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MEDICAL DEVICES MARKET DRIVER

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MEDICAL DEVICES MARKET DRIVER

1. INTRODUCTION

In this report, Medical Devices (MDev) are intended devices designed to interface with the human body. This category focuses on implantable or long-term-use external devices, rather than diagnosis devices used in a clinical setting, that will be analyzed in the specific Market Driver on Medical Diagnosis. MDevs have to be considered an important driver for future electronic market, as highlighted at the recent Sensors Summit held in December 2017 [1] where it was reported that "Wearable Medical Device Market is expected to exceed $7.9 Billion by 2021". Note that this is just a subset of the global market that medical devices can bring.

Medical devices can be classified in two general categories related to the application scenario in which they are used. These two different scenarios require diverse technological approaches, with a direct impact in terms of request of performance, cost, reliability, and accuracy:

1. *Clinical Applications*—related to "real" medical application for health and disease treatment or monitoring and requires the following:
    a. More reliable and precise performance
    b. Lower volumes, but higher costs are considered
2. *Consumer Applications*—related to sports or self-monitoring and requires the following:
    a. Low cost, but lower performances
    b. High volumes
    c. High user-friendliness of device interface

Biomedical technology has already achieved several successes improving the lives of a huge number of people. Nevertheless, there are still many challenges. The role of engineering in the medical and biological research is becoming evident year by year. Many improvements can be ascribed to the constant technology improvement.

In the future perspective, the innovations will grow not only in terms of technology, but in policies too. The relation between personal health and society wellness cannot be broken-up; the desire to open the innovation to more people and distribute healthcare worldwide is one of the major goals for future applications.

1.1. CURRENT STATE OF TECHNOLOGY AND RESEARCH

Present research trends can be clarified when taking into account the topics that are currently of high interest in scientific community.

Table 1 outlines the more important scientific journals in the biomedical technology during the last five years, as presented by Google Scholar and its metric tool. It is worth to note the great importance of materials and tissue engineering. Furthermore, the presence of the IEEE Transaction on Biomedical Engineering at the top of this list indicates the need of electronic engineering in biomedical innovation.

As reported in Table 2, in IEEE biomedical societies the discussed topics range from a wide variety of applications and methodologies from hardware to software and in a multidisciplinary framework. The table shows the most common keywords in the IEEE biomedical papers (considering IEEE Transactions on Biomedical Engineering and IEEE Transactions on Biomedical Circuits and Systems). This metric shows the topics on which researchers are more focused. It can be helpful to understand the future perspectives and the present achievements.

From Table 2 it is evident that research activities target the design of wirelessly connected small-size and low-power integrated electronic architectures that are adapted to implantable/wearable applications. Innovation leverages on new and efficient computation models, machine learning technique in particular, for classification and imaging. Brain computer interface (BCI) devices emerge too in the interest of biomedical research.

Table 1: Top-ten list of publications in the biomedical technology field in 2012-2016 (according the H-index) [2]

1.	Biomaterials
2.	Acta Biomaterialia
3.	IEEE Transactions on Biomedical Engineering
4.	Annals of Biomedical Engineering
5.	Journal of Biomedical Materials Research Part A
6.	Journal of the Mechanical Behavior of Biomedical Materials
7.	Journal of Neural Engineering
8.	Tissue Engineering Part A
9.	Tissue Engineering Part B: Reviews
10.	Journal of Tissue Engineering and Regenerative Medicine

Table 2: Top-ten list of most common keywords in IEEE Biomedical Journals

1.	Machine learning
2.	Wireless
3.	Integrated
4.	Implantable
5.	Imaging
6.	Classification
7.	Wearable
8.	Energy-efficient
9.	Neuromorphic
10.	Brain computer interface (BCI)

1.2 DRIVERS AND TECHNOLOGY TARGETS

In recent years, several goals were achieved, thanks to the growth of innovation. However, several challenges are left unsolved. The main topics that will lead the research and the market in the next future are strictly related to their impact on the society in terms of better quality of life.

Personalized Healthcare—The first goal to be achieved in the near-term future is the improvement of *personalized healthcare*: the advancing of person-centric and self-managed health, due to *precision medicine*. The goal is to improve medical care by exploiting expanded capabilities derived from technology improvements. In particular, telemedicine, early diagnosis, and non-invasive medical devices are key features to be considered [3].

The important technology improvements in biomedical technologies and solutions enable new scenarios for the implementation of medical devices and adapted to personal parameters and behaviors. Fundamental contributions are given by data availability thanks to electronic health records, recent advances in the study and manipulation of DNA, proteins and metabolites, and the possibility of continuous monitoring with low invasive devices. Scientific knowledge, coupled with detailed data about the specific person, will give the possibility to

- exploit large-scale databases, computational tools, and omics methodologies to characterize individuals and extract the needed information for tailoring the medical intervention [4];
- develop optimized prevention and screening strategies; and
- apply treatments at the most opportune times and adapting their dose to the specificities of the patient.

