization Guidance:** Results from these studies can inform future iterations of the device design, potentially guiding modifications to improve comfort and reduce the risk of skin irritation.
4. **Application Protocol Development:** Understanding how the skin responds to different wear durations can help in developing recommendations for optimal wear times and skin recovery periods.

In conclusion, these skin irritation studies provide essential data on the biocompatibility and skin-friendliness of the InSkin device. The findings from these tests are fundamental in validating the device's suitability for long-term wear and identifying any necessary improvements to ensure user safety and comfort.

3.3.5. Electrophysiological Recording Characterization

The ultimate test of the InSkin device's performance lies in its ability to record high-quality electrophysiological signals. To comprehensively evaluate this capability, we conducted a series of tests focusing on signal quality, spatial resolution, and practical application in gesture recognition.

Signal Quality Assessment

To quantify the fidelity of the recorded biopotential signals, we employed the following approach:

- **Equipment:** INTAN RHD recording system
- **Measurements:** Signal-to-noise ratio (SNR), baseline noise, signal amplitude

The use of the INTAN RHD recording system allowed for high-precision data acquisition, enabling us to capture subtle variations in the recorded signals. By analyzing the SNR, we could assess the device's ability to distinguish physiological signals from background noise, a critical factor in the accurate interpretation of electrophysiological data. Baseline noise measurements provided insights into the stability of the recording interface, while signal amplitude analysis helped determine the sensitivity of the device to various types of biopotential signals.

The significance of these measurements lies in their direct quantification of the recorded biopotential signals' quality. High SNR values and low baseline noise are indicative of

clear, reliable recordings, which are essential for accurate physiological monitoring and interpretation. These metrics serve as a benchmark for comparing the InSkin device's performance against existing electrophysiological recording technologies and validate its capability for high-fidelity biopotential acquisition.

Spatial Resolution Analysis

To evaluate the spatial discrimination capabilities of the InSkin device, we conducted high-density EMG mapping. This analysis focused on:

- Method: High-density EMG mapping
- Measurements: Spatial distribution of EMG signals, identification of motor unit innervation zones

By examining the spatial distribution of EMG signals across the electrode array, we could assess the device's ability to discern localized muscle activity patterns. The identification of motor unit innervation zones demonstrates the high spatial resolution achievable with the InSkin platform, showcasing its potential for detailed neuromuscular assessments.

This analysis is significant as it highlights a key advantage of the high-density electrode array design. The ability to perform high-resolution spatial mapping of muscle activity opens up new possibilities in fields such as rehabilitation medicine, sports science, and human-computer interaction, where precise localization of neuromuscular activity is crucial.

Gesture Recognition Accuracy

To demonstrate the practical application of the InSkin device in advanced human-machine interfaces, we conducted gesture recognition tests:

- Method: Machine learning classification of EMG patterns
- Software: Custom Python scripts using TensorFlow
- Measurements: Classification accuracy, confusion matrix

The use of machine learning techniques, specifically implemented through TensorFlow, allowed us to process the complex, multi-channel EMG data acquired by the InSkin device. By training classification algorithms on these EMG patterns, we could assess the device's capability to distinguish between different hand gestures or movements.

The significance of this analysis extends beyond mere technical performance. High gesture recognition accuracy demonstrates the InSkin device's potential for intuitive and responsive human-machine interfaces. This has far-reaching implications in fields such as prosthetics control, virtual reality interaction, and assistive technologies. The use of a confusion matrix provides detailed insights into which gestures are most reliably distinguished, guiding future optimizations of both the hardware design and signal processing algorithms.

In conclusion, these characterization techniques provide a comprehensive evaluation of the InSkin device's performance in electrophysiological recording. From fundamental signal quality metrics to advanced spatial analysis and practical gesture recognition applications, these assessments validate the device's capabilities across a spectrum of potential use cases. The results obtained from these methods, to be presented and discussed in detail in Chapter 4, offer a holistic understanding of the InSkin platform's performance and its potential impact in the field of skin-interfaced electronics for biopotential recording.

3.4. Human Studies

To rigorously evaluate the performance of the InSkin device across diverse populations and skin conditions, we conducted a series of comprehensive human studies. These studies were meticulously designed to assess the device's adaptability, signal quality, and user comfort in real-world scenarios. The importance of human studies in validating the performance of skin-interfaced electronics cannot be overstated, as they provide critical insights that are unattainable through in vitro or animal studies alone.

3.4.1. Participant Recruitment and Ethics

Ensuring ethical conduct and participant safety were paramount in the design and implementation of these studies. We adhered to stringent ethical guidelines and implemented robust protocols for participant recruitment and data protection.

Ethical Approval

The study protocol underwent rigorous review and received approval from the Institutional Review Board at Michigan State University (IRB reference number: 00008023, Appendix

D). This approval process ensured that our research design prioritized participant safety and rights, adhering to established research ethics principles. All procedures were conducted in strict compliance with the Declaration of Helsinki and Good Clinical Practice guidelines, upholding the highest standards of ethical research conduct.

Participant Recruitment

To ensure a diverse and representative sample, we employed a multi-faceted recruitment strategy:

- Recruitment methods: We utilized campus advertisements and the online platform ResearchMatch.org to reach a wide pool of potential participants.
- Sample size: A total of 20 participants were recruited for the study.
- Age range: Participants ranged in age from 19 to 83 years, providing a broad spectrum of age groups for assessment.
- Gender balance: We achieved an equal gender distribution with 50% male and 50% female participants.
- Inclusion criteria: Healthy adults with no known skin conditions or neuromuscular disorders were eligible for participation.
- Exclusion criteria: Individuals who were pregnant or had open wounds or skin infections in the areas of electrode placement were excluded from the study.

The significance of this diverse participant pool lies in its ability to assess the InSkin device's performance across a range of age groups and skin types. This diversity is crucial for validating the device's inclusivity and adaptability, ensuring its effectiveness across a broad spectrum of potential users.

Informed Consent

Upholding the ethical principle of autonomy, we implemented a thorough informed consent process:

- All participants provided written informed consent prior to any study procedures.
- Participants were clearly informed of their right to withdraw from the study at any time without consequence.

This process ensures that participants fully understand the study procedures, potential risks, and their rights, thereby upholding ethical research practices and fostering trust between researchers and participants.

Privacy and Data Protection

To protect participant privacy and comply with data protection regulations, we implemented stringent data management protocols:

- Participant data was anonymized using randomly generated identification numbers, ensuring that individual identities were protected throughout the research process.
- All data was stored securely in encrypted formats on password-protected devices, safeguarding against unauthorized access.

By implementing these comprehensive ethical and recruitment protocols, we established a solid foundation for our human studies. This approach not only ensures the protection of participant rights and safety but also enhances the validity and applicability of our research findings. The diverse participant pool and rigorous ethical standards provide a robust framework for evaluating the InSkin device's performance in real-world conditions, across a variety of user demographics and skin types.

3.4.2. sEMG Recording Protocol

The surface electromyography (sEMG) recording protocol was meticulously designed to comprehensively assess the InSkin device's performance under various conditions. This protocol allows for a thorough evaluation of the device's capabilities across different skin types, movement conditions, and recording durations.

Electrode Placement

The electrode placement strategy was crucial for ensuring consistent and comparable measurements:

- Test site: The biceps brachii muscle was selected as the primary recording site due to its accessibility and the ease of eliciting controlled contractions.
- Electrode types: Three distinct electrode types were used for comparison: a) Commercial dry electrodes (CE) b) Solution CP-G electrodes c) Solution CP-G electrodes

- Electrode size: To ensure a fair comparison, all electrode types maintained a consistent size with a diameter of 10 mm.
- Inter-electrode distance: A bipolar configuration with an inter-electrode distance of 20 mm was employed for all recordings.

The significance of this setup lies in its ability to directly compare the performance of the InSkin electrodes (WG and WGP solutions) against commercial alternatives. The consistent electrode size and spacing across all types ensure that any observed differences in performance can be attributed to the electrode properties rather than geometrical factors.

Experimental Conditions

To evaluate the adaptability and robustness of the InSkin device, we tested it under a variety of conditions:

- Skin types: Recordings were made on both smooth and wrinkled skin, as well as hairy and shaved skin. This variety allows for assessment of the device's performance across different skin textures and conditions commonly encountered in real-world applications.
- Movement conditions: Both static and dynamic recordings were conducted. The dynamic condition involved arm flexion while squatting, simulating realistic movement scenarios.
- Recording durations: We conducted both short-term (5 minutes) and long-term (24 hours) recordings to assess the device's performance over varying time scales.

The significance of these varied conditions lies in their ability to assess the device's adaptability to different skin types and its performance during movement. These factors are crucial for evaluating the real-world applicability of the InSkin device across diverse user populations and usage scenarios.

Task Protocol

A standardized task protocol was implemented to ensure consistent muscle activations across participants:

- Participants performed 5 repetitions of bicep contractions.

- Contraction intensity was set at 70-80% of maximal voluntary contraction, providing a robust EMG signal while minimizing fatigue.
- Rest periods of 1 second were included between contractions to allow for muscle recovery.

This protocol's significance lies in its ability to provide a standardized set of muscle activations. This standardization is crucial for comparing signal quality across participants and electrode types, ensuring that observed differences can be attributed to electrode performance rather than variations in task execution.

Data Acquisition

High-quality data acquisition was essential for subsequent analysis:

- **Equipment:** An INTAN RHD recording controller with a 32-channel amplifier was used, providing high-resolution, multi-channel recording capabilities.
- **Sampling rate:** A sampling rate of 2.5 kHz was employed, ensuring capture of the full frequency spectrum of sEMG signals.
- **Filtering:** Signal conditioning included a high-pass filter at 10 Hz to remove motion artifacts, a low-pass filter at 500 Hz to prevent aliasing, and a notch filter at 60 Hz and its harmonics to remove power line interference.

The significance of these acquisition parameters lies in their ability to ensure high-quality sEMG recordings suitable for detailed signal analysis. The high sampling rate and appropriate filtering enable accurate capture of the sEMG signal while minimizing common sources of interference.

By implementing this comprehensive sEMG recording protocol, we established a robust framework for evaluating the InSkin device's performance. The protocol's design allows for systematic comparison across electrode types, skin conditions, and movement scenarios, providing a thorough assessment of the device's capabilities in realistic usage conditions. This approach not only validates the InSkin device's performance but also provides valuable insights into its adaptability and potential for various applications in electrophysiological monitoring.

3.4.3. Data Analysis Methods

To quantify the performance of the InSkin device and compare it with existing technologies, we employed rigorous data analysis methods. These methods were designed to provide comprehensive insights into various aspects of device performance, from signal quality to user comfort.

Signal Quality Metrics

To assess the quality of the recorded sEMG signals, we utilized several key metrics:

- **Signal-to-Noise Ratio (SNR):** Calculated as the ratio of RMS amplitude during contraction to RMS amplitude during rest. This metric provides a quantitative measure of how well the signal of interest (muscle activity) stands out from background noise.
- **Baseline noise:** Measured during rest periods, this metric quantifies the level of background noise in the recording, which is crucial for determining the device's sensitivity to low-amplitude signals.
- **Signal amplitude:** Peak-to-peak amplitude during contractions was measured to assess the device's ability to capture the full range of muscle activity.

The significance of these metrics lies in their ability to provide quantitative measures of signal quality. They allow for objective comparison of performance across different electrode types and experimental conditions, crucial for evaluating the InSkin device against commercial alternatives.

Impedance Measurements

To assess the quality of the electrode-skin interface, we conducted impedance measurements:

- **Method:** Two-electrode impedance measurement at 1 kHz
- **Timing:** Measured before and after each recording session

The significance of these measurements lies in their ability to provide insights into the quality of the electrode-skin interface, a critical factor in signal quality. Changes in impedance over time can indicate alterations in the interface, such as electrode drying or skin hydration changes, which can affect signal quality.

Motion Artifact Quantification

To assess the device's performance during movement, we quantified motion artifacts:

- Method: SNR variation
- Metric: Percent variation of the SNR from static to dynamic recordings

This analysis is significant as it quantifies the device's susceptibility to motion artifacts, a crucial factor for wearable bioelectronics during real-world use. Lower SNR variation indicates better stability of recordings during movement, a key feature for practical applications.

Comfort Assessment

User comfort is a critical factor for the adoption and long-term use of wearable devices:

- Tool: Validated 6-point comfort scale
- Timing: Assessed after short-term use and at the end of long-term (24-hour) wear

The significance of this assessment lies in its ability to quantify user experience, a crucial factor for the practical applicability of the InSkin device. High comfort scores, particularly after long-term wear, indicate the device's suitability for extended use in real-world scenarios.

Statistical Analysis

To ensure the robustness and significance of our findings, we employed rigorous statistical analyses:

- Software: OriginPro (2024a)
- Tests:
 - Paired t-tests for comparing electrode types
 - Repeated-measures ANOVA for comparing skin conditions and time points
- Significance level: $p < 0.05$

The significance of this rigorous statistical approach lies in its ability to ensure that observed differences in performance are statistically significant and not due to chance variations. This adds validity to our comparisons between the InSkin device and commercial alternatives, as well as across different experimental conditions.

By implementing these comprehensive data analysis methods, we established a robust framework for evaluating the InSkin device's performance. This multi-faceted approach, combining quantitative signal analysis, impedance measurements, motion artifact quantification, comfort assessment, and statistical rigor, provides a thorough and objective assessment of the device's capabilities. The results derived from these analyses offer valuable insights into the InSkin device's performance across various conditions and in comparison to existing technologies, forming a solid foundation for evaluating its potential impact in the field of wearable bioelectronics.

3.4.4. Gesture Recognition Study

The gesture recognition study was designed to evaluate the practical application of the InSkin device in human-machine interfaces. This study demonstrates the device's potential for advanced prosthetic control and intuitive interaction with digital systems

Gesture Set

A diverse set of hand gestures was carefully selected to test the device's capabilities:

- 10 hand gestures were chosen (e.g., fist, open hand, pinch, point)
- These gestures were selected to represent common daily activities and prosthetic control commands

The significance of this gesture set lies in its ability to test the device's capacity to distinguish between fine motor movements. This is crucial for advanced prosthetic control and human-machine interfaces, where the ability to accurately recognize a wide range of gestures can greatly enhance the user's control and interaction capabilities.

Data Collection

To ensure robust and reliable data for analysis, we implemented a structured data collection protocol:

- Two sessions were conducted on separate days to create training and testing datasets
- Electrode array placement: Aligned over the elbow crease for consistent landmark-based positioning
- Recording duration: 5 seconds per gesture, repeated 10 times

- Rest periods: 10 seconds between gestures to prevent fatigue

The significance of this protocol lies in its ability to ensure a robust dataset for training and testing the gesture recognition algorithm. The use of separate sessions for training and testing data helps to validate the algorithm's generalization capabilities. The consistent electrode placement and the inclusion of rest periods address important factors like electrode positioning consistency and participant fatigue, which could otherwise introduce variability into the data.

Machine Learning Analysis

To process and interpret the collected EMG data, we employed advanced machine learning techniques:

- Feature extraction: Both time-domain and frequency-domain features were extracted from the raw EMG signals
- Classification algorithm: A Convolutional Neural Network (CNN) was employed for gesture classification
- Training/Testing split: 80% of the data was used for training, with the remaining 20% reserved for testing
- Performance metrics: Classification accuracy and confusion matrix were used to evaluate the algorithm's performance

The significance of this analysis lies in its demonstration of the InSkin device's capability to provide high-quality signals suitable for advanced machine learning applications in gesture recognition. The use of a CNN, which can automatically learn relevant features from the data, showcases the richness of the information captured by the InSkin electrodes.

Real-time Control Demonstration

To validate the practical applicability of the InSkin system, we conducted a real-time control demonstration:

- Task: Control of a robotic hand prototype
- Method: Real-time classification of EMG signals to actuate robotic hand movements

- Performance assessment: Success rate in achieving target hand configurations and time to complete gestures were measured

The significance of this demonstration lies in its practical validation of the InSkin system's potential for intuitive prosthetic control applications. By showing that the system can accurately classify gestures and control a robotic hand in real-time, we demonstrate its potential to significantly improve the functionality and user experience of advanced prosthetics.

This comprehensive gesture recognition study serves multiple important purposes:

1. It demonstrates the InSkin device's capability to capture high-quality EMG signals that contain sufficient information for distinguishing between complex hand gestures.
2. It showcases the potential of the device for advanced human-machine interface applications, particularly in the realm of prosthetic control.
3. The real-time demonstration provides a tangible example of how the InSkin technology could be applied to improve the lives of individuals using prosthetic devices.
4. The study's results offer valuable insights into the performance capabilities of the InSkin system, helping to guide future development and optimization efforts.

By combining rigorous data collection, advanced machine learning analysis, and a practical real-time demonstration, this gesture recognition study provides a comprehensive evaluation of the InSkin device's potential for advanced bioelectronic applications. The results of this study, to be presented in detail in the subsequent chapter, offer compelling evidence for the device's capabilities and its potential impact in the field of human-machine interfaces and prosthetic control.

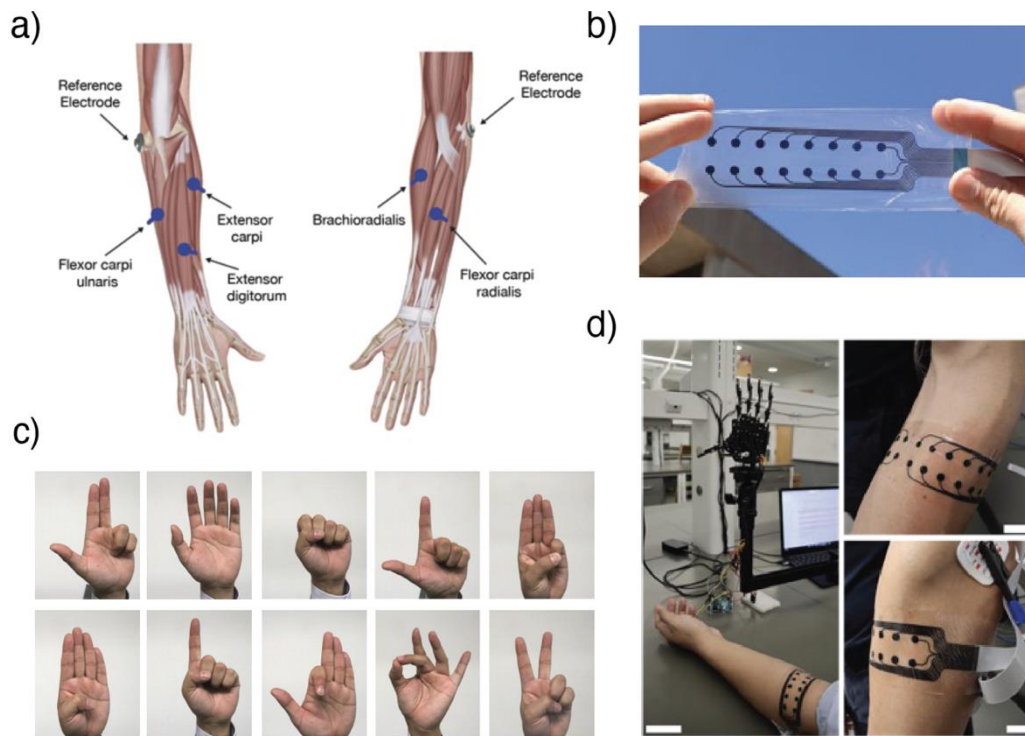


Figure 8: Overview of human studies protocol. (a) Electrode placement for the robotic hand control recordings. (d) Photograph of a 16-channel InSkin. (c) Examples of the 10 hand gestures used in the gesture recognition study. (d) Robotic hand prototype used for real-time control demonstration, and the 32-channel sEMG array applied to one of the subject's forearms.

3.4.5. Long-term Wearability Study

The long-term wearability study was crucial for assessing the InSkin device's suitability for continuous monitoring applications:

1. Duration: 24-hour continuous wear
2. Activities: Participants instructed to perform normal daily activities
3. Data collection:
 - Hourly EMG recordings during specified tasks
 - Continuous logging of device status (e.g., electrode contact)
4. Exit interview: Qualitative assessment of user experience, comfort, and any skin-related issues

- Significance: This study provides insights into the device's performance and user acceptability during extended wear in real-world conditions, critical for applications in continuous health monitoring.

These human studies were designed to provide a comprehensive evaluation of the InSkin device's performance across diverse user groups and usage scenarios. By combining quantitative performance metrics with qualitative user feedback, these studies offer a holistic assessment of the InSkin platform's potential for real-world applications.

The rigorous design of these studies, including diverse participant selection, standardized protocols, and comprehensive data analysis, ensures that the results provide a reliable and meaningful evaluation of the InSkin technology. Furthermore, the inclusion of both short-term performance assessments and long-term wearability studies addresses the full spectrum of potential use cases for skin-interfaced electronics.

Ethical considerations were at the forefront of study design and implementation, with particular attention paid to participant safety, informed consent, and data protection. These ethical practices not only protect study participants but also contribute to the overall integrity and reliability of the research findings.

The results from these human studies, presented and discussed in Chapter 4, provide crucial insights into the InSkin device's adaptability, signal quality, user comfort, and potential for real-world applications. These findings will inform future refinements of the technology and guide its development towards specific applications in healthcare, human-machine interfaces, and beyond.

3.5. Biopotential Recording Setup

The InSkin device was designed to record various biopotential signals, including surface electromyography (sEMG), electrocardiography (ECG), and electroencephalography (EEG). This versatility demonstrates the platform's potential for a wide range of applications in physiological monitoring and human-machine interfaces. This section details the specific setups used for each type of biopotential recording, highlighting the adaptability of the InSkin system.

3.5.1. Surface Electromyography (sEMG)

Surface electromyography represents a key application for the InSkin platform, offering valuable insights into muscle activity patterns for various medical and human-machine interface applications.

Recording System

The sEMG recording setup utilized state-of-the-art equipment to ensure high-quality data acquisition:

- Hardware: INTAN RHD recording controller
- Amplifier: 32-channel RHD recording headstage (INTAN Technologies)
- Software: RHX Data Acquisition Software (INTAN Technologies)

The significance of this high-channel-count system lies in its ability to facilitate high-density sEMG recordings. This capability is crucial for detailed muscle activity mapping, allowing for a more comprehensive understanding of complex muscle activation patterns.

