Trends in Analytical Chemistry 196 (2026) 118687

Contents lists available at ScienceDirect

Trends in Analytical Chemistry

journal homepage: www.elsevier.com/locate/trac

Wired for stress: Advances in electrochemical biosensors for monitoring of cortisol and catecholamines via wearable and point-of-care platforms

Ceren Karaman [a,b], Mustafa Aydemir [c], Onur Karaman [d,*]

[a] Akdeniz University, Department of Electricity and Energy, Antalya, 07070, Turkiye
[b] Akdeniz University, Renewable Energy Resources and Technologies, Antalya, 07070, Turkiye
[c] Akdeniz University, Faculty of Medicine, Department of Endocrinology, Antalya, 07070, Turkiye
[d] Akdeniz University, Department of Medical Imaging Techniques, Antalya, 07070, Turkiye

ARTICLE INFO

Keywords:
Electrochemical biosensors
Cortisol monitoring
Catecholamine detection
Hormone sensing
Wearable diagnostics
Point-of-care platforms
Personalized endocrine monitoring

ABSTRACT

Stress hormones including cortisol and catecholamines (epinephrine, norepinephrine, and dopamine) play crucial roles in regulating physiological responses to emotional, physical, and metabolic challenges. Their dynamic secretion patterns characterized by pulsatility, diurnal variation, and rapid concentration changes make timely monitoring essential for accurate assessment of stress-related conditions including adrenal disorders, mental health imbalances, cardiovascular dysfunction, and performance stress in athletes. Conventional diagnostic techniques, while precise, rely on invasive sampling, centralized laboratory infrastructure, and delayed feedback, limiting their utility for point-of-care (PoC) applications. Recent research has shown that electrochemical biosensors can meet the practical requirements of stress hormone analysis, offering both high sensitivity and adaptability for integration into wearable formats using sweat, saliva, or interstitial fluid as sample media. This review critically examines the current landscape of electrochemical biosensor technologies tailored for stress hormone detection, with a focus on sensor architecture, biorecognition strategies, signal amplification techniques, and the role of functional nanomaterials. Emphasis is placed on the integration of these sensors into wearable and PoC platforms, enabling rapid or near-continuous monitoring and supporting remote health assessment. Furthermore, key clinical applications, existing limitations, and the translational potential of these technologies within personalized and digital endocrinology are discussed. While several emerging wearable and microfluidic electrochemical systems demonstrate fast or semi-continuous operation, the majority of reported cortisol and catecholamine biosensors remain single-use or endpoint devices. Accordingly, this review highlights advances that enable rapid, on-demand electrochemical monitoring while outlining future directions toward fully continuous stress sensing.

1. Introduction

The human stress response is governed by a highly coordinated neuroendocrine network, primarily involving the hypothalamic–pituitary–adrenal (HPA) axis and the sympathetic nervous system (SNS) [1,2]. Upon exposure to physical or psychological stressors, the hypothalamus stimulates the anterior pituitary to secrete adrenocorticotropic hormone (ACTH), which in turn triggers the adrenal cortex to release cortisol, the body's primary glucocorticoid [3,4]. Concurrently, the SNS activates the adrenal medulla, initiating a rapid surge of catecholamines, including epinephrine (EP) (or adrenaline), norepinephrine (nEP) (or noradrenaline), and dopamine (DA), which orchestrate the classic "fight-or-flight" response [5,6].

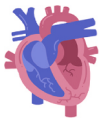
Cortisol and catecholamines are key biomarkers of both acute and chronic stress, holding diagnostic and prognostic value across a wide range of clinical conditions [7,8]. Elevated or dysregulated levels of these hormones have been implicated in mental health disorders such as depression and anxiety, adrenal dysfunctions including Cushing's syndrome and Addison's disease, metabolic syndromes like diabetes and obesity, as well as performance-related stress in athletes and military personnel [9]. Table 1 provides a comparative overview of the physiological roles of cortisol and catecholamines across major body systems. Cortisol primarily regulates long-term stress responses by modulating metabolism, suppressing immune activity, and promoting protein

This article is part of a special issue entitled: POCT devices published in Trends in Analytical Chemistry.

* Corresponding author.
E-mail address: onurkaraman@akdeniz.edu.tr (O. Karaman).

https://doi.org/10.1016/j.trac.2026.118687
Received 12 August 2025; Received in revised form 13 January 2026; Accepted 19 January 2026
Available online 20 January 2026
0165-9936/© 2026 Elsevier B.V. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

Table 1
Comparative physiological effects of cortisol and catecholamines on major body systems [13,14].

	Cortisol	Catecholamines
Central Nervous System 	• Enhances alertness and wakefulness • May impair memory and cognition under chronic exposure •Can cause mood changes (e.g., anxiety, depression	•Increases arousal and attention (fight-or-flight) •Heightens anxiety and vigilance •DA influences reward, motivation, and mood
Cardiovascular System 	•Increases sensitivity of blood vessels to catecholamines •Maintains vascular tone and blood pressure	•Increase heart rate (positive chronotropy) •Increase cardiac output and contractility (positive inotropy) •Vasoconstriction (nEP) increases blood pressure •Vasodilation in skeletal muscles (EP)
Metabolism 	•Increases gluconeogenesis and blood glucose levels •Promotes lipolysis and proteolysis •Induces insulin resistance	•Promote glycogenolysis and gluconeogenesis •Inhibit insulin secretion •Stimulate lipolysis (especially via β-adrenergic receptors)
Immune System 	•Suppresses immune response •Reduces inflammation by inhibiting cytokine production •Decreases lymphocyte and eosinophil counts	•Modulate immune cell trafficking •Acute stimulation may transiently boost immunity •Chronic elevation may suppress immune function
Musculoskeletal System 	•Promotes protein breakdown in muscles •Inhibits bone formation, can lead to osteoporosis over time	•Not directly catabolic but may contribute to muscle tension and tremor

catabolism [10]. In contrast, catecholamines mediate acute stress responses, enhancing cardiovascular output and increasing alertness [11]. Their combined action enables the body to adapt to both immediate and sustained stressors. Given their dynamic secretion patterns characterized by pulsatility, circadian rhythms, and rapid physiological fluctuations [8,12], accurate assessment of these hormones requires analytical methods that offer both high temporal resolution and physiological relevance.

Conventional techniques for hormone quantification, such as enzyme-linked immunosorbent assays (ELISA), high-performance liquid chromatography (HPLC), and mass spectrometry (MS), offer high sensitivity and specificity but are limited by several practical constraints [15]. These laboratory-based methods often involve invasive sample collection, lengthy processing times, and centralized infrastructure, making them unsuitable for continuous or point-of-care (PoC) use [16]. Consequently, they fail to capture the real-time dynamics of stress hormone secretion, which are essential for personalized diagnosis and monitoring. To address these limitations, there is a growing demand for wearable, non-invasive, and real-time sensing platforms capable of detecting hormonal changes as they occur [17,18]. Among emerging technologies, electrochemical biosensors have gained significant attention due to their high sensitivity, fast response times, portability, and compatibility with biofluids such as sweat, saliva, and interstitial fluid (ISF) [19]. These devices offer the potential to translate hormonal fluctuations into measurable electrical signals, enabling continuous monitoring and digital health integration for proactive endocrine management [20,21].

Several recent reviews have addressed different aspects of cortisol and catecholamine biosensing. Karachaliou et al. (2023) provided a comprehensive survey of cortisol immunosensors, covering both electrochemical and optical transduction with an emphasis on assay formats and analytical performance [22]. Weber et al. (2024) and Vignesh et al. (2024) summarized electrochemical and next-generation cortisol detection technologies in human biofluids, cataloguing recognition elements, electroanalytical techniques, and decentralized assay formats [23,24]. More recently, Li et al. (2025) [25], Balasamy et al. (2025) [26], and Sheffield et al. (2025) [27] have reviewed wearable and implantable cortisol-sensing platforms, highlighting advances in device architectures, functional materials, and electronic integration for on-body monitoring. In parallel, Ribeiro et al. (2016) [28], Fredj et al. (2023) [29], and related other works [30] have provided thorough overviews of electrochemical biosensors for catecholamines and dopamine, primarily from neuromodulator or nanomaterials standpoints, offering valuable depth on material platforms and electroanalytical strategies. Additional reviews have discussed cortisol detection methods at broader system levels, including signal processing, electronics, and stress-monitoring frameworks, and therefore offer complementary perspectives [31].

Together, these reviews offer important insights into specific components of hormone biosensing. In contrast, the present review aims to integrate these viewpoints by providing a stress-system-centric and electrochemistry-focused analysis that jointly (i) examines cortisol and catecholamines as complementary biomarkers; (ii) compares biorecognition and transduction strategies across saliva, sweat, and ISF; and (iii) critically evaluates how electrode architectures, sampling modules, and wearable or PoC form factors can be engineered for rapid or semi-continuous monitoring. Guiding this analysis is the central research question of *"How electrochemical biosensing strategies can be optimized to enable reliable real-time or near-real-time detection of stress hormones in minimally invasive formats?*". Literature surveyed in this review was identified primarily through Web of Science, Scopus, and PubMed searches, with emphasis on studies that directly address electrochemical sensing of cortisol and catecholamines, nanomaterial-enabled signal amplification, and wearable or PoC implementations. To maintain a coherent scope, the review prioritizes studies that report electrochemical detection of cortisol or catecholamines, provide mechanistic insight into biorecognition or signal amplification, or demonstrate relevance to wearable or PoC integration; non-electrochemical platforms are referenced only when they offer mechanistic principles directly informative for electrochemical sensor design. Particular emphasis is placed on the translational requirements for wearable and PoC devices, including stability, calibration, and dynamic sampling constraints. By combining endocrine physiology with electrochemical and material design principles and translational considerations, this work seeks to complement and extend existing reviews while offering a cohesive roadmap for next-generation biosensing platforms for endocrine diagnostics and personalized stress management.

2. Stress hormones as biomarkers

To enable non-invasive assessment of the physiological stress response, it is essential to understand how stress hormones transit from their sites of secretion into accessible biological matrices. As illustrated in Fig. 1, cortisol and catecholamines secreted by the adrenal gland enter the bloodstream and subsequently diffuse passively into peripheral biofluids such as sweat, urine, and saliva. Stress activates the HPA axis, initiating the release of corticotropin-releasing hormone (CRH), ACTH, and downstream secretion of cortisol from the adrenal cortex. In parallel, catecholamines (EP and nEP) are released from the adrenal medulla as part of the sympathetic–adrenal–medullary (SAM) response. Once in circulation, these hormones distribute into peripheral matrices through passive or facilitated diffusion. Cortisol and catecholamines can be measured in several sample types commonly used for non-invasive monitoring. They can also accumulate in hair, which reflects long-term hormonal exposure rather than biofluid composition [13,14,32].

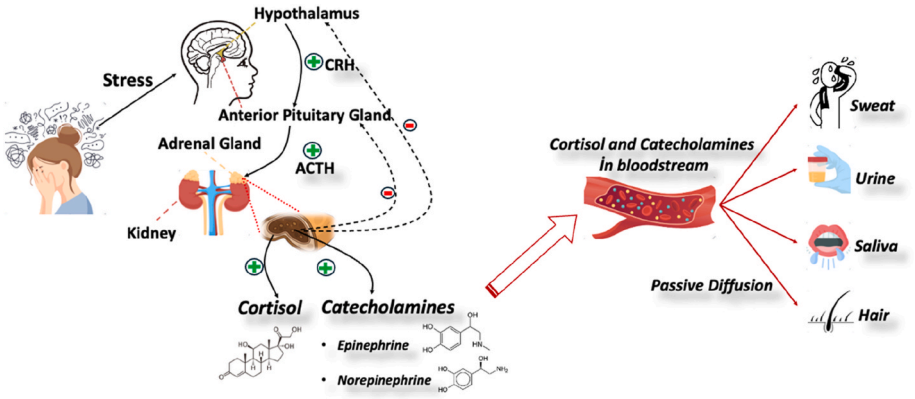


Fig. 1. Neuroendocrine stress pathways and distribution of cortisol and catecholamines in peripheral matrices.

The biofluids serve as valuable substrates for hormone monitoring, each offering unique advantages in terms of sampling convenience, analyte stability, and temporal resolution. The detectability of stress biomarkers in these matrices underpins the development of electrochemical biosensing platforms designed for continuous and non-invasive assessment of endocrine activity, a theme further elaborated in the subsequent sections [17,33].

Electrochemical sensor performance must be interpreted relative to the physiological concentration ranges of stress biomarkers. Cortisol concentrations differ across biofluids due to protein binding: blood and serum values reflect total cortisol (protein-bound + free), whereas saliva, sweat, and ISF contain only free cortisol, the biologically active fraction. In blood, total cortisol typically spans 50–230 ng/mL in healthy adults, with morning peaks around 100–230 ng/mL and afternoon values decreasing to 30–100 ng/mL, consistent with reported clinical ranges [34–36]. Clinical references confirm morning intervals of 45–250 ng/mL, encompassing the broad stated span due to time-of-day and individual factors [34,37,38]. Salivary cortisol, reflecting the unbound fraction of plasma, is approximately tenfold lower, with morning concentrations of 3.7–10 ng/mL and afternoon levels of 0.4–3 ng/mL [35,37,39–41]. Sweat cortisol shows broader variability (0.2–50 ng/mL), although most basal values fall within 2–8 ng/mL, with exercise, heat exposure, or acute stress occasionally producing higher readings [42–44].

Catecholamines present a more stringent analytical challenge. Basal plasma concentrations are typically 0.009–0.09 ng/mL for EP and 0.08–0.60 ng/mL for nEP, while acute psychological or physical stress can transiently elevate levels by 10- to 30-fold, producing short-lived peaks in the low-ng/mL range [45–48]. In sweat and ISF, concentrations may fall into the sub-nanomolar to picomolar range due to rapid enzymatic degradation and local clearance. Analytical challenges arise from these picomolar traces and rapid degradation [49,50]. Many reported biosensors demonstrate low limit of detection (LOD) values, but only a subset achieve physiologically meaningful thresholds across all matrices. These comparisons highlight that ultra-low detection limits are not merely desirable but essential to capturing biomarker dynamics within realistic biological ranges.

Although cortisol and catecholamines are jointly implicated in the stress response, their biochemical properties impose fundamentally different electrochemical sensing constraints. Catecholamines are intrinsically electroactive and undergo reversible redox reactions, enabling direct voltammetric detection but also introducing susceptibility to electrode fouling, oxidative degradation, and interference from structurally similar metabolites. Cortisol, by contrast, is redox-inactive and relies on affinity-based strategies, making sensor performance dependent on bioreceptor stability, immobilization chemistry, and mitigation of nonspecific adsorption in low-ionic-strength matrices such as sweat. Moreover, catecholamines fluctuate on a sub-second to minute scale, whereas cortisol exhibits slower ultradian and circadian rhythms, necessitating different temporal resolution and calibration strategies. These distinctions underscore that architectures optimized for neurotransmitter sensing cannot be directly translated to cortisol detection, highlighting the need for biomarker-specific design principles in integrated stress-monitoring platforms.

2.1. Cortisol

Cortisol, the primary glucocorticoid in humans, is synthesized in the zona fasciculata of the adrenal cortex under the control of the HPA axis. Its secretion is tightly regulated through a negative feedback loop involving CRH and ACTH. This hormone plays a critical role in metabolic regulation, immune response modulation, cardiovascular tone, and central nervous system function [13,32]. Its concentration fluctuates according to both circadian rhythms and pulsatile secretory patterns, peaking in the early morning hours (typically between 6 and 8 a.m.) and reaching its lowest around midnight. These temporal dynamics are further modulated by acute stressors, which transiently increase cortisol levels to support the body's adaptation to physiological demands [51].

Clinically, cortisol measurement is indispensable for the diagnosis and management of adrenal pathologies, including Cushing's syndrome (characterized by chronic hypercortisolemia), Addison's disease (primary adrenal insufficiency), and secondary adrenal insufficiency due to pituitary or hypothalamic dysfunction [52,53]. Beyond classical endocrinopathies, cortisol dysregulation is also associated with major depressive disorder, generalized anxiety, chronic fatigue syndrome, and post-traumatic stress disorder, positioning it as a biomarker of both endocrine and neuropsychiatric health. Furthermore, altered cortisol profiles have been implicated in obesity, insulin resistance, and cardiovascular risk, suggesting a broader systemic relevance [54,55].

Due to its lipophilic nature and widespread systemic effects, cortisol is detectable in multiple biological matrices, including venous blood, saliva, sweat, urine, and ISF. Each matrix presents distinct advantages and challenges in terms of analyte concentration, sampling ease, and temporal resolution [24]. Plasma cortisol remains the gold standard for diagnostic endocrinology, yet it requires venipuncture, is affected by binding protein levels, and does not always reflect free, bioactive hormone [37,56]. Salivary cortisol, by contrast, is a reliable surrogate for unbound serum cortisol and allows for non-invasive, repetitive sampling with minimal stress-induced bias [35,40]. Sweat and ISF are emerging as viable matrices for wearable biosensing platforms, though challenges persist regarding analyte stability, concentration variability, and calibration against plasma values [57,58]. Table 2 summarizes the physiological concentration ranges and stress-induced changes in cortisol levels across various biological matrices. These values highlight the inherent variability in cortisol distribution depending on sampling

Table 2
Physiological concentration ranges of cortisol and catecholamines across human biological samples [10,25,62].

Biological Fluid	Sampling Timing	Normal Range[a] (ng/mL)	Stress-Induced Change (ng/mL)
Blood	Morning	50–230	55 ± 10
	Evening	30–160	
Serum	Morning	45–250	55 ± 10 (assumed similar with blood)
	Evening	17–147	
Saliva	Morning	10.2–27.3	1.25 ± 0.39
	Evening	2.2–4.1	
Sweat	–	0.64–141.7	1.00 ± 0.29
Tear	–	1–40	b
Hair	–	55 pg/mL	
Urine	–	21–149 μg/day	
Interstitial Fluid	Morning	12–34 ng/mL	
	Evening	9–13 ng/mL	

[a] Blood and serum values represent total cortisol (protein-bound + free). Saliva, sweat, tear, ISF, and urine contain only free cortisol, the biologically active fraction. Hair cortisol reflects long-term cumulative cortisol incorporation and is not directly comparable to free or total cortisol concentrations.

[b] For urine, hair, tear fluid, and ISF, standardized acute stress-induced concentration changes are not consistently reported in the literature due to time-integrated sampling (urine, hair) or limited stress-challenge datasets (tear, ISF). Therefore, quantitative values are not provided to avoid extrapolation.

timing, biological fluid, and detection method. Notably, blood and serum levels exhibit marked diurnal variation and respond acutely to stress, while saliva provides a reliable proxy for free cortisol [35,39,40]. Sweat and ISF, although more variable and influenced by local collection methods, are increasingly recognized for their suitability in wearable biosensing. The wide dynamic range and matrix-specific concentration profiles of cortisol underscore the need for electrochemical biosensors with high sensitivity and broad quantification capability, tailored to the characteristics of each biofluid and the intended use-case, whether clinical diagnostics or continuous monitoring [20,21]. In particular, cortisol levels vary substantially between basal and stress-induced states and across biological matrices, requiring sensors that can accurately resolve low baseline concentrations while remaining responsive to transient elevations associated with physiological or psychological stress [59]. In parallel, high selectivity is essential because structurally related steroids, such as cortisone, progesterone, and prednisolone, can introduce significant cross-reactivity in affinity-based assays [60,61]. Accordingly, electrochemical biosensors for cortisol quantification must integrate highly specific recognition elements (e.g., monoclonal antibodies or aptamers) with robust transduction mechanisms capable of discriminating low analyte levels within complex biological backgrounds.

The continuous and non-invasive monitoring of cortisol is particularly valuable in ambulatory settings, stress research, and performance assessment, where dynamic hormone readouts can enhance individualized diagnostics and therapeutic decision-making. Consequently, the development of electrochemical biosensors optimized for cortisol detection in saliva, sweat, and ISF represents a critical step toward wearable platforms capable of rapid or semi-continuous stress monitoring.

2.2. Catecholamines

Catecholamines, comprising EP, nEP, and dopamine, are a class of biogenic amines synthesized from the amino acid tyrosine. These molecules serve as both hormones and neurotransmitters and play critical roles in the body's acute stress response, regulation of cardiovascular function, metabolic activity, and central nervous system signaling [11,63]. Upon activation of the SAM system, EP and nEP are rapidly released into the circulation from the adrenal medulla, facilitating immediate physiological adaptations such as increased heart rate, blood pressure, and glucose availability [11,14].

The clinical utility of catecholamines as stress biomarkers is well established in both acute and chronic stress assessment [63]. Elevated levels of EP and nEP are associated with conditions such as pheochromocytoma, paraganglioma, hypertension, anxiety disorders, and sympathoadrenal hyperactivity [11,64]. On the other hand, DA dysregulation is implicated in Parkinson's disease, schizophrenia, ADHD, and substance use disorders [65,66]. Due to their short half-lives (typically <2 min in plasma) and rapid degradation by catechol-*O*-methyltransferase (COMT) and monoamine oxidase (MAO), catecholamines are inherently challenging to measure reliably in real time using conventional techniques [67,68].

Quantification of catecholamines in biological samples is traditionally performed using HPLC coupled with either electrochemical or fluorescence detection techniques, or by liquid chromatography (LC) coupled with tandem MS (LC-MS) for enhanced analytical specificity, as well as spectroscopic techniques [67–69]. While effective, these methods are complex, time-consuming, and require specialized laboratory infrastructure, precluding their use in PoC or continuous monitoring applications. Furthermore, catecholamines are present at very low concentrations in peripheral biofluids, typically in the picomolar to nanomolar range, necessitating highly sensitive detection platforms [70].

Catecholamines can be detected in several biological matrices, including plasma, urine, saliva, and sweat [70]. Plasma remains the reference matrix for clinical diagnostics, but the instability of free catecholamines and their rapid clearance pose major analytical limitations. Urinary catecholamines, particularly their metabolites (e.g., metanephrines), provide integrated exposure over time but lack temporal resolution. Salivary and sweat-based monitoring has gained interest for wearable diagnostics, though catecholamine concentrations in these matrices are extremely low and highly variable, further complicating assay development [70,71].

Electrochemical sensing of catecholamines benefits from their electroactive nature, enabling direct oxidation at the electrode surface. However, this intrinsic electroactivity also introduces challenges, including susceptibility to interference from coexisting electroactive species (e.g., ascorbic acid and uric acid), signal instability arising from electrode fouling and surface passivation, and limited molecular discrimination among structurally similar catechol derivatives [29]. Immunosensor-based approaches that utilize antibodies or aptamers specific to catecholamines or their metabolites offer enhanced selectivity and compatibility with biological matrices. Moreover, signal amplification strategies using nanomaterials, redox mediators, or enzymatic cascades are often required to enable quantification at physiologically relevant concentrations [29].

Recent research have demonstrated the feasibility of miniaturized electrochemical biosensors for catecholamine detection using various nanostructures including metal nanoparticles, metal oxides, carbonaceous nanomaterials, MXene-based hybrid nanocomposites, and molecularly imprinted polymers (MIPs) [29]. Integration into microfluidic platforms and wearable devices, though still limited, represents a promising avenue for assessment of autonomic nervous system activity and stress-related endocrine responses [72–75]. Overall, the successful implementation of electrochemical biosensors for catecholamine monitoring demands careful optimization of biorecognition elements, electrode surface properties, and interference mitigation strategies. Their translation into practical, non-invasive, and rapid monitoring systems holds great potential for advancing personalized medicine, especially in the context of stress physiology, neuroendocrine disorders, and performance health.

3. Engineering electrochemical biosensor for stress hormones

Electrochemical biosensors have emerged as powerful analytical tools for the selective and sensitive detection of stress hormones such as

cortisol and catecholamines. Their ability to convert biochemical recognition events into measurable electrical signals makes them particularly attractive for miniaturized, wearable, and PoC platforms [10,23,50]. Fig. 2 provides an overview of the general workflow and core components involved in electrochemical biosensing of stress-related biomarkers. As shown in Fig. 2A, the process begins with sampling biological fluids (e.g., sweat, saliva, or ISF), which are then applied to an electrochemical transducer functionalized with specific biorecognition elements such as antibodies, nanobodies, aptamers, enzymes, MIPs, or even living cells. These elements selectively bind to target analytes like cortisol, EP, or nEP, converting molecular interactions into electrical signals. These signals are processed by a potentiostat and analyzed for diagnostic interpretation [76]. Fig. 2B outlines key electrochemical transduction strategies including amperometric, potentiometric, voltammetric, impedimetric, and conductimetric each offering unique advantages for hormone detection in different platforms and biofluids [77,78]. In the following subsections, we delve into the three foundational pillars of electrochemical biosensors for stress hormone monitoring: (i) sensor architectures and detection principles, (ii) biorecognition strategies, and (iii) functional nanomaterials with particular emphasis on their integration into wearable, and PoC platforms.

3.1. Sensor architectures and detection principles

The architecture of electrochemical biosensors determines how the specific interaction between hormones and their biorecognition elements is transduced into a measurable electrical signal [79]. For stress-related hormones like cortisol and catecholamines, which occur in low concentrations and require detection in real time, the choice of transduction method must consider not only sensitivity and selectivity but also signal stability, integration with wearable formats, and compatibility with complex, low-ionic-strength biofluids such as sweat and saliva [23,79].

3.1.1. Amperometric sensors

Amperometric sensors are widely used for hormone detection due to their high sensitivity and simple instrumentation. These sensors operate by applying a constant potential across the working and reference electrodes and measuring the current generated by redox reactions [80,81]. The resulting faradaic current is proportional to the analyte concentration. Amperometric sensors are particularly well-suited for cortisol detection in competitive immunoassays, where the hormone competes with a labeled analog for binding to immobilized antibodies. Xu and Suleiman (1997) reported one of the earliest studies on the amperometric detection of cortisol, in which they developed a reusable immunosensor based on the co-immobilization of horseradish peroxidase and cortisol-specific antibodies onto a chemically activated affinity membrane affixed to the tip of an oxygen electrode [82]. The immunosensor operates on an inhibition-based mechanism, wherein the binding of cortisol to the immobilized antibody suppresses the electrocatalytic current generated by the enzymatic reaction. The device demonstrated a rapid response time, straightforward analytical procedure, and high selectivity. Regeneration of the sensor was achieved through mild acid washing, enabling multiple reuse cycles. The calibration curve exhibited a linear response in the concentration range of 1×10^{-7} to 1×10^{-5} M cortisol [82]. Later, Vargas et al. (2020) introduced a dual amperometric immunosensor microchip capable of the simultaneous detection of cortisol and insulin in untreated serum samples, aiming to support improved glycemic regulation through enhanced biomarker monitoring [83]. The system integrated distinct immunoassay formats on a single platform including horseradish peroxidas (HRP)-labeled sandwich immunoassay for insulin and an alkaline phosphatase (ALP)-labeled competitive immunoassay for cortisol. By systematically optimizing the incubation protocols and amperometric readout conditions for each enzyme tag, the sensor achieved high analytical performance without cross-interference. The microchip enabled rapid analysis (within 25 min) using just a microliter of untreated serum, successfully detecting insulin at picomolar and cortisol at nanomolar concentrations. This dual-sensing platform presents a promising approach for decentralized monitoring of hormonal markers critical for personalized diabetes management [83]. Torrente-Rodríguez et al. (2020) developed a wearable amperometric sensor platform for the fast, non-invasive detection of cortisol in human sweat using a wireless system based on laser-induced graphene electrodes [84]. The flexible sensor, functionalized with cortisol-specific antibodies, enabled highly sensitive and selective amperometric detection with assay times as short as 1 min. This study was the first to report both the cortisol diurnal cycle

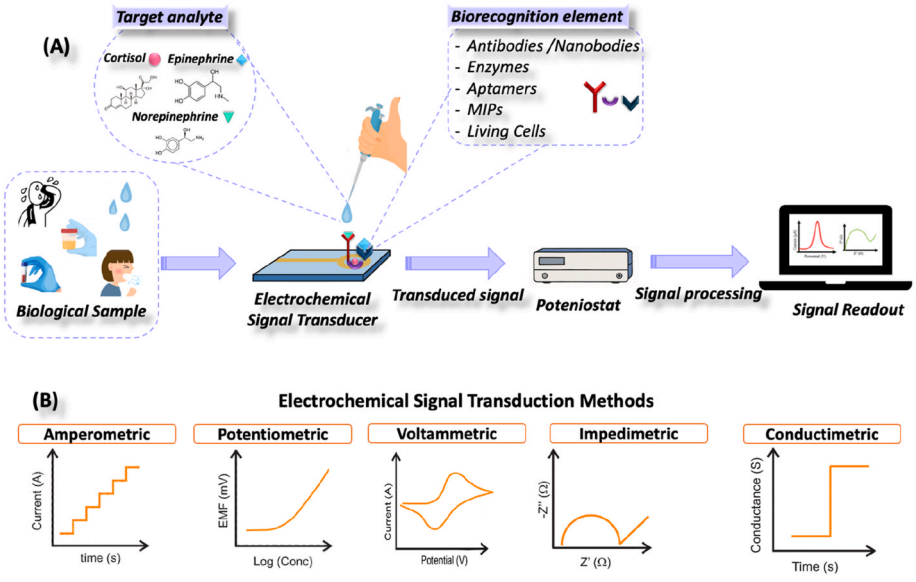


Fig. 2. Electrochemical biosensing workflow and signal-transduction strategies. **(A)** Schematic overview of stress-hormone detection, illustrating key components including biological sample acquisition, target analytes (cortisol and catecholamines), biorecognition elements, electrochemical transduction, signal processing, and digital readout. **(B)** Representative electrochemical signal-transduction methods employed in biosensors, including amperometric, potentiometric, voltammetric, impedimetric, and conductometric measurements.

and acute stress-response profiles derived from sweat, demonstrating a strong correlation with serum cortisol levels [84]. Tang et al. (2021) introduced a touch-based, non-invasive amperometric sensor for rapid cortisol detection in fingertip sweat, utilizing a molecularly imprinted polymer electropolymerized on polypyrrole (PPy) and embedded with Prussian blue redox probes [85]. This label-free electrochemical platform enabled highly selective and sensitive amperometric detection of cortisol within just 3.5 min. The sensor employed a porous hydrogel for efficient sweat collection and demonstrated excellent performance in capturing acute cortisol fluctuations during cold-pressor tests and daily circadian monitoring. A stretchable epidermal version was also applied to exercise-induced sweat, underscoring the system's potential for stress-free stress monitoring and quantitative mental health assessment [85]. Similarly, Carneiro et al. (2025) reported the development of conductive catecholamine–pyrrole (Py) copolymers as advanced platforms for amperometric biosensing [86]. To overcome the poor conductivity of polycatecholamines (PCA) such as polydopamine (PDA), the team co-electropolymerized DA, nEP, and catechol with Py, forming hybrid films (PDA/PPy, PNE/PPy, PCA/PPy) that synergistically combined strong adhesion with enhanced electroactivity. Detailed physicochemical characterization revealed tunable redox behavior, morphology, and dielectric properties, while cyclic voltammetry confirmed broad-range amperometric signal transduction due to the conductive PPy backbone and retained catechol functionality. Notably, the PDA/PPy copolymer exhibited strong adhesion and superior electrochemical performance for detecting gallic acid, demonstrating its suitability as a versatile transduction interface for polyphenol and catecholamine sensing [86]. In another work, Josypčuk et al. (2021) developed and evaluated four amperometric biosensors based on flow-through enzymatic mini-reactors filled with mesoporous silica powders (SBA-15 or MCM-41) functionalized with either laccase or tyrosinase [87]. Among them, the MCM-41 powder covalently bonded with laccase (Lac-MCM-41) demonstrated the highest performance for catecholamine detection. This biosensor exhibited the strongest relative current response toward DA (100 %), followed by Levodopa (32.1 %), nEP (26.2 %), and EP (0.71 %). Key operational parameters such as flow rate, injection volume, and detection potential were systematically optimized. The Lac-MCM-41 biosensor achieved high accuracy (relative standard deviation (RSD) = 1.82–5.18 %) and sensitivity (5.46–15.5 μmol L^{-1}), with a stable operational lifetime extending over several months. Its practical utility was validated through successful analysis of DA and nEP in clinical infusion solutions [87]. On the other hand, Casella et al. (2018) reported the electrochemical characterization and application of a glassy carbon electrode modified with multi-walled carbon nanotubes (MWCNTs) dispersed in a cellulose acetate matrix for the amperometric detection of catecholamines, including DA and EP [88]. The modified electrode exhibited enhanced surface area and favorable nanofiber distribution, leading to improved electroanalytical performance. Using differential pulse voltammetry (DPV) in 50 mM H_3PO_4, detection limits in the 1–10 μM range were achieved. Furthermore, the sensor was coupled with reverse-phase LC (pH 3.5) and a solid-phase extraction step, enabling separation and quantification of DA, EP, and vanillylmandelic acid within 10 min and reaching nanomolar-level detection [88]. Guliya et al. (2025) developed a novel amperometric biosensor for the sensitive and selective detection of catecholamines, including DA, adrenaline, and noradrenaline [89]. The sensor was fabricated by immobilizing cysteine-functionalized laccase nanoparticles (Lac-NPs) onto a pencil graphite electrode (PGE). Comprehensive physicochemical and electrochemical characterization confirmed successful biosensor assembly, with optimization of pH, temperature, and scan rate contributing to enhanced analytical performance. The Lac-NPs/PGE biosensor demonstrated excellent sensitivity (2320.0 μA/mM·cm^2), a low LOD value (0.12 μM), and a wide linear range (0.1–800.0 μM, $R^2 = 0.999$). High recovery rates (94–99 %) were achieved in pharmaceutical sample analysis, supporting the sensor's potential for catecholamine monitoring in clinical diagnostics and neurochemical studies [89].

