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Research Article

Design Perspectives of Bio Nanosensors Using Nanomaterials for Endocrine Hormones

Nibha M Desai [1], Prof. (Dr.) Vedvyas Jayprakashnarayanji Dwivedi [2], Dr. Chandni Upadhyaya [3], Dr. Mayur Mehta [4]

[1] *PhD Research Scholar, Department of Electronics & Communication Engineering*
Indus University, Ahmedabad, India.
Assistant Professor, Electronics Engineering (VLSI Design & Technology), Shah & Anchor Kutchhi Engineering College, Mumbai, India.
[2] *Professor, Department of Electronics & Communication Engineering, Indus University,*
Ahmedabad, India.
[3] *Associate Professor, Shree P. M. Patel Institute of Integrated M. Sc. In Biotechnology*
Sardar Patel University, Anand, India.
[4] *Industry Mentor, Department of Electronics & Communication Engineering*
Indus University, Ahmedabad, India.

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ABSTRACT

Stress is any change in the environment that the body requires to react and adjust in response, due to which different mental and physical illness symptoms are observed. Endocrine hormones are generated from the main part of the brain. Physical changes in the body like breathing rate, heart rate, sugar level, perspiration, and feeling of fear are observed when endocrine hormones enter the bloodstream. Cortisol is a stress hormone produced and released by adrenal glands on top of kidneys. It is a trigger factor to control diseases of Life style, Obesity, Hypertension. Cortisol level increased during stressful events. Balanced level of cortisol is essential. Extremely high and low cortisol cause diseases like Cushing's syndrome, Addison's disease, adrenal cancers. Bio-Nanosensors are used to detect the level of these hormones. These sensors detect biological elements and used different types of nanomaterials at nanoscale. Nanotechnology has enabled to design sensors with smaller size, better stability, and more sensitivity. Physical miniaturization of chip for Bio-Nanosensors are essential figure of merit. When cortisol level is high or low, sensor will biped the signal so that immediate treatment can be provided. Cortisol measurement should be dynamic such that rapid level of hormone can be detected. Non-Invasive based bio-nanosensors with different sensing materials can be used. Fabrication of sensor is depending on selecting different nanomaterials and defining different process. A wearable device consist of sensor and electronics can detect and monitor level of cortisol hormone for prevention of diseases in body which saves human life.

Keywords: : Endocrine hormones, Cortisol, Sweat, Biosensor, Nanosensor, Electrochemical, Nanotube, Nanowire

INTRODUCTION

The human brain is the command center for the nervous system. Endocrine is a chemical control system and aids in the regulation of internal body states [1]. Measurement of hormones help to diagnosis and control diseases associated with endocrine [2]. Biosensors provide many advantages in the terms of stability, sensitivity, selectivity, response time, calibration techniques and dynamic range. Biosensor made up of silicon enhances the performance of biosensors that results into improving the quality of human life for biomedical applications [3]. Similarly, CMOS technology-based sensor offers low power consumption, small size, and minimum cost [4] and health-related data are available in numerical or image formats in Biomedical research [5].

Nanosensors are used to detect different quantities at nanoscale level. Nanosensors track the electrical changes in the sensor materials based on mechanism used, the structure of sensor, the type of energy source, and applications like Environmental monitoring, Defense, Drug discovery, biomedical research, Medicine, Food analysis, quality, and safety [6]. Nanotechnology enables design of sensors with less power dissipation, and more sensitivity. Different types of nanosensors are available to detect endocrine hormones and its chemical substances. This research study identifies research gaps and scope in the field of Nanotechnology to detect cortisol hormones. The research design flow and technical details of sensors are discussed for designing the sensor to detect cortisol hormone. The challenges like experimental setup for continuous measurement of cortisol in real time is being focused. Challenges and future scope regarding cortisol detection, identifying bio-nanosensor, its method to detect cortisol are discussed. Modelling and characterization of nanotechnology-based sensor can be done based on CAD Tool. Different electrical, mechanical, and biological specifications required for detection of cortisol using nanosensors are discussed.

ENDOCRINE SYSTEM

Block diagram

A chemical control mechanism is the endocrine system and regulates internal body states. Chemicals called hormones are secreted by the eight major endocrine glands into the bloodstream in which they act as control agents to regulate various organic functions. Regulating metabolism, mood, behavior and reproductive functions are key functions of this system [7]. Different glands of endocrine system are shown in Figure 1.

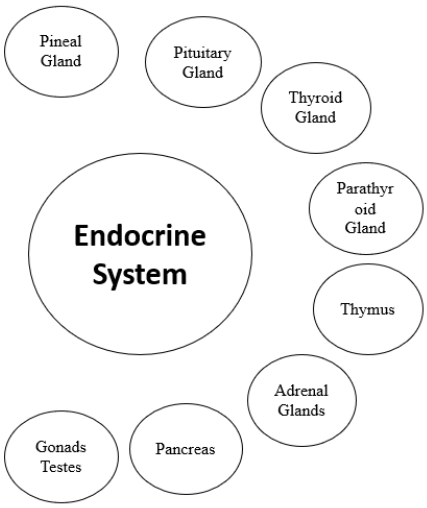

Figure 1: Basic understanding and Block diagram of Endocrine System

The Functions of various Endocrine glands are listed in below Table 1 [8].

S. No	Endocrine glands	Functions
1	Pineal Gland	To Control the cycle of reproduction and set the Circadian rhythm.
2	Pituitary Gland	To growth and fluid balance, control and regulate other endocrine glands
3	Thyroid Gland	To Control the metabolic rate and calcium levels
4	Parathyroid Gland	Similar like thyroid
5	Thymus	To Regulate the lymphocytes
6	Adrenal Glands	To balance water level, tissue metabolism, respiratory and cardiovascular activity
7	Kidneys	To Regulate RBC and Calcium
8	Pancreas	To Regulate sugar levels in the blood
9	Gonads Testes	To regulate reproductive functions in the human body

The difference and similarities between cortisol and Adrenaline is discussed in Table 2 [9] and Table 3 [10] respectively.

