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Exploring the Internet of Bio-Nano Things: Technologies, Applications, and Challenges

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ABSTRACT

The term "Internet of Things" (IoT), which refers to networked devices and items with embedded computing capabilities used to expand the Internet to numerous application fields, has gained significant attention in the past 10 years. There are numerous application fields where extremely small, covert, and non-intrusive items are required, even as research and development for generic IoT devices continues. The idea of the Internet of Nano Things (IoNT), which is based on the networking of nanoscale devices, was motivated by the characteristics of freshly researched nanomaterials like graphene. Although IoNT devices facilitate several uses, their artificial character can be harmful in situations where their deployment may have unintended health or pollution repercussions. Based on synthetic biology and nanotechnology methods that enable the fabrication of biological embedded computing devices, this study introduces the unique paradigm of the Internet of Bio-Nano Things (IoBNT). Using biological cells and their metabolic functions, Bio-NanoThings holds the potential to facilitate applications including environmental pollution and toxic agent control, intrabody sensing, and actuation networks. An interface to the electrical domain of the Internet is made possible by the Internet of Biomolecules , a concept that is revolutionizing communication and network engineering. The present study presents new challenges for the development of effective and secure methods for information exchange, interaction, and networking within the biochemical domain. Single nanomachines' capacities should increase as a result of connecting them and creating nanonetworks, since the information exchange that results will enable them to work together to achieve a shared objective. These days, systems typically use electromagnetic signals to encode, transmit, and receive data; nevertheless, molecular transceivers, channel models, or protocols use molecules in a revolutionary communication paradigm. To enhance comprehension of nanonetwork scenarios in biomedical applications, this article outlines the latest advances in nanomachines and their future architecture. Two applications for nanonetworks are also presented in order to emphasize the communication

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requirements between nanomachines: i) the Internet of NanoThings, a new networking paradigm that enables nanoscale devices to connect with preexisting communication networks, and ii) Molecular Communication, which involves the spread of chemical compounds such as drug particles.

Keywords: Nano communication, Nanotechnology, Internet of Bio-nano things, Nanosensors, Target drug delivery, Molecular communication

I. INTRODUCTION

All kinds of physical components in the real world, such as sensors, actuators, personal electronic devices or home appliances, among others, are connected and capable of interacting with each other on their own thanks to the Internet of Things (IoT) [1]. This new type of seamless connectivity makes it possible for a wide range of applications, including real-time industrial process monitoring, machineto-machine communication, smart cities, energy-management smart grids, intelligent transportation, environmental monitoring, infrastructure management, medical and healthcare systems, building and home automation, and large-scale deployments [1]. Over the past fifteen years, research and development has turned its attention to the Internet of Things. Governmental organisations and businesses around the world have made and continue to make significant investments in the Internet of Things [2]. Recent developments in nanotechnology and communication engineering have led to a revision of the Internet of Things concept [2].These developments allow for the creation of networks of embedded computing devices, known as nano things,that are based on nanomaterials like graphene or materials with scales ranging from one to a few hundred nanometres.Introduced initially in [3], the Internet of

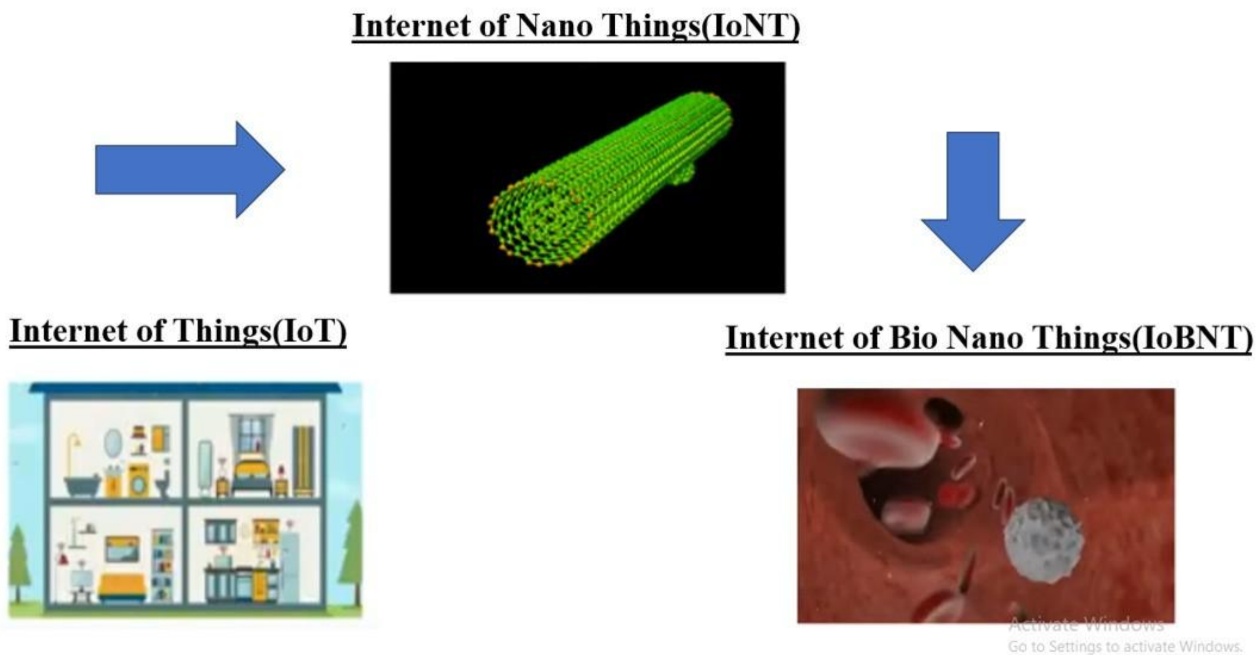

Figure 1: From IoT to IoNT to IoBNT[3]

Nano Things (IoNT) is envisioned as the foundation for a wide range of future applications, including in the fields of security, healthcare, and military, where the nano things can easily be implanted, hidden, and dispersed throughout the environment to perform networking, sensing, actuation, and processing in concert due to their small size. Since nano things are based on electronic circuits, synthesised materials, and electromagnetic (EM) communications, they are

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artificial in nature, even though they can push the engineering of devices and systems to previously unheard-of environments and scales. [2] For some application contexts, such as those found inside the body or in natural ecosystems, where the use of nanoparticles and their electromagnetic radiation may have unintended negative health or pollution impacts, these properties may be hazardous. By integrating nanotechnology with techniques from synthetic biology, a new avenue for research in the engineering of nanoscale devices and systems is being pursued in the field of biology. This approach aims to control, reuse, modify, and reengineer biological cells [3]. A biological cell can be efficiently used as a substrate to realise a so-called Bio Nano Thing by controlling, reusing, and reengineering biological cells' functions, including sensing, actuation, processing, and communication. This idea stems from an analogy between a biological cell and a typical IoT embedded computing device. The idea of Internet of Bio-Nano Thing (IoBNT), which is presented in this article, is anticipated to revolutionise many related fields, including communication and network engineering, which is the article's main focus, because cells are based on biological molecules and biochemical reactions rather than electronics. [3]

