Recent Advances in Body Area NanoNetworks: Electromagnetic, Materials and Communications

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ABSTRACT

In recent years, nanotechnology has emerged as a novel evolution in technology enabling the design of miniaturized devices (*i.e.*, nanodevices). At this scale, the behaviors and characteristics of nanodevices require a deep understanding and a revision of well-known features of devices at the macroscale level. Indeed, due to their specific nanoscale features, a fundamental requirement is to enable nanodevices to collaborate collectively to achieve a common objective. As a result, a set of nanodevices, sharing the same medium and collaborating for the same task, through communication and networking at the nanoscale, forms a nanonetwork.

Nanonetworks are expected expanding the capabilities of single nanodevice and enabling new nanotechnology applications including healthcare, biomedical, environmental, military, as well as industrial fields. In particular, through a nanoscale communication paradigm,as well a network of nanodevices can constitute a Body Area NanoNetwork (BANN), and new and revolutionary complex applications can be envisaged. This new context requires a deep analysis of the innovative technological solutions suitable for the specific features under consideration.

In this paper we aim to report the last advancements of the BANNs in a 360° vision, from three different perspectives, such as (*i*) electromagnetics, (*ii*) materials, and (*iii*) communications. We will also give a global vision of the three perspectives, by showing the glue elements of each other.

1. INTRODUCTION

Nanotechnology is a new research domain that is finding applications in several areas, from telecommunications to nanomedicine, from environmental to military and security, ust to mention some of the most common ones [3]. It is more and more gaining consensus in different fields, especially for (in)body applications, since the use of nanodevices, opportunistically functionalized, may improve the therapeutic index and increase their tolerability in the body, by drastically reducing the interferences at minimum.

In this context, a nanodevice is usually designed to perform a set of elementary actions, such as sensing and actuation. A dense wireless interconnection of nanodevices, could potentially accomplish novel and complex functionalities. Nanorobots distributed in or on top of the human body could enable pervasive and reactive continuous in-vivo monitoring.

The field of nanomedicine is a complex scenario, where the interaction of nanodevices is affected by the presence of the human body. This issue represents a very hot topic that only recently has started to be considered by researchers [28]. The interaction between the nanoparticulate system and the biological environment (*i.e.* the human body) is strictly correlated with the nanodevice material and the signaling considered for communication purpose.

From a "material" point of view, several types of nanoparticles can be exploited for body networks applications, constructed with a huge range of organic or inorganic materials, such as emulsions, Solid Lipid Nanoparticles (SLNs), gold nanoparticles, silver nanoparticles, titanium dioxide TiO_2 nanoparticles, dendrimers, Carbon Nano-Tubes (CNTs), etc. [24]. When these materials are opportunistically functionalized, it has been shown that can be used for localized Drug Delivery Systems (DDSs) and/or for diagnostic objectives.

Regarding the electromagnetic nanonetworks, the required downsize imposes the use of very high operating frequencies (several hundreds of Terahertz), thus limiting the feasibility of nanonetworks. In fact, according to the classical antenna theory, a one-micrometer-long antenna would radiate at approximately 150 THz with the assumption of a Perfect Electrical Conductor (PEC). Normally, at these higher frequencies, metallic materials are frequency-dependent and then far to be PEC material. Alternatively, nanomaterials (*e.g.* graphene or specific metamaterials (MMs)) enable the developments of nano-antennas that can operate at much

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lower frequencies. This type of considerations implies that there exists a very strict interrelation between the nature of the material constituting the antenna and the electromagnetic features.

Finally, from a communication point of view, different innovative communication paradigms have been proposed during the last few years, such as molecular and neural communications [13, 37], terahertz band communications [2], opto-ultrasonic communication [42], acoustic communication approaches [29].

The aim of this paper is to analyze the last advances of Body Area Nanonetworks from three different perspectives, such as (*i*) electromagnetics, (*ii*) (meta)materials, and (*iii*) communications. Furthermore, we try to identify the common points and the interdependencies of the three (sub)-domains.

