Wireless data transfer for Implanted Real-time Peripheral Nerve Interfaces

Chiara Quartana[1]*, Antonio Coviello[1]*, Paolo Motto Ros[2], Fabiana Del Bono[2], Danilo Demarchi[2], Umberto Spagnolini[1], and Maurizio Magarini[1]

[1] Department of Electronics, Information and Bioengineering, Politecnico di Milano, Piazza L. Da Vinci 32, 20133 Milan, Italy
[2] Department of Electronics and Telecommunications, Politecnico di Torino, Corso Duca Degli Abruzzi 24, 10129 Turin, Italy
*Both authors contributed equally to this research.
`chiara.quartana@mail.polimi.it`
`antonio.coviello@polimi.it`

Abstract. Rapid technological advancements have opened up exciting possibilities for incorporating electronic devices in medical applications, providing solutions to problems and diseases that were previously challenging to address using traditional treatments. This paper presents an optimization of the wireless communication between microcontrollers in the context of a biomedical application. Specifically, the research explores the utilization of Nordic Semiconductor© microcontrollers to establish reliable and efficient communication in real-time between an implanted device and an external unit, leveraging Bluetooth Low Energy (BLE) 5 protocol. To achieve a fast data transmission, careful consideration was given to selecting the optimal parameters for the BLE stack. Two distinct sets of tests were conducted to evaluate the wireless communication performance. Initially, offline tests were carried out, involving the transmission of a small amount of data. This allowed for assessing the coherence and reliability of the received data at close proximity. Subsequently, continuous streaming tests were performed to simulate real-time data transmission scenarios. Furthermore, the analysis encompassed an assessment of the implications arising from varying the distance between the two devices and the influence of biological tissues incorporated within the wireless communication system. These conditions were crucial in assessing the system's robustness and ability to overcome potential obstacles in a medical environment.

Keywords: Implanted Device · Firmware · Bluetooth Low Energy (BLE) · Performance Evaluation.

1 Introduction

Peripheral nerve injuries, resulting from various medical conditions and traumatic events, are increasingly affecting the global population. Their rising prevalence demands urgent and innovative solutions due to the range of debilitating symptoms they cause. These symptoms, which include loss or alteration of sensation and motor control, lead to significant dysfunction and disability, impacting both physical well-being and quality of life [4].

In traditional medicine, there are three different approaches to managing peripheral nerve injuries [7]:

- **Microsurgical Techniques**: These involve re-establishing nerve connections to facilitate neuronal regeneration.
- **Implantation of Grafts**: This method employs grafts to guide and support the correct regeneration of nerves, which can be enhanced by combining with drug delivery techniques.

However, these traditional approaches often face limitations in effectively addressing the complexities of such clinical issues. This gap has led to the emergence of non-traditional medicine techniques, notably in the field of neuroscience. A key development in this area is the advent of Peripheral Nerve Interfaces (PNIs), an example diagram is shown in Fig. 1. These implanted devices are designed to interface directly with the peripheral nervous system (PNS), offering new hope in situations where nerve damages are involved. PNIs function by bypassing injury sites to facilitate the flow of neural information, essential for restoring lost functionalities [23]. They achieve this by recording Electroneurographic (ENG) signals from downstream of nerve lesions and transmitting these signals to an external unit for detailed analysis and classification. This process is crucial for deciphering the types of information transmitted through nerves and determining appropriate stimuli for feedback to the PNS [25, 10].

The effectiveness of PNIs heavily relies on the efficiency and reliability of the communication system employed. This is critical as implanted devices, equipped with microcontrollers for signal recording, have inherent limitations in terms of processing power, storage capacity, and power consumption [9]. Therefore, optimizing this communication channel is key to maximizing the functional efficacy of PNIs. In addressing these communication needs, wireless systems have emerged as the superior choice over wired systems. Wired systems, while providing reliable data transmission, pose limitations such as reduced mobility, infection risks, and potential movement-induced noise [15, 6]. Wireless systems, on the other hand, enhance user mobility, reduce infection and skin complications, and are less conspicuous, improving both psychological well-being and the user's quality of life and optimizing patient comfort in real-world applications [14]. Despite challenges like limited battery life and potential signal interference, advancements in wireless technologies have made significant strides in addressing these issues.

An example of a case study that tries to implement a solution for a PNI is the SenseBack device [26]. This implantable system is semi-flexible and bidirectional designed to remain inside the body for up to six months. It is capable of both sensing and stimulating ENG signals, thereby creating an effective neural bypass. The device uses a wireless Bluetooth Low Energy (BLE) 5 communication for the bidirectional data transfer with an external unit where the analysis is conducted.

The preprocessing and the classification can be performed in many different ways such as the one present in [25, 10].

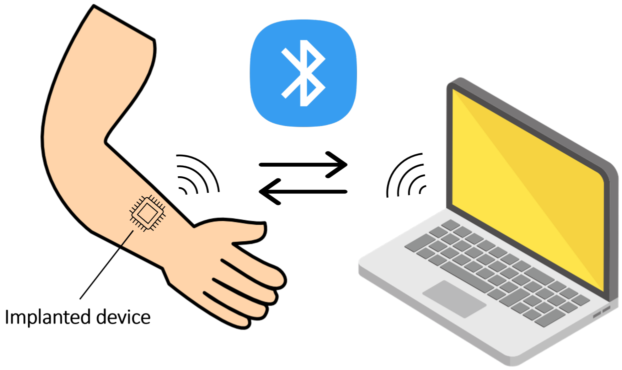

Fig. 1. Schematic idea behind a PNI using a wireless communication system. The implanted device records data from the nerve and sends it to the external unit through a wireless communication system

This paper focuses on leveraging BLE 5 technology for PNIs, this choice has been driven by the considerations made in Sections 2 and 3. Although BLE 5 has recently garnered increasing interest in the realm of PNIs as in [26, 20], the realization of real-time communication and the optimization of its data transfer rate present significant challenges. Addressing these challenges to fully exploit the capabilities of BLE 5 in the context of PNIs is the primary objective of this work.