3.1.2. Voltammetric sensors

Voltammetric sensors employ a varying potential to induce redox reactions and measure the corresponding current response. DPV and square-wave voltammetry (SWV) are the most employed techniques, offering high analytical resolution and low background current [23]. This modality is particularly advantageous for the direct detection of electroactive species such as catecholamines (DA, nEP, and EP undergo irreversible oxidation at electrode surfaces, typically within the 0.2–0.6 V potential window (vs. Ag/AgCl)) [90,91]. However, the electrochemical profiles of these analytes overlap with those of common interferents such as ascorbic acid and uric acid, necessitating the use of selective electrode coatings or differential potential shifts to improve specificity [10,70,92,93]. Strategies to mitigate this include size-exclusion membranes, electrocatalytic coatings, and the use of nanomaterial-based surface modifiers. Several studies have employed nanomaterial-based surface modifiers to resolve overlapping oxidation peaks. For example, Alizadeh et al. (2025) developed a cost-effective and highly sensitive electrochemical sensor for DA detection based on a flame-etched carbon fiber microelectrode (FE-CFME) modified with a pyrene acetic acid (PAA)-decorated single-walled carbon nanotube (SWCNT) nanocomposite [94]. The sensor exhibited excellent performance, with a wide linear range (0.5–22 μM), a low LOD (12.9 nM), and high reproducibility. Practical applicability was demonstrated through successful DA quantification in human serum and pharmaceutical samples [94]. In another work, Esmaeelzadeh et al. (2025) developed a carbon paste electrode modified with bimetallic yttrium–copper MOFs (Y–Cu-MOFs) for the voltammetric detection of DA [95]. The modified electrode exhibited enhanced electrocatalytic activity, leading to a significant improvement in oxidation signals. Using differential DPV, the sensor achieved a wide linear range (0.1–400.0 μM) and a low LOD (0.04 μM). Importantly, it enabled clear peak separation (170 mV) between DA and uric acid, demonstrating strong anti-interference capability [95]. Moreover, Liu et al. (2020) developed an ultrasensitive, smartphone-integrated immunosensor for the non-invasive detection of salivary cortisol using DPV [96]. The sensor employed a nanostructured transducer, functionalized with cortisol antibodies via a PEG-based self-assembled monolayer, and passivated with ethanolamine to prevent non-specific binding. The miniaturized system enabled cortisol quantification in the 0.5–200 nM range, with a LOD of 0.11 nM and high sensitivity (30 μA M^{-1}, $R^2 = 0.9947$). The device successfully differentiated cortisol from other salivary components and tracked diurnal variations, demonstrating its potential as a portable, PoC tool for stress monitoring [96].

While voltammetric and amperometric sensors offer high sensitivity, their real-world performance is often constrained by baseline drift, variable mass transport in sweat or saliva, and susceptibility to fluctuating pH or ionic strength. Wearable operation introduces additional challenges such as motion-induced artifacts and unstable sampling volumes, which can distort current responses and hinder quantitative interpretation. These limitations need careful control of electrode surface chemistry and dynamic calibration methods to maintain accuracy outside laboratory settings.

3.1.3. Impedimetric sensors

Electrochemical impedance spectroscopy (EIS) provides a label-free approach to detection by probing the interfacial properties of the electrode–electrolyte interface. When a target hormone binds to its immobilized bioreceptor on the electrode surface, it introduces steric hindrance and changes the surface charge distribution [96,97]. These effects alter the charge transfer resistance (R_{ct}), double-layer capacitance (C_{dl}) that are highly sensitive to surface functionalization and analyte binding. Although diffusion-related effects can also be represented in EIS spectra, the Warburg impedance (Z_w) mainly reflects mass-transport processes in the bulk solution rather than surface

chemistry. EIS responses are frequently analyzed using a Randles circuit or its modified variants, enabling extraction of R_{ct} and C_{dl} as quantitative indicators of recognition-layer formation, target binding, and sensor degradation [96]. Importantly, because EIS does not require electroactive analytes, enzymatic labels, or redox mediators, it is exceptionally well suited for wearable and PoC platforms where low sample volumes, minimal pretreatment, and stable long-term operation are required [98–100]. However, its performance can be influenced by the ionic composition of the matrix. In low-conductivity fluids such as sweat, the extended Debye length may reduce the capacitive sensitivity for small molecules like cortisol (<400 Da), which limits the signal-to-noise ratio [98,101]. For example, a label-free, noninvasive impedance immunosensor for cortisol detection was developed by coating PEDOT:PSS ((Poly(3,4-ethylenedioxythiophene):polystyrene sulfonate)-modified ITO glass with cortisol-specific antibodies [102]. The system employed non-faradaic EIS to detect changes in impedance upon antigen–antibody binding. The sensor achieved a linear response within the 50–200 ng/mL cortisol range, demonstrating strong correlation ($R^2 = 0.97$) and excellent repeatability [102]. This approach avoids external redox agents and offers a promising platform for stress monitoring and personalized diagnostics. In another example, Venugopal et al. (2011) developed a wearable electrochemical impedance-based immunosensor for cortisol monitoring in ISF [103]. ISF was non-invasively extracted through micropores created in the skin using a near-infrared laser--activated black dye layer, with pores remaining viable for up to three days. *In-vitro* studies demonstrated a linear detection range from 1 pM to 100 nM, and clinical tests confirmed strong correlation with commercial ELISA results in both saliva and ISF [103]. This study showcases the feasibility of a minimally invasive, impedance-based, disposable cortisol sensor, with future integration potential into wireless health monitoring systems for continuous, remote stress monitoring. Similarly, Arya et al. (2010) reported a disposable, label-free impedimetric biosensor for the ultrasensitive detection of cortisol in saliva. Using EIS, the sensor achieved a wide dynamic range from 1 pM to 10 nM with a sensitivity of 2.855 kΩ M^{-1} [104]. The platform demonstrated strong potential for PoC applications, offering accurate and noninvasive cortisol detection in complex biofluids like saliva. On the other hand, Ashton et al. (2025) developed two electrochemical impedance biosensors for the simultaneous detection of cortisol and human growth hormone (hGH) which is a key biomarker of HPA axis activity [105]. Both analytes were immobilized via antibody–antigen interactions on Au(111) slide electrodes and screen-printed gold electrodes, allowing swift, label-free detection based on impedance changes. The cortisol sensor demonstrated detection ranges of 30–300 ng/mL (Au slide) and 60–360 ng/mL (screen--printed chip), while hGH was detected across 5–30 ng/mL on both platforms [105]. This study highlights the potential of dual hormone biosensing for stress monitoring, clinical diagnostics, and performance assessment using practical, cost-effective electrode systems. Moreover, Pusomjit et al. (2021) developed a non-invasive, disposable electrochemical aptamer-based biosensor for the label-free detection of cortisol using screen-printed graphene electrodes (SPGEs) [106]. EIS revealed a dose-dependent decrease in R_{ct} upon cortisol binding, with a linear detection range from 0.10 to 100 ng/mL and a LOD value of 2.1 pg/mL. The biosensor showed high recovery (97.4–109.2 %) and low RSDs (5.7–6.6 %) in artificial sweat, supporting its promise as a low-cost, sensitive, and portable PoC platform for cortisol monitoring [106]. For highly sensitive and selective detection of DA, a molecularly imprinted impedimetric sensor was developed [107]. The sensor surface was functionalized with aminophenylboronic acid and pyrrole-3-carboxylic acid as monomers to form a DA-specific molecular imprint. EIS technique was used for label-free detection, yielding a linear response between 100 and 600 pM ($R^2 = 0.9517$), with a LOD value of 30.34 pM and a quantification limit of 95.82 pM [107]. This approach offers a promising low-cost and ultra-sensitive platform for monitoring DA in clinical diagnostics.

In real-world use, however, EIS sensors are vulnerable to non-specific adsorption and dielectric fluctuation induced by evaporative changes, temperature gradients, or skin contact variability. These effects can mask biomolecule-specific impedance changes and reduce analytical specificity. Therefore, despite their compatibility with miniaturization, EIS platforms require advanced antifouling chemistries and stable interface engineering to deliver reliable on-body measurements.

3.1.4. Potentiometric and field-effect transistor (FET)-based sensors

Potentiometric sensors operate by measuring the potential difference between a working and reference electrode at near-zero current, making them inherently low-power and well suited for miniaturized and wearable formats. In these systems, the measured potential is governed by changes in surface charge density at the sensing interface, typically described by the Nernst equation [108,109]. Although potentiometry is extensively used for ionic and pH sensing, its application to cortisol and catecholamines remains comparatively limited due to the lack of inherent charge changes upon binding and the requirement for highly selective ion-to-electron transduction mechanisms [110,111]. Nevertheless, emerging receptor–gated interfaces, such as aptamer-modified ion-selective membranes or polymeric receptors engineered to modulate interfacial charge, have enabled preliminary potentiometric hormone sensing in sweat and ISF [112–114]. These approaches highlight the potential of potentiometry for integration into low-power, continuous-monitoring platforms.

FET-based sensors, including ion-sensitive field-effect transistors (ISFETs), gate field-effect transistors (GFETs), extended floating gate field-effect transistors (EGFETs), and graphene-FETs, represent an important extension of potentiometric detection [115–118]. In FET biosensors, molecular recognition events occurring at or near the gate dielectric modulate charge carrier density within the semiconductor channel, producing sensitive, real-time electrical responses [119,120]. Recent studies have demonstrated that FET-based sensors can achieve physiologically relevant detection ranges for cortisol in ISF, even under high ionic strength conditions [109,115,116,121,122]. Indeed, Lee et al. (2025) demonstrated that a dual-gate FET architecture can reliably detect cortisol at sub-nanomolar levels, with a detection limit of 276 pM, even in artificial saliva containing high ionic strength and interfering species, underscoring the feasibility of achieving physiologically relevant sensing performance in complex biofluids [117]. Consistent with this trend, Nguyen et al. (2025) demonstrated a lab-on-chip cortisol biosensor with an ultra-low detection limit of 1 fM and a wide dynamic range spanning 1 fM–1 μM, confirming that advanced FET-compatible sensing platforms can reliably operate across physiologically relevant concentrations even in complex bodily fluids [123]. In another work, silicon nitride-based Immuno-FET-based sensor was developed for the quantification of salivary cortisol [109]. Device performance was initially assessed using potentiometry and EIS. The sensor exhibited excellent linearity ($R^2 > 0.99$), high selectivity against other biomarkers and an acceptable LOD of 0.005 ± 0.002 ng/mL [109]. Similarly, Jang et al. (2018) demonstrated a cortisol-detecting FET operating in 1 × PBS with a Debye length of only 0.2 nm, achieving a sensitivity spanning 10 fg/mL–10 ng/mL and a detection limit of 1 pg/mL, further confirming that engineered FET architectures can maintain high sensing performance even under severe ionic screening conditions [124]. Kim et al. (2025) further demonstrated that an immuno-graphene FET could achieve highly sensitive cortisol detection with a 500 fM LOD, a 500 fM–100 nM dynamic range, and a rapid 20 s response [125]. On the other hand, comparable performance in artificial sweat highlighted the ability of advanced FET architectures to operate effectively in complex, high-ionic-strength biofluids. Zhang et al. (2021) also demonstrated reliable cortisol detection using a liquid-gated graphene FET, achieving linear sensing across a broad seven-order concentration range (0.01–10^4 nM) and maintaining strong anti-interference capability in salivary matrices, further confirming that FET-based platforms can deliver robust, physiologically relevant performance in complex biofluids [126]. However, challenges remain, including susceptibility to

drift, sensitivity to microenvironmental pH and ionic fluctuations, and the need for encapsulation strategies that preserve gate–electrolyte coupling while ensuring mechanical durability in wearable devices.

Overall, potentiometric and FET-based platforms offer attractive advantages including ultralow power consumption, scalable fabrication, and compatibility with integrated electronics, but their current maturity for stress hormone monitoring lags behind amperometric, voltammetric, and impedimetric methods. Continued advances in receptor engineering, dielectric surface chemistry, and stable liquid-gate encapsulation will be essential for fully realizing their translational potential in wearable and PoC endocrine monitoring.

3.1.5. *Architectures for mitigating biofouling and environmental variability in electrochemical biosensors*

Beyond the core detection principles, both wearable and PoC architectures must account for the complexities of sensor–biofluid interfaces, where environmental, mechanical, and biological factors can significantly influence signal stability and analytical accuracy [9,127,128]. Although biofouling and environmental variability affect all electrochemical biosensors operating in complex biofluids, these challenges are particularly pronounced in wearable systems due to prolonged contact, dynamic sampling, and mechanical deformation. In wearable systems, these challenges may arise at the sensor–skin interface or within intermediate sampling modules such as microfluidic sweat collectors or ISF extraction patches. The impact of skin surface variability, sweat pH, and ionic strength must be considered in electrode design. Electrochemical signals can be distorted by nonspecific protein adsorption or biofouling at the electrode surface, especially during prolonged contact with complex biological fluids [129]. To address this challenge, Wang et al. (2025) developed an antifouling electrochemical sensor for cortisol detection using a molecularly imprinted conductive hydrogel composed of PEDOT/sodium alginate [130]. By integrating the selectivity of a molecularly imprinted polymer with the biofouling resistance of a conductive hydrogel, the sensor achieved exceptional performance in detecting cortisol across various fluids including sweat, saliva, and serum. Using EIS and chronocoulometry techniques, it demonstrated detection limits as low as 0.131–0.314 pM, along with wide dynamic ranges from 10^{-12} to 10^{-7} M [130]. This work highlights the growing utility of MIP-hydrogel composites as promising materials for real-world biosensing in wearable and continuous monitoring devices, providing both high sensitivity and operational stability in bioactive environments. Similarly, Xu et al. (2023) developed an antifouling electrochemical cortisol biosensor using a chondroitin sulfate (CS) functionalized polyaniline (PANI) nanocomposite combined with dendritic DNA–peptide conjugates [131]. The CS/PANI substrate, electrodeposited onto a glassy carbon electrode, enhanced conductivity and minimized surface fouling, while the DNA–peptide layer provided both signal amplification and antifouling protection. The sensor achieved ultrasensitive cortisol detection in sweat, saliva, and tears [131]. This work exemplifies how multifunctional nanocomposite coatings can offer both sensitivity and resistance to biofouling, crucial for the development of reliable PoC and wearable biosensors. Moreover, Li et al. (2024) developed a high-antifouling nanocrystalline boron-doped diamond microsensor grown on a carbon fiber substrate for DA monitoring [132]. The antifouling performance was found to be closely linked to both crystalline grain size and surface chemistry. In particular, oxygen-terminated nanocrystalline surfaces formed a robust hydration layer, acting as an energetic and physical barrier to protein adsorption. The sensor demonstrated high sensitivity (5.14 μA μM^{-1} cm^{-2}), a low LOD (25.7 nM), and was successfully applied in in vivo DA monitoring in rat brains under potassium chloride stimulation [132]. This study highlights the critical role of diamond-based nanomaterials and surface hydration engineering in the development of next-generation antifouling electrochemical sensors for neurological and clinical applications.

In summary, the electrochemical detection architecture must be carefully tailored to the specific properties of the target hormone, the operational matrix, and the intended device format. Amperometric systems provide strong performance in enzyme-based cortisol sensors, voltammetric methods offer high selectivity for electroactive catecholamines, and EIS presents a compelling route for label-free, miniaturized stress hormone sensors. The ongoing development of hybrid platforms and advanced amplification techniques is expected to further bridge the gap between laboratory-grade sensitivity and real-world usability in wearable and PoC endocrine monitoring systems. While the choice of transduction architecture defines the signal generation strategy, the biorecognition element remains central to the selectivity, affinity, and overall performance of the electrochemical immunosensor. The next section explores the key recognition agents used for stress hormone detection, including antibodies, aptamers, and nanobodies, and the challenges associated with their effective integration onto sensor interfaces.

3.2. *Biorecognition elements*

At the core of every electrochemical biosensor lies a biorecognition element that selectively binds the target analyte and initiates the signal transduction process [76]. The choice of receptor (its affinity, stability, and mode of immobilization) directly governs sensitivity, selectivity, and applicability for wearable or PoC deployment [23,79]. In stress-hormone sensing, bioreceptors must operate reliably in low-volume, complex biofluids (sweat, saliva, ISF), withstand environmental fluctuations, and support rapid or on-demand monitoring. In this section, biorecognition strategies are organized into protein-based receptors (antibodies and nanobodies), nucleic-acid-based receptors (aptamers), and synthetic molecular recognition systems (MIPs), followed by a dedicated subsection on immobilization chemistry.

3.2.1. *Protein-based bioreceptors: antibodies and nanobodies*

Antibodies, particularly monoclonal variants, remain the gold standard for biosensor applications owing to their strong and highly selective antigen-binding capabilities. Their ability to bind small-molecule hormones with high affinity has enabled sensitive detection of cortisol and catecholamines in diverse biofluids such as serum, saliva, sweat, and ISF [104,133,134].

A representative example is the flexible electrochemical immunosensor developed by Liu et al. (2021) for sweat cortisol detection [135]. They engineered a flexible cortisol immunosensor by integrating MWCNTs onto a polydimethylsiloxane (PDMS) substrate and electrodepositing AuNPs to promote covalent attachment of anti-cortisol monoclonal antibodies. This architecture (Fig. 3A) delivered high signal amplification, robust mechanical flexibility, and reliable cortisol quantification in sweat. The results demonstrated the utility of antibody-based platforms for non-invasive, on-body measurement [135]. However, despite their strong analytical performance, antibodies face inherent limitations such as structural fragility, batch-to-batch variability, and susceptibility to denaturation in wearable environments. These properties restrict their long-term use in continuous or semi-continuous monitoring and motivate the exploration of more robust protein scaffolds.

Nanobodies, or VHH (Variable Heavy-chain) fragments, along with recombinant nano-protein scaffolds, represent a next-generation class of protein-based bioreceptors that retain the high affinity of traditional antibodies while offering enhanced stability, controlled orientation, and superior scalability. Their compact size (~15 kDa—approximately one-tenth that of a conventional IgG) enables dense surface packing and improves the accessibility of binding epitopes at electrode interfaces. These attributes make nanobodies particularly well suited for compact, flexible, wearable electrochemical sensors and portable PoC devices, where mechanical resilience and environmental stability are essential. Although their application in electrochemical hormone sensing is still emerging, nanobodies have shown strong potential across various

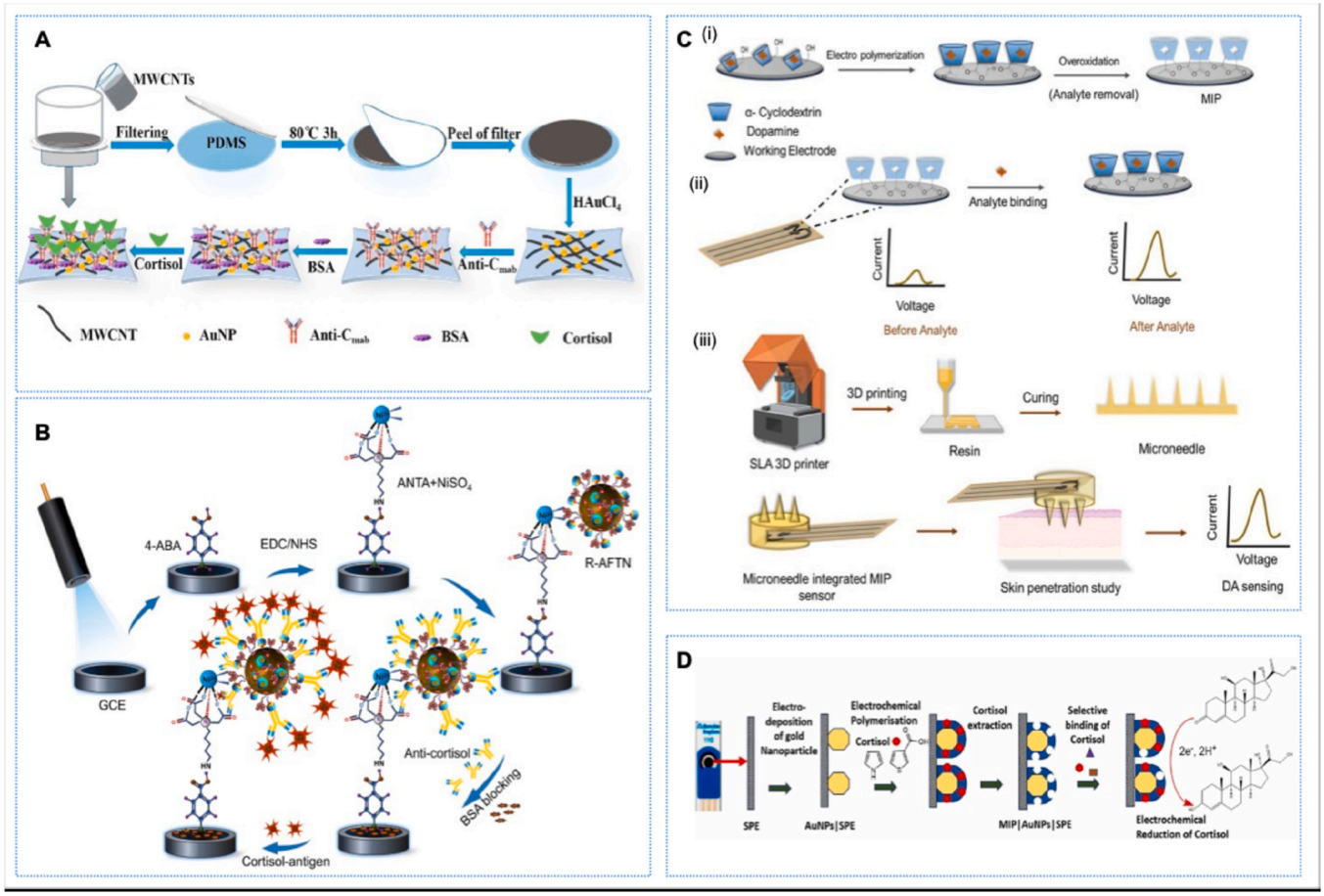


Fig. 3. Representative electrochemical sensor design strategies for cortisol and catecholamine detection. (A) Fabrication scheme of a flexible cortisol immunosensor based on AuNP/MWCNT/PDMS platform. Reprinted with the permission from Ref. [135] © *2021 Elsevier B.V.* (B) Oriented immobilization of histidine-tagged recombinant apoferritin nanoprobes (R-AFTN) on a functionalized glassy carbon electrode (GCE) for enhanced electrochemical cortisol sensing. Reprinted with the permission from Ref. [136] © *2021 Elsevier B.V.* (C) Microneedle-integrated MIP-based DA biosensor: (i) electropolymerization and template removal of α-cyclodextrin/DA complexes to form MIP binding sites; (ii) analyte rebinding and corresponding electrochemical response; and (iii) integration of the MIP layer onto a 3D-printed microneedle array for *in-situ* DA detection. Reprinted with the permission from Ref. [137] © *2025 Elsevier B.V.* (D) AuNP-modified MIP sensor for cortisol detection on a screen-printed electrode. Reprinted with the permission from Ref. [138] © *2024 Elsevier B.V.*

biosensing platforms and are being actively explored for cortisol and neurohormone detection. Their recombinant production in microbial systems also provides advantages in cost, batch consistency, and large-scale manufacturing compared to hybridoma-derived monoclonal antibodies. A strong example is the recombinant apoferritin nano-protein system developed by Chavan et al. (2022), where metal-chelating histidine tags facilitated well-oriented immobilization via Ni^{2+} coordination chemistry (Fig. 3B) [136]. This engineered orientation enhanced binding efficiency and yielded high-affinity cortisol detection in saliva with reduced steric hindrance compared to conventional antibodies. The biosensor enabled direct quantification of cortisol in saliva, achieving a detection limit of 0.95 ng/mL and a sensitivity of 7.91 μA ng^{-1} mL, highlighting its suitability for PoC applications [136]. It is important to note that the performance constraints driving the development of nanobodies, such as stability under variable temperature, prolonged operational lifetime, and compatibility with miniaturized transducers, apply broadly across wearable and PoC platforms, not only to sensors designed for direct skin contact.

Structural studies further support the promise of nanobody-based cortisol recognition. Ding et al. (2019) demonstrated that cortisol binds within a tunnel-like hydrophobic pocket in the NbCor nanobody (a cortisol-specific VHH antibody) [133]. The structure revealed that cortisol binds by embedding itself within a tunnel-like pocket formed primarily by the complementarity-determining region 1 (CDR1) of the nanobody. This encapsulation mechanism, distinct from the conventional flat or groove-based binding seen in IgG antibodies, was confirmed by microscale thermophoresis, which demonstrated high affinity and selectivity toward cortisol and related steroidal compounds [133]. These insights not only highlight the unique molecular recognition strategy of nanobodies for small molecules but also offer a valuable structural basis for engineering next-generation VHH biosensors with enhanced specificity for low-molecular-weight stress biomarkers.

It can be stated antibody-based biorecognition has enabled many of the highest-performing electrochemical cortisol and catecholamine sensors reported to date, particularly in early wearable and flexible platforms. Their high affinity and established conjugation chemistries make antibodies reliable benchmarks for assay validation and clinical comparability. However, the intrinsic structural fragility of immunoglobulins, their dependence on hydrated environments, and their susceptibility to mechanical and thermal denaturation impose important constraints on field-deployable, skin-mounted, or long-term operation. These vulnerabilities become increasingly significant when devices must withstand fluctuating pH, variable ionic strength, sweat composition, and repeated mechanical deformation. Additionally, batch-to-batch variation, relatively high production cost, and limited control over surface orientation complicate efforts to achieve reproducible sensing in miniaturized, PoC formats. Antibody-based electrochemical immunosensors therefore excel in single-use, rapid endpoint quantification but

face notable challenges in semi-continuous or wearable hormone monitoring. These limitations provide a clear rationale for the growing interest in more robust protein scaffolds, such as nanobodies, and synthetic biorecognition chemistries that offer improved stability and surface control for next-generation stress-monitoring platforms.

3.2.2. Nucleic-acid bioreceptors: aptamers

Aptamers provide a powerful and increasingly attractive alternative to antibodies, offering high affinity, excellent thermal and chemical stability, and complete synthetic tunability. Their ability to undergo target-induced conformational changes makes them uniquely compatible with electrochemical methods. These single-stranded DNA or RNA oligonucleotides are selected *in-vitro* through a process known as SELEX (Systematic Evolution of Ligands by EXponential enrichment) to bind specific targets with nanomolar to picomolar affinity [139,140]. Compared to protein-based receptors, aptamers offer superior thermal stability, ease of synthesis, low immunogenicity, and reusability. Their ability to undergo conformational changes upon target binding makes them particularly suitable for electrochemical signal transduction [141–143].