The rest of the paper is organized as follows. In the Section 2 we report the recent advances in the context of electromagnetism applied to nanonetwork domain. The Section 3 will be devoted to the description of the last results in terms of material and meta-material for nanonetworks and body area nanonetworks. In Section 4 we will revise the major considerations that have been done on the interferences between the body networks with the human immune system. In the Section 5 we will report the most recent results in terms of communication paradigms for BANNs. Finally, conclusions are drawn at the end of the paper, together with some directions for future works.

2. RECENT ADVANCES IN ELECTROMAGNETIC NANONETWORKS

On-going research on graphene-based nano-transceivers [19, 41] and nano-antennas [21, 46] witness the Terahertz Band (0.1−10 THz) as the communication frequency band for nanodevices. The peculiar propagation properties of electrons in graphene [14, 15] enable the creation of compact miniaturized RF components, alleviating the energy constraints of nanodevices.

The Terahertz Band brings many opportunities for communication among nanodevices, mainly due to the huge amount of available unlicensed band. Although long-range Terahertz Band communications are drastically limited by the molecular absorption loss [40], for short distances below one meter [20] the THz band acts as a single transmission window almost 10-THz-wide. This very large band can theoretically support data transmissions at very high rates, and also enables new communication mechanisms to be adopted by nanodevices with very limited capabilities.

In this direction, novel channel models need to be designed since existing models used for lower frequencies are not suitable in the THz band context. One of the main channel models for THz band has been presented in [20], where the authors investigate the effects due to molecular absorption and free space loss. Other works [22, 38] investigate the scattering effect in realistic environments for THz communications, while in [16] the authors present a channel model based on multi ray approach that considers both reflected, scattered, and diffracted rays.

Recently, it has been shown that the chirality effect of specific materials (*i.e.*, metamaterials) strongly affects the performance of channel in THz band [49, 50]. Metamaterials exhibiting Giant Optical Activity in a specific range of THz band (*i.e.*, from 4 to 10 THz) affect the channel response, and then it is possible to tune the working frequency in order to enhance the channel performances.

Following novel results in channel modeling in THz band, novel communication schemes need to be figured out. Recently, a technique based on the transmission of one-hundred-femtosecond-long pulses spread in time known as TS-OOK has been proposed in [19]. This modulation takes into account the difficulty of generating high-power carrier signals at Terahertz Band frequencies from a nano-transceiver and leverages the state of the art in pulse-based nano-transceivers.

3. ADVANCED MATERIALS FOR BANNS

Noble metals, like silver and gold, polymer based materials, silica nanoparticles, carbon nanotubes, etc. are largely employed in the design of nanoparticles and can be exploited to accomplish different tasks, e.g. they can be used as carriers of medicament and/or bioactive molecules to a desired intracellular cells, host materials for bioimaging and biosensing agents [45, 48].

Colloidal silver has been used as an antibacterial agent able to weakening DNA replication. Gold-based nano components have been often utilized since the low toxicity versus biological systems [7, 54]. In particular, Ti, Mg, steel and their alloys are considered important metallic materials for both *bioengineering* and for human *implants*; as well, their porous metal interface can be exploited as a drug delivery plate and stimuli reactive material.

The central point and the success of the usage of these metallic materials for the purpose of interest are governed by their capacity to develop biocompatible carriers allowing high loading of drug molecules with no any early release of the load before getting the target.

In order to serve as an efficient drug delivery system, among other characteristics, the carrier material should be biocompatible and it has to show (*i*) high loading ability for the chosen drug particles, (*ii*) cell type or tissue specificity, (*iii*) controlled release of the molecules with an appropriate ratio of release [10, 18]. Complementarily, surface chemistry and morphology are considered as key features for determining the biological performance of bio-metallic implants, to support or stimulate the preferred host response [53].

Modification of the physical properties of nano- and micro-particles radically changes their biological functions, representing an important aspect when drug delivery system is under development for highly specific sensibleness, e.g. long circulation. The effects that size [12], shape [8, 34], surface charge [9, 52] and hydrophobicity [17, 52] have on the transfer capabilities of particles have been extensively investigated during the time.

