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Multimodal Sensing Technologies Using Graphene in Health Monitoring: From Physical Signals to Chemical Biomarker Detection

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Abstract. Today in light of the growing demand for comprehensive health monitoring, technologies that can capture human physiological signals and chemical biomarkers in biological fluids simultaneously have become essential. As well as, due to its exceptional electrical and mechanical properties and biocompatibility, graphene is an ideal material for constructing multifunctional and multimodal wearable sensing platforms, offering a solution for real-time, non-invasive health monitoring. This paper provides a systematic review of research progress in graphene-based physical and chemical sensors for health monitoring, covering their operating principles, performance characteristics, and related applications. The focus of this study is on the strategies and key challenges involved in integrating diverse sensing modalities, such as physical and chemical sensing, into a single platform or system. Furthermore, this paper conducts an in-depth analysis of the critical challenges that must be overcome during the practical implementation of such multimodal sensors, and evaluates their biocompatibility, wearability, and long-term stability.

Keywords: Graphene; Multimodal; Wearable; Health Monitoring.

1. Introduction

Since its discovery in 2004, graphene has been widely studied. Research has found that graphene has excellent conductivity, mechanical strength, and flexibility, which enable it to monitor various physical and chemical signals, providing possibilities for its application in the field of sensors. On the other hand, its flexibility and low quality allow it to be made into wearable devices. The combination of the two provides a research direction for integrating different sensor modes into a single platform or system, making real-time monitoring and portability possible. At present, graphene has been widely used in the field of sensors, including the monitoring of physical and chemical signals [1,2]. In addition, graphene is widely used in wearable devices due to its flexibility. However, most of these wearable devices use a single type of sensor, such as wearable graphene sensors that use ambient light to monitor health [1,3], which cannot provide comprehensive and systematic monitoring of human health. The integration of disparate sensing modes into a unified platform or system by leveraging the multifaceted properties of graphene has the potential to revolutionise the field of mobile health technology. This approach will facilitate comprehensive monitoring of human health conditions, thereby circumventing the limitations of conventional devices that are limited in functionality and unable to correlate physiological status and metabolic levels. The prospect of real-time health monitoring through wearable devices becomes a tangible reality. This concept is in alignment with the prevailing trend of wearable sensors towards multi-functional and integrated development, which will provide a new paradigm for the lifestyle and commercialisation of graphene. In consideration of the practical applications of graphene wearable devices in daily life, this review will also explore their biocompatibility, wearing comfort, and long-term stability.

2. Graphene-Based Physical Sensing Modalities

2.1. Piezo-Resistive/Strain Sensing

In the absence of applied stress, the presence of overlapping graphene sheets results in the formation of interconnected conductive pathways. However, when tensile strain is applied, the graphene network structure undergoes an elongation, thereby reducing the overlapping area between the sheets. This has been shown to increase the tunnelling resistance for electron transfer between sheets, thus raising the overall electrical resistance. In contrast, compressive stress has been shown to reduce overall resistance [4]. This is the underlying mechanism that governs the resistance change in graphene network structures under pressure. In essence, stretching minimises the overlap/contact area between coated graphene sheets, thereby enhancing resistance. Upon release of strain, contact is restored and resistance reverts to its original state [5].

This mechanism facilitates the monitoring of pressure changes through current variations, making it suitable for use in sensor applications. As Zhu Chuang's research at Donghua University has demonstrated, a strain sensor based on cotton has been developed. This sensor consists of graphene coated onto cotton yarn using polydopamine, then encapsulated in flexible polytetrafluoroethylene (PTFE). The sensor's response to tensile forces is characterised by a decrease in the overlapping area between the graphene flakes and an increase in the gaps between them. This results in a smooth, reversible increase in resistance. When the strain ·is released, the yarn recoils, restoring contact between the graphene flakes and returning the resistance to baseline levels. Concurrently, the resistance gradually changes, making it suitable for measuring larger physiological activities (e.g. joint flexion amplitude and breathing depth) as opposed to merely weak pulse vibrations [4].

2.2. Temperature Sensing

The primary mechanism by which graphene, particularly reduced graphene oxide (rGO), is employed for temperature sensing is reliant on its electrical resistance, which is subject to temperature-dependent variations. These variations are governed by the behaviour of thermally activated charge carriers. As the temperature increases, the probability of charge carriers (electrons or holes) transitioning from the valence band to the conduction band rises, leading to an increase in carrier concentration. This phenomenon is accompanied by a change in electrical resistance, which typically manifests as a negative temperature coefficient. The negative temperature coefficient is characterised by a decrease in resistance with an increase in temperature [6].