Electrode Configuration

The electrode configuration was optimized for high-resolution muscle activity mapping:

- Array Design: 32-channel high-density array
- Electrode Spacing: 4 mm inter-electrode distance
- Reference Electrode: Placed on a bony prominence away from the recorded muscle (e.g., elbow)

The significance of this configuration is twofold. First, the high-density array with small inter-electrode distance enables high spatial resolution mapping of muscle activity. This allows for the detection of subtle variations in muscle activation across different regions of the muscle. Second, the careful placement of the reference electrode on a bony prominence minimizes crosstalk from other muscles, enhancing the signal specificity.

Signal Acquisition Parameters

The signal acquisition parameters were carefully selected to ensure optimal capture of the sEMG signals:

- Sampling Rate: 2.5 kHz
- Filtering:

- High-pass filter: 10 Hz
- Low-pass filter: 500 Hz
- Notch filter: 60 Hz and its harmonics

These parameters are significant as they ensure the capture of the full sEMG frequency spectrum while minimizing noise and interference. The high sampling rate of 2.5 kHz allows for an accurate representation of the high-frequency components of the sEMG signal, while the filtering strategy effectively removes low-frequency motion artifacts, high-frequency noise, and power line interference.

Muscle Groups Tested

To demonstrate the versatility of the InSkin system, multiple muscle groups were tested:

- Muscles: Forearm flexors and extensors

The significance of testing multiple muscle groups lies in demonstrating the adaptability of the InSkin system to various body locations and muscle sizes. This versatility is crucial for the system's potential applications in diverse fields such as rehabilitation, sports science, and prosthetic control.

Recording Protocol

A comprehensive recording protocol was implemented to assess the device's performance under various conditions:

- Resting state: 5 seconds
- Isometric contractions: 5 repetitions, 5 seconds each
- Dynamic movements: Flexion-extension cycles, 10 repetitions

The significance of this protocol is its ability to assess the device's performance under various muscle activation conditions, effectively mimicking real-world usage scenarios. The inclusion of both isometric and dynamic movements allows for evaluation of the system's ability to capture muscle activity during different types of contractions.

Real-time Visualization

Real-time visualization tools were employed to ensure data quality and provide immediate insights:

- Spectrograms for frequency content analysis

- Inter-spike interval histograms for motor unit firing pattern analysis

The significance of real-time visualization is twofold. First, it aids in ensuring data quality during recording, allowing for immediate identification and correction of any issues. Second, it provides instant insights into muscle activation patterns, which can be valuable for on-the-fly adjustments to experimental protocols or immediate feedback in clinical applications.

This comprehensive sEMG recording setup demonstrates the InSkin platform's capability to capture high-quality, high-resolution muscle activity data. The combination of advanced hardware, optimized electrode configuration, and carefully designed recording protocols positions the InSkin system as a powerful tool for detailed analysis of muscle function. The results obtained from this setup, to be presented in subsequent chapters, will provide crucial validation of the InSkin device's performance in capturing sEMG signals, a key indicator of its potential impact in fields ranging from clinical diagnostics to advanced human-machine interfaces.

3.5.2. Electrocardiogram (ECG)

The InSkin platform's ability to record ECG signals demonstrates its potential for continuous cardiac monitoring applications, significantly expanding its utility in healthcare settings. For ECG recordings, we employed the same INTAN RHD system used for sEMG, showcasing the versatility of the InSkin platform and its capacity for multi-modal physiological monitoring. This consistency in hardware across different signal types not only simplifies the overall system design but also potentially reduces costs in multi-modal monitoring scenarios.

We implemented a 3-electrode setup using a Modified Lead II configuration, with the positive electrode placed on the left lower chest, the negative electrode on the right upper chest, and the ground electrode on the left upper chest. This configuration is optimized for clear recording of the main ECG waveforms while minimizing motion artifacts. The Modified Lead II setup's widespread use in clinical practice allows for easy comparison with standard ECG recordings and seamless integration into existing medical workflows.

Signal acquisition parameters were carefully chosen to capture the full ECG frequency spectrum while addressing common challenges in ECG recording. We used a sampling rate of 2.5 kHz, with a high-pass filter at 0.5 Hz to minimize baseline wander, a low-pass filter at 100 Hz to remove high-frequency noise without losing important ECG waveform details, and a notch filter at 60 Hz to eliminate power line interference. Our recording protocol comprised three phases: a 5-minute resting state, 2 minutes of light exercise (stepping in place), and a 5-minute recovery period post-exercise. This protocol allows for assessment of ECG signal quality under both resting and mildly exertional conditions, simulating real-world usage scenarios. The inclusion of a light exercise phase is particularly important for evaluating the device's performance in capturing ECG signals during physical activity, a critical feature for continuous monitoring applications.

3.5.3. Electroencephalogram (EEG)

The InSkin platform's capacity to record EEG signals significantly expands its potential applications to include brain-computer interfaces and neurological monitoring. For EEG recordings, we again utilized the same INTAN RHD system used for sEMG and ECG, further demonstrating the platform's versatility and potential for comprehensive, multi-modal physiological monitoring. This capability is particularly valuable in research and clinical settings where simultaneous recording of multiple physiological signals is often required.

We implemented a 3-electrode setup optimized for alpha wave detection, a common marker of relaxation and cognitive state. The active electrodes were placed at FP1 and FP2 (frontal lobe), with the reference electrode at O2 (occipital lobe). This configuration allows for the capture of the characteristic anterior-posterior gradient of alpha activity, providing a robust test of the system's ability to detect spatially distributed brain activity.

Signal acquisition parameters for EEG were set to capture the frequency range of interest for most cognitive and clinical EEG applications. We used a sampling rate of 2.5 kHz, with a high-pass filter at 1 Hz to remove DC drift, a low-pass filter at 100 Hz to eliminate high-frequency noise, and a notch filter at 60 Hz to remove power line interference.

Our recording protocol consisted of two phases: 2 minutes with eyes open, followed by 2 minutes with eyes closed. This simple protocol allows for clear demonstration of alpha wave modulation, a key indicator of EEG signal quality. Our analysis focused on alpha wave detection (8-13 Hz) and changes in spectral power during different mental states, providing a straightforward validation of the InSkin system's ability to capture meaningful EEG signals.

The ability of the InSkin platform to effectively record ECG and EEG signals, in addition to sEMG, demonstrates its remarkable versatility. This multi-modal capability positions the InSkin device as a powerful tool for comprehensive physiological monitoring, with potential applications ranging from clinical diagnostics and patient monitoring to advanced brain-computer interfaces and cognitive state assessment.

3.5.4. Common Setup Features

Several features were common across all biopotential recording setups, ensuring consistency and reliability:

1. Skin Preparation:

- Gentle cleaning with water
- No abrasion to maintain skin integrity for testing InSkin's performance on unprepared skin
- Significance: Minimal skin preparation demonstrates the InSkin system's ability to function effectively in real-world conditions where extensive preparation may not be feasible. This approach simulates practical usage scenarios, where users may not have the time, expertise, or inclination to perform elaborate skin preparation procedures. By demonstrating high-quality signal acquisition on minimally prepared skin, the InSkin system showcases its potential for seamless integration into daily life monitoring applications.

2. Electrode-Skin Interface:

- Direct application of InSkin electrodes without additional conductive gels
- Monitoring of electrode-skin impedance throughout recordings

- Significance: This approach showcases the InSkin electrodes' ability to form a stable interface with the skin without additional conductive mediums, a key advantage for long-term wearability. The absence of conductive gels eliminates concerns about gel drying or irritation during extended wear. Continuous impedance monitoring provides real-time insight into the quality of the electrode-skin contact, allowing for immediate identification of any degradation in signal quality.

3. Data Storage and Processing:

- Raw data stored in proprietary INTAN format (RHD)
- Conversion to standard formats (e.g., EDF, CSV) for further analysis
- Python (Python, 3.12.3) used for signal processing and analysis
- Significance: The use of standard data formats and open-source analysis tools ensures reproducibility and facilitates comparison with other systems. By converting data to widely used formats like EDF and CSV, we enable interoperability with a broad range of analysis software and make our results accessible to the wider research community. The use of Python, a popular and well-documented programming language, further enhances the reproducibility of our analysis methods.

4. Quality Assurance:

- Continuous monitoring of signal quality during recordings
- Automatic detection and marking of artifacts
- Regular calibration of recording system using known signal inputs
- Significance: These measures ensure the reliability and validity of the recorded data, crucial for accurate interpretation of results. Real-time signal quality monitoring allows for immediate intervention if issues arise during recording sessions. Automatic artifact detection helps in post-processing by flagging potentially problematic data segments. Regular system calibration maintains the accuracy of our measurements over time, providing

confidence in the consistency of our results across different recording sessions.

This comprehensive biopotential recording setup enables the thorough evaluation of the InSkin device across various physiological signals. The ability to record sEMG, ECG, and EEG with the same system showcases the versatility of the InSkin platform, demonstrating its potential for multi-modal physiological monitoring in diverse applications ranging from healthcare to human-machine interfaces.

The consistency in recording equipment and protocols across different biopotential types allows for direct comparisons of performance, while the use of standard clinical electrode placements and recording parameters facilitates comparison with existing systems and integration into established clinical workflows. This approach not only validates the InSkin system's performance against current gold standards but also demonstrates its potential to seamlessly integrate into existing medical practices.

The results obtained from these recordings, presented and discussed in Chapter 4, will demonstrate the InSkin device's performance in capturing different types of biopotential signals, providing a comprehensive validation of its capabilities as a versatile platform for skin-interfaced electronics. These results will offer insights into the system's signal quality, stability over time, and ability to capture subtle physiological changes across different biopotential modalities, ultimately showcasing the InSkin platform's potential to advance the field of wearable bioelectronics.

3.5.5. Signal Processing and Analysis

The raw biopotential signals were processed using a custom Python script (version 3.13.4, python.org) to remove artifacts and extract relevant features. This custom approach allowed for tailored processing of the unique characteristics of the InSkin device's output. The processing pipeline included several sophisticated steps to ensure optimal signal quality:

1. Bandpass filtering (10-500 Hz for sEMG, 0.5-100 Hz for ECG, 1-50 Hz for EEG) using a 4th order Butterworth filter. This step was crucial for isolating the frequency ranges of interest for each biopotential signal type. The specific ranges were chosen

based on established physiological signal characteristics: sEMG requires a wider bandwidth to capture fast muscle fiber action potentials, ECG focuses on the lower frequency range typical of cardiac activity, and EEG targets the frequency band most relevant for cognitive and clinical applications.

2. Notch filtering at 60 Hz to remove power line interference. This step is essential for eliminating the ubiquitous electrical noise from power lines, which can significantly distort biopotential signals. The 60 Hz notch filter specifically targets the frequency of the North American power grid.
3. Adaptive noise cancellation using a least mean squares (LMS) algorithm to reduce motion artifacts. This advanced technique is particularly valuable for wearable systems like InSkin, as it can dynamically adjust to changing noise conditions often encountered in real-world use. The LMS algorithm continually updates its parameters to minimize the difference between the desired signal and the noise-corrupted signal.
4. Wavelet denoising using a sym4 wavelet with soft thresholding. This step provides an additional layer of noise reduction while preserving important signal features. The sym4 wavelet was chosen for its ability to effectively represent the types of signals encountered in biopotential recordings, while soft thresholding offers a more gradual approach to noise reduction compared to hard thresholding.

Following the noise reduction steps, feature extraction was performed on the processed signals. This step is crucial for transforming the raw time-series data into meaningful, quantitative metrics that can be used for analysis and classification. The extracted features included:

- Root mean square (RMS) amplitude: This provides a measure of the signal's power and is particularly useful for quantifying muscle activation in sEMG signals.
- Mean frequency: This offers insights into the overall frequency distribution of the signal, which can be indicative of fatigue in sEMG or cognitive states in EEG.
- Median frequency: Similar to mean frequency, but less sensitive to outliers, providing a robust measure of the signal's frequency content.

- Spectral entropy: This measure quantifies the complexity or irregularity of the signal in the frequency domain, which can be particularly informative for EEG analysis.

These features were carefully selected to provide a comprehensive representation of the signals' characteristics in both time and frequency domains. They serve a dual purpose: firstly, they allow for quantitative comparison of signal quality across different experimental conditions and electrode types. Secondly, they form the basis for more advanced analysis techniques.

The extracted features were used for subsequent analysis, providing insights into the performance of the InSkin device across different biopotential recording scenarios. Moreover, they served as inputs for the gesture recognition algorithm described in section 3.6, demonstrating the practical application of the InSkin system in advanced human-machine interface scenarios. This connection between signal processing and practical application highlights the translational potential of the InSkin technology, bridging the gap between basic signal acquisition and real-world use cases in fields such as prosthetics control and human-computer interaction.

3.6. Robotic Hand Control System

A robotic hand control system was developed to demonstrate the practical application of the InSkin device in human-machine interfaces. This system integrates the high-density sEMG recordings from the InSkin device with machine learning algorithms to enable intuitive control of a prosthetic hand prototype. This application showcases the potential of the InSkin platform for advanced prosthetic control and other human-machine interface applications.

3.6.1. Gesture Classification Algorithm

The gesture classification algorithm, a crucial component of the robotic hand control system, was designed to translate the sEMG signals into meaningful control commands with high accuracy and efficiency (Summarized in Table 4).

The process began with data preprocessing, which involved segmenting the sEMG data into 1-second non-overlapping windows. This segmentation approach allowed for

consistent analysis of the signal over time. A bandpass filter ranging from 20 to 500 Hz was then applied to remove motion artifacts and high-frequency noise, ensuring a clean signal for further processing. To account for inter-subject variability, Z-score normalization was performed on the filtered data. These preprocessing steps were critical in providing a consistent and noise-free input to the classification algorithm, thereby improving the overall system performance.

Feature extraction was the next crucial step in the process. A comprehensive set of features was derived from both the time and frequency domains to capture the full spectrum of information contained in the sEMG signals. Time-domain features included mean absolute value, waveform length, zero crossings, and slope sign changes. These features effectively captured the temporal characteristics of muscle activity. Complementing these, frequency-domain features were extracted by calculating the power spectral density in five frequency bands: 20-50 Hz, 50-100 Hz, 100-150 Hz, 150-200 Hz, and 200-250 Hz. This combination of time and frequency domain features provided a robust representation of the sEMG signals, encapsulating both temporal and spectral aspects of muscle activity.

The heart of the classification system was a Convolutional Neural Network (CNN), chosen for its ability to effectively learn spatial and temporal patterns in high-density sEMG data. The CNN architecture was carefully designed to balance complexity with performance. The input layer accepted data from 32 channels, each containing 2500 time points, corresponding to 1 second of data sampled at 2.5 kHz. The network consisted of three convolutional layers with 32, 64, and 128 filters respectively, each using a 3x3 kernel size and ReLU activation function. Max pooling layers were introduced after each convolutional layer to reduce spatial dimensions and computational load. Two fully connected layers with 128 and 64 nodes followed, incorporating a dropout rate of 0.5 for regularization to prevent overfitting. The output layer comprised 10 nodes, corresponding to the 10 gestures, with SoftMax activation for probabilistic classification.

The model training process was designed to ensure robust performance and generalization. The dataset was split with 80% used for training and 20% for testing. The Adam optimizer was employed along with a categorical cross-entropy loss function, chosen for its

effectiveness in multi-class classification problems. The model was trained for up to 50 epochs, with early stopping implemented based on validation loss to prevent overfitting. To further improve generalization, data augmentation techniques including random time shifts and Gaussian noise addition were applied to the training data.

For real-time classification, a sliding window approach was implemented with a 1-second window and a 200 ms step size, allowing for responsive yet stable gesture recognition. To ensure reliability, only predictions with a confidence level exceeding 95% were accepted. Additionally, a debouncing mechanism was introduced, requiring a minimum of 500 ms between gesture changes to prevent rapid fluctuations and enhance the smoothness of the robotic hand control.

This comprehensive approach to gesture classification, from preprocessing through to real-time implementation, enabled the InSkin system to provide accurate and responsive control of the robotic hand, representing a significant advancement in prosthetic control technology.

Table 4: Key Parameters of the InSkin Gesture Classification Algorithm

Component	Parameter	Value/Description
Data Preprocessing	Window Size	1 second
	Window Overlap	None (non-overlapping)
	Bandpass Filter	20-500 Hz
	Normalization	Z-score
Feature Extraction	Time-domain Features	Mean absolute value, waveform length, zero crossings, slope sign changes
	Frequency-domain Features	Power spectral density in 5 bands: 20-50 Hz, 50-100 Hz, 100-150 Hz, 150-200 Hz, 200-250 Hz

Table 4 (cont'd)

CNN Architecture	Input Layer	32 channels $\times$ 2500 time points
	Convolutional Layers	3 layers (32, 64, 128 filters)
	Kernel Size	3 $\times$ 3
	Activation Function	ReLU
	Pooling	Max pooling after each conv layer
	Fully Connected Layers	2 layers (128 and 64 nodes)
	Dropout Rate	0.5
	Output Layer	10 nodes with SoftMax activation
Model Training	Dataset Split	80% training, 20% testing
	Optimizer	Adam
	Loss Function	Categorical cross-entropy
	Max Epochs	200
	Early Stopping	Based on validation loss
	Data Augmentation	Random time shifts, Gaussian noise addition
Real-time Classification	Sliding Window	1-second window, 200 ms step size
	Confidence Threshold	>95%
	Debouncing	500 ms minimum between gesture changes

3.6.2. Hardware Framework

The hardware framework of the InSkin system integrates the device with a robotic hand prototype, demonstrating a complete human-machine interface system (Table 3). At the core of this setup is an anthropomorphic robotic hand designed to mimic human hand functionality. This hand features five individually actuated fingers, each controlled by a dedicated servo motor, allowing for intuitive control and the demonstration of fine motor skills.

The system's brain is an Arduino UNO microcontroller based on the ATmega328P chip from Microchip Technology. This versatile platform performs several crucial functions: convert analog sensor inputs to digital signals, control the servo motors via PWM (Pulse Width Modulation) signals, and communicate with the PC through a serial interface. The Arduino's flexibility and accessibility make it ideal for interfacing between the classification algorithm and the robotic hand.

To ensure precise control of the servo motors, a 16-channel PWM Servo Motor Driver (PCA9685 from NXP Semiconductors) is employed. This dedicated driver generates the accurate PWM signals necessary for smooth and stable motor control, which is essential for fluid hand movements.

Two separate power supplies meet the system's power requirements. A 5V, 5A supply is dedicated to the servo motors, while a separate 5V, 1A supply powers the microcontroller and logic circuits. This separation ensures stable operation of both the high-current motors and the sensitive control electronics, preventing potential interference.

Wireless communication is implemented using a Bluetooth module (HC-05) to enhance the system's practicality and user mobility. This module enables the untethered operation of the robotic hand by facilitating wireless communication between the PC and the microcontroller.

Table 5: Key Components and Specifications of the InSkin Robotic Hand Hardware Framework

Component	Specifications	Function
Robotic Hand	5 individually actuated fingers	Mimics human hand functionality
Actuation	5 servo motors (one per digit)	Provides precise finger control
Microcontroller	Arduino UNO (ATMega328P)	Processes inputs and controls outputs
Motor Driver	16 CH PWM Servo Motor Driver (PCA9685)	Generates precise PWM signals for motor control
Power Supply	5V, 5A (servo motors) 5V, 1A (microcontroller and logic)	Ensures stable power for all components
Wireless Communication	Bluetooth module (HC-05)	Enables untethered operation

3.6.3. Software Framework

The software framework of the InSkin system integrates various components to enable seamless operation from signal acquisition to robotic hand control (Table 6). At the heart of this framework is a signal processing pipeline implemented in Python 3.12. This pipeline utilizes NumPy for efficient numerical operations and SciPy for advanced signal processing tasks. By efficiently processing raw sEMG data into a format suitable for the classification algorithm, this pipeline forms the crucial first step in the data flow.

The machine learning component of the system is implemented using TensorFlow 2.6 with the Keras API. To achieve real-time processing of the high-dimensional sEMG data, the system leverages GPU acceleration through CUDA. This powerful combination allows for rapid classification of complex sEMG patterns, enabling responsive control of the robotic hand.

Custom C++ firmware runs on the Arduino microcontroller, handling motor control and sensor reading tasks. This firmware implements a simple yet effective communication protocol for PC communication, translating high-level commands from the classification algorithm into precise motor control signals for the robotic hand.

The user interface is developed in Python using the PyQt5 framework for GUI creation. This interface offers several key features: real-time visualization of sEMG signals, display of classified gestures, manual control options for system testing, and data logging for performance analysis. By providing real-time feedback to users and researchers, this graphical interface plays a crucial role in system evaluation and user training.

Table 6: Key Components and Implementation Details of the InSkin Software Framework

Component	Implementation Details	Function
Signal Processing Pipeline	Python 3.12 NumPy, SciPy libraries	Processes raw sEMG data for classification
Machine Learning	TensorFlow 2.6 with Keras API GPU acceleration (CUDA)	Classifies sEMG data in real-time
Arduino Firmware	Custom C++	Controls motors and reads sensors
PC Interface	Python with PyQt5	Provides GUI for system control and monitoring

3.6.4. System Integration and Workflow

The integration of the various components creates a complete closed-loop system for intuitive robotic hand control (Table 7). This system demonstrates the practical application of the InSkin technology in a real-world scenario.

The process begins with data acquisition, where high-quality sEMG signals are captured by the InSkin device. These signals are then streamed to a PC via Bluetooth using an

INTAN amplifier. This initial step showcases the InSkin device's capability to provide robust sEMG data in a practical application setting.

Once received by the PC, the data undergoes real-time processing. This involves continuous segmentation of the incoming data into 1-second windows, followed by feature extraction and normalization. The real-time nature of this processing is crucial for ensuring responsive control of the robotic hand.

The preprocessed data is then fed into the trained Convolutional Neural Network (CNN) model for gesture classification. This classification process occurs every 200 milliseconds, allowing for frequent updates that enable smooth and natural control of the robotic hand.