Table 2 Electrobio-difference cortisol and adrenaline [9]

Parameter	**Cortisol**	**Adrenaline**
Definition	A Hormone generated by the adrenal cortex [9]	A hormone produced by the adrenal medulla [9]
Nature	Corticosteroid Hormone	A peptide hormone
Normal Range	6 to 8 a.m.: 10 to 20 mcg/dL. 4 p.m.: 3 to 10 mcg/dL [9]	0 to 140 pg/mL [9]
Function	• Increased blood sugar level through gluconeogenesis • Stop the immune system to work • Aid fat in the metabolism of fat, protein, and carbohydrates • Decrease bone formation [9]	• Increase in blood flow to muscles • Increase the output of the heart, pupil dilation response • Increase Blood sugar level in the fight-to-fight response [9]
Medication	Treatment for a variety of skin conditions, insect bites, poison oak, eczema, dermatitis, allergies, rash, and itching [9]	Used to treat asthma attacks, cardiac arrest, and infection and is included in anesthesia to last longer [9]
Disease-Associated	Cushing's syndrome, a Pituitary tumour causes Cushing's disease, Pseudo Cushing's disease. Adrenal insufficiency, Nelson's syndrome, Pituitary tumor, Sheehan's syndrome [9]	Anxiety, depression, fibromyalgia, hypoglycemia, migraine, restless legs syndrome, and sleep disorders [9]

Table 3 Electrobio-similarity table [10]

Parameter	**Similarity (Both Hormones- Cortisol and Adrenaline)**
Produced by	Adrenal glands
Measurement Condition of Response	In stress
Level of Blood sugar	Increase
Regulation	ACTH (Adrenocorticotropic) hormone

The secreted cortisol gets within the circulatory system and can be detected in several bio-fluids in the human body. When compared with the other non-invasive bio-fluids, sweat is the one that has been most widely studied because it is full of medical information that can provide value for diagnosis. It is comparatively easier to stimulate, collect, and analyze. The monitoring through sweat will have lots of disadvantages above blood-based assays [11]. The sensing of sweat can address the pressing demand appropriately. Cortisol concentration in the sweat level ranges from 8–141 ng/mL and may be applied to non-invasively monitor diurnal rhythms. Rapid sampling enables simplified designs for long-term continuous monitoring systems with high sensitivity and selectivity. Sweat testing maps cortisol levels and helps model predicting anxiety attacks. There is a significant advantage in combining sweat sensing with electrochemical transduction [12]. Cortisol immunoassays are based on anti-cortisol antibody recognition and constitute the most common method to measure cortisol in clinical practice [13].

BIOSENSORS

Biosensors are analytical devices that consist of two elements one is a biological sensing system and the other a transducer. Here, the biological element may be a nucleic acid, an enzyme, or an antibody. The bio element communicates with the analyte to be tested and the bio-response can be converted into an electric signal using the transducer. The block diagram of the biosensor consists of three segments, sensor, transducer, and associated electrons [14]. The sensor is the biological part in the first segment. The detector part is in the second segment that modulates the resulting signal of the contact with the analyte and displays the results which is easy to access. Then an amplifier known as a signal conditioning circuit is comprised of a display unit and the processor as shown in Figure 2. Different types of biosensors like DNA, Immunosensors, Amperometric, Baroxymeter, Bioluminescent, Colorimetric, Conductometric, Fluorescence, FET-based, Impedance, Piezoelectric, Potentiometric are studied [15]. Various biosensors working on an electrochemical, optical, or surface plasmon resonance (SPR) basis have been recently developed to detect free cortisol in saliva. However, these optical and SPR techniques require expensive laser instrumentation, while electrochemical sensors need signal amplification at lower concentrations of cortisol due to poor signal-to-noise ratio (S/N) properties. In the current study, a thermal biosensor based on Bi nanowire was developed for detecting free cortisol in saliva. Bismuth nanowires were synthesized by the on-film formation of nanowires (OFF-ON) method [16].

