iDDS: An Edge-Device in IoMT for Automatic Seizure Control using On-Time Drug Delivery

Md Abu Sayeed
Dept. of Computer Science and Engineering
University of North Texas, USA.
Email: mdsayeed@my.unt.edu

Saraju P. Mohanty
Dept. of Computer Science and Engineering
University of North Texas, USA.
Email: saraju.mohanty@unt.edu

Elias Kougianos
Dept. of Electrical Engineering
University of North Texas, USA.
Email: elias.kougianos@unt.edu

Hitten Zaveri
Department of Neurology
Yale University, USA.
Email: hitten.zaveri@yale.edu

***Abstract*—Epilepsy affects around 1% of the world population, necessitating wearable or implantable solutions for seizure control. In this paper, an Internet of medical things (IoMT) based unified drug delivery system (iDDS) is proposed for automatic seizure detection and control. iDDS consists of two units: a seizure detection unit and a drug delivery unit. Seizure detection is performed in real time using statistical feature extraction and a deep neural network (DNN) classifier. Once a detection is complete, the drug is injected into the target area using a piezoelectric actuated valveless double reservoir micropump. iDDS presents a unique piezoelectric actuated double-reservoir based drug delivery system for fault-tolerance as well as better drug control. The proposed system was implemented in Simulink® and Thinkspeak, which reported a sensitivity of 100% and an average latency of 1.8 sec for the selected dataset.**

***Index Terms*—Smart Healthcare, Internet of Medical Things, Implantable, Epilepsy, Seizure, Deep neural network (DNN), Double Reservoir Micropump, Drug Delivery System (DDS)**

I. Introduction

Traditional healthcare needs to be updated to accommodate the demand of the growing population. Smart healthcare is gaining significant importance as it uses limited resources to their maximum potential [1]. An IoT based automated drug delivery system (DDS) is one of the crucial components of smart healthcare, and is used for automatic control of seizures. Epilepsy is a neurological disorder marked by recurrent seizures [2]. Seizure is abnormal electrical activity in the brain, marked by sensory disturbance or loss of consciousness [3]. Epilepsy can be treated by anti-convulsant drugs or surgery. Around 30% of epilepsy patients do not respond to medication. Epilepsy surgery could be an effective candidate for the refractory patients, but it can affect and damage the eloquent area of the cortex [4].The number of seizures can be reduced by responsive neuro-stimulation, which is approved by the Food and Drug Administration (FDA). Another approach is drug injection directly into the target area [5], [6], [7], [8]. Studies find that the drug injection into the epileptegenic zone increases the efficacy of the medication, and it can be used as an effective tool for controlling seizure.

EEG signals are used with the proposed iDDS, which mainly consists of two units: the seizure detection unit and the drug delivery unit. Seizure detection consists of a Neighborhood Component Analysis (NCA) unit, a feature extraction unit, and a DNN classifier unit. The drug delivery unit consists of two reservoirs, an actuator element, and a valveless micropump. The detection unit analyzes input EEG signals and detects seizure. Once a seizure occurs, the drug delivery unit injects anti-convulsant drug into the onset area for the termination of seizure progression. The inclusion of the Internet of medical things (IoMT) with the proposed framework helps to enhance remote healthcare monitoring and data recording. The proposed system has been conceptually depicted in Fig. 1.

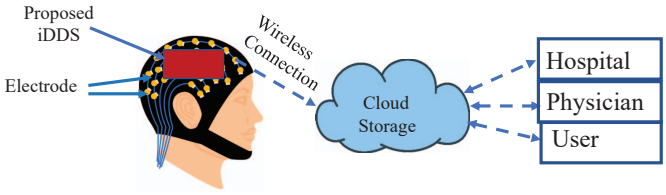

Fig. 1: Modules of the Proposed System

The paper is organized as follows: Section II discusses the novel contributions. Related prior research on drug delivery systems is presented in Section III. Section IV illustrates the proposed architecture of the seizure detection and drug delivery system. The simulation results of the proposed design are discussed in Section V. The paper concludes in Section VI.

