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IN VIVO NETWORKING (IVN): NEED OF PRESENT ERA.

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ABSTRACT

The emerging in vivo communication and networking system is a prospective component in advancing healthcare delivery and empowering the development of new applications and services. In vivo communications is based on networked cyber-physical systems of embedded devices to allow rapid, correct and cost- effective responses under various conditions. IVN overcomes fundamental challenges which have prevented past systems from powering up miniature sensors beyond superficial depths. These challenges include the significant signal attenuation caused by bodily tissues and the miniature antennas of the implantable sensors. This chapter presents the existing research which investigates the state of art of the in vivo communication. In this article attempt is done to throw a light on concept and method of in vivo communication technique. It focuses on characterizing and modeling the in vivo wireless channel and contrasting it with the other familiar channels. Furthermore, this article addresses in vivo nano communication which is presented for medical applications to provide fast and accurate disease diagnosis and treatment. Such communication paradigm is capable of operating inside the human body in real time and will be of great benefit for medical monitoring and medical implant communications.

KEYWORDS: In vivo communication, IVN in vivo, nano-communication, Miniature antenas.

INTRODUCTION

Oral controlled release dosage forms can provide efficacy for about 24 hours. The main drawback of oral dosage form is the long transit time of approximately 12hours through the gastrointestinal tract (GIT). If drug cannot be administered orally, a parenteral route of delivery is an alternative.

Many proteins/peptides and other drugs, which are susceptible to the adverse conditions of GIT, are action is short for majority of therapeutically active administered intravenously. Unfortunately, in intravenous drug administration, the duration of drug action is short for majority of therapeutically active agents and therefore frequent injections are required.

The development of injectable controlled-release dosage forms is more likely to succeed commercially than alternative routes of delivery, assuming that these dosage forms provide the desired efficacy and safety.

Implantable drug delivery devices are devoid of aforementioned limitations associated with oral, intravenous, topical drug administration vis-à-vis subcutaneously implantable drug delivery devices offer one unique advantage of a retrievable mechanism.

There is significant interest in bringing wireless networking capabilities to an emerging breed of in-vivo sensors and actuators.[1] (In contrast to traditional implantable medical devices such as cardiac pacemakers, are relatively large and have their own batteries)

These new devices need to be much smaller. They are swallowed or injected into the human body and used for:-

- Decoding brain circuits
- Delivering drugs
- Monitoring internal human vital signs

Despite the attention that these devices have received from the biomedical community, their networking capabilities are still very limited. This owes primarily to the very low power budget of these devices as well as their miniature form factor and biocompatibility requirements, which preclude incorporating batteries. The IVN presents a system that enables powering up and communicating with in-vivo battery-free biosensors and bio actuators.

IVN introduces a multi-antenna technique to remotely power up millimeter-sized in-vivo sensors and communicate with them.

Wireless Body Area Networks (WBANs) are a new generation of Wireless Sensor Networks (WSNs) dedicated for healthcare monitoring applications. The aim of these applications is to ensure continuous monitoring of the patients' vital parameters, while giving them the freedom of moving thereby resulting in an enhanced quality of health care. The aim of these applications is to ensure continuous monitoring of the patients vital parameters, while giving them the freedom of moving thereby resulting in an enhanced quality of healthcare. In fact, a WBAN is a network of wearable computing devices operating on, in, or around the body. It consists of a group of tiny nodes that are equipped with biomedical sensors, motion detectors, and wireless communication devices.[2]

The in vivo channel is a new frontier in wireless propagation and communications, compared to well-studied wireless environments such as cellular, WLAN, and deep-space. Characterizing in vivo wireless propagation is critical in optimizing communications and requires familiarity with both the engineering and the biological environments. Owing to the highly dispersive nature of the in vivo channel, achieving stringent performance requirements will be facilitated by the use of multiple-input multiple-output (MIMO) communications to achieve enhanced data rates. One potential application for MIMO in vivo communications is the MARVEL (Miniature Anchored Remote Video scope for Expedited Laparoscopy)[3] which is a wireless research platform for advancing MIS (Minimally Invasive Surgery) that requires high bit rates (~80–100 Mbps) for high-definition video transmission with low latency during surgery.[4] Actually, advanced health care delivery relies on both body surface and internal sensors since they reduce the invasiveness of a number of medical procedures.[5] Sensors such as those shown in Fig. 1 transmit data to monitoring devices of the hospital Information Technology (IT) infrastructure. Electrocardiogram (ECG), electroencephalography (EEG), body temperature, pulse oximetry (SpO2), and blood pressure are evolving as long-term monitoring sensors for emergency and risk patients.[4] Actually, advanced health care delivery relies on both body surface and internal sensors since they reduce the invasiveness of a number of medical procedures.[5] Sensors such as those shown in Fig. 1 transmit data to monitoring devices of the hospital Information Technology (IT) infrastructure. Electrocardiogram (ECG), electroencephalography (EEG), body temperature, pulse oximetry (SpO2), and blood pressure are evolving as long-term monitoring sensors for emergency and risk patients.[6,7]

