Advancement in Biosensor: 'Telediagnosis' and 'Remote Digital Imaging'

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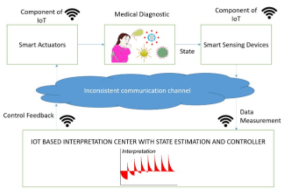
Abstract

Current developments in sensors and actuators are in the state of opening a new era to facilitate the things to be happened in effortless and efficient way with a proper communication. On the other hand, internet of things (IoT) have been boomed-up with a higher potential and occupies a wide range of disciplines. This study has choreographed the designing of algorithm and a smart data processing scheme to implement the obtained data from the sensing system to be transmitted to the receiving end. Technically it is called 'telediagnosis' and 'remote digital monitoring', a revolution in the field of medicine and artificial intelligence. For the proof of concept an algorithmic approach has been implemented for the telediagnosis with one of the regenerative diseases, Parkinson's disease. Using the data acquired for an improved interdigitated electrode sensing surface was evaluated with the attained sensitivity of 100 fM (*n*=3) and the limited of detection was calculated with the linear regression value co-efficient. By the designed algorithm and data processing with the assistance of IoT, further validation was performed and attested the co-ordination. This proven concept can be ideally used with all sensing strategies for immediate telemedicine, by the end-to-end communications.



Keywords: Medical diagnosis; Interdigitated electrode; Neurogenerative disease; Biomarker

Highlights

This study was designed using algorithm and a smart data processing scheme to implement the obtained data from the sensing system to be transmitted to the receiving end. The regenerative disease, Parkinson was demonstrated with the biomarker 'alpha-synuclein' as a model system. The improved interdigitated electrode sensing surface was evaluated with the averaged (*n*=3) sensitivity of 100 fM and the limited of detection and to be in the similar range with the linear regression co-efficient.

1. Introduction

'Telediagnosis' and 'remote digital monitoring' are the currently embarking terminologies with the massive demand in the field of medicine and diagnosis. This situation has been primarily emerged for the disease detection by evaluating the transmitted data to the station received from the high-performance sensing system, which monitors the patient in distant. Telediagnosis and remote digital monitoring are highly favourable to the elderly and disabled persons, including persons with obesity, bedridden, fatigue, heart-issue, pregnant women and in the case with the requirement of continuous monitoring. These necessities are the great future vision for simplifying the medical treatment in effortless way, and mandatory to elevate the past development in to the stream-line. Along with this research-line nanobiosensor became a main player; ideally, biosensor is a device that utilizes a biological recognition system towards targeting biomolecules and the clinical biomarkers.

Typically, biosensor comprised of primarily the biocomponents that can be enzyme, nucleic acid, glycan, antibody, and aptamer [1–3]. Current study demonstrates the potential sensing system with interdigitated electrodes for biomarker analysis. Interdigitated electrodes system is predominantly working with dual electrodes and extended with triple- and four-electrodes. These electrodes mediated sensing surfaces have been patterned with parallel or concentric electrodes at desired gap regions. These regions are critical to make the high-performance analysis and gaps can be patterned from nano- to micro-sizes. Upon immobilizing or interacting the molecules on the sensing surfaces, the system works based on dipole moment mechanism. The great thing with interdigitated electrodes sensor is suitable for portable sensors towards the ultimate aim for point-of-care analysis using alternate-/direct-currents. Further, output signal can be digitalized as directed in the current research by availing the modern technological inputs. The interaction between bioreceptor and analyte display the chemical and physical changes, and the signal processing system involves the amplification and display in the right format. Finally, the output signal is amplified and pass as microelectronics or in other modes followed by a data processor [2–5]. This strategy has the essence for a great impact in the medical front, permitting detection of emerging and emerged diseases at an early stage in a laboratory sampling and point-of-care. Recent researches are embarking on telemedicine and remote digital monitoring, with the participation of artificial intelligence in nanobiosensors. With this line of research and analysis, several information are missing while acquiring the knowledge due to the occurrence of plenty resources. With this basic demand, currently the big issue is making a proper communication between doctors and the disabled/elderly patients. As these patients are not able to move freely, it is an urgent and mandatory to create a telemedicine-remote diagnostic system. To fulfill this potential necessity, this study proposes to generate a system, which is able to diagnose the medical biomarker and hybrid with the internet of things (IoT) to facilitate the easier communication.