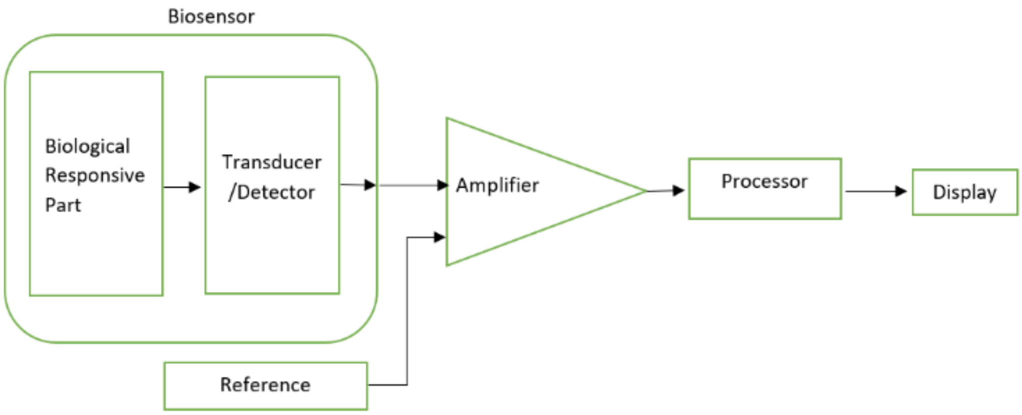

Figure 2: Research Model of Biosensor

NANOMATERIALS

The study of Nanomaterials having unique properties at nanoscale dimensions. Most of the nanomaterial's atoms are on or near their surface, which makes their essential physicochemical properties different due to size constraints. Based on electronic and mechanical properties and their advantages, they are used in enhanced biological signaling, and transduction mechanisms such as Carbon Nanotubes, Nanoparticles, Quantum dots, Nanowires, and Nanorods [17]. Nanomaterials helped biological sensing in accuracy and robustness. The most tunable electrochemical and physico-mechanical response attributes of the materials are related to the shape and the size-dependent physical and chemical attributes. Close energy levels as per quantum mechanical feasibility distinguish nanomaterials from bulk counterparts for accurate tracking of identified coordinates dependent upon interaction with these nanomaterials. The most widely used nanomaterials for biosensing are Au nanoparticles, graphene-based assemblies, carbon nanotubes, and magnetic nanoparticles [18].

Nanotubes, nanorods, and nanowires can be classified under one-dimensional nanoparticles which are characterized by their dimensions falling in the nanometric range or two-dimensional material under which at least one spatial dimension is at nanoscale range, such as graphitic carbon nitride thin films or nanosheets and phosphorenes. One, or in this case the term used as three dimensions, means that the 0D, 1D, and 2D components are in close, contact-forming surfaces, no matter if these are nanosized grains in dense polycrystals or 3D porous nanostructures [19]. Nanostructured materials display distinct surface effects when compared with micro or bulk materials due to a combination of three reasons: -

(a) Because dispersed nanomaterials have extremely large surface area and number of particles per unit mass (b) Gain in atoms at the surface fraction (c) Reduction in immediate neighboring atoms at the surface. These conceptual differences cause variations in the chemical and physical properties of nanomaterials with respect to the scale-up counterparts [20].

NANOSENSORS

Nanosensors provide biological or chemical information using nanoparticles. Nanosensor are tiny in the size of a few nanometers, about 10 to 100 nanometers. They can sense the presence of nanomaterials or molecules, and detect different quantities like temperature, humidity, moisture. Components of a nanosensor include analyte, sensor, transducer, and detector. Typically, a nanosensor works by monitoring electrical changes in sensor materials. The analyte from the solution diffuses into the surface of a sensor and reacts in a specific and efficient manner [6].

As depicted in Figure 3, Optical nanosensors measures change in intensity of light, biological nanosensors detect antibody and antigen interactions, DNA interaction and enzyme interactions, Electrochemical nanosensors measures change in electric quantities, and physical nanosensor detect physical parameters like pressure, force, mass, displacement.

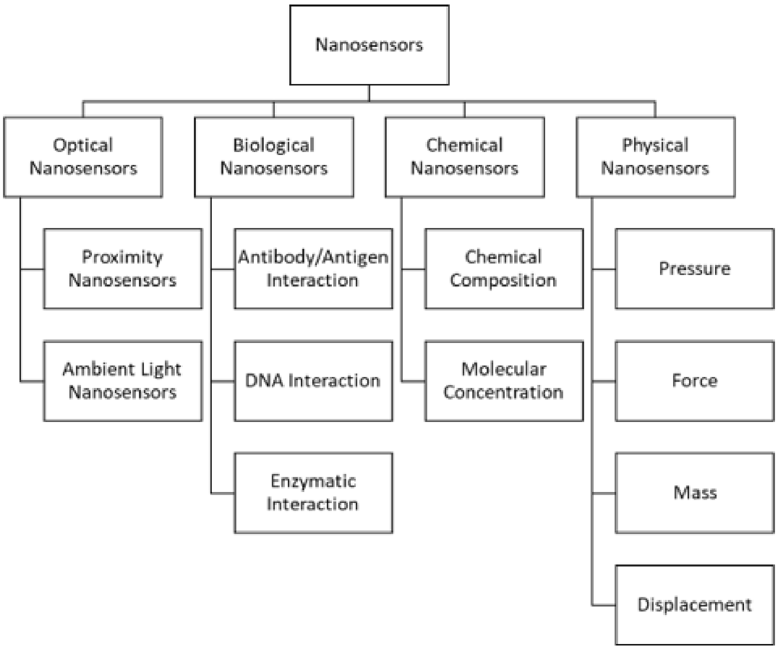

Figure 3: Classification of Nanosensors

The following are some examples of the different types of nanosensors:

Nanoparticle Based Sensors

1. *Acoustic Wave Biosensors*
   These are designed to increase the sensitivity and overall accuracy of the biodetection limits [17].
2. *Magnetic Biosensors*
   Biosensors based on magnetic nanoparticles are known as magnetic biosensors. Most of these sensors are having ferrite-based materials which are very useful for biomedical applications [17].

3. *Electrochemical Biosensors*
   These sensors use enhanced electrical methods to monitor metabolic reactions and rely on metallic nanoparticles. Metallic nanoparticles greatly aid in the immobilization of one of the reactants and make the chemical reactions between the biomolecules simple and effective to carry out [17].

Nanotube Based Sensors

Carbon nanotube is one of the most widely used in the field of material sciences and optoelectronics. It has remarkable properties such as electronic conductivity, elastic physical geometrical properties, and developing physicomechanical characteristics. Single-walled and multi-walled carbon nanotubes are used in the design of biosensors for higher performance due to these properties [17].

Nanowire Based Sensors

Like carbon nanotubes, nanowires are arranged in a cylindrical shape with diameters within the nano range and lengths ranging from a few micrometers to centimeters. One-dimensional nanostructures with excellent electron transport characteristics are called nanowires. Nanowires have greatly enhanced biological material detection and performance. The effectiveness of biosensors utilizing boron-doped silicon nanowires for the identification of chemical and biological substances [17].