The IoBNT will enable a wide range of applications, including the following: the transmission and reception of molecules, known as molecular communication (MC), the biochemical processing of data, the transformation of chemical energy, and the execution of DNA-based instructions [4]. Bio-Nano Things within the human body would work together to gather health-related data, send it to an outside healthcare provider over the Internet, and carry out instructions from the same source, such as the synthesis and release of medications, in an intra-body sensing and actuation system [4]. Intrabody connection control, in which Bio Nano Things would fix or stop malfunctions in the communication between our internal organs, including those that are based on the neurological and endocrine systems, which are underlying many illnesses. Bio-Nano Things placed in the environment, like a natural ecosystem, would monitor for harmful and polluting substances and work together to change them through bioremediation, such as bacteria used to clean up oil spills. [5]

A. Understanding the Internet of Bio-Nano Things (IoBNT)

The Internet of Bio-Nano Things (IoBNT) is a novel idea that combines the ideas of nanotechnology, biotechnology, and the Internet of Things (IoT) to build systems that can perform intelligent real-time operations on the nanoscale. Unprecedented interactions between the biological world and digital technology are made possible by this developing discipline, which combines biological systems with nanoscale electronics. Healthcare, environmental monitoring, agriculture, and smart cities will all undergo significant changes as a result of the potential for IoBNT to enable networked, adaptive, and autonomous systems that can sense, analyze, and communicate biological and environmental data. [6] Significance of IoBNT: By enabling the smooth integration of bionano devices within IoT infrastructures, IoBNT has the potential to completely transform our interactions with living things and the environment. Because these sensors can function at the molecular level, they enable real-time monitoring and data collection that is significantly more accurate and advanced than that possible with existing technologies. For instance, bio-nano sensors incorporated inside the human body might be used in healthcare to continually track vital signs and administer individualised therapy. Similarly, IoBNT can gather and analyse environmental data from nano-sensors placed in the soil to optimise crop management and increase resource efficiency in agriculture. [6] By bridging the gap between the biological and digital worlds, IoBNT has the potential to create systems that are not only responsive but also have the capacity to evolve and learn from the data they gather. Smarter systems with the ability to make decisions on their own will result from this convergence, opening the door to more effective, scalable, and sustainable solutions. [7]

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Table I: Comparison of IoT, IoNT, IoBNT[24]

Feature/Aspect	Internet of Things (IoT)	Internet of Nano Things (IoNT)	Internet of Bio-Nano Things (IoBNT)
Definition	Network of physical devices (sensors, actuators, appliances) that can interact with each other autonomously	Network of nano-sized devices (nano things) based on nanomaterials like graphene, designed for networking and processing	Integration of nanotechnology with synthetic biology to create biological cells that perform IoT functions like sensing and communication
Scale	Large-scale networks of interconnected devices, often on the human scale or larger	Nano-scale networks (1100 nanometers), focused on extremely small, embedded devices	Nano-scale networks using biological cells or engineered microorganisms to perform tasks at the molecular level
Materials	Electronics-based (e.g., sensors,actuators, and home appliances)	Nanomaterials like graphene and carbon nanotubes	Biological cells and molecules, combined with nanomaterials
Communication	Typically electromagnetic signals (e.g., Wi-Fi, Bluetooth, Zigbee)	Electromagnetic communication using nano-sized circuits and devices	Molecular communication, biochemical reactions, and DNA-based instructions
Energy Source	Powered by traditional electrical sources (batteries, mains power)	Often battery-powered or energy-harvesting from the environment (e.g., vibrations, heat)	Chemical energy or biochemical processes (e.g., biofuels, biological energy transformation)
Applications	Smart homes, smart cities, healthcare systems, industrial automation, environmental monitoring	Security, healthcare, military, environmental monitoring, smart materials, nanoscale sensing and processing	In-body health monitoring, drug release systems, environmental cleanup, molecular communication, and gene editing

B. IoT and Bio-Nano Technologies' Convergence:

Biological and environmental data may be collected, processed, and analysed in large quantities thanks to the integration of bio-nano sensors into IoT ecosystems. Because they may function at the molecular and cellular levels, bio-nano devices—like smart sensors, medication delivery systems, and biosensors—offer previously unattainable insights into biological processes. These gadgets allow for remote monitoring of ecosystems, the environment, and health concerns when linked to IoT networks, which results in quicker and more efficient treatments. [7] Two major trends are brought together by this convergence: IoT, which links physical things to digital networks for analysis and communication, and nanotechnology, which concentrates on creating materials and devices at the molecular scale. As a result, extremely complex systems with real-time sensing, decision-making, and automatic reactions are produced. The capacity to interact directly with biological systems and communicate at such small scales offers a revolutionary change in the way we monitor health, manage resources, and enhance our surroundings. [8]

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C. Special Contributions of This study

This study provides a thorough analysis of IoBNT, including its applications, problems, enabling technologies, and future directions. The objective is to give a comprehensive picture of IoBNT's current status and identify important areas for future advancement. [8]In particular, this review advances the field in the ways listed below:

- Comprehensive Overview of Enabling Technologies: The review focusses on the main technologies that propel IoBNT, including system integration, bio-nano device fabrication, and nanoscale communication protocols. We shed light on the qualities that make IoBNT viable and scalable by investigating these technologies. [9]
- Investigation of Real-World Applications: This study looks at a variety of IoBNT application cases, such as its effects on smart cities, healthcare, agriculture, and environmental monitoring, demonstrating how these technologies might enhance productivity, sustainability, and human wellbeing. [9]
- Identification of Research Gaps and Challenges: The review highlights the ethical and technical obstacles to the broad use of IoBNT systems, including the need for standardisation, security problems, and regulatory considerations. It also identifies research gaps that need to be filled in order to fully realise the potential of IoBNT. [10]
- Future Prospects and Technological Synergies: The article explores how new technologies can further expand IoBNT's potential and help it develop into a genuinely disruptive force across multiple sectors by looking at AI, quantum computing, and the development of 6G networks. [9]

II. HISTORY AND EVOLUTION

A historical review of the Internet of Bio-Nano Things (IoBNT) and molecular communication should highlight the evolution of concepts, methods, and technological advancements that have contributed to the development of IoBNT. [10]Below is a structured approach to understanding the history of IoBNT and molecular communication:

- Introduction to IoBNT and Molecular Communication: IoBNT, which combines biological and nanotechnology with IoT to create networks of bio-nano devices capable of detecting, processing, and communicating biological and chemical information [11]. Molecular communication as a form of data transfer that uses molecules as carriers, inspired by biological signaling pathways. Interdisciplinary Foundation introduces the intersection of fields like biotechnology, nanotechnology, communication engineering, and information technology that underpin IoBNT and molecular communication. [12]

  Early Stages of Molecular Communication (Pre-2005) Biological Inspiration and Theoretical Foundations: Concepts in molecular communication originated from biological systems where cells communicate through chemical signaling, such as neurotransmitter release and hormone signaling. Initial Models and Mechanisms: Early work focused on modeling how biological organisms transmit information, including studies on diffusion-based molecular communication and ligand-receptor binding. [10]