II. Novel Contributions of The Current Paper

1) A piezoelectric actuated double reservoir micropump has been introduced. If one reservoir does not work due to insufficient drugs or hardware problems, the other reservoir will become active, which enables continuous release of the drug. The double reservoir also increases the holding capacity and improves the lifetime of the DDS.

2) The proposed system provides a considerable reduction in power consumption, and increased detection accuracy making it suitable for use as a wearable or implantable device for seizure detection and control through drug delivery.
3) The proposed system reduces latency, while increasing sensitivity, making it a potential candidate for the use as a low latency implantable device for practical biomedical applications.

III. Different Methods for Seizure Control

Several methods for epileptic seizure control exists as presented in Fig. 2. Other than antiepileptic drugs and surgery, several alternative methods [2], [3], [4], [9] have been proposed to control drug resistant epilepsy such as: vagus nerve stimulation, deep brain stimulation, responsive neurostimulation (RNS), external nerve stimulation, subthreshold stimulation, and drug delivery. Seizure control through stimulation demonstrates potential for the treatment of epilepsy, but a significant portion of drug-resistant patients do not respond to stimulation. A recent work shows that RNS can be effective if the prediction of seizure is accurate [2]. Seizure control through drug delivery presents promising results, as direct drug injection into the target area improves the efficiency of the drugs. A unified and closed loop drug delivery system [9] has been proposed in which seizures have been detected through an asynchronous front end detector and the drug injection has been performed by micropump. The proposed unified system offers reduced power consumption. Embrace2 [10], a seizure detecting smartwatch, recently was approved by the Food and Drug Administration (FDA), and can detect generalized tonic-clonic seizures and alert the user immediately.

An IoT based unified drug delivery system [6] has been proposed using a machine learning classifier and an electromagnetic actuated micropump. The single reservoir associated with the electromagnetic micropump injects the required dosage once a seizure occurs. We also presented a unified seizure detection and control system in [5], which has a piezoelectric micropump. The current paper presents a double reservoir drug-delivery system with a piezoelectric actuated valveless micropump. Such a system can serve as fault-tolerant as well as provide better seizure control in the IoMT framework. The proposed system was validated with a scalp EEG dataset instead of the previously used icEEG dataset.

IV. Proposed drug delivery system - iDDS

The input EEG signals are pre-processed through a band pass filter. The redundant channels have been eliminated from the filtered signals using neighborhood component analysis (NCA). A DNN classifier analyzes the extracted features and detects the seizure in real time. Once a seizure detection is complete, the double reservoir micropump injects the required drug into the epileptogenic area to disrupt seizure propagation. The architecture and flowchart of the proposed drug delivery system (iDDS) are shown in Fig. 3 and Fig. 4, respectively.

A. Seizure Detection subsystem

This paper is focused on seizure control and an existing approach [11] has been considered for seizure detection. Fig. 5 shows the architecture of the proposed real time seizure detection system. EEG signals are fed to a band pass filter, which eliminates unwanted noise. NCA removes insignificant channels and only keeps the desired ones. The EEG signals have been equally divided to windows of length 6 sec. each. The moving window consists of three non-overlapping segments of length 2 sec. The arithmetic mean and standard deviation are extracted from each segment, and once the feature extraction is complete for a window, it moves to next window. This process repeats and forms the training and testing vector. Off-line, the classifier is trained with the training vector and in the detection phase, the testing vector from the moving window is continuously applied to the classifier. Once the classification of the current window is complete, the classifier moves to the next window. This process continues and becomes viable for real time seizure detection.