The structure of the paper is organized as follows: Section 2 provides an overview of potential wireless communication systems, Sec. 3 introduces BLE 5, Sec. 4 describes the experimental setup, and then in Sec. 5, the firmware loaded on the device is detailed. Finally, Sections 6, 7, and 8 present the results along with the corresponding discussions.

2 Communication Systems in Peripheral Nerve Interfaces

In the development of PNIs, various communication systems have been considered, each with distinct characteristics. This section offers a comparison of these systems, leading to the rationale behind selecting BLE 5 for this project.

- **Inductive Link**: Utilizes inductive coupling for data transmission and wireless power transfer. While efficient and non-invasive, challenges include design constraints, safety considerations at high data rates, and signal quality affected by tissue interference and coil misalignment [16].
- **Optical Systems**: Employs optogenetics and light-sensitive proteins for data transmission. These systems offer high data rates and are immune to

electromagnetic interference. However, they face challenges such as tissue absorption and scattering, limited penetration depth, and long-term biocompatibility concerns [13].
- **Ultrasound Systems**: Uses ultrasonic waves for communication, offering excellent spatial resolution and minimal energy attenuation in tissues. However, ultrasound systems have limitations in terms of range and potential interference with surrounding tissues [8, 17, 22].
- **Radio Frequency (RF)**: RF systems, particularly in the 2.4GHz ISM band (encompassing Wi-Fi, Bluetooth, and Zigbee), enable long-distance communication. These systems provide flexibility but are often energy-intensive, prone to environmental interference, and face challenges in effective miniaturization. The 2.4GHz ISM band, despite its widespread use, can suffer from congestion and interference in high-activity areas [18]. Among these, BLE 5 stands out due to its lower power consumption and compact form factor, making it particularly suited for implantable medical devices.

3 BLE 5

Among the available communication systems, Bluetooth, and specifically BLE 5, stands out as an attractive choice for PNIs applications, [21, 26], owing to several compelling reasons. Firstly, BLE 5 adheres to established industry standards and it is already integrated into many different devices. It is readily accessible in the market, especially in compact devices and offers a cost-effective solution. Moreover, it keeps the radio off as much as possible when no data has to be sent offering a lower power consumption.

BLE 5 employs radio frequency technology operating in the 2.4GHz Industrial, Scientific, and Medical (ISM) band, segmented into 2MHz channels, which corresponds to the raw data rate of this protocol [2]. This characteristic does impose limitations on the achievable maximum throughput, a challenge addressed in this work to optimize this communication protocol; a crucial step toward achieving real-time communication capabilities for PNIs. In this kind of system, it is important to keep in mind that Bluetooth technology is founded on a master-slave concept, in fact, the communication primarily involves two key roles [1]:

- *Peripheral* (Slave): advertises its presence and responds to central devices.
- *Central* (Master): scans for advertising packets and can initiate connections and establish the parameters that control the communication.

During a connection, central devices send connection requests to peripherals, and then a predetermined schedule is followed to synchronize frequencies, implement security, and exchange data. This communication utilizes a dynamic channel allocation, called Adaptive Frequency Hopping (AFH), across the 2.4 GHz ISM band to minimize interference [3]. To maintain the connection, both devices regularly exchange packets at least at every Connection Event (CE), Fig. 2. These packets could include application data or BLE control data that

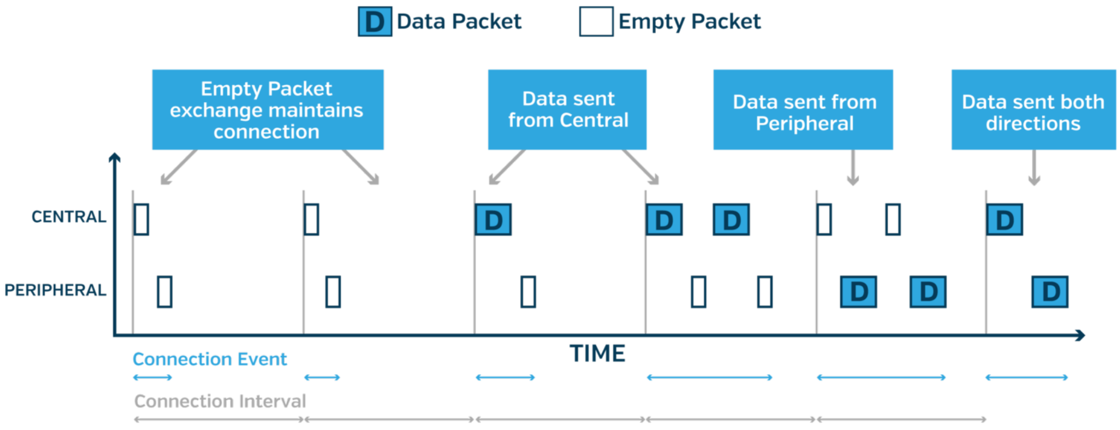

Fig. 2. Flow of what could happen in a connection [5].

correspond to the communication payload. In contrast, in the absence of these data, the devices send "empty packets" without any payload, [5]. As in Figure 2, multiple consecutive packet exchanges can occur within a CE serving to exchange data and maintain the connection. The interval between CEs, known as the Connection Interval (CI), will influence the throughput analysis as will be shown in Sec. 6.

The BLE protocol stack, based on the Open Systems Interconnection (OSI) model, comprises several layers with different functions [24]. The important layers to understand the developed firmware presented in this work are [1]:

- *Generic Access Profile* (GAP), that manages advertisements, connection establishment and device security.
- *Generic Attribute Profile* (GATT), which defines data exchange format and access procedures.
- *Physical layer* (PHY), responsible for data transfer in the radio. Channel bandwidth can be 1 Mbps or 2 Mbps, starting from Bluetooth version 5.0.

3.1 BLE throughput

The data throughput in BLE is primarily determined by the data rate of the PHY that is the bandwidth, which governs the transmission speed of the radio. From BLE 5 and beyond, this value depends on the operating mode and PHY selection. It can either be set to 1 Mbps or achieve an enhanced 2 Mbps when utilizing the high-speed feature. However, achieving these maximum data rates in real-world applications is influenced by several factors:

Table 1. Table captions should be placed above the tables.