Following classification, the system generates control signals. This involves mapping the classified gesture to predefined hand configurations and generating motor position commands based on the current and target hand configurations. This mapping process effectively translates abstract gesture classifications into concrete hand movements.

Finally, these control signals are sent to the Arduino microcontroller via Bluetooth. The Arduino interprets these commands and drives the servo motors accordingly. Importantly, the system utilizes position and force feedback for closed-loop control, ensuring accurate and stable hand movements (Figure 3.5).

Table 7: Key Stages and Processes in the InSkin Closed-Loop Robotic Hand Control System

Stage	Process	Update Frequency	Significance
Data Acquisition	sEMG capture and streaming	Continuous	Provides high-quality real-world data
Real-time Processing	Data segmentation and feature extraction	1-second windows	Enables responsive control
Gesture Classification	CNN model prediction	Every 200 ms	Allows smooth, natural hand control

Table 7 (cont'd)

Control Generation	Signal	Gesture-to-movement mapping	After each classification	Translates gestures to concrete movements
Robotic Actuation	Hand	Servo motor control with feedback	Continuous	Ensures accurate, stable hand movements

This integrated system demonstrates the InSkin device's capability to provide high-quality sEMG signals suitable for advanced prosthetic control. The combination of the high-density electrode array, sophisticated machine learning algorithms, and responsive robotic hand creates a platform for intuitive and precise control, potentially improving the functionality and user experience of prosthetic devices. The robotic hand control system serves as a proof-of-concept for the broader potential of the InSkin platform in human-machine interfaces. It showcases how the high-fidelity, multi-channel sEMG recordings enabled by InSkin can be translated into meaningful control signals for complex mechanical systems. This demonstration has implications beyond prosthetics, pointing to potential applications in fields such as robotics, virtual and augmented reality interfaces, and adaptive assistive technologies.

Furthermore, the system's modular design and use of widely available components (Arduino, TensorFlow, etc.) highlight future expansion and customization potential. This could facilitate adoption and further development by researchers and developers in various fields, potentially accelerating the translation of InSkin technology into diverse real-world applications.

Chapter 4 will present and discuss in detail the performance of this robotic hand control system, including metrics such as classification accuracy, response time, and user experience. These results will provide crucial insights into the practical applicability of the InSkin platform for advanced human-machine interfaces.

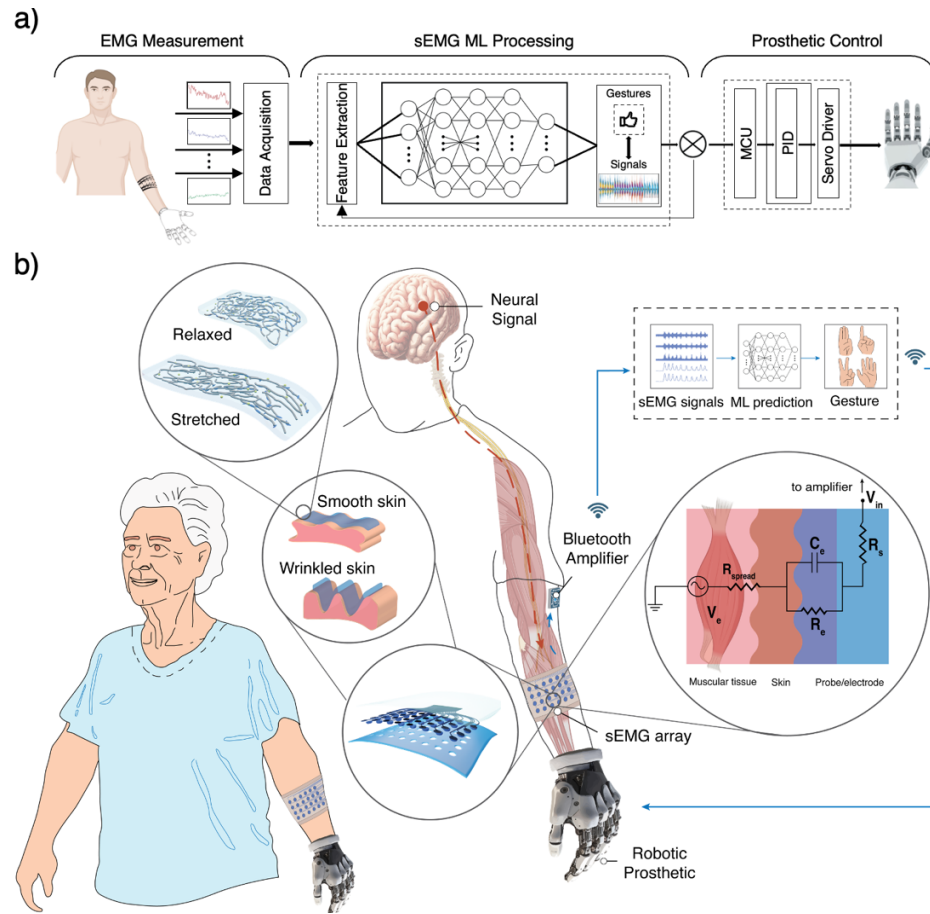


Figure 9: Robotic hand control system overview. (a) Block diagram of the entire system from sEMG acquisition to robotic hand movement. (b) Visual illustration of the InSkin application, from material properties to prosthetic control.

Chapter 4: Results and Discussion

This chapter presents a comprehensive analysis of the mechanical, electrical, and electrochemical properties of the InSkin device, alongside its performance in various sEMG applications. The findings are discussed in the context of the device's potential for practical implementation in wearable bioelectronics, with an emphasis on its adaptability to diverse skin conditions, long-term stability, and user comfort. Detailed statistical analyses and additional data supporting the results presented here can be found in Appendix B. These results underscore the advancements made by the InSkin device in comparison to existing technologies, highlighting its capability to maintain high-fidelity biopotential recordings under various mechanical strains and skin types. The implications of these findings for both research and clinical applications are considered, with particular attention given to the device's utility in high-density sEMG mapping, gesture recognition, and prosthetic control.

4.1. Mechanical Properties of InSkin

The InSkin device's mechanical properties are crucial for its ability to conform to diverse skin topographies and maintain performance during body movements. This section presents the results of our mechanical characterization studies and discusses their implications for the device's functionality.

4.1.1. Stretchability and Elasticity

The InSkin device, based on the optimized Solution CP-G 250 composite, demonstrated exceptional stretchability and elasticity. Its stress-strain behavior, as shown in Figure 4.1c, revealed an ultimate elongation of $1000\% \pm 15\%$ and a Young's modulus of 0.4 ± 0.1 MPa ($n = 10$ samples for both measurements). These values are comparable to human skin, which has an ultimate elongation of 35-115% and a Young's modulus of 0.1-0.8 MPa¹⁵⁷. Analysis of the stress-strain curves, presented in Figure 4.1c, revealed an initial toe region, followed by a linear elastic region and a plastic region. This behavior allows the device to stretch easily at low strains, effectively mimicking skin mechanics.

When compared to other skin-interfaced electronic materials, as shown in Table 8, InSkin demonstrated superior stretchability while maintaining a low Young's modulus.

Table 8: Extensive Summary of Mechanical Properties for Materials in Skin-Interfaced Electronic Devices and Applications

Material/Design	Young's Modulus (kPa)	Stretchability (%)	Biodegradability	References
InSkin (Solution CP-G250)	400 ± 100	1000 ± 15	Not reported	This work
Human Skin	100-800	35-115	N/A	92,157
EGaIn	≈ 2	>1000	Limited	67-69
Hydrogels	10-1000	Up to 1000	Good (natural polymers)	59-61
PEDOT:PSS	≈ 100	Up to 300	Limited	88-90
AgNWs/PDMS	≈ 100	Up to 500	Limited	63,64,96
Ultrathin Plastic	≈ 10	>100	Good (biodegradable plastics)	65,80,81
Serpentine	Tunable	Up to 800	Dependent on substrate	70-72
Mesh	Dependent on structure	Up to 1600	Dependent on materials	73-75

This comparison highlights the advantages of InSkin over traditional conductive polymers in terms of mechanical properties suited for skin-interfaced applications.

It's important to note that while the free-standing Solution CP-G250 shows an ultimate elongation of $250\% \pm 15\%$, the Artificial Skin (AS) supported material composing the InSkin interface achieves a remarkable stretchability of up to 1000%. At this maximum

elongation, the resistance ratio (R/R_0) is approximately 80 (Figure 4.1d). Considering the normal range of skin elasticity, this does not compromise the interface's functionalities and performance.

The stress-strain curve of InSkin exhibits characteristics of an elastoplastic material, primarily due to the waterborne polyurethane (WPU) that forms the material's elastic matrix. Adding glycerol softens the WPU, allowing for better flow of macromolecules and reducing internal polymer friction, improving the electromechanical behavior (Figure 4.1a).

4.1.2. Durability and Cyclic Performance

To assess the long-term mechanical stability of the InSkin device, we conducted comprehensive cyclic strain tests, the results of which are illustrated in Figure 4.1e. These tests provided crucial insights into the device's durability and performance under repeated stress conditions.

The stress-strain curves for 100 cycles at 100% strain, as depicted in Figure 4.1e, revealed minimal hysteresis (approximately 30%). This low hysteresis is indicative of excellent elastic recovery, suggesting that the InSkin device can maintain its structural integrity even after multiple stretching cycles. Furthermore, the maximum stress at 100% strain experienced only a marginal decrease of $5.2\% \pm 0.8\%$ after 100 cycles ($n = 5$ samples), underscoring the device's remarkable mechanical stability.

We also examined the resistance change under cyclic strain, with the results presented in Figure 4.1f. The graph displays the normalized resistance (R/R_0) during cyclic stretching, offering valuable information about the device's electrical performance under mechanical stress. Initially, at 100% strain, the normalized resistance (R/R_0) increased to 1.5 ± 0.1 in the first cycle. However, a notable improvement was observed over subsequent cycles. After 100 cycles, the maximum R/R_0 stabilized at 1 ± 0.05 , demonstrating enhanced electrical stability. This improvement can be attributed to the reorientation of conductive pathways within the composite material, which occurs as a result of repeated stretching.

To complement our quantitative analysis, we conducted a thorough mechanical fatigue analysis. Visual inspection of the InSkin device after 100 cycles at 100% strain revealed

no visible cracks or delamination. This qualitative assessment further supports the device's robust mechanical properties and its potential for long-term use in skin-interfaced applications.

These comprehensive cyclic strain tests collectively demonstrate the InSkin device's exceptional mechanical stability, elastic recovery, and electrical performance under repeated stress conditions, making it a promising candidate for durable and reliable skin-interfaced electronic systems.

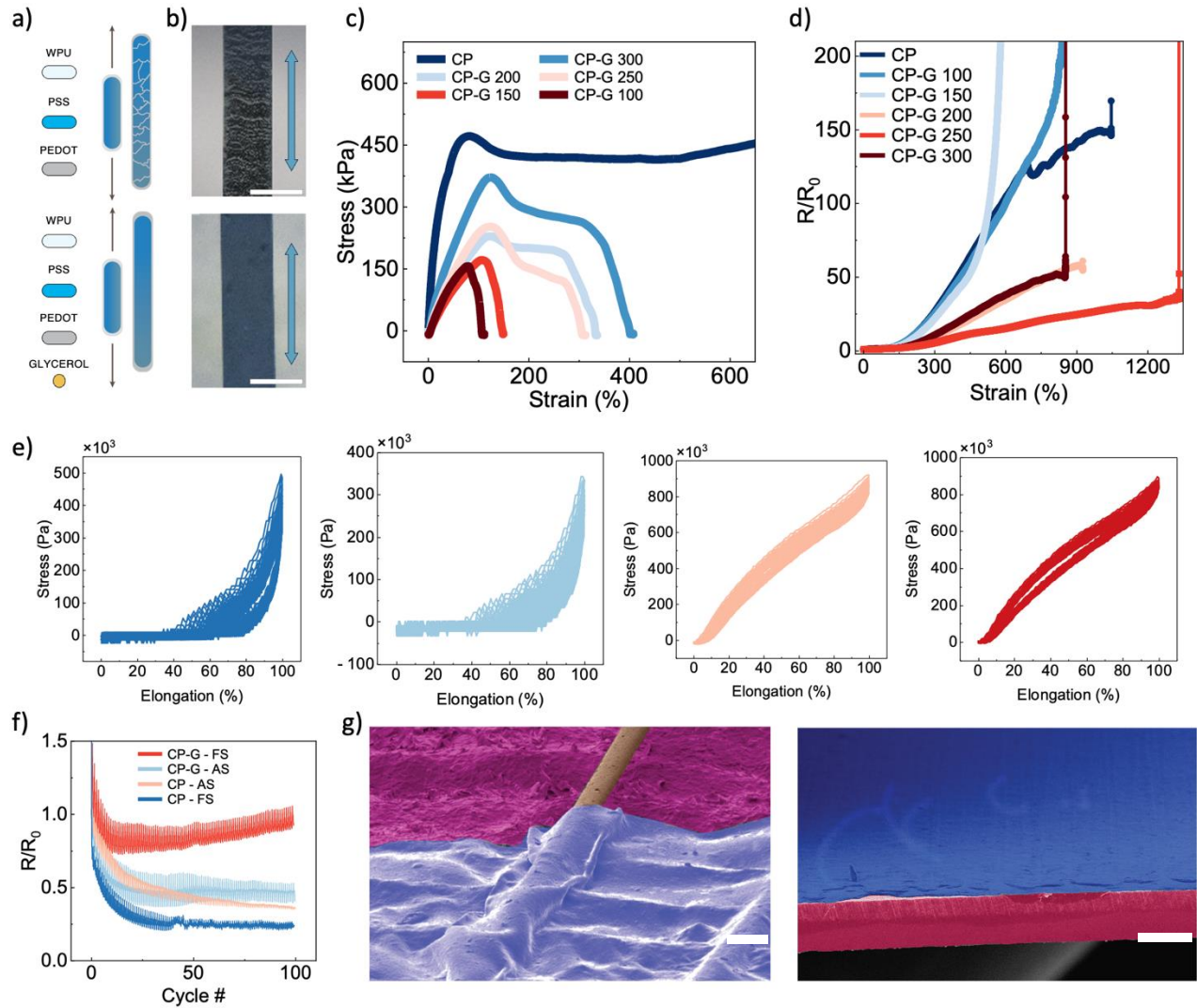


Figure 10: Mechanical characterization of InSkin. (a) illustration and (b) photo of the effect of the glycerol addition to the conductive composite during stretching: Solution CP (top) presents the formation of cracks along the transverse direction, whereas Solution CP-G (bottom) does not, scale bar: 1 cm. (c) Stress-strain curves, (d) Normalized resistance under strain, (e) Cyclic stress-strain curves for Solution CP, Solution CP-G, artificial skin-supported Solution CP, and artificial skin-supported Solution CP-G, (f) Normalized resistance under cyclic strain, and (g) SEM images showcasing the conformability of Solution CP-G on (left, scale bar 20 μ m) hairs and wrinkles and (right, scale bar 200 μ m) smooth skin.

4.1.3. Adhesion and Conformability

The ability of InSkin to adhere to and conform to the skin is a critical factor for stable electrophysiological recording, as illustrated in Figure 4.1g. To evaluate this crucial aspect, we conducted comprehensive long-term wear tests on human subjects ($n = 5$) over a 24-hour period. The results of these tests were highly encouraging, demonstrating that the InSkin device maintained more than 90% contact area throughout the entire duration of the test. This exceptional adherence is vital for ensuring consistent and reliable electrophysiological measurements, even during prolonged periods of wear and various daily activities.

The mechanical properties of the InSkin device collectively demonstrate its remarkable ability to mimic the mechanical behavior of human skin while simultaneously maintaining its essential electrical functionality. The synergistic combination of high stretchability, low modulus, and good adhesion enables the device to conform seamlessly to the complex topographies of human skin. This conformability is not limited to static situations but extends to accommodating the dynamic nature of body movements, which is crucial for maintaining stable electrode-skin contact.

The importance of these characteristics cannot be overstated in the context of electrophysiological recordings. By ensuring consistent contact and adaptability to movement, the InSkin device addresses one of the primary challenges in wearable bioelectronics: maintaining reliable measurements across diverse user populations and varying activity levels. Whether the wearer is sedentary or engaged in physical activity, the device's mechanical properties allow it to move with the skin, minimizing signal artifacts and ensuring data integrity.

In summary, the mechanical and adhesive properties of the InSkin device represent a significant advancement in skin-interfaced electronics. By closely mimicking the properties of human skin and demonstrating excellent long-term wearability with minimal irritation, the device sets a new standard for comfortable, reliable, and versatile electrophysiological monitoring systems.

4.2. Electrical and Electrochemical Characterization

The InSkin device's electrical and electrochemical properties are crucial for its ability to detect and transmit high-quality biopotential signals. This section presents the results of our comprehensive characterization studies and discusses their implications for the device's functionality in electrophysiological recording.

4.2.1. Conductivity Under Strain

The ability to maintain conductivity under mechanical deformation is essential for the InSkin device's performance during body movements:

The resistance-strain relationship of the InSkin device was thoroughly investigated, with results presented in Figure 4.2a. This graph shows the normalized resistance (R/R_0) as a function of applied strain for different WG compositions. Notably, Solution CP-G250 maintained conductivity up to 600% strain, with R/R_0 increasing to approximately 15 at maximum elongation. This performance surpasses many existing stretchable conductors, which typically fail electrically at lower strains^{81,158,159}

The strain-dependent conductivity mechanism of the InSkin device suggests a percolation-based conduction model. Figure 4.2b presents a schematic model of the conductive network reorganization under strain. The incorporation of glycerol in Solution CP-G250 likely facilitates the maintenance of conductive pathways during stretching, contributing to its superior performance.

The reversibility of electrical properties was also examined. Upon relaxation from 100% strain, the resistance of Solution CP-G250 returned to within 5% of its original value. This high reversibility was maintained for over 100 stretch-relax cycles, as demonstrated in Figure 4.1f. For Solution CP-G250-AS (artificial skin supported Solution CP-G 250), upon relaxation from 100% strain, the resistance returned to within 10% of its original value. This high reversibility was also maintained for over 100 stretch-relax cycles, highlighting the cycling stability of the material.

These results collectively demonstrate the InSkin device's ability to maintain conductivity under significant mechanical deformation, a crucial feature for its performance during various body movements and activities.

4.2.2. Impedance Analysis

Low electrode-skin impedance is crucial for high-quality biopotential recordings. We conducted extensive impedance spectroscopy studies:

Frequency-dependent impedance measurements, presented in Figure 4.2c and 4.2d as Nyquist and Bode plots, revealed the superior performance of the InSkin electrode (CP-G 250) compared to commercial dry Ag/AgCl electrodes (CE). At 100 Hz, a frequency relevant for EMG recordings, the InSkin electrode demonstrated an impedance of approximately 200 Ω (Figure 4.2e). This value is significantly lower than the impedance of commercial dry Ag/AgCl electrodes, which exhibited impedance around $10^4 \Omega$ at the same frequency.

To better understand the electrode-electrolyte interface, the impedance data were fitted to an equivalent circuit model, illustrated in Figure 4.2f. This model incorporates a constant phase element (C_{PE}) representing the electrode-electrolyte interface, in series with a resistance representing the bulk electrolyte. The CPE behavior ($\alpha = 0.85 \pm 0.03$) indicates a nearly ideal capacitive interface, which is beneficial for stable signal transduction. The equivalent circuit model can be represented as $R_s + C_{PE}$, where R_s is the solution resistance and C_{PE} is the constant phase element.

The stability of impedance under mechanical deformation was evaluated, with results shown in Figure 4.2g. The impedance magnitude at 100 Hz increased by only 38% when subjected to 100% strain, demonstrating excellent electrical stability under deformation. This characteristic is crucial for maintaining signal quality during body movements.

Finally, the consistency of the electrode array was assessed through impedance distribution measurements. Figure 4.2h displays the impedance distribution for a 32-channel array, showing a narrow distribution centered around 250-300 Ω . This tight distribution indicates consistent performance across all electrodes in the array, which is essential for reliable multi-channel recordings.

These electrical characterizations collectively demonstrate the InSkin device's excellent performance as an electrode material, combining low impedance, stability under deformation, and consistency across multiple channels.

4.2.3. Cyclic Voltammetry Results

Cyclic voltammetry (CV) was used to assess the electrochemical properties and stability of the InSkin electrodes:

Voltammogram analysis, presented in Figure 4.2i, shows cyclic voltammetry (CV) curves recorded in phosphate-buffered saline (PBS) for electrodes in Solution CP and Solution CP-G 250, unstretched and stretched at 60%. The Solution CP-G 250 electrodes demonstrated the largest enclosed area among the two, indicating high capacitance and rapid charge/discharge characteristics. Notably, the CV curves lack distinct redox peaks, suggesting a predominantly non-Faradaic charge transfer mechanism at the electrode-electrolyte interface.