B. Drug delivery subsystem

Currently a significant portion of biomedical research is focused on developing microfluidic systems for controlling small fluid volume. Micropumps have been a useful tool for this application, as they provide accurate flow control. Microumps can be categorized based on the actuation mechanisms, such as: piezoelectric (PZT), electro-osmotic, electromagnetic, and electrostatic. In this work, a valveless piezoelectric micropump is used for the drug delivery [5]. The piezoelectric mechanism renders higher actuation force, which leads to a higher deflection and faster response [12]. The elimination of inlet and outlet valves makes the micropump reliable and simplified in structure [13], [14], [6]. The pumping mechanism functions in two modes: the supply mode and the pumping mode. In the supply mode, the piezoelectric actuator deflects the diaphragm and drug flows through the inlet to the pump chamber, which increases the volume of the pump chamber. In the pumping mode, the volume of the pump chamber decreases, which enables the flow of drug to the outlet from the pump chamber. In the supply mode, the inlet element acts as a diffuser, whereas, in the pumping mode, the outlet element works as a diffuser, considering higher pressure loss in the nozzle direction. Once a moving window is classified as a seizure, the actuator unit is turned on. The applied voltage across the piezoelectric disc deflects the diaphragm, and leads to the pumping action. The supply mode increases the volume of the pump chamber and the pump mode reduces the volume. A primary reservoir supplies the drug dosages. If the volume of the drug at the primary reservoir is lower than the threshold value, the secondary reservoir become active and provides the required drug dosages. The drug flow can be obtained from the diffuser/nozzle geometry and other operating conditions, and finally, the required drug dosage is injected into the target area for effective treatment.

1) Design of the valveless micropump: Figure 6 shows the schematic diagram of the proposed valveless micropump

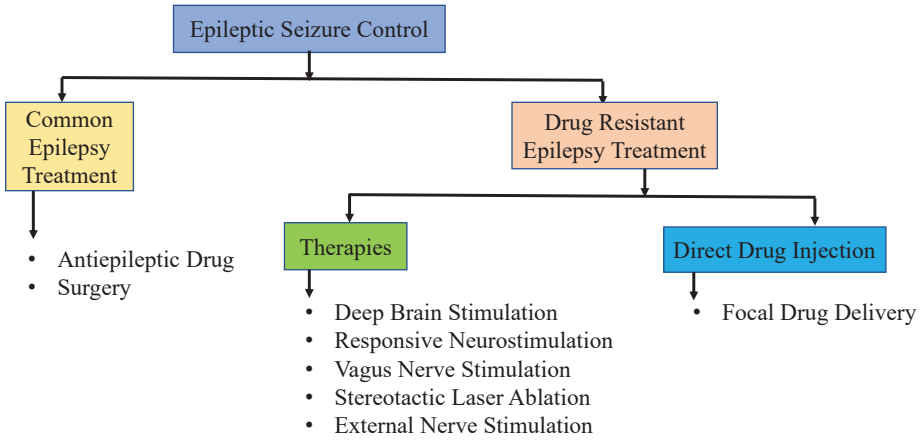

Fig. 2: Various Methods for Seizure Control.

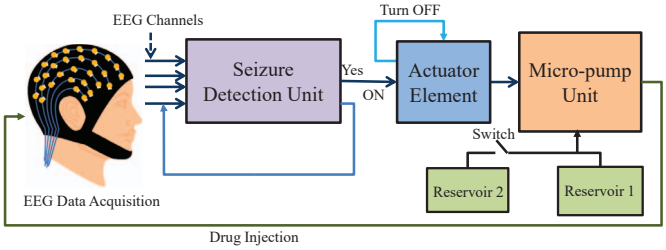

Fig. 3: Architecture of The Proposed Drug Delivery System.

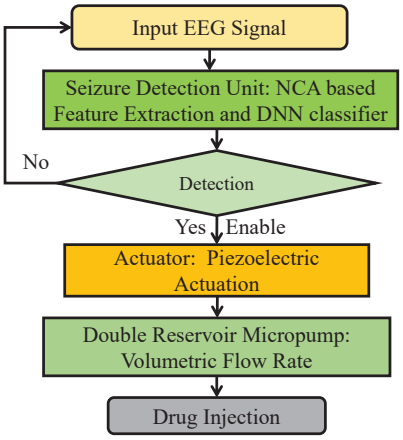

Fig. 4: Working Flow of The Proposed Drug Delivery System.