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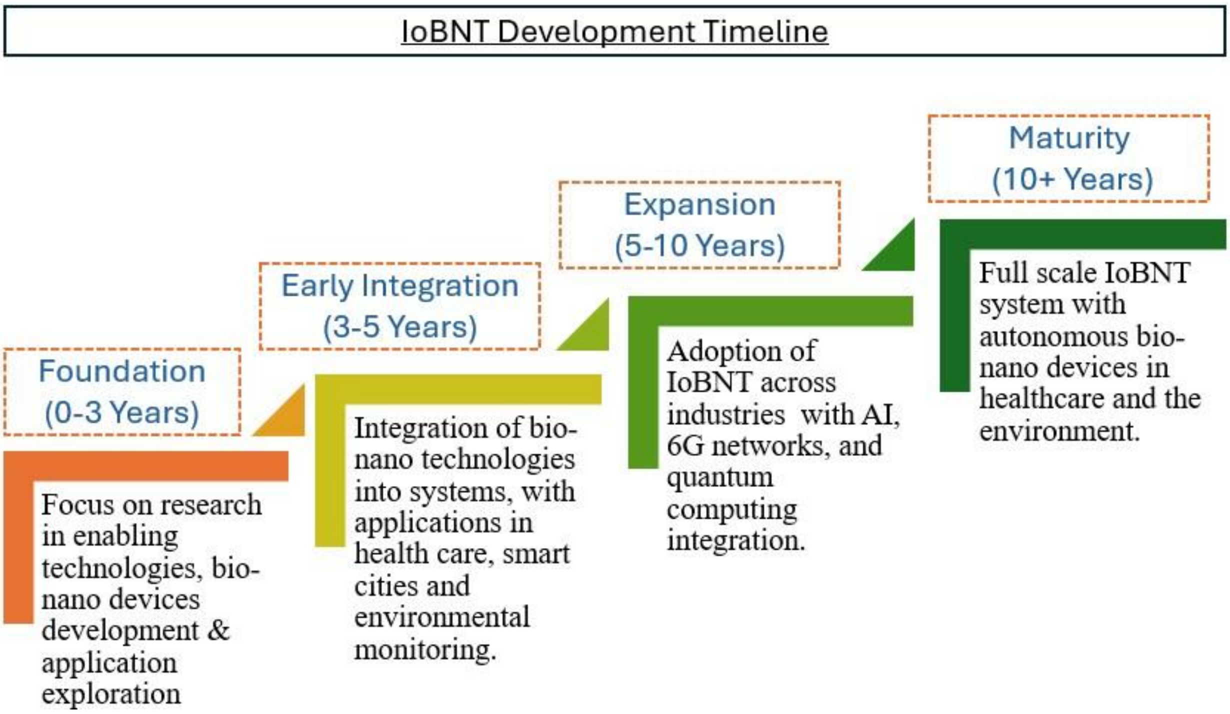

Figure 2: IOBNT Development Timeline[16]

- Emergence of Molecular Communication Research (2005 - 2010) First Molecular Communication Models: During this period, researchers proposed early models for molecular communication in synthetic and biological systems, studying mechanisms like diffusion and motor proteins to enable nano-scale data transfer. [12] Diffusion-Based Communication: Researchers began developing models where information is carried by molecules moving via diffusion, inspired by chemical signaling in cellular environments. This marked a major departure from traditional electromagnetic communication. Pioneering Experiments: Initial experimental studies were conducted to validate molecular communication models, including basic tests in controlled lab environments to measure molecule propagation and signal detection at nano-scales. [11]
- Foundation of IoBNT as a Concept (2010 - 2015) Introduction of IoBNT and Bio-Nano Networks: With advancements in nanotechnology and biosensors, the concept of IoBNT emerged as a way to connect nano-scale devices within biological systems or synthetic environments for IoTlike applications. [12]Notable Publications: Early papers formally introduced the term IoBNT, theorizing networks where nanodevices perform sensing, processing, and communication within living organisms or in microenvironments. Developments in Nano-Materials and Biosensors: Advances in nano-materials, including carbon nanotubes and graphene, enabled the creation of high-sensitivity nanosensors, which were essential for developing IoBNT devices that could interact with biological markers [12]. Synthetic Biology and Bioengineering: Synthetic biology contributed to IoBNT by enabling bioengineered cells that could perform specific sensing and signaling functions, such as detecting biomarkers and releasing therapeutic agents in response. [13]
- Expansion of Molecular Communication and IoBNT Applications (2015 - 2020)

Development of Communication Protocols and Architectures: Researchers proposed various net-

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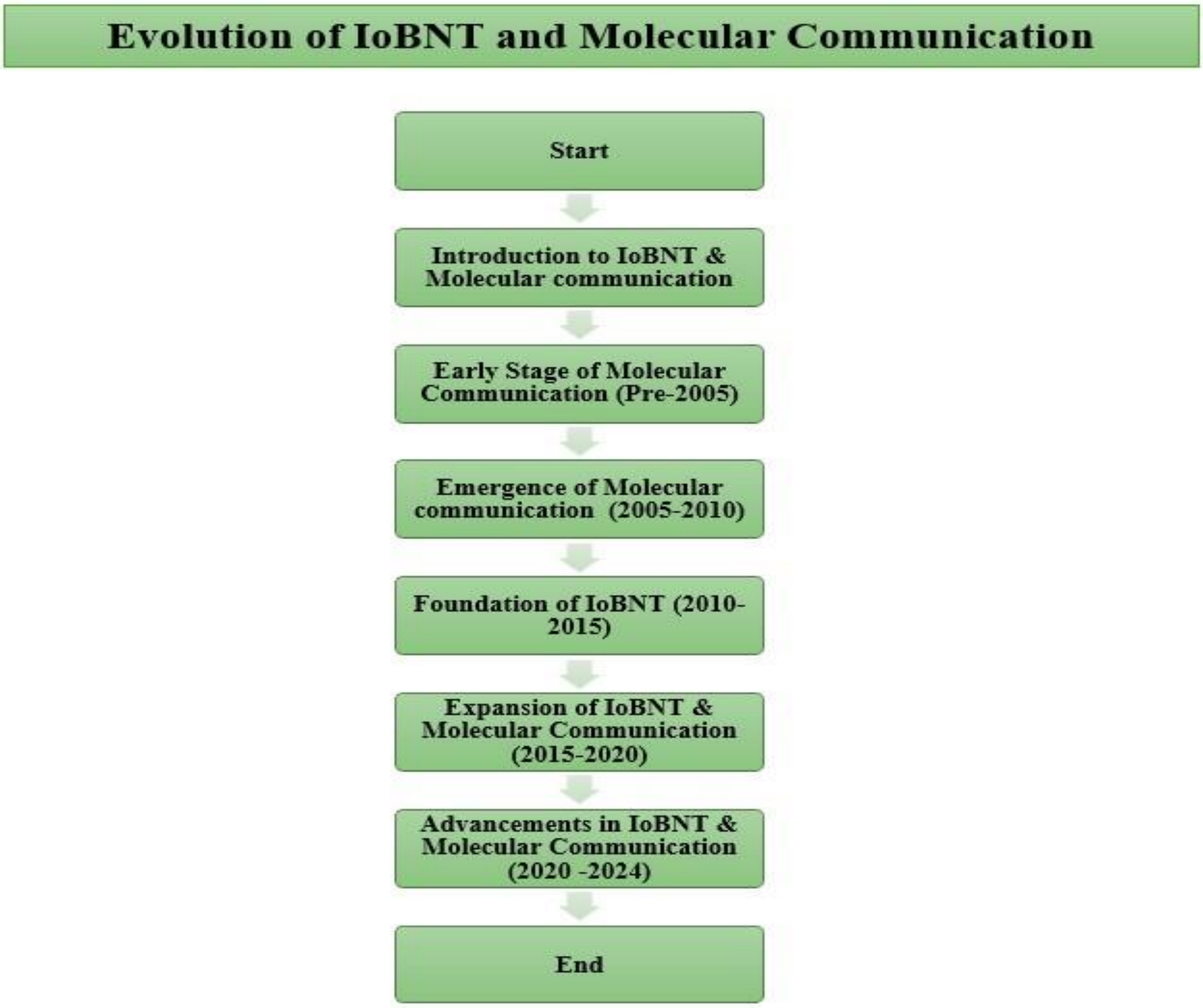