NANOMATERIALS AND NANOSENSORS FOR HORMNE

Nanomaterials such as graphene oxide (GO) have a self-assembly property. GO improves the sensitivity of biomolecule detection with high surface area to volume ratio and a small size similar to that of biomolecules [21]. There have been developments in nanomaterial-based strategies for making electrochemical sensors in recent years, namely gold and carbon-based nanoparticles that provide rapid and real-time analysis of cortisol concentrations in a variety of biological samples such as urine, plasma, or saliva. On account of its quick response time, electrochemical detection is a highly reliable method to quantify cortisol in biological matrices [22].

Nanomaterials can be classified into three groups: conductors, semiconductors, and insulators, depending on their electrical property or conductivity. Conductive nanomaterials, like carbon nanotubes and graphene, have exceptionally high electrical conductivity, enabling their versatile applications in current collecting, electrodes, and catalysts. Semi-conductive nanomaterials, like metal oxides and sulfides, show moderate conductivity and serve as active material in energy storage and conversion processes, while insulating nanomaterials, like metal-organic frameworks (MOFs) and covalent-organic frameworks (COFs), provide low electrical conductivity, high surface area, and porous volume and thus, can be suitable as supportive materials in electrochemical devices. Also, the electrical characteristics are modified by the composition of nanomaterials. Stimulating nanomaterials, such as MOFs, COFs, and MXenes, gained traction because of their tunable electrical properties and high surface area, which earmarks them as promising candidates for electrochemical device applications the synthesis of novel nanomaterials, such as metal-organic frameworks (MOFs), covalent organic frameworks (COFs), and MXenes, with applications in electrochemical devices [23].

Nanosensors for Endocrine Glands

Different types of Bio-Nanosensors are discussed for endocrine hormones. Molecular probes, chemosensors, and nanosensors are chemical sensing systems to detect biofluids (urine, blood, and saliva). Estrogenic cellular changes are detected by an ultra-sensitive nanosensor in Estrogen Receptor [24]. Cortisol is an adrenal steroid hormone. It is produced in the adrenal cortex of the kidneys and plays a role in regulating energy metabolism, stress responses, and the immune system [25]. Glucometer detects glucose using electrochemical means [26]. Immunosensor amplifies and detects an antigen–antibody reaction [15]. MIP (Molecularly imprinted polymer) sensor analytes are identified selectively by a standard biosensor, which then binds them into the designated binding layers [27].

Cortisol in sweat can serve as a biomarker in monitoring physiological stress. Gold nanoparticles were conjugated with cortisol-selective aptamers to attain a highly sensitive and specific sensor for cortisol [28].

Efforts have been made to develop the use of polymers and organic materials in a FET sensor because of their intrinsic flexibility and easy fabrication processes. In organic field effect transistors (OFET) sensors, the greatest technical challenge, however, is the instability of materials under solution-based testing, which leads to inferior low-sensitivity and selective detection when comparing the organic FET sensors with inorganic ones [29]. The EG-FET extended gate field effect transistor was designed to detect cortisol in biological buffers within the length of the Debye screening. This device exhibits very attractive experimental characteristics for real-time measurement of the level of cortisol in sweat as it varies over a circadian rhythm in humans. An hysteresis-free EG-FET shows good voltage sensitivity and current sensitivity across four decades of cortisol concentration [30].

The electrochemical sensors the job of the detector is done by modified electrode in the presence of the analyte. With carbon-based materials, high-sensitive sensors can be developed due to their exceptional conductivity, such as with the use of graphene, carbon nanotubes, and graphene quantum dots. Another great candidate for electrochemical sensors is metallic nanomaterials very well exemplified by iron oxide nanoparticles that may be used in the detection of analytes like glucose and heavy metals manganese oxide-detection of hydrogen peroxide titanium dioxide nanoparticles-detection of p-nonylphenol copper oxide-nonenzymatic pesticides detection and zinc oxide which detects glucose [31]. A voyage through history saw the synthesis and reporting of different kinds of nanomaterials from the noble gold nanoparticles of commerce, changing through new forms yet being either carbon- or transition-metal dichalcogenide (TMD)-based. These nanomaterials were employed either alone or in hybridization with other nanomaterials for highly sensitive biosensor development [32]. Electrodes' stability, sensitivity, and specificity are some of the many issues faced by sweat-based detection methods. Surface states of zinc oxide (ZnO) may be utilized for immobilizing various linker molecules for ultraspecific detection of biomolecules. [33]. Cortisol sensing has been performed highly sensitively, selectively, and efficiently using a flexible sensor array based on laser-induced graphene's exceptional electrochemical sensing capabilities [34]. Currently, such advances in nanomaterials, in particular fullerenes, carbon nanotubes, graphene, carbon quantum dots, nanodiamonds, carbon nanohorns, nanoporous materials, core-shell nanoparticles, silicene, antimonene, MXenes, 2D MOF nanosheets, boron nitride nanosheets, layered double hydroxides, and metallic nanomaterials have been made [35].

First, the advanced physical and chemical properties of one-dimensional conducting polymers (CPs) at the nanometer scale have helped in achieving outstanding sensing performances for biosensor applications. Of these, polypyrrole (PPy) is a biocompatible CP used extensively in polymer nanotube (NT) FET biosensors [36]. The EFC technology now allows us to measure trace levels of cortisol within the system by signal amplification using enzyme catalysis in conjunction with functionalized gold nanowires. Improved electron transfer across the functionalized electrodes is then expected due to the highly aligned structure of functionalized Au nanowires. Enhanced electron transfer between the electrodes could enable a stronger interaction with the substrate. Therefore, increased surface-to-volume ratio and high conductivity of the Au nanowires could further improve the sensitivity and detection limit of the biosensor [37]. From saliva and sweating samples of a representative subject, changes in cortisol levels were monitored during the day using cortisol aptamer-based field-effect transistor (FET) sensors. Elevated sensor responses were recorded in the morning when cortisol levels were high and were down in the afternoon when lower levels were recorded, showing response profiles to saliva and sweat samples [38].