[14], [15]. Figure 7 shows the flowchart of the drug injection operation. The diaphragm is attached to the PZT disc. In this micropump, the diaphragm is operated by piezoelectric actuation. An applied electric field across the piezoelectric disc moves the diaphragm in the vertical direction, which leads to the pumping action. The drug flow rate depends on the stroke volume which is a function of the oscillatory motion of the diaphragm. The required displacement can be obtained by applying voltage to the actuator [12], [14]. Stainless steel is a useful material because of its bio-compatibility and excellent corrosion resistance, hence it is widely used for building pump chambers. The dimensions of the pump chamber and the actuator are designed to provide the maximum flow rate to effectively address the healthcare problems. The diaphragm displacement has a proportional relationship with the applied driving voltage. The driving voltage can be obtained by DC to AC conversions and amplifications. The DC supply voltage is 5 V and the driving output voltage is 20 V.

2) Model of the double reservoir micropump: The displacement X of the diaphragm is a function of the tensile properties of the material (Young modulus E), and its geometry, namely its thickness t_d and radius R. It ts also dependent on the applied force F by the piezoelectric actuator which is proportional to the applied voltage [15], [5]:

$$X = \frac{0.55R^2F}{Et_d{}^3}, \tag{1}$$

Once the diaphragm displacement X is known, the flow volume V_{str} is represented by the cylinder volume which is expressed as [5]:

$$V_{str} = \left(\frac{2\pi}{3}\right) XR^2. \tag{2}$$

The overall volume flow Q depends on the pump frequency f and a factor η depending on pressure loss across the nozzle and diffuser [16]:

$$Q = 2V_{str} f \frac{\sqrt{\eta} - 1}{\sqrt{\eta} + 1}, \tag{3}$$

and

$$\eta = \left(\frac{\epsilon_{noz}}{\epsilon_{dif}}\right), \tag{4}$$

where ϵ_{noz} and ϵ_{dif} are the pressure loss coefficients across the nozzle and diffuser, respectively [17].

If we assume two reservoirs R1 and R2 connected in series with a switch S1, the volume of each reservoir is given by:

$$V_{ri} = \pi r^2 h, \tag{5}$$

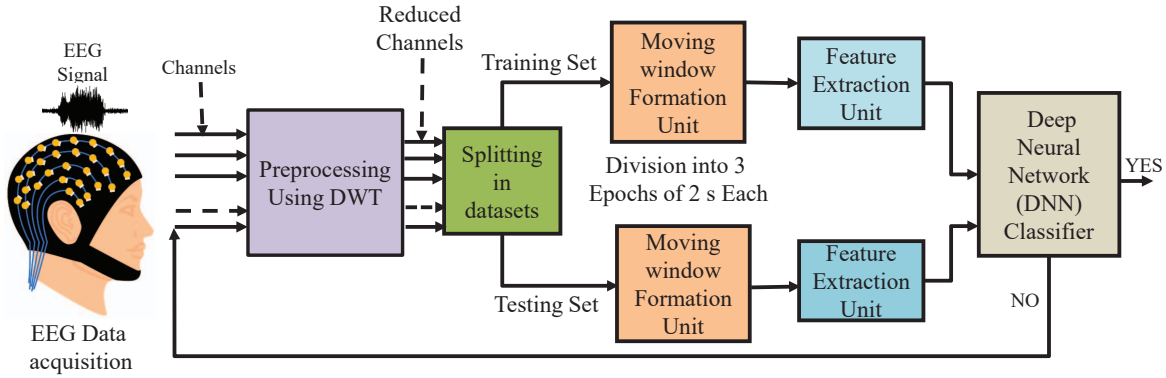

Fig. 5: Real Time Seizure Detection

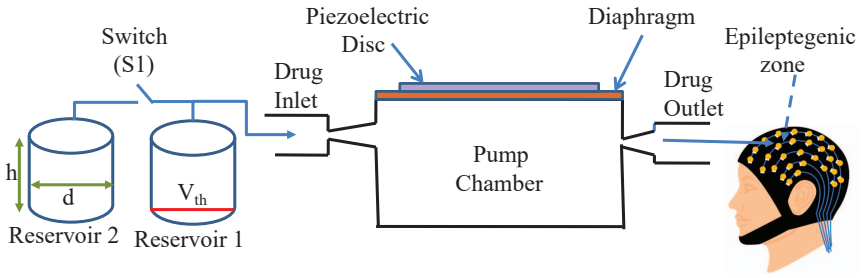

Fig. 6: A Valveless Micropump Explored for Use in iDDS

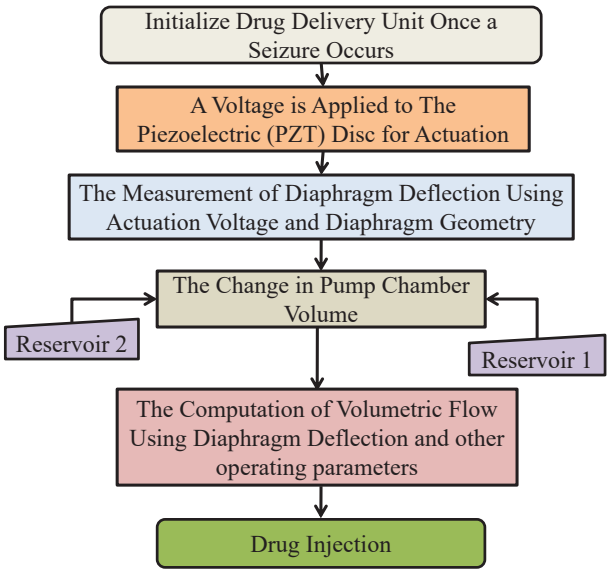

Fig. 7: The Steps for Drug Injection in iDDS.

where $i = 1, 2$ denotes the reservoir, D is its diameter, h is its height and $r = d/2$ is its radius. R1 is the primary reservoir and R2 is the secondary reservoir. A reservoir is considered empty if its volume drops beneath a threshold value V_{th}. Initially switch S1 is closed, thus providing drug from R1. If, at a later time $V_{r1} < V_{th}$, S1 opens disconnecting R1 from the system. At this point, the drug is pumped from R2.

V. Experimental Results

Fig. 8 shows the system level implementation of the proposed iDDS. The CHB-MIT scalp database [18] was used for validation. Epileptic subjects (chb01, chb02, chb03, and chb05), containing one hour of continuous EEG were taken into consideration. The data is sampled at a 256 Hz. Initially EEG signals were pre-processed through a band pass filter of frequency range 0-32 Hz. The filtered signals were analyzed and the significant channels were selected using NCA. A 10-fold cross validation was used to determine minimum loss which corresponds to the best λ. For epileptic subject1 chb01, the best lambda was $\lambda = 0.000264$. The following 8 channels were determined as significant channels where the channel weight is greater than the threshold value: (1) F7-T7 (2), P7-O1 (3), FP1-F3 (4), FP2-F8 (5), F8-T8 (6), FZ-CZ (7), T7-FT9 (8), FT9-FT10 (21).

At a 256 Hz sampling rate, the 6 sec. moving window comprised of 1536 points. The moving window was further subdivided into 3 non-overlapping epochs of 2 sec. each, each subdivision consisting of 512 points. Two features were extracted from the three subdivisions, and as a result, the moving window consists $8 \times 3 \times 2 = 48$ elements. The DNN classifier was trained with 2-4 hours of interictal data and 0.5-1 hour of normal EEG. The DNN classifier reported a sensitivity of 100% for two hidden layers with 10 neurons in each layer. The number of hidden layers as well as the number of neurons were determined by trial and error. It is observed that a sharp increase in hidden layers or neurons affects the performance

of the classifier. The average detection delay was measured as 1.8 sec. Fig. 9 shows the variation of detection delay for different epileptic subjects. The seizure detection subsystem is characterized in Table I.

TABLE I: Characterization of the seizure detection subsystem

Parameter	Value
Sampling frequency	256 HZ
Band pass filter's frequency range	0-32 HZ
No. of Hidden Layers	2
No. of neurons/Layers	10
Sensitivity	100 %
Latency	1.802 sec

TABLE II: Characterization of the drug delivery subsystem

Parameters	Value
Piezoelectric (PZT) disc diameter	9 mm
Piezoelectric (PZT) disc thickness	150 μm
Membrane diameter	10 mm
Membrane thickness	100 μm
Young modulus (PDMS)	0.8 MPa
Possions ratio	0.49
Fluidic diodicity (η)	2
Liquid density	1000 kg/m^3