Mobile-Health (m-Health) is becoming a reality, with implementing apps for clinical research. App-accompanied clinical trials (smartRCTs) can improve healthcare through daily and constant monitoring of patients [5].

Neurodegenerative Disorders—Neurodegenerative disorders are a major challenge to be addressed and, thanks to innovations in technology and engineering, they can be met with efficient solutions. Alzheimer's, Parkinson's, Epilepsy, Multiple Sclerosis, and other degenerative conditions are increasing due to population aging. In 2050, the percentage of population over 65 is expected to double [6]. The improvement and personalization of treatment of these diseases can dramatically increase the quality of life of people. Innovations, such as neuroimaging, is an example of strengthening clinical trials.

Neurostimulation used for treating Parkinson's and epilepsy gave remarkably positive effects in some patient cases. The problem is that current solutions are not suitable for everyone, and some diseases, such as Alzheimer's, are currently essentially untreatable. The application of neural engineering and targeted gene delivery to neurological disorders is a very promising approach for covering actual gaps between research results and their clinical application [7].

Combating Cancer—The fight against the cancer is a long-standing challenge that historically appears in any medical strategic plan. New technology innovations could produce further steps forward, as in the recent past. Engineering must continue to pursue this goal, as cancer is one of the most common problems afflicting people world-wide.

Nanomedicine is another fundamental player in this challenge, exploiting the properties of matter at the nanoscale for developing innovative and more efficient drugs, and with the important reduction of side effects than standard therapies [8]-[9].

Reducing Disparities—The access to treatments is not yet possible to everyone. In the next years a positive goal to achieve is to bring efficient medical solutions to the largest possible population. For reaching this target, engineering is a key enabler, to produce low-cost devices and instruments, thus enlarging the possibility of the access to efficient medical solution for a larger number of patients and from the less industrialized and poorer areas of the planet [10].

1.3. VISION OF FUTURE TECHNOLOGY

Thanks to the innovations brought by biomedical engineering healthcare can be improved. This progress is advanced by the birth of new techniques and methodologies. In this section some examples of emerging technologies that will be important in the future to address the current challenges are highlighted.

Machine learning—Machine learning and neural network techniques are becoming perfect solutions to a large variety of application fields of biomedical. The application of machine learning to the huge amount of data produced by emerging biomedical research solutions, that are produced by imaging and multiparametric sensors, is an efficient approach for analyzing the larger, more complex and heterogeneous, mostly unstructured, and poorly annotated information. Traditional data mining and statistical learning approaches typically need to first perform feature engineering to obtain effective and more robust features from those data, and then build prediction or clustering models on top of them. The application of machine learning algorithms, mapped into customized hardware, is a promising approach for bringing biomedical data into improved clinical devices [11].
As mentioned, precision and personalized medicine are becoming common and more important in medical practices. Big data and machine learning approaches are able currently to identify targeted active biomolecules from millions of candidate compounds quickly and cheaply [12]- [14]. The first exploitation of this outstanding result is the customization of healthcare, tailoring the treatments to individual patients as a consequence of machine-learning-based personalized monitoring and related medical decisions. The same considerations are valid for wearable and portable devices, where the quantity of data and the level of decisions to be made are requesting sophisticated methodologies. These are only possible if effective algorithms of machine learning and artificial intelligence in general are applied, mostly in optimized and low-consumption custom electronics.

Brain-computer interface (BCI)—BCI is used for interfacing human brain with electronic devices, then reading and interpreting encephalographic bio-signals with either invasive or non-invasive methods. There are different levels of invasiveness of BCI solutions, from non-invasive use of planar electrodes, such as from electroencephalography (EEG) to the implant of the device on the cortex electro cartography (ECoG) and up to the direct implant of electrodes on the brain's surface [15], [16].
The impact of BCI on healthcare is a reality, opening new scenarios in disease diagnosis, and therapeutic applications, such as in neurorehabilitation (restoration of upper limb function by implanted BCI [17] or in the spinal cord injury disease [16], [18]). The new challenges have an impact on all technology levels: on the processes for production of biocompatible bio-interfaces; on the devices, requiring miniaturization, low power and autonomy; at the system level, for the integration of multi-sensing capabilities with an efficient treatment and transmission of the information.