Aptamer-based sensors have demonstrated exceptional performance in detecting catecholamines and in multiplexed hormone analysis. For example, Farjami et al. (2013) immobilized a aptamer on a cysteamine-modified Au electrode, enabling rapid, selective amperometric detection across a physiologically relevant range, even in the presence of structurally similar interferents [141]. The aptamer conferred high specificity, allowing accurate DA quantification in the 100 nM to 5 μM range, while eliminating interference from other catecholamines and metabolites. The sensor exhibited a rapid response (<1 s) and high sensitivity (62 nA μM^{-1} cm^{-2}), highlighting the potential of aptamer-functionalized electrochemical platforms for in vivo neurotransmitter analysis under complex physiological conditions [141].

The adaptability of aptamers also enables simultaneous multiplexed detection of stress-related biomarkers with high specificity in noninvasive biofluids. A recent study introduced the AptaStrensor platform, which utilized dual aptamer-functionalized electrodes for the simultaneous detection of cortisol and neuropeptide Y (NPY) in ultra-low volumes (~2 μL) of human sweat using non-Faradaic electrochemical impedance spectroscopy (nF-EIS) [144]. This method leveraged changes in the capacitive properties of the electrical double layer upon target binding, allowing label-free and highly sensitive detection. The system achieved physiologically relevant detection ranges of 1–256 ng/mL for cortisol and 1–256 pg/mL for NPY, enabling precise monitoring of stress responses [144]. This work illustrates the suitability of aptamer-based biosensors for multi-analyte stress monitoring in wearable platforms, while also offering insights into the differential modulation of endocrine and neurochemical stress pathways.

The integration of aptamers with functional nanomaterials has enabled the construction of highly sensitive biosensors for catecholamine detection. In a recent study, a flexible voltammetric aptasensor was developed for the quantitative analysis of EP using a cerium-based MOF(CeMOF) loaded with AuNPs as the electrode modifier [145]. The EP-specific aptamer immobilized on the AuNPs@CeMOF-modified SPCE yielded a remarkably broad linear range (1 pM–10 nM) and a low detection limit (0.3 pM), outperforming many existing EP sensors. The platform also demonstrated high analytical reliability in spiked serum samples, with recovery values of 95.8–113 % and RSDs of 2.23–6.19 %. These results highlight how synergistic aptamer–nanomaterial interfaces can achieve ultrasensitive and selective neurochemical monitoring suitable for clinical and PoC contexts [145].

This growing body of research highlights the versatility, specificity, and adaptability of aptamer-based biosensors across a range of detection formats including electrochemical, colorimetric, and lateral flow assays for both single and multiplexed hormone analysis. However, despite their improved thermal stability, reusability, and miniaturization relative to antibodies, aptamers still face challenges related to non-specific interactions and environmental stability. This motivates parallel exploration of synthetic alternatives such as MIPs for next-generation biosensing platforms.

3.2.3. Synthetic recognition systems: MIPs

MIPs represent a synthetic, antibody-mimicking approach in which crosslinked polymer matrices are cast around a target molecule, creating selective binding cavities after template removal. MIPs offer excellent stability, reusability, cost efficiency, and tolerance to harsh environments making them highly suitable for wearable, sweat-based, or minimally invasive electrochemical designs.

Recent advances demonstrate increasingly sophisticated MIP configurations. A recent study reported the development of an integrated microneedle-strip-based electrochemical sensor for the label-free monitoring of DA [137]. Fig. 3C illustrates the fabrication of a DA-selective MIP using α-cyclodextrin as the functional monomer and its integration onto a microneedle-enabled SPCE. Analytical evaluation using amperometry and square wave voltammetry revealed a broad linear detection range (5 nM–100 μM in buffer; 0.5–100 μM in artificial ISF) with a LOD of 0.58 nM. The integration of MIP chemistry with a microneedle platform highlights the feasibility of non-invasive, wearable biosensors capable of monitoring neurological biomarkers with high sensitivity and specificity, reinforcing the promise of MIPs for personalized healthcare and continuous diagnostics [137].

Further validating the effectiveness of MIPs for hormone sensing, a recent study developed a salivary cortisol sensor by combining a MIP with AuNPs electrodeposited onto a screen-printed electrode (SPE) [138]. To guide the imprinting process, density functional theory (DFT) and molecular docking were employed to assess the electrostatic interactions and binding conformations between cortisol and functional monomers. A thin MIP film was formed by electropolymerizing pyrrole and thiophene-3-carboxylic acid in the presence of cortisol as a template (Fig. 3D). The modified surface was characterized via SEM, FTIR, and electrochemical techniques, and demonstrated excellent analytical performance, with a LOD value of 0.01 nmol L^{-1} and a broad linear range (0.05 nmol L^{-1} to 2.5 μmol L^{-1}) using DPV. This work exemplifies the potential of computationally optimized, nanostructure-enhanced MIP sensors for accurate, non-invasive cortisol detection in real saliva samples [138].

When integrated with conductive materials such as PANI, PPy, or graphene, MIP-based sensors have demonstrated impressive sensitivity and long-term robustness, even in harsh or biofouling-prone environments [146–148]. In a recent study, a computationally guided MIP sensor was developed for electrochemical detection of NE using 3-aminophenylboronic acid (3-APBA) as the functional monomer [149]. Molecular modeling techniques, including molecular mechanics and quantum chemical calculations, were employed to identify the optimal monomer-template interactions, with 3-APBA forming the most stable complex with nEP. The MIP film was electropolymerized directly onto a SPCE surface in the presence of nEP, forming highly specific binding sites. The resulting MIP sensor exhibited remarkable sensitivity (0.004 mA pM^{-1}), a detection limit as low as 0.03 pM, and a broad linear range (0.1–5 pM). Importantly, interference studies with DA, tyrosine, and serotonin confirmed the high selectivity of the sensor. Furthermore, its applicability was validated in plasma samples, underscoring the potential of MIP-engineered biosensors for real-world clinical diagnostics in neurological and endocrine monitoring [149].

MIPs offer a chemically robust and highly customizable alternative to biological receptors, enabling stable operation under variable pH, temperature, and biofluid conditions that challenge conventional affinity reagents. On the other hand, the analytical performance of both biological and synthetic recognition systems ultimately depends on how effectively they are integrated with the electrode interface. Parameters such as orientation, surface density, and anchoring chemistry govern the fidelity of target rebinding in MIPs just as critically as they influence antibody, nanobody, and aptamer performance. Thus, precise and

application-appropriate immobilization strategies are essential for translating recognition capability into reliable electrochemical signal generation, motivating a detailed examination of surface functionalization approaches.

3.2.4. Immobilization strategies for electrochemical bioreceptors

Regardless of whether a biosensor employs antibodies, nanobodies, aptamers, or MIPs, the immobilization of the recognition element onto the electrode surface is a decisive determinant of performance. Surface orientation, density, and stability govern binding efficiency, electron transfer, and background noise. Uncontrolled adsorption often leads to steric hindrance or loss of bioactivity, thereby compromising sensitivity and increasing nonspecific background. To address these challenges, various site-specific immobilization strategies have been developed [57, 150,151].

Protein-based receptors often rely on covalent EDC/NHS coupling, thiol–gold bonding, or Ni^{2+}–NTA coordination to achieve oriented and stable attachment. Nanobody and recombinant nano-protein systems particularly benefit from His-tag/NTA strategies that ensure controlled orientation. For example, a flexible biosensing platform based on conductive carbon yarn (CCY) functionalized with ellipsoidal Fe_2O_3 nanoparticles was developed to detect cortisol as a model stress biomarker in sweat [152]. The Fe_2O_3-modified CCY provided a high surface area and robust support for antibody immobilization, achieved through EDC/NHS chemistry, enabling strong covalent attachment of cortisol-specific antibodies. Electrochemical testing revealed an impressive detection range spanning from 1 fg/mL to 1 μg/mL, with an ultra-low LOD of 0.005 fg/mL and excellent linearity ($R^2 = 0.998$). The results were validated through comparison with a standard chemiluminescence immunoassay (CLIA) method, confirming both the specificity and clinical relevance of the antibody-based detection platform [152].

Aptamers frequently employ thiolated termini for Au–S bonding, aryldiazonium electrografting, or click-like reactions. For example, Chen et al. (2024) introduced a poly(tannic acid)–derived o-quinone surface to covalently graft DA aptamers onto carbon fiber microelectrodes for in vivo sensing [153]. This site-specific surface functionalization preserved aptamer bioactivity and minimized nonspecific adsorption, resulting in a highly selective and stable interface. The fabricated aptasensor showed a linear amperometric response between 0.2 and 20 μM, a LOD of 88 nM, and sensitivity of 0.09 nA/μM suitable for probing dynamic DA fluctuations in the brain. The strategy's success in live animal models illustrates how rational chemical modification of electrode surfaces can profoundly improve recognition specificity and biological integration in neurochemical sensing applications [153].

Further demonstrating the impact of surface engineering, a study by Pérez-Benito et al. (2022) employed an aryldiazonium electrografting strategy to immobilize either DA or tyrosinase on a screen-printed carbon electrode (SPCE) for catalytic sensing applications [154]. The electrode was first modified with 4-nitrobenzenediazonium ions, which were electrochemically reduced to form covalently attached aminophenyl layers. These amine-functionalized surfaces enabled DA immobilization via glutaraldehyde cross-linking, forming stable imine bonds. The immobilized DA retained redox activity, confirmed by the catechol/hydroquinone voltammetric response, and significantly enhanced electrode sensitivity, yielding redox signals up to 14-fold higher than the bare electrode using ferricyanide as a probe. Additionally, grafting tyrosinase onto the same platform produced a biosensor with 10-fold greater response toward catechol, underscoring the role of enzyme orientation and surface anchoring chemistry in tuning electrocatalytic performance. This work exemplifies how aryldiazonium-based grafting and controlled bioconjugation strategies can be used to construct stable, catalytically active sensing surfaces, offering versatile platforms for neurotransmitter detection and environmental monitoring [154].

MIPs use electropolymerization or sol–gel deposition to tightly anchor the imprinted film onto electrode surfaces, ensuring reproducible template rebinding and mechanical robustness. A recent example is provided by Sullivan et al. (2026), who synthesized ~65 nm cortisol-specific nanoMIPs in situ on laser-induced graphene electrodes via cyclic-voltammetric electropolymerization [155]. This approach formed a conformal, strongly adhered imprinted layer that remained stable during both static and microfluidic flow assays, enabling sub-nanomolar affinity (KD ≈ 0.79 nM), clinically relevant detection limits (~0.27–0.28 ng mL^{-1}), and highly reproducible rebinding (>95 % recovery under flow) [155]. Their findings underscore how electropolymerization provides a robust immobilization strategy for MIP-based electrochemical bioreceptors, improving mechanical durability and operational reproducibility compared to non-covalent deposition methods. Similarly, Sharma et al. (2025) demonstrated that electropolymerization enables highly stable immobilization of MIP recognition layers on carbon-based microelectrode platforms [156]. In their work, cortisol-imprinted PPy/Prussian blue films were grown in situ on laser-engraved graphene, forming a tightly integrated hybrid interface that preserved redox activity while providing selective and durable cortisol-binding sites. The conformal electropolymerized layer supported a broad dynamic range (0.10–10,000 pg mL^{-1}), an ultralow LOD (0.08 pg mL^{-1}), and maintained structural integrity during repeated measurements and real-sample testing. Notably, the strong electrode–polymer adhesion achieved through electropolymerization enabled rapid 3-min assays and highly reproducible operation in saliva, yielding a good correlation with ELISA and clinical laboratory benchmarks ($r = 0.9948$) [156]. These results reinforce that electropolymerization not only defines the molecular imprint but also serves as a robust immobilization method for achieving mechanically stable, reproducible, and scalable MIP-based electrochemical biosensors. This principle is also exemplified in the work of Santos et al. (2025), who developed an affordable and rapid cortisol sensor for aquaculture monitoring by synthesizing a pyrrole-based MIP film via electropolymerization directly on reduced graphene oxide (rGO)/Prussian blue nanocube–functionalized screen-printed carbon electrodes [157]. The in situ electropolymerization process ensured strong interfacial adhesion between the imprinted polymer and the nanostructured electrode surface, producing a mechanically robust and chemically stable MIP layer. After polymerization in the presence of cortisol and subsequent template extraction through pyrrole overoxidation, the resulting sensor displayed selective and reproducible rebinding behavior, enabling a wide linear detection range (0.1 nM–0.1 mM) in artificial saltwater [157].

These works proved that the development of effective biorecognition layers remains at the heart of high-performance electrochemical biosensors. While traditional antibodies provide strong affinity and well-established protocols, alternatives like aptamers, nanobodies, and molecularly imprinted materials are rapidly gaining ground for their resilience, tunability, and compatibility with emerging sensor technologies. Optimizing immobilization strategies, ensuring functional orientation, and leveraging nanostructured supports will be key to advancing the next generation of biosensors for non-invasive stress hormone monitoring.

3.3. Nanomaterials and signal amplification strategies in electrochemical biosensing

Signal amplification plays a pivotal role in hormone sensing because cortisol, EP, nEP, and DA appear at inherently low concentrations and exhibit low molecular weights that limit direct electrochemical transduction [157–159]. To address these challenges, several amplification strategies have emerged. While redox-active tags such as methylene blue and ferrocene have been integrated into aptamer-based systems to provide direct readout mechanisms, functional nanomaterials have become central to amplification strategies by simultaneously enhancing electrode conductivity, increasing electroactive surface area, improving bioreceptor loading density, and facilitating rapid charge-transfer kinetics [160]. The physicochemical versatility of nanomaterials,

including tunable surface terminations, high catalytic activity, electrical conductivity, and ease of functionalization, enables sensitive and selective detection in complex biofluids such as saliva, sweat, interstitial fluid, and serum [29,160–162].

Together, nanomaterial-enabled signal amplification and electrode engineering constitute an integrated design space, where material choice dictates both the sensitivity limits and the translational feasibility of biosensors intended for wearable or PoC applications.

Among the most widely used carbon-based nanomaterials, graphene and its derivatives (graphene oxide (GO), rGO, 3-dimensional graphene, etc.) stand out due to their exceptional electrical conductivity, mechanical flexibility, and high specific surface area [163]. Graphene facilitates rapid electron transfer and supports the high-density immobilization of antibodies, aptamers, or MIPs [164–166].

A notable example is presented by Yogalakshmi et al. (2025), who synthesized activated graphene using various chemical agents and demonstrated its utility in constructing highly responsive electrochemical sensors for the simultaneous detection of DA and uric acid [167]. Among the tested agents, potassium hydroxide–activated graphene exhibited the most pronounced electrocatalytic performance, delivering distinct oxidation peaks for DA and uric acid with a peak separation of 0.23 V, even in the presence of interfering analytes such as ascorbic acid. The potassium hydroxide–activated graphene-modified SPCEs displayed excellent sensitivity and selectivity, achieving detection limits as low as 0.09 μM for DA using DPV [167]. These findings underscore the effectiveness of chemically activated graphene in enhancing electrochemical resolution and enabling multi-analyte biosensing, particularly in physiologically relevant environments. To further support the application of graphene-based materials, Ghosh et al. (2024) developed flexible, disposable laser-induced graphene (LIG) sensors for the simultaneous detection of DA and interleukin-6 (IL-6) [168]. Modified with graphene–PANI (G-PANI) conductive inks, the sensors achieved outstanding analytical performance, including a low LOD of 0.408 μM for DA and 2.623 pg/mL for IL-6, while maintaining excellent mechanical stability (RSD = 4.39 % after repeated bending). Notably, the LIG/G-PANI platform provided a 41-fold improvement in DA selectivity compared to standard SPEs. These results underscore the promise of LIG–polymer nanocomposites for high-performance, wearable electrochemical biosensors [168]. Further illustrating the versatility of graphene-based hybrid materials, a recent study demonstrated the fabrication of a PANI–GO modified GCE for the selective electrochemical detection of cortisol in human saliva [169]. Fig. 4 illustrates the synthesis and functionalization of a PANI–GO nanocomposite via Hummer's method and its subsequent drop-casting onto a GCE. This PANI–GO nanocomposite, known for its excellent conductivity and high surface area, enabled substantial improvements in redox peak currents compared to bare and singly modified electrodes. Through cyclic voltammetry, the sensor exhibited a low detection limit of 30 μM, high reproducibility (95 % over 8 replicates), and exceptional long-term stability, retaining over 95 % of its initial signal after 11 weeks of storage at −20 °C. The enhanced electrocatalytic performance of the composite not only facilitated efficient cortisol detection over a wide linear range (100 μM–10 mM) but also allowed successful validation in real saliva samples. These results underscore the significance of PANI-GO composites in constructing robust, non-invasive electrochemical biosensors for hormone monitoring [169].

Further supporting the potential of graphene-based platforms, a recent study employed a liquid-gated graphene-FET functionalized with cortisol-specific aptamers for sensitive detection of cortisol in ISF [140]. The device demonstrated excellent performance within the physiological range (1 pM–1 μM), achieving a sensitivity of ~154 nA/dec under high ionic strength conditions, and highlighted the utility of 2D materials and aptamer integration for wearable biosensing applications [140].

While graphene provides unmatched conductivity, its aggregation tendency and hydrophobicity can compromise long-term stability in sweat-based wearable platforms, underscoring the need for composite or polymer-supported architectures. In a recent study, a cost-effective electrochemical sensor was developed by sequentially modifying a GCE with poly(L-serine), GO, and β-cyclodextrin for the simultaneous detection of lidocaine and EP in serum [170]. The integration of GO notably enhanced the electrode's surface area and electron transfer kinetics, enabling a 5.3-fold increase in anodic current response for EP, along with a 79 mV negative shift in oxidation potential [170]. These enhancements underscore the critical role of graphene derivatives in boosting signal transduction and sensitivity for catecholamine detection in complex biological samples.

Similarly, carbon nanotubes (CNTs), both SWCNTs and MWCNTs, offer excellent electrocatalytic properties and tubular nanostructures that facilitate molecular diffusion and enhance signal transduction. A recent study by Singh et al. (2024) exemplifies this, where nickel selenide nanoparticles were encapsulated within CNTs to construct a nonenzymatic electrochemical sensor for DA [171]. The composite was synthesized via a one-step, environmentally benign chemical vapor deposition method, resulting in a hybrid nanostructure with high conductivity and robust electrocatalytic activity. Electrochemical

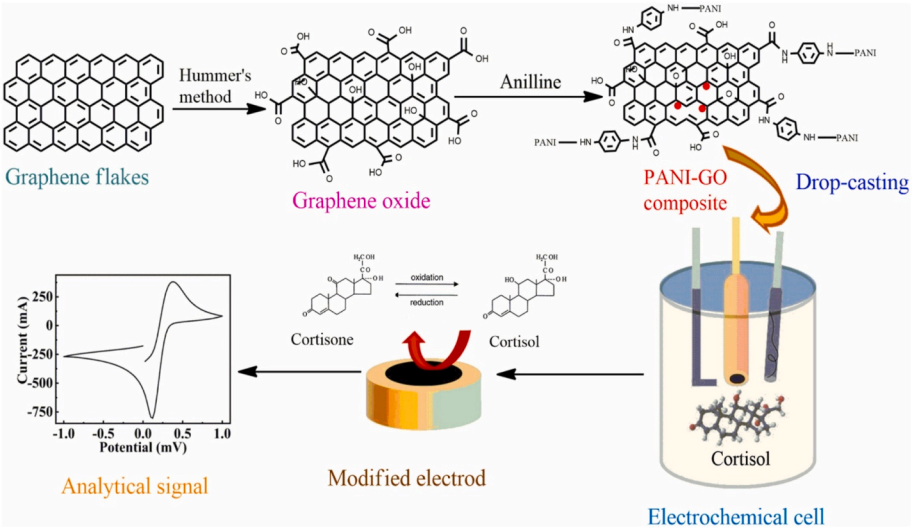


Fig. 4. Schematic representation of a PANI–GO composite-based electrochemical sensor for cortisol detection. Reprinted with permission from Ref. [169] © *2024 Elsevier Ltd.*

evaluations revealed remarkable performance, including a high sensitivity of 19.62 μA μM^{-1} cm^{-2}, a wide linear detection range (5 nM–640 μM), and exceptional selectivity. These outcomes were attributed to the synergistic interaction between the electroactive $NiSe_2$ core and the conductive CNT shell, which collectively enhanced molecular diffusion and electron transfer. Such findings underscore the utility of CNT-based architecture in designing sensitive and reliable electrochemical platforms for on-demand neurotransmitter monitoring [171]. These findings further reinforce the value of MWCNT-based hybrid nanostructures in electrochemical sensing. Complementarily, Kumar et al. (2024) developed a multi-walled carbon nanotube-based hybrid sensor platform functionalized with metallic nanoparticles for enhanced DA detection [172]. The incorporation of MWCNTs served as an efficient electron-conducting backbone, while the embedded metal nanoparticles provided abundant active sites for redox reactions. The resulting hybrid sensor exhibited high electrocatalytic efficiency, a low detection limit, and reliable operational stability under physiological conditions [172]. Their work highlights how the high surface area and conductive architecture of MWCNTs, when synergistically combined with catalytically active components, markedly improve both sensitivity and selectivity in neurotransmitter detection. Such MWCNT-integrated platforms underscore the importance of nanotube engineering in advancing the performance of next-generation electrochemical biosensors for stress biomarkers. In parallel, Zeng et al. (2024) demonstrated the utility of a dual-analyte electrochemical sensor based on a MWCNT–polymer hybrid film for the simultaneous determination of nEP and serotonin in complex biological matrices [173]. Their sensor design leveraged the high surface area and electron transfer capabilities of MWCNTs, combined with a selective polymer layer that provided strong molecular discrimination. The developed platform achieved excellent resolution of oxidation signals for both analytes, minimizing peak overlap and matrix interference. Notably, the sensor maintained linear response ranges suitable for physiological concentrations, along with low detection limits in the nanomolar range [173]. Its successful application to real samples, including cerebrospinal fluid, underscores the versatility and diagnostic relevance of MWCNT-based multiplexed sensors. These results highlight CNTs as powerful amplification scaffolds capable of multiplexed sensing when paired with selective polymer matrices. CNTs outperform graphene in mass transport and diffusion but require careful dispersion and surface functionalization to mitigate potential cytotoxicity and ensure reproducibility, an especially important consideration for wearable systems.

MXenes, particularly $Ti_3C_2T_x$, are emerging class of 2D transition metal carbides with exceptional hydrophilicity, metallic conductivity, and tunable surface terminations [174,175]. Their negatively charged, layered structure facilitates strong electrostatic interactions with positively charged neurotransmitters like DA, while offering abundant sites for bioreceptor anchoring. Chavan et al. (2024) introduced a $Ti_3C_2T_x$-MXene-based electrochemical sensor, modified with in situ polymerized 4-aminophenylboronic acid (4-APBA), for highly sensitive DA detection [176]. The sensor integrated into a label-free screen--printed carbon electrode achieved a detection limit of 1.3 nM in PBS and 1.9 nM in human serum, with a linear detection range of 40–500 nM. The exceptional sensitivity was attributed to the conductive 2D MXene architecture, which enhanced charge transfer and bioreceptor density [176]. This work highlights the role of emerging 2D nanomaterials in building ultrasensitive PoC platforms for neuromolecular biomarkers. Supporting this trend, Ankitha et al. (2024) developed a novel MXene-integrated single-stranded carbon yarn-based sensor patch capable of detecting DA directly from artificial human sweat [177]. The sensor employed a minimalist three-thread electrode configuration and utilized $Ti_3C_2T_x$ MXene-coated CCY as the sensing element. This design leveraged MXene's exceptional conductivity and large surface area to achieve a low detection limit of 316 pM and a broad linear range (1 nM–1 μM), with excellent reproducibility and selectivity. Notably, the sensor could be seamlessly integrated into textiles via sewing or weaving, enabling close contact with the skin for unobtrusive on-body application. The flexible, lightweight structure and real-sample validation demonstrated its potential in wearable diagnostics, offering a promising avenue for the monitoring of stress-related biomarkers in individuals with neurological conditions [177]. This work highlights the transformative role of MXene-functionalized yarn-based platforms in advancing the future of personalized healthcare and PoC diagnostics. Further advancing the field, Liu et al. (2023) introduced a highly sensitive molecularly imprinted electrochemical biosensor for cortisol detection, employing a porous nanocomposite comprised of $Ti_3C_2T_x$ MXene sheets and graphene [178]. In this configuration, MXene acts as a nanoscale conductive scaffold, providing a high surface area and excellent electrical conductivity, which are critical for enhancing charge transfer kinetics at the electrode interface. The integration of MXene with graphene significantly increased the density of molecularly imprinted cavities, thereby improving the selective recognition of cortisol molecules. The sensor demonstrated an ultralow detection limit of 0.4 fM and a wide dynamic range spanning from 1 fM to 10 μM, while maintaining strong selectivity against structurally similar steroid hormones. Notably, its applicability was validated through successful detection of cortisol in human saliva, confirming the platform's potential for noninvasive monitoring of psychological and physiological stress [178]. This work underscores the value of MXene nanoparticles not only as passive conductive additives but as active nanostructured materials that facilitate precise molecular recognition and transduction in next-generation biosensing platforms. In alignment with these advancements, Boobphahom et al. (2021) developed a multifunctional hydrogel-based electrochemical sensor by integrating TiO_2/MXene with a polyvinyl alcohol/GO(PVA/GO) matrix for the detection of nEP in urine samples [179]. The resulting TiO_2/MXene-PVA/GO hydrogel was applied onto a SPCE, where each component contributed distinct functional advantages: TiO_2 offered electrocatalytic activity, MXene provided high electrical conductivity and surface area, and the PVA/GO hydrogel acted as a preconcentration medium due to its hydrophilic and porous nature. This synergistic configuration enabled efficient oxidation of nEP at +0.4 V (vs. Ag|AgCl), yielding excellent analytical performance with a low detection limit of 6 nM and wide linear ranges (0.01–60.0 μM). Importantly, the sensor exhibited high selectivity in complex biological matrices and strong agreement with HPLC-validated results, with recovery rates between 97.6 % and 102 % and RSDs below 4.9 %. Moreover, the successful integration of this hydrogel sensor into pantyliners underscored its potential for noninvasive, wearable monitoring of stress-related biomarkers such as nEP, enabling early screening of neurological disorders through routine urinalysis [179]. Supporting this, Shankar et al. (2018) developed a MXene/graphite composite paste electrode for adrenaline sensing, demonstrating superior electrocatalytic activity compared to bare electrodes [180]. The sensor achieved a low detection limit of 9.5 nM and effectively resolved overlapping signals from adrenaline, ascorbic acid, and serotonin. It also showed high accuracy in pharmaceutical sample analysis, with recoveries between 99.2 % and 100.8 %, underscoring MXene's utility in multi-analyte electrochemical sensing [179]. These examples highlight MXenes are ideally suited for wearable biofluidics due to hydrophilicity but face oxidative degradation challenges. Stabilizing coatings or polymer encapsulation will be crucial for long-term deployment.

Metal nanoparticles, particularly gold nanoparticles (AuNPs), are widely utilized for their biocompatibility, high surface energy, and ease of functionalization via thiol or amine linkers. These nanoparticles facilitate electron transfer and provide nanoscale platforms for the immobilization of biomolecules. Their inclusion in electrode surfaces increases the electroactive surface area and enhances charge transfer kinetics. This is well exemplified by the work of He et al. (2021), who developed a flexible electrochemical sensor incorporating AuNPs and graphene layers for the simultaneous detection of DA and uric acid in the presence of ascorbic acid [181]. The inclusion of electroneutral AuNPs not only facilitated electron transfer but also improved peak separation

and enhanced molecular diffusion at the electrode surface. The resulting electrode achieved a low detection limit of 10 nM for DA and demonstrated excellent selectivity due to the engineered charge distribution at the heterogeneous interface [181]. These findings highlight the critical role of metal nanoparticles like AuNPs in enhancing the sensitivity, selectivity, and electrochemical resolution of neurotransmitter sensors. Similarly, Aryan et al. (2024) developed a highly selective and sensitive electrochemical sensor using a nanocomposite of AuNPs anchored onto ultrathin graphitic carbon nitride (utg-C_3N_4) nanosheets for DA detection [182]. The AuNPs/utg-C_3N_4 hybrid significantly enhanced the electrode's electrochemical performance by providing abundant active sites and facilitating efficient electron transfer. The sensor exhibited an impressive detection limit of 0.24 nM and demonstrated two broad linear ranges for DA quantification [182]. This study underscores the synergistic effect of metal nanoparticles and 2D nanomaterials in improving sensitivity, selectivity, and real-sample applicability in electrochemical neurotransmitter sensing. Another good example is early reported by Sun et al. (2017) (Fig. 5). Although this work predates the most recent advances in wearable cortisol platforms, it is included here because it represents one of the earliest high-performance graphene–gold nanoparticle electrochemical immunosensors and established architectural principles that continue to underpin modern sensor designs. They demonstrated the successful development of a highly sensitive electrochemical immunosensor for cortisol detection by integrating AuNPs with magnetic functionalized rGO (AuNPs/MrGO) [183]. In their system, AuNPs were electrochemically deposited onto the MrGO-modified glassy carbon electrode, significantly enhancing the sensor's electrochemical performance. The incorporation of AuNPs provided a large electroactive surface area and superior biocompatibility, enabling efficient immobilization of biomolecules such as cortisol and horseradish peroxidase-labeled antibodies. Moreover, the high electrical conductivity of AuNPs contributed to the amplification of the electrochemical signal, thereby facilitating more efficient electron transfer. This resulted in a broad dynamic detection range (0.1–1000 ng/mL) and a low detection limit (0.05 ng/mL), outperforming conventional methods like ELISA in terms of sensitivity, stability, and reproducibility [183].

