Internet of Nano and Bio-Nano Things: A Review

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Abstract In recent years, advances in biotechnology, nanotechnology and materials science have led to the development of revolutionizing applications in Internet of Things (IoT). In particular, the interconnection of nanomaterials, nanoimplants, and nanobiosensors with existing IoT networks has inspired the concepts of Internet of Nano Things (IoNT), and Internet of Bio-Nano Things (IoBNT). To date, although there are several survey papers that addressed these concepts separately, there is no current survey covering all studies in IoNT and IoBNT. Therefore, in this paper, we provide the complete overview of the recent studies in these three areas. Furthermore, we emphasize the research challenges, potential applications, and open research areas.

1 Introduction

The number of Internet usage and Internet-based applications in our daily life is increasing day by day [1]. This increase also brings about an exponential increase in number of devices with internet access. In this context, it is estimated that the number of connected devices to the Internet will exceed 75 billion by 2025 [2]. As a natural consequence of these developments, the concept of the Internet of Things (IoT) has become the focus of research and development, especially in the last 15 years [3]. IoT concept represents the connection and communication of all kinds of physical things such as sensors, actuators, personal electronic devices in the real world via the Internet [4]. Today, IoT applications appear in many areas such as smart transportation, real-time monitoring systems, smart cities, smart grids, smart environmental monitoring,

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medical and health systems, and smart buildings [5]. On the other hand, thanks to the advancements in materials science and nanotechnology, IoT application areas are expanding further and beating a path for the formation of new concepts like the Internet of Nano Things (IoNT) and the Internet of Bio-Nano Things (IoBNT).

Although these concepts are just emerging today, the history of nanotechnology, which forms the basis of these concepts, goes back to the 1950s. In 1959, Richard Feynman first discussed the possibility of straightly handling materials at the atomic scale and the idea of reproducing everything by miniaturization on nanoscale in his famous talk entitled "There's Plenty of Room at the Bottom" [11]. In 1974, the term "Nanotechnology" was first coined by Norio Taniguchi to describe dimensional accuracy [12]. Nanotechnology is the study and use of extremely small objects on an atomic and molecular scale. It has the potential to produce many new technological materials and devices for the benefit of people by bringing together many disciplines such as engineering, medicine, biology, physics, and chemistry [6]. Nano things are devices ranging from 1 to 100 nanometers (nm) and can perform tasks such as collecting, creating, computing, processing, and transmitting data at nanoscale [13, 14]. Today, it has revealed promising networking paradigms such as IoNT and IoBNT, which are formed by interconnecting nano-things with existing communication networks via high-speed Internet. These network paradigms have high application potential in different fields such as healthcare, biomedical, military, smart environment, industry, energy, and multimedia [4, 7]. Therefore, there is a need for up-to-date studies that comprehensively explain all these network paradigms. As shown in Table 1, although there are several studies in the literature that individually address IoT, IoNT, and IoBNT, there is currently no review article that encompasses all three subjects together. This suggests a need for a comprehensive examination of these related technologies in a single publication. Based on this motivation, in this paper, we present a survey that fills the existing gaps in the literature. The following is a summary of the survey's main contributions:

- We present a review paper on IoNT and IoBNT network paradigms, which may have many potential applications in the future.
- We then detail the potential application areas, architectural models, and communication structures of all presented network paradigms.
- We also discuss several IoNT and IoBNT problems, outstanding topics, and future research possibilities.

The remainder of this paper is organized as follows. In Sect. 2, we provide an overview of IoNT, IoBNT, and their applications. In Sect. 3, We also discuss several IoNT and IoBNT problems, outstanding topics, and future research possibilities. Finally, Sect. 4 concludes the paper.