Quantitative analysis of the electrochemical performance under mechanical stress is illustrated in Figure 4.2j. This graph displays the normalized enclosed area (A/A_0) of CV curves as a function of elongation for the two electrodes. The Solution CP-G 250 electrodes exhibited superior stability, maintaining over 90% of their initial enclosed area even when subjected to 100% strain. This performance significantly outpaces other electrode types

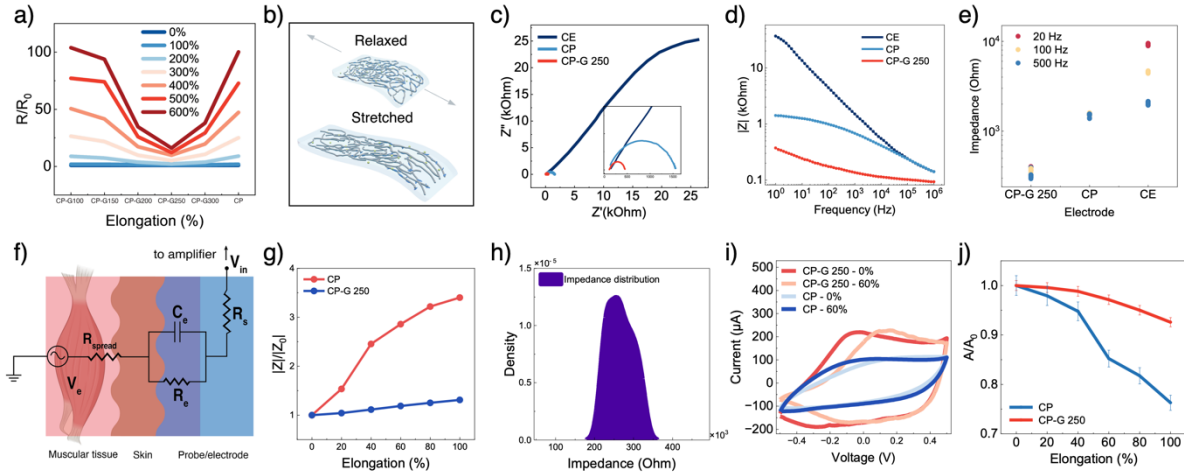


Figure 11: Electrical and electrochemical characterization of InSkin. (a) Normalized resistance vs. strain for Solution CP and the different Solution CP-G formulations, (b) Schematic of the conductive network under strain, (c) Nyquist plot for the different materials tested in this study, inset: zoom in the 0 – 1.5kΩ, (d) Bode plot of impedance, (e) Impedance at various frequencies of interest, (f) Equivalent circuit model for electrode-skin impedance, (g) Impedance change under strain, (h) impedance distribution density, (i) Cyclic voltammograms, (j) Normalized enclosed area as function of the elongation.

tested. The ability to maintain electrochemical stability under such substantial deformation is crucial for ensuring consistent performance during long-term use and accommodating various body movements.

The electrical and electrochemical characterization results demonstrate the exceptional performance of the InSkin device. The combination of high conductivity under strain and low electrode-skin impedance addresses key challenges in skin-interfaced electronics. These properties enable the device to maintain high-quality, stable biopotential recordings across diverse skin conditions and during various body movements, supporting its potential for long-term, reliable electrophysiological monitoring.

4.3. sEMG Performance Across Different Skin Conditions

A key objective of the InSkin project was to develop a device that performs consistently across diverse skin conditions. This section presents the results of our sEMG performance studies across different skin types, ages, and conditions.

4.3.1. Performance on Hairy vs. Shaved Skin and Wrinkled vs. Smooth Skin

We evaluated the performance of two electrode types (CE, and InSkin) across different skin conditions (smooth, wrinkled, and hairy) to assess their adaptability to various skin textures (Figure 4.3a and Figure 4.4a), measuring the sEMG signal (Fig 4.3c and Figure 4.4b-c). Figure 4.3b illustrates the mechanism of signal attenuation through the skin.

Impedance: InSkin demonstrated consistently low impedance across all skin conditions, ranging from 25 to 30 k Ω . This stability indicates excellent skin contact regardless of skin texture. CE exhibited the highest overall impedance, ranging from 380 to 580 k Ω across different skin conditions (Figure 4.3d-f and Figure 4.4f). **Signal Amplitude:** InSkin consistently outperformed the other electrode types, maintaining high signal amplitudes ranging from 0.48 to 0.62 mV across all skin conditions. CE demonstrated the lowest signal amplitudes, ranging from 0.08 to 0.20 mV, indicating poorer signal detection and transmission than the other types (Figure 4.3e and Figure 4.4e).

Signal-to-Noise Ratio (SNR): InSkin exhibited superior SNR performance across all skin conditions, with values ranging from 17 to 35. WG showed moderate SNR performance,

with values between 4 and 16. CE demonstrated the lowest SNR values, ranging from 2 to 10, suggesting higher susceptibility to noise interference (Figure 4.3f and Figure 4.4d). Direct Comparison: InSkin consistently outperformed CE across all metrics and skin conditions. It maintained the lowest impedance, highest signal amplitude, and best SNR, demonstrating superior adaptability to various skin textures. CE consistently showed the poorest performance, with high impedance, low signal amplitude, and low SNR across all skin conditions.

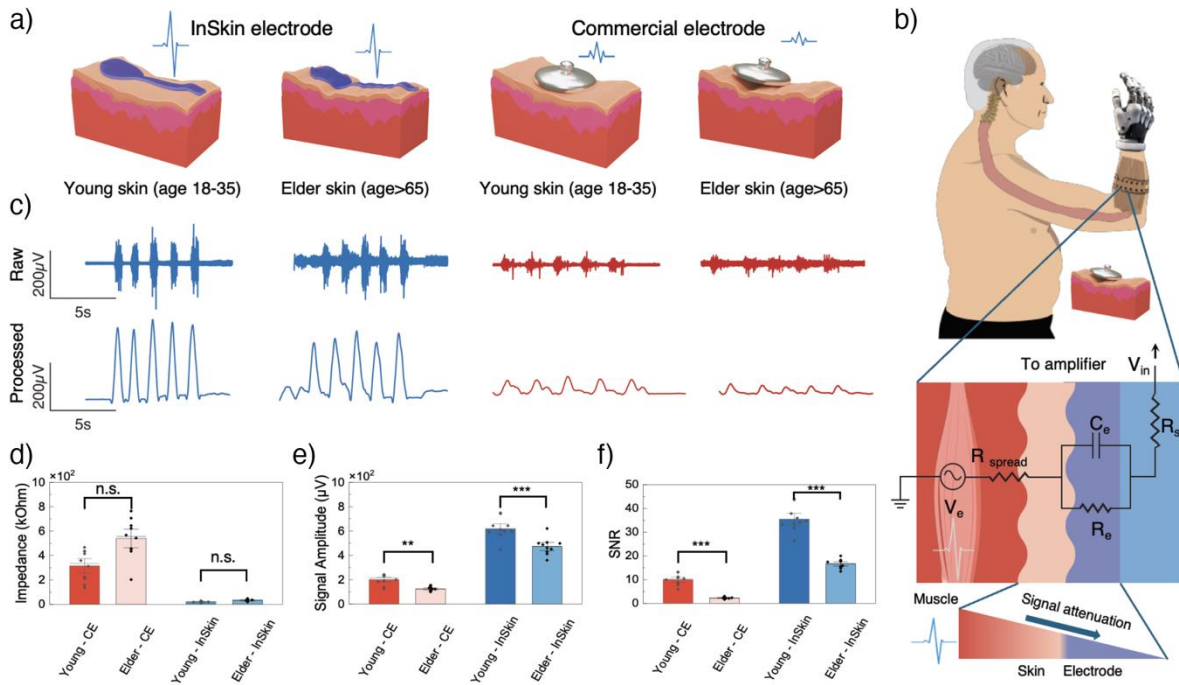


Figure 12: (a) Illustration of the electrode configurations employed to record sEMG signals, showing their different capability to conform to the skin's surface features. (b) Schematic diagram highlighting the importance of skin-electrode interface for signal attenuation. (c) Raw and processed sEMG signals recorded with CE and InSkin. (d) Impedance measurements for the three electrodes on a smooth, wrinkled, and hairy skin. (e) Signal amplitude for the three electrodes across different skin types. (f) Signal-to-noise ratio (SNR) for the electrodes on smooth, wrinkled, and hairy skin. (** n.s. not significant, ** $p < 0.05$, *** $p < 0.005$).

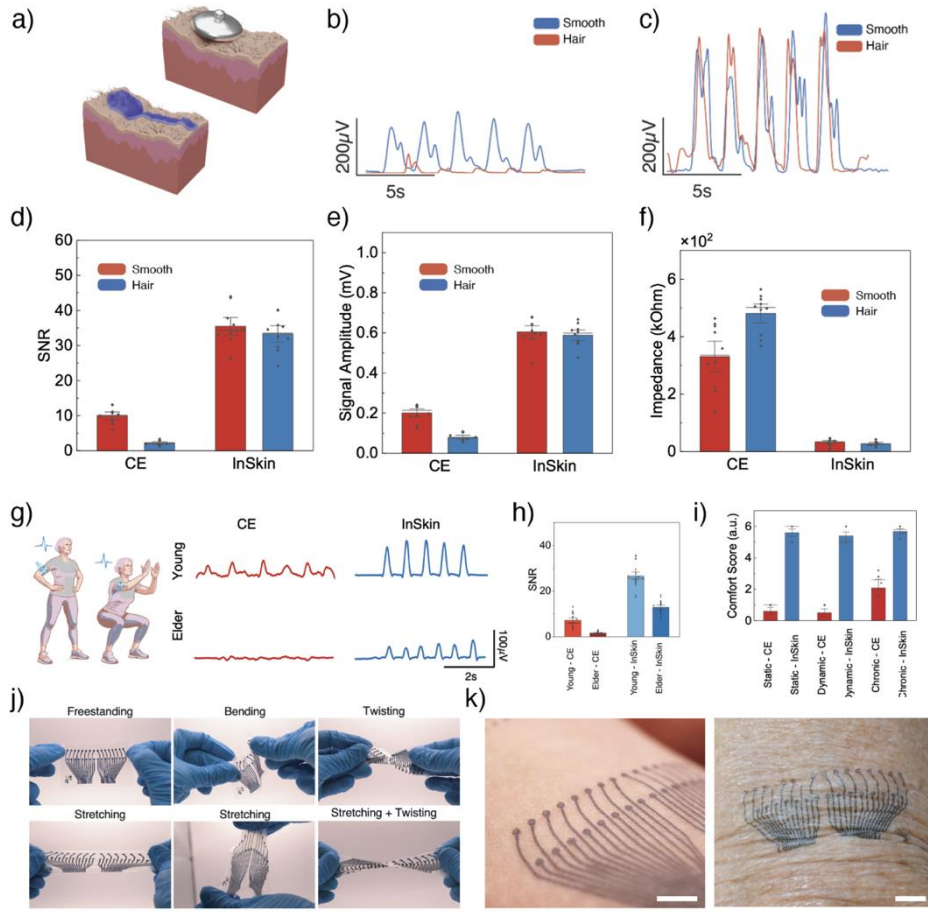


Figure 13: (a) Schematic illustration of the commercial electrode (CE) and solution CP-G 250 electrodes on hairy skin surfaces. (b), (c). Representative sEMG recordings from smooth (blue) and hairy (red) skin using CE (b) and CP-G 250 (c) electrodes. The CP-G 250 electrode demonstrates higher signal fidelity, particularly on hairy skin. (d). SNR comparison between CE and CP-G 250 electrodes on smooth and hairy skin, showing significantly higher SNR for CP-G 250, particularly on hairy skin. (e) Signal amplitude comparison, highlighting enhanced signal capture with CP-G 250 electrodes across both skin types. (f) Electrode-skin impedance measurements, with CP-G 250 showing significantly lower impedance on both skin types, indicating superior skin-electrode interface stability. (g) Illustration of an elderly individual performing activities while equipped with surface electrodes and sEMG signals during motion tests with CE and InSkin electrodes for young and elderly participants. (h) SNR comparison of sEMG signals between commercial and InSkin electrodes during motion for young and elderly participants. (i) User comfort scores for different electrodes during static, dynamic, and long-term wear, with statistical significance noted. (j) Photographs of the 32-channel sEMG array showing flexibility and stretchability under twisting, stretching, and complex deformation. (k) Photograph of an array made with Solution CP-G on skin, highlighting its conformality with skin's microscale features (scale bar: 5mm).

These results collectively demonstrate WGP's exceptional performance and adaptability across varying skin conditions, particularly its ability to maintain high signal quality and low impedance on wrinkled and hairy skin. This addresses key challenges in skin-interfaced electronics for diverse user populations, making WGP a promising option for applications requiring reliable electrode performance across different skin types and textures.

The difference in signal amplitude across different electrode types and skin conditions reflects how well each electrode can detect and transmit the electrical signals from muscle activity. Higher amplitudes generally indicate better signal detection and transmission. For example, Solution CP-G 250 (InSkin) consistently shows higher signal amplitudes across all skin conditions than CE and WG electrodes, suggesting it maintains better contact and signal quality regardless of skin type. The lower signal amplitude observed on wrinkled skin, often associated with elderly participants, can be attributed to multiple factors related to aging. As people age, their muscles typically weaken due to a process called sarcopenia, which involves the loss of muscle mass and strength. This muscular weakening results in lower electrical activity during muscle contractions, leading to reduced signal amplitude in electromyography (EMG) measurements.

These results collectively demonstrate InSkin's exceptional performance and adaptability across varying skin conditions, particularly its ability to maintain high signal quality and low impedance on wrinkled and hairy skin. This addresses key challenges in skin-interfaced electronics for diverse user populations.

Table 9: Comprehensive Comparison of Electrode Performance Across Smooth, Wrinkled, and Hairy Skin Surfaces in Bioelectronic Applications

Electrode Type	Skin Condition	Signal Amplitude (mV)	SNR	Impedance (kΩ)
CE	Smooth	0.20	10	310
	Wrinkles	0.12	2	580
	Hairs	0.08	2	330

Table 9 (cont'd)

InSkin	Smooth	0.62	35	30
	Wrinkles	0.48	17	25
	Hairs	0.62	33	25

4.3.2. Performance during Motion and Static Conditions

Figure 4.4 illustrates the performance of InSkin electrodes during motion, particularly comparing their efficacy between young and elderly subjects. The schematic (g) depicts an elderly individual engaged in two activities - standing and squatting - while wearing surface electrodes, setting the context for the subsequent data.

The sEMG signals in (g) show a clear difference in signal quality between CE and InSkin, with InSkin demonstrating much clearer and more defined waveforms for both young and elderly subjects. The SNR data in (h) quantifies this difference, showing that InSkin electrodes maintain a high SNR (around 35 for young and 25 for elderly subjects) compared to CE (about 7 for young and 5 for elderly subjects).

To evaluate user comfort, we compared the InSkin device (WGP) directly with commercial electrodes (CE) across static, dynamic, and long-term (chronic) wear conditions. As shown in Figure 4.4i, participants consistently rated the InSkin device significantly more comfortable than CE across all conditions ($p < 0.01$, $n = 20$ participants). The comfort scores for InSkin were notably higher, with mean scores around 5.5-6 out of 6 for all conditions, compared to CE scores which ranged from approximately 0.5 to 2. The difference in comfort was particularly pronounced during dynamic wear, where InSkin maintained its high comfort rating while CE received the lowest scores. Participants reported minimal skin irritation with InSkin and noted improved comfort during movement compared to CE.

Figure 4.4j showcases the array's exceptional flexibility and stretchability, demonstrating its ability to conform to complex body movements. The images show the InSkin array maintaining its integrity while freestanding, bending, twisting, stretching, and combining these deformations.

Finally, Figure 4.4k provides close-up views of the InSkin array adhering to skin, illustrating its remarkable conformality to microscale skin features. The images show the array conforming perfectly to skin textures and wrinkles, which is crucial for maintaining signal quality during motion.

These results highlight InSkin's superior performance, especially for elderly participants where motion artifacts typically pose greater challenges. The combination of high signal quality, comfort, and conformability to skin demonstrates InSkin's potential for reliable electrophysiological monitoring across diverse populations and movement conditions. The InSkin device's superior user experience, especially for extended monitoring applications where long-term comfort is crucial, further underscores its advantages over traditional electrodes.

4.3.3. Long-Term Stability and Comfort

The sEMG performance results demonstrate the superior adaptability and inclusivity of the InSkin device across various skin conditions. The device maintains high signal quality and low impedance on both smooth and wrinkled skin, as well as on hairy skin. This consistency in performance addresses a significant challenge in skin-interfaced electronics, particularly for elderly users or those with diverse skin types.

Furthermore, our comprehensive assessment of the InSkin device's long-term performance and user comfort over a 24-hour period yielded promising results (Figure 4.5a). The InSkin electrode maintained 75% of its initial signal-to-noise ratio (SNR) after 24 hours of continuous wear, as illustrated in Figure 4.5b. This demonstrates the device's ability to provide consistent, high-quality readings over extended periods, which is crucial for long-term monitoring applications.

The long-term stability and high user comfort of InSkin, combined with its adaptability to various skin conditions, strongly support its potential for extended wear in both clinical and everyday settings. These findings address key challenges in skin-interfaced electronics and pave the way for more inclusive and user-friendly bioelectronic devices.

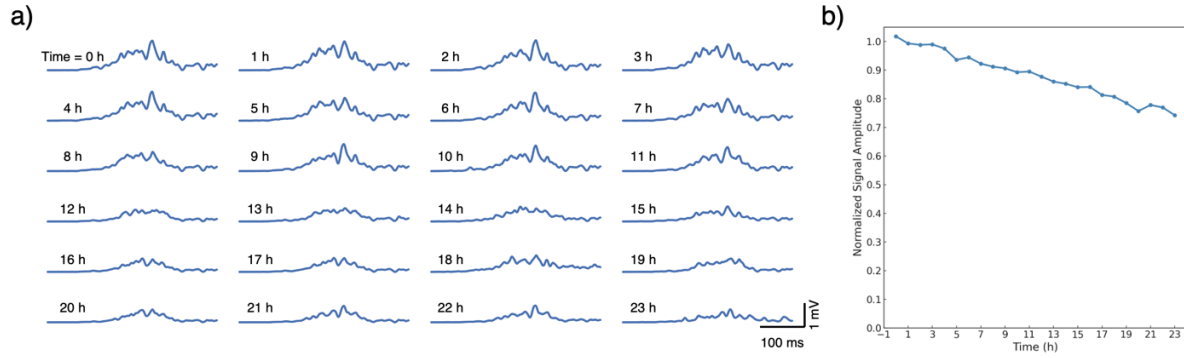


Figure 14: (a) sEMG recordings from a bicep brachii contraction at 1h intervals. (b) SNR evolution over 24 hours.

4.4. High-Density sEMG Mapping

The high-density electrode array of the InSkin device enables detailed mapping of muscle activity, providing insights into motor unit activation patterns and muscle fiber dynamics. This section presents the results of our high-density sEMG mapping studies and discusses their implications for both research and clinical applications.

4.4.1. Spatial Resolution and Signal Fidelity

We evaluated the spatial resolution and signal fidelity of the InSkin high-density array compared to conventional electrode configurations:

- 32-channel InSkin array
- Inter-electrode distance: 15 mm
- Total coverage area: 27 cm x 6 cm

Our evaluation of the InSkin high-density array revealed significant advancements in spatial resolution and signal fidelity compared to conventional electrode configurations. The layout of the 32-channel InSkin array, as depicted in Figure 4.6a, showcases sophisticated designs that maximizes spatial sampling capabilities.

One of the most striking improvements is the dramatic increase in sampling density. Within the same area where conventional setups typically employ only 4-6 electrodes, the InSkin array provides 32 sampling points (Figure 4.6b). This substantial increase in spatial resolution enables much more precise localization of muscle activity, offering researchers and clinicians unprecedented detail in their electrophysiological recordings.

The combination of high spatial density and consistent performance across all electrodes positions the InSkin array as a powerful tool for detailed muscle activity mapping. This level of precision opens up new possibilities for both research applications and clinical diagnostics, potentially enabling more accurate identification of specific muscle activation patterns and subtle changes in neuromuscular function.

4.4.2. Muscle Activity Visualization

The InSkin device's high-density mapping capabilities provide detailed visualization of muscle activity patterns, offering significant benefits for both research and clinical applications.

A key feature of the device is its ability to identify innervation zones with clarity. As shown in Figure 4.6c, an overlaid sEMG trace of the average sEMG amplitude during sustained contraction reveals a distinct band of high amplitude signals, indicating the innervation zone. This information is valuable for optimal electrode placement in clinical sEMG applications, potentially improving the accuracy of diagnoses and treatment plans.

The system's capability for high-resolution muscle mapping is illustrated in Figure 4.6d, which shows sEMG mapping of the forearm using a 32-channel array. The heatmaps, updated at 100ms intervals, provide a dynamic visualization of normalized signal amplitude changes across each channel. This level of detail allows for thorough analysis of muscle activation patterns during complex movements, offering insights that are challenging to obtain non-invasively with conventional methods. Notably, the InSkin device shows strong performance in gesture prediction, particularly for older subjects. Figure 4.6e presents a comparison of gesture prediction heatmaps between younger and older subjects, as well as between InSkin and conventional electrode (CE) arrays.

The results indicate improved machine learning performance of InSkin, with a particularly strong showing in elder subjects - a demographic that often faces challenges with existing technologies.

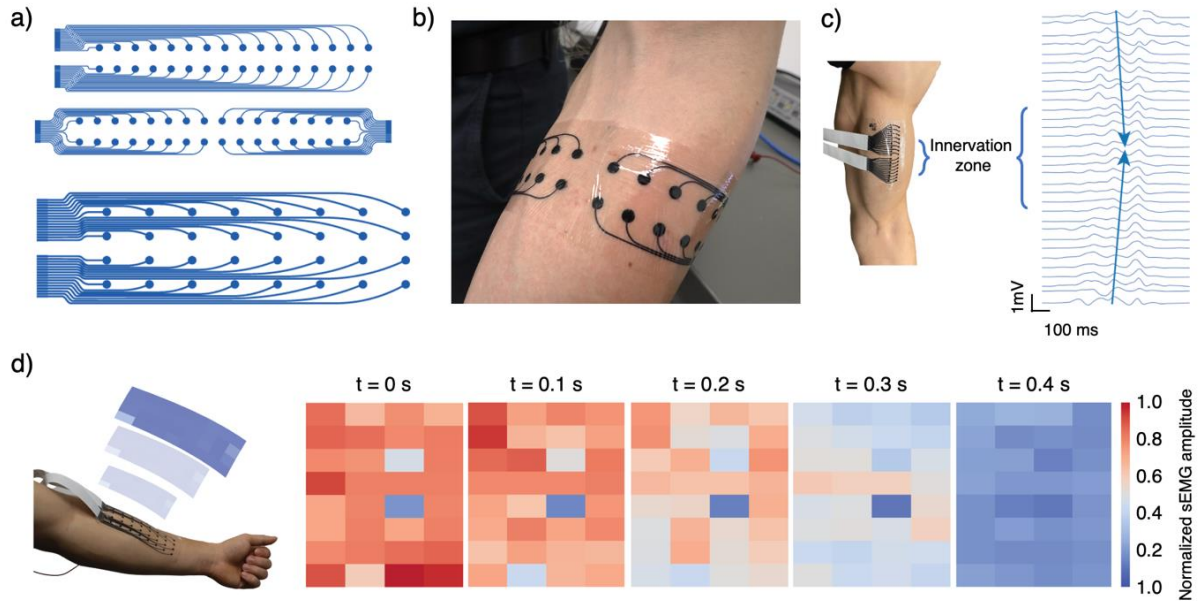


Figure 15: High-density sEMG mapping with InSkin. (a) 32-channel array layout, (b) Photo of the 3D-channel array used for prosthetic hand control, (c) sEMG signal for innervation zone localization, (d) sEMG mapping of the forearm.