Figure 3: History and Evolution[30]

work models and protocols to address the unique challenges of bio-nano communication, including diffusion-based communication for intracellular networks and signal relay models for larger-scale systems [13].Bio-Inspired Communication Models:Research explored new communication models that mimic biological processes, such as quorum sensing and gap junctions, for applications in both intra-body and environmental networks. IoBNT Applications in Healthcare and Environmental Monitoring: IoBNT systems began finding applications in healthcare for diagnostics and treatment, including systems for real-time health monitoring, drug delivery, and pathogen detection.[13] Environmental IoBNT networks were proposed for applications in pollution monitoring and biodegradation. Standardization Efforts: The need for standardized protocols and frameworks in molecular communication and IoBNT became a focus, as researchers highlighted interoperability challenges in bio-nano communication. [14]

- Advancements in IoBNT and Molecular Communication (2020 - 2024) Integration of AI and Machine Learning: With the growth of AI, researchers began integrating machine learning algorithms to process the complex data generated by IoBNT devices and optimize molecular communication protocols. [13]AI-based models are now applied in predictive diagnostics, molecular signal interpretation, and real-time decision-making. Breakthroughs in Synthetic

Molecular Machines: Advances in synthetic biology have produced molecular machines and programmable nanodevices capable of specific actions, such as targeted drug release or pathogen neutralization. [15]These developments enable more sophisticated IoBNT applications in personalized medicine and therapeutic monitoring. Hybrid Communication Models: Recent studies have combined molecular communication with traditional electromagnetic models to create hybrid IoBNT systems that can operate within biological environments while communicating with external devices. [15]

III. BACKGROUND AND FUNDAMENTAL CONCEPTS

It is essential to establish the fundamentals of bio-nano technologies and the Internet of Things (IoT) in order to comprehend the Internet of Bio-Nano Things (IoBNT) and how they are integrated into this new field. The fundamentals of these technologies are covered in this section, along with important elements that are essential to IoBNT operation, such as bio-nano devices, molecular communication, and nano-networks [16].

A. *The fundamentals of bio-nanotechnology*

Because bio-nano technologies apply nanotechnology to biological systems, they allow biological materials to be controlled and manipulated at the molecular and nanoscale levels. [16] By using the special qualities of materials at the nanoscale, such as enhanced surface area, chemical reactivity, and biocompatibility, these technologies are able to develop tools that can precisely and carefully interact with biological entities, such as cells, tissues, and DNA. [17] Important ideas in bio-nano technology consist of: Nanomaterials: Materials with nanoscale (usually 1–100 nanometre) structures that have special qualities, like increased strength, reactivity, and conductivity, and are used to make bio-nano devices. [18] Nanoengineering: The creation of nanoscale systems and devices, such as drug delivery systems, biosensors, and nanosensors, that can communicate with biological systems. [19] Biocompatibility: One of the most important factors in bio-nano technologies is making sure that the nano-devices are safe and non-toxic enough to be integrated into biological habitats, such as the human body or natural ecosystems. [19]

B. *Core Internet of Things (IoT) Principles*

In order to gather and share data over the internet, a network of physical devices with sensors, actuators, and software built in them is known as the Internet of Things (IoT). [17]These gadgets, which range from wearable health monitors to smartphones, are networked and have the ability to provide remote control and real-time insights. [17] The following are essential elements of the Internet of Things: • Sensors: Equipment that picks up biological signals (like heart rate or glucose levels) or physical phenomena (like temperature, pressure, or light) and transforms them into digital data for transmission. [16] Connectivity: The networks of communications, such as Wi-Fi, Bluetooth, cellular, and newer technologies like 5G and 6G, that enable data transmission from IoT devices. [17] Data processing and cloud computing: the systems that store, analyse, and analyse data produced by Internet of Things devices—often in real-time—to produce insights that can be put to use. [18]

C. *Combining IoT with Bio-Nano Technologies to Create IoBNT*

Intelligent, real-time communication between digital networks and biological systems is made possible by the Internet of Bio-Nano Things (IoBNT), which is the result of the convergence of bio-nano devices and IoT.[18] In this integrated ecosystem, IoT offers the network infrastructure for data exchange, storage, and analysis, while bio-nano devices carry out functions like monitoring environmental conditions, delivering tailored treatments, and sensing biological markers. [18] The following are important facets of IoBNT integration:

- Bio-Nano Devices: These are specialised devices that can interact directly with biological systems and function at the nanoscale. [18] Examples include implanted devices for ongoing health monitoring, nanoscale medication delivery systems, and biosensors for identifying

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particular proteins. These gadgets can connect to IoT networks for real-time data transfer and analysis, and they can be integrated into living things like the human body. [19]

- Molecular Communication: The foundation of IoBNT is the idea of molecular communication, in which bio-nano devices use biological molecules (such proteins, DNA, or ions) to encode and transmit data at the molecular level. [19]Bypassing the conventional electrical or radio frequency communication protocols employed in classical IoT, this mode of communication enables direct interaction with biological ecosystems. [19]
- Nano-Networks: These are the communication systems that link bio-nano devices at the nanoscale, enabling the construction of dispersed networks capable of exchanging data and working together on challenging projects. [20] For dependable and effective data transfer, these networks frequently rely on molecular communication protocols and nano-scale routing strategies. [21]

D. Essential Elements of IoBNT

It is necessary to introduce a few crucial elements that serve as the basis for IoBNT in order to better comprehend its operation: [20]

- Bio-Nano Devices: As previously stated, these devices serve as the foundation for IoBNT. They include nanosensors that can identify particular biological or environmental cues and nanoactuators that can react to such cues by performing tasks like environmental cleanup or medication administration. [20] For these devices to work, biological processes or nanomaterials are frequently required. [21]
- Molecular Communication: Bio-nano devices can share data using biological signals, such as diffusion of molecules in a fluid environment or electrochemical impulses in cells, thanks to this new communication paradigm. An essential component of IoBNT applications is molecular communication, which permits ultra-low power, short-range interactions between devices at the nanoscale. [21]
- Nano-Networks: These are the communication systems that enable a number of bio-nano devices to cooperate in a planned, coordinated way. [21]These networks use molecular communication as well as other methods like optical or electromagnetic radiation to function at the nanoscale.[21] They enable data sharing, condition monitoring, and cooperative tasks like tracking environmental changes or detecting disease biomarkers. [22]

E. The Role of IoBNT in Real-World Applications

The integration of bio-nano devices and IoT into IoBNT has the potential to revolutionize various sectors by enabling real-time monitoring and autonomous decision-making at unprecedented scales. For example: [22]

- Healthcare: IoBNT can enable personalized medicine, where bio-nano sensors continuously monitor a patient's health and send real-time data to healthcare providers. [23]Nano-drug delivery systems could automatically adjust medication doses based on continuous feedback from sensors embedded within the body. [23]
- Agriculture: In agriculture, IoBNT can optimize resource use by deploying bio-nano sensors in the soil to monitor moisture levels, nutrient content, and plant health, enabling more efficient irrigation and fertilization. [24]
- Environmental Monitoring: Bio-nano devices could be used for pollution monitoring, detecting toxic substances in air or water at the nanoscale and transmitting data to a central system for analysis and response. [23]