One attractive feature of the emerging Internet of Things is to consider in vivo networking for WBANs as an important application platform that facilitates continuous wirelessly-enabled healthcare.[8,9] In vivo communication, also known Fig. 1. Sensor network of biomedical monitoring applications. As Intra Body Communication (IBC), uses the human body to transmit electrical signals, where the radiated energy is mostly confined within the body.[10]

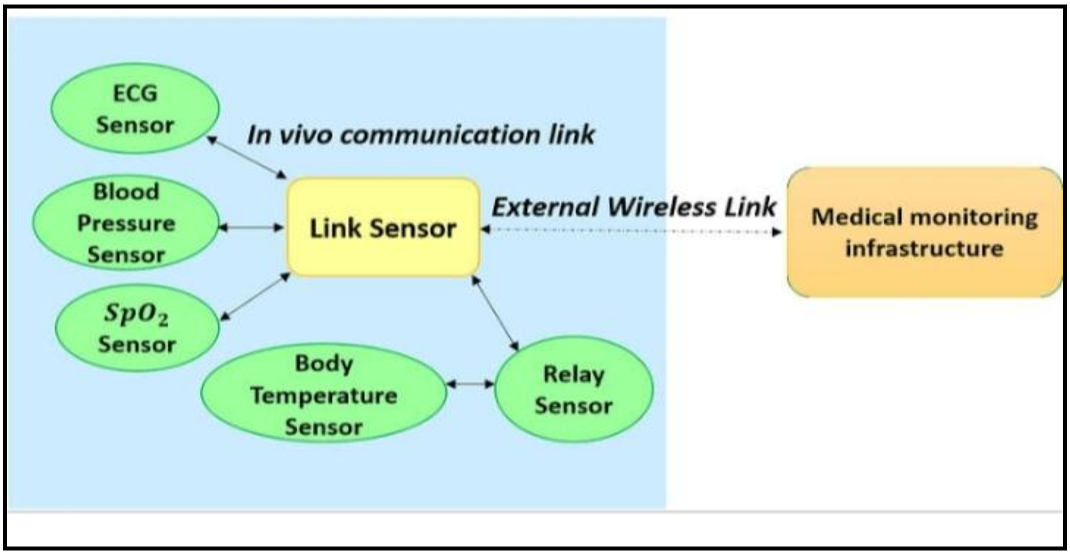

Fig. 1: Simplified overview of the in vivo communication network.

STATE OF ART OF IN VIVO COMMUNICATION

In vivo communication is a genuine signal transmission field which utilizes the human body as a transmission medium for electrical signals.[11] The body becomes a vital component of the transmission system. Electrical current induction into the human tissue is enabled through sophisticated transceivers while smart data transmission is provided by advanced encoding and compression. Fig.2 below shows the main components of an in vivo communication link.

A transmitter unit permits sensor data to be compressed and encoded. It then conveys the data by a current-controlled coupler unit. The human body acts as the transmission channel. Electrical signals are coupled into the human tissue and distributed over multiple body regions. On the other hand, the receiver unit is composed of an analog detector unit that amplifies the induced signal and digital entities for data demodulation, decoding, and extraction.[7]