In conclusion, the high-density sEMG mapping capabilities of the InSkin device make it a useful tool with diverse applications. Its combination of high spatial resolution, good signal fidelity, and adaptability to various skin conditions enables detailed, non-invasive assessment of muscle function. These capabilities create opportunities for studying motor control, diagnosing neuromuscular disorders, personalizing rehabilitation strategies, and developing advanced human-machine interfaces. As research progresses, the InSkin device may play a significant role in advancing our understanding of neuromuscular function and in developing more effective, personalized treatment strategies.

4.5. Gesture Recognition and Prosthetic Control

The high-fidelity sEMG signals and spatial resolution provided by the InSkin device offer significant potential for advanced gesture recognition and intuitive prosthetic control. This section presents the results of our gesture recognition studies and demonstrates the

application of InSkin in controlling a prosthetic hand prototype. The code developed for gesture recognition and robotic hand control is detailed in Appendix C).

4.5.1. Classification Accuracy

Our evaluation of the gesture recognition performance compared the InSkin device with commercial electrodes (CE) and Solution CP-G electrodes. The results demonstrate the capabilities of InSkin across various metrics.

In terms of overall accuracy, as shown in Figure 4.7a, InSkin achieved a classification accuracy of $97.7\% \pm 1.2\%$ for 10 hand gestures (Figure 4.7b, $n = 20$ participants). This performance was significantly higher than that of commercial electrodes, which achieved $62\% \pm 3.5\%$ accuracy. The difference in accuracy was statistically significant ($p < 0.001$, paired t-test).

A more detailed analysis of InSkin's performance is presented in the confusion matrix in Figure 4.7c. Most gestures were recognized with over 98% accuracy. The most challenging distinction was between the "one sign" and "four-finger up sign", which still achieved 91.8% accuracy.

The study also examined performance across different age groups, comparing younger (18-29 years) and older (65-85 years) participants. As illustrated in Figure 4.5c, InSkin maintained consistent accuracy in both groups ($95\% \pm 1.0\%$ for younger, $94\% \pm 1.4\%$ for older). In contrast, commercial electrodes showed a noticeable decrease in accuracy for older participants ($68\% \pm 1.0\%$ for younger, $62\% \pm 1.4\%$ for older).

Lastly, we analyzed the learning curve for gesture recognition. Figure 4.7d illustrates how classification accuracy changes as the number of gestures increases. InSkin maintained over 98% accuracy for up to 8 gestures, while commercial electrodes maintained this level of accuracy for only 2 gestures.

These results indicate that the InSkin device offers improved gesture recognition performance compared to commercial electrodes, particularly in maintaining accuracy across age groups and for a larger number of gestures.

4.5.2. Prosthetic Control Application

The signal processing pipeline, illustrated in Figure 4.7f, provides an overview of the steps from EMG measurement to machine learning-based prosthetic control. This pipeline encompasses data acquisition, feature extraction, gesture classification, and control signal generation, forming the foundation for accurate prosthetic hand control.

Figure 4.7i demonstrates the correlation between hand gestures and their respective sEMG signal patterns. This visual representation serves as a reference for gesture classification and highlights the distinct patterns associated with different hand movements, emphasizing the system's ability to differentiate various gestures.

A custom algorithm for gesture recognition in sEMG prosthetic control is detailed in Figure 4.7h. The algorithm segments EMG data into 1-second non-overlapping windows, classifying windows with accuracy exceeding 70% as valid gestures and others as transitions. A sliding observation window compares the signal with specific criteria, and recognized gestures are converted into finger angles for prosthetic hand control.

Classification performance is extensively analyzed through several visualizations. Figure 4.7a presents a confusion matrix showing prediction accuracy for ten trained gestures. Figure 4.7c compares gesture prediction heatmaps between younger and older subjects, as well as between InSkin and CE arrays. The relationship between the number of gestures and classification accuracy for different subject groups and electrode types is graphed in Figure 4.7d. Figure 4.7e displays sequential sEMG signals for different gesture states, demonstrating robust classification over time.

The practical application of the system is showcased in Figure 4.7g, which presents photos of the prosthetic robotic hand control setup with the multi-channel HD-sEMG array. The array is wrapped around the subject's forearm and connected to a wireless amplifier, illustrating the system's potential for real-world use.

The gesture recognition and prosthetic control results demonstrate the superior performance of the InSkin device in translating high-fidelity sEMG signals into intuitive and accurate control commands. The high classification accuracy, robustness to real-

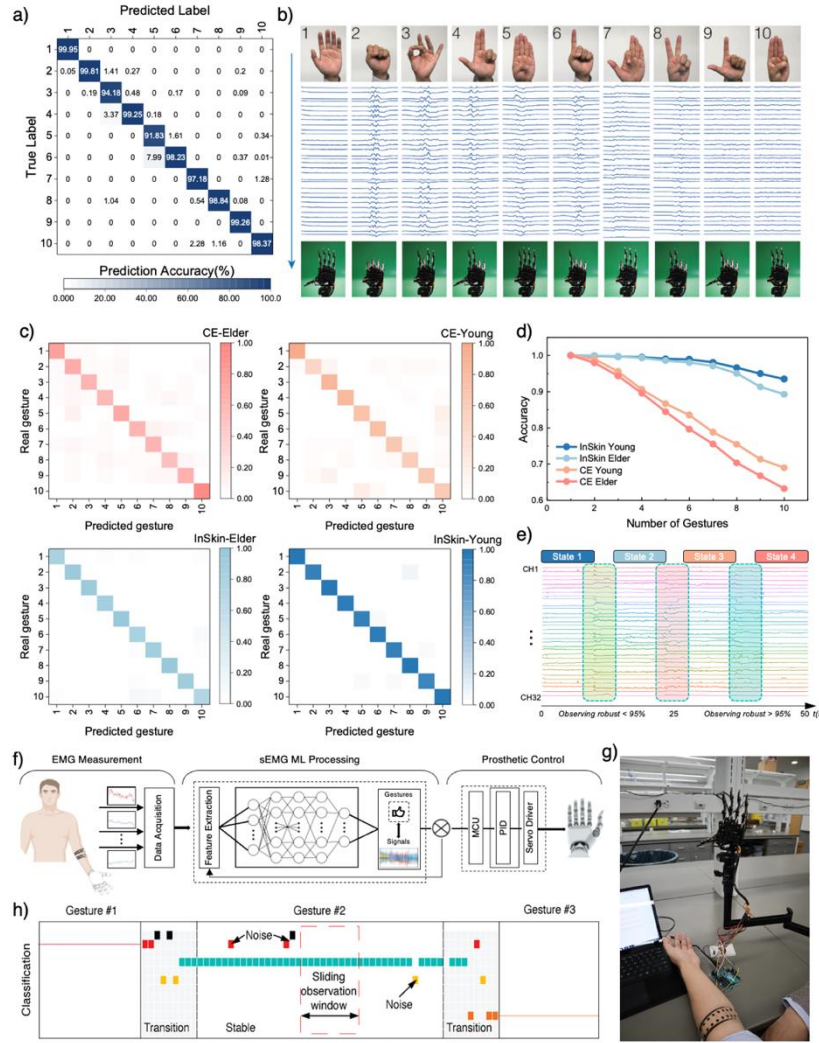


Figure 16 : (a) Confusion matrix of the DNN model used for gesture recognition showing the prediction accuracy values for each of the ten gestures used to train the model. I, Visual demonstration of hand gestures correlated with their respective sEMG signal patterns, providing a reference for gesture classification. (c) Comparison of gesture prediction heatmaps between younger and elder subjects and between InSkin and CE arrays, highlighting differences in machine learning performance. (d) Graph illustrating the relationship between the number of gestures and classification accuracy for younger and elder subjects with InSkin and CE sEMG arrays. (e) Sequential sEMG signals for different gesture states, displaying the robustness of signal classification over time. (f) An overview of the signal processing pipeline from EMG measurement to machine learning-based prosthetic control. (g) Photo of the prosthetic robotic hand control with the multi-channel HD-sEMG array, (h) Graphical representation of the gesture recognition algorithm. EMG data is segmented into 1-second windows, analyzed for valid gestures (>70% accuracy) or transitions, and processed through a sliding observation window. Recognized gestures are converted to finger angles for prosthetic hand control.

world conditions, and consistent performance across age groups highlight its potential for inclusive design, catering to users with diverse skin conditions and motor capabilities.

The successful integration with a prosthetic hand prototype showcases the practical impact of these improvements, enabling more natural and dexterous control of assistive devices. This has significant implications for enhancing the quality of life for individuals with limb differences, potentially increasing prosthetic adoption rates and expanding the range of activities users can perform confidently.

4.6. Limitations and Potential Sources of Error

While the results demonstrate the promising performance of the InSkin device, it is important to acknowledge the limitations of the current study:

1. Sample size: The human studies involved 20 participants, which may limit the generalizability of the results. Future studies with larger, more diverse populations are needed to confirm the findings.
2. Long-term performance: While 24-hour wear tests were conducted, the long-term stability and performance of the InSkin device beyond this timeframe remain to be fully characterized.
3. Environmental factors: The controlled laboratory conditions of this study may not fully represent the range of environmental conditions (temperature, humidity, etc.) that the device would encounter in real-world use.
4. Inter-individual variability: Despite efforts to include diverse skin types, the full range of human skin conditions and physiological variations may not be captured in this study.
5. Potential bias in gesture recognition: The current gesture set may not fully represent the range of movements required for all potential applications, and the classification algorithm may be biased towards the specific gestures used in training.

These limitations provide important directions for future research and development of the InSkin technology

4.7. Discussion

The comprehensive characterization and evaluation of the InSkin device presented in this chapter demonstrate its potential to address key challenges in skin-interfaced electronics

and advance the field of electrophysiological monitoring. The results highlight several significant achievements and implications:

Mechanical Adaptability: With exceptional stretchability (up to 1000%) and low Young's modulus (0.4 ± 0.1 MPa), the InSkin device conforms to diverse skin topographies while maintaining functionality. This adaptability ensures consistent performance across different body locations and user populations, addressing a major limitation of traditional rigid electrodes.

Electrical Stability Under Deformation: The device maintains conductivity up to >1000% strain, with only a 38% increase in impedance at 100% strain. This stability ensures reliable signal acquisition during body movements, significantly expanding the potential applications of wearable biosensors.

Consistent Performance Across Skin Conditions: InSkin maintains high signal quality and low impedance on smooth, wrinkled, and hairy skin, addressing a critical challenge in inclusive design for bioelectronics. Its performance on elderly skin is particularly noteworthy, potentially enabling more accurate health monitoring for an aging population.

High-Density Mapping Capabilities: The 32-channel array provides detailed muscle activity visualization, opening new possibilities in research and clinical applications. It clearly identifies innervation zones and enables long-term, high-resolution muscle mapping, which could enhance our understanding of neuromuscular disorders and improve rehabilitation strategies.

Advanced Gesture Recognition: The device achieves high classification accuracy (97.7% for 10 gestures) with consistent performance across age groups, demonstrating its potential for intuitive human-machine interfaces. This could lead to more natural and effective control of prosthetic devices and other assistive technologies.

Long-Term Wearability: InSkin maintains 75% of its initial SNR after 24 hours of wear, coupled with high user comfort ratings. This supports its potential for continuous, long-term health monitoring applications.

These advancements collectively position the InSkin device as a significant step forward in wearable bioelectronics, offering improved performance, comfort, and versatility across a wide range of applications.

However, several areas warrant further investigation:

1. **Biocompatibility and Skin Health:** While initial results show minimal skin irritation, longer-term studies are needed to ensure the safety and comfort of extended wear.
2. **Signal Processing Algorithms:** Further development of adaptive algorithms could potentially compensate for variations in signal quality due to factors like sweat accumulation or electrode shift during long-term use.
3. **Power Management:** Integration of energy harvesting, or wireless power technologies will be crucial for realizing fully self-contained, long-term wearable systems.
4. **Clinical Validation:** While the results are promising, extensive clinical studies across diverse patient populations are necessary to validate InSkin's efficacy in various healthcare applications.
5. **Environmental Factors:** The device's performance under various environmental conditions (e.g., temperature, humidity) needs to be thoroughly evaluated to ensure reliability in real-world scenarios.

In conclusion, the InSkin device represents a significant step forward in skin-interfaced electronics, offering a combination of mechanical adaptability, electrical stability, and high-fidelity signal acquisition that addresses many limitations of existing technologies. Its potential applications span from advanced prosthetics and human-machine interfaces to personalized healthcare and continuous monitoring. As research continues, addressing the identified challenges will be crucial in translating this technology from the laboratory to practical, real-world applications that can significantly impact human health and quality of life.

Chapter 5: Applications and Future Directions

The InSkin platform represents a significant advancement in skin-interfaced electronics, offering unprecedented capabilities in electrophysiological monitoring and human-machine interfaces. This chapter explores the diverse landscape of potential applications and examines future directions for this technology.

5.1. Potential Applications in Healthcare

The InSkin device's advanced signal acquisition capabilities, adaptability to diverse skin conditions, and long-term wearability position it to revolutionize various aspects of healthcare.

5.1.1. Continuous Health Monitoring

InSkin enables transformative approaches to long-term patient monitoring:

- **Cardiovascular Care:** Continuous ECG monitoring could serve as an early warning system for cardiac events in high-risk patients, potentially reducing hospitalization rates and improving outcomes.
- **Respiratory Function:** By monitoring intercostal and diaphragm muscle activity, InSkin may facilitate early detection of respiratory distress in conditions like COPD (chronic obstructive pulmonary disease) or sleep apnea, enabling timely interventions.
- **Neurological Disorders:** The technology offers opportunities for continuous EEG monitoring in epilepsy patients and precise tracking of tremors and muscle activity in Parkinson's disease, potentially leading to more personalized treatment regimens.

5.1.2. Rehabilitation and Physical Therapy

InSkin's high-resolution muscle activity mapping capabilities can revolutionize rehabilitation practices:

- **Stroke Recovery:** Precise tracking of muscle activation patterns during recovery could inform personalized exercise regimens and provide real-time feedback to patients, potentially accelerating rehabilitation.

- **Sports Medicine:** By analyzing muscle activation patterns, InSkin may help optimize athletic performance and identify early signs of overuse or imbalance, contributing to injury prevention strategies.
- **Orthopedic Rehabilitation:** Monitoring muscle activity around joints post-surgery or injury could guide physical therapists in tailoring treatment plans, potentially improving recovery outcomes and reducing rehabilitation time.

5.1.3. Assistive Technologies

InSkin's advanced sensing capabilities open new possibilities in assistive devices:

- **Next-Generation Prosthetics:** Integration with prosthetic limbs could offer more intuitive control, adapting to individual user patterns and potentially improving the adoption rates of advanced prosthetics.
- **Exoskeleton Control:** InSkin arrays could facilitate more natural control of powered exoskeletons, expanding their applications in both medical rehabilitation and industrial settings.
- **Silent Speech Interfaces:** By detecting subtle facial and throat muscle movements, InSkin might enable the development of new communication devices for individuals with vocal cord paralysis or laryngectomy.

5.1.4. Preventive Healthcare

InSkin's long-term monitoring capabilities create opportunities for proactive health management:

- **Ergonomic Assessment:** Continuous monitoring of muscle activity in workplace settings could help prevent repetitive strain injuries and inform the design of more ergonomic work environments.
- **Stress and Mental Health:** Analysis of muscle tension patterns may provide insights into stress levels and mental health status, potentially integrating with mindfulness applications for holistic well-being management.
- **Sleep Quality Assessment:** Monitoring muscle activity and movement during sleep could enhance the detection and management of sleep disorders, potentially improving overall health outcomes.

5.1.5. Personalized Medicine

InSkin technology has the potential to significantly advance personalized healthcare approaches:

- **Medication Response Tracking:** By monitoring changes in muscle activity in response to medications, InSkin could facilitate real-time drug dosage optimization, particularly beneficial in conditions like Parkinson's disease.
- **Aging Population Care:** Long-term monitoring of muscle strength and activity patterns in elderly individuals could enable early detection of mobility issues or fall risks, supporting aging-in-place initiatives.
- **Advanced Diagnostics:** High-resolution mapping of muscle activity could lead to more accurate diagnosis of neuromuscular disorders and potentially enable early detection of conditions like motor neuron disease or muscular dystrophy.

While these applications show great promise, extensive clinical validation studies and collaborations with healthcare institutions and regulatory bodies will be crucial to fully realize InSkin's potential in medical settings.

5.2. Human-Machine Interfaces

InSkin's high-fidelity, multi-channel capabilities create new paradigms for human-machine interaction across various domains.

5.2.1. Advanced Prosthetics

InSkin technology could significantly enhance prosthetic functionality:

- **Multi-Degree Freedom Control:** Utilization of high-density sEMG patterns may enable simultaneous control of multiple joint movements, creating more natural and dexterous prosthetic limbs.
- **Sensory Feedback Integration:** Combining InSkin-based control with tactile sensors and neural stimulation could create closed-loop systems, potentially restoring a sense of touch for prosthetic users.
- **Adaptive Learning Systems:** AI-driven algorithms could continuously adapt to users' changing muscle patterns and intentions, potentially reducing the learning curve for prosthetic control.

5.2.2. Virtual and Augmented Reality Interactions

InSkin's ability to detect subtle muscle activations could enhance immersion and control in VR/AR environments:

- **Gesture-Based Navigation:** Fine hand and finger movements could be translated into intuitive controls for virtual spaces, potentially replacing or augmenting traditional handheld controllers.
- **Facial Expression Tracking:** InSkin arrays applied to the face could enable real-time avatar animation in social VR platforms, enhancing non-verbal communication in virtual environments.
- **Haptic Feedback Systems:** Integration with haptic actuators could create more realistic tactile experiences in VR/AR, potentially revolutionizing fields like virtual training and remote operations.

5.2.3. Human-Robot Collaboration

InSkin could facilitate more natural and efficient interactions between humans and robotic systems:

- **Intuitive Robot Control:** Muscle activity patterns could be used for direct, intuitive control of robotic arms or mobile robots, potentially improving efficiency in manufacturing and healthcare settings.
- **Safety Enhancements:** Monitoring operator muscle tension and fatigue could prevent accidents in human-robot collaborative tasks, creating safer work environments.
- **Teleoperation Advancements:** High-fidelity muscle activity detection could enable precise control of remote robotic systems, potentially improving outcomes in telesurgery or hazardous environment operations.

5.2.4. Wearable Computing

InSkin technology could enable novel interaction paradigms for wearable devices:

- **Subtle Command Interfaces:** Detection of small, socially acceptable gestures could provide expanded control options for smartwatches or augmented reality glasses.

- Context-Aware Systems: Muscle activity patterns could be used to infer user context, allowing devices to adapt their behavior accordingly.
- Bio-Authentication: Unique muscle activation patterns could serve as a secure, hands-free method for device authentication, potentially replacing or augmenting traditional biometric systems.

5.2.5. Neurorehabilitation Interfaces

InSkin could play a crucial role in creating engaging and effective interfaces for neurorehabilitation:

- Gamified Rehabilitation: Development of video games controlled by specific muscle movements could encourage more engaging and effective rehabilitation exercises.
- Virtual Reality Therapy: Integration with VR systems could create immersive, targeted rehabilitation experiences, potentially improving patient engagement and outcomes.
- Brain-Computer Interface Hybrids: Combining InSkin-based muscle control with BCI systems could enhance control capabilities for severely paralyzed patients, potentially improving their quality of life.

5.2.6. Artistic and Creative Interfaces

The sensitivity and multi-channel capabilities of InSkin open up new possibilities for artistic expression:

- Novel Musical Instruments: Creation of instruments controlled by subtle muscle movements could expand the boundaries of musical performance and composition.
- Intuitive Digital Art Tools: Full-body muscle activity monitoring could enable more natural and expressive control of digital sculpting or painting tools.
- Interactive Performances: Integration with stage lighting and sound systems could create new forms of interactive, body-driven performances.

While these applications show immense promise, realizing their full potential will require addressing several challenges:

1. Development of robust algorithms for real-time interpretation of complex, multi-channel sEMG data.
2. Creation of standardized protocols for integrating InSkin with various technological systems.
3. Addressing potential privacy and security concerns related to the collection and transmission of physiological data.
4. Conducting extensive user studies to ensure that these new interfaces enhance rather than complicate user experiences.
5. Overcoming potential social and cultural barriers to the adoption of skin-interfaced technologies.

As research progresses and these challenges are addressed, InSkin technology has the potential to reshape human-machine interaction across numerous fields, from healthcare and assistive technologies to entertainment and creative expression. The future directions of this technology will likely involve further miniaturization, increased computational power at the edge, and integration with other emerging technologies such as artificial intelligence and advanced materials science.

5.3. Limitations and Areas for Improvement

While the InSkin technology demonstrates significant advancements in skin-interfaced electronics, it is important to critically evaluate the limitations of the current research:

Long-term Durability: Although our tests demonstrated stable performance over 24 hours, the longevity of InSkin beyond this period remains uncertain. Extended testing over weeks or months is necessary to fully evaluate the device's durability in real-world conditions.

Diverse Skin Conditions: Our study tested InSkin on smooth, wrinkled, and hairy skin but did not include individuals with dermatological conditions or extreme skin types. Further investigation is required to assess InSkin's performance on these types of skin.

Environmental Factors: Our tests were conducted in controlled laboratory settings. The effects of varying environmental factors such as temperature, humidity, and UV exposure on InSkin's performance need to be studied further.

Motion Artifacts: While InSkin showed improved resistance to motion artifacts compared to commercial electrodes, we did not test the device under high-intensity movements or impacts. Further evaluation is needed to understand its performance under extreme motion conditions.

