Bioelectronic Medicines: A review

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Abstract - Today every individual strive to improve the quality of life to face societal and technological challenges. So in this hustle, Bioelectronic medicine has revolutionized the way we practice medicines and has demonstrated to drastically improve the results of healthcare. This technology focuses on targeting and customized treatments of neurological based infections and conditions in control systems.This technology employs various approaches like neuromodulation whichprovides an opportunity to treat the specific disease, disorder or injury. For better emergence there has been development of BEM technology Roadmap that serves as a planning tool in diagnosing the disease and to guide the future investments in this emerging field of medicines. This road map has been further divided into eight chapters. Hence this review article focuses on the brief information about this roadmap and its chapters.

Keywords: Bioelectronic medicine, targeted delivery, neuromodulation, simulation.

Introduction

Bioelectronic medicines may be defined as a new class of treatment that depends on the precision, detection and modulation of electrical signaling patterns in the nervous system. Since the functions controlled by peripheral nervous system are extensive during chronic diseases, therefore more targeted modulation is achieved. Small implantable devices are attached to the nerves of the individual in the viscera of peripheral nervous systemwhich are able to decode and regulate neural signaling patterns and accomplishing therapeutic effects targeted at specific organs. So as to upgrade the precision these devices record neural electrical activity, physiological parameters and analyze the data in real time and modulate neural signal accordingly.

With the developing research pioneers from scholarly world, industry and government have met up to characterize theexploration way towards Bioelectronic medicines. For better emergence there has been development of BEM technology Roadmap that serves as a planning tool which collects the meaningful information related to neurotechnology based diagnosis and treatment of disease at a quickened rate along with the gaps that needs greater consideration. This roadmap is proposed to give best evaluation of current abilities, projections of innovation needs, research priorities to support industries and institutes on important coordinated effort to accomplish the expected advantages.

BEM GOALS:

Following are the goals which are needed to be achieved in BEM therapy:

1. Identification of targeted diseases is considered as good candidate for Bioelectronic medicine.
2. For better understanding of mechanism there is need of investigative devices which would integrate to understand the remaining gaps in the therapy.
3. There is a requirement forcoordinated efforts between biologic/medical//computing disciplines.
4. Relative to normal state, there must be such biological, chemical, electrical and mechanical models which could help in understanding the proper and complete body’s system behavior when in diseased state.

BEM MICROSYSTEM

The whole system of a closed loop BEM microsystem has been shown in the figure:

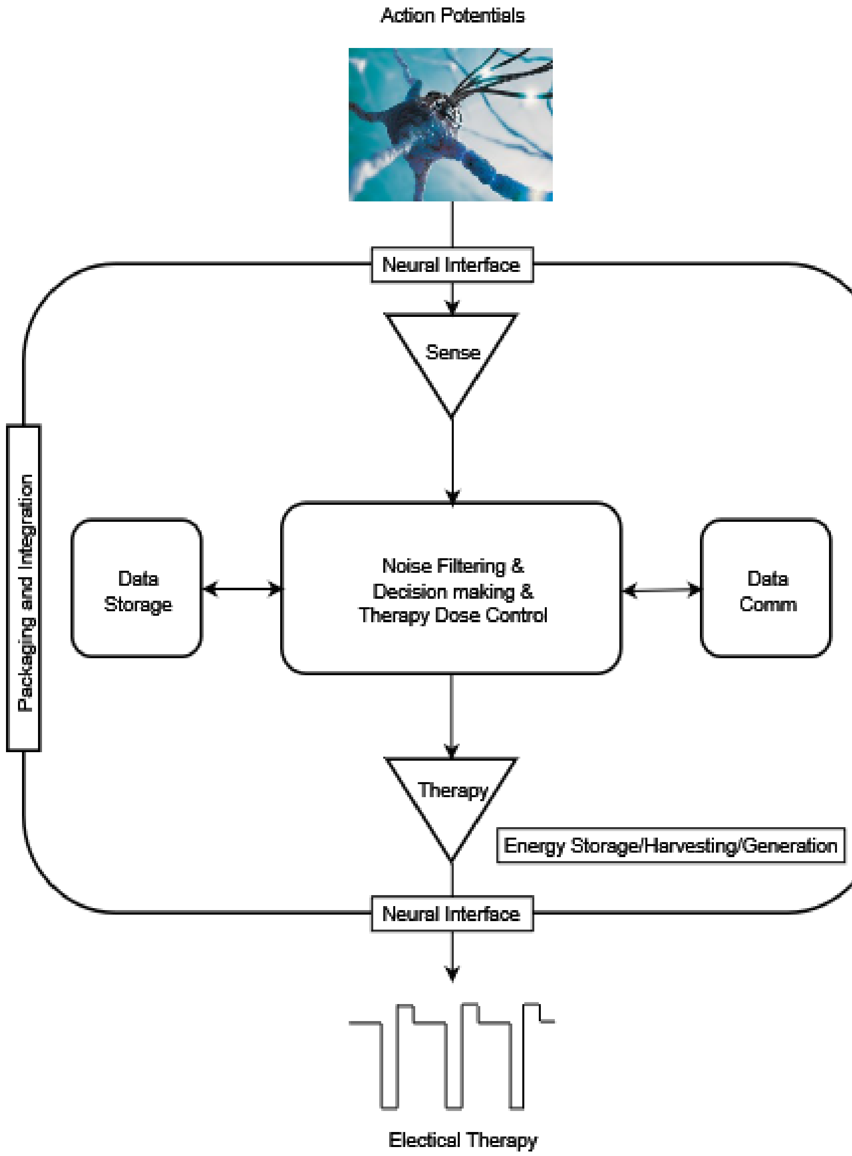

Figure: 1 Block diagram of an implantable neuromodulation device

The device processes the bio signals which are obtained from the implantable electrode through neural interface that either stimulates or blocks the nerve activity. After processing the data is stored in the device. So while designing the device there are five areas which needs focus:

1. Senstivity: to sense and decode the signals from neurons
2. Selectivity: able to target the main nucleic by avoiding off target neurons.
3. Responsiveness: capable of detecting biomarkers.
4. Acceptance: must be accepted by patients with minimum invasive implantation.
5. Closing the loop: should form a closed loop system so as to achieve the targeted function.

So following technologies are important in BEM technology roadmap:

1. **BIOLOGY**: Biomarkers, sensors, neural interface, hermetic packaging
2. **TECHNOLOGY**:Electronics, energy storage
3. **BIOLOGICAL MEDIUM**: wireless communication, surgical tools, wireless powering packaging
4. **USE CASE**: industrial design

The BEM roadmap has been organized into eight chapters [8]:

1. **Chapter 1**: (BEM roadmap overview): Bioelectronic Medicines provide a platform where we can treat many diseases by the use of neurotechnology precisely. It has brought revolution in terms of practice, cost and outcomes in the field of healthcare and medicines. Hence this chapter covers an overview describing the purpose of BEM Technology roadmap, its success factors and various technologies employed.
2. **Chapter 2:** (BEM Platform Functionality): BEM platform can be characterized as a blend of electronic equipment, segments and calculations combined in a manner that explains the system's basic operational attributes.

BEM microsystem is composed of:

1. Energy
2. Analog blocks
3. Communication unit
4. Logic unit
5. Non-volatile memory
6. Packaging enclosure/ encapsulation

1. *Energy source*: one of the major challenges is to keep the implants powered to sustain a long stimulation time. So for meeting the energy demand caseless micro batteries were suggested as a solution which consisted of two electrodes immersed in fluids like blood, serum etc.[1]. With regards to BEM system, energy harvesting alludes to gathering of energy from external source and converting it into power.[2,3,4].so these external sources can be in the form of radiation (light, RF) , mechanical energy, (ultrasound, vibrations) or thermal energy. Some other hidden sources of energy present inside the body which consider some research are:

- Fuel cells
- Temperature gradients
- Electric potential in inner-ear from cochlea
- Muscle/organ movement

2 *Logic/ Analog Mixed signal circuits*: The system intelligence is usually determined by its capability to validate the decisions regarding actuation using combination of mixed signals, logic and memory elements which should be maximized in order to reduce the latency.