MOFs, characterized by their tunable porosity, high surface area, and modular chemistry, have recently emerged as advanced signal amplification platforms. In another work, Chang et al. (2023) demonstrated the use of defective UiO-66 metal–organic framework (MOF) thin films as effective signal amplifiers in electrochemical DA sensing [184]. Though UiO-66 is inherently insulating, introducing controlled missing-linker defects enabled a hopping-based electrochemical signal enhancement for irreversibly adsorbed DA. When layered atop a GO-modified electrode, the bi-layer system exhibited 6.4x higher sensitivity, 0.23x lower detection limit, and improved selectivity over ascorbic acid and uric acid, compared to GO alone [184]. This work underscores the potential of engineered MOF-based coatings as amplification layers in complex electrochemical sensing systems. This is supported by the work of

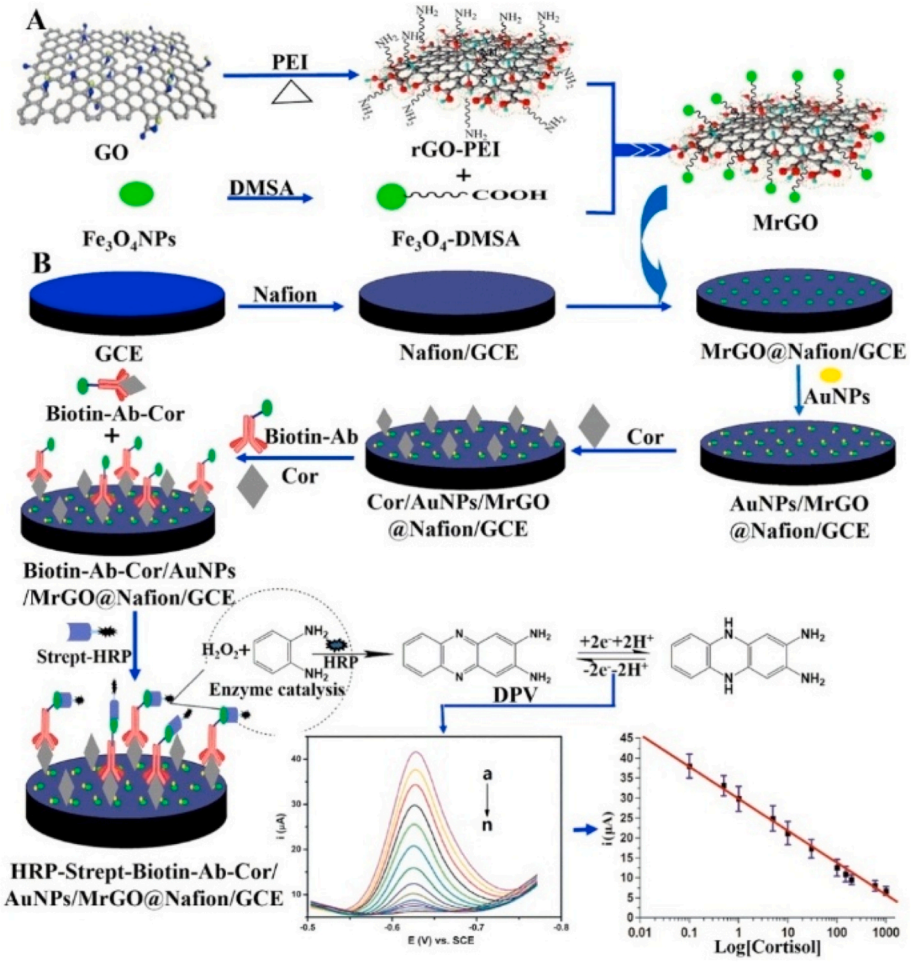


Fig. 5. Fabrication and operating principle of an electrochemical cortisol immunosensor based on AuNPs/MrGO. **(A)** Preparation of MrGO nanocomposites through PEI functionalization and Fe_3O_4 nanoparticle conjugation. **(B)** Step-wise construction of the immunosensor on a Nafion-modified GCE, involving immobilization of biotinylated anti-cortisol antibodies (Ab-Cor), cortisol binding, and signal amplification using HRP–streptavidin. Reprinted with permission from Ref. [183] © *2016 Elsevier B.V.*

Soosaimanickam et al. (2024), who designed a bi-metallic Co–Ni/BTC/4,4′-BiPy MOF as an advanced electrode material for the electrochemical detection of EP and nEP [185]. The MOFs were synthesized via a solvothermal approach and further functionalized with benzene-1,3,5-tricarboxylic acid and amine-rich 4,4′-bipyridine to enhance electron transfer through π–π interactions. The resulting MOF-based electrode provided a sensitive and selective platform for dual-analyte detection, with detection limits of 0.724 μM for EP and 0.815 μM for nEP and demonstrated reliable performance in complex biological matrices such as blood and urine [185]. This study highlights how the tunable porosity, high surface area, and modular chemistry of MOFs can be strategically exploited to create signal-amplifying electrochemical interfaces for simultaneous neurotransmitter monitoring in clinical settings. Moreover, Zhou et al. (2025) developed a non-enzymatic electrochemical sensor based on Au@Ni-MOF hybrids for the sensitive detection of DA [186]. By integrating AuNPs into a Ni-MOF framework synthesized via in situ growth, the platform demonstrated enhanced electrocatalytic activity and electron transfer efficiency. The sensor exhibited a wide linear detection range for DA (0.1 μM–2 mM) and was validated using DPV and EIS [186]. This study underscores the effectiveness of MOF-based hybrid materials in enabling precise DA sensing through improved surface interaction and signal amplification. In another work, Chowdury et al. (2024) reported the synthesis of bimetallic Zn–Co BTC-based MOFs and their subsequent pyrolytic conversion into hierarchical porous Co/C hybrids for DA sensing [187]. Among the materials tested, the carbonized Zn-rich MOF demonstrated superior electrochemical performance, with a low detection limit of 0.04 μM, a broad linear range (0.1–500 μM), and excellent sensitivity. The enhanced sensing capability was attributed to the material's high surface area, mesoporosity, and abundant electroactive sites. Importantly, the modified electrode exhibited strong selectivity against common interferents and retained stability over two weeks, highlighting the promise of MOF-derived porous carbon materials in reliable, long-term DA detection [187].

Cerium-based MOFs (CeMOFs) have also been used to support aptamer immobilization for EP detection. This is further supported by recent findings where cerium-based MOFs have been employed as precursors for advanced electrochemical sensing platforms. In particular, a study demonstrated the synthesis of a mesoporous $CePO_4$@carbon composite via high-temperature calcination of a Ce-MOF (Fig. 6), resulting in a uniformly structured material with enhanced electrical conductivity and abundant catalytic active sites [188]. These features facilitated efficient electron transfer and redox reactions. The composite-modified glassy carbon electrode exhibited excellent performance in the simultaneous detection of DA, uric acid, and acetaminophen, achieving low detection limits down to 0.009 μM for DA. Although the study focused on DA, UA, and acetaminophen (APAP), it underscores the electrochemical potential of CeMOF-derived materials, which can likewise support aptamer immobilization for EP detection, due to their favorable surface chemistry, high conductivity, and mesoporous architecture [188]. This reinforces the role of CeMOFs as a promising scaffold in biosensing applications.

Conducting polymers, such as PANI, and PPy, are often used either as standalone matrices or as composites with nanomaterials to provide electrochemical responsiveness, biocompatibility, and anti-fouling capabilities. This is exemplified by a recent study where a cortisol biosensor was constructed using double-conducting polymer nanowires, demonstrating the unique advantages of conducting polymers in biosensing applications [189]. By integrating PPy and PEDOT into a dual-mode electrochemical platform utilizing DPV and chronoamperometry (CA), the sensor achieved ultralow detection limits down to 0.131×10^{-14} M in DPV mode and reliable performance in human saliva samples (Fig. 7). The enhanced electrochemical responsiveness and antifouling properties provided by the conducting polymer nanowires were critical to achieving both sensitivity and specificity, highlighting the pivotal role of conducting polymers in high-performance biosensor design [189].

Another recent study demonstrated the development of a wearable electrochemical biosensor based on PANI hydrogel integrated with hydrophilic polypeptides for reliable cortisol detection in sweat [190]. The PANI hydrogel not only provided excellent electrochemical responsiveness but also acted as a water-retentive matrix, facilitating consistent signal stability and conductivity. Additionally, the incorporation of antifouling peptides significantly minimized nonspecific adsorption in complex biological environments like sweat. The resulting sensor exhibited high sensitivity, with a detection limit as low as 33 pg/mL and effectively tracked cortisol's circadian fluctuations in human sweat samples [190]. This wearable PANI-based cortisol biosensor also

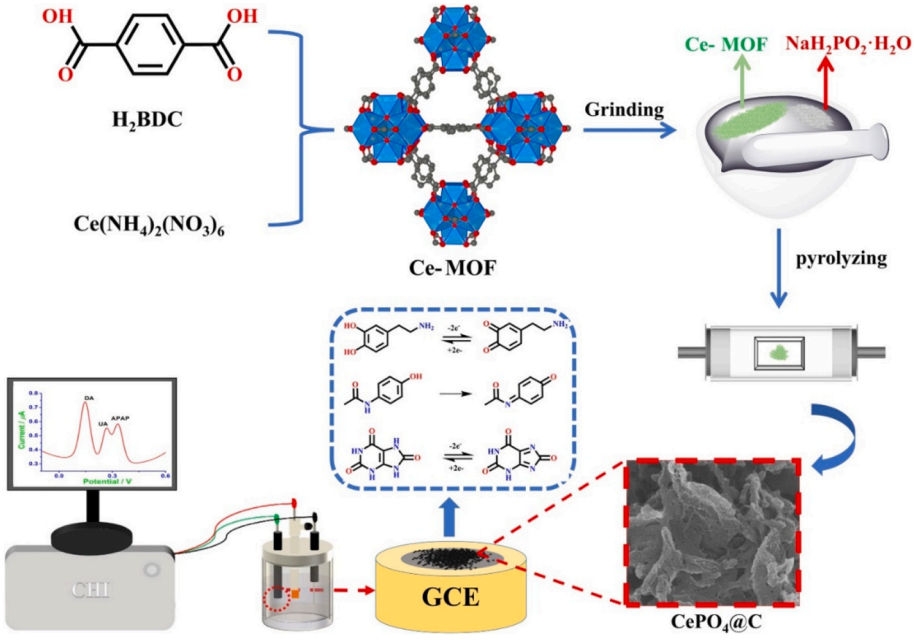


Fig. 6. Synthesis and electrochemical application of $CePO_4$@C composite derived from a Ce-MOF precursor for simultaneous detection of DA, UA, and APAP. Reprinted with permission from Ref. [188] © *2024 Elsevier B.V.*

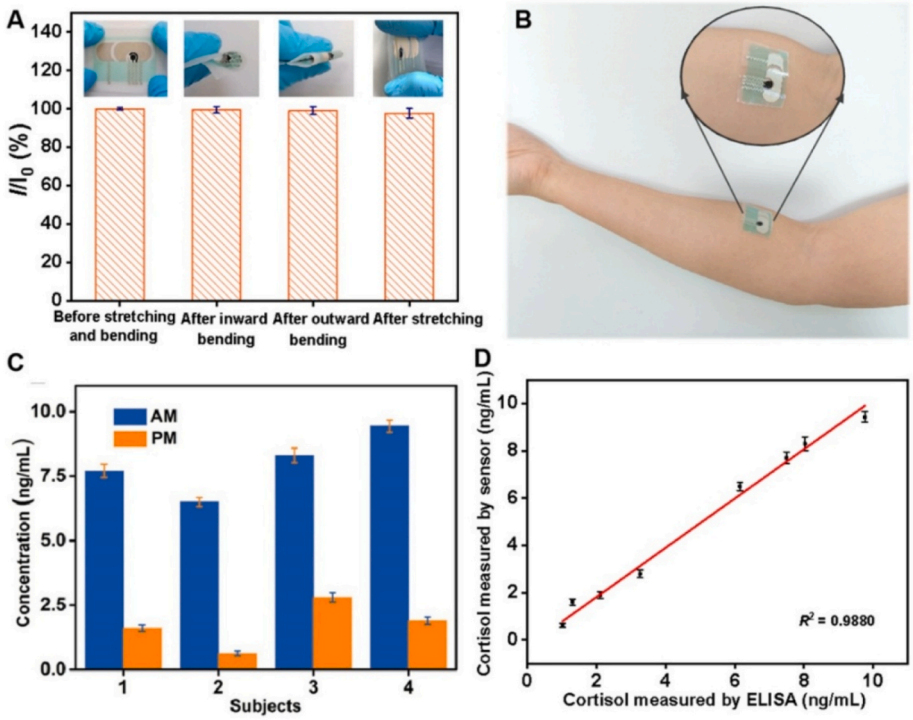


Fig. 7. Performance evaluation of the wearable PANI-based cortisol biosensor. **(A)** Mechanical durability of the sensor under repeated stretching and bending. **(B)** On-skin application of the wearable patch. **(C)** Circadian cortisol variations measured in human sweat across multiple subjects. **(D)** Correlation between sensor-derived cortisol levels and ELISA measurement. Reprinted with permission from Ref. [190] *© 2025 Published by Elsevier B.V. on behalf of Chinese Chemical Society and Institute of Materia Medica, Chinese Academy of Medical Sciences.*

demonstrated excellent mechanical robustness and practical applicability, as shown in Fig. 7A and B, where its sensing performance remained stable under stretching and repeated bending. The sensor was comfortably adhered to the forearm, enabling swift, noninvasive monitoring. Importantly, as illustrated in Fig. 7C, it successfully captured diurnal variations in cortisol levels across multiple subjects, showing higher levels in the morning compared to the evening, consistent with known circadian rhythms. Furthermore, a strong correlation ($R^2 = 0.9880$) was observed between sensor readings and ELISA measurements (Fig. 7D), validating the sensor's accuracy and clinical potential [190].

Across graphene, CNTs, MXenes, metal nanoparticles, MOFs, and conducting polymers, each material class provides distinct amplification pathways including catalytic boosting, electron-transfer acceleration, molecular preconcentration, or increased immobilization density. These mechanisms directly shape LOD, linear range, selectivity, and stability. However, no single nanomaterial universally outperforms others. Application-specific constraints such as biofluid chemistry, required detection dynamic range, wearable form factor, mechanical stress, and storage stability must guide rational material selection.

Table 3 presents a comprehensive comparison of recent electrochemical biosensors designed for cortisol and catecholamine monitoring, with a focus on the transformative contributions of functional nanomaterials. Graphene and CNTs, while offering exceptional conductivity, require anti-fouling treatments for prolonged use. MXenes excel in biofluid interfacing due to their hydrophilicity but suffer from oxidative instability. Metal nanoparticles, especially AuNPs, enhance electron transfer and immobilization density but often lack inherent selectivity. MOFs provide highly tunable architectures and signal amplification capabilities, though challenges remain in mechanical robustness and scale-up. The successful integration of these nanomaterials into biosensor platforms has enabled the development of miniaturized, wearable, and PoC devices capable of continuous, non-invasive stress hormone monitoring. These systems are poised to support personalized monitoring of stress biomarkers across both clinical and field settings. Moving forward, hybridization strategies that pair complementary material strengths (e.g., MXene–polymer, AuNP–-graphene, MOF–carbon composites) represent the most promising route for clinically reliable, on-demand or semi-continuous electrochemical monitoring of stress biomarkers.

Bearing all aforementioned information in mind, it can be stated that the integration of functional nanomaterials into electrochemical biosensors has transformed sensor performance by enabling ultra-low detection limits, broad dynamic ranges, and robust operation in complex biological fluids. Beyond their physicochemical advantages, these materials enable system-level innovations including mechanical flexibility, anti-fouling surfaces, and multiplexing which are essential for stress hormone monitoring. Moving forward, rational selection and synergistic hybridization of nanomaterials, tailored to specific sample matrices and form factors, will be critical for translating lab-scale prototypes into clinically relevant wearable and PoC diagnostics.

From a performance standpoint, the analytical performance of stress-hormone biosensors depends not only on the choice of nanomaterials but also on the interplay between biorecognition chemistry and electrochemical transduction. Antibody-based systems typically deliver high selectivity and picomolar–nanomolar detection limits under DPV or amperometric interrogation, whereas aptamers provide comparable sensitivity with improved stability and reversible binding dynamics, particularly advantageous for SWV and EIS-based measurements. Nanobodies and recombinant nano-proteins offer enhanced orientation control and robustness and have shown strong promise when integrated into FET or impedance platforms, although reports are still emerging. MIPs, while exceptionally stable and matrix-tolerant, achieve sub-nanomolar to nanomolar LODs primarily in voltammetric assays but show broader binding distributions than biological receptors. Transduction modality further shapes performance. While DPV and SWV consistently enable the lowest LODs, amperometry excels in rapid or repeated measurements. On the other hand, EIS is highly sensitive to

Table 3
Comparative performance of electrochemical biosensors for stress hormone monitoring.

Target Analyte	Electrode material	Sensor type	Transduction Technique	Sample Matrix	LOD	Linear ranges	Ref.
Cortisol	PEDOT:PSS	MIP-gated OECT on a laser-patterned microfluidic wearable skin-mounted patch-type	OECT	Sweat	N/A	0.1–1.0 μM	[191]
	Gold electrode modified with MXene/MWCNT	Immunosensor	DPV	Artificial and human sweat	0.03 fg/mL	0.1 fg/mL – 1.0 μg/mL	[192]
	TiO_2 nanostructure-modified carbon yarn	Immunosensor	CV	Human sweat	10 fg/mL	10 fg/mL – 1.0 μg/mL	[193]
	PBASE-NHS modified GF	Immunosensor	DPV	Human salvia	0.24 fg/mL	1.0 fg/mL - 10,000 pg/mL	[194]
	APTES/ZnO Nanorods	Immunosensor	DPV	Human serum	2×10^{-4} nM	10^{-6} nM and 106 nM	[195]
	MOF with oriented cortisol monoclonal antibody	Immunosensor (wearable, label-free)	DPV	Human sweat	0.26 pg/mL	1.0 pg/mL – 1.0 μg/mL	[134]
	AuNPs/MoS_2/AuNPs with SH-PEG-COOH functionalization	Immunosensor (POC, portable)	DPV	Salvia	0.11 nM	0.5–200 nM	[96]
	AuNPs@SnS_2/NiCo MOFs	Label-free Immunosensor	SWV	Saliva	29 fg/mL	100 fg/mL – 100 ng/mL	[196]
	Au Single-Atom Nanozymes with HRP-labeled Anti-Cortisol Antibody	Immunosensor	SWV	Salvia	0.48 pg/mL	0.15–300 ng/mL	[197]
	Inkjet-printed graphene/silver electrodes	Immunosensor (wearable)	CA	Sweat	10 pM	10 pM to 100 nM	[198]
	3D nanostructured Au/PDMS electrode	Immunosensor (wearable Label-Free Impedimetric; Lab-on-a-Patch)	EIS	Sweat	1.0 pg/mL	1.0 pg/mL - 1.0 μg/mL	[199]
	PANI electrodeposited on graphene	Immunosensor	EIS	Dog salvia	3.57 fg/mL	0.0005–50 μg/mL	[200]
	$Ti_3C_2T_x$ MXene-loaded LBG on PDMS	Immunosensor (Wearable Impedimetric)	EIS	Sweat	88 pM	0.01–100 nM	[201]
	Graphene-FET integrated into soft contact lens	Wearable Graphene-FET-based Sensor (Smart Contact Lens)	FET	Tears	10 pg/mL	1–40 ng/mL	[202]
	Gold electrode with MB-labeled aptamer	Aptamer-Based Sensor	SWV	Human serum	0.05 ng/mL	0.05–100 ng/mL	[143]
	Ni–Co MOF nanosheets on CNTs/PVA/PU film	Wearable Aptamer-Based Sensor	DPV	Sweat	0.032 ng/mL	0.1–100 ng/mL	[203]
	MOF-derived Ni–P bundle-like nanorods	Aptamer-Based Sensor (label-free)	EIS	Urine	10 aM	0.1 fM – 700 nM	[204]
	AuNW with MB-tagged aptamer/PVDF antifouling nanocomposite	Aptamer-Based Sensor	DPV and CA	Human serum (undiluted) and buffer	0.68 nM (serum), 0.51 nM (buffer)	1.0–1000 nM	[36]
	MoS_2 nanopore edge rings	Bio-FET Aptamer-Based Sensor	FET	Salvia and serum	1 ag/mL	3.6×10^{-10}–360 ng/mL	[122]
Dopamine	Au–SiO_2 nanocomposite	Non-enzymatic	DPV	Human serum	1.98 μM	10–100 μg/mL; 200–500 μg/mL	[205]
	CD-crosslinked prepolymer with graphene sheets and MWCNTs			Buffer	0.05 μM	0.15–21.65 μM	[206]
	Nano-Fe_3O_4/few-layer graphene			Human serum	0.413 nM	3.33–19 nM	[207]
	Pd nanoparticles on rGO			Buffer	1.0 μM	3–15 μM; 15–42 μM	[208]
	rGO/PEDOT			Buffer	1.92 μM	19.6–122.8 μM	[209]
	Au@SiO_2–APTES			Human urine and plasma (spiked)	14 nM	47–100 nM; 125–875 nM	[210]
	CeO_2/rGO			Buffer	2.0 μM	10–150 μM	[211]
	AuNPs/PANI			Buffer	16 μM	20–100 μM	[212]
	Spindle-shaped NH_2-MIL-101(Fe)			Buffer	0.025 μM	0.3–450 μM	[213]
	Vein-like Ni-BTC@Ni_3S_4			Buffer	0.016 μM	0.05–750 μM	[214]
	WS_2/MWCNT				0.55 μM	1–22 μM	[172]
	Nanostructured silver chromate	Non-enzymatic (IoT-integrated)		Buffer	1.05 μM	5–45 μM	[215]
	carbon nitride-supported zinc oxide	Non-enzymatic (Extended Gate FET)	Extended Gate FET	Buffer	0.36 μM	1–6 μM	[216]
		Non-enzymatic (paper based)	SWV	Buffer	2.66 μM	N/A	
Epinephrine	Polydopamine-decorated CeO_2	Non-enzymatic	DPV	Buffer & spiked human serum	8.37 μM (buffer); 14.79 μM (serum)	10–200 μM (buffer); 20–100 μM (serum)	[217]
	Potassium ferrite ($K_2Fe_4O_7$) on GCE	Non-enzymatic	DPV	Buffer	0.27 μM	2–260 μM	[218]

(*continued on next page*)

Table 3 (*continued*)

Target Analyte	Electrode material	Sensor type	Transduction Technique	Sample Matrix	LOD	Linear ranges	Ref.
	Cu^{2+}/double-stranded DNA on Au electrode	DNA-based label-free	DPV	Spiked mouse serum, EP hydrochloride injection	47 nM	1.0–12.5 μM and 12.5–1000 μM	[219]
	Boron-doped MWCNTs decorated with AuNPs	Non-enzymatic, multi-analyte	DPV	Pig blood serum	0.30 μM	0.323–1.020 mM	[220]
	rGO/$Ti_3C_2T_x$ MXene on ITO	Non-enzymatic	DPV	Human urine	3.5 nM	1–60 μM	[221]
	$NiMoS_4$ nanowire arrays on graphene foam	Non-enzymatic	DPV	Real samples	0.02 μM	0–60 μM	[222]
	Cu/CuO–Vertical Graphene microelectrode	Non-enzymatic, flexible, multi-analyte	DPV	Human blood and urine	0.13–0.18 μM	0.5–100 μM	[223]
	CQDs/CuO nanocomposite on GCE	Non-enzymatic	SWV	Chicken blood serum, EP injection	15.99 μM	10–100 μM	[224]
	Poly-ferulic acid/MWCNT on GCE	Non-enzymatic	CV, CA	EP hydrochloride injection	22.2 μM	73–1406 μM	[225]
	MWCNTs dispersed in cellulose acetate on GCE	Non-enzymatic	CV, DPV, Amperometry	Pharmaceutical vials, urine samples	10 μM	30–170 μM	[88]
	CQDs-modified carbon paste electrode	Non-enzymatic	CA, CV	Adrenaline bitartrate injection (real sample)	6 nM	0.05–2 μM	[226]
Norepinephrine	Co–Ni/BTC/4,4′-BiPy MOF-modified electrode	Non-enzymatic	DPV	Spiked blood and urine samples	0.815 μM	10–50 μM	[227]
	NiFe-LDH nanosheets decorated with carbon black	Non-enzymatic	DPV	Rat serum	3 nM	0.1–100 μM	[228]
	MIL-88B(FeCu)/COF core–shell integrated in chitosan-acrylamide hydrogel	Non-enzymatic	DPV	Spiked serum samples	0.02 μmol/L	0.06–10 μmol/L	[229]
	La(III)-based HPOM hybrid ($[Ln_4(H_2O)_4W_6(H_2GA)_4O_{12}(B\text{-}\alpha\text{-}TeW_9O_{33})_4]$) on carboxyl-functionalized MWCNT-modified GCE	Non-enzymatic	DPV	Buffer	1.50 μmol/L	2–900 μmol/L	[230]
	AuNPs@NH_2-VMSF modified pre-activated GCE	Non-enzymatic	DPV	Human whole blood	10 nM	50 nM–2 μM and 2–50 μM	[231]
	Honeycomb-like NiO–RGO nanocomposite on GCE	Non-enzymatic	DPV	PC12 cell culture (real-time NE release)	5 nM	20 nM–14 μM and 14–80 μM	[232]
	N-doped carbon hollow trunk on IDA	Non-enzymatic	Portable IDA	PC12 cell secretion (in vitro)	5 nM	10–300 μM	[233]
	De-bundled SWCNTs (D-SWCNTs) modified screen-printed carbon electrode	Non-enzymatic	DPV	Ex vivo rat tissue samples	62.0 nM	100 nM–2.0 μM	[234]
	CNTs(COOH)-modified GCE	Non-enzymatic	DPV	Human serum	35 nM	0.3–3.3 μM	[235]
	Au/rGO on GCE	Non-enzymatic	DPV	Blood plasma, pharmaceutical injection	57 nM	–	[236]
	Graphene quantum dots and ionic liquid modified carbon paste electrode	Non-enzymatic	DPV	Real samples	60 nM	0.2–400.0 μM	[237]
	ADPC-assisted Fe_2O_3@CeO_2 core–shell NPs modified carbon paste electrode	Non-enzymatic	DPV	Real samples	40 nM	0.6–10.0 μmol/L	[238]
	$MnCr_2O_4$ nanocomposite modified carbon paste electrode	Non-enzymatic	CV	Injection samples	34 nM	0.3 μM–4.5 μM	[239]
	Poly-terephthalic acid and poly-4-amino-3-hydroxy-1-naphthalenesulfonic acid modified GCE	Non-enzymatic	CV, DPV	Blood, urine, pharmaceutical samples	2.08 nM	5.0 nM–1600.0 μM	[240]
	C-, N-doped NiO broccoli-like hierarchy	Non-enzymatic	DPV	Living cells (PC12)	0.009 μM	0.5–32 μM	[241]
	Silica–titania/AuNPs	Non-enzymatic	SWV	Simulated biological fluids	0.35 μM	20–180 μM	[242]
	Sulfur-doped carbon spheroidal nanomaterial	Label-free	DPV	Human fluids, neuronal cell line (in vitro)	0.001 μM	0.01–0.8 μM	[243]

OECT (Organic Electrochemical Transistor); PBASE-NHS (1-pyrenebutyric acid N-hydroxysuccinimide ester); GF (graphene foam); APTES (3-aminopropyltriethoxysilane); SH-PEG (thiol-polyethylene glycol-acid); PDMS (Polydimethylsiloxane); LBG (Laser-Burned Graphene; MB (methylene blue); PU (Polyurethane); AuNW (Gold nanowires); PVDF (Polyvinylidene fluoride); CD (cyclodextrin); ITO (Indium tin oxide); CQDs (Carbon quantum dots); IDA (interdigitated electrode array); ADPC (6-amino-4-(3,4-dihydroxyphenyl)-3-methyl-1,4-dihydropyrano[2,3-c],pyrazole-5-carbonitrile).

interfacial changes but less suited for dynamic quantification, and GFET-based approaches offer ultrahigh sensitivity with greater fabrication complexity. These comparative insights highlight that optimal sensor architecture requires matching receptor type and transduction method to the biochemical nature of the hormone, the sampling matrix, and the intended operational context, whether rapid PoC testing or wearable monitoring.

4. Sampling matrices and integration into wearable and PoC systems

4.1. Sweat, saliva, and ISF as alternative biofluids

The development of electrochemical biosensors for stress hormone detection has increasingly shifted focus toward non-invasive and minimally invasive sampling matrices that enable fast, on-body monitoring

[244,245]. While serum remains the gold standard for clinical diagnostics, its use in PoC or wearable applications is impractical due to the need for venipuncture, trained personnel, and centralized laboratories [73,246]. In contrast, sweat, saliva, and ISF offer accessible alternatives that support continuous sampling and integration with flexible, skin-conformal sensing platforms. However, their physicochemical properties, hormone transport mechanisms, and matrix-specific challenges must be addressed for reliable deployment [57,129,247].

The temporal distribution of stress biomarkers across biofluids is a critical parameter for interpreting wearable sensor outputs. Cortisol rapidly equilibrates from blood into saliva through passive diffusion, resulting in short lag times of approximately 5–10 min [38,248]. In contrast, sweat reflects circulating cortisol levels with a longer and more variable delay (≈10–30 min), strongly influenced by sweat rate, glandular secretion dynamics, and local microcirculation [42,248,249]. ISF, accessed through microneedle devices, exhibits diffusion-driven delays comparable to or slightly longer than sweat (≈15–30 min) due to tissue transport resistance [250,251]. Catecholamines display even more transient and complex profiles. Owing to rapid clearance, oxidation, and low basal concentrations, their appearance in peripheral fluids is often delayed, attenuated, or influenced by local metabolic processing [252]. These physiological lag times are essential for contextualizing measurements from wearable electrochemical platforms and for distinguishing acute hormonal pulses from slower, integrated endocrine responses.