Based on different parameters such as Types, Materials, methods of detection, properties, advantages and limitations, comparison of bionanosensors for cortisol detection are shown in Table 4.

Table 4 Comparison of bionanosensors for cortisol detection

Sr No	Type of Bio-nanosensor	Materials/Molecules/Hormone	Method	Properties	Substance	Advantages	Limitations	References
1	Electrochemical Sensor	Carbon/Gold NPs/ neurological drugs	Invasive	Electrical, optical, and catalytic	Cell	Tunability, self-assemble, sensitivity, selectivity, and versatility.	Simultaneous detection of multiple targets, integration of microfluidic strategies, real time monitoring	[39]
2	Fluorescent single walled carbon nanotubes	Colloidal Nanoparticle /Insulin	Invasive	Fluorescent intensity	Blood	Selectivity, and Sensitivity	Better in the detection limit, Development of sensor as	[40]

							implantable device non-invasively	
3	Optical Nanosensor (LSPR-based cuvette-type)	Cortisol	Localized surface plasmon resonance based cuvette type sensor	Local refractive index and a shift in the wavelength	Serum	High sensitivity, Rapid detection	Long-term stability remains for its commercialization	[41]
4	Electrochemical immunosensor (Yarn-based)	Gold Nanoparticles/ Cortisol	Non-invasive, ZnO nanorods(1D) ZnO nanoflaxes(2D)	Mechanical stability, super-wetting, morphology, crystallinity, and specific surface area	Sweat	Excellent Electrical Conductivity, Excellent detection limit	Transformation as portable device	[42]
5	Field effect transistor (FET) sensors	SiNW/Cortisol	Aptamer-functionalized nanoscopic	Electrical	Saliva	Label-free and portable	Debye screening length limitations	[43]
6	Single-Walled Carbon Nanotube-Based Field-Effect Transistors	SWCNT /Cortisol	Non-Invasive	Structure and Physicochemical	Artificial sweat	Good LOD, Sensitivity, Linear response	Analytical challenge due to low concentrations	[44]
7	Fluorescent-based bioprobes	Biological macromolecules	Non-Invasive	Optical and Electronic	Blood	Good sensitivity, Selectivity, High surface-to-volume ratio	Sensor's lifetime	[45]
8	CMOS-silicon nanowire field effect transistor (SiNW-FET)	3 Aminopropyltriethoxysilane (APTES), Glutaraldehyde, and Bovine serum albumin (BSA), Silicon nanowire / carbon nanotube /Thyroid stimulating hormone (hTSH)	Electrical Measurements	Semiconductor	Serum	Low-cost and large-scale production, label-free and rapid electrical detection	Anisotropic etching with self-stop limitation	[46]

9	Fluorescent sensors	Quantum dots , neurohormones (Cortisol)	Optical	Fluorescent, electronic, or Photoluminescent	Saliva/Blood	Miniaturisation and cost-effectiveness	Problem with many analysis steps and with the integration of sample pretreatment.	[47]
10	Nanowell array biosensors	Cortisol	Nanowell array design, Non-invasive	Impedance characterization	Serum	Rapid and low volume, Monitoring the real-time binding evets, Highly sensitive, Label free detection, Cost effective	Measurement inconsistency	[48]
11	Chemical impedance sensors	Gold electrodes/Cortisol	Electrochemical impedance spectroscopy	Temperature and pH	Sweat	Robust sensor for continuous monitoring	A redox-based probing system requires an amperometric system, which in turn modifies the target biomarker being studied.	[49]
12	Vertically-aligned metal electrode sensor	MoS2 nanosheets /cortisol	Electrochemical impedance spectroscopy	Changes in Impedances	Sweat	Low volume, specificity	Robustness and reliability necessary for commercial implementation.	[50]
13	Electromagnetic biosensor	Brainwaves	Non-Invasive	Extremely low frequency	Brainwaves	Good Accuracy	Limited range of frequency	[51]

SPECIFICATIONS

As required to identify and specify technical and biological specifications for implementation of bionanosensor to detect a hormone, detailed specifications are mentioned in Table 5 and Table 6 respectively.

Table 5 Technical specifications of the sensor

Type of Specification	**Details of Parameter**
Mechanical	Stability, Sensitivity, Reliability, Repeatability, Potential for miniaturization, Specificity, Selectivity
Electrical	SNR, Thermal stability, Response time, Energy consumption, Speed

Table 6 Details of the biological specification [7]

Biological Specification	**Details of Biological parameters**	
Level of biomolecular	DNA, RNA and Protein [7]	
Carbon compounds	Bisphenol A,Vinclozolin,Propylparaben,Hormone receptor,Estrone,Fenoxycarb [7]	
Biofluid	Sweat, Saliva, Blood, Urine	
	Name of Gland	***Name of Hormones***
Hormones	Pineal gland	Melatonin
	Pituitary Gland	Luteinising hormone (LH), Follicle-stimulating hormone (FSH), Prolactin, growth hormone, Thyroid stimulating hormone (TSH), Adrenocorticotrophic hormone (ACTH) [7]
	Thyroid gland	Tri-iodothyronine (T3), Thyroxine (T4), Calcitonin [7]
	Parathyroid Gland	Parathyroid hormone (PTH) [7]
	Thymus	Lymphocytes [7]
	Adernal Glands	Adrenaline, Cortisol [7]
	Pancreas	Insulin [7]
	Gonads Testes	Male - Testosterone, anti-mullerian hormone (AMH), Estradiol, inhibin B [7]
		Female - Oestrogen, Progesterone, Testosterone, Anti-mullerian hormone (AMH), Inhibin A and Inhibin B [7]

PROCESS FLOW OF RESEARCH DESIGN

The design steps from specification to validation are shown in Figure 4 for detecting endocrine hormones. The first step is to set the biological, mechanical, chemical, and electronic specifications of desired sensors. The second step is to select the type of sensor based on the quantity to detect. The third step is to select type of methodology for sensor detection. The fourth step is to model the sensor as a device in a CAD tool by setting the environment. The fifth step is to simulate the device for characterization as per the properties of the sensors defiled and simulate for analysis. Final steps to validate sensor as per defined function.