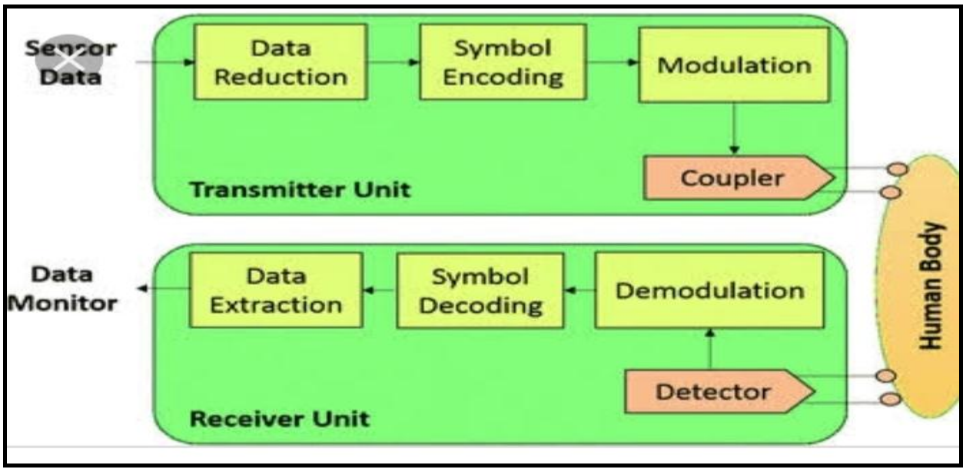

Fig. 2: In vivo communication for data transmission between sensors enabled by transmitter and receiver units.

CHARACTERIZATION OF THE IN VIVO CHANNEL

Understanding the characteristics of the in vivo channel is necessary to optimize in vivo physical layer signal processing and communications techniques, and designing efficient networking protocols that ultimately will make possible the deployment of wireless body area networks and remote health monitoring platforms in the in vivo environment. The characteristics of the in vivo channels are significantly different than those of classical wireless cellular and WiFi systems.[12,13,14] There are many challenges in characterizing the in vivo channel. Firstly, the in vivo environment is an inhomogeneous and very lossy medium. Secondly, the far field assumption used to develop channel models for classical RF wireless communication systems is not always valid for the in vivo environment. Finally, additional factors need to be considered, such as near-field effects and highly variable propagation speeds through different organs and tissues. Researcher's long-term research goal is to model the in vivo wireless channel, including building a phenomenological path loss model and validating the path loss, angular dependency, and fading characteristics.[15]

Basically, in an in vivo channel, the electromagnetic wave passes through various dissimilar media that have different electrical properties, as displayed in Fig. 3. This leads to the reduction in the wave propagation speed in some organs and the stimulation of significant time dispersion that differs with each organ and body tissue.[16]

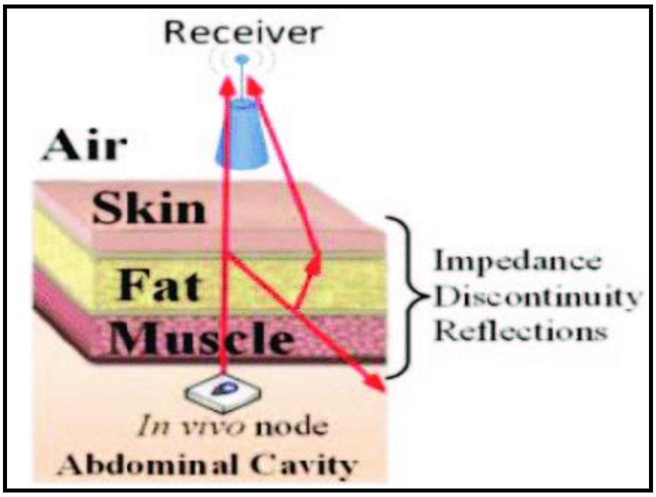

Fig. 3: In vivo multi-path channel.[3]

ADVANTAGES OF IVN

1. Mobility

Monitor patients' vital parameters; while giving them the opportunity of moving-in thereby bringing about an improved nature of healthcare.

2. Long-term monitoring

Keeps track of patients' health over a period of time and reacts accordingly. For example, Absence or insufficient production of insulin, or an inability of the body to properly use insulin causes diabetes. IVN can be used to monitor blood sugar levels and can be used to trigger the pancreas to release insulin to lower blood glucose.

3. Complex monitoring

During critical surgeries and medical examinations patients, health or organ conditions may change and monitoring during this time is crucial. With the help of In Vivo networks potential risks can be reduced.

4. Internal drug administration

The route of drug administration is important since it affects drug metabolism, drug clearance, and thus dosage. By placing the device inside a smart pill and managing the controlled delivery of the drug can cure diseases faster and more efficiently. Fig 3 shows path to internal drug administration using IVN.