Interestingly, the next emerging IoT technologies can be utilized for IoT application development will be effective to follow the physical systems such as garage, emergency alarms, wristwatches, home utilities, and smart body sensors from the remote control center (Figure 1a) [6]. It has seen that all electronic surrounding to aid daily life operations are well-linked to the IoT and monitored by the controlled remote [7]. Notably, the IoT assisted sensors are integrated into the physical systems for instance the automated systems [8] and telemedicine [9]. Technically, the diagnostic information by IoT devices either from elderly or patients is passed to the control centre by varied communication topologies like internet, ZigBee, and WiFi [10–13]. It is fair to indicate that estimation and control of smart system are highly relied on the measurement accuracy [14] and sensor precision[15]. On the other hand, the measurements received by the installed sensors are vulnerable to packet loss and cyber-attacks [16]. This enhances the security and safety concerns which may cause the financial crisis and social issues [17]. By taking this motivation, the current work elevates an algorithm for controlling the telediagnosis system using the IoT technologies under the packet loss conditions, especially for elderly/disabled people (Figure 2).

To implement the above idea, this research integrates the biosensing application with designing algorithm and smart data processing. To make the proof-of-concept, one of the prevalent neurogenerative diseases, ‘Parkinson’s disease’ was considered and demonstrated on the finely-tuned interdigitated electrode surface. Upon setting-up this strategy of IoT will connect to the plug-in devices and smart phones, to transmit the generated reports as the output to the doctors in the nearest clinics (telediagnosis-remote diagnosis). For this goal the proper transceiver, receiver and data-interpreting display can be created. The major benefit of this research is to conjugate the current advancement in the medical diagnosis and IoT, to be suitable for all levels of stakeholders.

2. Experimental

2.1. Materials

Gold nanorod with 700 nm in size was purchased from Nanocs, USA. Phosphate buffer saline (PBS), (3-Aminopropyl) triethoxysilane (APTES), Ethanolamine, Carbonyldiimidazole (CDI), and 16-mercaptoundecanoic acid (16-MHA) were acquired from Sigma-Aldrich (USA). N-hydroxysuccinimide and N-ethyl-N'-(3-dimethylaminopropyl) carbodiimide hydrochloride were obtained from GE Healthcare (USA). Aggregated form of α-synuclein was made in Glycine-NaOH buffer (pH 7.4) by placing at 37°C with a mild shaking (for 5 days).

2.2. System Model for a Controlled IoT System

Generally, the IoT entails of smart body sensors, actuators and smart processors to create an informative remote digital monitoring [18]. For designing such an interconnected telediagnosis network, the following system was considered:

$$q_{k+1} = Aq_k + Bu_k + n_k \tag{1}$$

where q_k is the state at time step k, A and B are the given matrices, u_k is the control input and n_k is the process noise with Q_k covariance matrix. In order to sense the telediagnosis, the practitioners deploy the IoT sensors where analysis y_k are,

$$y_k = Hq_k + w_k \tag{2}$$

where H is the sensing matrix, and w_k is the noise with R_k covariance matrix. This sensing information transfers to the center management system where packet loss is as below [19]:

$$z_k = \beta_k Hq_k + \beta_k w_k \tag{3}$$

where z_k is the analysis under packet loss condition, and packet loss $\beta_k \in \{0, 1\}$ can be modelled to be,

$$\beta_k = \begin{cases} 1, & with\ \gamma_k \\ 0, & with\ 1 - \gamma_k \end{cases}$$

where γ_k is the packet loss probability.

Considering packet dropouts IoT network in remote monitoring, the filtering problem is written as,

$$\hat{q}_{k|k} = \hat{q}_{k|k-1} + K_k(z_k - \beta_k H\hat{q}_{k|k-1}) \tag{4}$$

Here, $\hat{q}_{k|k-1}$ and $\hat{q}_{k|k}$ are the predicted and updated state estimation, and K_k is the filter gain. With previous state $\hat{q}_{k-1|k-1}$ and it error covariance $P_{k-1|k-1}$, the following function is obtained:

$$\hat{q}_{k|k-1} = A\hat{q}_{k-1|k-1} + Bu_{k-1} \tag{5}$$

$$P_{k|k-1} = AP_{k-1|k-1}A' + Q_{k-1} \tag{6}$$

Thus, it is important to design the optimal K_k and analyse the algorithmic convergence. From Figure 1b, it was noticed that the sensing measurements/control signals are influenced by intermittent IoT communication [20].