Scalability of Fabrication: Our current fabrication process works well for prototypes, but its scalability for mass production has yet to be fully assessed. Transitioning to industrial-scale manufacturing may present challenges.

Power Requirements: The current prototype uses wired connections for power. Integrating wireless power solutions and assessing their impact on device performance and user comfort are necessary next steps.

Data Privacy and Security: As with any technology that collects physiological data, robust encryption and privacy protection measures must be developed and rigorously tested.

User Adaptation: Initial user feedback was positive, but long-term studies are needed to assess user adaptation, comfort, and potential behavioral changes resulting from continuous monitoring.

Comparative Studies: We compared InSkin with commercial dry electrodes, but broader comparisons with a wider range of existing technologies could provide a more comprehensive evaluation of InSkin's strengths and weaknesses.

Biocompatibility: Initial tests showed good biocompatibility, but more extensive long-term studies are required to ensure safety during prolonged skin contact, especially for diverse populations and individuals with sensitive skin.

5.4. Future Research Directions

Building upon the achievements of the InSkin project and addressing its current limitations, several promising research directions emerge. These avenues of investigation have the potential to further advance the field of skin-interfaced electronics and expand the capabilities of the InSkin technology.

Material Enhancements

Research into conductive polymers with self-healing properties could enhance the durability and longevity of InSkin devices. Biomimetic approaches, such as microcapsule-based or vascular self-healing systems, offer potential improvements in functionality. Exploring biodegradable conductive materials could lead to environmentally friendly, disposable InSkin variants, while investigating controlled degradation mechanisms might benefit time-limited applications. The integration of shape-memory polymers could create adaptive electrode structures, with temperature or electrically activated shape changes potentially improving skin contact.

Multi-modal Sensing Integration

Developing hybrid electrophysiological and biochemical sensing capabilities could advance InSkin's utility, as could exploring sweat analysis for continuous biomarker monitoring. Integrating flexible optical sensors for combined electrophysiological and photoplethysmography (PPG) measurements, along with near-infrared spectroscopy (NIRS) for muscle oxygenation monitoring, could enhance the system's capabilities. Incorporating high-resolution temperature sensors and exploring infrared thermal imaging integration might enable more comprehensive physiological monitoring.

Advanced Signal Processing and AI Integration

Developing advanced neural network architectures for real-time processing of high-density sEMG data and exploring transfer learning approaches could reduce user-specific training requirements. Research into advanced adaptive filtering techniques might improve motion artifact reduction, while multi-sensor fusion approaches combining sEMG, IMU, and other data could enhance signal quality. Developing AI models to predict physiological states or impending health events based on long-term InSkin data could lead to personalized, adaptive alerting systems for healthcare applications.

Expanded Biomedical Applications

Large-scale, long-term studies could validate the clinical utility of continuous InSkin monitoring and investigate data patterns as early indicators of various health conditions. Clinical trials might quantify the impact of InSkin-based feedback on rehabilitation

outcomes and explore personalized rehabilitation protocols. Research into hybrid systems combining InSkin with non-invasive brain-computer interfaces (BCIs) could lead to advanced prosthetic control. High-resolution sEMG arrays for non-invasive neural interfacing and signal processing techniques for extracting neural information from surface recordings represent other potential areas of study. Exploring InSkin-based neurofeedback systems for rehabilitation and cognitive enhancement and investigating closed-loop stimulation systems combining InSkin with transcutaneous electrical nerve stimulation (TENS), could yield valuable insights.

Energy Harvesting and Power Management

Developing techniques to harvest energy from body heat or motion and exploring biofuel cells using sweat as a power source, could create self-sustaining InSkin systems. Research into efficient, long-range wireless power transfer methods and body-area wireless power networks for multiple distributed sensors might enhance usability. Novel circuit designs and materials for extreme low-power operation, along with event-driven architectures and intermittent computing, could improve energy efficiency.

Fabrication and Scalability

Developing roll-to-roll processing techniques could enable large-scale production of InSkin devices. Exploring additive manufacturing methods might lead to customized, patient-specific InSkin arrays. Investigating novel encapsulation methods could further improve long-term stability and biocompatibility.

Clinical Translation and Validation

Conducting large-scale, long-term studies could validate the clinical utility of continuous InSkin monitoring. Designing clinical trials to quantify the impact of InSkin-based feedback on rehabilitation outcomes might lead to personalized rehabilitation protocols. Collaborating with regulatory bodies could establish clear pathways for InSkin technology approval in various applications.

Ethical and Societal Implications

Developing robust data privacy and security protocols for continuous physiological monitoring and studying the psychological and social impacts of long-term use of skin-

interfaced electronics are worthy considerations. Exploring InSkin's potential in reducing healthcare disparities through improved access to continuous monitoring could ensure ethical and societal acceptance.

Environmental Impact and Sustainability

Developing life cycle assessments for InSkin devices could optimize their environmental footprint. Investigating recycling and refurbishment processes for used InSkin devices and exploring sustainable and renewable materials in InSkin fabrication could enhance the technology's sustainability.

These research directions represent opportunities to address current limitations, unlock new capabilities, and progress toward the seamless integration of electronics with the human body. The interdisciplinary nature of these paths highlights the potential for collaborative efforts across various scientific and engineering disciplines, potentially contributing to advancements in wearable technology, human-machine interfaces, and personalized medicine.

5.5. Ethical Considerations and Societal Impact

The development and potential widespread adoption of skin-interfaced electronics like InSkin raise important ethical considerations:

1. Privacy and data security: The continuous collection of physiological data raises concerns about data ownership, storage, and potential misuse. Future development must prioritize robust data protection measures and transparent data management policies.
2. Accessibility and equity: While InSkin aims to be more inclusive, advanced bioelectronic technologies could exacerbate healthcare disparities if not made widely accessible. Efforts should be made to ensure equitable access to these technologies.
3. Human enhancement and identity: As skin-interfaced electronics become more advanced, they may blur the line between medical devices and human enhancement technologies, raising questions about human identity and the ethics of augmenting human capabilities.

4. Psychological impact: Long-term use of skin-interfaced electronics may have unforeseen psychological effects, such as increased anxiety from continuous health monitoring or changes in body image.

5. Regulatory challenges: The rapid advancement of this technology may outpace current regulatory frameworks, necessitating proactive engagement with policymakers to ensure appropriate oversight and safety standards.

Addressing these ethical considerations will be crucial for developing and deploying InSkin and similar technologies. Future research should include interdisciplinary collaboration with ethicists, policymakers, and social scientists to fully explore and address these issues.

Chapter 6: Conclusion

This dissertation presented the InSkin project, a comprehensive exploration into developing and validating a novel, adaptive, and stretchable bioelectronic platform for high-fidelity, inclusive electrophysiological recording. Driven by the need for improved skin-interfaced electronics that cater to diverse populations and dynamic conditions, this research has addressed key limitations of existing technologies and yielded a platform with transformative potential across healthcare, human-machine interfaces, and scientific research.

6.1. Summary of Key Findings and Contributions

The InSkin project has made significant advancements in the field of skin-interfaced electronics, culminating in the following key findings:

1. **Novel Material Design:** The InSkin platform is based on a water-soluble, solution-processable conductive polymer composite, Solution CP-G, that combines high electrical conductivity with exceptional mechanical properties. This unique material exhibits a freestanding stretchability up to 250% while maintaining electrical functionality and significantly reducing electrode-skin impedance compared to commercial electrodes.
2. **Adaptive Performance Across Diverse Skin Conditions:** The InSkin electrodes demonstrate consistent signal quality on both smooth and wrinkled skin, as well as on hairy skin, outperforming commercial electrodes in each scenario. They exhibit long-term stability, maintaining 75% of initial signal quality after 24 hours of continuous wear.
3. **High-Density sEMG Mapping Capabilities:** The 32-channel array with 20 mm inter-electrode distance enables detailed visualization of muscle activity patterns, including motor unit action potential propagation and innervation zone identification. This opens new possibilities for non-invasive assessment of neuromuscular disorders and personalized rehabilitation strategies.

4. **Advanced Gesture Recognition and Prosthetic Control:** The InSkin system achieves 97.7% accuracy in classifying 10 hand gestures, maintaining high accuracy across age groups. Its successful integration with a prosthetic hand prototype demonstrates potential for intuitive and high-precision control of assistive devices.
5. **Scalable Fabrication Process:** The developed fabrication process, combining solution processing, laser patterning, and transfer techniques, achieves a minimal feature size of 50 μm and enables the production of high-density electrode arrays. This scalable approach holds promise for large-area fabrication, potentially enabling full-body monitoring systems.

These findings represent a significant step forward in creating skin-interfaced electronics that are adaptable, high-performing, and suitable for long-term use across diverse user populations.

6.2. Significance and Impact of the Research

The InSkin project has significant implications across various fields:

1. **Inclusive Design in Bioelectronics:** By maintaining consistent performance across diverse skin types and ages, InSkin promotes more equitable access to advanced bioelectronic technologies, particularly benefiting elderly populations who have been historically underserved.
2. **Advancements in Healthcare:** InSkin's capabilities open doors for continuous health monitoring, personalized medicine, and data-driven rehabilitation strategies, potentially transforming cardiovascular care, respiratory monitoring, neurological assessment, and preventive healthcare.
3. **Next-Generation Human-Machine Interfaces:** InSkin's high-fidelity, multi-channel capabilities enable more intuitive and responsive prosthetic limbs, enhance control interfaces for virtual and augmented reality, and offer new input methods for various devices based on subtle muscle movements.
4. **Pushing the Boundaries of Materials Science and Wearable Technology:** The development of Solution CP-G contributes to the broader field of stretchable

electronics and wearable technology, inspiring new approaches to creating more comfortable, longer lasting, and seamlessly integrated devices.

5. **Accelerating Neuromuscular Research:** The high-resolution sEMG mapping capabilities provide researchers with a powerful, non-invasive tool for studying muscle function and neuromuscular disorders, potentially accelerating research in fields like sports science, ergonomics, and neurology.

In conclusion, this research has successfully met its objectives by:

1. Developing a novel, water-soluble conductive polymer composite (Solution CP-G) that demonstrates exceptional stretchability and electrical performance.
2. Creating a fabrication process for high-density, stretchable electrode arrays that can be scaled for potential mass production.
3. Demonstrating consistent performance across diverse skin conditions and age groups, addressing a critical gap in current skin-interfaced electronics.
4. Validating the InSkin platform's capabilities in high-resolution sEMG mapping and advanced gesture recognition for prosthetic control.

These achievements support the thesis that intrinsically stretchable, inclusive skin bio-interfaces can overcome the limitations of current technologies and expand the potential applications of wearable bioelectronics. The InSkin platform represents a significant step towards realizing seamless electronics integration with the human body, with far-reaching implications for healthcare, human-machine interfaces, and our understanding of human physiology.

6.3. Discussion of Research Implications

The findings of the InSkin project have far-reaching implications, potentially impacting:

- Personalized medicine and treatment optimization
- Rehabilitation and physical therapy practices
- Advanced prosthetics and assistive technology design
- Occupational health and ergonomics
- Sports science and performance enhancement
- Neuroscience and cognitive studies

- Aging population care and telemedicine
- Ethical and societal considerations surrounding continuous health monitoring

6.4. Final Remarks and Future Outlook

The InSkin project addresses current challenges in skin-interfaced electronics and paves the way for a future where the biological and the digital boundaries become increasingly seamless. Future research should focus on:

- Further miniaturization and multi-modal sensing integration
- Advanced signal processing and AI-driven interpretation
- Integration with emerging technologies like soft robotics and augmented reality
- Biocompatible and biodegradable material development
- Large-scale clinical validation and addressing ethical considerations

As technology continues to evolve, the InSkin platform and its successors have the potential to transform healthcare, enhance human capabilities, and reshape our interactions with the world. This research serves as a foundation for future innovations in bioelectronic devices that will undoubtedly play an increasingly important role in improving human health and quality of life for diverse populations worldwide.

BIBLIOGRAPHY

1. Oh, J. Y. & Bao, Z. Second Skin Enabled by Advanced Electronics. *Adv. Sci. Lett.* (2019) doi:10.1002/advs.201900186.
2. Li, J. *et al.* Ultrathin, Soft, Radiative Cooling Interfaces for Advanced Thermal Management in Skin Electronics. *Science Advances* (2023) doi:10.1126/sciadv.adg1837.
3. Chen, S. Innovations in Flexible Electronic Skin: Material, Structural and Applications. *Highlights in Science Engineering and Technology* (2023) doi:10.54097/hset.v63i.10887.
4. Chung, H. U. *et al.* Skin-Interfaced Biosensors for Advanced Wireless Physiological Monitoring in Neonatal and Pediatric Intensive-Care Units. *Nat. Med.* (2020) doi:10.1038/s41591-020-0792-9.
5. Han, S. Editorial: Skin-Interfaced Platforms for Quantitative Assessment in Public Health. *Frontiers in Bioengineering and Biotechnology* (2024) doi:10.3389/fbioe.2024.1406483.
6. Brown, L. Conducting Electroencephalography With Black Individuals: Barriers, Recommendations, and Impact on Generalizability. *Policy Insights From the Behavioral and Brain Sciences* (2023) doi:10.1177/23727322231197739.
7. Wang, Y. *et al.* Validation of Low-Cost Wireless EEG System for Measuring Event-Related Potentials. (2018) doi:10.1109/issc.2018.8585297.
8. Vaz Mello, L. J., Seifi, A., Perez, I. A. & Godoy, D. A. Electroencephalography During the Acute Phase of Encephalitis: A Brief Review. *J. Neurol. Res.* (2020) doi:10.14740/jnr568.
9. Xu, S. & Wu, W. Ink-Based Additive Nanomanufacturing of Functional Materials for Human-Integrated Smart Wearables. *Advanced Intelligent Systems* (2020) doi:10.1002/aisy.202000117.
10. He, B., Sohrabpour, A., Brown, E. N. & Li, Z. Electrophysiological Source Imaging: A Noninvasive Window to Brain Dynamics. *Annu. Rev. Biomed. Eng.* (2018) doi:10.1146/annurev-bioeng-062117-120853.
11. Hassan, A. M. & El-Shenawee, M. Biopotential Signals of Breast Cancer Versus Tumor Types and Proliferation Stages. *Physical Review E* (2012) doi:10.1103/physreve.85.021913.

12. Wu, Z. *et al.* Integrated All-Fiber Electronic Skin Toward Self-Powered Sensing Sports Systems. *ACS Appl. Mater. Interfaces* (2021) doi:10.1021/acsami.1c13420.
13. You, Y.-W. *et al.* Biofuel-Powered Soft Electronic Skin With Multiplexed and Wireless Sensing for Human-Machine Interfaces. *Science Robotics* (2020) doi:10.1126/scirobotics.aaz7946.
14. Dong, K. *et al.* A Stretchable Yarn Embedded Triboelectric Nanogenerator as Electronic Skin for Biomechanical Energy Harvesting and Multifunctional Pressure Sensing. *Adv. Mater.* (2018) doi:10.1002/adma.201804944.
15. Zhu, L. *et al.* Fully Elastomeric Fingerprint-Shaped Electronic Skin Based on Tunable Patterned Graphene/Silver Nanocomposites. *ACS Appl. Mater. Interfaces* (2020) doi:10.1021/acsami.0c09653.
16. Yang, X. Electronic Skin for Health Monitoring Systems: Properties, Functions, and Applications. *Adv. Mater.* (2024) doi:10.1002/adma.202402542.
17. Lee, Y. *et al.* Mimicking Human and Biological Skins for Multifunctional Skin Electronics. *Adv. Funct. Mater.* (2019) doi:10.1002/adfm.201904523.
18. Roy, S. 3D Printed Electronic Skin for Strain, Pressure and Temperature Sensing. *Adv. Funct. Mater.* (2024) doi:10.1002/adfm.202313575.
19. Lee, K. *et al.* Artificially Intelligent Tactile Ferroelectric Skin. *Adv. Sci. Lett.* (2020) doi:10.1002/advs.202001662.
20. Zhao, P. *et al.* Strain-Discriminable Pressure/Proximity Sensing of Transparent Stretchable Electronic Skin Based on PEDOT:PSS/SWCNT Electrodes. *ACS Appl. Mater. Interfaces* (2020) doi:10.1021/acsami.0c16546.
21. Yokota, T. *et al.* Ultraflexible Organic Photonic Skin. *Science Advances* (2016) doi:10.1126/sciadv.1501856.
22. Wang, X. *et al.* Recent Progress in Electronic Skin. *Adv. Sci. Lett.* (2015) doi:10.1002/advs.201500169.
23. Patel, S. *et al.* Wearable electronics for skin wound monitoring and healing. *Soft Sci* **2**, (2022).
24. Dahiya, A. S. *et al.* 1D nanomaterial-based highly stretchable strain sensors for human movement monitoring and human–robotic interactive systems. *Adv. Electron. Mater.* **6**, 2000547 (2020).
25. Zhu, P. Latest Developments and Trends in Electronic Skin Devices. *Soft Science* (2024) doi:10.20517/ss.2024.05.

26. Zhang, X. *et al.* Direct Fabrication of High-Performance Multi-Response E-Skin Based on a Graphene Nanosheet Film. *Soft Science* (2022) doi:10.20517/ss.2022.18.
27. Li, P., Anwar Ali, H. P., Cheng, W., Yang, J. & K. Tee, B. C. Bioinspired Prosthetic Interfaces. *Advanced Materials Technologies* (2020) doi:10.1002/admt.201900856.
28. Jahed, Z. *et al.* Nanocrown Electrodes for Parallel and Robust Intracellular Recording of Cardiomyocytes. *Nat. Commun.* (2022) doi:10.1038/s41467-022-29726-2.
29. Xu, D., Mo, J., Xie, X. & Hu, N. In-Cell Nanoelectronics: Opening the Door to Intracellular Electrophysiology. *Nano-Micro Letters* (2021) doi:10.1007/s40820-021-00655-x.
30. Mehrali, M. *et al.* Blending Electronics With the Human Body: A Pathway Toward a Cybernetic Future. *Adv. Sci. Lett.* (2018) doi:10.1002/advs.201700931.
31. Cerone, G. L., Botter, A., Vieira, T. & Gazzoni, M. Design and Characterization of a Textile Electrode System for the Detection of High-Density sEMG. *IEEE Trans. Neural Syst. Rehabil. Eng.* (2021) doi:10.1109/tnsre.2021.3086860.
32. Ерофеев, А. И. *et al.* An Open-Source Wireless Electrophysiological Complex for in Vivo Recording Neuronal Activity in the Rodent's Brain. *Sensors* (2021) doi:10.3390/s21217189.
33. Ko, C.-Y. *et al.* Linear- And Nonlinear-Electromyographic Analysis of Supracutaneous Vibration Stimuli of the Forearm Using Diverse Frequencies and Considering Skin Physiological Properties. *J. Biomech. Eng.* (2013) doi:10.1115/1.4025777.
34. Chi, M., Zhao, J., Dong, Y. & Wang, X. Flexible Carbon Nanotube-Based Polymer Electrode for Long-Term Electrocardiographic Recording. *Materials* (2019) doi:10.3390/ma12060971.
35. Park, H. *et al.* A Skin-Friendly Soft Strain Sensor With Direct Skin Adhesion Enabled by Using a Non-Toxic Surfactant. *J. Mater. Chem.* (2023) doi:10.1039/d3tc01150j.
36. Wang, C. *et al.* Stretchable, Multifunctional Epidermal Sensor Patch for Surface Electromyography and Strain Measurements. *Advanced Intelligent Systems* (2021) doi:10.1002/aisy.202100031.
37. Gao, Y. Ultraconformal Skin-Interfaced Sensing Platform for Motion Artifact-Free Monitoring. *ACS Appl. Mater. Interfaces* (2024) doi:10.1021/acsami.4c04357.

38. Ershad, F. *et al.* Ultra-Conformal Drawn-on-Skin Electronics for Multifunctional Motion Artifact-Free Sensing and Point-of-Care Treatment. *Nat. Commun.* (2020) doi:10.1038/s41467-020-17619-1.
39. Tian, Q. *et al.* Hairy-Skin-Adaptive Viscoelastic Dry Electrodes for Long-Term Electrophysiological Monitoring. *Adv. Mater.* **35**, e2211236 (2023).
40. Wang, H. *et al.* MEMS Devices-Based Hand Gesture Recognition via Wearable Computing. *Micromachines (Basel)* **14**, (2023).
41. Park, J., Xu, L., Sridhar, V., Chi, M. & Cauwenberghs, G. Wireless dry EEG for drowsiness detection. in *2011 Annual International Conference of the IEEE Engineering in Medicine and Biology Society* 3298–3301 (2011).
42. Rao, Z. *et al.* Soft Electronics for the Skin: From Health Monitors to Human–Machine Interfaces. *Advanced Materials Technologies* (2020) doi:10.1002/admt.202000233.
43. Yamagami, M. *et al.* Assessment of Dry Epidermal Electrodes for Long-Term Electromyography Measurements. *Sensors* **18**, (2018).
44. Chowdhury, R. H. *et al.* Surface electromyography signal processing and classification techniques. *Sensors* **13**, 12431–12466 (2013).
45. Campbell, A. & Wu, C. Chronically Implanted Intracranial Electrodes: Tissue Reaction and Electrical Changes. *Micromachines (Basel)* **9**, (2018).
46. Wood, S. M., Jarratt, J. A., Barker, A. T. & Brown, B. H. Surface electromyography using electrode arrays: a study of motor neuron disease. *Muscle Nerve* **24**, 223–230 (2001).
47. Hwang, W. *et al.* A Breathable and Stretchable Metastructure for a Versatile Hybrid Electronic Skin Patch With Long-Term Skin Comfort. *Advanced Materials Technologies* (2022) doi:10.1002/admt.202200477.
48. Jang, K. I. *et al.* Ferromagnetic, Folded Electrode Composite as a Soft Interface to the Skin for Long-Term Electrophysiological Recording. *Adv. Funct. Mater.* (2016) doi:10.1002/adfm.201603146.
49. Zhu, Y. *et al.* Skin-interfaced electronics: A promising and intelligent paradigm for personalized healthcare. *Biomaterials* **296**, 122075 (2023).
50. Sophocleous, M. & Atkinson, J. K. A review of screen-printed silver/silver chloride (Ag/AgCl) reference electrodes potentially suitable for environmental potentiometric sensors. *Sens. Actuators A Phys.* **267**, 106–120 (2017).