Nanomedicine—The biomedical devices and bio-nanotechnology, thanks to the application of innovative micro and nano techniques, are effective for developing bio-devices and bio-systems for interfacing living cells and biomolecules in general. The most important purposes for building devices for nanomedicine are the development of nano-bio-sensors, of devices for living cell imaging and analysis, for implantable devices for disease treatment and smart diagnosis, of integrated devices for point-of-care in vitro and in-vivo diagnosis (see following chapter on Implantable, Ingestible, and Injectable Devices).
In general, a nanomedicine device can be defined as a miniaturized system for delivering nanocarriers, nanotherapeutics, or nanodrugs. The best application target is the improvement of the therapeutic efficacy of currently available therapeutic agents, combining nanoscale delivery components, control electronics, and, in some cases, nanoparticles [19].
New scenarios will appear in this framework in the following years; the nanoelectronics will provide architectures small enough to be drunk or to fly in the human bodies as small drones, both to deliver drugs and to monitor the patient metabolism [20]. These types of applications are defined as IIIDs—Implantable, Ingestible and Injectable Devices.

1.3.1 Implantable, Ingestible and Injectable Devices (IIIDs)

A specific analysis has to be dedicated to the **in-body** solutions (Figure 1) that are appearing on the market and are present currently more in research, but are of very high interest for the future of medical devices [21]:

1. *Implantable*: devices implanted inside the human body
2. *Ingestible*: devices ingested like regular pills
3. *Injectables*: devices injected into the human body via needles

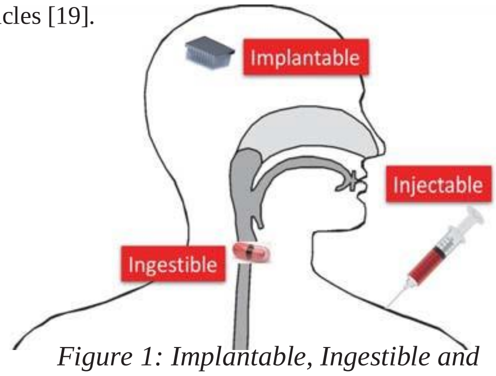

Figure 1: Implantable, Ingestible and Injectable Devices

A key technology need common to all in-body devices is the **wireless communication** for interconnecting the IIID with external components for monitoring and control, avoiding the use of intrusive wires or penetrating structures. The main target is to implement devices always less unobtrusive for medical diagnosis, prevention, prognosis, and disease treatment.

1: Implantable devices are typically installed in the human body (generally immediately under the skin) with a surgical operation. Their purpose is in general for both sensing and stimulating/delivery functionalities. One of the most important future market requests will be to build closed-loop systems for measuring physical parameters and taking decision for actuation in terms of stimuli or drug delivery, for example. Some of the most interesting implantable applications are:

- *Neurosensors*: devices used for many applications, applied to diseases as Epilepsy, Parkinson's and Alzheimer's
- *Neurostimulators*: devices for stimulating the nervous system and recover functionality, used for example in spinal cord stimulation for back pain treatment [22]
- *Pacemakers*: miniaturized devices, installed inside the chest or abdomen, devoted to help the control of cardiac arrhythmias, detecting the heart status, and stimulating heart beat in case of anomalies. Pacemakers are the most mature devices of this category
- *Cardiovascular Pressure Monitors*: devices placed as catheters or wires inside cardiovascular system for long-term monitoring of blood pressure. Applied both in case of chronic blood pressure monitoring as well as for tracking real-time the progress of surgical interventions
- *Intra-cranial Pressure Monitors*: devices placed in the skull for measuring intra-cranial pressure, preventing the risk of severe brain damage in case of localized intracranial mass lesion or cerebral edema, but also in case of cerebrospinal fluid disorder head injury.

2: Ingestible devices are in general miniaturized devices with a capsule-shape, normally taken as a regular pill for drug ingestion. They travel inside the gastrointestinal and digestive system for collecting information about their status. The most diffused solutions are based on real-time videos, images, measurement of physiological parameters for monitoring or diagnostic purposes, or the release of drugs. One of the most important targets is the collection of data that need to be wirelessly transmitted for display or processing. The most representative applications in this field are as follows:

- *Imaging capsules*: used for imaging the gastrointestinal tract and digestive system. They are smart endoscopy capsules, some present already in the market produced as the PillCam by Given Imaging and Medtronic [23], [24]. This is the most advanced area in this field in actual market, but several open issues are image quality, real-time monitoring, and capsule control;
- *Drug delivery capsules*: electronic pills used to deliver a precise quantity of a drug along the gastrointestinal tract.

3: Injectable devices are minimally invasive in respect to the others and are considered the most promising solution for next generation of this type of medical devices. Injectables can be associated to:

- Highly miniaturized Micro-sensors or Micro-stimulators, exploiting the reduced dimensions for flowing in the cardiovascular system, and injected by means of a needle. They are the less invasive and unobtrusive alternative to the implantable devices previously described;
- Three-dimensional medical electronics that are directly built inside the human body through sequential injections, such as the device for electrocardiogram (ECG) and stimulator electrodes developed by Jin et al. [25].