Table 1 Existing survey papers and relation to this paper

Paper	IoT	IoNT	IoBNT	Description
[6]	×	✓	×	This study discusses the usage scenarios, network architecture, communication paths, pros and cons of IoNT and nano-sensors in modern healthcare
[7]	×	✓	×	This paper presents the features, network architecture, application possibilities, key challenges, and future trends of IoNT
[8]	×	✓	×	This paper briefly summarizes the network models of IoNT and the difficulties encountered in its implementation in healthcare
[9]	✓	×	×	Solid waste management was controlled and cost analysis of this system was carried out by using IoT
[10]	×	×	✓	This paper presents the key components, applications, technological challenges, and future research directions of IoBNT
Our work	✓	✓	✓	Our paper covers all nano-network paradigms and potential application areas, architectural models, and communication structures. It also comprehensively addresses current challenges and future research directions

2 Internet of Nano Thing and Internet of Bio-Nano Things

The interconnection of nano-scale devices and machines via the Internet has paved the way for the emergence of new network architectures such as IoNT and IoBNT. These network architectures are based on existing technologies such as IoT, sensor networks, edge, fog, cloud computing and newly developed nano-scale sensor, machine, and smart antenna technologies [15]. In this context, the concept of IoNT was described as "*The interconnection of nanoscale devices with existing communication networks and ultimately the Internet defines a new networking paradigm that is further referred to as the Internet of Nano Things*" in 2010 by Ian F. Akyildiz and Josep Miguel Jornet from the Georgia Institute of Technology [16]. On the other hand, IoBNT is a developed version from IoNT and focuses on information exchange, interaction, and networking within the biochemical field using synthetic biology and nanotechnology tools [4]. The main purpose of IoBNT is to communicate with cells that enable real-time and accurate detection and control of complex biological dynamics occurring in the human body [17]. In other words, while IoNT is based on the integration of nanoscale devices with existing network and communication technologies, IoBNT is additionally based on the behavior and properties of in vitro environments such as molecular communication, Ca^{2+} com-

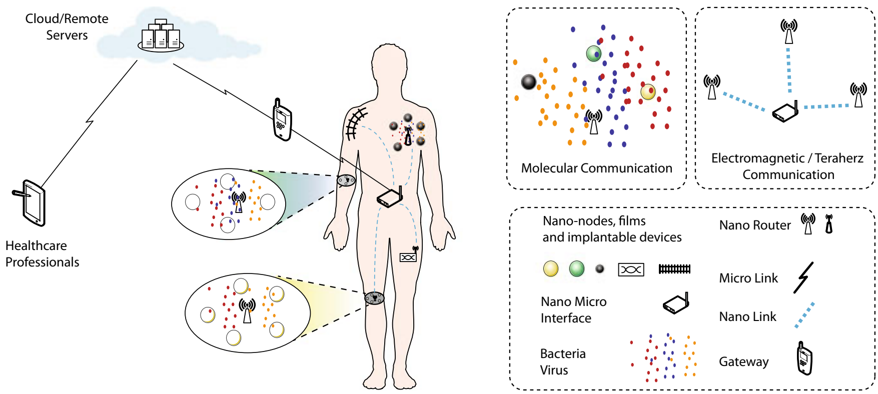

Fig. 1 A typical nano-network architecture for healthcare applications

munication, hormonal communication [18]. The nanodevices used in these network architectures can be created from materials such as biological materials, magnetic fragments, or gold nanoparticles. Here, biological devices are created by reprogramming many biological materials such as cells, viruses, bacteria, bacterial phages, erythrocytes [19].

In recent years, scientific and technological developments in biomaterial fields have enabled the development of smart biomaterials with high bio functions. The smartness level of these biomaterials is divided into four classes as inert, active, responsive, and autonomous. Showing their biofunctionality, these smart materials require a wide range of internal and exterior stimuli. Examples of internal stimuli are proteins, enzymes, molecules, antigens, and ionic factors. Examples of external factors are magnetic field, electric fields, light, temperature, and mechanical stress [20].

In the light of the information given above, nano and bio-nano device-based network architectures have many potential application areas such as health, military, environmental monitoring, multimedia, and entertainment. Therefore, we first present the network architectures and communication models of IoNT and IoBNT in Sect. 2.1. We then provide comprehensive examples of application areas in Sect. 2.2 (Fig. 1).