51. Suzuki, H., Hiratsuka, A., Sasaki, S. & Karube, I. Problems associated with the thin-film Ag/AgCl reference electrode and a novel structure with improved durability. *Sens. Actuators B Chem.* **46**, 104–113 (1998).
52. M, Y., Jung, T. & Cauwenberghs, G. Dry-Contact and Noncontact Biopotential Electrodes: Methodological Review. *IEEE Rev. Biomed. Eng.* (2010) doi:10.1109/rbme.2010.2084078.
53. Vidhya, C. M., Maithani, Y. & Singh, J. P. Recent Advances and Challenges in Textile Electrodes for Wearable Biopotential Signal Monitoring: A Comprehensive Review. *Biosensors* (2023) doi:10.3390/bios13070679.
54. Guo, X., Avila, R. & Xie, Z. Flexible Electronics With Dynamic Interfaces for Biomedical Monitoring, Stimulation, and Characterization. *International Journal of Mechanical System Dynamics* (2021) doi:10.1002/msd2.12017.
55. Moin, A. *et al.* A wearable biosensing system with in-sensor adaptive machine learning for hand gesture recognition. *Nature Electronics* **4**, 54–63 (2020).
56. Cho, K. W. *et al.* Soft Bioelectronics Based on Nanomaterials. *Chem. Rev.* (2021) doi:10.1021/acs.chemrev.1c00531.
57. Yao, K. *et al.* Recent Advances in Materials, Designs and Applications of Skin Electronics. *Ieee Open Journal of Nanotechnology* (2023) doi:10.1109/ojnano.2022.3218960.
58. Sung, M. K. A Review of Soft Electronic Devices Based on Flexible and Stretchable Materials for Cardiac Monitoring. *International Journal of Students Research in Technology & Management* (2023) doi:10.18510/ijsrtm.2023.1113.
59. Yang, C. & Suo, Z. Hydrogel ionotronics. *Nat. Rev. Mater.* **3**, 125–142 (2018).
60. Sun, J.-Y. *et al.* Highly stretchable and tough hydrogels. *Nature* **489**, 133–136 (2012).
61. Annabi, N. *et al.* 25th anniversary article: rational design and applications of hydrogels in regenerative medicine. *Adv. Mater.* **26**, 85–124 (2014).
62. Gao, D., Parida, K. & Lee, P. S. Emerging Soft Conductors for Bioelectronic Interfaces. *Adv. Funct. Mater.* (2019) doi:10.1002/adfm.201907184.
63. Choi, S., Han, S. I., Kim, D., Hyeon, T. & Kim, D.-H. High-performance stretchable conductive nanocomposites: materials, processes, and device applications. *Chem. Soc. Rev.* **48**, 1566–1595 (2019).

64. Matsuhisa, N. *et al.* Printable elastic conductors by in situ formation of silver nanoparticles from silver flakes. *Nat. Mater.* **16**, 834–840 (2017).
65. Kaltenbrunner, M. *et al.* An ultra-lightweight design for imperceptible plastic electronics. *Nature* **499**, 458–463 (2013).
66. Chitrakar, C., Hedrick, E., Adegoke, L. & Ecker, M. Flexible and Stretchable Bioelectronics. *Materials* (2022) doi:10.3390/ma15051664.
67. Dickey, M. D. Stretchable and soft electronics using liquid metals. *Adv. Mater.* **29**, 1606425 (2017).
68. Ladd, C., So, J.-H., Muth, J. & Dickey, M. D. 3D printing of free standing liquid metal microstructures. *Adv. Mater.* **25**, 5081–5085 (2013).
69. Byun, S.-H. *et al.* Mechanically transformative electronics, sensors, and implantable devices. *Sci. Adv.* **5**, eaay0418 (2019).
70. Khang, D.-Y., Jiang, H., Huang, Y. & Rogers, J. A. A stretchable form of single-crystal silicon for high-performance electronics on rubber substrates. *Science* **311**, 208–212 (2006).
71. Someya, T. *et al.* A large-area, flexible pressure sensor matrix with organic field-effect transistors for artificial skin applications. *Proc. Natl. Acad. Sci. U. S. A.* **101**, 9966–9970 (2004).
72. Xu, S. *et al.* Soft microfluidic assemblies of sensors, circuits, and radios for the skin. *Science* **344**, 70–74 (2014).
73. Lanzara, G., Salowitz, N., Guo, Z. & Chang, F.-K. A spider-web-like highly expandable sensor network for multifunctional materials. *Adv. Mater.* **22**, 4643–4648 (2010).
74. Wang, S. *et al.* Skin electronics from scalable fabrication of an intrinsically stretchable transistor array. *Nature* **555**, 83–88 (2018).
75. Choi, S. *et al.* Highly conductive, stretchable and biocompatible Ag-Au core-sheath nanowire composite for wearable and implantable bioelectronics. *Nat. Nanotechnol.* **13**, 1048–1056 (2018).
76. Kwon, Y. *et al.* Printed, Wireless, Soft Bioelectronics and Deep Learning Algorithm for Smart Human–Machine Interfaces. *ACS Appl. Mater. Interfaces* (2020) doi:10.1021/acsami.0c14193.
77. Tepole, A. B., Gosain, A. K. & Kuhl, E. Stretching skin: The physiological limit and beyond. *Int. J. Non Linear Mech.* **47**, 938–949 (2012).

78. Hagler, J. *et al.* Flexible and Stretchable Printed Conducting Polymer Devices for Electrodermal Activity Measurements. *Flexible and Printed Electronics* (2022) doi:10.1088/2058-8585/ac4d0f.
79. Dorsainvil, J. S. Cellulosic Nanofibers Utilizing a Silicone Elastomeric Core to Form Stretchable Paper. *Advanced Materials Interfaces* (2023) doi:10.1002/admi.202300487.
80. Sekitani, T. *et al.* Organic nonvolatile memory transistors for flexible sensor arrays. *Science* **326**, 1516–1519 (2009).
81. Kim, D.-H. *et al.* Stretchable and foldable silicon integrated circuits. *Science* **320**, 507–511 (2008).
82. Zhe Fan, Zhong Wang, Guanglin Li & Ruomei Wang. A canonical correlation analysis based EMG classification algorithm for eliminating electrode shift effect. *Conf. Proc. IEEE Eng. Med. Biol. Soc.* **2016**, 867–870 (2016).
83. Chortos, A., Liu, J. & Bao, Z. Pursuing Prosthetic Electronic Skin. *Nat. Mater.* (2016) doi:10.1038/nmat4671.
84. Bora, D. J. & Dasgupta, R. Estimation of skin impedance models with experimental data and a proposed model for human skin impedance. *IET Syst. Biol.* **14**, 230–240 (2020).
85. Goyal, K., Borkholder, D. A. & Day, S. W. Dependence of Skin-Electrode Contact Impedance on Material and Skin Hydration. *Sensors* (2022) doi:10.3390/s22218510.
86. Wu, H. *et al.* Materials, devices, and systems of on-skin electrodes for electrophysiological monitoring and human-machine interfaces. *Adv. Sci.* **8**, 2001938 (2021).
87. Wang, Y. *et al.* Epidermal electrodes with enhanced breathability and high sensing performance. *Materials Today Physics* **12**, 100191 (2020).
88. Wang, Y. *et al.* A highly stretchable, transparent, and conductive polymer. *Sci. Adv.* **3**, e1602076 (2017).
89. Oh, J. Y. *et al.* Intrinsically stretchable and healable semiconducting polymer for organic transistors. *Nature* **539**, 411–415 (2016).
90. Kang, J., Tok, J. B.-H. & Bao, Z. Self-healing soft electronics. *Nat. Electron.* **2**, 144–150 (2019).

91. Hurlow, J. & Bliss, D. Z. Dry skin in older adults. *Geriatr. Nurs.* **32**, 257–262 (2011).
92. Krueger, N. & Luebberding, S. Age-Related Changes in Skin Mechanical Properties. in *Textbook of Aging Skin* (eds. Farage, M. A., Miller, K. W. & Maibach, H. I.) 309–317 (Springer Berlin Heidelberg, Berlin, Heidelberg, 2017).
93. Taji, B., Shirmohammadi, S., Groza, V. & Batkin, I. Impact of skin–electrode interface on electrocardiogram measurements using conductive textile electrodes. *IEEE Trans. Instrum. Meas.* **63**, 1412–1422 (2014).
94. Williams, R., Pawlus, A. D. & Thornton, M. J. Getting under the skin of hair aging: the impact of the hair follicle environment. *Exp. Dermatol.* **29**, 588–597 (2020).
95. Zou, X., Xue, J. & Lai, K. W. C. Optimizing silver nanowires on-skin electrode shape for improved electromyography signal quality in detecting adjacent muscles. in *2023 IEEE 23rd International Conference on Nanotechnology (NANO)* (IEEE, 2023). doi:10.1109/nano58406.2023.10231213.
96. Lipomi, D. J. *et al.* Skin-like pressure and strain sensors based on transparent elastic films of carbon nanotubes. *Nat. Nanotechnol.* **6**, 788–792 (2011).
97. Liu, C. *et al.* Multifunctional materials strategies for enhanced safety of wireless, skin-interfaced bioelectronic devices. *Adv. Funct. Mater.* **33**, (2023).
98. Watkins, Z., McHenry, A. & Heikenfeld, J. Wearing the Lab: Advances and Challenges in Skin-Interfaced Systems for Continuous Biochemical Sensing. *Adv. Biochem. Eng. Biotechnol.* **187**, 223–282 (2024).
99. Min, J. *et al.* Skin-Interfaced Wearable Sweat Sensors for Precision Medicine. *Chem. Rev.* **123**, 5049–5138 (2023).
100. Kim, T. & Park, I. Skin-interfaced wearable biosensors: A mini-review. *J. Sens. Sci. Technol.* **31**, 71–78 (2022).
101. Liang, W. *et al.* Enhancing Efficiency of Organic Solar Cells With Alkyl Diamines Doped PEDOT: PSS. *Acs Materials Letters* (2023) doi:10.1021/acsmaterialslett.2c01078.
102. Wen, Y. & Xu, J. Scientific Importance of Water-Processable PEDOT–PSS and Preparation, Challenge and New Application in Sensors of Its Film Electrode: A Review. *J. Polym. Sci. A Polym. Chem.* (2017) doi:10.1002/pola.28482.

103. Ahmad Ruzaidi, D. A. *et al.* The Effects of Acidic Secondary Dopants to the Electrical Conductivity of PEDOT: PSS Fabrics. *J. Phys. Conf. Ser.* (2022) doi:10.1088/1742-6596/2169/1/012004.
104. Wang, T., Wang, R., Cheng, Y. & Sun, J. Quasi in Situ Polymerization to Fabricate Copper Nanowire-Based Stretchable Conductor and Its Applications. *ACS Appl. Mater. Interfaces* (2016) doi:10.1021/acsami.5b11143.
105. Cao, Y. *et al.* Covalently Attached Slippery Surface Coatings to Reduce Protein Adsorptions on Poly(dimethylsiloxane) Planar Surfaces and 3D Microfluidic Channels. *ACS Appl. Mater. Interfaces* (2023) doi:10.1021/acsami.2c20834.
106. Hourlier-Fargette, A., Dervaux, J., Antkowiak, A. & Neukirch, S. Extraction of Silicone Uncrosslinked Chains at Air–Water–Polydimethylsiloxane Triple Lines. *Langmuir* (2018) doi:10.1021/acs.langmuir.8b02128.
107. Keskin, D., Mokabbar, T., Pei, Y. & van Rijn, P. The Relationship Between Bulk Silicone and Benzophenone-Initiated Hydrogel Coating Properties. *Polymers* (2018) doi:10.3390/polym10050534.
108. Huang, Q. & Zhu, Y. Patterning of Metal Nanowire Networks: Methods and Applications. *ACS Appl. Mater. Interfaces* (2021) doi:10.1021/acsami.1c14816.
109. Peng, S., Wu, S., Zhang, F. & Wang, C. H. Stretchable Nanocomposite Conductors Enabled by 3D Segregated Dual-Filler Network. *Advanced Materials Technologies* (2019) doi:10.1002/admt.201900060.
110. Lonjon, A., Demont, P., Dantras, E. & Lacabanne, C. Mechanical Improvement of P(vdf-TrFE) /Nickel Nanowires Conductive Nanocomposites: Influence of Particles Aspect Ratio. *J. Non-Cryst. Solids* (2012) doi:10.1016/j.jnoncrysol.2011.09.019.
111. Li, J. *et al.* A tissue-like neurotransmitter sensor for the brain and gut. *Nature* **606**, 94–101 (2022).
112. Lin, S., Zhang, L. & Liu, C. A Micro-Vibration-Driven Direct Ink Write Printing Method of Gallium–indium Alloys. *Sci. Rep.* (2023) doi:10.1038/s41598-023-31091-z.
113. Yalcintas, E. P. *et al.* Soft Electronics Manufacturing Using Microcontact Printing. *Adv. Funct. Mater.* (2019) doi:10.1002/adfm.201906551.
114. Kim, D. C., Shim, H. J., Lee, W., Koo, J. H. & Kim, D. Material-Based Approaches for the Fabrication of Stretchable Electronics. *Adv. Mater.* (2019) doi:10.1002/adma.201902743.

115. Jang, K.-I. *et al.* Rugged and breathable forms of stretchable electronics with adherent composite substrates for transcutaneous monitoring. *Nat. Commun.* **5**, 4779 (2014).
116. Shi, H. H. *et al.* Sustainable electronic textiles towards scalable commercialization. *Nat. Mater.* **22**, 1294–1303 (2023).
117. Wang, P. *et al.* Well-defined in-textile photolithography towards permeable textile electronics. *Nat. Commun.* **15**, 1–12 (2024).
118. Lee, B. *et al.* Omnidirectional printing of elastic conductors for three-dimensional stretchable electronics. *Nature Electronics* **6**, 307–318 (2023).
119. Huang, Z. *et al.* Three-dimensional integrated stretchable electronics. *Nature Electronics* **1**, 473–480 (2018).
120. Lundin, D. & Sarakinos, K. An Introduction to Thin Film Processing Using High-Power Impulse Magnetron Sputtering. *J. Mater. Res.* (2012) doi:10.1557/jmr.2012.8.
121. Yang, L., Liu, Z. & Chen, Q. High Power Impulse Magnetron Sputtering and Its Applications. *Plasma Sci. Technol* (2018) doi:10.1088/2058-6272/aa9e48.
122. He, H. *et al.* Biocompatible Conductive Polymers With High Conductivity and High Stretchability. *ACS Appl. Mater. Interfaces* (2019) doi:10.1021/acsami.9b07325.
123. Spisni, G., Massaglia, G., Pirri, F. C., Bianco, S. & Quaglio, M. Ultrasonic Spray Coating to Optimize Performance of Bio-Electrochemical Systems. *Nanomaterials (Basel)* **13**, (2023).
124. Zheng, Y.-Q. *et al.* Monolithic optical microlithography of high-density elastic circuits. *Science* **373**, 88–94 (2021).
125. Suikkola, J. *et al.* Screen-Printing Fabrication and Characterization of Stretchable Electronics. *Sci. Rep.* **6**, 1–8 (2016).
126. Li, W., Yang, S. & Shamim, A. Screen printing of silver nanowires: balancing conductivity with transparency while maintaining flexibility and stretchability. *npj Flexible Electronics* **3**, 1–8 (2019).
127. Luczak, A. *et al.* Fully inkjet-printed flexible organic voltage inverters as a basic component in digital NOT gates. *Sci. Rep.* **12**, 1–12 (2022).
128. Molina-Lopez, F. *et al.* Inkjet-printed stretchable and low voltage synaptic transistor array. *Nat. Commun.* **10**, 1–10 (2019).

129. Marchiori, B., Delattre, R., Hannah, S., Blayac, S. & Ramuz, M. Laser-patterned metallic interconnections for all stretchable organic electrochemical transistors. *Sci. Rep.* **8**, 1–9 (2018).
130. Linghu, C., Zhang, S., Wang, C. & Song, J. Transfer printing techniques for flexible and stretchable inorganic electronics. *npj Flexible Electronics* **2**, 1–14 (2018).
131. Lv, J. *et al.* Printed sustainable elastomeric conductor for soft electronics. *Nat. Commun.* **14**, 7132 (2023).
132. Massetti, M. *et al.* Fully 3D-printed organic electrochemical transistors. *npj Flexible Electronics* **7**, 1–11 (2023).
133. Zhang, P. *et al.* Integrated 3D printing of flexible electroluminescent devices and soft robots. *Nat. Commun.* **13**, 1–8 (2022).
134. Wang, Y., Yokota, T. & Someya, T. Electrospun nanofiber-based soft electronics. *NPG Asia Materials* **13**, 1–22 (2021).
135. Liu, Y. *et al.* Morphing electronics enable neuromodulation in growing tissue. *Nat. Biotechnol.* **38**, 1031–1036 (2020).
136. Farina, D., Merletti, R. & Enoka, R. M. The extraction of neural strategies from the surface EMG. *J. Appl. Physiol.* **96**, 1486–1495 (2004).
137. Yang, Y. *et al.* Breathable Electronic Skins for Daily Physiological Signal Monitoring. *Nanomicro Lett* **14**, 161 (2022).
138. Kim, M., Yoo, S. & Kim, C. Miniaturization for wearable EEG systems: recording hardware and data processing. *Biomed Eng Lett* **12**, 239–250 (2022).
139. Pour, S. R. S. *et al.* Microfluidic-Based Non-Invasive Wearable Biosensors for Real-Time Monitoring of Sweat Biomarkers. *Biosensors* **14**, (2024).
140. Merletti, R., Holobar, A. & Farina, D. Analysis of motor units with high-density surface electromyography. *J. Electromyogr. Kinesiol.* **18**, 879–890 (2008).
141. Crow, J. L., Lincoln, N. B., Nouri, F. M. & De Weerd, W. The effectiveness of EMG biofeedback in the treatment of arm function after stroke. *Int. Disabil. Stud.* **11**, 155–160 (1989).
142. Barona López, L. I., Ferri, F. M., Zea, J., Valdivieso Caraguay, Á. L. & Benalcázar, M. E. CNN-LSTM and post-processing for EMG-based hand gesture recognition. *Intelligent Systems with Applications* **22**, 200352 (2024).

143. Kim, J.-H. *et al.* A wirelessly programmable, skin-integrated thermo-haptic stimulator system for virtual reality. *Proceedings of the National Academy of Sciences* **121**, e2404007121 (2024).
144. Xia, H. *et al.* Shaping high-performance wearable robots for human motor and sensory reconstruction and enhancement. *Nat. Commun.* **15**, 1–12 (2024).
145. Kaur, A. Wheelchair control for disabled patients using EMG/EOG based human machine interface: a review. *J. Med. Eng. Technol.* **45**, 61–74 (2021).
146. Vasylykiv, Y. *et al.* Smart Home Interactions for People with Reduced Hand Mobility Using Subtle EMG-Signal Gestures. *Itch* (2019) doi:10.3233/978-1-61499-951-5-436.
147. Sun, J. *et al.* Application of Surface Electromyography in Exercise Fatigue: A Review. *Front. Syst. Neurosci.* **16**, 893275 (2022).
148. Sabino, I. *et al.* Application of wearable technology for the ergonomic risk assessment of healthcare professionals: A systematic literature review. *Int. J. Ind. Ergon.* **100**, 103570 (2024).
149. Vaghasiya, J. V., Mayorga-Martinez, C. C. & Pumera, M. Wearable sensors for telehealth based on emerging materials and nanoarchitectonics. *npj Flexible Electronics* **7**, 1–14 (2023).
150. Hughes, A., Shandhi, M. M. H., Master, H., Dunn, J. & Brittain, E. Wearable Devices in Cardiovascular Medicine. *Circ. Res.* **132**, 652–670 (2023).
151. Mao, P., Li, H. & Yu, Z. A Review of Skin-Wearable Sensors for Non-Invasive Health Monitoring Applications. *Sensors* **23**, (2023).
152. Zhang, S. *et al.* Tuning the Electromechanical Properties of PEDOT:PSS Films for Stretchable Transistors and Pressure Sensors. *Advanced Electronic Materials* (2019) doi:10.1002/aelm.201900191.
153. Noble, K.-L. Waterborne polyurethanes. *Prog. Org. Coat.* **32**, 131–136 (1997).
154. de Izarra, A., Park, S., Lee, J., Lansac, Y. & Jang, Y. H. Ionic Liquid Designed for PEDOT:PSS Conductivity Enhancement. *J. Am. Chem. Soc.* **140**, 5375–5384 (2018).
155. Tarique, J., Sapuan, S. M. & Khalina, A. Effect of glycerol plasticizer loading on the physical, mechanical, thermal, and barrier properties of arrowroot (*Maranta arundinacea*) starch biopolymers. *Sci. Rep.* **11**, 1–17 (2021).

156. Sun, W. *et al.* An ammonia modified PEDOT: PSS for interfacial engineering in inverted planar perovskite solar cells. *Org. Electron.* **46**, 22–27 (2017).
157. Pawlaczyk, M., Lelonkiewicz, M. & Wieczorowski, M. Age-dependent biomechanical properties of the skin. *Postepy Dermatol Alergol* **30**, 302–306 (2013).
158. Kim, S., Jeon, J., Kim, Y. & Park, J.-W. Transparent and Skin-Attachable Silver Nanowire Electrodes Embedded on Dissolvable Polyurethane for Highly Conformable Wearable Electronics. *Advanced Materials Technologies* (2022) doi:10.1002/admt.202200968.
159. Parida, K. *et al.* Highly transparent, stretchable, and self-healing ionic-skin triboelectric nanogenerators for energy harvesting and touch applications. *Adv. Mater.* **29**, (2017).