According to [5], modulating the elasticity of nano- and micro-particles is a feasible approach to control some biological interactions. In-vitro studies pointed out that softer particles show lower internalization in immune cells which is supported by in-vivo studies that jointly demonstrate that softer particles circulate for longer periods as compared to their hard counterparts. Additionally, computational studies in detail described how hard particles have individual returns over their soft counterparts in cellular internalization. The transformation of the metal-based materials surface into a porous network obtained by different methods (surface anodization, plasma or laser treatments, chemical etching, ultrasonic technique, sol-gel route, etc.), as well as amplification of their biocompatibility, lead obtaining an intelligent metal surface (spongy like material). Such a biometal becomes more attractive for functional molecules (surface attached pills) in a complex biological system, where the strict control over the physical or chemical absorption of functional biomolecules and cells is encouraged. As for example, a textured bio-metal surface with a fully hydrophilic nature, determining a positive reaction of distinguished cells to the surface and their attachment(s) has been discussed in [6].

Development of a passive oxide layer on the bio-metallic implant surfaces is considered as one of the crucial element as concerns the protection of their surfaces and their biocompatibility: once the implant will be embedded, the biological environment will be in contact with the oxide layer and not with the metal themselves. Additionally, the developed oxide layer could guarantee the chemical attachment of functional molecules (pharmaceutical agents, drugs, etc.).

The modification of the metal surfaces can further prevent the introduction and release of toxic compounds from the surface of the bio-device [35], [36]. Supplementary, an intelligent metal surface is capable to control the behavior of the biomolecules during the time. The properties of such surfaces can be manipulated externally (humidity, temperature, pH change, presence of an electric or magnetic field, etc.) giving rise to different structures to be selectively used for particular applications [11], [43]. Appropriately modified metallic surfaces can present advanced features: e.g. Ti wires and nanotubes groups are considered innovative drug releasing structures with the additional benefit related to a localized approach, that reduces the toxic effect of drug to the healthy tissues and at the same time diminishes the severity of side effects [23].

As well, local treatment allows high drug concentration at the target site and prolonged pharmacological exposure. Ionic dissolution is strictly related to the specific surface area of the materials and affects the biocompatibility of the materials. Specific surface area increases as particle size decreases, and the chemical reactivity of the system is more evident.

In most cases, the interaction of materials with cells and tissue starts from ionic dissolution and is an expression of the materials toxicity, which is directly correlated to the corrosion resistance of the material [33]. Rise in specific surface area, typically counted as the nanosizing effect, origins the improvement of the chemical reactivity and toxicity for soluble materials. In the case of a non-soluble and biocompatible material, like Ti and TiO_2, when the particle size is 200 nm or minor, they are less stimulative and their identification by the body protection systems becomes weaker. They can arrive into the organism through the respiratory or the digestive apparatus and then spread out inside the whole body [51].

In the last a few years the research field of material science has a bit changed its primary focus, by shifting it for engineering materials with specific features instead of studying the properties and characteristics of the existing materials. This new field of research is well represented by the field of metamaterials. Metamaterials are complex materials with artificial structures and are particularly interesting, since they exhibit features that are not existing in nature, *e.g.* negative refraction index [4, 44]. These characteristics have attracted several researchers in several research areas [55]. One of the most prominent example of scientific and technical applications concerned with metamaterial is certainly nanotechnology. The typical feature of metamaterials construction is the possibility to achieve the user defined electromagnetic response at a precisely controlled target frequency and this represents a very interesting aspect in the context of photonic/phononic domain [47].

Normally, the parameters of an MM are established from the beginning and cannot be altered later (*e.g.* programmatically). On the other hand, the concept of reprogrammable metamaterial has been considered for the first time in [25], where the authors propose a new class of real-time reconfigurable MMs, named Software Defined Metamaterials (SDMs).

4. IMMUNE HUMAN SYSTEM CONSIDERATIONS

One of the most important considerations that need to be done related to the context of BANNs is about the impact that the Immune Human System (IHS) can exert on the nanoparticulate system performance, as well as how this latter stimulates a response of IHS. Of course, the desirable effect would be to have as minimum interference as possible.