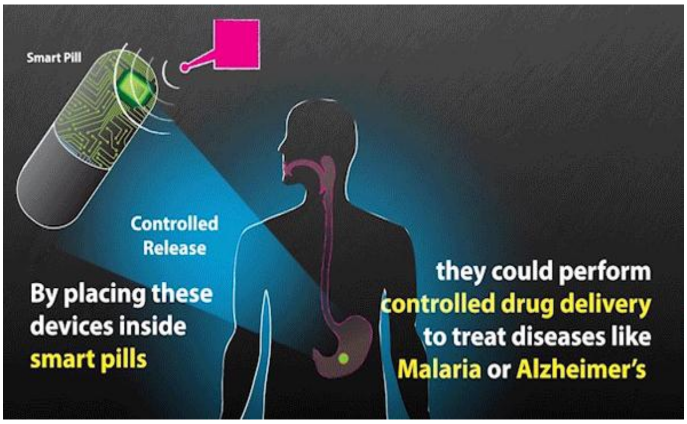

Fig-3: Internal drug administration using IVN.

5. A cure for Brain Disorders

IVN can be integrated with neurostimulators, implanted inside the brain to perform deep brain stimulation to treat diseases like Parkinson's, epilepsy and Alzheimer's disease. It can also control neural circuits through optogenetics manipulation.[17]

DISADVANTAGES OF IVN[18]

1. **Tissue warming:** There is a direct relationship between frequency and tissue warming in which the higher the frequency of the electromagnetic signal, the higher is its absorption bythe tissue, thereby the greater the tissue warming.
2. **Variation in energy consumption:** Because of the diversity found in the human body including fluids, fats, bones, and muscles, variation in energy absorption exists coupled with the possibility of tissue damage due to heating by radiation
3. **Biocompatibility:** any sensor must not only be biologically inert but also it should not perturb the normal biology it's interrogating.

CHALLENGES OF IVN

1. Low-latency wireless communications and networking
2. Electronic and mechanical miniaturization of complex systems
3. Localization and mapping of the intra-body camera unit and surrounding organs and tissues (*How can IVN power up and communicate with these devices when they have no batteries?*

- transmits wireless signals and reach the tiny implanted sensor
- uses multiple antennas
- uses a sophisticated signal generation technique that allows the signals to combine constructively at the sensors.[19]

IN VIVO NANO COMMUNICATION

Nanotechnology opens the door towards a new communication paradigm that introduces a variety of novel tools. This technology enables engineers to design and manufacture nanoscale electronic devices and systems with substantially new properties.[20] These devices cover radio frequencies in the Terahertz (THz) range and beyond, up to optical frequencies. The interconnections of Nano devices build up into Nano networks enabling a plethora of potential applications in the biomedical, industrial, environmental and military fields. A number of challenges exist in the creation of in vivo Nano sensor networks, which range from the development of nanoantennas for in vivo operation to the characterization of the intra-body channel environment from the nanosensor perspective.[21] In order to develop in vivo wireless nanosensor networks (iWNSNs), plas monic nanoantennas for intra-body communication must be utilized.[22]

COMPARISON BETWEEN EX VIVO AND IN VIVO COMMUNICATIONS

The different characteristics between ex vivo and in vivo channels are summarized in[13] as shown in Table 1 below.

Sr. no	feature	Ex vivo	In vivo
1	Physical wave propagation	Constant speed, multipath reflection. scattering and diffraction	Variable speed, multipath and penetration
2	Attenuation and path loss	Lossless medium, decreases inversely with distance.	Very lossy medium, Angular (direction) dependent
3	Dispersion	Multipath delays time dispersion	Multipath delays of variable speed frequency dependency time dispersion
4	Directionality	Propagation essentially uniform	Propagation varies with direction. Directionality of antennas changes with position.
5	Near field communication	Deterministic near field region around antenna	Inhomogeneous near field region changes with angel and position inside the body.
6	Power limitations	Average and peak	Plus specific absorption rate.(SAR)
7	Shadowing	Follows a long normal distribution	To be determined.
8	Multipath fading	Flat fading and frequency selective fading	To be determined.
9	Antenna Gains	constant	Angular and position dependent. Gains highly attenuated.
10	Wavelength	The speed of light in free space divided by frequency.	$\lambda = c/\sqrt{\in} rf$ At 2.4GHz average dielectric constant =35.which is roughly 6 times than the wavelength in free space