Preamble	**Access Address**	**PDU** (2-257 bytes)						**CRC**
		LL Header	**Payload** (0-251 bytes)				**MIC** (Optional)	
			L2CAP Header	**ATT Data** (0-247 bytes)				
				ATT Header		**ATT Payload**		
				OpCode	**Attribute Handle**			
1 byte (1M PHY) 2 bytes (2M PHY)	4 bytes	2 bytes	4 bytes	1 byte	2 bytes	Up to 244 bytes		3 bytes

- *Packet overhead*: Various protocol layers introduce bytes of overhead. Reducing this overhead by maximizing the data payload in each packet is essential for efficient data transfer, Tab. 1.
- *CI*: The CI affects the number of packets sent within a CE and the time gaps between consecutive CEs.
- *Data Length Extension* (DLE): Enabling DLE allows for larger payloads in packets, up to 251 bytes.
- *Attribute Maximum Transmission Unit* (ATT MTU): Setting the ATT MTU to 247 bytes (accounting for the L2CAP header) allows all ATT data to fit into a single packet.
- *Operation type*: These can be different, however, Notifications, which do not require acknowledgement packets, are preferred for fast data transfer.

Considering these parameters, a simple connection between one peripheral and one central, and assuming that only the peripheral transmits data continuously as Notifications while the central sends back just empty packets as shown

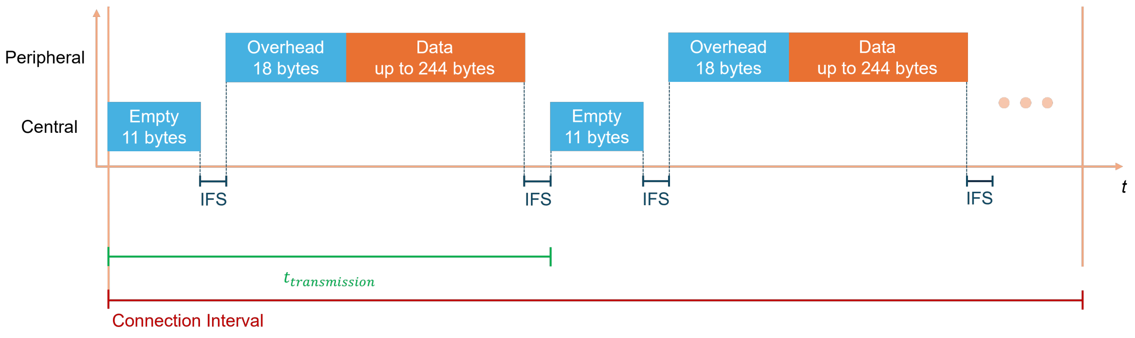

Fig. 3. Example of the communication simulated in this work

in Fig. 3, the theoretical throughput can be calculated following the subsequent steps:

1. Set the PHY to 2Mbps.
2. Set the payload of a data packet as 244 bytes through the DLE and the ATT MTU parameters. This leads to a $size(data\,type[bits])_{ATTPayload}$ equal to 1952 bits.
3. Calculate the transmission time for the single data packet and the empty packet, accounting for PHY speed, Inter Frame Space (IFS) of 150µs between every packet in the air, and packet structure.
4. Determine the maximum number of packets that can be transmitted within a CI for instance of 50ms.

Then using Eq. 1, the **theoretical throughput (Thr) of BLE 5** can reach 1.366 Mbps.

$$Thr = \frac{\#Packets_{perCI} \cdot size(data\,type[bits])_{ATTPayload}}{CI} \tag{1}$$

Section 3.2 details the analysis of the throughput necessary for real-time data transmission in an implantable device functioning as a PNI. This analysis is crucial to determine whether BLE can meet the specific requirements of this application.

3.2 Throughput requirement for a PNI

To determine the required data rate Thr_r needed to meet real-time requirements in such systems, various factors must be taken into account:

- *Sampling frequency* f_s that is imposed by the characteristics of the ENG signal [12, 19]. In particular, since its energy is concentrated between 0.5 and 2.5 kHz, a $f_s \geq 5$ kHz can be used without losing information.
- *Number of electrodes* n that are used for the recording, supposed equal to 16.
- $size(data\,type[bits])$ is the bit representation of the data to be transmitted. It depends on the digitalization of the recorded signal and the unit of information of the communication protocol. It can be hypothesized to be 16 bits (2 bytes).

$$Thr_r = f_s \cdot n \cdot size(data\,type[bits]) \tag{2}$$

Considering these hypothetical values, using the Eq. 2 the Thr_r is equal to 1.28 Mbps. This value is lower than the theoretical value reachable with BLE of 1.366 Mbps, as seen in Sec. 3.1, meaning that BLE if accurately optimized could be suitable for these systems. In this context, this project aims to develop and optimize the firmware for wireless communication using this protocol.

3.3 Packet Error Rate (PER)

Besides the optimization of the transmission rate, it is also important to account for the number of retransmitted packets over the total transmitted ones. In this way, it is important to assess the performance of the communication.

Let

$$r = [r_1, r_2, \ldots, r_n] \tag{3}$$

be the vector of n retransmissions that occurred during a test and

$$p = [p_1, p_2, \ldots, p_m] \tag{4}$$

be the vector of the total transmissions that occurred during the same test. With these two values, it is possible to calculate the PER as:

$$PER = \frac{n}{m} \tag{5}$$

As will be seen in Sec. 6, in BLE, increased PER does not significantly impact throughput due to several key features of the protocol. One such feature is adaptive frequency hopping (AFH), which significantly reduces interference-related errors. This technique involves dynamically switching communication channels to avoid interference-prone frequencies. Since BLE operates in the 2.4 GHz ISM band, which is crowded with various other wireless signals like Wi-Fi and other BLE devices, AFH helps in identifying and avoiding channels with high interference. By rapidly shifting across frequencies, BLE minimizes the likelihood of collision and interference from other devices, thereby enhancing the overall reliability and reducing further packet errors. Furthermore, BLE employs efficient retransmission protocols that utilize a stop-and-wait flow control mechanism based on cumulative acknowledgements for error recovery. Each data packet header contains Sequence Number (SN) and Next Expected Sequence Number (NESN) fields to manage packet identification and acknowledgement. This system ensures quick recovery of lost data by resending packets as needed, which minimizes throughput degradation [11].