2.3. Generated State Estimation Scheme

The optimal gain is designed based on the mean squared error principle. For doing this, let ϕ denotes the system calculation error as:

$$\phi_{k|k-1} = q_k - \hat{q}_{k|\,k-1} \tag{7}$$

$$\phi_{k|k} = q_k - \hat{q}_{k|\,k} \tag{8}$$

Substituting (4) into (7) yields:

$$\phi_{k|k} = (I - \beta_k K_k H)\phi_{k|k-1} - \beta_k K_k w_k \tag{9}$$

Now, the error covariance $P_{k|k}$ is:

$$P_{k|k} = E(\phi_{k|k}\phi'_{k|k}) \tag{10}$$

By putting (9) into (10):

$$P_{k|k} = \gamma_k(I - K_kH)P_{k|k-1}(I - K_kH)' + (1 - \gamma_k)P_{k|k-1} + \gamma_kK_kR_kK'_k \quad (11)$$

Taking the partial derivative yields:

$$\frac{\partial[trP_{k|k}]}{\partial K_k} = -2\gamma_kP_{k|k-1}H' + 2\gamma_kK_kHP_{k|k-1}H' + 2\gamma_kK_kR_k \quad (12)$$

Putting $\frac{\partial[trP_{k|k}]}{\partial K_k} = 0$ in (12) and K_k is expressed as Rana et al., 2017c [21]:

$$K_kHP_{k|k-1}H' + K_kR_k = P_{k|k-1}H' \quad (13)$$

$$\Rightarrow K_k = P_{k|k-1}H'[HP_{k|k-1}H' + R_k]^{-1}$$

2.4. Proposed Control Scheme for IoT Telediagnosis System

With the help of Figure 1b and utilizing separation principle, the proposed controller is defined as:

$$u_k = \alpha_kDq_k \quad (14)$$

Considering following objective function:

$$J = E\left[\lim_{N\to\infty}\frac{1}{N}\sum_{k=0}^{N-1}(q'_kM_xq_k + u'_kN_uu_k)\right] \quad (15)$$

Given D is the state feedback gain, N_u and M_x are control and state matrices, packet loss α_k is represented as

$$\alpha_k = \begin{cases} 1, & \text{ideal} \\ \lambda_k, & \text{unreliable network} \end{cases}$$

Here, λ_k is the packet arrival rate. Using Hu and Yan, 2007 [22], it assumes that $\lambda = \gamma$. The closed-loop system is:

$$q_{k+1} = (A + \alpha_kBD)q_k + n_k \quad (16)$$

By using (14) and $m'Ln = tr[Lnm']$, (15) can be formed to be,

$$J = E\left[\lim_{N\to\infty}\frac{1}{N}\sum_{k=0}^{N-1} tr(M_x q_k q'_k + \alpha_k D' N_u D q_k q'_k \alpha_k)\right] \quad (17)$$

$$J = tr(M_x + \lambda_k D' N_u D)P$$

where $P = E\left[lim_{N\to\infty}\frac{1}{N}\sum_{k=0}^{N-1} q_k q'_k\right]$. It assumes that initial value of $E\left[q_o q'_o\right] = 0$ as the system stability does not depend on initial value. By using (16) with noise covariance $E[n_k n'_k] = Q_k$ it can be expressed as:

$$P = E\left[\lim_{N\to\infty}\frac{1}{N}\sum_{k=0}^{N-2} q_{k+1} q'_{k+1}\right] + \lim_{N\to\infty}\frac{1}{N}\, E\left[q_o q'_o\right]$$

$$P = E\left[\lim_{N\to\infty}\frac{1}{N}\sum_{k=0}^{N-2}(A + \alpha_k BD) q_k q'_k (A + \alpha_k BD)']\right] + Q_k \quad (18)$$