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IV. LITERATURE REVIEW

Table II: Review of IOBNT[43]

Paper/Study/Year	Focus/Topic	Methodology	Key Findings/Results	Relevance to IoBNT
Internet of Bio-Nano Things: The Paradigm and its Applications 2015 [1]	Concept of IoBNT and its potential applications in healthcare and environmental monitoring	Theoretical framework, simulation	Introduces the concept of IoBNT, explores applications in health and environment	Foundational paper for the development of IoBNT systems, essential for IoT integration in nanomedicine
Bio-Nano Things for Smart Healthcare: Enabling Technologies 2016 [4]	Bio-Nano technology's role in smart healthcare systems	Experimental studies, simulations	Discusses sensorbased bio-nano systems for health monitoring, wireless communication	Explores critical enabling technologies for IoBNT in healthcare
Nanotechnology and IoT: The Integration of Nano-Devices in the Internet of Things 2017 [39]	Integration of nano-devices with IoT for smarter biomedical applications	Modeling and simulation of IoT systems	Analyzes the potential of integrating nanosensors with IoT platforms for real-time data processing	Illustrates the synergy between IoT and nanotechnology in healthcare and IoBNT
Applications of IoBNT in Personalized Medicine 2019 [49]	Personalized medicine enabled by IoBNT	Experimental data, clinical trials	Explores personalized therapeutic interventions using bio-nano devices and IoT integration	Directly relevant to healthcare applications in IoBNT for precision medicine
Molecular Communication for IoBNT: Challenges and Opportunities 2020 [44]	Molecular communication mechanisms in IoBNT	Simulation and theoretical modeling	Addresses the challenges of molecular communication, such as reliability and energy efficiency	Crucial for understanding communication protocols in IoBNT systems
Enabling Technologies for the Internet of BioNano Things in Healthcare 2021 [37]	Review of enabling technologies Like nanosensors, energy harvesters, and ommunication protocols	Literature review, technology comparison	Reviews the key technologies that enable IoBNT, including sensor miniaturization and power-efficient protocols	Key for identifying the technological infrastructure of IoBNT in healthcare

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Challenges and Future Directions of IoBNT in Medicine 2022 [43]	Challenges in deploying IoBNT systems for medical applications	Survey of current solutions, expert interviews	Identifies key challenges in deployment, such as biocompatibility, data security, and network reliability	Provides insight into the hurdles IoBNT must overcome for widespread medical use
IoBNT for Smart Wearables-A New Frontier in Health Monitoring 2024 [30]	Smart wearables based on IoBNT for continuous health monitoring	Prototype development, real-time monitoring	Demonstrates IoBNTbased wearable devices for continuous biometric data collection	Bridges the gap between bio-nano systems and wearable health monitoring devices

- Aspects of Nanoscale Information Transmission in Nanonetworks-based Molecular Communication: The paper explores how molecular signals can be used to encode, transmit, and decode information within nanonetworks, focusing on biological and synthetic environments where traditional electromagnetic communication is ineffective. [24] Molecular communication at the nanoscale leverages chemical signals, typically via diffusion, to carry information across tiny distances. This method faces unique challenges, including signal noise, propagation delays, and energy constraints. [24] Key solutions explored include using various modulation techniques, enhancing receiver sensitivity and selectivity, and developing error control mechanisms. By addressing these aspects, molecular communication can enable applications in biomedicine, environmental monitoring, and the Internet of Bio-Nano Things, offering a novel framework for information transmission at a microscopic scale. [25]
- A Molecular Communication System Model for Particulate Drug Delivery Systems is to develop a theoretical framework for using molecular communication to control and optimize the delivery of drug particles (e.g., nanoparticles) within the body.[25] The paper integrates principles of molecular communication, which involves the transmission of biochemical signals, with targeted drug delivery mechanisms to create more efficient and precise therapeutic systems. [25]Overall, the paper outlines how molecular communication can be leveraged to create smart, responsive drug delivery systems that operate autonomously within biological systems, improving precision, reducing adverse effects, and potentially transforming treatments in areas such as cancer therapy and chronic disease management. [25]
- A molecular communications model for drug delivery: The paper presents a molecular communications model for drug delivery, which uses molecular signals to enable precise and targeted delivery of therapeutic agents within the body [26].The model simulates the transmission of drug molecules through biological media, with transmitters (e.g., nanoparticles) releasing the drug, channels (biological environments) facilitating its movement, and receivers (target cells) responding to the drug. [25] This system offers potential for improving the effectiveness of treatments by ensuring controlled and targeted drug release. The paper also discusses challenges such as signal degradation and diffusion, while highlighting the potential for personalized medicine through bio-nano technologies. [26]
- A Physical Channel Model and Analysis for Nanoscale Molecular Communications With Förster Resonance Energy Transfer (FRET) :presents a detailed model for molecular communication in nanoscale systems. [27] It specifically focuses on the use of Förster Resonance Energy Transfer (FRET), a phenomenon where energy is transferred non-radiatively between molecules over short distances. [27] The paper proposes a physical channel model that accounts for various factors affecting the communication process, including molecular interactions, environmental conditions, and energy transfer dynamics. [24] It also analyzes the performance of FRET-based communication in terms of signal attenuation,

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capacity, and reliability, providing insights into how to optimize molecular communication systems at the nanoscale. [27]

- A Survey of Molecular Communication in Cell Biology: Establishing a New Hierarchy for Interdisciplinary Applications : It explores the concept of molecular communication (MC) within biological systems, specifically in the context of cell biology. It provides a comprehensive overview of how cells communicate using molecular signals, including signaling pathways, chemical signals, and receptor-ligand interactions. [28] The paper proposes a novel hierarchical framework to categorize the different levels of molecular communication, helping to bridge the gap between biological systems and interdisciplinary fields such as synthetic biology, bioengineering, and nanotechnology. This hierarchy aims to guide future research and applications of molecular communication, particularly in areas like bio-nano interfaces, medicine, and IoT. [28]
- A Systematic Review of Bio-Cyber Interface Technologies and Security Issues for Internet of Bio-Nano Things: provides a comprehensive analysis of the integration of bio-cyber systems with the Internet of Bio-Nano Things (IoBNT) [29].It explores the key technologies that enable the interaction between biological and cyber systems, such as bio-sensors, nano-scale devices, and cyber-physical systems[29].The review also highlights the security challenges in this emerging field, focusing on the risks associated with data privacy, bio-hacking, system vulnerabilities, and the potential for misuse of bio-nano technologies. The paper emphasizes the need for robust security protocols, encryption methods, and authentication mechanisms to ensure the safe and reliable functioning of IoBNT systems. [29]
- A Cross-Layer Approach for Optimization of MolCom Systems Toward the Internet of BioNanoThings: discusses a framework for optimizing molecular communication (MolCom) systems, which are a key enabler for the Internet of Bio-Nano Things (IoBNT). It proposes a crosslayer approach that integrates multiple system layers—such as physical, medium access control (MAC), and network layers—to improve communication efficiency in bio-nano systems. [30] The optimization strategy addresses challenges like energy efficiency, data transmission reliability, and scalability in highly constrained bio-nano environments. By taking into account the interaction between different layers, this approach aims to enhance the overall performance of MolCom systems in IoBNT applications. [30]
- . Analytical framework for end-to-end channel capacity in molecular communication system: The paper discusses an analytical framework for evaluating the end-to-end channel capacity of molecular communication systems [31]. It highlights the unique characteristics of molecular signaling, such as diffusion and noise, and presents models to describe the transmission, propagation, and reception of molecular signals. [31] The framework includes the calculation of mutual information between the transmitted and received signals to determine the channel capacity. Environmental factors, inter-symbol interference, and noise sources are considered, and optimization methods for improving capacity are outlined. The paper also addresses the impact of spatial and temporal constraints on communication performance. [31]
- Applications of molecular communications to medicine: a survey: The paper Applications of Molecular Communications to Medicine: A Survey explores the emerging field of molecular communications (MC) and its potential applications in medicine [32]. Molecular communications involve the transmission of information through the movement of molecules, which can be harnessed for advanced medical technologies.The paper surveys various applications such as targeted drug delivery, diagnostics, and therapeutic treatments, highlighting how MC can improve precision and efficiency in medical interventions. It also discusses the challenges in implementing molecular communication systems, such as scalability, reliability, and integration with existing technologies, while envisioning future possibilities for bio-nano communication in healthcare. [32]
- Biologically Inspired Bio-Cyber Interface Architecture and Model for Internet of Bio-Nano Things Applications: proposes a novel interface architecture and model that bridges biological