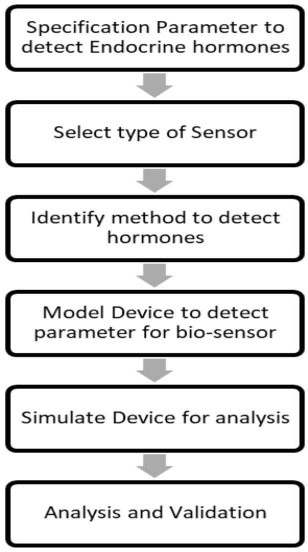

Figure 4 : Research Process flow

The CAD Tools are used for device-level modelling of bio-nanosensor for implementation.

CHALLENGES AND FUTURE SCOPE

We discussed few challenges associated with implementing real-time sensor. Materials availability and cost planning should be aligned with the designated timeline. Sensor fabrication poses a significant challenge, and support of grants and facilities. The laboratory facility is equipped with an experimental setup specifically designed for testing the equipment. Approval from regularity authorities is necessary for conducting clinical trials on human sweat or artificial prototypes.

The nanosensor is a nanotechnology-based instrument capable of detecting chemical and physical changes, monitoring biochemical and biomolecular changes. Defining fabrication and operation of nanosensor to detect cortisol hormone for better sensitivity and stability to be focused in future as real time application.

CONCLUSION

Cortisol is identified as one of key hormone in Endocrine system for stress measurement. Biosensor is used to detect biological elements and converting bio signals into electrical signal using transducer. Different types of Biosensors like FET-based, Impedance type and many more are studied. Nanotechnology enabled different Nanosensors are available in small size, with less power consumption and with high sensitivity. Different types of nanosesnors like Nanoparticle, Nanotube and Nanowire are used as per their sensing mechanism and materials for required application. Nanotechnology enabled endocrine sensors and comparison of bionanosensor to detect cortisol are surveyed. Non-Invasive sweat based continuous monitoring nanosensor is promising future in biomedical application. The research design flow and technical details of sensors are defined to detect cortisol hormone. With the help of nanotechnology, bionanosensor can be implemented in further research environments.

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REFERENCES

[1] Carr, J. J., & Brown, J. M. (2001). Introduction to biomedical equipment technology (4th ed.). Pearson Education.

[2] Faridbod, F., Ganjali, M. R., Larijani, B., Norouzi, P., & Hosseini, M. (2014). Biosensors in Endocrinology - Review Article. Iranian Journal of Public Health, Vol. 43, Supple. 1, pp. 94-104.

[3] Xu, Y., Hu, X., Kundu, S., Nag, A., Afsarimanesh, N., Sapra, S., ... Han, T. (2019). Silicon-Based Sensors for Biomedical Applications: A Review. Sensors, 19, 2908. https://doi.org/10.3390/s19132908

[4] Li, H., Liu, X., Li, L., Mu, X., Genov, R., & Mason, A. J. (2017). CMOS electrochemical instrumentation for biosensor microsystems: A review. Sensors, 17(1), 74. https://doi.org/10.3390/s17010074

[5] Weiss, R., Karimijafarbigloo, S., Roggenbuck, D., & Rödiger, S. (2022). Applications of neural networks in biomedical data analysis. Biomedicines, 10(1469). https://doi.org/10.3390/biomedicines10061469

[6] Munawar, A., Khan, R. F. H., Iqbal, M. Z., Rehman, A., Bajwa, S. Z., & Khan, W. S. (2022). Drug-detection performance of carbon nanotubes decorated with metal oxide nanoparticles. In Carbon nanotubes for biomedical applications (Chapter 18). Elsevier. Retrieved from https://www.sciencedirect.com/science/article/abs/pii/B9780128226940000016

[7] https://www.healthdirect.gov.au/endocrine-glands-and-their-hormones

[8] https://www.uc.edu/content/dam/uc/ce/docs/OLLI/Page%20Content/The%20Endocrine%20System.pdf https://www.youtube.com/watch?v=nCwRX7seya0

[9] Dr. Samanthi. (2022, May 13). What is the difference between cortisol and epinephrine? Difference Between. Retrieved from https://www.differencebetween.com

[10] https://www.elprocus.com/what-is-a-biosensor-types-of-biosensors-and-applications/

[11] Sekar, M., Pandiaraj, M., Bhansali, S., Ponpandian, N., & Viswanathan, C. (2019). Carbon fiber-based electrochemical sensor for sweat cortisol measurement. Scientific Reports, 9, 403. https://doi.org/10.1038/s41598-018-37243-w

[12] Pali, M., Jagannath, B., Lin, K.-C., Upasham, S., Sankhala, D., Upasham, S., Muthukumar, S., & Prasad, S. (2021). CATCH (Cortisol Apta WATCH): 'Bio-mimic alarm' to track anxiety, stress, immunity in human sweat. Electrochimica Acta, 2021, 138834. https://doi.org/10.1016/j.electacta.2021.138834

[13] Karachaliou, C.-E., Koukouvinos, G., Goustouridis, D., Raptis, I., Kakabakos, S., Petrou, P., & Livaniou, E. (2023). Cortisol immunosensors: A literature review. Biosensors, 13(2), 285. https://doi.org/10.3390/bios13020285

[14] Alawsi, T. (2015). Nanosensors: Basics, design, and applications. https://doi.org/10.13140/RG.2.2.26047.51362

[15] Singh, S., Kumar, V., Dhanjal, D. S., Datta, S., Prasad, R., & Singh, J. (2020). Biological biosensors for monitoring and diagnosis. In Microbial biotechnology: Basic research and applications (pp. 317–335).