4 Experimental Setup

This section details the experimental setup designed to simulate a realistic scenario involving implanted medical devices communicating with an external unit via BLE. Our primary objective was to assess the reliability and efficiency of BLE communication in conditions that closely mimic implanted environments. To achieve this, we utilized a single transmitter and a single receiver setup, as depicted in Fig. 4, employing nRF52832 development kits from Nordic Semiconductor©.

Additionally, to gain deeper insights into the intricacies of the BLE communication process, we employed a nRF52840 Dongle, also from Nordic Semiconductor©, as a packet sniffer. This setup allowed us to monitor and analyze the communication flow during the tests using Wireshark software in conjunction with the

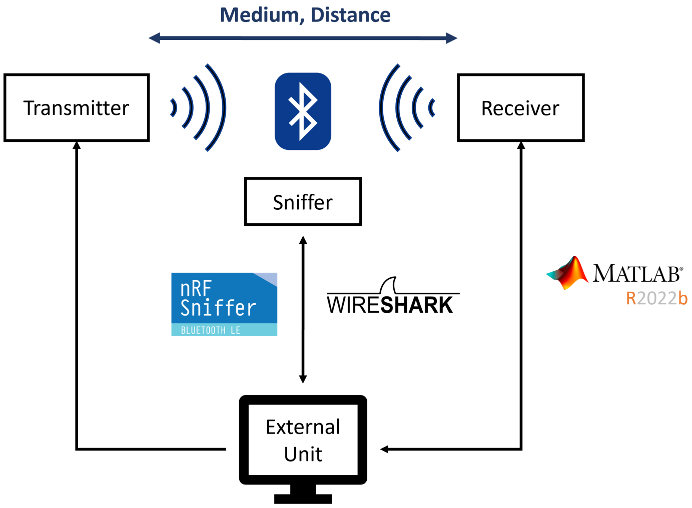

Fig. 4. Diagram of the experimental setup.

nRF Sniffer Tool. The role of Matlab in our setup was twofold: firstly, it served to facilitate the transmission of commands from the receiver to the transmitter over BLE, and secondly, in our offline data transmission tests, it was instrumental in evaluating the communication reliability by computing the discrepancies between the received and expected data.

Following the establishment of our experimental setup, we configured the BLE stack parameters used in the BLE communication tests. The specific parameters chosen were as follows:

- PHY Layer Rate: 2Mbps, to facilitate high data rate transmission.
- DLE: Enabled, allowing for extended data packet length.
- ATT MTU: Set to 247, maximizing the data payload per packet and minimizing the overall communication overhead.
- Operation Type: Notifications, suitable for continuous data transfer.

It is important to note that these parameters align closely with those employed in the theoretical throughput calculations for BLE 5, except for the CI. The latter impacts the overall throughput, and this was a key focus of our investigation. In addition to this technical parameter, our tests were designed to explore the system's robustness in various environmental conditions. This approach was crucial to replicate the diverse scenarios likely to be encountered in implanted settings. Our tests aimed to provide comprehensive insights into the transmission system's capabilities and limitations in real-world applications by varying environmental factors and analysing the system's performance under these conditions.

In particular, our experimental design included two primary sets of tests:

- **Distance Variation Tests:** The first set focused on the impact of varying distances between the transmitter and receiver. We selected distances of 0cm, 10cm, and 50cm to simulate possible proximities between a subject with an implanted device and the external unit. This range was chosen based on the hypothesis that the external unit is a wearable device.
- **Transmission Medium Tests:** The second set examined the transmission medium's influence on communication efficacy. To emulate the internal body environment, tissue samples of approximately 10mm thickness were placed atop the transmitter. This setup, with the transmitter 50cm from the receiver, allowed us to test under conditions mimicking those encountered by implanted devices. We used two types of tissue samples, high ($> 30kg/m^2$) and low ($< 18.5kg/m^2$) Body Mass Index (BMI), to evaluate the system's adaptability to varying tissue compositions. The chosen tissue thickness mirrors real-world considerations such as skin thickness, implantation depth variability, and the presence of fibrotic capsules around implants.

To derive robust conclusions from these setups, two distinct types of tests were conducted:

1. *Offline Data Transmission Test:* This test involved the offline transmission of a predetermined data volume over the BLE connection. Critical to this test was the analysis of factors affecting throughput, such as BLE connection parameters (packet size and CI), signal generation rate, and data consistency. The primary objective was to evaluate the system's reliability and identify the maximum data rate achievable in an offline application.
2. *Online Data Transmission Test:* Building upon the offline test setup, these tests involved continuous data streaming for a duration of 4 minutes. The focus here was on evaluating the performance and stability of data transmission in continuous applications, under the various environmental conditions established in our experimental framework.

Each of these tests was meticulously designed to address specific hypotheses about the BLE communication system, contributing significantly to our understanding of its potential and limitations in medical applications.

5 Firmware

A crucial aspect of testing the communication system outlined in Sec. 4 involves the development of specialized firmware for the microcontrollers and the appropriate configuration of auxiliary programs.

5.1 Transmitter

The transmitter operates as a Finite State Machine (FSM), taking on the role of a Peripheral device in the BLE connection. Its operation can be delineated into several key states:

- **OFF State**: The initial dormant state.
- **ON State**: Activates the device and initializes the system.
- **ADVertising State**: In this phase, the transmitter broadcasts advertising packets and awaits a connection.
- **CONNection State**: This state is entered upon successful pairing.
- **TX State**: Triggered by a START command received over BLE, the transmitter mimics data reception from an FPGA at a rate of 80 kHz, which comes from 16 channels of ENG at 5kHz of sampling rate. For simplicity, the data was emulated as a stair-step signal pattern, illustrated in Fig. 5. After completing data transmission or receiving a STOP command, it reverts to the CONNection state.