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systems with cyber systems, particularly in the context of the Internet of Bio-Nano Things (IoBNT). [33] The authors focus on the integration of biological components, like bio-nano devices, with cyber-physical systems through advanced bio-cyber interfaces.[33] These interfaces facilitate communication and interaction between biological entities (e.g., cells, proteins, or tissues) and digital systems, enabling new possibilities for IoBNT applications, such as healthcare monitoring, environmental sensing, and personalized medicine. The paper emphasizes the need for a biologically inspired design to optimize the functionality and adaptability of bio-nano systems in real-world applications. [33]

- Body Area Nano Networks with Molecular Communications in Nanomedicine: explores the concept of using molecular communication for creating nano-networks within the human body, particularly for medical applications . It highlights the integration of nanotechnology with the Internet of Things (IoT) to enable advanced healthcare solutions through Body Area Networks (BANs). [34]The primary focus is on the use of nanoscale devices that communicate through molecular signals, which can be used for tasks like disease detection, monitoring, and drug delivery. The paper discusses the technical challenges and benefits of molecular communications, including the miniaturization of sensors and devices, power efficiency, and real-time monitoring. It also covers the potential of these networks to revolutionize personalized medicine, providing more precise, scalable, and less invasive treatments. [34]
- Nanomedicine: Treatment of Chronic Disease Using Gold Nano Thermo Robot (GNTR) Empowered With Nanotechnology Approaches: The paper discusses the use of Gold Nano Thermo Robots (GNTR) powered by nanotechnology for the treatment of chronic diseases [35]. It highlights how these advanced nanodevices leverage the unique properties of gold nanoparticles, such as their biocompatibility, stability, and ease of functionalization, to deliver targeted therapies. The GNTRs are designed to interact with biological systems in a controlled manner, responding to thermal stimuli to release therapeutic agents precisely where needed [35]. The paper explores various nanotechnology approaches, such as drug delivery, gene therapy, and diagnostic tools, showcasing their potential to revolutionize the management of chronic diseases by improving efficacy, reducing side effects, and offering personalized treatment options [35].
- Cooperative Molecular Communication for Nanonetworks: investigates how chemical signals can be used in nanonetworks to facilitate communication between nanoscale devices like sensors or nanobots [36]. In order to improve molecular communication’s dependability, range, and energy efficiency, it presents the idea of cooperative molecular communication (CMC), in which several devices work together. This method assists with issues such as noise, interference, and signal deterioration in nanonetworks.The study also addresses possible uses in industrial automation, environmental monitoring, and medical diagnostics, highlighting the necessity of developing new methods and models to optimise CMC protocols for reliable, scalable communication in upcoming nanotechnology-based systems [36].
- Efficient Framework Analysis for Targeted Drug Delivery Based on Internet of Bio-Nano Things: explores the integration of bio-nanotechnology with the Internet of Things (IoT) to enhance drug delivery systems [37].It presents an efficient framework that utilizes bio-nano devices, such as nanoparticles and sensors, combined with IoT infrastructure to enable real-time monitoring, precise drug targeting, and controlled release. The framework aims to improve the efficacy of drug delivery, minimize side effects, and ensure optimal therapeutic outcomes by leveraging the connectivity and intelligence of IoT networks in conjunction with the unique properties of bio-nano materials. [37]
- Efficient Nanosystem for Nanomedicine Applications Based on Molecular Communications: An efficient nanosystem for nanomedicine applications based on molecular communications leverages the principles of molecular signaling for inter-nanodevice communication [38]. This approach enables precise and targeted drug delivery, enhanced diagnostics, and real-time monitoring of disease progression at the molecular level. By utilizing nanoparticles as carriers

and molecular signals for transmission, these nanosystems can communicate within the body to detect specific biomarkers or release therapeutic agents in response to environmental cues [38]. This technology holds significant promise for advancing personalized medicine, improving treatment efficacy, and minimizing side effects. The integration of molecular communication with nanoscale devices allows for more sophisticated, dynamic medical interventions. [35]

- Biocyber Interface-Based Privacy for Internet of Bio-nano Things : The concept of a biocyber interface-based privacy for the Internet of Bio-Nano Things (IoBNT): focuses on safeguarding personal and sensitive biological data transmitted through interconnected bio-nano devices. This interface integrates biological systems with cyber-technological elements, ensuring secure data exchange in environments where bio-nano devices monitor, collect, and communicate healthrelated information [39]. The goal is to prevent unauthorized access or misuse of data, maintain confidentiality, and protect user privacy by leveraging advanced encryption, biometric authentication, and other privacy-preserving technologies. As the IoBNT involves highly sensitive biological information, ensuring robust privacy measures is critical to fostering trust and promoting widespread adoption of these technologies. [39]
- Embedded Nano Relay for Intra-Body Network-Based Molecular Communications : The concept of an embedded nano relay for intra-body network-based molecular communications refers to the integration of nanoscale relays into biological environments for communication purposes. [40]These nano relays serve as intermediaries that facilitate the transfer of molecular signals, typically in the form of nanoparticles or biomolecules, within the human body. This is particularly useful for intra-body communication systems, where data is transmitted via molecular or biochemical signals instead of traditional electrical signals. The technology could enable advanced healthcare applications, such as targeted drug delivery, real-time monitoring of biological processes, and efficient communication between bio-nano devices in the body [40]. The relay helps to extend the range and improve the reliability of molecular communications, paving the way for sophisticated medical treatments and personalized medicine. [40]
- Fundamentals of Molecular Information and Communication Science: explores the foundational principles and techniques of molecular communication, a field that applies concepts from molecular biology, information theory, and communication engineering. [41]. It discusses how molecules can be used for transmitting and processing information at the molecular level, akin to traditional communication systems but within biological or synthetic molecular environments. The paper outlines key topics such as molecular signaling, DNA computing, molecular communication models, and applications of these technologies in areas like bio-nano systems and biomedical engineering . [40]. The work highlights the potential of using molecular communication for applications in areas like medical diagnostics, drug delivery, and bio-inspired systems. It also addresses challenges such as noise, interference, and scalability that need to be overcome to make molecular communication systems practical. [41]
- Internet of Bio Nano Things-based FRET nano communications for eHealth: investigates the application of fluorescence resonance energy transfer, or FRET, in bio-nano devices for medical uses [42]. Advanced communication mechanisms for real-time data transmission in eHealth systems are made possible by FRET, which permits energy transfer between light-sensitive molecules [42]. When utilised for biological parameter monitoring or incorporated in the human body, these technologies can increase data security, accuracy, and efficiency in remote health monitoring, diagnosis, and treatment. The study also discusses issues with FRET-enabled bionano devices' scalability, energy consumption, and miniaturisation in medical settings [43].
- Internet of Bio-Nano Things: A Review of Applications, Enabling Technologies and Key Challenges: provides an overview of the emerging field of the Internet of Bio-Nano Things (IoBNT), where biological and nanoscale devices are interconnected to create a new class of