[16] Lee, S., Lee, J. H., Kim, M. G., Kim, J., Song, M.-J., Jung, H.-I., & Lee, W. (2013). Bi nanowire-based thermal biosensor for the detection of salivary cortisol using the Thomson effect. Applied Physics Letters, 103(14), 143114. https://doi.org/10.1063/1.4824015

[17] Malik, P., Katyal, V., Malik, V., Asatkar, A., Inwati, G., & Mukherjee, T. K. (2013). Nanobiosensors: Concepts and variations. ISRN Nanomaterials, 2013, Article 327435, https://doi.org/10.1155/2013/327435

[18] Malik, P., Gupta, R., Malik, V., & Ameta, R. K. (2021). Emerging nanomaterials for improved biosensing. Measurement: Sensors, 18, 100050. https://doi.org/10.1016/j.measen.2021.100050

[19] Khan, Y., Sadia, H., Shah, S. Z. A., Khan, M. N., Shah, A. A., Ullah, N., Ullah, M. F., Bibi, H., Bafakeeh, O. T., Khedher, N. B., Eldin, S. M., Fadhl, B. M., & Khan, M. I. (2022). Classification, synthetic, and characterization approaches to nanoparticles, and their applications in various fields of nanotechnology: A review. Catalysts, 12(11), 1386. https://doi.org/10.3390/catal12111386

[20] Joudeh, N., & Linke, D. (2022). Nanoparticle classification, physicochemical properties, characterization, and applications: A comprehensive review for biologists. Journal of Nanobiotechnology, 20(262). doi:10.1186/s12951-022-01477-8

[21] Poudyal, S. S. (2017). Screen printed carbon electrode based microfluidic biosensor for sweat cortisol detection (Master's thesis). South Dakota State University. Retrieved from https://openprairie.sdstate.edu/etd/2156

[22] Abu Shama, N., Aşır, S., Göktürk, I., Yılmaz, F., Türkmen, D., & Denizli, A. (2023). Electrochemical detection of cortisol by silver nanoparticle-modified molecularly imprinted polymer-coated pencil graphite electrodes. ACS Omega, 8(32), 29202–29212. doi:10.1021/acsomega.3c02472

[23] Saleh, H. M., & Hassan, A. I. (2023). Synthesis and characterization of nanomaterials for application in cost-effective electrochemical devices. Sustainability, 15(14), 10891. doi:10.3390/su151410891

[24] Le, N. D. B., Wang, X., Geng, Y., Tang, R., Tonga, G. Y., Jiang, Z., & Rotello, V. M. (2017). Rapid and ultrasensitive detection of endocrine-disrupting chemicals using a nanosensor-enabled cell-based platform. Chemical Communications, 53(62), 8794–8797.

[25] Kusov, P. A., Kotelevtsev, Y. V., & Drachev, V. P. (2023). Cortisol monitoring devices toward implementation for clinically relevant biosensing in vivo. Molecules.

[26] Eun-Hyung, & Lee, S.-Y. (2010). Glucose biosensors: An overview of use in clinical practice. Sensors, 10, 4558–4576.

[27] Bezbaruah, A. N., & Kalita, H. (2013). Sensors and biosensors for endocrine disrupting chemicals: State-of-the-art and future trends. IWA Publishing. ISBN: 9781843393160.

[28] Dalirirad, S., & Steckl, A. J. (2018). Aptamer-based lateral flow assay for point-of-care cortisol detection in sweat. Sensors and Actuators B: Chemical. https://doi.org/10.1016/j.snb.2018.11.161

[29] Jang, H.-J., Lee, T., Song, J., Russell, L., Li, H., Dailey, J., ... Katz, H. E. (2018). Electronic cortisol detection using an antibody-embedded polymer coupled to a field-effect transistor. ACS Applied Materials & Interfaces, 10, 16233–16237. https://doi.org/10.1021/acsami.7b18855

[30] Sheibani, S., Capua, L., Kamaei, S., Akbari, S. S. A., Zhang, J., Guerin, H., & Ionescu, A. M. (2020). Extended gate field-effect transistor for sensing cortisol stress hormone. Communications Engineering, 1(14). https://doi.org/10.1038/s43246-020-00114-x

[31] Zubarev, A., Cuzminschi, M., Iordache, A.-M., Iordache, S.-M., Rizea, C., Grigorescu, C. E. A., & Giuglea, C. (2022). Graphene-based sensor for the detection of cortisol for stress level monitoring and diagnostics. Diagnostics, 12(11), 2593. https://doi.org/10.3390/diagnostics12112593

[32] Yoon, M., Shin, M., Lee, T., & Choi, J.-W. (2020). Highly sensitive biosensors based on biomolecules and functional nanomaterials depending on the types of nanomaterials: A perspective review. Materials, 13(2), 299. Retrieved from https://doi.org/10.3390/ma13020299

[33] Munje, R. D., Muthukumar, S., & Prasad, S. (2016). Interfacial tuning for detection of cortisol in sweat using ZnO thin films for wearable biosensing. In Proceedings of the IEEE Nanotechnology Materials and Devices Conference (NMDC) (pp. 1–4). IEEE. Retrieved from https://doi.org/10.1109/NMDC.2016.7886773