Future directions of IIIDs

It is a fact that recent advances in electronics, materials, power harvesting and smart systems can be a boost for the clinical application of *implantable devices*. First application domain examples are well listed in [21]:

- heart stents for wirelessly transmitting the health of an artery;
- implants for detecting performance-enhancing drugs;
- closed-loop glucose meters and insulin pumps for monitoring and controlling blood sugar levels;
- implants capable of detecting the presence of oral cancers.

In terms of *ingestible devices*, they can be very effective for personalized drug delivery, using capsules for treating digestive disorders and diseases. The possibility of having higher-bandwidth data transmission can improve the quantity of information exchanged with the capsule and so enable better diagnosis. By ingesting capsules equipped with sensors, taken may be with regular pills, gives the possibility of monitoring that the patient has taken the correct dosage. Electronic capsules can better monitor the physiological reactions due to the released dose of drug. It is possible to imagine devices that track the electrical activity at the gastrointestinal system, measuring transit times. The merge of sensing and actuation capabilities, can drive the implementation of smart capsules that release specialized drug profiles when they reach a specific location or when they detect specific species in the environment.

Last but not least, *injectable devices* are a promising solution too. Future challenges for this type of devices are mostly powering issues, due to the high level of miniaturization, requiring fabrication of injectable antennas/electronics with micrometric footprints.

2. CHALLENGES AND TECHNOLOGY REQUIREMENTS

All the mentioned targets, in particular mHealth, personalization of the diagnosis and cure, portability of the solutions, are high demanding in terms of technology challenges.

For *Wearable Devices*, as depicted in Figure 2, Bonato et al. [26] highlighted the impact of mHealth on all the implementation levels both in terms of devices and communication systems.

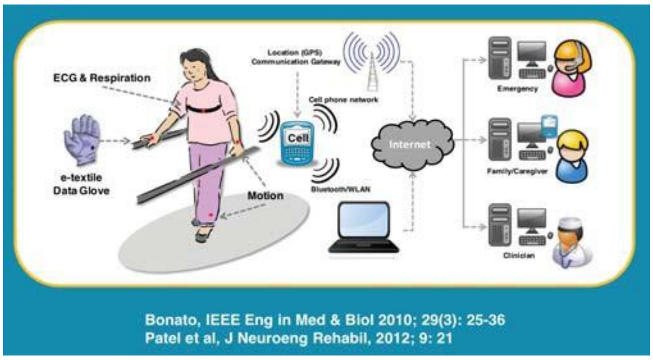

Figure 2: mHealth impact on different implementation levels

The most important challenges to face are:

- Biocompatibility in devices in contact with human skin or tissues;
- for mHealth solutions
    - Ultra-Low Power (ULP) using low-leakage devices such as SOI devices [31];
    - Always connected devices (real monitoring)
    - Cloud Management
- Closed Loop Systems for measuring the patient data, elaborating them efficiently, transmitting them in case and, for example, taking decisions for actuating countermeasures or raising alarms;
- Biosignal detection and interpretation (BCIs, EMGs, ECG, …);
- Efficient and fast decision making;
- Realization of customized patches, implants, … exploiting Additive Manufacturing potentialities.

Medical Devices must be able to become much more personalized for:

- Building Personal Emergency Response Systems;
- Implementing Wearable devices for monitoring for example:
    - Heart, Respiration;
    - Skin for Hydration;
    - Movements;
    - Brain Activity;
- Implementing Methods for taking best decisions based on smart and efficient technologies, where machine learning and neuromorphic/bio-inspired approaches will take a key role.

About *in-body devices*, their design is performed starting from human body analytical models and advanced Multiphysics simulation software, as by Finite Element Methods. Then it is performed the experimental validation using in-vitro phantoms emulating biological tissues electrical properties, and/or by in-vivo using animals (rats, pigs, etc.) and, where possible, human subjects. In this case the most important challenges to consider are:

a) The selection of the optimized *Operation Frequency*. For this choice several trade-offs have to be considered. Working at low frequencies (ex. ISM 13.5-6MHz) is a good option because they have lower losses passing through the biological tissues. As negative effect, low frequencies limit the communications speed and request large antennas and components, increasing the size of the device. Because of it, ingestible devices typically employ high-frequency links (ex. ISM 2.4-5GHz), achieving a better miniaturization, reaching higher data rates and obtaining an improved image resolution.
b) *Integration of Wireless interface*s (inductive links to antennas) into the in-body device. This aspect is highly critical and is the best enabler of unobtrusive and efficient communication with the external monitoring and control equipment. These equipment can be today smart phones, smart watches or in general more customized smart wearable garment. Antenna solutions useful for in-body devices are [21]:
    a. planar Inverted-F antennas (for implantables);
    b. helical antennas (for ingestibles). They provide a circular polarization and an omnidirectional radiation pattern, having too a consistent bandwidth for good range of different tissues;
    c. loop or dipole antennas (for injectables) that has to be designed considering the strict specification in terms of size and shape of the device.