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smart systems [41]. The review explores key applications, such as healthcare, environmental monitoring, and agriculture, where IoBNT can have a transformative impact. It delves into the enabling technologies behind these systems, including bio-sensors, nano-materials, communication networks, and data analytics. Additionally, the paper highlights the major challenges facing the development of IoBNT, such as scalability, energy efficiency, security, and ethical [43]concerns.

- Moving Forward With Molecular Communication: From Theory to Human Health Applications: explores the development of molecular communication (MC), an emerging communication paradigm inspired by biological systems. [44] The study examines how theoretical models of MC, which traditionally focused on the transmission of information using molecules, are evolving into practical applications, particularly in the realm of human health. It delves into the potential of MC for biomedical applications, such as drug delivery, disease monitoring, and the development of novel diagnostic tools. The paper highlights both the challenges and promising opportunities in translating MC from a theoretical framework to tangible, real-world healthcare solutions. [44]
- Molecular Communication Modeling of Antibody-Mediated Drug Delivery System: This paper models antibody-mediated drug delivery using molecular communication principles. [45] It focuses on designing antibodies to target specific cells, analyzing the body as a communication medium, and using simulations to optimize delivery. The aim is to improve targeting accuracy and delivery efficiency in antibody-based therapeutic systems. [45]
- Molecular communication nanonetworks inside human body: The idea of molecular communication nanonetworks within the human body entails the use of nanoscale devices or particles, such as proteins, ions, or synthetic nanocarriers, to transfer information through biochemical signals. As opposed to conventional wireless networks, these nanonetworks imitate biological processes to facilitate disease detection, tailored drug delivery, and health monitoring [46]. For instance, illness indicators can be detected by bloodstream nanosensors, which can then initiate therapeutic reactions like the release of medication at particular locations [46]. Control over molecular signals, interference in the intricate biological milieu, and biocompatibility are among the difficulties. In order to provide real-time, localised healthcare, research attempts to create reliable communication protocols for safe and efficient medical applications. [48]
- Molecular Communication Among Biological Nanomachines: presents a framework for molecularlevel communication between biological nanomachines [47]. It suggests a tiered design that includes molecular signal encoding, transmission, reception, and processing, much like conventional network models like the OSI model. The main obstacles in creating molecular protocols, enhancing signal transmission, and guaranteeing dependable data transfer are identified with the aid of this methodical methodology. Future studies in the Internet of Bio-Nano Things (IoBNT) for environmental and biomedical applications are intended to be supported by the framework. [47]
- Nanonetworks: A New Communication Paradigm: According to the literature, nanonetworks are revolutionary systems that make it possible for nanoscale objects to carry out actuation, computing, and sensing functions [48]. Because of the shortcomings of conventional approaches, other communication strategies like terahertz-based and molecular mechanisms are being investigated. Creating effective protocols, controlling molecular noise, and maintaining security are major obstacles. Their potential in the biological, industrial, and environmental sectors is highlighted by applications that include smart materials, targeted medicine delivery, and environmental monitoring [48].

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V. KEY ENABLING TECHNOLOGIES FOR IOBNT

Table III: Key Enabling Technologies for IoBNT[10]

Technology	Description	Impact on IoBNT	Challenges
Nanoscale Communication	Techniques enabling communication between bio-nano devices at the molecular level	Facilitates ultra-low power, high-density networks of bio-nano devices for real-time data exchange	Requires overcoming interference and energy efficiency issues
Bio-Nano Device Design	Integration of biological and nanoscale components to create devices capable of sensing or actuation	Enables the creation of highly sensitive and responsive devices for healthcare, environmental monitoring, and more	Design complexity, biocompatibility, and miniaturization
Quantum Comput-ing	Use of quantum algorithms and processing power for complex calculations	Provides higher data processing power for real-time analysis and simulation of biological systems	Need for quantumsafe communication and integration into existing systems
6G Networks	Advanced communication protocols with ultralow latency and high bandwidth	Supports seamless connectivity for billions of bionano devices, enabling largescale deployments in smart cities and healthcare	Deployment challenges in remote areas and managing vast amounts of data
AI andMachine Learning	Use of algorithms to analyze large data sets and make realtime decisions	Enhances system adaptability, predictive capabilities, and automation in IoBNT applications	Need for training data, model accuracy, and computational resources

The Internet of Bio-Nano Things' (IoBNT) success is contingent upon a collection of enabling technologies that offer the fundamental framework for system integration, device design, and communication [49]. These technologies are essential to IoBNT's scalability, effectiveness, and efficiency in handling the various problems that arise in real-world applications. With an emphasis on nanoscale communication, bio-nano device design, and system integration, this section examines the major technologies advancing IoBNT and shows how they meet the real-world needs of IoBNT applications [49].

A. Nanoscale Communication Paradigms

Nanoscale communication is one of the most critical components enabling the functionality of IoBNT. This communication paradigm allows for data exchange between bio-nano devices at the molecular and nanoscale levels, facilitating the interaction between biological systems and digital networks [50].

Key aspects of nanoscale communication include: Molecular Communication: Molecular communication is the primary method for transmitting data in IoBNT. It uses biomolecules (e.g.,

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proteins, DNA, ions) to encode, transmit, and decode information at the nanoscale [51]. Unlike traditional electrical communication methods (e.g., electromagnetic waves), molecular communication allows devices to directly interface with biological systems and environments [51]. For example, DNAbased communication can be used to encode and transmit data, offering high capacity and stability, especially in biological environments. This technology is crucial for in-body health monitoring and biosensing applications, where real-time data exchange between devices embedded in the human body or biological systems is required [52]. Nano-scale Communication Protocols: The design of communication protocols for nano-networks is another essential aspect of nanoscale communication [53]. These protocols ensure efficient data transfer between bio-nano devices while minimizing power consumption [53]. Current research is focused on developing energy-efficient, reliable, and scalable communication protocols tailored for the constraints of nanoscale systems, such as limited range, low power, and high interference. Diffusion-based communication (where molecules spread through the environment) and electromagnetic-based communication (using terahertz or microwave frequencies) are key examples of the techniques being explored for nanoscale communication [53]. Hybrid Communication Methods: The integration of molecular communication with traditional communication methods (e.g., wireless communication via radio frequency) can overcome the limitations of both approaches [54]. By leveraging both biological and digital communication paradigms, IoBNT systems can achieve long-range communication, as well as localized, molecular-level interactions [51].