Sweat is a biofluid secreted primarily by eccrine glands and contains a mixture of electrolytes, metabolites, and a subset of circulating hormones, including cortisol and catecholamines [57,108,253]. The transport of cortisol into sweat occurs via passive diffusion driven by the concentration gradient between serum and glandular tissues [253]. Although its concentration in sweat is generally lower than in plasma, ranging between 1 and 10 ng/mL, several studies have demonstrated a strong correlation between sweat and serum cortisol under both basal and stress-induced conditions [44,254]. The feasibility of label-free cortisol sensing in naturally expressed sweat has been significantly advanced by recent developments in electrochemical aptasensors. A notable example is the work by Ganguly et al. (2020), who engineered an autonomous, nonfaradaic electrochemical sensor designed to operate over prolonged durations (~8 h) using sub-microliter volumes of sweat [255]. The sensor employed a highly selective single-stranded DNA (ssDNA) aptamer that binds cortisol with high affinity, triggering a conformational shift that modulates the interfacial electrical properties. The sensor achieved a dynamic detection range of 1–256 ng/mL and exhibited a strong linear response ($R^2 = 0.97$), with an output signal modulation between 20 and 50 %. Notably, the aptasensor demonstrated high resistance to signal degradation from common interferents and buffer constituents, which typically challenge antibody-based biosensors in complex biofluids. Comparative evaluation with previously established biosensors revealed that the aptamer-based system exhibited superior surface charge modulation, improved signal-to-noise ratios, and a broader response window across equivalent analyte concentrations. Moreover, the platform's robustness and sensitivity were validated through continuous dosing experiments and human subject trials, confirming its applicability [255]. Despite its potential, sweat analysis poses challenges due to episodic secretion, inter-individual variability, and the need for active sweat stimulation under resting conditions [57,247]. Furthermore, local skin temperature, hydration status, and electrolyte content can affect analyte concentration and sensor response. To address these issues, microfluidic sweat harvesting systems with flow rate monitoring and integrated calibration channels are being developed to decouple hormone fluctuations from sweat rate variability [74,201].

Saliva represents another promising, non-invasive matrix that closely reflects the free (biologically active) fraction of circulating cortisol, as it is not subject to binding by corticosteroid-binding globulin [50,256]. This makes salivary cortisol particularly valuable for diurnal rhythm assessment and psychoneuroendocrinology studies [96,138]. Typically, salivary cortisol levels range from 0.1 to 10 ng/mL, and exhibit a predictable circadian variation, peaking 20–30 min after awakening (the cortisol awakening response) [257]. Electrochemical immunosensors tailored for saliva must be sensitive to proteolytic degradation, pH variability (typically pH 6.0–7.5), and the presence of mucins that may interfere with antibody-antigen binding or electrode conductivity [22,50,96]. A recent study by Zea et al. (2024) demonstrated the development of a fully inkjet-printed electrochemical paper-based analytical device for salivary cortisol detection, providing a compelling example of how low-cost, disposable sensor formats can be adapted for on-demand hormone analysis [258]. Utilizing gold ink on paper substrates, the researchers achieved covalent immobilization of monoclonal cortisol antibodies via electrochemical grafting of 4-carboxymethylaniline, followed by ethanolamine passivation to minimize non-specific interactions. The resulting sensor exhibited a linear response across the physiological salivary cortisol range (5–20 ng/mL), with excellent sensitivity and R^2 values exceeding 0.97. Importantly, the device maintained high specificity in the presence of potential cross-reactive species, underscoring its suitability for complex biological matrices [258]. This work illustrates the viability of environmentally friendly, scalable fabrication strategies for cost-effective endocrine biosensing and further supports the adoption of non-invasive matrices like saliva for time-resolved stress hormone monitoring. Further supporting the viability of saliva as a diagnostic matrix, Khan et al. (2017) developed a disposable paper-based biosensor incorporating a nanocomposite of graphene nanoplatelets and poly(styrene)-block-poly (acrylic acid) on filter paper, followed by micro-gold electrode deposition [259]. This configuration enabled highly sensitive cortisol detection down to 1 pg/mL, across a broad range up to 10 ng/mL ($R^2 = 0.9777$). Coupled with a handheld impedance analyzer, the device showed strong agreement with ELISA ($R^2 = 0.9386$) and demonstrated excellent performance in both standard solutions and real saliva samples. The platform's simplicity, portability, and selectivity position it as a promising tool for PoC psychological stress monitoring [259]. Nevertheless, variability in flow rate and potential contamination with food or oral bacteria require either pre-processing modules or antifouling surface chemistries, such as zwitterionic polymers or polyethylene glycol coatings.

ISF, which fills the space between cells and capillaries, offers a more stable and less contaminated alternative for hormone detection [21]. Because ISF is in dynamic equilibrium with blood plasma, it contains hormones such as cortisol and catecholamines in concentrations closely approximating their systemic levels [58,260]. For cortisol, ISF concentrations typically range from 5 to 20 ng/mL, depending on the sampling depth and local perfusion. Unlike sweat and saliva, ISF exhibits minimal influence from environmental or behavioral factors, making it suitable for applications requiring quantitative and temporally consistent monitoring [58,260]. Continuous ISF sampling is enabled by minimally invasive approaches such as microneedle arrays, iontophoresis, and reverse iontophoresis [261–264].

From a systems-integration perspective, each biofluid imposes distinct constraints on the design of sensor interfaces, sampling modules, and analytical algorithms. Sweat-based sensors often require continuous flow assessment or periodic recalibration to account for variable secretion rates and dynamic composition changes. Saliva-based systems benefit from direct sampling but must cope with a higher likelihood of matrix interference and variability. ISF-accessing platforms offer the highest fidelity but require material and mechanical optimization to ensure long-term comfort and stability. The selection of an optimal biofluid for stress hormone sensing must be dictated by the application context, balancing trade-offs between invasiveness, signal fidelity, and sampling robustness. For short-term stress tracking, sweat and saliva provide accessible solutions when supported by appropriate sensor calibration and antifouling strategies. On the other hand, for longitudinal hormone monitoring, ISF presents a compelling matrix, especially

when integrated with microneedle or electroosmotic sampling systems. Future efforts should focus on developing unified platforms capable of adaptive sampling and matrix-specific signal normalization to enable precise and continuous endocrine monitoring in real-world conditions.

Direct comparison of cortisol and catecholamine concentrations across sweat, saliva, and ISF remains challenging due to the absence of harmonized sampling protocols, matrix-specific partitioning behavior, and variable lag times relative to blood. Salivary cortisol reflects the unbound plasma fraction (typically 10–20 %), but catecholamine levels correlate poorly with blood because of rapid enzymatic degradation in saliva. Sweat concentrations are strongly influenced by sweat rate, evaporation, pH, and ionic strength, often introducing ≥20–40 % variability independent of physiological secretion. ISF more closely approximates blood but exhibits measurable delays (typically 5–15 min for cortisol) and may show attenuated catecholamine peaks due to rapid local clearance. As a result, identical sensing chemistries frequently produce matrix-specific calibration curves, and no universally accepted conversion factors currently exist between sweat, saliva, ISF, and plasma. Reference intervals for non-blood matrices also remain insufficiently validated in clinical cohorts. These matrix-dependent discrepancies impose inherent accuracy limits on wearable and PoC biosensors and highlight the need for standardized calibration frameworks before real-time hormonal measurements can be reliably interpreted in clinical practice.

4.2. Wearable and PoC platforms

The growing demand for personalized and decentralized health monitoring has spurred rapid development in wearable and PoC sensing technologies for endocrine biomarkers [24,50]. These platforms aim to provide continuous and fast physiological data acquisition outside of clinical environments, supporting early intervention, stress management, and personalized therapy [73,246]. Among the most promising configurations are epidermal patches, microneedle-based systems, and integrated biosensor arrays with wireless communication capabilities. The integration of electrochemical biosensors into these wearable formats requires addressing challenges related to mechanical flexibility, biofluid sampling, power management, and data fidelity, all while ensuring biocompatibility and user comfort [57,129].

Patch-based wearable sensors have emerged as a dominant class for non-invasive sweat and saliva endocrine hormone monitoring [265,266]. These platforms typically consist of a flexible polymer substrate integrated with patterned electrodes and functionalized recognition layers. Supporting this trend, Singh et al. (2023) developed a wearable electrochemical biosensor tailored for cortisol detection in sweat, addressing key limitations of traditional stress monitoring method [265]. Cortisol recognition is achieved through a conformation-switching aptamer functionalized with a pseudoknot, which enhances target specificity and minimizes background signal by locking the aptamer into only two energetically favorable states. This design enables repeatable and regenerable binding events, crucial for continuous monitoring over extended periods. The sensor demonstrated an ultra-low detection limit (0.2 pM) and a wide linear range (1 pM–1 μM), fully encompassing the physiologically relevant concentrations of cortisol in sweat. Real-world validation was achieved via on-body testing with human participants undergoing an induced stress protocol, during which the patch provided stable and continuous cortisol readings for up to 90 min, with in situ signal regeneration [265]. Together, these innovations showcase how patch-based wearable sensors have evolved into highly specialized platforms for non-invasive, biomolecular stress monitoring, offering unprecedented levels of specificity, temporal resolution, and personalization. These systems go beyond generic physiological indicators, such as heart rate variability, by directly quantifying endocrine biomarkers, thereby establishing a new paradigm in wearable stress diagnostics. Moreover, Lee et al. (2020) developed a fully integrated, conformable lab-on-a-patch (LoP) platform designed for on-body, non-invasive detection of cortisol in sweat [199]. This wearable system combined a stretchable, label-free impedimetric biosensor with a stretchable microfluidic component, all embedded on a soft, flexible substrate (Fig. 8). The platform enabled precise sweat collection, controlled reagent delivery, and one-touch operation. Notably, the use of three-dimensional nanostructured gold electrodes significantly enhanced sensitivity, allowing for accurate detection of cortisol at picomolar levels during exercise. The successful integration of microfluidics and biosensing elements into a single soft patch underscores the potential of these wearable platforms for endocrine hormone monitoring, particularly through sweat [199]. This study exemplifies how flexible polymer-based wearable patches, outfitted with patterned electrodes and functionalized recognition elements, are redefining the landscape of non-invasive biosensing for hormone biomarkers, thereby substantiating the claim regarding their dominant role in modern bioanalytical applications.

Microneedle-integrated systems represent another transformative approach, particularly for accessing interstitial fluid. These devices leverage arrays of polymeric or metallic microneedles to penetrate the stratum corneum without reaching pain receptors, enabling continuous sampling of ISF in a minimally invasive manner. Early human studies have already demonstrated the feasibility of electrochemical microneedle sensors for minimally invasive cortisol monitoring, including clinical evaluations showing correlation with serum cortisol levels and acceptable safety profiles. These examples illustrate that electrochemical ISF-based platforms have begun to progress beyond bench testing toward initial clinical validation. In example, Jing et al. (2024) developed a conductive microneedle electrochemical biosensor functionalized with dendritic AuNPs and a cortisol-specific aptamer [139]. The device demonstrated a low LOD (~0.2 nM), a broad dynamic range, and a calibration slope indicative of high analytical sensitivity. In human studies, sensor readings showed strong correlation with blood cortisol levels, underscoring the potential of microneedle platforms for accurate, painless endocrine biomarker detection directly beneath the skin [139]. In another work, Mugo et al. (2023) advanced microneedle-integrated platforms by developing a low-cost, multiplexed electrochemical sensor array for simultaneous detection of pH, EP, DA, and lactate in human sweat (Fig. 9) [267]. Built on a PDMS microneedle substrate with a conductive PDMS/CNT/cellulose nanocrystal (CNC)/silver nanoparticle composite, the sensors employed molecularly imprinted PANI-based layers for high specificity and rapid response (~2 min). The system achieved impressive detection limits (e.g., 0.7 nM for EP, 2.11 nM for DA) and accurately measured analytes in real sweat samples [267]. This study showcases the potential of wearable microneedle systems for comprehensive, non-invasive sweat analytics at the point of need.

Beyond mechanical integration, the electronic backbone of wearable biosensors is critical for enabling on-device data analytics and Internet-of-Things (IoT) functionalities [268,269]. Onboard electronics typically include low-power potentiostats, microcontrollers for signal processing, and wireless modules (e.g., BLE, near-field communication (NFC)) for data transmission [270,271]. The incorporation of edge computing allows for on-device anomaly detection and trend prediction, reducing the need for cloud-dependent analysis. Several recent prototypes have demonstrated continuous or event-driven cortisol readouts with visual biofeedback delivered to smartphones, enabling users to associate hormonal variations with behavioral or environmental factors [272]. These capabilities are particularly relevant in sports science, occupational health, and mental wellness applications [273,274].

In summary, wearable and PoC cortisol sensors represent a confluence of biosensing, materials science, and wireless electronics, offering significant potential to revolutionize stress hormone monitoring. However, challenges remain in ensuring sensor longevity, calibration stability, and biofouling resistance during extended wear. The ongoing refinement of these platforms, toward higher fidelity, lower cost, and greater user integration, will be critical to realizing the vision of

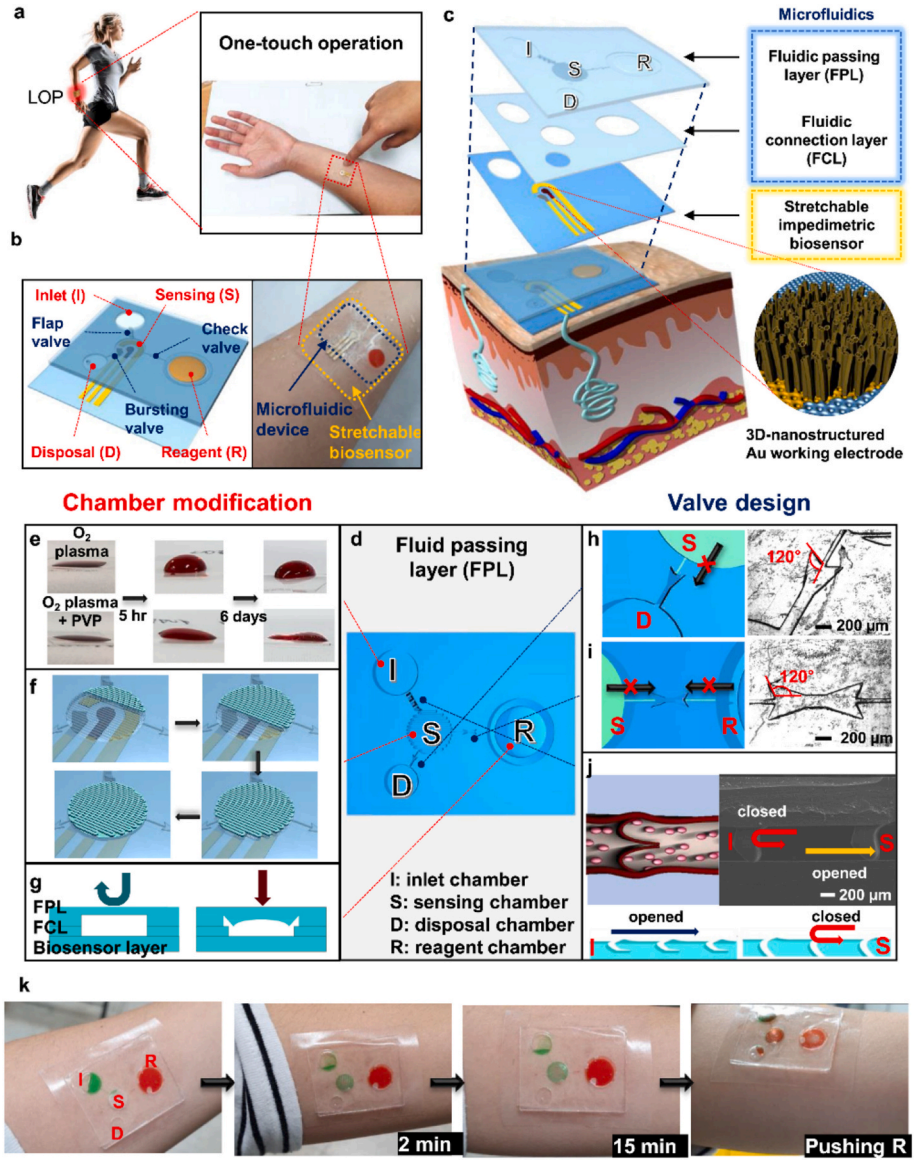


Fig. 8. Design and on-body application of a stretchable LoP platform for wearable cortisol sensing via integrated microfluidics and nanostructured biosensor. Reprinted with permission from Ref. [199]. © *2020 Elsevier B.V.*

personalized, proactive, and precision-based endocrine health management.

4.3. Multiplexing: dual or panel hormone detection

Capturing the full spectrum of stress-related hormonal dynamics often requires the concurrent measurement of multiple biomarkers, such as cortisol and catecholamines, which exhibit distinct secretion kinetics, chemical properties, and physiological roles [275]. As single-analyte measurements may offer only limited insight, multiplexed biosensing platforms are being developed to enable synchronized detection of hormone panels from a single sample, thus improving diagnostic accuracy and contextual interpretation [17,276]. These systems are particularly valuable for distinguishing between chronic baseline dysregulation and acute stress surges, supporting their relevance in precision health and behavioral monitoring applications [18,276,277].

Multiplexed electrochemical immunosensors and aptasensors offer a powerful route toward dual-analyte or panel hormone detection. These platforms often utilize spatially separated working electrodes within a shared microfluidic or sensor interface, each functionalized with a distinct biorecognition element (e.g., antibodies or aptamers) specific to the target analyte [17,267,277]. The integration of electrochemical readouts typically via DPV, EIS, and CA allows for parallel data acquisition from multiple channels without crosstalk. Signal deconvolution is further enhanced by the use of redox mediators with distinct potentials or frequency-resolved impedance analysis, enabling analyte-specific resolution in on-device measurements [278,279].

Recent advances in microfluidics and Lab-on-a-Chip (LoC) technology have played a pivotal role in enabling such multiplexed configurations [280]. These systems allow precise fluid handling, sample partitioning, and analyte preconcentration, all within compact, low-volume architectures. In another work, Alachkar et al. (2022) developed a 3D-printed microfluidic syringe-type biosensor (μSyringe) for the detection of DA in ultralow fluid volumes [281]. The device employed PGEs and leveraged additive manufacturing to create a compact and cost-effective platform capable of continuous amperometric monitoring. It demonstrated excellent analytical performance, with a quantification limit of 0.1 nM and a linear range extending up to 500 nM, validated in cerebrospinal fluid from freely moving mice [281]. This work underscores the growing potential of LoC systems to combine

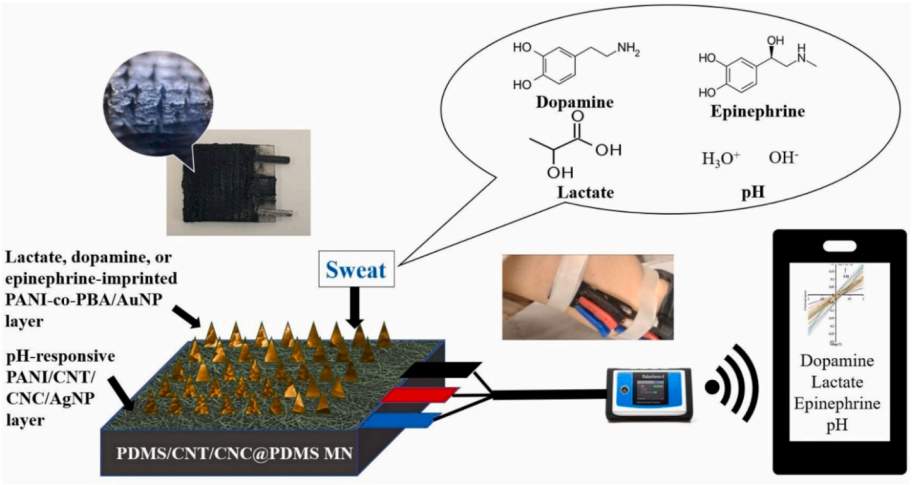


Fig. 9. Schematic illustration of a multiplexed microneedle-based wearable sensor platform for sweat analysis of dopamine, EP, lactate, and pH. Reprinted with permission from Ref. [267]. © *2023 Elsevier B.V.*

miniaturization, precision, and robustness, enabling in situ biochemical analysis of biofluids in dynamic and physiologically relevant environments. Further advancing the utility of microfluidic systems, a study by Liu et al. (2018) demonstrated the integration of an electrochemical sensor comprising PDDA-rGO modified multi-walled carbon nanotube carbon paste electrode (MWCNT-CPE/PDDA-rGO) within a microfluidic device for the simultaneous detection of DA and 5-hydroxytryptamine in microliter-scale samples [282]. This hybrid nanomaterial-based configuration exhibited a strong synergistic electrocatalytic effect, enabling dual-analyte quantification with high sensitivity and selectivity. The system achieved low limits of detection (0.016 μM for DA and 0.0098 μM for 5-HT) across wide linear ranges using only 20 μL of plasma, illustrating the efficiency of microfluidic-enabled multiplexing [282]. The successful application of this platform in rat plasma highlights its potential for multi-biomarker monitoring in both in vitro and in vivo settings, underscoring the power of miniaturized microfluidic systems in complex biological analysis. The versatility of microfluidic platforms for simultaneous multi-analyte detection is further exemplified by a paper-based capillary electrophoresis-amperometric detection system developed using wax printing and screen-printing techniques [283]. This low-cost microchip enabled electrophoretic separation and in-channel amperometric detection of DA, EP, and serotonin within a single 2 μL serum sample without the need for decouplers or pre-treatment. The device achieved efficient separation within 650 s and was validated using spiked fetal bovine serum, highlighting its potential for PoC neurochemical diagnostics [283]. This simplified configuration underscores how microfluidics can integrate separation and detection in compact, field-deployable systems for clinically relevant applications.

A critical consideration in multiplexed designs is the electrochemical compatibility of recognition chemistries and electrode interfaces. Co-functionalization must avoid steric hindrance, surface fouling, and cross-binding events that may affect sensor specificity [284]. Surface patterning techniques such as microcontact printing and inkjet deposition have been utilized to spatially isolate sensing domains [285]. Furthermore, antifouling coatings and nanomaterial scaffolds (e.g., AuNPs, GO films) have been incorporated to enhance signal fidelity and electrode regeneration during multi-analyte detection cycles [284].

Beyond simultaneous detection, multiplexed biosensors enable the generation of endocrine profiles that reveal dynamic interactions between biomarkers. For example, diurnal patterns of cortisol may be interpreted in conjunction with pulsatile nEP spikes to distinguish between circadian rhythm disruptions and acute stress responses. Such analytical capabilities are particularly valuable in the context of psychiatric disease classification, personalized medicine, and sports physiology, where a single biomarker often provides insufficient diagnostic granularity.

Importantly, data handling and visualization strategies for multiplexed systems are evolving to support continuous interpretation. Multichannel electrochemical analyzers, edge-computing algorithms, and machine learning-based signal classification tools are being deployed to extract clinically relevant patterns from complex biosignal datasets. As miniaturization continues, the convergence of microfluidics, nanomaterial-enabled sensing, and multivariate analytics will shape the next generation of intelligent PoC systems for endocrine monitoring.

5. Challenges and future directions

Despite the rapid evolution of electrochemical biosensors for stress hormone monitoring, several scientific and translational barriers remain unresolved, limiting their widespread clinical adoption and long-term field deployment beyond controlled laboratory studies. While many current systems are innovative in concept, most remain confined to proof-of-concept or short-term experimental applications, with few demonstrating the reliability, reproducibility, and robustness necessary for routine endocrine health assessment.

A persistent challenge is maintaining high selectivity while achieving low detection limits in complex, low-volume biofluids such as sweat, saliva, and interstitial fluid. These matrices present fluctuating ionic composition, variable secretion rates, and numerous electroactive interferents that can compromise surface-bound bioreceptors. Many recently reported platforms achieve low detection limits under controlled laboratory conditions, but their performance often deteriorates when exposed to dynamic, multi-analyte *in-vivo* environments. For instance, label-free impedance sensors, while advantageous for miniaturization, are especially vulnerable to non-specific adsorption and dielectric noise, which can obscure analyte-specific responses. Continued development of antifouling chemistries, high-specificity molecularly imprinted polymers, next-generation aptamers, and engineered nanobody constructs will be essential to sustain selectivity under real physiological conditions.

Lack of standardized calibration protocols represents another major limitation, especially for wearable and PoC formats. Unlike laboratory assays such as ELISA or LC-MS/MS, on-body biosensors must contend with fluctuating sampling volumes, variable skin or mucosal contact, and uncontrolled environmental conditions (e.g., humidity, temperature, motion). The absence of a universally accepted calibration method leads to significant inter-study variability and hinders meta-analysis or

regulatory benchmarking. Dynamic referencing strategies, incorporation of on-device calibration modules, and development of matrix-specific reference standards will be essential to achieving clinically meaningful and interoperable biosensing platforms.

Long-term biostability remains a technical bottleneck for continuous hormone tracking. Enzyme-labeled systems are prone to degradation over time, especially under fluctuating pH and ionic conditions. Similarly, antibody-based and aptamer-based sensors often suffer from conformational instability, sensor drift, or denaturation over extended wear periods. Although emerging strategies such as nanobody-based constructs, supramolecular recognition systems, and regenerable self-assembled monolayers offer improved stability, few studies evaluate operational longevity over clinically relevant timescales (e.g., 24–72 h). Systematic durability and drift studies under real-world conditions are needed to establish reliability for continuous monitoring.

Calibration drift remains one of the most persistent obstacles to deploying hormone sensors outside controlled laboratory settings. Sweat composition, ISF osmolarity, temperature, and motion artifacts can alter charge-transfer kinetics and C_{dl} over time, producing sensor drift independent of biomarker concentration. Additionally, biofouling, gradual dehydration of hydrogels, and mechanical strain during wear can distort sensor baselines. Most reported devices demonstrate stability only over short testing windows (1–4 h) and lack validation under typical daily-life conditions such as exercise, variable humidity, or extended wear. Overcoming these challenges will require self-calibrating architectures, internal reference channels, drift-compensation algorithms, and materials engineered for mechanical and biochemical resilience.

From a clinical translational standpoint, electrochemical sensors must ultimately be evaluated against gold-standard laboratory methods including LC–MS/MS, HPLC, and immunoassays. While biosensors excel in capturing real-time trends, circadian patterns, and acute hormonal fluctuations, they currently lack the accuracy and standardization required to fully replace centralized diagnostics. Instead, their near-term role is likely complementary, enabling preliminary screening, stress-pattern tracking, and decentralized monitoring.

Translational progression of electrochemical hormone sensors also depends on alignment with regulatory expectations. However, regulatory classification and clinical validation pathways for stress hormone biosensors remain underdeveloped. Wearable or minimally invasive cortisol devices fall under FDA Class II or EU IVDR Class B/C classifications, requiring analytical validation, clinical performance studies, biocompatibility testing (ISO 10993), and cybersecurity provisions for connected platforms. Although most current biosensors remain at TRL 3–5, several wearable electrochemical devices including sweat electrolyte sensors and microneedle glucose monitors demonstrate clear regulatory precedents for future cortisol and catecholamine systems. Establishing standardized protocols for clinical validation, including comparison with LC–MS/MS or immunoassay benchmarks, will be essential to accelerate regulatory submission and market adoption. Furthermore, agencies require well-established clinical utility endpoints such as diagnostic thresholds or decision-making algorithms which do not yet exist for real-time stress monitoring. These gaps must be addressed before wearable or PoC hormone sensors can enter regulated healthcare pathways. Bridging this gap will require collaborative efforts to define clinical utility endpoints, generate normative hormone fluctuation databases, and build robust clinical validation pipelines in partnership with endocrinologists and behavioral health experts.

Beyond analytical performance, the translational feasibility of wearable and PoC electrochemical biosensors is shaped by practical considerations that remain insufficiently addressed in current literature. The material cost of high-performance platforms often limits scalability, and several emerging nanomaterials still lack mature, high-yield, batch-consistent synthesis routes. Sustainability is an additional concern for disposable skin-mounted patches or microneedle systems, where polymer substrates, adhesives, and nanomaterial residues raise environmental and waste-management challenges that are rarely evaluated. Reproducibility represents a major barrier. Batch-to-batch variability in antibodies, aptamers, and MIPs, as well as morphological heterogeneity in nanostructured electrodes, can generate significant drift in calibration curves and limit inter-device comparability. Finally, data integration challenges persist for wearable hormone sensors. These devices require secure, low-power transmission, standardized data formats, and robust on-device or cloud-based algorithms capable of compensating for matrix effects, lag times, and sensor drift. Without unified frameworks for signal processing and cross-platform interoperability, biosensor outputs cannot be reliably incorporated into digital health ecosystems or clinical decision-support tools. Collectively, these considerations underscore that analytical performance alone is insufficient for clinical translation. Cost, sustainability, reproducibility, and data integration must be co-optimized to enable scalable, real-world deployment.

Looking ahead, the convergence of biosensing with artificial intelligence, edge computing, and digital therapeutics is expected to redefine the future landscape of stress hormone monitoring. Machine learning algorithms can correct matrix-dependent variability, compensate for drift, harmonize signals across individuals or devices, and integrate multiple biomarkers into composite stress indices. AI-driven calibration transfer and domain adaptation could also enable standardized interpretation across heterogeneous platforms that is an essential step toward regulatory approval and clinical integration. Predictive algorithms trained on multimodal datasets including biosensor output, circadian rhythm data, and behavioral inputs could enable anticipatory stress management strategies. In parallel, closed-loop feedback systems that trigger therapeutic interventions (e.g., neuromodulation, pharmacological release) in response to biosensed hormonal cues are beginning to emerge. However, these innovations must be balanced with ethical considerations regarding data ownership, biometric surveillance, and algorithmic bias.

Commercial translation of electrochemical cortisol and catecholamine biosensors has progressed slowly, not due to lack of analytical innovation but because most research prototypes have not yet demonstrated the level of reproducibility, long-term reliability, and validation required for regulatory approval and commercialization. Unlike glucose monitoring, which benefits from decades of clinical calibration standards and market infrastructure, stress biomarkers lack established clinical decision thresholds and standardized reference ranges. This makes product certification and reimbursement pathways less straightforward. For manufacturers, uncertainties in defining clinically actionable outputs create additional barriers to investment. Moving toward viable market products will require *(i) multi-site clinical studies that link sensor readouts to validated physiological or behavioral endpoints; (ii) manufacturing workflows capable of producing stable and reproducible electrode–bioreceptor interfaces; and (iii) integration of on-device calibration and AI-based signal correction to ensure reliable longitudinal performance.* As these elements mature, electrochemical stress-hormone sensing platforms will be better positioned for regulatory evaluation and adoption in digital health or wellness markets.