5.2 Receiver

Similarly, the receiver board is designed as a FSM and functions as a Central device in the BLE setup. Its state transitions are as follows:

- **OFF State**: The initial state before activation.
- **ON State**: Starts up and prepares the device for operation.
- **SCANning State**: Here, it listens for advertising packets and searches for the Nordic UART Service (NUS) used by the transmitter to send data over BLE.

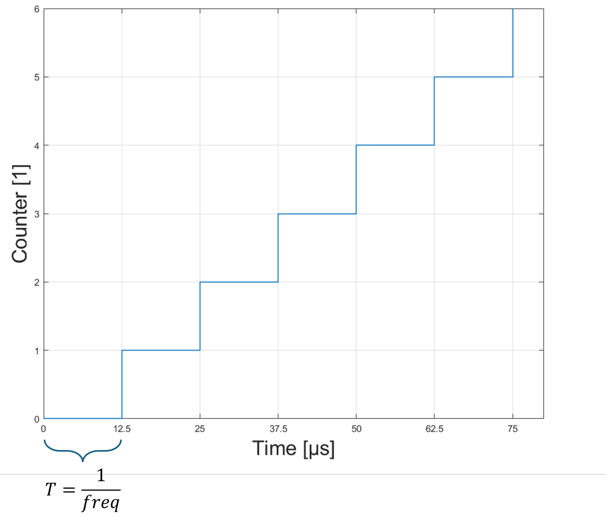

Fig. 5. Signal sent over the BLE communication simulating the correct frequency of the ENG signal to send. This signal was generated using just a counter incremented at 80kHz.

- **CONNection State**: Entered upon locating the service of the transmitter, and at this point the Central and the Peripheral negotiate the specific parameters of the communication.
- **RX State**: Upon receiving a START command from a Matlab script, it begins data reception, buffering the data, and forwarding it to a computer via UART protocol. On receiving a STOP signal, it calculates throughput using the formula in Eq. 6.

$$Thr = \frac{bits_{received}}{t_{elapsed}} \tag{6}$$

5.3 Dongle

The nRF52840 Dongle, in conjunction with Wireshark and the nRF Sniffer firmware, serves as a critical tool for BLE network analysis. It captures data packets during transmission, enabling us to analyze the PER. This is achieved by counting the number of retransmissions and transmitted packets that occurred during a specific test, followed by the calculation of PER using Eq. 5.

5.4 Matlab script

Two distinct Matlab scripts were developed for the offline and online tests. During offline tests, the script manages transmission initiation and data reception for reliability analysis, comparing expected and received data to calculate errors. For online tests, due to the memory constraints of the receiver and the slower data rate of the UART connection with the computer, the script primarily handles the transmission of "START\n" and "STOP\n" commands.

6 Results

6.1 Ideal Case Analysis

In our examination of an ideal scenario, where the devices are positioned at a distance of 0cm from each other with only air as the transmission medium, we conducted both offline and online data transmission tests. The findings, illustrated in Fig. 6, reveal a significant disparity in throughput between these two modes. Specifically, the offline transmission achieved a maximum throughput of approximately 1.4 Mbps, whereas the online transmission was limited to around 1.07 Mbps. This variance primarily stems from the operational dynamics of the CI.

In offline streaming scenarios, particularly when the CI is approximately 200 ms or higher, all transmitted data fit within a single CE, as depicted in Fig. 7. Conversely, in online streaming or scenarios where the CI is shorter than the total time required for data transmission, there is a noticeable latency between the transmission of the last packet in one CE and the commencement of the next as reported in Fig. 8. This interval contributes to a reduction in throughput. Additionally, in the streaming case, as the throughput decreases, the delay caused by data buffering within the transmitter is worsened, leading to a further reduction in throughput. These observations underscore the need for optimization in the firmware of the transmitter. Specifically, a refinement in the buffering and transmission strategy could minimize the impact on throughput, enhancing the system's efficiency, especially in applications where continuous data streaming is critical.

Importantly, in offline tests, the receiver consistently obtained the correct data sent by the transmitter, showcasing the reliability of the BLE communication. This reliability was quantitatively assessed using a Matlab-based error calculation, which consistently yielded a zero error rate. The same result was confirmed across various experimental setups, ensuring consistency in the system's performance. Acknowledging these findings, alongside the practical significance of online data transmission in real-world applications, the subsequent sections of this paper will shift focus exclusively to the examination of online tests.

6.2 Distance Analysis

The analysis of distance effects on transmission, as depicted in Fig. 9, indicates that distances up to 50cm have a minimal impact on the transmission rate. This finding underscores the suitability of our communication system for medical scenarios where devices operate in close proximity. However, the influence of high CI values on system performance warrants careful consideration. Our tests suggest that excessively high CIs, especially in conjunction with a higher PER observed at distances of 50cm, might have been suboptimal. This combination can potentially lead to diminished transmission rates and an increased risk of data loss. The higher PER at this distance (reaching 0.15%-0.20%) implies a

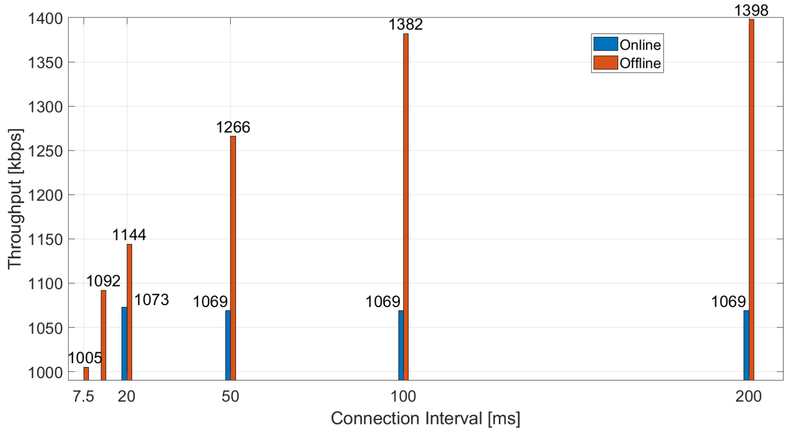

Fig. 6. Comparison of Offline-Online tests in the ideal configuration.