Despite the great importance of this research topic, it has only recently started to be investigated by the researchers [26, 31]. The main difficulty in this context, is to identify a “right” model that can capture the necessary features of the IHS in a way that the interferences can be correctly modeled by keeping the system as “tractable” as possible (*i.e.* not too much complex). In [32], the authors review the different effects of nanoparticles on the specific immune cells (*i.e.*, dendritic cells, neutrophils, mast cells, T cells, B cells, etc.). The authors distinguish two types of immune response such as (*i*) innate, and (*ii*) adaptive immunity. Innate response is the non specific and first response of the immune system, and plays a very important role in the early recognition and proinflammatory response. The adaptive immune response of the IHS is antigen specific and reacts with the organism that induced the response. Normally, nanoparticles are identified as “foreign” entities and then are eliminated by the IHS, as it has also already mentioned in the previous paragraph.

However, the human body can also identify the foreign elements but does not consider them as a threat. In this case the IHS will tolerate the nanoparticles. The response of the immune system to the presence of the nanoparticles has to be considered when developing a nanomaterial for in-vivo applications. As outlined in [32] a different perspective is given by a different application, such as nanoparticles targeting immune cells that have to manipulate or control immunological diseases. In this case, the material of nanodevices has to be designed to opportunistically modify the immune response.

In any case, the conclusion is that a deep and accurate knowledge of a nanoparticulate system with the IHS is fundamental. This purpose has been pursued by the researchers in [30] and [31], where the authors introduced a mathematical model to effectively represent the IHS and to be able to also incorporate both time and spatial correlations with an external system composed of nanoparticles.

5. COMMUNICATION PARADIGMS FOR BANNS

One key factor of BANN technology is represented by data communications, and specifically the need for short-range data communications. Several new communication paradigms in the context of BANNs have been proposed in the last few years. Among them, electromagnetic communications in the terahertz band [2], neural communications [13], chemical communication or molecular communications [37], opto-ultrasonic [42], and phonon-based [27] communication techniques have been proposed.

In particular, in [39], the authors investigate electromagnetic propagation and communication in human tissues, by demonstrating the challenges that characterize a similar environment as transmitting medium. A terahertz channel characterization inside the human skin has been derived in [1], where the authors propose a novel radio channel model inside the human skin and compare the model with terahertz time-domain spectroscopy based measurement of skin sample.

Chemical and molecular communications represent a kind of straightforward and natural way to communicate at this size, since molecules and cells naturally communicate in living beings. The counter side of this type of communications is based from one side by the high communication latency that generally characterize this type of communication, and from another side the still scarce control on molecules. In fact, targeting specific actions at this level is not at all trivial, and *synthetic biology* is still in its infancy.

A different point of view in terms of BANN communications is represented by the approach considered in [42]. The authors exploit the optoacoustic effects enabling the generation of high-frequency acoustic waves when the medium is irradiated with electromagnetic energy at the optical frequency. In [27], the authors argue that quantum phenomena may represent a natural direction for developing nanotechnology. A specific type of nanoparticles is considered, namely phonons, and by considering them as specific information carriers, it is possible to compute the theoretical capacity in a body network context.

6. CONCLUSIONS

Based on the recent advancements on electromagnetism, (meta)material for nanodevices and nanocommunication approaches, it is clear a very strict interrelation existing among these three fundamentals aspects of BANNs. In particular, electromagnetic communication seems a viable solution for BANN if innovative materials with specific properties are considered, such as graphene, carbon nanotubes or metamaterial with specific features. On the other hand, the type of communication is strictly dependent on the specific technology selected that depends on the characteristics of the material used as transmission means. Most important, in biological contexts not only the transmission features matters but also fundamental aspects such as bio-compatibility and low impact in terms of immune systems have to be taken into consideration.

From one side it is clear that a global and multi-disciplinary approach has to be considered in order to investigate novel and revolutionary solutions in the context of BANNs that takes into considerations the different aspects we have envisaged in this position paper. On the other hand, we realize that a convergence of different disciplines is always a complex process and is more complicated in this case where all the research domains (*i.e.* electromagnetism, material and communications) for BANNs are still in infancy.

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