Assumption: For steady state case and it assumes that $E[v_k v'_k] = \mathrm{I}$, i.e., constant time-invariant value. Using this assumption, (18) can be,

$$P = (A + \lambda BD)P(A + \lambda BD)' + Q \quad (19)$$

If there exists a stabilising gain D then inequality $A_{cl} X A_{cl} - X + Q < 0$ hold to reduce the error, where A_{cl} is the closed-loop system state matrix and $P > 0$. Based on aforementioned condition, considered the inequality below:

$$(A + \lambda BD)PP - 1P(A + \lambda BD)' - P + Q < 0 \quad (20)$$

Consider $G = DP$, the function (20) can be expressed as follows:

$$(AP + \lambda BG)P - 1(AP + \lambda BG)' - P + Q < 0 \quad (21)$$

With Schur's complement, (21) can be estimated as shown below:

$$\begin{bmatrix} Q - P & AP + \lambda BG \\ \star & -P \end{bmatrix} < 0 \quad (22)$$

From (17), the gain and positive definite matrix can be found as follows:

$$\text{minimize}_{P,D} \qquad tr[M_x + \lambda D' N_u D]P \quad \text{subject to (22)} \tag{23}$$

Based on $G = DP$, (23) can be written as follows:

$$\text{minimize}_{P,S,G} \qquad tr[M_x P] + tr[S] \tag{24}$$

$$\text{subject to} \qquad S > \lambda N_u^{1/2} G P^{-1} G' M_u^{1/2} \tag{25}$$

Hold (22).

Now (25) can be rewritten as:

$$\begin{bmatrix} S & \sqrt{\lambda} N_u^{1/2} G \\ \sqrt{\lambda} G' N_u^{1/2} & P \end{bmatrix} > 0 \tag{26}$$

The gain is received considering the following problem:

$$\text{minimize}_{P,S,G} \qquad tr[M_x P] + tr[S]$$

$$\text{subject to} \qquad \text{Hold (22) and (26).} \tag{27}$$

Finally, the controller gain is received as:

$$D = GP - 1 \tag{28}$$

This optimization problem can be solved utilizing linear matrix inequality toolbox.

2.5. Preparation of dielectrode surface

As stated earlier, silver dielectrode has been prepared on the silicon wafer by the wet etching method. The positive photoresist was layered on the wafer, and then soft baked (~90 sec). Ultraviolet light was exposed (~10 sec) for pattern transferring from the original mask design to the surface. Then, the developmental processes were done (~15 sec) with RD-6 developer. Followed by baking was at 110 ^{0}C to eliminate the moisture and enhanced the adhesion effect. At the end, the unexposed area was removed using a silver etchant (~23 sec) and then cleaned [2-3]. The surface characterization of the sensing surface was studied by Scanning Electron Microscopy and 3D-nanoprofiler.

2.6. Chemical modification and interaction of alpha-synuclein

The surface chemical modification followed by the interactive analysis was done as stated earlier [23]. In brief, CDI-modified surface was hybrid with goldrod-antibody conjugates by the aid of APTES, 16-MHA, EDC and NHS. Upon modification and blocking with ethanolamine, the surface was exposed with antibodies to interact alpha-synuclein. The dose-dependent interaction was carried out from low-femtomolar to low-nanomolar concentrations of alpha-synuclein. The limit of detection (LOD) was calculated by 3σ (LOD = standard deviation of the baseline + 3σ) against the background (S/N = 3:1). All data were averaged with triplicates (n=3) and estimated the mean standard deviation for sensitivity analysis (on lower concentrations with a linear determination regression curve). All the measurements were carried out with wet-condition at ambient room temperature. Washings between each modification step were performed with 10 mM PBS (pH 7.0) of 20 reaction volumes. Current-volt measurements were by Keithley ammeter from 0 to 2 V (~2 min) on three different devices fabricated from the same batch.