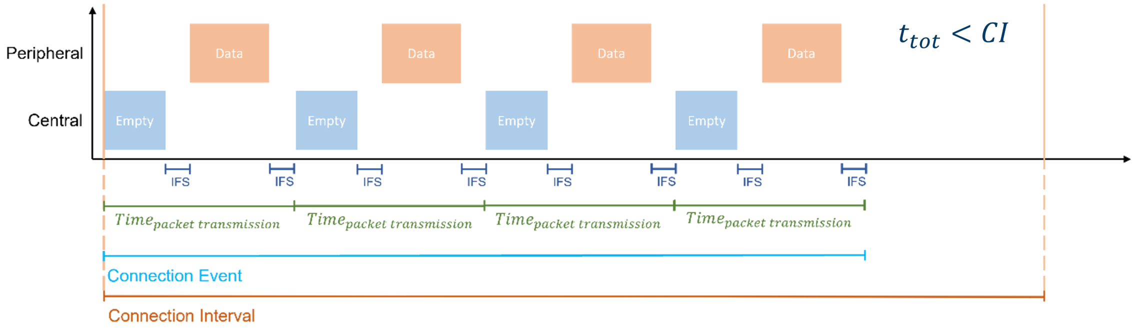

Fig. 7. When $t_{tot} < CI$, there is no time delay between the packets sent.

greater likelihood of packet errors. Combined with a longer CI, this can delay the detection and retransmission of erroneous packets, exacerbating the risk of data loss. That's why for the case of 50cm the results are shown for values of the CI just up to 100ms. In fact, in this scenario, a data loss was experienced, with not all data being received on the receiver side.

Notably, even with these higher PER values, the system maintained stable throughput and robust data transfer capabilities as in the tests at shorter distances (10cm and 0cm) with nearly 0% PER. This resilience is attributed to the system's effective error correction and retransmission mechanisms, which mitigate the impact of errors and ensure data integrity. However, the combined effect of higher PER and longer CI at 50cm impacts the permissible CI values. This could be because the higher amount of packet errors necessitates more frequent retransmissions, making shorter CIs more effective in maintaining data integrity and throughput.

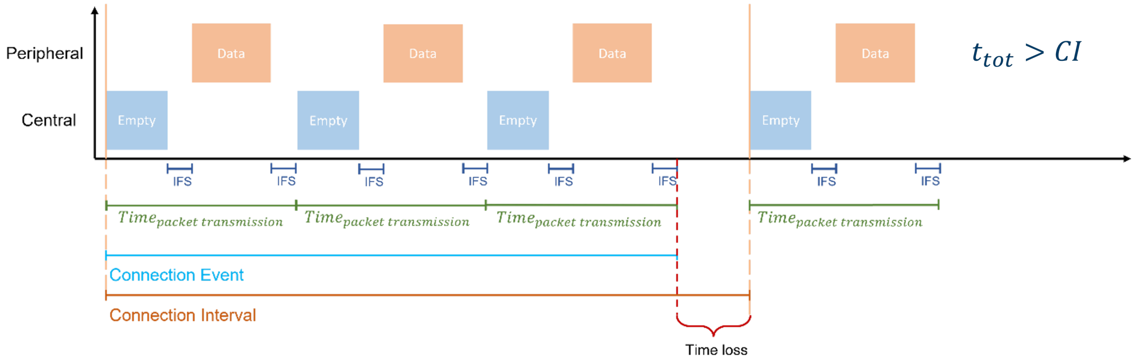

Fig. 8. When $t_{tot} > CI$, a noticeable latency occurs between the end of one CE's last packet transmission and the start of the next.

These findings provide crucial insights for the practical deployment of our communication system, laying the groundwork for its application and further enhancement in diverse real-world scenarios.

6.3 Medium Analysis

The impact of different tissue samples on throughput and acceptable CIs was analyzed in Fig. 10. Tissues corresponding to high BMI significantly constrained the viable CIs to a narrow range of 20ms-50ms, mirroring the constraints observed at a distance of 50cm. This observation underscores the importance of considering the characteristics of the medium for ensuring reliable data transmission. The

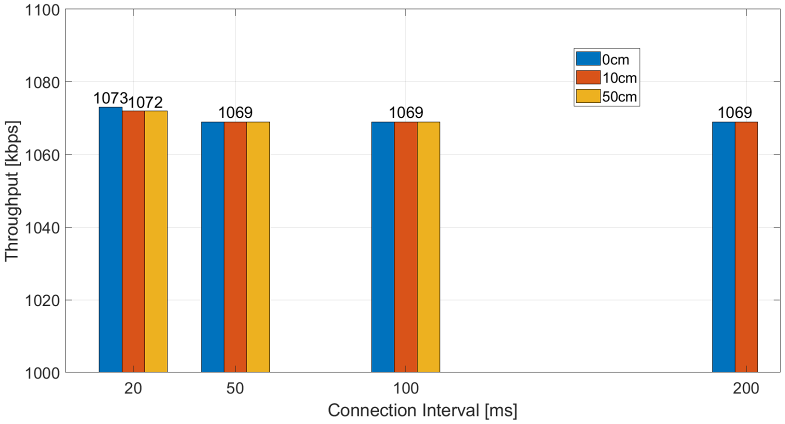

Fig. 9. Results of the Online tests using different distances.