TABLE III: Characterization of the drug delivery system

Parameter	Value
Input voltage	5 V
Divergence angle (Diffuser)	10°
Frequency	130 Hz
Power Consumption	$\approx$ 29 mW
Volume flow	3.08 ml/min

The optimal divergence angle of the diffuser element was computed to be 10°. It is observed that the net volume flow has a quadratic relationship with the diaphragm diameter, as an increase in the diameter quadratically increases the net flow rate. However, the increase in chamber diameter increases the dead volume, which is undesirable for on-chip biomedical applications. Considering all these, the diameter of the pump chamber was chosen as 10 mm. Table II characterizes the drug delivery unit. Polydimethylsiloxane (PDMS) was chosen as a diaphragm membrane because of its lower Young Modulus. The diaphragm thickness is an important parameter for obtaining maximum flow rate. An increase in thickness of the diaphragm reduces the volumetric flow rate. The diaphragm thickness was chosen as 100 μm. Fig 10a. shows the variation of net flow rate with diaphragm diameter at a fixed diaphragm thickness of 100um. The change in the flow rate with actuation frequency is shown in Fig. 10b. The proposed design reports a maximum flow rate of 3.08 ml/min. A pattern independent method has been adopted to measure the power consumption, and the total power consumption has been calculated as $\approx$ 29 mW. ThingSpeak, an open data platform was used for the implementation of IoT. Table III characterizes the drug delivery system. Table IV shows a comparison with existing systems.

VI. Conclusions and Future Research

In this paper, an automated and unified drug delivery system has been proposed in the IoT platform. The validation with MIT scalp datasets demonstrates that the proposed system reduces latency considerably, which is essential for effective seizure control. A double reservoir mechanism improves the lifetime, making it a viable tool for practical biomedical applications. Simulation results also show that proposed system offers reduced power consumption. Future research includes developing an embedded chip by advanced integrated circuit technologies and testing on an animal model of epilepsy.

Our future research of this work will involve the integration of security in drug delivery system to ensure that no hacker can trigger the device or alter the flow rate as it is a IoMT enabled device [22], [23], [24]. We intend to explore both Physical Unclonable Function (PUF) based security as well as blockchain based security and compare their applicability for implantable medical devices (IMD).

References

[1] P. Sundaravadivel, E. Kougianos, S. P. Mohanty, and M. K. Ganapathiraju, "Everything You Wanted to Know about Smart Health Care," *IEEE Consumer Electronics Magazine*, vol. 7, no. 1, pp. 18–28, Jan 2018.

[2] C. Liu, X.-W. Wen, Y. Ge, N. Chen, W.-H. Hu, T. Zhang, J.-G. Zhang, and F.-G. Meng, "Responsive neurostimulation for the treatment of medically intractable epilepsy," *Brain Research Bulletin*, vol. 97, pp. 39 – 47, 2013.

[3] P. Boon, "Electrical Stimulation for the Treatment of Epilepsy," *Neurotherapeutics*, vol. 6, no. 2, pp. 218–27, 2009.

[4] W. H. Theodore and R. S. Fisher, "Brain Stimulation for Epilepsy," *Neurology*, vol. 3, no. 8, pp. 111–8, 2004.

[5] M. A. Sayeed, S. P. Mohanty, and E. Kougianos, "cSeiz: An Edge-Device for Accurate Seizure Detection and Control for Smart Healthcare," *arXiv preprint*, vol. arXiv:1908.08130, 2019.

[6] M. A. Sayeed, S. P. Mohanty, E. Kougianos, and H. Zaveri, "An IoT-based Drug Delivery System for Refractory Epilepsy," in *Proc. IEEE Int. Conf. Consum. Electron. (ICCE)*, Las Vegas, NV, 2019, pp. 1–4.

[7] M. A. Sayeed, S. P. Mohanty, E. Kougianos, and H. P. Zaveri, "iDDS: An IoT based System for Refractory Epilepsy in Smart Healthcare," Abstract, IEEE MetroCon 2018 Conference, Arlington Convention Center, TX., November 07, 2018.