FUTURE DIRECTIONS

The major future research direction focuses on investigating high throughput, efficient, and robust novel networking technologies that enable reliable information transmission between devices. In order to achieve a system with such specifications, great focus should be spent on architecting, realizing and networking a family of wirelessly controlled in vivo devices. The first aspect that should be regarded in order to ensure improved future in vivo communication is frequency. Indeed, the frequency range selected for such communications plays a significant role in the design and performance of the system. Actually, there is a direct relationship between frequency and tissue warming in which the higher the frequency of the electromagnetic signal, the higher is its absorption by the tissue, thereby the greater the tissue warming. Thus, it is favorable to use lower frequencies for communications. Yet, the lower the frequency, the larger the antenna dimensions. As a result, a tradeoff between antenna dimensions and greater tissue warming should be achieved.[23] Moreover, limitations exist when transmitting at high frequencies from in vivo devices to ex vivo transceivers since the maximum transmit power is restricted by the SAR safety guidelines.[22]

As a result of the diversity found in the human body including fluids, fats, bones, and muscles, variation in energy absorption exists coupled with the possibility of tissue damage due to heating by radiation. Such issues result in complicating the design of biosensors and biosensor networks; therefore, careful attention must be paid in future work to overcome 2015 Loughborough Antennas & Propagation Conference (LAPC) such limitations.[22] Finally, testing using real animals to validate the simulation results is one of the fundamental research directions[23] in addition to hardware emulation with human body phantoms.

CONCLUSIONS

In this paper, an overview of the in vivo communication and networking is provided. The overview focuses on the state of art of the in vivo communication, the in vivo channel modeling and characterization, and the concept of MIMO in vivo. The paper also discusses few potential research areas covering the development of parametric models and the in-depth study of MIMO in vivo technology. Frequency range, power levels and SAR requirements are few aspects that should be carefully regarded in any upcoming research associated with this field.

REFERENCES

1. P. Honeine, F. Mourad, M. Kallas, H. Snoussi, H. Amoud, and C. Francis, "Wireless sensor networks in biomedical: Body area networks," in Systems, Signal Processing and their Applications (WOSSPA), 2011 7th International Workshop on, May 2011; 388–391.
2. D. Cypher, N. Chevrollier, N. Montavont, and N. Golmie, "Prevailing over wires in healthcare environments: benefits and challenges," Com- munications Magazine, IEEE, April 2006; 44(4): 56–63.
3. C. A. Castro, S. Smith, A. Alqassis, T. Ketterl, Y. Sun, S. Ross, A. Rosemurgy, P. P. Savage, and R. D. Gitlin, "MARVEL: A wireless Miniature Anchored Robotic Videoscope for Expedited Laparoscopy," in 2012 IEEE International Conference on Robotics and Automation (ICRA), 2012; 2926–2931.
4. C. Castro, A. Alqassis, S. Smith, T. ketterl, Y. Sun, S. Ross, A. Rosemurgy, P. Savage, and R. Gitlin, "A Wireless Miniature Robot for Networked Expedited Laparoscopy," IEEE Transactions on Biomedical Engineering, Apr. 2013; 930–936.
5. T. Ketterl, G. Arrobo, A. Sahin, T. Tillman, H. Arslan, and R. Gitlin, "In vivo wireless communication channels," in Wireless and Microwave Technology Conference (WAMICON), 2012 IEEE 13th Annual, April 2012; 1–3.
6. M. S. Wegmuller ¨ et al., "Intra-body communication for biomedical sensor networks," Ph.D. dissertation, Diss., Eidgenossische Technische ¨ Hochschule ETH Zurich, Nr. 17323, 2007, 2007.
7. M. S. Wegmuller ̈et al., "Intra-body communication for biomedical sensor networks," Ph.D. disserM. dissertation, Diss., Eidgen ̈ossische Technische Hochschule ETH Z ̈urich, Nr. 17323, 2007, 2007.
8. C. He, Y. Liu, T. Ketterl, G. Arrobo, and R. Gitlin, "Performance evaluation for mimo in vivo wban systems," in RF and Wireless Technologies for Biomedical and Health- care Applications (IMWS-Bio), 2014 IEEE MTT-S International Microwave Workshop Series on, Dec 2014, pp. 1–3.tation, Diss., Eidgenossische Technische ¨ Hochschule ETH Zurich, Nr. 17323, 2007, 2007.
9. C. He, Y. Liu, T. Ketterl, G. Arrobo, and R. Gitlin, "Performance Evaluation for MIMO In Vivo WBAN Systems," in RF and Wireless Technologies for Biomedical and Healthcare Applications (IMWS-Bio), 2014 IEEE MTT-S International Microwave Workshop Series on, Dec 2014; 1–3.
10. A. Ruaro, J. Thaysen, and K. Jakobsen, Head-Centric Body-Channel Propagation Paths Characterization. IEEE, 2015.