Ultimately, enabling commercial and clinical adoption will require coordinated progress across materials science, electrochemical engineering, microfluidics, and data analytics, together with sustained engagement from clinicians and regulators. Multi-site clinical validation, harmonized calibration standards, and rigorous long-term stability assessments under on-body conditions will be essential to establish trust and regulatory readiness. With these elements in place, electrochemical platforms for cortisol and catecholamines can progress from research prototypes toward reliable diagnostic and digital-health tools for endocrine assessment, mental-health monitoring, and personalized stress management.

6. Conclusion

Electrochemical biosensors have emerged as powerful tools for translating the complex endocrine stress response into measurable signals across accessible biofluids such as saliva, sweat, and interstitial fluid. By jointly considering cortisol and catecholamines, this review has highlighted how sensor architecture, biorecognition chemistry, nanomaterial engineering, and sampling-matrix selection collectively shape analytical performance and translational potential. Comparative analysis of recent devices shows that thoughtful pairing of recognition elements with tailored electrode materials and suitable biofluids can yield platforms that are both highly sensitive and compatible with wearable or PoC operation.

At the same time, the discussion of sampling dynamics, device integration, and data handling underscores that successful stress-hormone monitoring will depend not only on incremental gains in limit of detection, but also on robust calibration strategies, long-term stability, and clinically meaningful interpretation of temporal hormone patterns. In this context, promising future directions include hybrid nanomaterial architectures optimized for specific biofluids, semi-continuous or multiplexed sensing formats capable of capturing the interplay between cortisol and catecholamines, and deeper integration with computational frameworks for signal correction, pattern extraction, and decision support. If these scientific and translational elements can be harmonized within validated clinical workflows, electrochemical biosensors are well positioned to bridge molecular endocrinology with connected-health technologies, enabling more precise stress assessment, earlier detection of endocrine dysfunction, and new opportunities for personalized interventions in mental health, occupational medicine, and performance monitoring.

CRediT authorship contribution statement

Ceren Karaman: Writing – review & editing, Writing – original draft, Visualization, Conceptualization. **Mustafa Aydemir:** Writing – review & editing, Writing – original draft. **Onur Karaman:** Writing – review & editing, Writing – original draft, Visualization, Conceptualization.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used ChatGPT in order to improve the readability and language of the manuscript. After using this tool/service, the author(s) reviewed and edited the content as needed and took full responsibility for the content of the publication.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

References

[1] A. Agorastos, G.P. Chrousos, The neuroendocrinology of stress: the stress-related continuum of chronic disease development, Mol. Psychiatr. 27 (2022), https://doi.org/10.1038/s41380-021-01224-9.

[2] L. Palego, G. Giannaccini, L. Betti, Neuroendocrine response to psychosocial stressors, inflammation mediators and brain-periphery pathways of adaptation, Cent. Nerv. Syst. Agents Med. Chem. 21 (2020), https://doi.org/10.2174/1871524920999201214231243.

[3] A. Flak, D. Bartusik-Aebisher, D. Aebisher, Adrenocorticotropic hormone (ACTH), in: The Biochemical Guide to Hormones, 2023, https://doi.org/10.1016/b978-0-12-379260-0.50019-4.

[4] S.L. Lightman, M.T. Birnie, B.L. Conway-Campbell, Dynamics of ACTH and cortisol secretion and implications for disease, Endocr. Rev. 41 (2021), https://doi.org/10.1210/ENDREV/BNAA002.

[5] J.B. Young, R.M. Rosa, L. Landsberg, Dissociation of sympathetic nervous system and adrenal medullary responses, Am. J. Physiol. 247 (1984).

[6] A.S.P. Jansen, X. Van Nguyen, V. Karpitskiy, T.C. Mettenleiter, A.D. Loewy, Central command neurons of the sympathetic nervous system: basis of the fight-or-flight response, Science (1995) 270, https://doi.org/10.1126/science.270.5236.644, 1979.

[7] U.M. Nater, N. Skoluda, J. Strahler, Biomarkers of stress in behavioural medicine, Curr. Opin. Psychiatr. 26 (2013), https://doi.org/10.1097/YCO.0b013e328363b4ed.

[8] K. Shah, R. Kumari, M. Jain, Unveiling stress markers: a systematic review investigating psychological stress biomarkers, Dev. Psychobiol. 66 (2024), https://doi.org/10.1002/dev.22490.

[9] S. Kaur, N. Gupta, B.D. Malhotra, Recent developments in wearable & non-wearable point-of-care biosensors for cortisol detection, Expert Rev. Mol. Diagn 23 (2023), https://doi.org/10.1080/14737159.2023.2184260.

[10] J. Ok, S. Park, Y.H. Jung, T. il Kim, Wearable and implantable cortisol-sensing electronics for stress monitoring, Adv. Mater. 36 (2024), https://doi.org/10.1002/adma.202211595.

[11] R. McCarty, P.E. Gold, Catecholamines, stress, and disease: a psychobiological perspective, Psychosom. Med. 58 (1996), https://doi.org/10.1097/00006842-199611000-00007.

[12] E.A. Young, J. Abelson, S.L. Lightman, Cortisol pulsatility and its role in stress regulation and health, Front. Neuroendocrinol. 25 (2004), https://doi.org/10.1016/j.yfrne.2004.07.001.

[13] L. Thau, J. Gandhi, S. Sharma, Physiology, cortisol, StatPearls January (2021). https://www.ncbi.nlm.nih.gov/sites/books/NBK538239/.

[14] S. Paravati, A. Rosani, S.J. Warrington, Physiology, Catecholamines, StatPearls, 2024.

[15] V. Vignesh, B. Castro-Dominguez, T.D. James, J.M. Gamble-Turner, S. Lightman, N.M. Reis, Advancements in cortisol detection: from conventional methods to next-generation technologies for enhanced hormone monitoring, ACS Sens. 9 (2024) 1666–1681, https://doi.org/10.1021/acssensors.3c01912.

[16] M. Plebani, J.H. Nichols, P.B. Luppa, D. Greene, L. Sciacovelli, J. Shaw, A.I. Khan, P. Carraro, G. Freckmann, W. Dimech, M. Zaninotto, M. Spannagl, J. Huggett, G. J. Kost, T. Trenti, A. Padoan, A. Thomas, G. Banfi, G. Lippi, Point-of-care testing: state-of-the art and perspectives, Clin. Chem. Lab. Med. 63 (2025) 35–51, https://doi.org/10.1515/cclm-2024-0675.

[17] H. Kim, J. Song, S. Kim, S. Lee, Y. Park, S. Lee, S. Lee, J. Kim, Recent advances in multiplexed wearable sensor platforms for real-time monitoring lifetime stress: a review, Biosensors (Basel) 13 (2023), https://doi.org/10.3390/bios13040470.

[18] S. Klinghammer, T. Voitsekhivska, N. Licciardello, K. Kim, C.K. Baek, H. Cho, K. J. Wolter, C. Kirschbaum, L. Baraban, G. Cuniberti, Nanosensor-based real-time monitoring of stress biomarkers in human saliva using a portable measurement system, ACS Sens. 5 (2020), https://doi.org/10.1021/acssensors.0c02267.

[19] J. Lee, M.C. Kim, I. Soltis, S.H. Lee, W. Yeo, Advances in electrochemical sensors for detecting analytes in biofluids, Adv. Sensor Res. 2 (2023), https://doi.org/10.1002/adsr.202200088.

[20] R. Ghaffari, D.S. Yang, J. Kim, A. Mansour, J.A. Wright, J.B. Model, D.E. Wright, J.A. Rogers, T.R. Ray, State of sweat: emerging wearable systems for real-time, noninvasive sweat sensing and analytics, ACS Sens. 6 (2021), https://doi.org/10.1021/acssensors.1c01133.

[21] S. Cha, M.Y. Choi, M.J. Kim, S.B. Sim, I. Haizan, J.-H. Choi, Electrochemical microneedles for real-time monitoring in interstitial fluid: emerging technologies and future directions, Biosensors (Basel) 15 (2025) 380, https://doi.org/10.3390/bios15060380.

[22] C.E. Karachaliou, G. Koukouvinos, D. Goustouridis, I. Raptis, S. Kakabakos, P. Petrou, E. Livaniou, Cortisol immunosensors: a literature review, Biosensors (Basel) 13 (2023), https://doi.org/10.3390/bios13020285.

[23] C.J. Weber, O.M. Clay, R.E. Lycan, G.K. Anderson, O. Simoska, Advances in electrochemical biosensor design for the detection of the stress biomarker cortisol, Anal. Bioanal. Chem. 416 (2024), https://doi.org/10.1007/s00216-023-05047-1.

[24] V. Vignesh, B. Castro-Dominguez, T.D. James, J.M. Gamble-Turner, S. Lightman, N.M. Reis, Advancements in cortisol detection: from conventional methods to next-generation technologies for enhanced hormone monitoring, ACS Sens. 9 (2024) 1666–1681, https://doi.org/10.1021/acssensors.3c01912.

[25] Z. Li, D. Luo, Y. Zhang, X. Niu, H. Liu, Smart health monitoring: review of electrochemical biosensors for cortisol monitoring, Adv. Healthcare Mater. 14 (2025), https://doi.org/10.1002/adhm.202404454.

[26] S. Balasamy, R. Atchudan, S. Arya, A.K. Sundramoorthy, Emerging trends in wearable and non-invasive cortisol sensing technologies – a review, J. Mater. Chem. B 13 (2025) 13154–13183, https://doi.org/10.1039/D5TB01519G.

[27] Z. Sheffield, P. Paul, S. Krishnakumar, D. Pan, Current strategies and future directions of wearable biosensors for measuring stress biochemical markers for neuropsychiatric applications, Adv. Sci. 12 (2025), https://doi.org/10.1002/advs.202411339.

[28] J.A. Ribeiro, P.M.V. Fernandes, C.M. Pereira, F. Silva, Electrochemical sensors and biosensors for determination of catecholamine neurotransmitters: a review, Talanta 160 (2016), https://doi.org/10.1016/j.talanta.2016.06.066.

[29] Z. Fredj, M. Sawan, Advanced nanomaterials-based electrochemical biosensors for catecholamines detection: challenges and trends, Biosensors (Basel) 13 (2023), https://doi.org/10.3390/bios13020211.
[30] S. Lakard, I.A. Pavel, B. Lakard, Electrochemical biosensing of dopamine neurotransmitter: a review, Biosensors (Basel) 11 (2021), https://doi.org/10.3390/bios11060179.
[31] U.A. Wankhade, Y.N. Thakare, B.M. Hardas, R.S. Pande, Cortisol detection methods for stress monitoring: current insight and future prospect: a review, IEEE Sens. J. 24 (2024) 23389–23400, https://doi.org/10.1109/JSEN.2024.3404399.
[32] M. Dutt, C.J. Wehrle, I. Jialal, Physiology, adrenal gland, StatPearls (2023). https://www.ncbi.nlm.nih.gov/books/NBK538239/.
[33] E. Mansour, W. Saliba, Y.Y. Broza, O. Frankfurt, L. Zuri, K. Ginat, E. Palzur, A. Shamir, H. Haick, Continuous monitoring of psychosocial stress by non-invasive volatilomics, ACS Sens. 8 (2023), https://doi.org/10.1021/acssensors.3c00945.
[34] N. Ljubijankić, R. Popović-Javorić, S. Šćeta, A. Šapčanin, I. Tahirović, E. Sofić, Daily fluctuation of cortisol in the saliva and serum of healthy persons, Bosn. J. Basic Med. Sci. 8 (2008) 110–115, https://doi.org/10.17305/bjbms.2008.2962.
[35] M. Kosák, V. Hána, M. Hill, K. Šimůnková, Z. Lacinová, M. Kršek, J. Marek, Serum cortisol seems to be a more appropriate marker for adrenocortical reserve evaluation in ACTH test in comparison to salivary cortisol, Physiol. Res. 63 (2014), https://doi.org/10.33549/physiolres.932611.
[36] N.K. Singh, S. Chung, M. Sveiven, D.A. Hall, Cortisol detection in undiluted human serum using a sensitive electrochemical structure-switching aptamer over an antifouling nanocomposite layer, ACS Omega 6 (2021), https://doi.org/10.1021/acsomega.1c03552.
[37] C. Jung, S. Greco, H.H.T. Nguyen, J.T. Ho, J.G. Lewis, D.J. Torpy, W.J. Inder, Plasma, salivary and urinary cortisol levels following physiological and stress doses of hydrocortisone in normal volunteers, BMC Endocr. Disord. 14 (2014), https://doi.org/10.1186/1472-6823-14-91.
[38] C.E. Hernandez, T. Thierfelder, K. Svennersten-Sjaunja, C. Berg, A. Orihuela, L. Lidfors, Time lag between peak concentrations of plasma and salivary cortisol following a stressful procedure in dairy cattle, Acta Vet. Scand. 56 (2014) 61, https://doi.org/10.1186/s13028-014-0061-3.
[39] R.M. Estrada-Y-Martin, P.R. Orlander, Salivary cortisol can replace free serum cortisol measurements in patients with septic shock, Chest 140 (2011), https://doi.org/10.1378/chest.11-0448.
[40] S. Ciancia, S.A.A. van den Berg, E.L.T. van den Akker, The reliability of salivary cortisol compared to serum cortisol for diagnosing adrenal insufficiency with the Gold standard ACTH stimulation test in children, Children 10 (2023), https://doi.org/10.3390/children10091569.
[41] R.F. Vining, R.A. McGinley, J.J. Maksvytis, K.Y. Ho, Salivary cortisol: a better measure of adrenal cortical function than serum cortisol, Ann. Clin. Biochem. 20 (1983), https://doi.org/10.1177/000456328302000601.
[42] E. Tu, P. Pearlmutter, M. Tiangco, G. Derose, L. Begdache, A. Koh, Comparison of colorimetric analyses to determine cortisol in human sweat, ACS Omega 5 (2020) 8211–8218, https://doi.org/10.1021/acsomega.0c00498.
[43] M. Jia, W.M. Chew, Y. Feinstein, P. Skeath, E.M. Sternberg, Quantification of cortisol in human eccrine sweat by liquid chromatography – Tandem mass spectrometry, Analyst 141 (2016) 2053–2060, https://doi.org/10.1039/C5AN02387D.
[44] P. Pearlmutter, G. DeRose, C. Samson, N. Linehan, Y. Cen, L. Begdache, D. Won, A. Koh, Sweat and saliva cortisol response to stress and nutrition factors, Sci. Rep. 10 (2020), https://doi.org/10.1038/s41598-020-75871-3.
[45] E. Grouzmann, C. Cavadas, D. Grand, M. Moratel, J.F. Aubert, H.R. Brunner, L. Mazzolai, Blood sampling methodology is crucial for precise measurement of plasma catecholamines concentrations in mice, Pflugers Arch 447 (2003), https://doi.org/10.1007/s00424-003-1140-x.
[46] L.A. Morrow, O.A. Linares, T.J. Hill, J.A. Sanfield, M.A. Supiano, S.G. Rosen, J. B. Halter, Age differences in the plasma clearance mechanisms for epinephrine and norepinephrine in humans, J. Clin. Endocrinol. Metab. 65 (1987), https://doi.org/10.1210/jcem-65-3-508.
[47] T. Nisha, V.G. Vishnu, C.K. Mukhopadhyay, Catecholamine stress hormones regulate cellular iron homeostasis by a posttranscriptional mechanism mediated by iron regulatory protein: implication in energy homeostasis, J. Biol. Chem. 290 (2015), https://doi.org/10.1074/jbc.M114.592519.
[48] D.B. Bastos, B.A.M. Sarafim-Silva, M.L.M.M. Sundefeld, A.A. Ribeiro, J.D. P. Brandão, É.R. Biasoli, G.I. Miyahara, D.E. Casarini, D.G. Bernabé, Circulating catecholamines are associated with biobehavioral factors and anxiety symptoms in head and neck cancer patients, PLoS One 13 (2018), https://doi.org/10.1371/journal.pone.0202515.
[49] D. Sim, M.C. Brothers, J.M. Slocik, A.E. Islam, B. Maruyama, C.C. Grigsby, R. R. Naik, S.S. Kim, Biomarkers and detection platforms for human health and performance monitoring: a review, Adv. Sci. 9 (2022), https://doi.org/10.1002/advs.202104426.
[50] P. Pandit, B. Crewther, C. Cook, C. Punyadeera, A.K. Pandey, Sensing methods for stress biomarker detection in human saliva: a new frontier for wearable electronics and biosensing, Mater. Adv. 5 (2024), https://doi.org/10.1039/d3ma00937h.
[51] N.A. O'Byrne, F. Yuen, W.Z. Butt, P.Y. Liu, Sleep and circadian regulation of cortisol: a short review, Curr. Opin. Endocr. Metab. Res. 18 (2021), https://doi.org/10.1016/j.coemr.2021.03.011.
[52] M.H. Choi, Clinical and technical aspects in free cortisol measurement, Endocrinol. Metab. 37 (2022), https://doi.org/10.3803/EnM.2022.1549.
[53] A. Lewis, A.A. Thant, A. Aslam, P.P.M. Aung, S. Azmi, Diagnosis and management of adrenal insufficiency, Clin. Med. J. Royal College Phys. London 23 (2023), https://doi.org/10.7861/clinmed.2023-0067.
[54] E. Knezevic, K. Nenic, V. Milanovic, N.N. Knezevic, The role of cortisol in chronic stress, neurodegenerative diseases, and psychological disorders, Cells 12 (2023), https://doi.org/10.3390/cells12232726.
[55] E. Dziurkowska, M. Wesolowski, Cortisol as a biomarker of mental disorder severity, J. Clin. Med. 10 (2021), https://doi.org/10.3390/jcm10215204.
[56] A.K. Sahi, N. Varshney, R.K. Sidu, S. Poddar, Pallawi, K. Singh, S.K. Mahto, Clinical implications of cortisol and bioanalytical methods for their determination in various biological matrices, in: Immunodiagnostic Technologies from Laboratory to point-of-care Testing, 2020, https://doi.org/10.1007/978-981-15-5823-8_11.
[57] A. Childs, B. Mayol, J.A. Lasalde-Ramírez, Y. Song, J.R. Sempionatto, W. Gao, Diving into sweat: advances, challenges, and future directions in wearable sweat sensing, ACS Nano 18 (2024) 24605–24616, https://doi.org/10.1021/acsnano.4c10344.
[58] Z. Wu, Z. Qiao, S. Chen, S. Fan, Y. Liu, J. Qi, C.T. Lim, Interstitial fluid-based wearable biosensors for minimally invasive healthcare and biomedical applications, Commun. Mater. 5 (2024), https://doi.org/10.1038/s43246-024-00468-6.
[59] T. Iqbal, A. Elahi, W. Wijns, A. Shahzad, Cortisol detection methods for stress monitoring in connected health, Health Sci. Rev. 6 (2023), https://doi.org/10.1016/j.hsr.2023.100079.
[60] G. Casals, F.A. Hanzu, Cortisol measurements in Cushing's syndrome: immunoassay or mass spectrometry? Ann. Lab. Med. 40 (2020) https://doi.org/10.3343/alm.2020.40.4.285.
[61] M.D. Krasowski, D. Drees, C.S. Morris, J. Maakestad, J.L. Blau, S. Ekins, Cross-reactivity of steroid hormone immunoassays: clinical significance and two-dimensional molecular similarity prediction, BMC Clin. Pathol. 14 (2014), https://doi.org/10.1186/1472-6890-14-33.
[62] F. Rossi, T. Trakoolwilaiwan, V. Gigli, C. Tortolini, A. Lenzi, A.M. Isidori, N.T. K. Thanh, R. Antiochia, Progress in nanoparticle-based electrochemical biosensors for hormone detection, Nanoscale 16 (2024) 18134–18164, https://doi.org/10.1039/D4NR02075H.
[63] I. Maimari, Stress hormones, in: Stress in the Modern World [2 Volumes]: Understanding Science and Society [2 Volumes], 2017, https://doi.org/10.1093/oso/9780190088859.003.0025.
[64] P.F. Plouin, A.P. Gimenez-Roqueplo, Pheochromocytomas and secreting paragangliomas, Orphanet J. Rare Dis. 1 (2006), https://doi.org/10.1186/1750-1172-1-49.
[65] S. Latif, M. Jahangeer, D. Maknoon Razia, M. Ashiq, A. Ghaffar, M. Akram, A. El Allam, A. Bouyahya, L. Garipova, M. Ali Shariati, M. Thiruvengadam, M. Azam Ansari, Dopamine in Parkinson's disease, Clin. Chim. Acta 522 (2021), https://doi.org/10.1016/j.cca.2021.08.009.
[66] L. Speranza, M.C. Miniaci, F. Volpicelli, The role of dopamine in neurological, psychiatric, and metabolic disorders and cancer: a complex web of interactions, Biomedicines 13 (2025) 492, https://doi.org/10.3390/biomedicines13020492.
[67] J. Bicker, A. Fortuna, G. Alves, A. Falcão, Liquid chromatographic methods for the quantification of catecholamines and their metabolites in several biological samples - a review, Anal. Chim. Acta 768 (2013), https://doi.org/10.1016/j.aca.2012.12.030.
[68] R.T. Peaston, C. Weinkove, Measurement of catecholamines and their metabolites, Ann. Clin. Biochem. 41 (2004), https://doi.org/10.1258/000456304322664663.
[69] M.V. Gorbunova, S.V. Gutorova, D.A. Berseneva, V.V. Apyari, V.D. Zaitsev, S. G. Dmitrienko, Y.A. Zolotov, Spectroscopic methods for determination of catecholamines: a mini-review, Appl. Spectrosc. Rev. 54 (2019), https://doi.org/10.1080/05704928.2018.1470980.
[70] E. Grouzmann, F. Lamine, Determination of catecholamines in plasma and urine, Best Pract. Res. Clin. Endocrinol. Metabol. 27 (2013), https://doi.org/10.1016/j.beem.2013.06.004.
[71] J. Jiang, M. Zhang, Z. Xu, Y. Yang, Y. Wang, H. Zhang, K. Yu, G. Kan, Y. Jiang, Recent advances in catecholamines analytical detection methods and their pretreatment technologies, Crit. Rev. Anal. Chem. 55 (2025), https://doi.org/10.1080/10408347.2023.2258982.
[72] A.M. Nightingale, C.L. Leong, R.A. Burnish, S. ul Hassan, Y. Zhang, G.F. Clough, M.G. Boutelle, D. Voegeli, X. Niu, Monitoring biomolecule concentrations in tissue using a wearable droplet microfluidic-based sensor, Nat. Commun. 10 (2019), https://doi.org/10.1038/s41467-019-10401-y.
[73] S. Kumar, S. Kumar, M.A. Ali, P. Anand, V.V. Agrawal, R. John, S. Maji, B. D. Malhotra, Microfluidic-integrated biosensors: prospects for point-of-care diagnostics, Biotechnol. J. 8 (2013), https://doi.org/10.1002/biot.201200386.
[74] M.A. Zahed, D.K. Kim, S.H. Jeong, M. Selim Reza, M. Sharifuzzaman, G. B. Pradhan, H. Song, M. Asaduzzaman, J.Y. Park, Microfluidic-integrated multimodal wearable hybrid patch for wireless and continuous physiological monitoring, ACS Sens. 8 (2023), https://doi.org/10.1021/acssensors.3c00148.
[75] M. Safarkhani, B. Farasati Far, E.C. Lima, S. Jafarzadeh, P. Makvandi, R.S. Varma, Y.S. Huh, M. Ebrahimi Warkiani, N. Rabiee, Integration of MXene and microfluidics: a perspective, ACS Biomater. Sci. Eng. 10 (2024), https://doi.org/10.1021/acsbiomaterials.3c01361.
[76] K. Sankar, U. Kuzmanović, S.E. Schaus, J.E. Galagan, M.W. Grinstaff, Strategy, design, and fabrication of electrochemical biosensors: a tutorial, ACS Sens. 9 (2024) 2254–2274, https://doi.org/10.1021/acssensors.4c00043.
[77] S. Majeed, S.T.R. Naqvi, M.N. ul Haq, M.N. Ashiq, Electroanalytical techniques in biosciences: conductometry, coulometry, voltammetry, and electrochemical