[8] I. L. Olokodana, S. P. Mohanty, E. Kougianos, and M. Manzo, "Towards Photonic Sensor based Brain-Computer Interface (BCI)," in *Proc. IEEE International Smart Cities Conference (ISC2)*, Sep. 2018, pp. 1–5.

[9] M. T. Salam, M. Mirzaei, M. S. Ly, D. K. Nguyen, and M. Sawan, "An Implantable Closedloop Asynchronous Drug Delivery System for the Treatment of Refractory Epilepsy," *IEEE Trans. Neural Syst. Rehabil. Eng.*, vol. 20, no. 4, pp. 432–442, July 2012.

[10] "Embrace2: Medical quality technology for epilepsy management," Nov. 2018. [Online]. Available: https://www.empatica.com/embrace2

[11] M. A. Sayeed, S. P. Mohanty, E. Kougianos, and H. P. Zaveri, "Neuro-Detect: A Machine Learning Based Fast and Accurate Seizure Detection System in the IoMT," *IEEE Transactions on Consumer Electronics*, vol. 65, no. 3, pp. 359–368, August 2019.

[12] S. Singh, N. Kumar, D. George, and A. Sen, "Analytical Modeling, Simulations and Experimental Studies of a PZT Actuated Planar Valveless PDMS Micropump," *Sens. Actuator A-Phys.*, vol. 225, pp. 81 – 94, 2015.

[13] X. He, W. Xu, N. Lin, B. Uzoejinwa, and Z. Deng, "Dynamics Modeling and Vibration Analysis of a Piezoelectric Diaphragm Applied in Valveless Micropump," *J. Sound Vib.*, vol. 405, pp. 133 – 143, 2017.

[14] P. Kawun, S. Leahy, and Y. Lai, "A Thin PDMS Nozzle/diffuser Micropump for Biomedical Applications," *Sens. Actuator A-Phys.*, vol. 249, pp. 149 – 154, 2016.

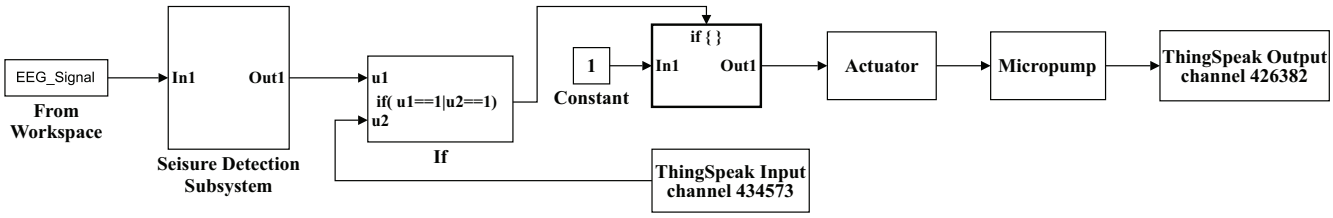

Fig. 8: Simulink® Model of The Proposed Drug Delivery System (DDS).

TABLE IV: Comparison with existing systems

Existing Works	Seizure Detection Method	Sensitivity	Latency	Drug Delivery Unit	Power Consumption on DDS[b]
Altaf, et al. 2015 [19]	Linear Support vector machines (LSVM)	95.7 %	1 sec	X	X
Vidyaratne, et al. 2017 [20]	Fractal dimension (FD), Relevance vector machine (RVM)	96.0 %	1.89 sec	X	X
Sayeed, et al. 2019 [21]	Signal rejection algorithm (SRA)	96.8 %	3.6 sec	X	X
Sayeed, et al. 2019 [6]	κ-NN classifier and statistical feature extraction	98.6 %	X	Electromagnetic actuated micropump	12.81 mW
Our Proposed System	Deep neural network (DNN) classifier	100.0 %	1.8 sec	PZT based double reservoir micropump	$\approx$ 29 mW