3 *Non-volatile Memory*: The most important attributes of a BEM memory unit are reliability and its long life time. At present Ferroelectric random-access memory technology has huge potential for applications in implantable therapeutic gadgets as it empowers rapid, low power and virtually unlimited [5]. Some other technologies are: i) magnetic (MRAM), ii) phase-changing (PCRAM) and iii) resistive (RRAM) memory technologies.

4 *Communication*: An important function of BEM is continuous communication with external monitoring, so mostly ultrasound is operated as RF communication becomes inefficient in small systems. Ultrasound communication in comparison to RF communication undergoes small propagation losses i.e. it is being used for battery-less communication [6].

5 *Electronic packaging*: generally small packaged device is preferred as it will cause less difficulty during implantation.

3. **CHAPTER 3**: (Instrumentation capabilities): This chapter focuses on instrumentation to support organ-nerve mapping relying on biosensors that are embedded in human body which convert the received biological signals into electrical form for the understanding of the nervous system as data system. New advancements in the semiconductor technology are expected to give the revolutionary tools and instrumentation for fundamental organic disclosure and medical applications.
4. **CHAPTER 4**: (Modeling and simulation): this portrays the modeling and recreation needs for Bioelectronic medicines. So to increase the progress of BEM systems, several cell-level and organ-level biological models are needed so that they could be used to obtain the measure of responses due to variety of stimuli. Hence such models should be small and compact and must describe the biological functions accurately. These models can be created either from theoretical biology or it can be experimental stimulus response based.
5. **CHAPTER 5** (Neural Interface): Human body is a complex network which constitute of several systems which performs specific body functions. Out of all systems nervous system is one of systems which regulate and coordinate through different network of nerves. This network is known as autonomic nervous system (ANS). So BEM focuses on neurostimulation therapies thathelp in mapping neural signals using techniques like ultrasonic and tomography techniques for recording and modulation. For example: *Spinal cord leads* stimulates spinal cord which can be used in the treatment of bowel and bladder dysfunction by masking the pain signals to the brain. Hence this chapter includes information about neurostimulation, recording, its types and target precision.
6. **CHAPTER 6**(Biocompatibility packaging): This chapter focuses on different aspects in which BEM devices are packaged. Ultraminiature packaging technology is required for these BEM implants which are placed near to the targeted neurons so as to provide thousands of independent conductors.
7. **CHAPTER 7**: This chapter focuses on implementation of research into practice so that benefit could be provided to patients through more efficient therapies.
8. **CHAPTER 8**: this chapter defines the applications of BEM in exploring clinical opportunity and laying business opportunity by combining BEM with pharmacological intervention.

CONCLUSION:

With the vision of revolutionizing the system of medicines, Bioelectronic medicines hold the promise in achieving the therapeutic intervention by modulating the signaling patterns of the nerves impulses. These medicines include such devices which are implanted anywhere in the viscera and record the neural activity. Further this information is then decoded and analyzed. However there are three principal research areas [7]i) Making of an instinctive nerve atlas is pivotal as this focuses on mapping the innervation of visceral organs for example, the lungs, heart, liver, pancreas, kidney, bladder, gastrointestinal tract and lymphoid and reproductive organs with the objective of achieving resolution at the level of nerve fibers and action potentials. ii) Neural interfacing technology helps in mapping neural signals which includes techniques like ultrasonic and tomography techniques for recording and modulation. iii) When the particular signaling pattern is characterized then focus drifts towards confirmation of rule which implies characterizing which neural circuit exerts impact over which disease in representative animal model. After that an experimental phase is sought after, which includes developing the correlation of neural signals and biomarkers patterns and also investigating the effect of blocking and stimulating neural activity during established disease. Finally this new research delineated here aims to fill in as a guide for developing community and bringing them a new class of precision medicines to patients.

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