sensors, in: Analytical Techniques in Biosciences: from Basics to Applications, 2022, https://doi.org/10.1016/B978-0-12-822654-4.00004-X.
[78] E.B. Bahadir, M.K. Sezgintürk, Electrochemical biosensors for hormone analyses, Biosens. Bioelectron. 68 (2015), https://doi.org/10.1016/j.bios.2014.12.054.
[79] J. Tu, J. Yeom, J.C. Ulloa, S.A. Solomon, J. Min, W. Heng, G. Kim, J. Dao, R. Vemu, M. Pang, C. Wang, D.-H. Kim, W. Gao, Stressomic: a wearable microfluidic biosensor for dynamic profiling of multiple stress hormones in sweat, Sci. Adv. 11 (2025), https://doi.org/10.1126/sciadv.adx6491.
[80] F. Rossi, T. Trakoolwilaiwan, V. Gigli, C. Tortolini, A. Lenzi, A.M. Isidori, N.T. K. Thanh, R. Antiochia, Progress in nanoparticle-based electrochemical biosensors for hormone detection, Nanoscale 16 (2024) 18134–18164, https://doi.org/10.1039/D4NR02075H.
[81] D. Grieshaber, R. MacKenzie, J. Vörös, E. Reimhult, Electrochemical biosensors - sensor principles and architectures, Sensors 8 (2008), https://doi.org/10.3390/s8031400.
[82] Y. Xu, A.A. Suleiman, Reusable amperometric immunosensor for the determination of cortisol, Anal. Lett. 30 (1997), https://doi.org/10.1080/00032719708001813.
[83] E. Vargas, E. Povedano, S. Krishnan, H. Teymourian, F. Tehrani, S. Campuzano, E. Dassau, J. Wang, Simultaneous cortisol/insulin microchip detection using dual enzyme tagging, Biosens. Bioelectron. 167 (2020), https://doi.org/10.1016/j.bios.2020.112512.
[84] R.M. Torrente-Rodríguez, J. Tu, Y. Yang, J. Min, M. Wang, Y. Song, Y. Yu, C. Xu, C. Ye, W.W. IsHak, W. Gao, Investigation of cortisol dynamics in human sweat using a graphene-based wireless mHealth system, Matter 2 (2020), https://doi.org/10.1016/j.matt.2020.01.021.
[85] W. Tang, L. Yin, J.R. Sempionatto, J.M. Moon, H. Teymourian, J. Wang, Touch-based stressless cortisol sensing, Adv. Mater. 33 (2021), https://doi.org/10.1002/adma.202008465.
[86] D.M. Carneiro, L.C. Almeida, D.R. Santos, J.P. Correia, A.S. Viana, Conductive polycatecholamine (or polycatechol)/polypyrrole copolymers enriched in catechol moieties for amperometric sensing application, Electrochim. Acta 524 (2025) 146004, https://doi.org/10.1016/j.electacta.2025.146004.
[87] O. Josypčuk, J. Barek, B. Josypčuk, Amperometric determination of catecholamines by enzymatic biosensors in flow systems, Electroanalysis 30 (2018), https://doi.org/10.1002/elan.201800078.
[88] I.G. Casella, D. Gioia, M. Rutilo, A multi-walled carbon nanotubes/cellulose acetate composite electrode (MWCNT/CA) as sensing probe for the amperometric determination of some catecholamines, Sensor. Actuator. B Chem. 255 (2018), https://doi.org/10.1016/j.snb.2017.09.188.
[89] H. Guliya, S. Lata, R. Chaudhary, Fabrication of a sensitive neurotransmitter detecting amperometric biosensor employing laccase nanoparticles on a pencil graphite electrode, J. Biotechnol. 404 (2025) 152–161, https://doi.org/10.1016/j.jbiotec.2025.04.021.
[90] M. Hu, I. Fritsch, Application of electrochemical redox cycling: toward differentiation of dopamine and norepinephrine, Anal. Chem. 88 (2016), https://doi.org/10.1021/acs.analchem.6b00427.
[91] N.G. Mphuthi, A.S. Adekunle, E.E. Ebenso, Electrocatalytic oxidation of Epinephrine and Norepinephrine at metal oxide doped phthalocyanine/MWCNT composite sensor, Sci. Rep. 6 (2016), https://doi.org/10.1038/srep26938.
[92] K. Nasa Irkham, I. Kurnia, Y.W. Hartati, Y. Einaga, Low-interference norepinephrine signal on dopamine detection using nafion-coated boron doped diamond electrodes, Biosens. Bioelectron. 220 (2023), https://doi.org/10.1016/j.bios.2022.114892.
[93] J.C. Hidalgo-Acosta, A.M. Jaramillo, M.T. Cortés, Distinguishing catecholamines: dopamine determination in the presence of epinephrine in water/acetonitrile mixtures, Electrochim. Acta 359 (2020), https://doi.org/10.1016/j.electacta.2020.136932.
[94] V. Alizadeh, G. Mahmoudi, M. Hosseinifard, A. Jamali Moghadam, M. Servati Gargari, Modification of flame etched carbon-fiber microelectrode (FE-CFME) by single walled carbon nanotube/pyreneacetic acid (SWCNT/PAA) nanocomposite for sensitive and selective detection of dopamine, J. Electroanal. Chem. 991 (2025) 119199, https://doi.org/10.1016/j.jelechem.2025.119199.
[95] S. Esmaeelzadeh, N. Akbarzadeh–T, S. Tajik, H. Beitollahi, Bimetallic yttrium-copper-metal-organic framework-based voltammetric sensor for detection of dopamine in the presence of uric acid, Inorg. Chem. Commun. 172 (2025) 113712, https://doi.org/10.1016/j.inoche.2024.113712.
[96] J. Liu, N. Xu, H. Men, S. Li, Y. Lu, S.S. Low, X. Li, L. Zhu, C. Cheng, G. Xu, Q. Liu, Salivary cortisol determination on smartphone-based differential pulse voltammetry system, Sensors (Switzerland) 20 (2020), https://doi.org/10.3390/s20051422.
[97] H.S. Magar, R.Y.A. Hassan, A. Mulchandani, Electrochemical impedance spectroscopy (Eis): principles, construction, and biosensing applications, Sensors 21 (2021), https://doi.org/10.3390/s21196578.
[98] A.C. Lazanas, M.I. Prodromidis, Electrochemical impedance spectroscopy—a tutorial, ACS Measurement Sci. Au 3 (2023), https://doi.org/10.1021/acsmeasuresciau.2c00070.
[99] F. Gao, C. Liu, L. Zhang, T. Liu, Z. Wang, Z. Song, H. Cai, Z. Fang, J. Chen, J. Wang, M. Han, J. Wang, K. Lin, R. Wang, M. Li, Q. Mei, X. Ma, S. Liang, G. Gou, N. Xue, Wearable and flexible electrochemical sensors for sweat analysis: a review, Microsyst. Nanoeng. 9 (2023), https://doi.org/10.1038/s41378-022-00443-6.
[100] J.A. Ribeiro, P.A.S. Jorge, Applications of electrochemical impedance spectroscopy in disease diagnosis—A review, Sens. Acutators Rep. 8 (2024) 100205, https://doi.org/10.1016/j.snr.2024.100205.
[101] V. Kesler, B. Murmann, H.T. Soh, Going beyond the debye length: overcoming charge screening limitations in next-generation bioelectronic sensors, ACS Nano 14 (2020), https://doi.org/10.1021/acsnano.0c08622.
[102] C. Gupta, S.K. Pattanayek, B. Mukherjee, S. Kumar, Multilayer label-free non-faradic electrochemical impedance immunosensor for cortisol detection, IEEE Sens. J. 24 (2024), https://doi.org/10.1109/JSEN.2023.3344470.
[103] M. Venugopal, S.K. Arya, G. Chornokur, S. Bhansali, A realtime and continuous assessment of cortisol in ISF using electrochemical impedance spectroscopy, Sens. Actuator. A Phys. (2011), https://doi.org/10.1016/j.sna.2011.04.028.
[104] S.K. Arya, G. Chornokur, M. Venugopal, S. Bhansali, Antibody functionalized interdigitated μ-electrode (IDμE) based impedimetric cortisol biosensor, Analyst 135 (2010), https://doi.org/10.1039/c0an00242a.
[105] R. Ashton, M. Rizwan, C. Gwenin, Development of low-cost impedimetric biosensors for the quantitative detection of cortisol and the human growth hormone, Sens. Acutators Rep. 9 (2025) 100325, https://doi.org/10.1016/j.snr.2025.100325.
[106] P. Pusomjit, P. Teengam, N. Thepsuparungsikul, S. Sanongkiet, O. Chailapakul, Impedimetric determination of cortisol using screen-printed electrode with aptamer-modified magnetic beads, Microchim. Acta 188 (2021), https://doi.org/10.1007/s00604-020-04692-y.
[107] H.D. Ertuğrul Uygun, M.N. Demir, A novel molecularly imprinted polymers on self-assembly monolayer gold electrode impedimetric detection of dopamine, J. Mater. Sci. Mater. Electron. 36 (2025) 441, https://doi.org/10.1007/s10854-025-14375-0.
[108] A. Cazalé, W. Sant, F. Ginot, J.C. Launay, G. Savourey, F. Revol-Cavalier, J. M. Lagarde, D. Heinry, J. Launay, P. Temple-Boyer, Physiological stress monitoring using sodium ion potentiometric microsensors for sweat analysis, Sensor. Actuator. B Chem. 225 (2016), https://doi.org/10.1016/j.snb.2015.10.114.
[109] H. Ben Halima, F.G. Bellagambi, F. Brunon, A. Alcacer, N. Pfeiffer, A. Heuberger, M. Hangouët, N. Zine, J. Bausells, A. Errachid, Immuno field-effect transistor (ImmunoFET) for detection of salivary cortisol using potentiometric and impedance spectroscopy for monitoring heart failure, Talanta 257 (2023), https://doi.org/10.1016/j.talanta.2022.123802.
[110] N.R. Jalal, T. Madrakian, M. Ahmadi, A. Afkhami, S. Khalili, M. Bahrami, M. Roshanaei, Wireless wearable potentiometric sensor for simultaneous determination of pH, sodium and potassium in human sweat, Sci. Rep. 14 (2024) 11526, https://doi.org/10.1038/s41598-024-62236-3.
[111] R. Liang, L. Zhong, Y. Zhang, Y. Tang, M. Lai, T. Han, W. Wang, Y. Bao, Y. Ma, S. Gan, L. Niu, Directly using Ti3C2Tx MXene for a solid-contact potentiometric pH sensor toward wearable sweat pH monitoring, Membranes 13 (2023), https://doi.org/10.3390/membranes13040376.
[112] F. Zhu, Y. Liu, Z. Sun, J. Ni, Y. Jiang, Aptamer-based galvanic potentiometric sensor for real-time monitoring of serotonin signaling under psychosocial stress, Angew. Chem. 137 (2025), https://doi.org/10.1002/ange.202501701.
[113] M.A. Fathy, P. Bühlmann, Next-generation potentiometric sensors: a review of flexible and wearable technologies, Biosensors (Basel) 15 (2025) 51, https://doi.org/10.3390/bios15010051.
[114] H. Richardson, A. Kline, S. Pavlidis, Performance of an aptamer-based neuropeptide Y potentiometric sensor: dependence on spacer molecule selection, Electroanalysis 36 (2024), https://doi.org/10.1002/elan.202300387.
[115] J. Ok, S. Park, Y.H. Jung, T. Kim, Wearable and implantable cortisol-sensing electronics for stress monitoring, Adv. Mater. 36 (2024), https://doi.org/10.1002/adma.202211595.
[116] Y. Li, H. Hu, J. Shu, G. Zhang, Flexible field-effect transistor sensors for next-generation health monitoring: materials to advanced applications, Small 21 (2025), https://doi.org/10.1002/smll.202504059.
[117] S.-J. Lee, W.-J. Cho, Emerging dual-gate FET sensor paradigm for ultra-low concentration cortisol detection in complex bioenvironments, Biosensors (Basel) 15 (2025) 134, https://doi.org/10.3390/bios15030134.
[118] S. Sheibani, L. Capua, S. Kamaei, S.S.A. Akbari, J. Zhang, H. Guerin, A.M. Ionescu, Extended gate field-effect-transistor for sensing cortisol stress hormone, Commun. Mater. 2 (2021), https://doi.org/10.1038/s43246-020-00114-x.
[119] M. Kaisti, Detection principles of biological and chemical FET sensors, Biosens. Bioelectron. 98 (2017) 437–448, https://doi.org/10.1016/j.bios.2017.07.010.
[120] D. Sadighbayan, M. Hasanzadeh, E. Ghafar-Zadeh, Biosensing based on field-effect transistors (FET): recent progress and challenges, TrAC, Trends Anal. Chem. 133 (2020), https://doi.org/10.1016/j.trac.2020.116067.
[121] B. Wang, C. Zhao, Z. Wang, K.A. Yang, X. Cheng, W. Liu, W. Yu, S. Lin, Y. Zhao, K. M. Cheung, H. Lin, H. Hojaiji, P.S. Weiss, M.N. Stojanović, A.J. Tomiyama, A. M. Andrews, S. Emaminejad, Wearable aptamer-field-effect transistor sensing system for noninvasive cortisol monitoring, Sci. Adv. 8 (2022), https://doi.org/10.1126/sciadv.abk0967.
[122] H. Park, S. Baek, A. Sen, B. Jung, J. Shim, Y.C. Park, L.P. Lee, Y.J. Kim, S. Kim, Ultrasensitive and selective field-effect transistor-based biosensor created by rings of MoS2 nanopores, ACS Nano 16 (2022), https://doi.org/10.1021/acsnano.1c08255.
[123] T.T.H. Nguyen, C.M. Nguyen, M.A. Huynh, Q.T. Trinh, P. Tanner, S. Ingebrandt, X.T. Vu, T.-K. Nguyen, N.-T. Nguyen, Ultra-sensitive aptameric field-effect transistor for cortisol sensing, Sens. Acutators Rep. 9 (2025) 100324, https://doi.org/10.1016/j.snr.2025.100324.
[124] H.-J. Jang, T. Lee, J. Song, L. Russell, H. Li, J. Dailey, P.C. Searson, H.E. Katz, Electronic cortisol detection using an antibody-embedded polymer coupled to a field-effect transistor, ACS Appl. Mater. Interfaces 10 (2018) 16233–16237, https://doi.org/10.1021/acsami.7b18855.

[125] K.H. Kim, J.-T. Kim, S.E. Seo, H.G. Lee, O.S. Kwon, Immuno-graphene field-effect transistor-based cortisol bioelectronics using a novel cortisol antibody, Biochip J. 19 (2025) 194–203, https://doi.org/10.1007/s13206-024-00176-w.
[126] R. Zhang, Y. Jia, A disposable printed liquid gate graphene field effect transistor for a salivary cortisol test, ACS Sens. 6 (2021) 3024–3031, https://doi.org/10.1021/acssensors.1c00949.
[127] J. Xu, Y. Fang, J. Chen, Wearable biosensors for non-invasive sweat diagnostics, Biosensors (Basel) 11 (2021), https://doi.org/10.3390/bios11080245.
[128] H.C. Ates, P.Q. Nguyen, L. Gonzalez-Macia, E. Morales-Narváez, F. Güder, J. J. Collins, C. Dincer, End-to-end design of wearable sensors, Nat. Rev. Mater. 7 (2022), https://doi.org/10.1038/s41578-022-00460-x.
[129] C.C. dos Santos, G.N. Lucena, G.C. Pinto, M.J. Júnior, R.F.C. Marques, Advances and current challenges in non-invasive wearable sensors and wearable biosensors—A mini-review, Med. Device. Sens. 4 (2021), https://doi.org/10.1002/mds3.10130.
[130] J. Wang, L. Sun, Y. Zuo, N. Hui, A highly sensitive molecularly-imprinted electrochemical sensor based on a conducting PEDOT/SA hydrogel for the detection of cortisol with exceptional antifouling properties, Sensor. Actuator. B Chem. 426 (2025) 137133, https://doi.org/10.1016/j.snb.2024.137133.
[131] K. Xu, J. Yang, L. Shen, X. Wang, N. Hui, J. Wang, An antifouling electrochemical biosensor based on chondroitin sulfate-functionalized polyaniline and DNA-peptide conjugates for cortisol determination in body fluids, Microchim. Acta 190 (2023), https://doi.org/10.1007/s00604-023-06083-5.
[132] H. Li, Y. Zhang, Z. Deng, B. Lu, L. Ma, R. Wang, X. Wang, Z. Jiao, Y. Wang, K. Zhou, Q. Wei, Constructing a hydrophilic microsensor for high-antifouling neurotransmitter dopamine sensing, ACS Sens. 9 (2024), https://doi.org/10.1021/acssensors.3c02042.
[133] L. Ding, Z. Wang, P. Zhong, H. Jiang, Z. Zhao, Y. Zhang, Z. Ren, Y. Ding, Structural insights into the mechanism of single domain VHH antibody binding to cortisol, FEBS Lett. 593 (2019), https://doi.org/10.1002/1873-3468.13398.
[134] G. Tian, Z. Zhou, M. Li, X. Li, T. Xu, X. Zhang, Oriented antibody-assembled metal-organic frameworks for persistent wearable sweat cortisol detection, Anal. Chem. 95 (2023), https://doi.org/10.1021/acs.analchem.3c02392.
[135] Q. Liu, W. Shi, L. Tian, M. Su, M. Jiang, J. Li, H. Gu, C. Yu, Preparation of nanostructured PDMS film as flexible immunosensor for cortisol analysis in human sweat, Anal. Chim. Acta 1184 (2021), https://doi.org/10.1016/j.aca.2021.339010.
[136] S. Ganpat Chavan, A. Kumar Yagati, A. Koyappayil, A. Go, S. Yeon, M.H. Lee, Recombinant histidine-tagged nano-protein-based highly sensitive electro-sensing device for salivary cortisol, Bioelectrochemistry 144 (2022), https://doi.org/10.1016/j.bioelechem.2021.108046.
[137] L.R. Panicker, A. Joy, P.R. Anusree, S. Kadian, R. Narayan, A. Padmesh, Y. G. Kotagiri, Molecular imprinted polymer based microneedle-strip electrochemical sensor for label-free dopamine monitoring: advancing neurological disorder diagnostics, Chem. Eng. J. 516 (2025) 163870, https://doi.org/10.1016/j.cej.2025.163870.
[138] P. Karthika, S. Shanmuganathan, V. Subramanian, C. Delerue-Matos, Selective detection of salivary cortisol using screen-printed electrode coated with molecularly imprinted polymer, Talanta 272 (2024), https://doi.org/10.1016/j.talanta.2024.125823.
[139] L. Yue Jing, Y. Fan, B. Zhi Chen, D. Li, Y. Ting He, G. Liang Zhang, L. Liang, J. Du, Y. Wang, X. Dong Guo, An aptamer-integrated conductive microneedle biosensor for real-time transdermal cortisol monitoring, Chem. Eng. J. 502 (2024) 157488, https://doi.org/10.1016/j.cej.2024.157488.
[140] A. Gilani, A. Saeidi, S. Sheibani, J. Longo, S. Kamaei, A. Ameti, N. Niederländer, N. Pitteloud, A.M. Ionescu, Aptamer-decorated graphene channel array with liquid-gating for sensing cortisol stress hormone, in: 2024 IEEE Biosensors Conference (Biosensors), IEEE, 2024, pp. 1–4, https://doi.org/10.1109/BioSensors61405.2024.10712663.
[141] E. Farjami, R. Campos, J.S. Nielsen, K.V. Gothelf, J. Kjems, E.E. Ferapontova, RNA aptamer-based electrochemical biosensor for selective and label-free analysis of dopamine, Anal. Chem. 85 (2013), https://doi.org/10.1021/ac302134s.
[142] S. Ben Aissa, A.E.G. Cass, Systematic optimisation of an integrated electrochemical aptamer-based sensor for cortisol detection, Sensor. Actuator. B Chem. 444 (2025) 138284, https://doi.org/10.1016/j.snb.2025.138284.
[143] G. Karuppaiah, J. Velayutham, S. Hansda, N. Narayana, S. Bhansali, P. Manickam, Towards the development of reagent-free and reusable electrochemical aptamer-based cortisol sensor, Bioelectrochemistry 145 (2022), https://doi.org/10.1016/j.bioelechem.2022.108098.
[144] N.K.M. Churcher, C. Greyling, S. Upasham, K.-C. Lin, P. Rice, M. Pali, J. Spiro, S. Prasad, AptaStrensor (aptamer-based sensor for stress monitoring): the interrelationship between NPY and cortisol towards chronic disease monitoring, Biosens. Bioelectron. X 10 (2022) 100145, https://doi.org/10.1016/j.biosx.2022.100145.
[145] Z. Fredj, P. Wang, F. Ullah, M. Sawan, A nanoplatform-based aptasensor to electrochemically detect epinephrine produced by living cells, Microchim. Acta 190 (2023), https://doi.org/10.1007/s00604-023-05902-z.
[146] C.G. Ann Maria, A. Varghese, M. Nidhin, Recent advances in nanomaterials based molecularly imprinted electrochemical sensors, Crit. Rev. Anal. Chem. 53 (2023), https://doi.org/10.1080/10408347.2021.1937925.
[147] X. Dong, C. Zhang, X. Du, Z. Zhang, Recent advances of nanomaterials-based molecularly imprinted electrochemical sensors, Nanomaterials 12 (2022), https://doi.org/10.3390/nano12111913.
[148] A.A. Lahcen, A. Amine, Recent advances in electrochemical sensors based on molecularly imprinted polymers and nanomaterials, Electroanalysis 31 (2019), https://doi.org/10.1002/elan.201800623.
[149] K. Murugesan, M.D. Kumar, G. Kaniraja, P. Ananthappan, V.S. Vasantha, C. Karunakaran, Theoretical screening and electrochemical sensor for determination of norepinephrine using a molecularly imprinted poly (3-amiophenylboronic acid), Anal. Biochem. 696 (2025) 115676, https://doi.org/10.1016/j.ab.2024.115676.
[150] S. Patle, D. Rotake, Recent advances, technological challenges and requirements to predict the future treads in wearable sweat sensors: a critical review, Microchem. J. 200 (2024) 110457, https://doi.org/10.1016/j.microc.2024.110457.
[151] Q. ul A. Zahra, S. Ullah, F. Shahzad, B. Qiu, X. Fang, A. Ammar, Z. Luo, S. Abbas Zaidi, MXene-based aptasensors: advances, challenges, and prospects, Prog. Mater. Sci. 129 (2022), https://doi.org/10.1016/j.pmatsci.2022.100967.
[152] M. Sekar, M. Pandiaraj, S. Bhansali, N. Ponpandian, C. Viswanathan, Carbon fiber based electrochemical sensor for sweat cortisol measurement, Sci. Rep. 9 (2019), https://doi.org/10.1038/s41598-018-37243-w.
[153] J. Chen, F. Xia, X. Ding, D. Zhang, Universal covalent grafting strategy of an aptamer on a carbon fiber microelectrode for selective determination of dopamine in vivo, Anal. Chem. 96 (2024) 10322–10331, https://doi.org/10.1021/acs.analchem.4c01167.
[154] J.M. González-Costas, S. Caruncho-Pérez, E. González-Romero, Enhanced catalytic surfaces for catechol sensing: combining grafted aryldiazonium derivative with cross-linking dopamine or coupling tyrosinase immobilizations, Appl. Sci. 15 (2025) 4250, https://doi.org/10.3390/app15084250.
[155] M.V. Sullivan, M. Klein, J.M. Mohan, A.Q. Shen, Highly sensitive, real-time cortisol sensing with molecularly imprinted polymer nanoparticles on graphene electrodes in a microfluidic biosensor, Talanta 299 (2026) 129141, https://doi.org/10.1016/j.talanta.2025.129141.
[156] A. Sharma, R. Owyeung, A. Thomas, S. Siraj, B.K. Keshari, P. Sahatiya, S. Sonkusale, Facile and scalable fabrication of molecularly imprinted polymer (MIP) sensors on poriferous laser-engraved graphene electrodes for stress monitoring, Analyst (2025), https://doi.org/10.1039/D4AN01389A.
[157] H.G. Santos, D.S. Oliveira, F.T.C. Moreira, Innovative molecular imprinting sensor for quick, non-invasive cortisol monitoring in fish welfare, Biosensors (Basel) 15 (2025) 204, https://doi.org/10.3390/bios15040204.
[158] S. Park, J. Kim, S. Kim, G. Kim, N.S. Lee, Y.H. Yoon, H. Yang, Combined signal amplification using a propagating Cascade reaction and a redox cycling reaction for sensitive thyroid-stimulating hormone detection, Anal. Chem. 91 (2019), https://doi.org/10.1021/acs.analchem.9b01740.
[159] K. Ghoshal, Recent advances in biosensing technologies for detecting hormones, in: Advanced Sensor Technology: Biomedical, Environmental, and Construction Applications, 2022, https://doi.org/10.1016/B978-0-323-90222-9.00012-1.
[160] C.P. Kurup, N.F. Mohd-Naim, M.U. Ahmed, Recent trends in nanomaterial-based signal amplification in electrochemical aptasensors, Crit. Rev. Biotechnol. 42 (2022), https://doi.org/10.1080/07388551.2021.1960792.
[161] M. Aydemir, A.İ. Kömür, E.S. Gündüz, C. Karaman, O. Karaman, Breaking the silence: AI-enhanced multi-omics biosensors for liquid biopsy-based early diagnosis of pancreatic cancer, Microchem. J. 215 (2025) 114118, https://doi.org/10.1016/j.microc.2025.114118.
[162] H. Ehtesabi, S.O. Kalji, Carbon nanomaterials for sweat-based sensors: a review, Microchim. Acta 191 (2024), https://doi.org/10.1007/s00604-023-06162-7.
[163] F. Karimi, H. Karimi-Maleh, J. Rouhi, N. Zare, C. Karaman, M. Baghayeri, L. Fu, S. Rostamnia, E.N. Dragoi, A. Ayati, P. Krivoshapkin, Revolutionizing cancer monitoring with carbon-based electrochemical biosensors, Environ. Res. 239 (2023), https://doi.org/10.1016/j.envres.2023.117368.
[164] J.A. Buledi, H. Shaikh, A.R. Solangi, A. Mallah, Z.U.H. Shah, M.M. Khan, A. L. Sanati, H. Karimi-Maleh, C. Karaman, M.B. Camarada, D.E. Niculina, Synthesis of NiO-Doped ZnO nanoparticle-decorated reduced graphene oxide nanohybrid for highly sensitive and selective electrochemical sensing of bisphenol A in aqueous samples, Ind. Eng. Chem. Res. 62 (2023), https://doi.org/10.1021/acs.iecr.2c04091.
[165] M. Mehmandoust, N. Erk, O. Karaman, F. Karimi, M. Bijad, C. Karaman, Three-dimensional porous reduced graphene oxide decorated with carbon quantum dots and platinum nanoparticles for highly selective determination of azo dye compound tartrazine, Food Chem. Toxicol. 158 (2021), https://doi.org/10.1016/j.fct.2021.112698.
[166] M.A. Abdelfattah, S.S. Jamali, N. Kashaninejad, N.-T. Nguyen, Wearable biosensors for health monitoring: advances in graphene-based technologies, Nanoscale Horiz. 10 (2025) 1542–1574, https://doi.org/10.1039/D5NH00141B.
[167] V. Yogalakshmi, S.R. Aishwarya, M. Rajkumar, S.R. Srither, R. Balaji, Fabrication of activated graphene based electrodes for ultrasensitive simultaneous electrochemical detection of uric acid and dopamine, Talanta Open (2025) 100477, https://doi.org/10.1016/j.talo.2025.100477.
[168] D. Ghosh, R. Tabassum, P.P. Sarkar, M.A. Rahman, A.H. Jalal, N. Islam, A. Ashraf, Graphene nanocomposite ink coated laser transformed flexible electrodes for selective dopamine detection and immunosensing, ACS Appl. Bio Mater. 7 (2024) 3143–3153, https://doi.org/10.1021/acsabm.4c00166.
[169] Z. Hassan, S.A. Alsalhi, N. Drissi, S.A.M. Abdelmohsen, J. Sattar, P. Tehreem, H. Noor, H. Alqurashi, A.M.A. Henaish, H.M.T. Farid, Graphene nanoplatelets-polyaniline composite for the detection of cortisol, J. Phys. Chem. Solid. 191 (2024) 112031, https://doi.org/10.1016/j.jpcs.2024.112031.
[170] Y.M. Ahmed, M.R. El-Zanaty, A. Galal, N.F. Atta, Synergistically enhanced electrochemical detection of lidocaine and epinephrine simultaneously in human serum samples at poly(L-serine)/graphene oxide/β-cyclodextrin composite sensor, Microchem. J. 208 (2025) 112406, https://doi.org/10.1016/j.microc.2024.112406.