2.1 *Network Architecture and Communication in IoNT and IoBNT*

Effective integration and communication between nanodevices and macroscale components are required for the IoNT and IoBNT network paradigms to be fully operational. For this reason, the design of network architectures that include several alternative communication paradigms, such as electromagnetic, acoustic, mechani-

Table 2 Features of communication modes at the nanoscale

Approach	Biocompatibility	Range in body	Energy
Nano wireless	Medium to low	1 cm to 1 m	High
Nano acoustic	Low	1 cm to 10 cm	High
Molecular	High to medium	1 nm to 1 cm	Very low
Nanomechanic	Medium to low	1 mm to 1 nm	Very low
Bacteria-based	High to medium	1 mm to 1 cm	Very low

cal, and molecular communication, comes to the fore [21]. Within these networks, nano-things are expected to interact with each other by exchanging various types of information such as synchronization signals, sensed chemical/physical parameter values, logical operation results, instruction sets, and commands [4].

For the time being, communication in IoNT and IoBNT networks is mainly envisaged as molecular communication and nano-electromagnetic communication [22]. Since these two network paradigms are intertwined, similar technologies can be used in terms of communication. Molecular communication is created by releasing and reacting to certain molecules to transmit or receive information. on the other hand, the transmission and receiving of electromagnetic radio-frequency waves in the terahertz (THz) range constitute nano-electromagnetic communication[23]. However, there are difficulties in using these communication technologies such as coverage, compatibility, energy, and transferred data rate. Although there are strong theoretical knowledge and practical models in the literature on communication today, communication at the nanoscale is quite complex and difficult due to the biocompatibility problems of nanodevices and the signal propagation properties of tissues in the body [21] (Table 2).

IoNT and IoBNT network architectures consist of a series of components that connect the electrical field and the biochemical field with devices at the nano or bio-nano-scale. More specifically, the main components of the IoNT architecture are nano-nodes, nano-routers, nano-micro interface devices, and gateways [13]. IoBNT, on the other hand, may contain additional components that have the function of reading and transferring biochemical domain information. In this context, IoBNT architecture can consist of Bio-cyber interface, gateway, and application-specific server components [19]. All these components are described in Table 3.

2.2 *IoNT and IoBNT Applications*

IoNT and IoBNT network paradigms have added new dimensions to the existing application areas of IoT such as healthcare and communication networking. Therefore, in this section, we present current studies on these two application areas.

Table 3 The components of the IoNT and IoBNT network architectures

Components	Description
Nano-nodes	Data sensing, transmission, and processing are all performed by nano-nodes, which are the simplest nanodevices
Nano-routers	Nano-routers are more advanced devices than nano-nodes in terms of features such as computing and storage. They are responsible for collecting information from nano-nodes and controlling nano-nodes with basic control commands such as on/off, read, and sleep
Nano-micro interface device	Nano-micro interfaces are hybrid devices that can both communicate at the nanoscale and use existing communication paradigms in traditional communication networks. They are in charge of gathering data from nano-routers and transmitting it to micro-scale devices. This component is used in IoNT
Bio-cyber interface	The bio-cyber interface is a hybrid device that converts the biochemical signal received from in-body nano-networks into an electrical signal that can be processed in external networks
Gateways	Gateways are hybrid devices that can be used in both classical and nano-networks at micro and macro scales. These devices allow remote control of the designed IoNT and IoBNT networks via the Internet
Application-specific servers	These devices are responsible for the storage, analysis, and real-time monitoring of information from nano-networks. They can be used in the realization of many applications such as healthcare, medicine, entertainment, or multimedia

In healthcare, it has been shown that these network paradigms can be used in the treatment of circulatory system diseases, infectious diseases, diabetes, thrombosis, and many physical or psychological diseases. Today, due to the Covid-19 pandemic, remote work has become increasingly common in many areas. In this context, studies have been carried out regarding the electronic and remote provision of health services [19]. In this way, it has become possible to transmit data collected from patients connected to the IoNBT network directly and in real time to healthcare professionals. Thanks to the remote collection of patient data, the patient may not need to go to the laboratory for testing. In addition, in case of any infection, the disease can be detected even before the patient shows symptoms and medical support can be given to the patient [17]. Telemedicine applications related to these sample scenarios have been included in our lives with the Covid-19 epidemic. For example, Jarmakiewicz et al. set forth standards and guidelines for the research and development of nano-sensor networks for some telemedicine applications. They also demonstrated that some applications can be implemented with a nano-sensor network by testing it with a nano-network developed for human circulatory system [24].