c) *Powering*. Nowadays almost all in-body devices on the market use batteries for powering. But batteries are usually large, and so they dramatically increase the size of the device. And it has to be considered too the raise of patient safety, being in general batteries based on not biocompatible materials. They add too an important issue in terms of maintenance and long-term operating time, requiring frequent replacement and/or recharging. Batteries are still the largest component present inside in-body devices. For the success IIIDs it is so fundamental to find efficient power harvesting techniques, avoiding the presence of the battery and allowing a self-sustainability in terms of power supply. Possible choices are related to harvesting energy from environmental or bodily sources. Electromagnetic energy (RF, ultrasound) are a valid option. Mechanical vibrations are an interesting power source, exploiting heartbeat or tissue and human motion. In the body are present thermal gradients that can be used for thermoelectric energy generation. Electrochemical reactions can be a further possibility, like extracting power from glucose oxidization [27], [28]. Simpler, but less efficient and integrated solutions, are related to RFID, with the drawback of requiring an exterior interrogator in close proximity of the device and inducing an undesired heating inside the tissues.

d) *Biocompatibility* is a further critical issue to be considered. Several techniques have been explored to achieve biocompatibility for in-body devices, including use of biocompatible materials, coating with thin biocompatible polymers or the addition of superstrates to cover the exposed metal parts, the most critical to protect. Actually, steel jackets are the most common solution, as is in pacemakers, but more flexible and integrated approaches have to be studied, as *Biodegradable Electronics*, that are bringing very important results having today the possibility of realizing active devices and so to integrate in future implementations signal detection and wireless transmission [29], [30].

2.1. CHALLENGES AND POSSIBLE SOLUTIONS

Challenges	Metrics	Roadblocks	Potential solutions
Form Factor	#Sensors, #ICs, #Antennas, #Components PCB routing complexity Flexibility Miniaturization	Increasing PCB footprint occupied by connectors and components Need of Flexible PCB Substrates	1. Package-level integration 2. 3D integration
		Integration of heterogeneous components	3. 3D integration 4. Unified technology (CMOS RF/CMOS MEMS)
		Die area explosion due to more functionalities	5. Technology scaling
Power Consumption	Max frequency, Operating Speed, Low Standby current, Sensor Power Consumption, Low-noise AFE Battery Power Density (Watt-Hr/Liter)	System Power Consumption increasing	1. Neuromorphic/Bio-Inspired Architectures 2. Asynchronous and Event Driven computing 3. Approximate computing 4. Quality/Energy Tradeoff 5. Low-leakage SOI devices
	Peak Tx/Rx current (mA for wearables, <μA for IIIDs), Tx/Rx power per bit (μW/bit for Wearables, nW/bit for IIIDs)	Increase of data to be transmitted	6. Optimization of amount of Tx/Rx data by on-site elaboration 7. Machine Learning / Neuromorphic for data filtering
Heating Reduction	#ICs, Max Frequency	Die &PCB areas increase due to more functionalities	1. Best trade-off choice of Operational Frequency 2. Heating reduction at device level by technological improvements
	Heating for Tx/Rx & Remote Powering	Tissue Filtering requests more power for remote powering	3. Quality/Energy Tradeoff 4. Increase of efficiency in power transmission
Biocompatibility	Toxicity level, Inflammation	Need of different materials because of the increase in functionalities request	1. Study of new materials (material science and engineering)
Communication Bandwidth Scaling	RF Data rate	Increasing communication modes/bandwidth requirement for RF communication	1. Technology scaling for high performance RF devices 2. High-performance RF/baseband 3. Integrated multi-standard communication circuits
IP/Sensor integration and scaling (More than Moore)	#Sensors, Max Sensor Power (μW for wearable, < μW for IIDs), DC-DC efficiency (%), DC-DC power density (W/mm^2)	Exclusive technology (analog, MEMS, logic… etc.)	1. Heterogeneous 3D integration 2. Sensor Fusion
Supply voltage scaling challenge	Lowest VDD	Threshold voltage scaling and performance requirement	1. Quality/Energy Tradeoff 2. Technology scaling

2.2. IMPACT ON IRDS IFTS

IFT	*Personalized Healthcare*	*Neurodegenerative disorders*	*Combating cancer*	*Reducing Disparities*
Application Benchmark (AB)	*	**	-	-
System Architecture (SA)	***	***	**	***
Outside System Connectivity (OSC)	***	***	*	***
Packaging Integration (PI)	***	**	***	*
More Moore (MM)	-	**	-	-
Beyond CMOS (BC)	-	-	-	-
Emerging Research Materials (ERM)	***	**	***	*
Metrology (MET)	*	*	*	*
Environment, Safety, and Health (ESH)	***	***	***	***