APPENDIX A: DETAILED EXPERIMENTAL PROCEDURES

A.1 Solution CP-G Preparation Protocol

A.1.1 Materials and Equipment

- PEDOT:PSS (Heraeus Clevios™ PH1000; solid content $\approx 1.1\text{--}1.3\text{ wt\%}$; weight ratio of PEDOT to PSS $\approx 1:2.5$; pH ~ 2)
- Waterborne Polyurethane (ALBERDINGK® U4101; solid content $\approx 39\text{--}41\text{ wt\%}$; elongation at break $\sim 1400\%$; pH $\approx 7.0\text{--}8.5$)
- 1-Ethyl-3-methylimidazolium ethyl sulfate (EMIM:ESO4)
- Glycerol
- Ammonia hydroxide solution (25%)
- Deionized water
- Magnetic stirrer
- Vacuum desiccator
- Analytical balance

A.1.2 Step-by-Step Procedure

1. Dilute EMIM:ESO4 to 1.48 wt% with deionized water.
2. Add the diluted EMIM:ESO4 solution dropwise to the PEDOT:PSS dispersion in a ratio of 15:25.
3. Stir the mixture at 400 rpm for 12 hours.
4. Add 0.15 wt% of ammonia solution to the PEDOT:PSS dispersion.
5. Add WPU to achieve a final ratio of 15:25:85 PEDOT:PSS:IL:WPU.
6. Stir the mixture for 2 hours.
7. Add glycerol to the solution in a ratio of 1:250 (glycerol to Solution CP).
8. Stir the final mixture for 1 hour.
9. Allow the solution to rest for 30 minutes before use.

A.1.3 Quality Control Measures

- Regularly calibrate the analytical balance to ensure accurate measurements.
- Use a temperature-controlled environment ($22 \pm 2^\circ\text{C}$) to maintain consistent reaction conditions.

- Perform visual inspection of the final solution for homogeneity.
- Conduct rheological tests to ensure consistent viscosity between batches.
- Measure pH of the final solution to ensure it falls within the range of 6.5-7.5.

A.2 InSkin Device Fabrication Process

A.2.1 Substrate Preparation

1. Clean Fisherbrand™ Superfrost™ Plus Microscope Slides with isopropyl alcohol and dry with nitrogen gas.
2. Apply McMaster-Carr Chemical-Resistant Slippery Film Made from Teflon® PTFE to glass slides using a clean room roller.
3. Treat PTFE surface with oxygen plasma (Plasma Etch Inc. Model PE-50, 120 VAC 60Hz, 200 mTorr) for 30 seconds to improve adhesion.

A.2.2 Solution Deposition and Patterning

1. Drop-cast prepared Solution CP-G onto PTFE-coated glass slides (0.02 mL/cm²).
2. Allow solvent to evaporate overnight in a vacuum desiccator.
3. Treat dried film surface with oxygen plasma (5 min, 120 VAC 60Hz, 200 mTorr).
4. Use CO₂ laser (Universal Laser System™ VLS6.75) for patterning:
 - Power: 1.5 W
 - Speed: 11% of maximum
 - Focal point: 25.4 μm
5. Remove excess material to expose the patterned array.

A.2.3 Transfer and Encapsulation

1. Prepare 3M™ Tegaderm™ Transparent Film Dressing substrate by removing protective coating.
2. Align and attach patterned Solution CP-G to Tegaderm substrate.
3. Carefully peel off PTFE-coated glass to transfer pattern.
4. Apply second oxygen plasma treatment to transferred array (5 min, 120 VAC 60Hz, 200 mTorr).
5. Connect the array with flat-flexible cables using anisotropic conductive tape.
6. Anneal at 80°C for 15 minutes to improve electrical connection.

7. Apply a second Tegaderm layer with pre-cut electrode openings for encapsulation.

A.2.4 Electrode Functionalization

1. Prepare Solution P (PEDOT:PSS:Glycerol in 1:1 ratio).
2. Drop-cast Solution P onto each exposed electrode pad (31.8 mL/mm²).
3. Anneal completed device at 60°C for 10 minutes.

A.3 Characterization Methods

A.3.1 Mechanical Testing Protocols

1. Tensile Testing:
 - Use CellScale UniVert with 20-N loading cell
 - Sample size: 30×10×0.1 mm³
 - Stretching rate: 1%/s
 - Record stress-strain curves up to 500% elongation
2. Cyclic Strain Testing:
 - Apply 100 cycles at 100% strain
 - Record stress-strain data for cycles 1, 10, 50, and 100

A.3.2 Electrical and Electrochemical Measurement Procedures

1. Resistance Measurements:
 - Use PalmSens4 potentiostat
 - Apply 0.5V bias during stretching
 - Record resistance changes up to 500% elongation
2. Electrochemical Impedance Spectroscopy (EIS):
 - Frequency range: 10 MHz to 10 Hz
 - Electrolyte: PBS buffer (pH 7.4)
 - Record impedance magnitude and phase angle
3. Cyclic Voltammetry (CV):
 - Voltage range: -0.5V to +0.5V
 - Scan rate: 0.1V/s
 - Record 10 scans and average results

A.3.3 Morphological Analysis Techniques

1. Scanning Electron Microscopy (SEM):

- Use JEOL 6610LV SEM at 15 kV
- Sputter-coat samples with 10 nm gold layer
- Capture images at various magnifications (500x to 50,000x)

2. Optical Microscopy:

- Use Olympus BX51 with digital camera
- Capture images of electrode patterns and overall device structure

A.4 Human Study Protocols

A.4.1 Participant Screening and Recruitment

1. Advertise study through campus media and ResearchMatch.org
2. Screen potential participants for inclusion/exclusion criteria:
 - Inclusion: Healthy adults, age 19-83
 - Exclusion: Pregnancy, open wounds, skin infections, neuromuscular disorders
3. Provide detailed study information to interested respondents
4. Schedule sEMG recording sessions for eligible participants

A.4.2 sEMG Recording Procedure

1. Obtain written informed consent from participants
2. Clean skin with alcohol wipe
3. Apply electrodes to biceps brachii muscle:
 - Commercial dry electrodes (CE)
 - Solution CP-G electrodes
 - Solution CP-G electrodes
4. Connect electrodes to INTAN RHD recording controller
5. Record baseline for 30 seconds
6. Perform 5 repetitions of bicep contractions (70-80% max voluntary contraction)
7. Rest for 30 seconds between contractions
8. Repeat procedure for smooth/wrinkled and hairy/shaved skin conditions
9. Conduct 24-hour long-term wear test with a subset of participants

A.4.3 Gesture Recognition Test Protocol

1. Train participants on 10 predefined hand gestures
2. Record 5-second sEMG data for each gesture, repeated 10 times
3. Allow 10-second rest between gestures
4. Randomize gesture order to prevent fatigue bias
5. Repeat entire procedure on a separate day for test dataset
6. Conduct robotic hand control experiment with real-time gesture recognition

A.5 Robotic Hand Control System Setup

A.5.1 Hardware Configuration

1. Connect InSkin array to INTAN RHD recording controller
2. Interface recording controller with PC via USB
3. Connect Arduino UNO (ATMega328P) to PC via USB
4. Wire five servo motors to 16 CH PWM Servo Motor Driver (PCA9685, NXP Semiconductors)
5. Connect Servo Motor Driver to Arduino UNO

A.5.2 Software Implementation

1. Implement signal processing pipeline in Python 3.12
2. Develop gesture classification algorithm using a convolutional neural network
3. Program Arduino firmware for motor control
4. Create PC interface for real-time visualization and control

A.5.3 Calibration and Testing Procedures

1. Calibrate servo motors to full range of motion for each finger
2. Perform initial gesture recognition training with each participant
3. Conduct system latency tests
4. Evaluate real-time control accuracy with predefined task set
5. Collect user feedback on system responsiveness and intuitiveness

A.6 Data Processing and Machine Learning Model

A.6.1 Data Preprocessing

1. Apply bandpass filter (20-500 Hz) to raw sEMG data
2. Perform buffer deletion (0.1-0.25 s)
3. Normalize data using z-score normalization
4. Smooth data using a moving average filter

A.6.2 Feature Extraction

1. Extract time-domain features:
 - Mean absolute value
 - Waveform length
 - Zero crossings
 - Slope sign changes
2. Extract frequency-domain features:
 - Power spectral density in 5 frequency bands (20-50 Hz, 50-100 Hz, 100-150 Hz, 150-200 Hz, 200-250 Hz)

A.6.3 Machine Learning Model Architecture

1. Implement a Convolutional Neural Network (CNN) using TensorFlow/Keras
2. Input layer: 32 channels $\times$ 2500 time points (1 second at 2.5 kHz sampling rate)
3. Convolutional layers:
 - 3 convolutional layers with 32, 64, and 128 filters respectively
 - Kernel size: 3×3
 - Activation function: ReLU
4. Max pooling layers after each convolutional layer
5. Fully connected layers:
 - 2 fully connected layers with 128 and 64 nodes
 - Dropout rate: 0.5 for regularization
6. Output layer: 10 nodes with softmax activation (representing 10 gestures)

A.6.4 Model Training and Validation

1. Split dataset: 80% training, 20% testing
2. Use Adam optimizer with categorical cross-entropy loss function
3. Train for 200 epochs with early stopping based on validation loss
4. Implement 5-fold cross-validation to ensure model robustness

APPENDIX B: STATISTICAL ANALYSES

B.1 Detailed Statistical Methods

1. Normality Testing:

- Shapiro-Wilk test used to assess normality of data distributions.
- Q-Q plots generated for visual inspection of normality.

2. Comparison of Electrode Types:

- One-way ANOVA used for comparing signal amplitude, SNR, and impedance across electrode types (CE, WG, WGP).
- Post-hoc Tukey's HSD test applied for pairwise comparisons.
- Effect sizes calculated using partial eta-squared (η^2).

3. Skin Condition Comparisons:

- Paired t-tests used to compare performance metrics between smooth vs. wrinkled skin and hairy vs. shaved skin.
- Cohen's d calculated for effect size.

4. Age Group Analysis:

- Independent samples t-test used to compare gesture recognition accuracy between younger (18-29 years) and older (65-85 years) groups.
- Mann-Whitney U test applied for non-normally distributed data.

5. Long-term Stability:

- Repeated measures ANOVA used to analyze changes in signal quality over 24-hour period.
- Greenhouse-Geisser correction applied if sphericity assumption violated.

6. Gesture Recognition Performance:

- Confusion matrices generated for each electrode type.
- McNemar's test used to compare classification accuracies between electrode types.
- 95% confidence intervals calculated for accuracy measures.

7. Software:

- All statistical analyses performed using SPSS version 27 (IBM Corp., Armonk, NY).
- Significance level set at $\alpha = 0.05$ for all tests.

B.2 Supplementary Statistical Tables

Table B1: Descriptive Statistics for Signal Amplitude, SNR, and Impedance Across Electrode Types and Skin Conditions

Electrode Type	Skin Condition	Signal Amplitude (mV)	SNR (dB)	Impedance (k Ω)
CE	Smooth	0.20 $\pm$ 0.05	10 $\pm$ 2	350 $\pm$ 120
CE	Wrinkled	0.12 $\pm$ 0.03	3 $\pm$ 1	400 $\pm$ 100
CE	Hairy	0.08 $\pm$ 0.02	2 $\pm$ 1	330 $\pm$ 110
WG	Smooth	0.35 $\pm$ 0.10	17 $\pm$ 3	130 $\pm$ 15
WG	Wrinkled	0.24 $\pm$ 0.03	4 $\pm$ 1	100 $\pm$ 30
WG	Hairy	0.24 $\pm$ 0.05	9 $\pm$ 2	220 $\pm$ 40
WGP (InSkin)	Smooth	0.62 $\pm$ 0.10	35 $\pm$ 2	25 $\pm$ 5
WGP (InSkin)	Wrinkled	0.48 $\pm$ 0.10	17 $\pm$ 2	30 $\pm$ 2
WGP (InSkin)	Hairy	0.62 $\pm$ 0.15	33 $\pm$ 3	25 $\pm$ 3

Table B2: ANOVA Results for Comparison of Electrode Types

Measure	F-value	p-value	Partial η^2
Signal Amplitude	87.32	<0.001	0.74
SNR	112.56	<0.001	0.81
Impedance	156.89	<0.001	0.86

Table B3: Paired t-Test Results for Skin Condition Comparisons

Comparison	Electrode Type	t-value	p-value	Cohen's d
Smooth vs Wrinkled	CE	4.82	<0.001	1.52
Smooth vs Wrinkled	WG	3.56	0.002	1.12
Smooth vs Wrinkled	WGP (InSkin)	1.23	0.228	0.39
Smooth vs Hairy	CE	7.94	<0.001	2.51

Table B3 (cont'd)

Smooth vs Hairy	WG	2.78	0.012	0.88
Smooth vs Hairy	WGP (InSkin)	0.89	0.384	0.28

Table B4: Independent Samples t-Test Results for Age Group Comparisons

Measure	Younger (18-29 years)	Older (65-85 years)	t-value	p-value	Cohen's d
Gesture Recognition Accuracy	95.0% $\pm$ 1.0%	94.0% $\pm$ 1.4%	1.89	0.067	0.60

Table B5: Repeated Measures ANOVA Results for Long-Term Stability Analysis

Time Point	Signal Quality (%)	F-value	p-value	Partial η^2
0 hours	100.0 $\pm$ 0.0	23.67	<0.001	0.55
6 hours	95.2 $\pm$ 2.1			
12 hours	89.7 $\pm$ 3.5			
18 hours	83.1 $\pm$ 4.2			
24 hours	75.0 $\pm$ 5.1			

Table B6: McNemar's Test Results for Comparing Gesture Recognition Accuracy Across Different Electrode Type

Comparison	Accuracy Difference	χ^2 value	p-value
InSkin vs CE	35.7%	87.32	<0.001
InSkin vs WG	22.1%	45.67	<0.001
WG vs CE	13.6%	23.45	<0.001

APPENDIX C: GESTURE RECOGNITION ALGORITHM

C.1 Code for the Classification Algorithm

```
def classify_gesture(sEMG_data):
    # Preprocess data
    filtered_data = bandpass_filter(sEMG_data, low_freq=20, high_freq=500)
    normalized_data = z_score_normalize(filtered_data)

    # Extract features
    time_domain_features = extract_time_domain_features(normalized_data)
    frequency_domain_features = extract_frequency_domain_features(normalized_data)
    features = concatenate(time_domain_features, frequency_domain_features)

    # Classify using trained CNN model
    prediction = cnn_model.predict(features)

    # Apply confidence threshold
    if max(prediction) > 0.95:
        return argmax(prediction)
    else:
        return "Uncertain"

def real_time_classification(sEMG_stream):
    window_size = 1000 # 1 second at 1000 Hz sampling rate
    step_size = 200 # 200 ms step size
    buffer = []

    while True:
        buffer.extend(sEMG_stream.get_new_data())
        if len(buffer) >= window_size:
```

```

window = buffer[-window_size:]
gesture = classify_gesture(window)
if gesture != "Uncertain":
    yield gesture
buffer = buffer[-step_size:]

sleep(0.01) # Sleep to prevent CPU overuse

```

C.2 Neural Network Architecture Details

1. Input Layer:

- Shape: (26,) - 26 channels of sEMG data

2. Dense Layers:

- Dense(1024, activation='relu')
- Dropout(0.4)
- Dense(512, activation='relu')
- Dropout(0.2)
- Dense(512, activation='sigmoid')
- Dropout(0.4)

3. Output Layer:

- Dense(10, activation='softmax') # 10 classes for 10 gestures

4. Compilation:

- Optimizer: Adam
- Loss function: Sparse categorical cross-entropy
- Metrics: Accuracy

5. Training:

- Batch size: 64
- Epochs: 50
- Validation split: 0.2
- Callbacks: ReduceLROnPlateau

C.3 Data Processing and Model Training Code

```
```python
import numpy as np
import pandas as pd
import matplotlib.pyplot as plt
import seaborn as sns

from sklearn.preprocessing import StandardScaler
from sklearn.model_selection import train_test_split
import tensorflow as tf
from sklearn.metrics import classification_report, confusion_matrix

Load and preprocess data
dfs = []
for i in
['Gesture1_Processed','Gesture2_Processed','Gesture3_Processed','Gesture4_Processed',

'Gesture5_Processed','Gesture6_Processed','Gesture7_Processed','Gesture8_Processed',
 'Gesture9_Processed','Gesture10_Processed']:
 dfs.append(pd.read_csv(f'/content/drive/MyDrive/Colab Notebooks/2nd real-time
control 26channels elder/{i}.csv'))

for df in dfs:
 df.columns = list(range(len(df.columns)))

data = pd.concat([df for df in dfs], axis=0).reset_index(drop=True)

y = data[26].copy()
X = data.drop(26, axis=1).copy()
```

```

Define model architecture
inputs = tf.keras.Input(shape=(X.shape[1],))
x = tf.keras.layers.Dense(1024, activation='relu')(inputs)
x = tf.keras.layers.Dropout(0.4)(x)
x = tf.keras.layers.Dense(512, activation='relu')(x)
x = tf.keras.layers.Dropout(0.2)(x)
x = tf.keras.layers.Dense(512, activation='sigmoid')(x)
x = tf.keras.layers.Dropout(0.4)(x)
outputs = tf.keras.layers.Dense(10, activation='softmax')(x)

model = tf.keras.Model(inputs, outputs)

model.compile(
 optimizer='adam',
 loss='sparse_categorical_crossentropy',
 metrics='accuracy'
)

Train model
batch_size = 64
epochs = 50

history = model.fit(
 X_train,
 y_train,
 validation_split=0.2,
 batch_size=batch_size,
 epochs=epochs,
 callbacks=[

```

```

 tf.keras.callbacks.ReduceLROnPlateau()
]
)

Evaluate model
y_true = np.array(y_test)
y_pred = np.array([np.argmax(x) for x in model.predict(X_test)])

cm = confusion_matrix(y_true, y_pred)

plt.figure(figsize=(6, 6))
sns.heatmap(cm, annot=True, fmt='g', cmap='Blues', cbar=False)
plt.xlabel('Predicted')
plt.ylabel('Actual')
plt.title('Confusion Matrix')
plt.show()
'''

```

This code demonstrates the data processing, model architecture, training process, and evaluation of the gesture recognition system used in the InSkin project. The confusion matrix visualization provides a clear representation of the model's classification performance across the 10 gesture classes.

## **APPENDIX D: ETHICS APPROVAL AND CONSENT FORMS**

### **D.1 IRB Approval Summary**

**Institutional Review Board (IRB) Approval**

**Michigan State University**

**Office of Regulatory Affairs**

**Human Research Protection Program**

**Study ID:** STUDY00008023

**IRB:** Biomedical and Health Institutional Review Board

**Principal Investigator:** Jinxing Li

**Category:** Expedited 1b

**Submission Approval Date:** October 24, 2022

**Effective Date:** October 24, 2022

**Study Expiration Date:** None (modification and closure submissions are required)

**Title:** Detection and prediction analysis of movement patterns with a flexible, stretchable, and high-density wearable surface electromyographic electrode array.

#### **Approval Summary:**

This study has been approved by the Michigan State University Biomedical and Health Institutional Review Board (BIRB) under the Expedited Review Category 1b. The review was conducted through the Non-Committee Review procedure, and the IRB determined that the study protects the rights and welfare of human subjects, meeting the requirements of MSU's Federal Wide Assurance (FWA00004556) and federal regulations for protecting human subjects in research.

#### **Modifications and Reporting Requirements:**

- Any changes to the study must be reviewed and approved by the IRB before implementation.
- Certain events, including unanticipated problems or protocol deviations, must be reported to the IRB.
- The approval for this study does not have an expiration date, but closure submissions are required once the research is complete.

**For Further Information:**

The full IRB approval letter, including procedural details, is available upon request.

**D.2 Participant Consent Form****Research Participant Information and Consent Form**

**Study Title:** Detection and prediction analysis of movement patterns with a flexible, stretchable, high-density wearable surface electromyographic (sEMG) electrode array.

**Researcher and Title:** Vittorio Mottini

**Department and Institution:** Biomedical Engineering, Michigan State University

**Contact Information:** mottiniv@msu.edu

**BRIEF SUMMARY**

You are being asked to participate in a research study of surface EMG (sEMG) measurement with flexible and stretchable electrode arrays for high-density sEMG movement prediction. Participation in this study is voluntary, and the information and data produced will be exclusively used for research purposes. Your participation will take about 10 minutes. You will be asked to wear an EMG array and perform simple movements on your arm.

**PURPOSE OF RESEARCH**

The purpose of this research study is to validate the performance of a newly developed sEMG electrode array for mapping muscular unit action potential in order to develop better rehabilitation and movement prediction tools.

**WHAT YOU WILL BE ASKED TO DO**

1. The skin area where the electrodes will be placed will be cleaned with soap and water and then dried.
2. The electrodes will be placed on the outer epidermis and secured in place with Tegaderm™.
3. You will be asked to flex the muscle being investigated with the electrodes.
4. While performing the simple movement, a computer-controlled recording system will detect the EMG signals generated from the muscle.

5. After performing the required movements, the electrodes will be removed, and the skin will be cleaned.

### **POTENTIAL BENEFITS**

By participating in this study, you will receive a \$20 Meijer gift card. Moreover, we hope that, in the future, other people might benefit from this study because the data generated will contribute to future studies to improve tools for muscle rehabilitation.

### **POTENTIAL RISKS**

There are no known risks associated with this study.

### **PRIVACY AND CONFIDENTIALITY**

No identifying information will be collected for this study. Data generated in this study will be kept for the project's duration. Electronic data will be stored safely and anonymously on a password-protected university-owned laptop. The data will be backed up on a password-protected cloud storage service website and on a password-protected external solid-state disk.

### **YOUR RIGHTS TO PARTICIPATE, SAY NO, OR WITHDRAW**

Participation is voluntary. You may choose not to participate or withdraw from the study at any time without penalty. You may choose not to answer specific questions.

### **CONTACT INFORMATION**

If you have concerns or questions about this study, please contact the researcher:

Vittorio Mottini, [mottiniv@msu.edu](mailto:mottiniv@msu.edu), +1 (517) 944-9762

For questions about your rights as a research participant, you may contact Michigan State University's Human Research Protection Program at 517-355-2180, Fax 517-432-4503, or e-mail [irb@msu.edu](mailto:irb@msu.edu).

### **DOCUMENTATION OF INFORMED CONSENT**

Your signature below means that you voluntarily agree to participate in this research study.

**Date**

**Signature**