Thrombosis is one of the most common causes of mortality in the world, killing one out of every four individuals. In thrombosis, a blood clot forms in a vein, once the blood clot forms, it can stop or delay blood flow, or it can be found in organs. Froud et al. [3] developed a new IoBNT model with a bio-cyber communication interface that allows for better prediction and analysis of blood vessel coagulation. Thanks to this model, the information in the blood vessel is collected and the bio-cyber interface is used to convert the information into electrical equivalent. Moreover, the optical or thermal response has also been used to stimulate the release of certain nanocarrier molecules such as liposomes, nanodevices that can be transported through the bloodstream and predict clots.

IoBNT can also be used in the early diagnosis and mitigation of infectious diseases. For instance, cystic fibrosis disease is a genetic disease that can be seen in organs and systems such as lungs, pancreas, intestines, and sweat glands. It develops in waves and causes the death of patients. In [17], Akyildiz et al. proposed an IoBNT network called PANACEA, which provides an end-to-end solution to infectious diseases. In this network, a submillimeter implantable bio-electronic device that senses communication within body cells is used to determine the level of infection.

Another common disease today is diabetes. Abbasi et al. [25] focused on modeling IoBNT applications that will improve the diagnosis, management, and treatment practices of the insulin-glucose system for this disease. Through an IoBNT network to be developed, insulin and glucose concentration values can be transmitted directly to healthcare providers. In this way, besides monitoring the health status, pump life can be extended by ensuring that the insulin cartridge lasts longer. In addition, thanks to such smart systems, the body is protected from the side effects of excess insulin. On the other hand, preventive health services can be provided by methods such as pre-illness therapy with a holistic approach to physical and psychological diseases. In this context, it is predicted that healthy living conditions can be created by making changes in people's lifestyles with IoBNT [26].

Since IoNT and IoBNT are emerging network paradigms, the developed applications in these networks are also at the beginner level. Moreover, the integration of nanomachines into the human body, their architectural design, and efficient operation (communication, computing, storage, etc.) of these devices within the heterogeneous network structure are among the main challenges. Therefore, there is an increasing number of research efforts aimed at eliminating existing and potential challenges. Al-Turjman proposed an energy-efficient framework focusing on data delivery in nano-networks. With this framework, it is aimed to realize data distribution with energy-sensitive routing protocols by considering the shortest path [14].

It is clear that IoNT has different architectural requirements for different network models and applications. In these networks, communication model design is also another challenge. In [8], Ali et al. investigated the structure of communication models in the IoNT network that was developed for drug delivery and disease detection. In the study, they evaluated the advantages and disadvantages of these two models by establishing non-additive and single-layer communication models. In [27], Stelzner et al. introduced a new concept of function-centered Nano-network (FCNN) focusing on intra-body communication scenarios. FCNN aims to minimize memory requirements by combining the location and function capabilities of nanomachines. In another study, Canovas-Carrasco et al. [28] emphasized that the development of optimal transmission policies to be used in nano-networks, reducing implementation costs and in vivo monitoring of nano-sensors depending on the generation of smart policies. For this reason, the authors proposed the Markov decision process model, which enables the derivation of smart policies.

From the network architecture perspective, Galal and Hesselbach [29] presented a multi-layered architectural model in nano networking that combines software-defined networking (SDN), network function virtualization (NFV), and IoT technologies. In the study, the authors proposed a number of functionalities and usage scenarios that could be implemented for nanodevices. In addition, significant challenges and gaps in implementing the proposed functions with nanotechnology are discussed. In [6], the usage possibilities, architecture, communication models, advantages, and challenges of nanotechnology through nano biosensors and IoNT in modern health care were determined. It has been emphasized that the concept of placing nanoscale devices in the human body has the potential to be used in all health and medical applications that exist today (Table 4).

3 Challenges, Open Issues, and Future Research Directions

IoNT and IoBNT networks have wide application potential to improve the health and quality of life of living things. However, many challenges are encountered in real-life applications of these networks. These challenges also present the topic of open research issues and future research directions.