The high thermal conductivity of rGO (approximately 5300W·m-1·K-1) also enables it to respond rapidly to temperature changes, thereby enhancing sensor sensitivity [6]. The Marzia team has successfully transformed discarded graphene-based electronic textiles into conductive recycled powders through the process of pyrolysis at a temperature of 1000°Cin an inert atmosphere. Subsequently, these recycled materials and raw graphene were separately coated on Tencel fabric to create wearable electrodes. The resistance value of the material is known to be subject to change in accordance with the temperature coefficient of resistance of graphene. Consequently, the temperature can be deduced through the measurement of the resistance change. The experiment measured the resistance changes of raw graphene and recycled graphene-coated fabric electrodes in the temperature range of 25°C to 55°C. It is evident that both exhibit negative temperature coefficient characteristics, whereby resistance decreases with increasing temperature [7]. This finding demonstrates the high practicality of graphene-based temperature sensors and provides a feasible method for producing sensors through the recycling of waste. This approach underscores the dual advantages of resource recycling, which is beneficial in terms of reducing environmental impact and potential costs. Additionally, the strong adhesion between graphene and fabrics provides sensors with flexibility, breathability, and comfortable wearing characteristics, thereby expanding their application prospects in long-term, close-fitting health monitoring.

3. Graphene-Based Chemical/Biological Sensing Applications

The primary benefit of graphene and its derivatives is their capacity to effectively transform biorecognition events (e.g. antigen-antibody binding and enzyme-substrate reactions) into quantifiable physical signals. This transformation is accomplished principally via two predominant methodologies: electrochemical sensing and field-effect transistor (FET) sensing.

Electrochemical sensing represents the most prevalent chemical detection modality within the realms of wearable and point-of-care diagnostics. Fundamentally, the target analyte undergoes redox reactions at the interface of the graphene working electrode, thereby inducing measurable alterations in current or impedance. The exceptional electrical conductivity and substantial specific surface area (approximately2630m2/g) of graphene furnish a copious number of active sites and expeditious electron transfer pathways for reactions, culminating in a substantial enhancement in detection performance. This renders it especially well-suited for the detection of biomarkers in complex biological fluids, such as sweat and saliva [5,8,9].

In accordance with the detection principles underlying their operation, graphene-based electrochemical sensors can be categorised into two distinct types: current-type (amperometric) and impedance-type sensors. Current-type sensors achieve quantitative detection by measuring redox currents at a constant potential, and as a result, these sensors have a wide range of applications, including in the field of enzyme-catalyzed reaction detection. For instance, a glucose sensor that demonstrated excellent performance in plasma detection was constructed by Cardoso through the utilisation of 3D-printed graphene/polylactic acid electrodes [10]. One of the most typical applications of graphene-based electrochemical sensors is as part of a wearable immunosensor that is based on laser-induced graphene and Ti3C2TxMXene composites for the non-invasive sweat cortisol detection, which is capable of achieving a picomolar level of detection [1].

Graphene-based FET biosensors are reliant on the extreme sensitivity of their channel conductance to surface charge. When charged targets (e.g. proteins or DNA) bind to recognition elements modified on graphene channels, they induce changes in the surface electrostatic potential, thereby modulating the carrier concentration and source-drain current within the channel [11]. This label-free, direct electrical readout mechanism endows the FET sensor with exceptional sensitivity, rendering it particularly suitable for real-time analysis of trace biomarkers. Such sensors demonstrate unique advantages in detecting ultra-low concentration biomarkers, such as inflammatory factors. For example, Hao's team developed a dual-channel aptamer-functionalised graphene FET sensor for simultaneous detection of multiple cytokines, such as IFN-γand TNF-α. This sensor employs a functional sensing channel and an unfunctionalised reference channel to effectively eliminate environmental interference through differential signalling. The instrument has been shown to achieve detection limits as low as 10-15mol/L in various biological fluids, including serum and saliva, with analysis completed within minutes. This provides a state-of-the-art solution for rapid monitoring of severe infections or immune disorders [12].

4. Multimodal Integration Strategies, Challenges, and Prospects

The integration of diverse physical and chemical sensing modalities onto a single flexible platform is an inevitable trend in the development of next-generation intelligent, multifunctional wearable health monitoring systems. This integration provides more comprehensive and reliable physiological information across multiple dimensions and parameters, enabling a holistic assessment of complex health conditions.