11. T. G. Zimmerman, "Personal Area Networks (PAN): Near-field Intra- Body Communication," Master of Science in Media Arts and Sciences, Massachussetts Institute of Technology, 1995.
12. K. Sayrafian-Pour, W.-B. Yang, J. Hagedorn, J. Terrill, K. Yekeh Yazdandoost, and K. Hamaguchi, "Channel Models for Medical Implant Communication," International Journal of Wireless Information Networks, 2010; 17(3): 105–112.
13. A. Alomainy and Y. Hao, "Modeling and Characterization of Biotelemetric Radio Channel From Ingested Implants Considering Organ Contents," IEEE Transactions on Antennas and Propagation, Apr. 2009; 57(4): 999–1005.
14. D. Kurup, W. Joseph, G. Vermeeren, and L. Martens, "In-body Path Loss Model for Homogeneous Human Tissues," IEEE Transactions on Electromagnetic Compatibility, Jun. 2012; 54(3): 556–564.
15. Y. Liu, T. Ketterl, G. Arrobo, and R. Gitlin, "Modeling the wireless in vivo path loss," in RF and Wireless Technologies for Biomedical and Healthcare Applications (IMWS-Bio), 2014 IEEE MTT-S International Microwave Workshop Series on, Dec 2014; 1–3.
16. C. He, Y. Liu, T. Ketterl, G. Arrobo, and R. Gitlin, "MIMO In Vivo," in Wireless and Microwave Technology Conference (WAMICON), 2014 IEEE 15th Annual, June 2014; 1–4.
17. Carta, r., tortora, g., thone, j., lenaerts, b., valdastri, p., menciassi, a., dario, p., and puers, r. Wireless powering for a self-propelled and steerable endoscopic capsule for stomach inspection. Biosensors and Bioelectronics 25, 4 (2009), 845–851.
18. Charthad, J., weber, M. J., chang, T. C., and arbabian, a. A mm-sized implantable medical device (imd) with ultrasonic power transfer and a hybrid bi-directional data link. IEEE Journal of solid-state circuits 50, 8 (2015), 1741–1753.
19. 19 Chaudhuri, S. K., and lovley, D. R. Electricity generation by direct oxidation of glucose in mediatorless microbial fuel cells. Nature biotechnology 21, 10 (2003), 1229.
20. P. Russer and N. Fichtner, "Nanoelectronics in radio-frequency technology," Microwave Magazine, IEEE, May 2010; 11(3): 119–135.
21. J. M. Jornet, "Fundamentals of plasmonic communication for in vivo wireless nanosensor networks," in 36th Annual International Conference on IEEE Engineering in Medicine and Biology Society (EMBC), Chicago, IL, USA, 2014.
22. Q.-H. Park, "Optical antennas and plasmonics," Contemporary physics, 2009; 50(2): 407–423.

23. L. Schwiebert, S. K. Gupta, and J. Weinmann, "Research challenges in wireless networks of biomedical sensors," in Proceedings of the 7th Annual International Conference on Mobile Computing and Networking, ser. MobiCom '01. New York, NY, USA: ACM, 2001; 151–165. [Online]. Available: http://doi.acm.org/10.1145/381677.381692
24. T. Ketterl, G. Arrobo, and R. Gitlin, "SAR and BER Evaluation Using a Simulation Test Bench for In Vivo Communication at 2.4 GHz," in Wireless and Microwave Technology Conference (WAMICON), 2013 IEEE 14th Annual, April 2013; 1–4.
25. Q. Abbasi, M. Qaraqe, and E. Serpedin, "Numerical characterisation and modeling of in-vivo radio communication," in Biomedical Engineering (MECBME), 2014 Middle East Conference on, Feb 2014; 365–367.