- No impact
* Low Impact
** Medium Impact
*** High Impact

3. CONCLUSIONS AND RECOMMENDATIONS

3-1 Findings and Highlights:

Medical Devices (MDev) are intended devices designed to interface the human body, that are analyzed in the specific Market Driver on Medical Diagnosis. "Wearable Medical Device Market is expected to exceed $7.9 Billion by 2021". Medical devices can be classified into (1) *Clinical Applications*, related to "real" medical application for health and disease treatment or monitoring, requiring more reliable and precise performances, and (2) *Consumer Applications*, like for sports or self-monitoring, requiring low cost, but lower performances and high user friendliness of device interface.

Biomedical technology has already achieved several successes, improving the lives of a huge number of people. Nevertheless, a lot of challenges are still open. The important technology improvements in biomedical technologies and solutions open new scenarios for the implementation of medical devices, fitting the personal parameters and behaviors.

- Personalized Health Care is given by data availability thanks to electronic health records, recent advances in the study and manipulation of DNA, proteins and metabolites, and the possibility of continuous monitoring with low invasive devices. to characterize individuals and extract the needed information for tailoring the medical intervention. It also develops optimized prevention and screening strategies, applying treatments at the most opportune times and adapting their dose to the specificities of the patient.
- Mobile-Health (m-Health) is becoming a reality, trying to implement apps for clinical research. App-accompanied clinical trials (smartRCTs) can improve health care following all-day-long the patients.
- Neurodegenerative disorders are a major challenge to be addressed and, thanks to the innovation in technology and engineering, they can be faced with efficient solutions. Alzheimer, Parkinson, Epilepsy, Multiple Sclerosis and other degenerative conditions are increasing due to population ageing. The improvement and personalization of treatment of these diseases can dramatically increase the quality of life of people, as example strengthening clinical trials with neuroimaging.
- Neurostimulation used for treating Parkinson and epilepsy gave remarkably positive effects in some patient cases. The problem is that current solutions are not suitable for everyone, and some diseases, as for example Alzheimer, are still nowadays essentially

untreatable. The application of neural engineering and targeted gene delivery to neurological disorders is a very promising approach for covering actual gaps between research results and their clinical application.

- Combating Cancer could produce further step forward, as already done in the recent past. The engineering must continue to strike on this goal, as one of the most common problems which afflicts people all around the world.
- Nanomedicine is another fundamental player in this challenge, exploiting the properties of matter at the nanoscale for developing innovative and more efficient drugs, with in parallel the important reduction of side effects than standard therapies.
- Reducing Disparities are to bring efficient medical solutions to the largest possible population. Low cost devices and instruments, enlarging the possibility of the access to efficient medical solution to a larger number of patients, also from less industrialized and poor areas of the planet.

3-2 CHALLENGES AND TECHNOLOGY REQUIREMENTS

- **Machine learning**. Machine learning and neural network techniques are becoming perfect solutions to a huge variety of application fields, comprising biomedical. The application of machine learning to the huge amount of data produced by emerging biomedical research solutions, that are based on imaging and multiparametric sensors, is the efficient approach for analyzing the produced larger, more complex and heterogeneous, mostly unstructured and poorly annotated information. Traditional data mining and statistical learning approaches typically need to first perform feature engineering to obtain effective and more robust features from those data, and then build prediction or clustering models on top of them. The application of machine learning algorithms, mapped into customized hardware, is a promising approach for bringing biomedical data into improved clinical devices.

- **Brain-computer interface (BCI)**. BCI are used for interfacing human brain with electronic devices, reading and interpreting encephalographic bio-signals, with either invasive or non-invasive methods. The impact of BCI on healthcare is a fact, opening new scenarios in disease diagnosis, therapeutic applications, as example in neurorehabilitation. The new open challenges have an impact on all technology levels: on the processes for production of biocompatible bio-interfaces; on the devices, requiring miniaturization, low power and autonomy; on system level, for the integration of multi-sensing capabilities with an efficient treatment and transmission of the information.

- **Nanomedicine.** The biomedical devices and bio-nanotechnology, thanks to the application of innovative micro & nano techniques, are effective for developing bio-devices and bio-systems for interfacing living cells and biomolecules in general. The most important purposes for building devices for nanomedicine are the development of nano-bio-sensors, of devices for living cell imaging and analysis, for implantable devices for disease treatment and smart diagnosis, of integrated devices for point-of-care in vitro and in-vivo diagnosis.