4.1. Multimodal Integration Strategy

4.1.1. Multifunctional Single Materials and Composite Synergy.

Materials such as graphene oxide have been shown to exhibit discernible responses to a variety of physical and chemical stimuli. An exemplar of this is provided by the graphene oxide heterostructure bilayer film reported by Wang et al. Wang constructed a bilayer structure with a gradient oxygen content by regulating the oxygen content of oxidised graphene sheets through a thermal reduction process. This structure is capable of responding to changes in ultraviolet light, humidity, and temperature. Oxygen functional groups induce proton generation and migration upon external stimulation, while oxygen concentration differences between bilayers create asymmetric charge distributions, thereby generating distinct electrical signal response patterns [13]. This strategy relies on precise control over the micro- and nanostructures and physicochemical properties of materials to achieve the goal of integrating multiple modalities into a single system by leveraging the multifunctional characteristics of a single material.

In addition, a more common strategy is to composite graphene or its derivatives with other functional materials. For example, combining laser-induced graphene with single-walled carbon nanotubes to construct a sandwich structure for enhancing the sensitivity of sweat lactate sensors [14]. Another common composite is the combination of graphene with conductive polymers, hydrogels, etc., to simultaneously obtain excellent electrical properties, mechanical flexibility and biocompatibility, laying the foundation for integrated biosensors and physical sensors [15,16].

4.1.2. From Micro-Heterogeneous Interfaces to Macro-Heterogeneous Integration.

Building special structures within or at the interface of materials is the key to achieving multifunctionality of a single material or enhancing a single function. As an illustration, consider the earlier mentioned graphene oxide bilayer heterojunction interface, which itself represents a sophisticated structural design. This design is the catalyst for the creation of a built-in proton migration-driven potential field and thus forms the structural basis for multi-signal response [14]. Similarly, in terms of physical sensing, designing graphene films with porous, wrinkled, or micro pyramid structures can greatly enhance their sensitivity to pressure and strain, providing high-performance units for integrated tactile perception [17,18].

The simplest way to achieve multimodal sensing is to integrate macro-heterogeneous units. This involves arranging and encapsulating sensing units that operate on different principles in a specific manner. For instance, Li demonstrated that combining LIG interdigitated electrodes with long-period fibre gratings encapsulated in PDME enabled the integration of photochemical and electrochemical sensing units. This formed a photoelectric hybrid structure capable of simultaneously monitoring glucose and biomechanical parameters within a compact space [16].

4.1.3. Acquisition and Processing of Mixed-Signal Data.

One of the core challenges of multimodal integration is how to accurately and independently extract various modal information from mixed signals, which is related to the accuracy of health monitoring. We can use the different nature of signals generated by different sensing mechanisms on physical carriers (such as light and electricity) to achieve synchronous but independent measurement. For example, in optoelectronic hybrid sensors, glucose concentration is encoded as resistance, while biomechanical information is encoded as resonant wavelength shift. These two signals are naturally separated and do not interfere with each other during transmission and detection, achieving true parallel operation [16].

4.1.4. Synergy Between Flexible Electronics and Intelligent Systems.

For a comprehensive health monitoring system, we must integrate all types of sensors into a complete wearable system, which necessitates an integrated design at the system level.

This can be achieved through flexible electronic hybrid technology, integrating flexible sensors with rigid or flexible chips such as microcontrollers, wireless communication modules, and power management units to build an integrated flexible patch system that combines sensing, signal processing, and data transmission capabilities. For example, the multimodal sweat sensing system employs a three-tier wireless topology comprising a “patch-relay-host” configuration [14]. The flexible sensor patch receives wireless power and transmits data via near-field communication from a relay unit attached to clothing. The relay unit then communicates with host devices such as smartphones via Bluetooth [14]. This design eliminates the battery on the patch, enhancing safety and wearability.

More importantly, future system integration will inevitably incorporate intelligent algorithms. This involves not only back-end signal analysis but also front-end real-time calibration, drift compensation, and data fusion [1]. Embedding artificial intelligence into wearable systems is key to achieving device autonomy, providing real-time feedback and alerts, and represents an advanced stage of “smart integration” [19].

4.2. Analysis of Key Practical Challenges

For multimodal wearable sensors to be effectively applied in long-term, reliable personal health management, the following interconnected core challenges must be systematically addressed.