3. Results

3.1. Convergence Analysis

Let consider the Lyapunov function, which is given by (Rana et al., 2017c):

$$V[\phi_{k|k}] = \phi'_{k|k}(P_{k|k})^{-1}\phi_{k|k} \tag{29}$$

The small enhancement of $E\left[\Delta V\left(\phi_{k|k}\right)\right]$ is written as:

$$\begin{aligned} E\left[\Delta V\left(\phi_{k|k}\right)\right] &= E\left[V\left(\phi_{k+1|k+1}\right) - V\left(\phi_{k|k}\right)\right] \\ &= E[\phi'^{i}_{k+1|k+1}\left(P^{i}_{k+1|k+1}\right)^{-1}\phi^{i}_{k+1|k+1} - \phi'^{i}_{k|k}\left(P^{i}_{k|k}\right)^{-1}\phi^{i}_{k|k}] \end{aligned} \tag{30}$$

Similar to (9), $\phi^{i}_{k+1|k+1}$ can be written as:

$$\begin{aligned} \phi_{k+1|k+1} &= q_{k+1} - \hat{q}_{k+1|k+1} \\ &= (I - \beta_{k+1}K_{k+1}H)[A\left(q_k - \hat{q}_{k|k}\right) + n_k] - \beta_{k+1}K_{k+1}w_{k+1} \\ &= (I - \beta_{k+1}K_{k+1}H)\left(A\phi_{k|k} + n_k\right) - \beta_{k+1}K_{k+1}w_{k+1} \end{aligned} \tag{31}$$

Without disturbance, $E\left[\phi'_{k+1|k+1}\phi_{k+1|k+1}\right]$ can be written as follows:

$$E\left[\phi'_{k+1|k+1}\phi_{k+1|k+1}\right] = \lambda_{k+1}(I - K_{k+1}H)'A\phi_{k|k}\phi'_{k|k}A'(I - K_{k+1}H) + (1 - \lambda_{k+1})A\phi_{k|k}\phi'_{k|k}A' \tag{32}$$

Using (30), $E\left[\Delta V\left(\phi_{k|k}\right)\right]$ can be written as:

$$E\left[\Delta V\left(\phi_{k|k}\right)\right] = \lambda_{k+1}\left\{(I - K_{k+1}H)'A\phi_{k|k}\left(P_{k+1|k+1}\right)^{-1}\phi'_{k|k}A'(I - K_{k+1}H)\right\} + (1 - \lambda_{k+1})A\phi_{k|k}\left(P_{k+1|k+1}\right)^{-1}\phi'_{k|k}A' - \phi'_{k|k}\left(P_{k|k}\right)^{-1}\phi_{k|k} \tag{33}$$

If $E\left[\Delta V\left(\phi_{k|k}\right)\right] \leq 0$, then the designed algorithm is in stable state. The considered simulation is carried out using raw data given by Letchumanan et al. [2,3]. The telediagnosis state versus time step information is displayed in Figure 1b. It can be seen the designed scheme can well-estimate the system states where it needs only few seconds (k × Δt) to predict the system states.

3.2. Determination Alpha-synuclein: A Proof-of-concept with Algorithm

To provide an evidence for the above stable state algorithm, alpha-synuclein was detected in aggregated condition on interdigitated electrode sensor and the obtained data has been applied into the above algorithm. For the preparation of materials and surface chemical functionalization chemistry, the procedures from the recent study were followed [23]. However, instead of the gold-nanourchin, gold nanorod (700 nm) was used as recommended by Hussaini et al. [24]. The surface characterization of the fabricated interdigitated electrode surface was studied as outlined in our earlier studies [2,3]. The surface has uniformly arranged gap and finger regions with dielectrode as assessed by the high-resolution microscopy observations (Figure 3a-d), creates the signal responses based on the changes in the electrical flow upon the molecular interaction. The target alpha-synuclein (PDB accession: 2N0A) was aggregated and interacted with the anti-alpha synuclein on the gold nanorod embedded interdigitated electrode surface (Figure 4a). With this interaction, could evaluate the sensitivity of 100 fM (Figure 4b) and LOD falls in the close range at 100 fM with the acceptable linear regression coefficient (Figure 4c). An algorithm was substituted in the obtained results and the output clearly illustrates a genuine co-incidence between true and estimated states. The displayed co-ordination displayed in the figure 4, attests the reliability the derived algorithm for the sensing applications (Figure 5).

4. Discussion

In the past, different classes of epidemic diseases were reported and found to be infectious, pose a threat to the economy and public health. In addition, several other communicable and non-communicable diseases have been transmitted. On the other hand, development of high-performance nanobiosensors could be a central importance for the medical diagnosis, surveillance of emerging diseases. Apart from these, a great current issue is setting-up the telemedicine and remote diagnosis, especially with disabled and elderly patients. This lacuna needs to be solved by the current advancement with the interdisciplinary sciences. An immediate solution proposed in this study is setting-up a coupling system of IoT and medical diagnosis for making an easier communication between medical practitioners and the patients.