- **Implantable, Ingestible and Injectable Devices (IIIDs).** Implantable devices are typically installed in the human body (generally immediately under the skin) with a surgical operation. Their purpose is in general for both sensing and stimulating/delivery functionalities. Some of the most interesting implantable applications are Neurosensors, Neurostimulators, Pacemakers, Cardio Vascular Pressure Monitors, Intra-cranial Pressure Monitors. Ingestible devices are in general miniaturized devices with capsule-shape, normally taken as the regular pills for drug ingestion. They travel inside the gastrointestinal and digestive system for collecting information about their status. The most diffused solutions are based on real-time videos, images, measurement of physiological parameters for monitoring or diagnostic purposes, release of drugs. One of the most important targets is the collection of data that have to be wirelessly transmitted for display or processing. Injectable devices are minimally invasive in respect to the others and are considered the most promising solution for next generation of this type of medical devices.

All the mentioned targets, mHealth, personalization of the diagnosis and cure, portability of the solutions, are high demanding in terms of technology challenges. About in-body devices, their design is performed starting from human body analytical models and advanced Multiphysics simulation software, as by Finite Element Methods. Then it is performed the experimental validation using in-vitro phantoms emulating biological tissues electrical properties, and/or by in-vivo using animals (rats, pigs, etc.) and, where possible, human subjects.

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REFERENCES

[1] Sensors Global Summit 2017, Retrieved: Nov. 2017. [Online]. Available: http://sensorsglobalsummit.com.

[2] Google contributors, "Google Scholar, top publication", Retrieved: Nov. 2017. [Online]. Available: https://scholar.google.com/citations?view_op=top_venues&hl=en&vq=eng_biomedicaltechnology.

[3] United States Department of Health and Human Services, "Federal Health IT Strategic Plan 2015-2020", 2016.

[4] United States Department of Health and Human Services, "NIH-Wide Strategic Plan Fiscal Years 2016-2020", 2016.

[5] M. M. E. Vogel, S. E. Combs, and K. A. Kessel, "mHealth and application technology supporting clinical trials: Todays limitations and future perspective of smartRCTs", Frontiers in Oncology, vol. 7, p. 37, 2017.

[6] L. E. Hebert, L. A. Beckett, P. A. Scherr, and D. A. Evans, "Annual incidence of Alzheimer disease in the united states projected to the years 2000 through 2050", 2001.

[7] United States Department of Health and Human Services, "National Plan to Address Alzheimer Disease: 2017 Update", 2017.

[8] L. Bregoli, D. Movia, J. D. Gavigan-Imedio, J. Lysaght, J. Reynolds, and A. Prina-Mello, "Nanomedicine applied to translational oncology: A future perspective on cancer treatment", Nanomedicine: Nanotechnology, Biology and Medicine, vol. 12, no. 1, pp. 81–103, 2016.

[9] F. Iommelli, V. De Rosa, C. Terlizzi, and S. Del Vecchio, "Preclinical imaging in oncology: advances and perspectives", The quarterly journal of nuclear medicine and molecular imaging: official publication of the Italian Association of Nuclear Medicine (AIMN) the International Association of Radiopharmacology (IAR), vol. 61, p. 3347, 2017.

[10] C. o. F. American Institute for Medical and B. Engineering, "Medical and biological engineering in the next 20 years: The promise and the challenges", IEEE Transactions on Biomedical Engineering, vol. 60, pp. 1767–1775, 2013.

[11] R. Miotto, F. Wang, S. Wang, X. Jiang, and J. T. Dudley, "Deep learning for healthcare: review, opportunities and challenges", Briefings in Bioinformatics, 2017.

[12] F. Celesti, A. Celesti, L. Carnevale, A. Galletta, S. Campo, A. Romano, P. Bra- manti, and M. Villari, "Big data analytics in genomics: The point on Deep Learning solutions", in 2017 IEEE Symposium on Computers and Communications (ISCC), pp. 306–309, 2017.

[13] L. Zhang, J. Tan, D. Han, and H. Zhu, "From machine learning to deep learning: progress in machine intelligence for rational drug discovery", Drug Discovery Today, vol. 22, no. 11, pp. 1680-1685, 2017.

[14] M. Rais, A. Lachkar, A. Lachkar, and S. E. A. Ouatik, "A comparative study of biomedical named entity recognition methods-based machine learning approach", in 2014 Third IEEE International Colloquium in Information Science and Technology (CIST), pp. 329–334, 2014.

[15] K. Casimo, K. E. Weaver, J. Wander, and J. G. Ojemann, "BCI use and its relation to adaptation in cortical networks", IEEE Transactions on Neural Systems and Rehabilitation Engineering, vol. 25, pp. 1697–1704, 2017.