- Nano-network architecture: Traditional IoT networks are usually built with three, five, and seven layers. In nano-networks, it is very difficult to establish a layered network structure in terms of device size, computation, storage capacity, and communication types.
- Nano communication and Standards: There are short and limited (from 1 nm to 1 m) in vivo communication modes in nano-networks. There is also a high level of biological noise in the environment. These communication difficulties can cause data loss, delay, and network congestion in nano communication. In addition, since these networks differ from conventional networks in many aspects such as operating environment and communication mode, the OSI/TCP model is not fully suitable for these networks. In this context, the foundation of new communication standards is quite necessary [6, 10].
- Bio-cyber Interface: As mentioned earlier, different bio-cyber interfaces have been proposed for each considered network. However, these interfaces are not yet at the

Table 4 Summary of some selected papers in the area of IoNT and IoBNT

Paper	Scope	Domain	Technology	Obtained/used datasets	Contribution of the work
[24]	IoNT	Healthcare	Nanosensor Radio channels	Simulation Data	The telemedicine applications in the literature were examined and the points that could be improved were determined. It has been stated that it would be beneficial to support these applications by using a nano-sensor network that has the potential to be applied in some scenarios and that works in the human circulatory system
[27]	IoNT	Biomedical (Human Body)	Sensor Actuator	None	They tried to minimize memory requirements by combining the data collected about the location and function of the respective nano-devices, using the Function-centered Nano-network (FCNN) architecture.
[28]	IoNT Nano Networks	Healthcare (Human Cardiovascular System)	Nanodevices Nano-routers	Cardiovascular system	A Markov-based decision process model is proposed to generate optimal transmission policies to be used by nano-nodes. In addition, a series of simulations were executed.
[29]	Nano Networks	Healthcare	Nanodevices Nano-antennas	Nano drugs Wearable devices	It is represented an approach which is combining SDN, NFV, and IoT. Also, a composite architecture model of nano-network communication is proposed.
[30]	IoNT	Human Body	RF radio channels	Simulation Data	The paper defines challenges and opportunities of IoNT systems. Also it is constructed simulation area for human body area network technology using nano-devices

practical and clinically desirable level. For these reasons generalized and realistic biointerface deployments are needed [10, 31].

- Data Management and Analysis: It is predicted that there will be a rapid increase in the number of new devices connected to the internet together with nano-networks. Currently, data method and analysis are a serious challenge. This challenge will become a hot topic with nano-networks. In addition, the development of smart data analysis algorithm models that can work on nano-scale devices is open to research [32].
- Smart Biomaterials: Although there are many types of biocompatible in-capsular sensors (camera, pH, temperature, gas, ultrasound imaging, physisorption, surface acoustic wave, etc.), the field of ingestible sensors and smart biomaterials is still in its absolute infancy [20, 33].

- Security and Privacy: The new nano-network paradigms mostly include applications that have not yet established standards and frameworks in the medical, biological, chemical, or personal fields. Therefore, these networks are now exposed to a wide range of threats, including multidimensional attack vectors [34]. At this point, ensuring the confidentiality, integrity, and availability of the data stored and circulating on the network is more critical than other application areas. The weakness that will arise in this regard may harm individuals and societies by laying the groundwork for negative situations such as data manipulation, theft, espionage and even bioterrorism [35]. Therefore, trust management systems, user access control systems, lightweight data encryption, and compression models are needed.
- Other challenges:Besides the current challenges, there are many uncovered research topics such as content management, mobility management, service aggregation and discovery, energy conservation, energy harvesting, power transfer, nanodevice addressing, integration with next-generation technologies (SDN, NFV, Blockchain, NFTs, Metaverse and etc.) [10, 32].

4 Conclusion

This paper provides comprehensive literature to contribute to a holistic understanding of emerging nano-networks. For this purpose, we present all of the promising network paradigms such as IoNT, and IoBNT that have emerged based on nanoscale devices and materials in connection with the "All-thing connected" vision. We give comprehensive explanations of communication, network architecture, and application domains of these network paradigms. Moreover, we comprehensively provide the challenges of these networks, open issues, and future research guidelines. In this work, we comprehensively present all emerging nano-network paradigms in a single survey paper, and we hope that the paper will shed light on future works.

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