Current technological enhancement with a smart communication system has become a mandatory. The coming generation will be highly occupied to the social internet networking, can make use for the medical and telecommunication digital monitoring, in an economical way for healthcare, especially with elderly and disabled patients. In the present investigation, it was proposed the application IoT for monitoring and capturing the data and transmits in a digital form [25]. IoT is able generate a non-traditional healthcare arrangement; a digital monitoring system to elevate the proper communication between the medical practitioner and patients. In other words, IoT can couple with the digital technologies to glean the patient data from the home to the hospital. It is an electronic transmission of the information from the healthcare providers in one location to the remote location, where the recommendation and assessment are necessary. In addition, an implementation of non-invasive strategy has a potential now being connected to the management of diseases [26]. In this flow, the digital approaches are widely adopted as an ideal system for the healthcare system monitoring. In that way, the professionals from healthcare are ability to consult in order to save the time and drastically minimize the expenses to the poor patients. Further, the non-invasive system with the desired devices can be automated to transmit patient's health issue without intense action by the patient using the wearable device. This system can easily opt for the common disease such as, hypertension, diabetes, Parkinson and other neurogential diseases, in addition to monitor the breathing level, weight and heartbeat. The obtained data may be shared at a secure web-site and smartphone for a personal care assessment [26].

Remote- or tele-diagnosis needed personnel with special skills at the location of patient to ascertain the acquired clinical data to transmit for the analysis at the tail-end to subside the current demand. Even though, there is initiation of several schemes with this scenario, due to the lack of in-depth information, poor data processing and the involvement of expensive equipment, there is a further gearing-up is mandatory to attain the estimated future vision in the technology of telediagnosis with two-ways telecommunications. A few schemes have this assessment with the location of patient for the complete consultation, however, in most of the cases this strategy is feasible with only for an initial screening, ultimately its anomaly suspected to visit the advanced medical centre.

On the other hand, IoTs have been already in the main flow for creating the reality with the advanced multiple applications in smart sensors, automation and fulfilling the requirement of the industries, potentially in medicine. IoT sensor solutions are the better option for the data acquisition, capable to extract the raw data and computationally pass through the network to the capable device. Further, the significant enhancement in data-mining, transmission with a broad-band, clouds and big-data, uploads the meaningful data communications. To mitigate these potentials, artificial intelligence (AI) showed the milestone for the generation of a new revolution. With the logistics of AI, several reinvestigations are necessary and the currently research has taken the direction of telediagnosis and remote digital monitoring by availing the above advantages to pave the way for the next generation developments in telemedicine with the nanobiosensing technology. In addition, the logistic algorithms have been added for the development of data transmission with nanobiosensors. Interestingly, privacy and data protection can be installed with the system and stored for the future reference [27].

Nanobiosensors display the real appreciations in the past by showing the portable and wearable sensors for delivering the diagnosed issue, to be applicable for the bed-side/point-of-care analysis. Potential users of these developments can be the people with difficulties, such as obesity, bedridden, heart-issues, drug-abuse, pregnancy and handicap (Figure 6). By embedding the micro-processing core into the sensor along the strategy is shown in this study boosting the benefits. The obtained data by the nanobiosensing with human diseases is in turn converting in to the readable output and facilitates to recommend the right medicine.

Apart from these appealing advantages, this system can be implemented with the implanted sensors. To make the proof-of-concept, the designed algorism was implemented for the detection of parkinson's disease biomarker, alpha-synuclein [28] (PDB accession: 2N0A) to determine the neurogenerative disorder. The demonstrated data is convincible with a good sensitivity and reached at 100 fM. Further, the designed algorithm was validated this result and found to be well-coordinated. The above-mentioned sensing strategy for alpha-synuclein is also applicable for animal, as Parkinson's diseases are widely testing in experimental monkey as a good *in vivo* model to be mimicked in human (Figure 7). It is an implantable sensor has been commonly tested in animal and human systems [29]. Current demand in the medical scenario is implementing high-performance sensing system for the clinical applications. The above sensing strategy can be implemented for clinical analysis with patient specimens such as, tissue and blood. Further, highly suitable for point-of-care/bed-side analysis to be for immediate and high-throughput screening. The approach followed in the current study has been attested by the earlier literature on telemedicine and remote sensing analysis [30,31].