[16] J. E. Huggins, C. Guger, M. Ziat, T. O. Zander, D. Taylor, M. Tangermann, A. Soria-Frisch, J. Simeral, R. Scherer, R. Rupp, G. Ruffini, D. K. R. Robin- son, N. F. Ramsey, A. Nijholt, G. Mller-Putz, D. McFarland, D. Mattia, B. J. Lance, P.-J. Kindermans, I. Iturrate, ChristianHerff, D. Gupta, A. H. Do, J. L. Collinger, R. Chavarriaga, S. M. Chase, M. Bleichner, A. Batista, C. W. Anderson, and E. J. Aarnoutse, "Workshops of the Sixth International Brain Computer Interface Meeting: brain computer interfaces past, present, and future", Brain-Computer Interfaces, 2017.

[17] G.R. Müller-Putz, P. Plank, B. Stadlbauer, K. Statthaler, J. Bosco Uroko. "15 Years of Evolution of Non- Invasive EEG-Based Methods for Restoring Hand & Arm Function with Motor Neuroprosthetics in Individuals with High Spinal Cord Injury: A Review of Graz BCI Research", Journal of Biomedical Science and Engineering, Vol.10 n.06, 2017.

[18] A. Athanasiou, G. Arfaras, I. Xygonakis, P. Kartsidis, N. Pandria, K. R. Kavazidi, A. Astaras, N. Foroglou, K. Polyzoidis, and P. D. Bamidis, "Commercial BCI control and functional brain networks in spinal cord injury: A proof-of-concept", in 2017 IEEE 30th International Symposium on Computer- Based Medical Systems (CBMS), pp. 262–267, 2017.

[19] H. Jahangirian, E. Lemraski, T. Webster, R. Rafiee-Moghaddam, and Y. Ab- dollahi, "A review of drug delivery systems based on nanotechnology and green chemistry: green nanomedicine", pp. 2957–2978, 2017.

[20] W. Ngwa, R. Kumar, M. Moreau, R. Dabney, and A. Herman, "Nanoparticle drones to target lung cancer with radiosensitizers and cannabinoids", Frontiers in Oncology, vol. 7, p. 208, 2017.

[21] A. Kiourti, S.N. Konstantina, "A review of in-body biotelemetry devices: implantables, ingestibles, and injectables", IEEE Transactions on Biomedical Engineering, 2017.

[22] C.R. Abrecht, E.L. Ross, “Spinal Cord Stimulation”. In: Yong R., Nguyen M., Nelson E., Urman R. (eds) Pain Medicine. Springer, 2017.

[23] P. Dionisio, S. Gurudu, J. Leighton, G. Leontiadis, D. Fleischer, A. Hara, et al. “Capsule Endoscopy as a Significantly Higher Diagnostic Yield in Patients with Suspected and Established Small-Bowel Crohn’s Disease: A Meta-Analysis”. Am J Gastroenterol. 105:1240-8, 2010.

[24] G. Rogler, L. Biedermann, “Clinical Utility of Biomarkers in IBD”. Current Gastroenterology Reports, 17:26, 2015.

[25] C. Jin et al., “Injectable 3-D fabrication of medical electronics at the target biological tissues,” Sci. Rep., vol. 3, Art. no. 3442, 2013.

[26] S. Patel, H. Park, P. Bonato, L. Chan, M. Rodgers, “A review of wearable sensors and systems with application in rehabilitation”, J Neuroeng Rehabil. 20; 9: 21, 2012.

[27] C. Dagdeviren, Z. Li, Z.L. Wang, “Energy Harvesting from the Animal/Human Body for Self-Powered Electronics”, Annual Review of Biomedical Engineering,19:1, 85-108, 2017.

[28] J. Gross, X. Chen, F. Giroud, C. Abreu, A. Le Goff, M. Holzinger, S. Cosnier, “A High Power Buckypaper Biofuel Cell: Exploiting 1,10-Phenanthroline-5,6-dione with FAD-Dependent Dehydrogenase for Catalytically-Powerful Glucose Oxidation”, ACS Catalysis 7(7), 4408-4416, 2017

[29] R. Li, L. Wang, D. Kong, L. Yin, “Recent progress on biodegradable materials and transient electronics”, Bioactive Materials, https://doi.org/10.1016/j.bioactmat.2017.12.001, 2017.

[30] G. Lee, S.-K. Kang, S. M. Won, P. Gutruf, Y. R. Jeong, J. Koo, S.-S. Lee, J. A. Rogers, J. S. Ha, “Fully Biodegradable Micro supercapacitor for Power Storage in Transient Electronics”, Adv. Energy Mater., 7, 1700157, https://doi.org/10.1002/aenm.201700157, 2017.

[31] H. Rahmani, A. Babakhani, “A wireless power receiver with an on-chip antenna for millimeter-size biomedical implants in 180 nm SOI CMOS”, 2017 IEEE MTT-S International Microwave Symposium (IMS), pp. 300–303, 2017.