[34] Torrente-Rodríguez, R. M., Tu, J., Yang, Y., Min, J., Wang, M., Song, Y., Yu, Y., Xu, C., Ye, C., IsHak, W. W., & Gao, W. (2020). Investigation of cortisol dynamics in human sweat using a graphene-based wireless mHealth system. Matter, 2(4), 921–937. doi:10.1016/j.matt.2020.01.021

[35] Baig, N., Kammakakam, I., & Falath, W. (2021). Nanomaterials: A review of synthesis methods, properties, recent progress, and challenges. Materials Advances, 2(6), 1821–1871. doi:10.1039/D0MA00807A

[36] Kim, K. H., Lee, S. H., Seo, S. E., Bae, J., Park, S. J., & Kwon, O. S. (2020). Ultrasensitive stress biomarker detection using polypyrrole nanotube coupled to a field-effect transistor. Micromachines, 11(4), 439. doi:10.3390/mi11040439

[37] Kumar, A., Aravamudhan, S., Gordic, M., Bhansali, S., & Mohapatra, S. S. (2007). Ultrasensitive detection of cortisol with enzyme fragment complementation technology using functionalized nanowire. Biosensors and Bioelectronics, 22(9–10), 2138–2144. doi:10.1016/j.bios.2006.09.035

[38] Wang, B., Zhao, C., Wang, Z., Yang, K.-A., Cheng, X., Liu, W., Yu, W., Lin, S., Zhao, Y., Cheung, K. M., Lin, H., Hojaiji, H., Weiss, P. S., Stojanović, M. N., Tomiyama, A. J., Andrews, A. M., & Emaminejad, S. (2022). Wearable aptamer-field-effect transistor sensing system for noninvasive cortisol monitoring. Science Advances, 8(1), eabk0967. doi:10.1126/sciadv.abk0967

[39] Sanghavi, B. J., Wolfbeis, O. S., Hirsch, T., & Swami, N. S. (2014). Nanomaterial-based electrochemical sensing of neurological drugs and neurotransmitters. Springer.

[40] Bisker, G., Bakh, N. A., Lee, M. A., Ahn, J., Park, M., O'Connell, E. B., Iverson, N. M., & Strano, M. S. (2018). Insulin detection using a corona phase molecular recognition site on single-walled carbon nanotubes. ACS Sensors, 3(2), 367–377. https://doi.org/10.1021/acssensors.7b00788

[41] Jeon, J., Uthaman, S., Lee, J., Hwang, H., Kim, G., Yoo, P. J., Hammock, B. D., Kim, C. S., Park, Y.-S., & Park, I.-K. (2018). Indirect localized surface plasmon resonance (LSPR)-based nanosensors for highly sensitive and rapid detection of cortisol. Sensors and Actuators B: Chemical. https://doi.org/10.1016/j.snb.2018.03.167

[42] Sfrazzetto, G. T., & Santonocito, R. (2022). Nanomaterials for cortisol sensing. Nanomaterials, 12(3790). https://doi.org/10.3390/nano12213790

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

[44] Bian, L., Shao, W., Liu, Z., Zeng, Z., & Alexander, S. (2022). Detection of stress hormone with semiconducting single-walled carbon nanotube-based field-effect transistors. Journal of The Electrochemical Society, 169(057519). https://doi.org/10.1149/1945-7111/ac6b16

[45] Sargazi, S., Fatima, I., Kiani, M. H., Mohammadzadeh, V., Arshad, R., Bilal, M., Rahdar, A., Díez-Pascual, A. M., & Behzadmehr, R. (2022). Fluorescent-based nanosensors for selective detection of a wide range of biological macromolecules: A comprehensive review. International Journal of Biological Macromolecules, 206, 115–147.

[46] Lu, N., Dai, P., Gao, A., Valiaho, J., Kallio, P., Wang, Y., & Li, T. (2014). Label-free and rapid electrical detection of hTSH with CMOS-compatible silicon nanowire transistor arrays. ACS Applied Materials & Interfaces, 6(20), 20378–20384. https://doi.org/10.1021/am505915y

[47] Halicka, K., Meloni, F., Czok, M., Spychalska, K., Baluta, S., Malecha, K., Pilo, M. I., & Cabaj, J. (2022). New trends in fluorescent nanomaterials-based bio/chemical sensors for neurohormone detection: A review. ACS Omega, 7, 33749–33768. https://doi.org/10.1021/acsomega.2c04134

[48] Mahmoodi, S. R., Xie, P., Zachs, D. P., Peterson, E. J., Graham, R. S., Kaiser, C. R. W., Lim, H. H., Allen, M. G., & Javanmard, M. (2021). Single-step label-free nanowell immunoassay accurately quantifies serum stress hormones within minutes. Science Advances, 7, eabf4401. https://doi.org/10.1126/sciadv.abf4401

[49] Kinnamon, D., Ghanta, R., Lin, K.-C., Muthukumar, S., & Prasad, S. (2017). Portable biosensor for monitoring cortisol in low-volume perspired human sweat. Scientific Reports, 7, 13312. https://doi.org/10.1038/s41598-017-13684-7

[50] Sankhala, D., Muthukumar, S., & Prasad, S. (2018). A four-channel electrical impedance spectroscopy module for cortisol biosensing in sweat-based wearable applications. SLAS Technology, 23(6), 529–539. https://doi.org/10.1177/24726303187592

[51] Aparnathi, R., & Dwivedi, V. V. (2013). Electromagnetic biosensor for extremely low-frequency brain waves. International Journal of Advanced Research in Electrical, Electronics and Instrumentation Engineering, 2(9).