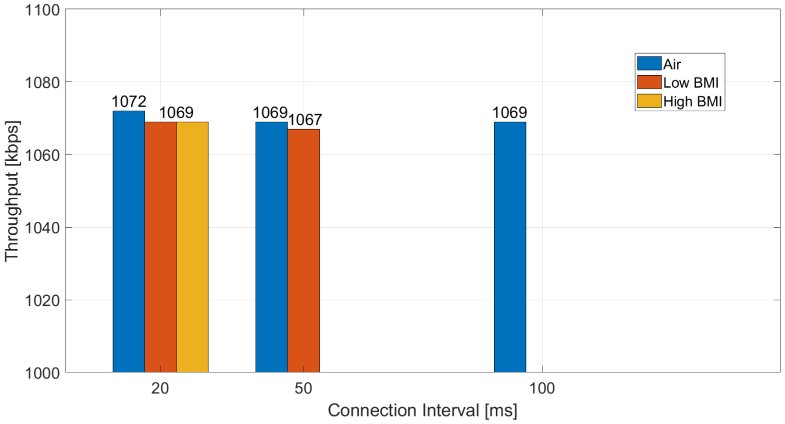

Fig. 10. Results of the Online tests using different mediums.

influence of tissues with varying BMI on PER was noteworthy, with higher PER values in comparison to scenarios where air was the sole medium. Specifically, tissues representative of high BMI exhibited a PER of around 1%, while those indicative of low BMI showed a PER between 0.7%-0.9%. This disparity in PER associated with different BMI categories indicates a direct relationship between tissue composition and the effectiveness of data transmission.

The increased PER in tissues representative of high BMI, similar to the trend observed at longer distances, highlights the need for adapting both CI and error correction strategies to the specific challenges posed by these mediums. The increased PER requires a careful choice of CIs and improved error handling to reduce data loss and maintain strong data reliability. In practical applications, particularly in medical device contexts involving varied BMI tissues, these insights are crucial for devising communication solutions that are responsive to the unique challenges of the medium, thereby improving the system's reliability and performance.

These findings emphasize the necessity for customized solutions and optimization strategies that account for medium variability, such as different BMI tissues, to advance communication in real-world scenarios involving biological tissues.

7 Discussion

Our comprehensive testing has yielded critical insights into the reliability and efficiency of our transmission mechanism. The minimal PER and consistent error-free data reception across various scenarios affirm the robustness of our approach.

Offline tests performed under ideal conditions showcased the system's maximum achievable data rate with the selected parameters, enabling efficient and high-speed data transmission. This outcome holds particular significance for scenarios involving asynchronous downlink of packets, such as in nerve stimulation applications. Assuming the same setup as discussed in this paper and considering only the data direction where stimulation is transmitted from the central to the peripheral unit, we anticipate achieving the same data throughput as calculated in Sec. 3.1 and observed in the offline tests. Given that this involves sending a single packet of 244 bytes, we estimate the transmission time for this packet to be less than 2ms. This rapid transmission capability presents a compelling avenue for further investigation, particularly in the development of a complete nerve bypass system.

On the other hand, the online tests provided valuable insights into the system's performance for real-time applications. These tests demonstrated the system's ability to maintain stable and consistent data delivery, despite a slightly lower throughput than ideal for real-time needs. The factors contributing to this, including delays in packet transmission, CI optimization, and buffering time, emerge as key areas for further development. Overcoming these challenges is critical for boosting real-time transmission capabilities.

Particularly noteworthy is the system's performance at short distances, up to 50cm, where the transmission rate remains largely unaffected. This finding is encouraging for implanted settings. However, our tests indicate the need for firmware optimization to enhance transmission efficiency at a proper CI. Moreover, the system demonstrated commendable resilience in the face of higher PERs, particularly at extended distances. The effective error correction and retransmission strategies in place were instrumental in maintaining reliable data transfer, underscoring the system's robustness.

The exploration of data transmission in the presence of biological tissues, representing varying BMI, brought to light some challenges. It highlighted the critical need for solutions and optimization strategies tailored to these specific mediums. This aspect of our research paves the way for enhanced system performance and reliability in complex biological environments.

In summary, this analysis paints a comprehensive picture of our system's current capabilities and areas of potential improvement. By addressing the identified challenges and fine-tuning the system, we aim to significantly enhance the practical utility and dependability of our communication system, especially in the demanding realm of real-time medical applications.

8 Conclusions and future developments

This research successfully demonstrates the efficacy of the BLE 5 protocol in achieving efficient, reliable, and robust wireless communication, particularly tailored for biomedical applications. Through extensive experimentation, we optimized the system's firmware, achieving data rates of up to 1.4 Mbps in offline tests and approximately 1.07 Mbps in online scenarios. Although the online test results show a slightly lower data rate than the generation rate of the data, leading to minor transmission delays due to buffering, these results are still highly promising for practical applications.

A critical aspect of our study was the assessment of communication performance in the face of varying distances and the presence of biological tissues. These findings underscore the system's applicability and potential effectiveness in implanted settings, where such factors are prevalent.

The robustness and flexibility of the firmware established in this study lay a strong foundation for its implementation in a wide range of biomedical applications. Looking ahead, there are several key areas for further research that we have identified. Understanding the nuances of the delay introduced during transmission and optimising the firmware to minimize this delay. Moreover, it is important to investigate other critical parameters like power consumption, data encapsulation, security measures, and compression techniques are essential. These factors must be examined thoroughly to ensure the safety, functionality, and optimal throughput of the system in biomedical applications.

In conclusion, this study not only demonstrates the practical viability and reliability of our proposed communication system for real-time medical applications but also provides invaluable insights into the realm of wireless data transmission in implanted settings. The groundwork laid here paves the way for future advancements in this field, promising enhanced data transmission capabilities in diverse medical scenarios.

Acknowledgment

This work was supported by the Italian Ministry of Foreign Affairs and International Cooperation, grant number US23GR04 (CUP: D43C23000350001).