Conclusion

To help in developing a coordinated effort, this research prioritized nanotechnology as a key factor to strive today's world scenario. Recent researches are embarking on telediagnosis and remote digital monitoring, IoTs controller with the use of artificial intelligence in fusion with nanobiosensors. On the other hand, with the current diagnostics towards developing novel biosensors, several information are missing while acquiring the knowledge due to the occurrence of plenty resources. To implement the current necessity, telediagnosis (a new health resource for the community) and remote digital monitoring have been outlined by designing algorithm and smart data processing. A model system to connect biosensing analysis on interdigitated electrode for Parkinson's disease was evaluated with IoTs. Further, this strategy is applicable for other sensor systems to analyse a wide range disease biomarker interaction with partner molecules. This research clearly demonstrated the possible networking between disabled patient and the treating end by an e-diagnostic. It closes the gap between laboratory and industry by changing older laboratory set-up to the novel hand-held device by amending micro/nanodevices and making communication between two ends.

Potentially, this approach is minimizing the cost and time for treatment and maintaining the healthcare.

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Figure legends

Figure 1: (a) Basic concept on telediagnosis. The communication between wearable sensor and smart phone is shown. (b) IoT-linked Telediagnosis state estimation and stabilization. The steps and strategy involved are shown.

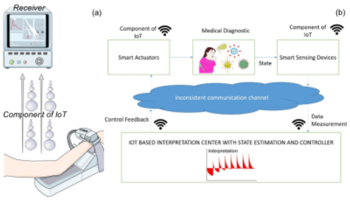

Figure 2: A proposed strategy for telediagnosis with IoT technologies. This two-ends communication is involved between biosensor user and analyser.

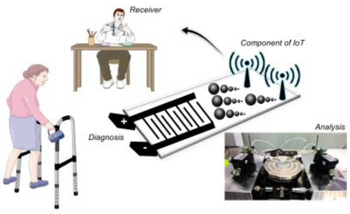

Figure 3: Surface morphology of interdigitated electrode. Surface Gaps and fingers are by (a) 3D-profiler normal image; (b) 3D-profiler 3D image; (c) High-performance microscopy image; (d) Scanning Electron Microscopy image.

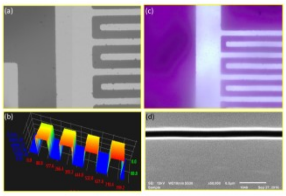

Figure 4: Analaysis for determining Parkinson's disease. (a) Basic scheme of detection by the selected molecule and the sensing system; (b) Dose-dependent analysis on interdigitated electrode sensor; (c) Estimation of limit of detection. Calculated by 3σ (LOD = standard deviation of the baseline + 3σ) against the background (S/N = 3:1). Data was averaged with triplicates (n=3) and the standard mean calculated as ± 0.05 x 10^{-5} A. The reliable determination co-efficient regression was noticed.

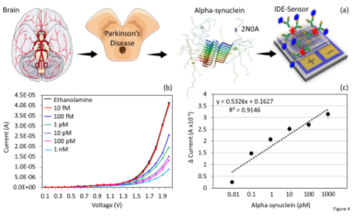

Figure 5: Algorithm and data processing. The data obtained from interdigitated electrode sensor analysis was stimulated and the co-ordination was found between the true and the estimated states.

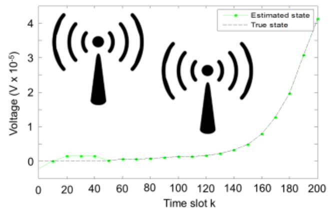

Figure 6: Potential user of the proposed telediagnosis. Different levels of disabilities are displayed.

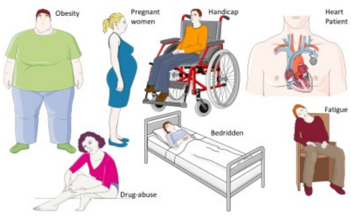

Figure 7: Potential model for *in vivo* studies. The implanted sensor model for the Parkinson's disease is shown.