4.2.1. Biocompatibility and Wear Comfort

Biocompatibility and wear comfort are prerequisites for the practical application of multimodal sensing systems. Biocompatibility requires that all materials in direct contact with the skin(including the substrate, active layer, and encapsulation layer)must be non-toxic, non-irritating, and ideally resistant to biofouling. There is literature that clearly indicates that achieving long-term stable non-invasive monitoring requires the development of biocompatible encapsulation materials and the establishment of standardized protocols for verifying materials and devices under physiologically relevant conditions [1]. When developing graphene piezoresistive wearable sensors, researchers specifically conducted biocompatibility testing to assess potential risks associated with long-term contact with the human body [4]. Wear comfort is crucial for user experience and compliance, requiring devices to be ultra-thin, soft, breathable, and stretchable to minimize movement restrictions and skin irritation. For instance, to monitor fragile surfaces such as the ocular surface, researchers developed graphene field-effect transistor sensors with ultra-thin substrates capable of withstanding large deformations, demonstrating the importance of mechanical matching with biological tissues [11]. Integrating sensors with electronic textiles is an effective approach to enhancing breathability and natural wearability [5,20].

4.2.2. Long-Term Stability and Reliability

It is a well-established fact that long-term exposure to complex biological fluids, such as sweat and sebum, causes biofouling of the sensor's active interface. This biofouling includes deposits of protein and salt. This phenomenon is characterised by a decline in sensitivity and baseline drift, as well as a deterioration in the signal-to-noise ratio. All of these things together make it hard to get continuous monitoring without having to calibrate often [21]. Some solutions to this problem are making anti-fouling coatings, like zwitterionic polymers, using strong immobilisation methods, like covalent bonding, to make the retention rate of biometric elements better, and designing renewable sensing interfaces [1].

In addition, under repeated wearing and movement induced bending and stretching, the interface between the conductive network, functional coating, and substrate of the sensing material may experience fatigue or delamination, leading to performance degradation or even failure. Debnath listed mechanical degradation as one of the three main failure modes of graphene wearable biosensors. He emphasized the need to design robust structures that can withstand repeated strains without compromising conductivity or receptor integrity. Arwani team built a strain-insensitive chemical detection platform by introducing graphene-based hydrogel to maintain electrical stability under mechanical deformation [22].

4.3. Outlook for the Future

Future research on graphene-based multimodal wearable sensors should focus on overcoming core bottlenecks in integrated applications to achieve the leap from laboratory prototypes to reliable, practical devices. Research directions require systematic advancement. At the material level, novel flexible encapsulation materials that combine biocompatibility, mechanical compatibility, and long-term stability should be developed, alongside the establishment of a standardized biocompatibility evaluation system. At the system level, the key lies in integrating edge computing with artificial intelligence algorithms to achieve real-time intelligent calibration of data, as well as the decoupling and fusion of multimodal signals. This ensures data quality while reducing power consumption.

With the maturation of technology, this field demonstrates broad application prospects. Its core value lies in driving the transformation of healthcare models from passive, intermittent treatment to proactive, continuous personalized health management. By continuously collecting multidimensional physiological and biochemical data in real time and over extended periods, combined with artificial intelligence analysis, this technology holds promise as a transformative tool for chronic disease management, early disease screening, and precision diagnostics and treatment based on "digital twins." Ultimately, it will be applied to preventive medicine and personalized healthcare systems.

5. Conclusion

In summary, graphene offers an exceptional platform for wearable sensing applications owing to its unique two-dimensional structure and outstanding physicochemical properties. In terms of physical sensing, its exceptional mechanical strength, high conductivity, and atomic-level thickness endow it with extreme sensitivity and a wide detection range for physical stimuli such as pressure and strain. In the field of chemical/biosensing, its enormous specific surface area, ease of functionalization, and highly efficient electron transfer capability enable it to selectively detect a wide range of biochemical markers.

It is evident that the capacity of single-modality sensor data to satisfy the requirement for comprehensive and precise interpretation of complex physiological states has reached its limits. Consequently, multimodal integration, defined as the collaborative integration of physical and chemical sensing mechanisms onto a single flexible platform, is an inevitable trend in the development of next-generation comprehensive health monitoring systems. The core concept of achieving multimodal sensing lies in the efficient and synergistic integration of sensing capabilities for different target signals onto a single flexible platform. This integration is not merely a simple aggregation of functions, but rather a systematic engineering endeavour spanning material design, structural engineering, signal processing, and system construction.

In conclusion, it is vital to articulate that biocompatibility, long-term wear comfort and system stability in real-world applications represent the core obstacles hindering advanced sensing technologies from transitioning from laboratory research to clinical validation and large-scale market deployment. Consequently, surmounting these challenges necessitates profound interdisciplinary integration and collaborative innovation across materials science, artificial intelligence, biomedicine and clinical research. It is imperative that both academia and industry direct their efforts towards these critical scientific questions and technical challenges, augment research investment and facilitate the integration of resources, and collectively propel the advancement of graphene-based multimodal sensing technology. This will accelerate its practical application in the field of personalised health management.

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