References

1. Bluetooth low energy: A primer, https://interrupt.memfault.com/blog/bluetooth-low-energy-a-primer, accessed Jun. 05, 2023
2. Bluetooth low energy (ble): A complete guide, https://novelbits.io/bluetooth-low-energy-ble-complete-guide/, accessed Jun. 05, 2023
3. How bluetooth technology uses adaptive frequency hopping to over-come packet interference, https://www.bluetooth.com/blog/how-bluetooth-technology-uses-adaptive-frequency-hopping-to-overcome-packet-interference/, accessed Jun. 05, 2023
4. Peripheral nerve injuries market size & share report, 2030., https://www.grandviewresearch.com/industry-analysis/peripheral-nerve-injuries-market-report, accessed Jul. 03, 2023
5. Ultimate guide to managing your ble connection, https://punchthrough.com/manage-ble-connection/, accessed Jun. 05, 2023
6. Barua, N., Woolley, M., Bienemann, A., Johnson, D., Lewis, O., Wyatt, M., Irving, C., O'Sullivan, S., Murray, G., Fennelly, C., Skinner, P., Gill, S.: Intermittent convection-enhanced delivery to the brain through a novel transcutaneous bone-anchored port. Journal of Neuroscience Methods **214**(2), 223–232 (2013). https://doi.org/https://doi.org/10.1016/j.jneumeth.2013.02.007, https://www.sciencedirect.com/science/article/pii/S0165027013000733
7. Caillaud, M., Richard, L., Vallat, J.M., Desmoulière, A., Billet, F.: Peripheral nerve regeneration and intraneural revascularization. Neural regeneration research **14**(1), 24 (2019)
8. Charthad, J., Weber, M.J., Chang, T.C., 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), 1741–1753 (2015). https://doi.org/10.1109/JSSC.2015.2427336
9. Coviello, A., Bersani, A., Ros, P.M., Del Bono, F., Demarchi, D., Spagnolini, U., Magarini, M.: Comparison of data compression methods for implanted real-time peripheral nervous system. In: IEEE MetroXRAINE 2023 Proceedings, pp. 110–115 (2023)
10. Coviello, A., Porta, F., Magarini, M., Spagnolini, U.: Neural network-based classification of eng recordings in response to naturally evoked stimulation. In: Proceedings of the 9th ACM International Conference on Nanoscale Computing and Communication. pp. 1–7 (2022)
11. Gomez, C., Oller, J., Paradells, J.: Overview and evaluation of bluetooth low energy: An emerging low-power wireless technology. Sensors **12**(9), 11734–11753 (2012). https://doi.org/10.3390/s120911734, https://www.mdpi.com/1424-8220/12/9/11734

12. Hoffer, J., Kallesoe, K.: How to Use Nerve Cuffs to Stimulate, Record or Modulate Neural Activity (09 2000)
13. Jeong, J.W., McCall, J.G., Shin, G., Zhang, Y., Al-Hasani, R., Kim, M., Li, S., Sim, J.Y., Jang, K.I., Shi, Y., Hong, D.Y., Liu, Y., Schmitz, G.P., Xia, L., He, Z., Gamble, P., Ray, W.Z., Huang, Y., Bruchas, M.R., Rogers, J.A.: Wireless optofluidic systems for programmable in-vivo pharmacology and optogenetics. Cell **162**(3), 662–674 (2015). https://doi.org/https://doi.org/10.1016/j.cell.2015.06.058, https://www.sciencedirect.com/science/article/pii/S0092867415008284
14. Kim, H., Rigo, B., Wong, G., Lee, Y.J.: Advances in wireless, batteryless, implantable electronics for real-time, continuous physiological monitoring. Nano-Micro Letters **16** (12 2023). https://doi.org/10.1007/s40820-023-01272-6
15. Koch, J., Schuettler, M., Pasluosta, C., Stieglitz, T.: Electrical connectors for neural implants: design, state of the art and future challenges of an underestimated component. Journal of Neural Engineering **16**(6), 061002 (oct 2019). https://doi.org/10.1088/1741-2552/ab36df, https://dx.doi.org/10.1088/1741-2552/ab36df
16. Lee, B., Ghovanloo, M.: An overview of data telemetry in inductively powered implantable biomedical devices. IEEE Communications Magazine **57**(2), 74–80 (2019). https://doi.org/10.1109/MCOM.2018.1800052
17. Meng, H., Sahin, M.: An electroacoustic recording device for wireless sensing of neural signals. Conference proceedings : ... Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society. Conference **2013**, 3086–3088 (07 2013). https://doi.org/10.1109/EMBC.2013.6610193
18. Nelson, B., Karipott, S., Wang, Y., Ong, K.: Wireless technologies for implantable devices. Sensors **20**, 4604 (08 2020). https://doi.org/10.3390/s20164604
19. Raspopovic, S., Carpaneto, J., Udina, E., Navarro, X., Micera, S.: On the identification of sensory information from mixed nerves by using single-channel cuff electrodes. Journal of neuroengineering and rehabilitation (2010)
20. Schönle, P., Michoud, F., Brun, N., Guex, A., Lacour, S.P., Wang, Q., Huang, Q.: A wireless system with stimulation and recording capabilities for interfacing peripheral nerves in rodents. In: 2016 38th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC). pp. 4439–4442 (2016). https://doi.org/10.1109/EMBC.2016.7591712
21. Schönle, P., Michoud, F., Brun, N., Guex, A., Lacour, S.P., Wang, Q., Huang, Q.: A wireless system with stimulation and recording capabilities for interfacing peripheral nerves in rodents. In: 2016 38th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC). pp. 4439–4442 (2016). https://doi.org/10.1109/EMBC.2016.7591712
22. Seo, D., Carmena, J., Rabaey, J., Alon, E., Maharbiz, M.: Neural dust: An ultrasonic, low power solution for chronic brain-machine interfaces. Available at: ArXiv.org/abs/1307.2196. (07 2013)
23. Shahriari, D., Rosenfeld, D., Anikeeva, P.: Emerging frontier of peripheral nerve and organ interfaces. Neuron **108**(2), 270–285 (2020). https://doi.org/https://doi.org/10.1016/j.neuron.2020.09.025
24. Tanenbaum, A., Wetherall, D.: Computer Networks - 5th Edition (2011)
25. Vasta, E., Coviello, A., Spagnolini, U., Magarini, M.: Classification of sensory neural signals through deep learning methods. In: IEEE EUROCON 2023-20th International Conference on Smart Technologies. pp. 313–318. IEEE (2023)

26. Williams, I., Brunton, E., Rapeaux, A., Liu, Y., Luan, S., Nazarpour, K., Constandinou, T.G.: Senseback - an implantable system for bidirectional neural interfacing. IEEE Transactions on Biomedical Circuits and Systems **14**(5), 1079–1087 (2020). https://doi.org/10.1109/TBCAS.2020.3022839