[171] H. Singh, J. Wu, K.A.L. Lagemann, M. Nath, Highly efficient dopamine sensing with a carbon nanotube-encapsulated metal chalcogenide nanostructure, ACS Appl. Nano Mater. 7 (2024), https://doi.org/10.1021/acsanm.3c05422.
[172] S. Kumar, R. Sharma, D. Singh, A. Awasthi, V. Kumar, K. Singh, Tungsten sulphide decorated carbon nanotube based electroanalytical sensing of neurotransmitter dopamine, Electrochim. Acta 475 (2024), https://doi.org/10.1016/j.electacta.2023.143584.
[173] C. Zeng, Y. Li, M. Zhu, Z. Du, H. Liang, Q. Chen, H. Ye, R. Li, W. Liu, Simultaneous detection of norepinephrine and 5-hydroxytryptophan using poly-alizarin/multi-walled carbon nanotubes-graphene modified carbon fiber microelectrode array sensor, Talanta 270 (2024), https://doi.org/10.1016/j.talanta.2023.125565.
[174] R. Khan, S. Andreescu, Mxenes-based bioanalytical sensors: design, characterization, and applications, Sensors (Switzerland) 20 (2020), https://doi.org/10.3390/s20185434.
[175] U. Amara, I. Hussain, M. Ahmad, K. Mahmood, K. Zhang, 2D MXene-Based biosensing: a review, Small 19 (2023), https://doi.org/10.1002/smll.202205249.
[176] S.G. Chavan, P.R. Rathod, A. Koyappayil, A. Go, M.H. Lee, "Two-step" signal amplification for ultrasensitive detection of dopamine in human serum sample using Ti3C2Tx-MXene, Sensor. Actuator. B Chem. 404 (2024), https://doi.org/10.1016/j.snb.2024.135308.
[177] M. Ankitha, F. Shamsheera, P.A. Rasheed, MXene-Integrated single-stranded carbon yarn-based wearable sensor patch for On-Site monitoring of dopamine, ACS Appl. Electron. Mater. 6 (2024), https://doi.org/10.1021/ACSAELM.3C01668.
[178] H. Liu, W. Qin, X.X. Li, L. Feng, C. Gu, J. Chen, Z. Tian, J. Chen, M. Yang, H. Qiao, X. Guo, Y. Zhang, B. Zhao, S. Yin, Molecularly imprinted electrochemical sensors based on Ti3C2Tx-MXene and graphene composite modifications for ultrasensitive cortisol detection, Anal. Chem. 95 (2023), https://doi.org/10.1021/acs.analchem.3c01715.
[179] S. Boobphahom, T. Siripongpreda, D.D. Zhang, J. Qin, P. Rattanawaleedirojn, N. Rodthongkum, TiO2/MXene-PVA/GO hydrogel-based electrochemical sensor for neurological disorder screening via urinary norepinephrine detection, Microchim. Acta 188 (2021), https://doi.org/10.1007/s00604-021-04945-4.
[180] S.S. Shankar, R.M. Shereema, R.B. Rakhi, Electrochemical determination of adrenaline using MXene/Graphite composite paste electrodes, ACS Appl. Mater. Interfaces 10 (2018), https://doi.org/10.1021/acsami.8b11741.
[181] W. He, X. Ye, T. Cui, Flexible electrochemical sensor with graphene and gold nanoparticles to detect dopamine and uric acid, IEEE Sens. J. 21 (2021), https://doi.org/10.1109/JSEN.2021.3122326.
[182] Z. Aryan, H. Khajehsharifi, S. Shahrokhian, AuNPs-Ultrathin/Graphitic-C3N4 nanosheets as a sensitive platform for electrochemical detection and determination of dopamine, Microchem. J. 198 (2024), https://doi.org/10.1016/j.microc.2024.110087.
[183] B. Sun, Y. Gou, Y. Ma, X. Zheng, R. Bai, A.A. Ahmed Abdelmoaty, F. Hu, Investigate electrochemical immunosensor of cortisol based on gold nanoparticles/magnetic functionalized reduced graphene oxide, Biosens. Bioelectron. 88 (2017), https://doi.org/10.1016/j.bios.2016.07.047.
[184] Y.N. Chang, C.H. Shen, C.W. Huang, M.D. Tsai, C.W. Kung, Defective metal-organic framework nanocrystals as signal amplifiers for electrochemical dopamine sensing, ACS Appl. Nano Mater. 6 (2023), https://doi.org/10.1021/acsanm.2c05402.
[185] C. Soosaimanickam, K. Murugavel, S. Alwarappan, Bimetallic MOFs-Based electrodes for the simultaneous electrochemical detection of epinephrine and norepinephrine, J. Electrochem. Soc. 171 (2024) 097501, https://doi.org/10.1149/1945-7111/ad6c80.
[186] F. Zhou, L. Gai, H. Liu, D. Qin, T. Abudouwufu, Y. Liu, Enhanced electrochemical detection of dopamine and uric acid using Au@Ni-MOF and employing 2D structure DFT simulation, Sci. Rep. 15 (2025) 8686, https://doi.org/10.1038/s41598-025-89797-1.
[187] S. Chowdhury, A.S. Nugraha, R. O'May, X. Wang, P. Cheng, R. Xin, S.M. Osman, M.S. Hossain, Y. Yamauchi, M.K. Masud, Y.V. Kaneti, Bimetallic metal-organic framework-derived porous one-dimensional carbon materials for electrochemical sensing of dopamine, Chem. Eng. J. 492 (2024) 152124, https://doi.org/10.1016/j.cej.2024.152124.
[188] Z.-A. Zhao, Y.-L. Li, J. Yang, Y.-H. Luo, X.-M. Jia, D.-E. Zhang, Porous CePO4@carbon composite derived from cerium-based metal–organic framework for the simultaneous detection of dopamine, uric acid, and acetaminophen, Microchem. J. 202 (2024) 110834, https://doi.org/10.1016/j.microc.2024.110834.
[189] N. Li, Z. Zhang, T. Tian, L. Sun, L. Xu, J. Wang, N. Hui, A double-conducting polymer nanowire-based electrochemical aptasensor for highly sensitive and low fouling detection of cortisol in saliva, Microchim. Acta 191 (2024) 600, https://doi.org/10.1007/s00604-024-06695-5.
[190] X. Qiao, Z. Xu, Z. Wei, Y. Hou, F. Gao, X. Yu, X. Luo, A wearable electrochemical biosensor based on antifouling and conducting polyaniline hydrogel for cortisol detection in sweat, Chin. Chem. Lett. (2025) 110884, https://doi.org/10.1016/j.cclet.2025.110884.
[191] O. Parlak, S.T. Keene, A. Marais, V.F. Curto, A. Salleo, Molecularly selective nanoporous membrane-based wearable organic electrochemical device for noninvasive cortisol sensing, Sci. Adv. 4 (2018), https://doi.org/10.1126/sciadv.aar2904.
[192] L. Tian, M. Jiang, M. Su, X. Cao, Q. Jiang, Q. Liu, C. Yu, Sweat cortisol determination utilizing MXene and multi-walled carbon nanotube nanocomposite functionalized immunosensor, Microchem. J. 185 (2023), https://doi.org/10.1016/j.microc.2022.108172.
[193] S. Madhu, S. Ramasamy, P. Manickam, P. Nagamony, V. Chinnuswamy, TiO2 anchored carbon fibers as non-invasive electrochemical sensor platform for the cortisol detection, Mater. Lett. 308 (2022), https://doi.org/10.1016/j.matlet.2021.131238.
[194] A. Sharma, A. Wulff, A. Thomas, S. Sonkusale, Ultrasensitive electrochemical sensor for detection of salivary cortisol in stress conditions, Microchim. Acta 191 (2024), https://doi.org/10.1007/s00604-023-06169-0.
[195] M. Zhang, C. Li, C. Huang, A facile electrochemical cortisol sensing based on zinc oxide nanostructures for monitoring stress and recovery in high-performance athletes, Alex. Eng. J. 88 (2024), https://doi.org/10.1016/j.aej.2023.12.068.
[196] B. Yang, H. Li, C. Nong, X. Li, S. Feng, A novel electrochemical immunosensor based on SnS2/NiCo metal-organic frameworks loaded with gold nanoparticles for cortisol detection, Anal. Biochem. 669 (2023), https://doi.org/10.1016/j.ab.2023.115117.
[197] Y. Du, M. Guo, Y. Chen, X. Mo, J. Cao, F. Hu, Ultrasensitive cortisol electrochemical immunosensor amplifying by Au single-atom nanozymes and HRP enzymes, Anal. Chim. Acta 1303 (2024), https://doi.org/10.1016/j.aca.2024.342462.
[198] A.R. Naik, Y. Zhou, A.A. Dey, D.L.G. Arellano, U. Okoroanyanwu, E.B. Secor, M. C. Hersam, J. Morse, J.P. Rothstein, K.R. Carter, J.J. Watkins, Printed microfluidic sweat sensing platform for cortisol and glucose detection, Lab Chip 22 (2022), https://doi.org/10.1039/d1lc00633a.
[199] H.B. Lee, M. Meeseepong, T.Q. Trung, B.Y. Kim, N.E. Lee, A wearable lab-on-a-patch platform with stretchable nanostructured biosensor for non-invasive immunodetection of biomarker in sweat, Biosens. Bioelectron. 156 (2020), https://doi.org/10.1016/j.bios.2020.112133.
[200] H. Perkins, M. Higgins, M. Marcato, P. Galvin, S.R. Teixeira, Immunosensor for assessing the welfare of trainee guide dogs, Biosensors (Basel) 11 (2021), https://doi.org/10.3390/BIOS11090327.
[201] J.S. Nah, S.C. Barman, M.A. Zahed, M. Sharifuzzaman, H. Yoon, C. Park, S. Yoon, S. Zhang, J.Y. Park, A wearable microfluidics-integrated impedimetric immunosensor based on Ti3C2Tx MXene incorporated laser-burned graphene for noninvasive sweat cortisol detection, Sensor. Actuator. B Chem. 329 (2021), https://doi.org/10.1016/j.snb.2020.129206.
[202] M. Ku, J. Kim, J.E. Won, W. Kang, Y.G. Park, J. Park, J.H. Lee, J. Cheon, H.H. Lee, J.U. Park, Smart, soft contact lens for wireless immunosensing of cortisol, Sci. Adv. 6 (2020), https://doi.org/10.1126/sciadv.abb2891.
[203] T. Su, Z. Mi, Y. Xia, D. Jin, Q. Xu, X. Hu, Y. Shu, A wearable sweat electrochemical aptasensor based on the Ni–Co MOF nanosheet-decorated CNTs/PU film for monitoring of stress biomarker, Talanta 260 (2023), https://doi.org/10.1016/j.talanta.2023.124620.
[204] Z. Rahmati, M. Roushani, H. Hosseini, MOF-derived Ni-P bundle-like nanorods as high-performance substrate for design of electrochemical aptasensor toward cortisol detection, IEEE Sens. J. 23 (2023), https://doi.org/10.1109/JSEN.2022.3229403.
[205] S. Immanuel, T.K. Aparna, R. Sivasubramanian, A facile preparation of Au—SiO2 nanocomposite for simultaneous electrochemical detection of dopamine and uric acid, Surf. Interfaces 14 (2019), https://doi.org/10.1016/j.surfin.2018.11.010.
[206] Y. Zhang, R. Yuan, Y. Chai, W. Li, X. Zhong, H. Zhong, Simultaneous voltammetric determination for DA, AA and NO2- based on graphene/poly-cyclodextrin/MWCNTs nanocomposite platform, Biosens. Bioelectron. 26 (2011), https://doi.org/10.1016/j.bios.2011.03.017.
[207] H. Maseed, V.M. Reddy Yenugu, S.S.B. Devarakonda, S. Petnikota, M. Gajulapalli, V.V.S.S. Srikanth, Peroxidase-like Fe3O4 Nanoparticle/Few-layered graphene composite for electrochemical detection of dopamine, ascorbic acid, and uric acid, ACS Appl. Nano Mater. 6 (2023), https://doi.org/10.1021/acsanm.3c04018.
[208] Y. Wei, Y. Liu, Z. Xu, S. Wang, B. Chen, D. Zhang, Y. Fang, Simultaneous detection of ascorbic acid, dopamine, and uric acid using a novel electrochemical sensor based on palladium nanoparticles/reduced graphene oxide nanocomposite, Int. J. Anal. Chem. 2020 (2020), https://doi.org/10.1155/2020/8812443.
[209] S. Cogal, Electrochemical determination of dopamine using a Poly(3,4-Ethylenedioxythiophene)-Reduced graphene oxide-modified glassy carbon electrode, Anal. Lett. 51 (2018), https://doi.org/10.1080/00032719.2017.1387791.
[210] A. Dhaffouli, P.A. Salazar-Carballo, S. Carinelli, M. Holzinger, B.V.M. Rodrigues, H. Barhoumi, Electrochemical detection of dopamine with a non-enzymatic sensor based on Au@SiO2-APTES composite, Chemosensors 13 (2025) 87, https://doi.org/10.3390/chemosensors13030087.
[211] A. Murali, Y.P. Lan, P.K. Sarswat, M.L. Free, Synthesis of CeO2/reduced graphene oxide nanocomposite for electrochemical determination of ascorbic acid and dopamine and for photocatalytic applications, Mater. Today Chem. 12 (2019) 222–232, https://doi.org/10.1016/j.mtchem.2019.02.001.
[212] S. Mahalakshmi, V. Sridevi, In situ electrodeposited gold nanoparticles on polyaniline-modified electrode surface for the detection of dopamine in presence of ascorbic acid and uric acid, Electrocatalysis 12 (2021), https://doi.org/10.1007/s12678-021-00665-8.
[213] P. Chen, H. Wang, H. Li, B. Niu, H. Guo, Z. Chen, A high-activity Fe-based MOFs fabricated through ultrasound strategy for electrochemical sensor of heavy metal ions and dopamine, J. Electroanal. Chem. 957 (2024), https://doi.org/10.1016/j.jelechem.2024.118129.
[214] B. Niu, M. Liu, X. Li, H. Guo, Z. Chen, Vein-like Ni-BTC@Ni3S4 with sulfur vacancy and Ni3+ fabricated in situ etching vulcanization strategy for an electrochemical sensor of dopamine, ACS Appl. Mater. Interfaces 15 (2023), https://doi.org/10.1021/acsami.2c22586.
[215] L. Mgenge, C. Saha, P. Kumari, S.K. Ghosh, H. Singh, K. Mallick, Electrochemical sensing of dopamine using nanostructured silver chromate: development of an

IoT-integrated sensor, Anal. Biochem. 698 (2025) 115726, https://doi.org/10.1016/j.ab.2024.115726.
[216] C. Saha, S.K. Ghosh, P. Kumari, V.K. Perla, H. Singh, K. Mallick, Carbon nitride-supported zinc oxide nanocomposite for the electrochemical detection of dopamine and the development of disposable sensors, Electroanalysis 37 (2025), https://doi.org/10.1002/elan.202400236.
[217] S. Yadav, M.A. Sadique, S. Singhai, R. Khan, Rapid electrochemical detection of epinephrine in human serum based on polydopamine-wrapped cerium oxide nanocomposite, Hybrid Adv. 4 (2023), https://doi.org/10.1016/j.hybadv.2023.100108.
[218] M. Jiang, D. Zeng, X. Zheng, H. Yuan, Detection of epinephrine using a K 2 Fe 4 O 7 modified glassy carbon electrode, RSC Adv. 14 (2024) 15408–15412, https://doi.org/10.1039/D4RA00242C.
[219] Z. Wang, J. Chen, H. Ma, Y. Deng, Y. Li, L. Geng, Y. Huang, Y. Fan, A novel copper ion enhanced electrochemical DNA biosensor for the determination of epinephrine, Talanta 276 (2024) 126274, https://doi.org/10.1016/j.talanta.2024.126274.
[220] N.G. Tsierkezos, U. Ritter, Y. Nugraha Thaha, A. Knauer, D. Fernandes, A. Kelarakis, E.K. McCarthy, Boron-doped multi-walled carbon nanotubes as sensing material for analysis of dopamine and epinephrine in presence of uric acid, Chem. Phys. Lett. 710 (2018), https://doi.org/10.1016/j.cplett.2018.09.007.
[221] Z. Li, Y. Guo, H. Yue, X. Gao, S. Huang, X. Zhang, Y. Yu, H. Zhang, H. Zhang, Electrochemical determination of epinephrine based on Ti3C2Tx MXene-reduced graphene oxide/ITO electrode, J. Electroanal. Chem. 895 (2021), https://doi.org/10.1016/j.jelechem.2021.115425.
[222] H. Zhang, H. Yue, S. Huang, X. Gao, S. Yang, Y. Xie, J. Li, Design and synthesis of 3D hierarchical NiMoS4 nanowire arrays in situ grown on graphene foam: electrochemical determination of epinephrine, J. Mater. Sci. Mater. Electron. 33 (2022), https://doi.org/10.1007/s10854-021-07528-4.
[223] Y. Sun, H. Li, C. Li, L. Wang, X. Xuan, M. Li, Preparation of a Cu/cuO-Vertical graphene microelectrode for the simultaneous determination of epinephrine and 2-aminoadenosine, Mater. Today Chem. 33 (2023), https://doi.org/10.1016/j.mtchem.2023.101685.
[224] S.E. Elugoke, O.E. Fayemi, A.S. Adekunle, P.S. Ganesh, S.Y. Kim, E.E. Ebenso, Sensitive and selective neurotransmitter epinephrine detection at a carbon quantum dots/copper oxide nanocomposite, J. Electroanal. Chem. 929 (2023), https://doi.org/10.1016/j.jelechem.2022.117120.
[225] L.V. da Silva, C.B. Lopes, W.C. da Silva, Y.G. de Paiva, F. de A. dos S. Silva, P. R. Lima, L.T. Kubota, M.O.F. Goulart, Electropolymerization of ferulic acid on multi-walled carbon nanotubes modified glassy carbon electrode as a versatile platform for NADH, dopamine and epinephrine separate detection, Microchem. J. 133 (2017), https://doi.org/10.1016/j.microc.2017.04.014.
[226] S.S. Shankar, R.M. Shereema, V. Ramachandran, T.V. Sruthi, V.B.S. Kumar, R. B. Rakhi, Carbon quantum dot-modified carbon paste electrode-based sensor for selective and sensitive determination of adrenaline, ACS Omega 4 (2019), https://doi.org/10.1021/acsomega.9b00230.
[227] C. Soosaimanickam, K. Murugavel, S. Alwarappan, Bimetallic MOFs-Based electrodes for the simultaneous electrochemical detection of epinephrine and norepinephrine, J. Electrochem. Soc. 171 (2024) 097501, https://doi.org/10.1149/1945-7111/ad6c80.
[228] H. Yao, N. Lal, X. Wu, M. Liu, H. Jiang, Q. Yu, R. Zhang, Q. Zhou, F. Cui, Carbon black nanoparticles-functionalized NiFe-Layered double hydroxide nanosheets as nanoenzymes for the electrochemical sensing of norepinephrine, ACS Appl. Nano Mater. 8 (2025) 11508–11520, https://doi.org/10.1021/acsanm.5c01681.
[229] W. Sun, G. Sun, J. Liu, X. Huang, Y. Wang, Integration of MOF/COF core-shell composite material with wrinkled supramolecular hydrogel: a portable electrochemical sensing platform for noradrenaline bitartrate detection, Compos. B Eng. 291 (2025) 112029, https://doi.org/10.1016/j.compositesb.2024.112029.
[230] M. Liu, Y. Zhang, J. Jiang, D. Wang, Y. Li, J. Zhao, L. Chen, Hydroxyl-and-carboxyl ligand concatenating multi-lanthanide substituted tellurotungstates and electrochemical detection of noradrenaline, J. Rare Earths 40 (2022), https://doi.org/10.1016/j.jre.2021.09.015.
[231] L. Huang, R. Su, F. Xi, Sensitive detection of noradrenaline in human whole blood based on Au nanoparticles embedded vertically-ordered silica nanochannels modified pre-activated glassy carbon electrodes, Front. Chem. 11 (2023), https://doi.org/10.3389/fchem.2023.1126213.
[232] M. Su, X. Cao, H. Gao, C. Zhu, W. Peng, Q. Jiang, C. Yu, Honeycomb-like nickel oxide-reduced graphene oxide based sensor for the electrochemical tracking of norepinephrine in neuronal cells, Anal. Chim. Acta 1262 (2023), https://doi.org/10.1016/j.aca.2023.341247.
[233] M.Y. Emran, M.A. Shenashen, A. Elmarakbi, M.M. Selim, S.A. El-Safty, Nitrogen-doped carbon hollow trunk-like structure as a portable electrochemical sensor for noradrenaline detection in neuronal cells, Anal. Chim. Acta 1192 (2022), https://doi.org/10.1016/j.aca.2021.339380.
[234] T. Rajarathinam, D. Thirumalai, M. Kwon, S. Lee, S. Jayaraman, H. jong Paik, J. Lee, S.C. Chang, Screen-printed carbon electrode modified with de-bundled single-walled carbon nanotubes for voltammetric determination of norepinephrine in ex vivo rat tissue, Bioelectrochemistry 146 (2022), https://doi.org/10.1016/j.bioelechem.2022.108155.
[235] E.A. Khudaish, A. Al-Badri, A modified hummers soft oxidative method for functionalization of CNTs: preparation, characterization and potential application for selective determination of norepinephrine, Synth. Met. 277 (2021), https://doi.org/10.1016/j.synthmet.2021.116803.
[236] E.A. Khudaish, A. Al-Khodouri, A surface network based on reduced graphene oxide/gold nanoparticles for selective determination of norepinephrine in real samples, J. Electrochem. Soc. 167 (2020), https://doi.org/10.1149/1945-7111/abc5db.
[237] P.M. Jahani, M. Jafari, V.K. Gupta, S. Agarwal, Graphene quantum dots/ionic liquid-modified carbon paste electrode-based sensor for simultaneous voltammetric determination of norepinephrine and acetylcholine, Int. J. Electrochem. Sci. 15 (2020), https://doi.org/10.20964/2020.01.45.
[238] M. Mazloum-Ardakani, Z. Alizadeh, F. Sabaghian, B.B.F. Mirjalili, N. Salehi, Novel Fe2O3@CeO2 coreshell-based electrochemical nanosensor for the voltammetric determination of norepinephrine, Electroanalysis 32 (2020), https://doi.org/10.1002/elan.201900454.
[239] S.R. Priyanka, K.P. Latha, MnCr2O4 nanocomposite modified carbon paste electrode based electrochemical sensor for determination of norepinephrine: a cyclic voltammetry study, Chem. Data Collect. 35 (2021), https://doi.org/10.1016/j.cdc.2021.100769.
[240] M.G. Gopika, B. Sajeevan, A.S. Murali, S. lekshmi, M. Govindasamy, B. Saraswathyamma, A surfactant-electropolymer modified dual sensor for the monitoring of norepinephrine at nanomolar levels in biological samples and pharmaceutical formulations, Mater. Chem. Phys. 318 (2024) 129266, https://doi.org/10.1016/j.matchemphys.2024.129266.
[241] M.Y.Y. Emran, M. Mekawy, N. Akhtar, M.A.A. Shenashen, I.M.M. EL-Sewify, A. Faheem, S.A.A. El-Safty, Broccoli-shaped biosensor hierarchy for electrochemical screening of noradrenaline in living cells, Biosens. Bioelectron. 100 (2018), https://doi.org/10.1016/j.bios.2017.08.050.
[242] F. de M. Morawski, B.B. Xavier, A.H. Virgili, K. dos S. Caetano, E.W. de Menezes, E.V. Benvenutti, T.M.H. Costa, L.T. Arenas, A novel electrochemical platform based on mesoporous silica/titania and gold nanoparticles for simultaneous determination of norepinephrine and dopamine, Mater. Sci. Eng. C 120 (2021) 111646, https://doi.org/10.1016/j.msec.2020.111646.
[243] M.Y. Emran, M.A. Shenashen, S.A. El-Safty, M.M. Selim, T. Minowa, A. Elmarakbi, Three-dimensional circular surface curvature of a spherule-based electrode for selective signaling and dynamic mobility of norepinephrine in living cells, ACS Appl. Bio Mater. 3 (2020), https://doi.org/10.1021/acsabm.0c00882.
[244] J. Xu, H.J.A. Smaling, J.W. Schoones, W.P. Achterberg, J.T. van der Steen, Noninvasive monitoring technologies to identify discomfort and distressing symptoms in persons with limited communication at the end of life: a scoping review, BMC Palliat. Care 23 (2024), https://doi.org/10.1186/s12904-024-01371-0.
[245] Z. Ying, L. Qiao, B. Liu, L. Gao, P. Zhang, Development of a microfluidic wearable electrochemical sensor for the non-invasive monitoring of oxidative stress biomarkers in human sweat, Biosens. Bioelectron. 261 (2024) 116502, https://doi.org/10.1016/j.bios.2024.116502.
[246] Q. Ning, S. Feng, Y. Cheng, T. Li, D. Cui, K. Wang, Point-of-care biochemical assays using electrochemical technologies: approaches, applications, and opportunities, Microchim. Acta 189 (2022), https://doi.org/10.1007/s00604-022-05425-z.
[247] N. Davis, J. Heikenfeld, C. Milla, A. Javey, The challenges and promise of sweat sensing, Nat. Biotechnol. 42 (2024), https://doi.org/10.1038/s41587-023-02059-1.
[248] B. Charlton, J.M. Lanyon, C. Madden, W. Phillips, T. Keeley, Salivary cortisol as a measure of acute stress and diurnal adrenal activity in bottlenose dolphins, Mar. Mamm. Sci. 41 (2025), https://doi.org/10.1111/mms.70044.
[249] M.A. King, S.D. Brown, K.A. Barnes, P.J.D. De Chavez, L.B. Baker, Regional and time course differences in sweat cortisol, glucose, and select cytokine concentrations during exercise, Eur. J. Appl. Physiol. 123 (2023) 1727–1738, https://doi.org/10.1007/s00421-023-05187-3.
[250] M.A. Lee, N. Bakh, G. Bisker, E.N. Brown, M.S. Strano, A pharmacokinetic model of a tissue implantable cortisol sensor, Adv. Healthcare Mater. 5 (2016) 3004–3015, https://doi.org/10.1002/adhm.201600650.
[251] P.P. Samant, M.M. Niedzwiecki, N. Raviele, V. Tran, J. Mena-Lapaix, D.I. Walker, E.I. Felner, D.P. Jones, G.W. Miller, M.R. Prausnitz, Sampling interstitial fluid from human skin using a microneedle patch, Sci. Transl. Med. 12 (2020), https://doi.org/10.1126/SCITRANSLMED.AAW0285.
[252] C. Tortolini, A.E.G. Cass, R. Pofi, A. Lenzi, R. Antiochia, Microneedle-based nanoporous gold electrochemical sensor for real-time catecholamine detection, Microchim. Acta 189 (2022), https://doi.org/10.1007/s00604-022-05260-2.
[253] L.B. Baker, A.S. Wolfe, Physiological mechanisms determining eccrine sweat composition, Eur. J. Appl. Physiol. 120 (2020), https://doi.org/10.1007/s00421-020-04323-7.
[254] J.H.D.M. Westerink, R.J.E. Rajae-Joordens, M. Ouwerkerk, M. van Dooren, S. Jelfs, A.J.M. Denissen, E. Penning de Vries, R. van Ee, Deriving a cortisol-related stress indicator from wearable skin conductance measurements: quantitative model & experimental validation, Front. Comput. Sci. 2 (2020), https://doi.org/10.3389/fcomp.2020.00039.
[255] A. Ganguly, K.C. Lin, S. Muthukumar, S. Prasad, Autonomous, real-time monitoring electrochemical aptasensor for circadian tracking of cortisol hormone in sub-microliter volumes of passively eluted human sweat, ACS Sens. 6 (2021), https://doi.org/10.1021/acssensors.0c01754.
[256] C.R. Ferrari, S.M. Moraes, M.A.R. Buzalaf, Saliva-based hormone diagnostics: advances, applications, and future perspectives, Expert Rev. Mol. Diagn (2025) 1–15, https://doi.org/10.1080/14737159.2025.2505527.
[257] M. Yamaguchi, S. Yoshikawa, Y. Tahara, D. Niwa, Y. Imai, V. Shetty, Point-of-use measurement of salivary cortisol levels, in: Proceedings of IEEE Sensors, 2009, https://doi.org/10.1109/ICSENS.2009.5398143.
[258] M. Zea, H. Ben Halima, R. Villa, I.A. Nemeir, N. Zine, A. Errachid, G. Gabriel, Salivary cortisol detection with a fully inkjet-printed paper-based electrochemical sensor, Micromachines 15 (2024) 1252, https://doi.org/10.3390/mi15101252.

[259] M.S. Khan, K. Dighe, Z. Wang, A.S. Schwartz-Duval, S.K. Misra, D. Pan, Ultra-sensitive paper-based biosensor for cortisol sensing in human saliva with electrical impedance analyzer, in: 2017 IEEE Healthcare Innovations and Point of Care Technologies, HI-POCT, 2017, https://doi.org/10.1109/HIC.2017.8227615, 2017.
[260] T. Saha, S. Mukherjee, M.D. Dickey, O.D. Velev, Harvesting and manipulating sweat and interstitial fluid in microfluidic devices, Lab Chip 24 (2024), https://doi.org/10.1039/d3lc00874f.
[261] K.M. Saifullah, Z. Faraji Rad, Sampling dermal interstitial fluid using microneedles: a review of recent developments in sampling methods and microneedle-based biosensors, Adv. Mater. Interfac. 10 (2023), https://doi.org/10.1002/admi.202201763.
[262] T. Abbasiasl, F. Mirlou, H. Mirzajani, M.J. Bathaei, E. Istif, N. Shomalizadeh, R. E. Cebecioğlu, E.E. Özkahraman, U.C. Yener, L. Beker, A wearable touch-activated device integrated with hollow microneedles for continuous sampling and sensing of dermal interstitial fluid, Adv. Mater. 36 (2024), https://doi.org/10.1002/adma.202304704.
[263] N. Kashaninejad, A. Munaz, H. Moghadas, S. Yadav, M. Umer, N.T. Nguyen, Microneedle arrays for sampling and sensing skin interstitial fluid, Chemosensors 9 (2021), https://doi.org/10.3390/chemosensors9040083.
[264] K. Takeuchi, N. Takama, K. Sharma, O. Paul, P. Ruther, T. Suga, B. Kim, Microfluidic chip connected to porous microneedle array for continuous ISF sampling, Drug Deliv. Transl. Res. 12 (2022), https://doi.org/10.1007/s13346-021-01050-0.
[265] N.K. Singh, S. Chung, A.Y. Chang, J. Wang, D.A. Hall, A non-invasive wearable stress patch for real-time cortisol monitoring using a pseudoknot-assisted aptamer, Biosens. Bioelectron. 227 (2023), https://doi.org/10.1016/j.bios.2023.115097.
[266] M. Hu, K. Zhu, J. Wei, Z. Xu, K. Yang, L. Wu, S. Zong, Z. Wang, Wearable microfluidic SERS patch based on silk fibroin for the non-invasive monitoring of sweat cortisol and pH, Sensor. Actuator. B Chem. 427 (2025) 137152, https://doi.org/10.1016/j.snb.2024.137152.
[267] S.M. Mugo, S.V. Robertson, W. Lu, A molecularly imprinted electrochemical microneedle sensor for multiplexed metabolites detection in human sweat, Talanta 259 (2023), https://doi.org/10.1016/j.talanta.2023.124531.
[268] S. Majumder, A.K. Roy, T. Mondal, M.J. Deen, Flexible sensors for IoT-Based health monitoring, IEEE J. Flexible Electr. 4 (2025) 63–88, https://doi.org/10.1109/JFLEX.2025.3538808.
[269] V. Abhinav, P. Basu, S.S. Verma, J. Verma, A. Das, S. Kumari, P.R. Yadav, V. Kumar, Advancements in wearable and implantable BioMEMS devices: transforming healthcare through technology, Micromachines 16 (2025) 522, https://doi.org/10.3390/mi16050522.
[270] S.C. Kishore, K. Samikannu, R. Atchudan, S. Perumal, T.N.J. Immanuel Edison, M. Alagan, A.K. Sundramoorthy, Y.R. Lee, Smartphone-operated wireless chemical sensors: a review, Chemosensors 10 (2022), https://doi.org/10.3390/chemosensors10020055.
[271] A.C. Sun, D.A. Hall, Point-of-Care smartphone-based electrochemical biosensing, Electroanalysis 31 (2019), https://doi.org/10.1002/elan.201800474.
[272] F. Akhtar, M. Belal Bin Heyat, A. Sultana, S. Parveen, H. Muhammad Zeeshan, S. F. Merlin, B. Shen, D. Pomary, J. Ping Li, M. Sawan, Medical intelligence for anxiety research: insights from genetics, hormones, implant science, and smart devices with future strategies, WIREs Data Min. Knowledge Discov. 14 (2024), https://doi.org/10.1002/widm.1552.
[273] M.O. Sekeroglu, M. Pekgor, A. Algin, T. Toros, E. Serin, M. Uzun, G. Cerit, T. Onat, S.A. Ermis, Transdisciplinary innovations in athlete health: 3D-printable wearable sensors for health monitoring and sports psychology, Sensors 25 (2025) 1453, https://doi.org/10.3390/s25051453.
[274] R. Alhejaili, A. Alomainy, The use of wearable technology in providing assistive solutions for mental well-being, Sensors 23 (2023), https://doi.org/10.3390/s23177378.
[275] C.R. Ferrari, S.M. Moraes, M.A.R. Buzalaf, Saliva-based hormone diagnostics: advances, applications, and future perspectives, Expert Rev. Mol. Diagn (2025) 1–15, https://doi.org/10.1080/14737159.2025.2505527.
[276] A. Chmayssem, N. Verplanck, C.E. Tanase, G. Costa, K. Monsalve-Grijalba, S. Amigues, M. Alias, M. Gougis, V. Mourier, S. Vignoud, A.M. Ghaemmaghami, P. Mailley, Development of a multiparametric (bio)sensing platform for continuous monitoring of stress metabolites, Talanta 229 (2021), https://doi.org/10.1016/j.talanta.2021.122275.
[277] T. Beduk, D. Beduk, M.R. Hasan, E. Guler Celik, J. Kosel, J. Narang, K.N. Salama, S. Timur, Smartphone-based multiplexed biosensing tools for health monitoring, Biosensors (Basel) 12 (2022), https://doi.org/10.3390/bios12080583.
[278] M. Díaz-González, X. Muñoz-Berbel, C. Jiménez-Jorquera, A. Baldi, C. Fernández-Sánchez, Diagnostics using multiplexed electrochemical readout devices, Electroanalysis 26 (2014), https://doi.org/10.1002/elan.201400015.
[279] T. Ozer, C.S. Henry, Review—recent advances in sensor arrays for the simultaneous electrochemical detection of multiple analytes, J. Electrochem. Soc. 168 (2021), https://doi.org/10.1149/1945-7111/abfc9f.
[280] C.İ. Kuru, F. Ulucan-Karnak, S. Akgöl, Lab-on-a-chip sensors: recent trends and future applications, in: Fundamentals of Sensor Technology: Principles and Novel Designs, 2023, https://doi.org/10.1016/B978-0-323-88431-0.00012-0.
[281] A. Alachkar, S. Alhassan, M. Senel, Lab-In-A-Syringe: a novel electrochemical biosensor for On-Site and real-time monitoring of dopamine in freely behaving mice, ACS Sens. 7 (2022), https://doi.org/10.1021/acssensors.1c02525.
[282] Z. Liu, M. Jin, J. Cao, R. Niu, P. Li, G. Zhou, Y. Yu, A. van den Berg, L. Shui, Electrochemical sensor integrated microfluidic device for sensitive and simultaneous quantification of dopamine and 5-hydroxytryptamine, Sensor. Actuator. B Chem. 273 (2018), https://doi.org/10.1016/j.snb.2018.06.123.
[283] A. Roychoudhury, K.A. Francis, J. Patel, S.K. Jha, S. Basu, A decoupler-free simple paper microchip capillary electrophoresis device for simultaneous detection of dopamine, epinephrine and serotonin, RSC Adv. 10 (2020), https://doi.org/10.1039/d0ra03526b.
[284] Z. Liao, J. Wang, P. Zhang, Y. Zhang, Y. Miao, S. Gao, Y. Deng, L. Geng, Recent advances in microfluidic chip integrated electronic biosensors for multiplexed detection, Biosens. Bioelectron. 121 (2018), https://doi.org/10.1016/j.bios.2018.08.061.
[285] I.M. Handrea-Dragan, I. Botiz, A.S. Tatar, S. Boca, Patterning at the micro/nano-scale: polymeric scaffolds for medical diagnostic and cell-surface interaction applications, Colloids Surf. B Biointerfaces 218 (2022), https://doi.org/10.1016/j.colsurfb.2022.112730.