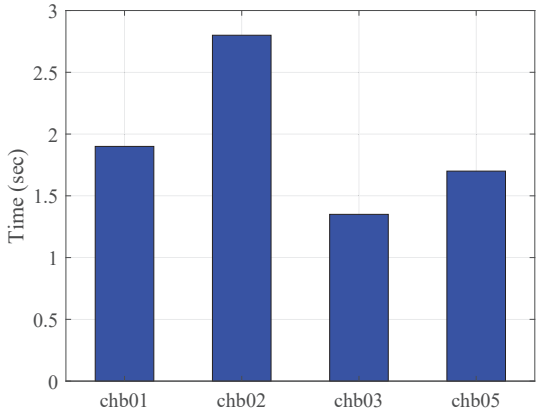

Fig. 9: Variation of Latency for Different Epileptic Subjects

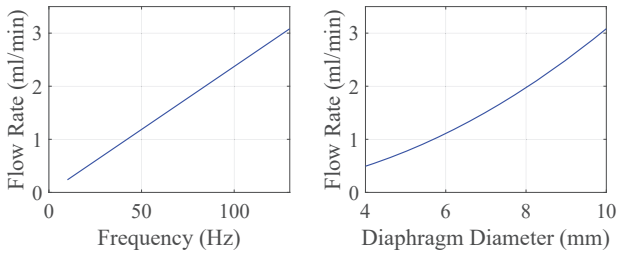

Fig. 10: Volumetric Flow Rate as a Function of (a) Actuation Frequency (b) Diaphragm Diameter.

[15] N. Ramaswamy, N. Karanth, S. Kulkarni, and V. Desai, "Modeling of micropump performance and optimization of diaphragm geometry," *IJCA Proc. Int. Symp. Devices MEMS, Intell. Syst. Commun. (ISDMISC)*, no. 5, pp. 14–19, 2011.

[16] A. Olsson, G. Stemme, and E. Stemme, "A Valve-less Planar Fluid Pump With Two Pump Chambers," *Sens. Actuator A-Phys.*, vol. 47, no. 1-3, pp. 549–556, 1995.

[17] E. Stemme and G. Stemme, "A Valveless Diffuser/nozzle Based Fluid Pump ," *Sens. Actuator A-Phys.*, vol. 39, no. 2, pp. 159–167, 1993.

[18] A. L. Goldberger, "PhysioBank, PhysioToolkit, and PhysioNet: Components of a new research resource for complex physiologic signals," *Circulation*, vol. 101, no. 23, pp. e215–e220, Jun. 2000.

[19] M. A. B. Altaf, C. Zhang, and J. Yoo, "A 16-Channel Patient-Specific Seizure Onset and Termination Detection SoC With Impedance-Adaptive Transcranial Electrical Stimulator," *IEEE J. Solid-State Circuits*, vol. 50, no. 11, pp. 2728–2740, Nov. 2015.

[20] L. S. Vidyaratne and K. M. Iftekharuddin, "Real-Time Epileptic Seizure Detection Using EEG," *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, vol. 25, no. 11, pp. 2146–2156, Nov 2017.

[21] M. A. Sayeed, S. P. Mohanty, E. Kougianos, and H. P. Zaveri, "eSeiz: An Edge-Device for Accurate Seizure Detection for Smart Healthcare," *IEEE Transactions on Consumer Electronics*, vol. 65, no. 3, pp. 379–387, August 2019.

[22] V. P. Yanambaka, S. P. Mohanty, E. Kougianos, and D. Puthal, "PMsec: Physical Unclonable Function-Based Robust and Lightweight Authentication in the Internet of Medical Things," *IEEE Transactions on Consumer Electronics*, vol. 65, no. 3, pp. 388–397, Aug 2019.

[23] S. P. Mohanty, V. P. Yanambaka, E. Kougianos, and D. Puthal, "PUFchain: Hardware-Assisted Blockchain for Sustainable Simultaneous Device and Data Security in the Internet of Everything (IoE)," *arXiv Computer Science*, vol. 1909.06496, Sep 2019.

[24] D. Puthal, S. P. Mohanty, P. Nanda, E. Kougianos, and G. Das, "Proof-of-Authentication for Scalable Blockchain in Resource-Constrained Distributed Systems," in *Proceedings of IEEE International Conference on Consumer Electronics (ICCE)*, Jan 2019, pp. 1–5.