B. Bio-Nano Device Design

The design of bio-nano devices is central to IoBNT's ability to interact with biological systems and the environment at the nanoscale. These devices are engine ered to sense, act, and communicate with biological entities, facilitating the desired outcomes in applications ranging from healthcare to environmental monitoring [53]. Key aspects of bio-nano device design include: Nanosensors: Nanosensors are designed to detect specific biological markers or environmental conditions with high precision. These devices can be engineered using nanomaterials (e.g., carbon nanotubes, graphene, quantum dots) that exhibit unique properties at the nanoscale, such as increased surface area and enhanced chemical reactivity [51]. These sensors can detect biomolecules, pathogens, chemical pollutants, and environmental factors such as temperature and pressure. In healthcare, for example, biosensors could continuously monitor glucose levels, detecting early signs of diseases like diabetes [55]. Nanoactuators: Nanoactuators are devices capable of initiating physical actions in response to signals received from nanosensors [56]. These actuators can be used in applications such as drug delivery, where they release a therapeutic agent in response to the detection of specific biomolecules [57]. For instance, nanorobots could be deployed to deliver drugs to targeted cells in the body, ensuring that treatment is personalized and efficient [57]. Bio-compatible Materials: One of the significant challenges in bionano device design is ensuring that devices are biocompatible—that is, they must not elicit adverse biological responses. For this, devices are often made from materials that are non-toxic, bio-degradable, and safe for integration into living systems. Common materials include gold nanoparticles, silica, and biopolymers, all of which have been shown to be well-tolerated by biological tissues [56]. Power Harvesting and Low-Power Operation: Bio-nano devices typically operate in environments with limited energy sources. To address this, devices are designed to operate with ultra-low power consumption, and energy harvesting techniques, such as vibration-based, solar, or biochemical energy harvesting, are employed to power these devices without the need for external batteries [58].

C. System Integration Challengess

The integration of bio-nano devices into a cohesive, functioning IoBNT ecosystem presents significant challenges. These challenges arise from the need to combine biological components, nano-devices, and digital networks into a unified system that can operate efficiently, scale effectively, and be deployed in real-world applications [58]. Key system integration challenges

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include: Interfacing Biological Systems and Nano-devices: One of the primary challenges is achieving seamless integration between bio-nano devices and biological systems. For instance, ensuring that nano-sensors can accurately detect biological signals (such as the presence of pathogens or changes in biomarkers) within the human body without interference or degradation is a significant hurdle. The biocompatibility of devices and the ability to integrate them into biological systems without causing harm or rejection are essential factors to consider [58]. Data Synchronization and Management: Given the distributed nature of IoBNT systems, which may involve large numbers of bio-nano devices embedded in diverse biological environments, data synchronization and real-time communication are challenging tasks. The data generated by each device must be processed and transmitted to a central system for analysis and action. This requires highly efficient data management systems, capable of handling large volumes of data from multiple sources, including sensors and actuators, in real time [55]. Scalability and Robustness: As IoBNT systems are deployed across multiple sectors and environments, scalability and robustness are key considerations. Designing systems that can expand efficiently while maintaining their performance is critical. For example, a system that monitors environmental pollution via bio-nano devices must be able to scale to monitor large geographic areas without compromising data quality or reliability [59]. Security and Privacy: Given the sensitive nature of biological data and the potential for IoBNT devices to be deployed in personal and healthcare contexts, security and privacy are significant concerns. Robust encryption protocols and secure communication channels must be integrated into IoBNT systems to protect against potential breaches, unauthorized access, and malicious attacks [59].

D. Addressing the Demands of Real-World Applications

The technologies described above are not merely theoretical—they are central to addressing the practical demands of IoBNT applications: In healthcare, IoBNT can revolutionize personalized medicine, where bio-nano devices continuously monitor patient health, detect diseases early, and provide targeted treatments without the need for invasive procedures [60]. In agriculture, bio-nano sensors can monitor soil conditions and optimize resource usage, resulting in more sustainable farming practices and improved crop yields [60]. For environmental monitoring, IoBNT can facilitate real-time pollution detection, enabling swift responses to environmental hazards such as chemical spills or airborne toxins [60]. By driving innovation in communication, device design, and system integration, these enabling technologies ensure that IoBNT systems are practical, scalable, and capable of providing meaningful solutions to pressing global challenges [61].

VI. BIO NANO AND MOLECULAR COMMUNICATION

A. Bio Nano Thing

Bio-Nano Things, as described by the IoBNT, are distinctly recognisable fundamental structural and functional units that function and interact in the biological environment. Bio-Nano Things, which

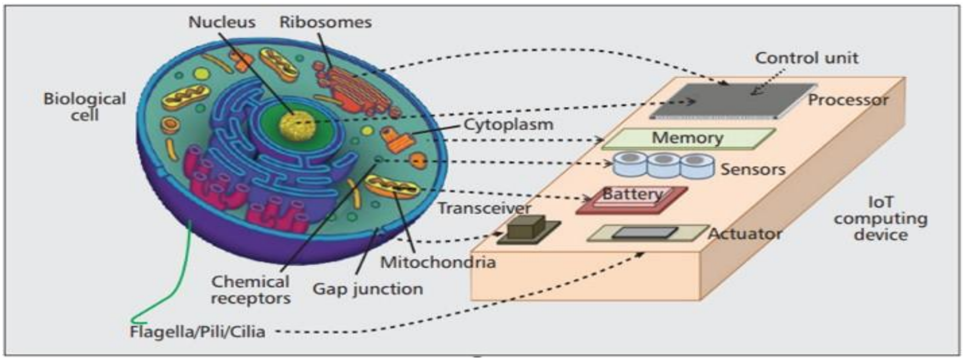

Figure 4: Components of a typical Internet of Things device and elements of a biological cell[1]

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are derived from biological cells and made possible by synthetic biology and nanotechnology, are anticipated to carry out operations and features common to embedded computing devices in the Internet of Things, including sensing, processing, actuation, and inter-device interaction [56]. Biological Cells as the substrate of BIO NANO THINGS: A biological cell is the fundamental building block of life. It is made up of a membrane containing a variety of highly specialised molecules with distinct chemical compositions and functions, some of which may be arranged into functional structures [57]. It is possible to see a connection between the constituents of a cell and the components of a typical Internet of Things embedded computing device by comparing the way electrons propagate in semiconductors to functionally similar but far more complex physiological reactions. [61]

The device's embedded software, found in the control unit, would be equivalent to the genetic instructions that are tightly packed into the DNA molecules of the cells. These instructions encode protein structures, the cell's "data units," and regulatory sequences that are comparable to the software conditional expressions. [56] The memory unit would correspond to the chemical content of the cytoplasm, or the inside of the cell, which is made up of molecules the cell synthesises in response to DNA instructions and other molecules or structures, like vesicles, that are exchanged with the outside world. [57] It would also contain the values of the embedded system data. The processing unit, which runs software programs and controls memory and peripherals, is analogous to the molecular machinery that creates protein molecules with types and concentrations that depend on instructions from DNA molecules via a process known as transcription and translation [60]. The adenosine triphosphate (ATP) molecule, which is produced by the cell from energy received from th// eexternal environment in various forms and provides the energy required for the cell's biochemical reactions to occur, would be equivalent to the power unit, which provides the energy to maintain the electrical currents in the embedded system's circuits [61].The transceivers that enable information sharing between embedded systems would be equivalent to the particular chemical reaction chains, or signalling routes, that cells use to exchange chemicals that carry information. Sensing and actuation, which enable embedded systems to gather information and communicate with their surroundings, would be analogous to a cell's ability to chemically identify external molecules or physical stimuli, like light or mechanical stress, and to alter the environment's chemical composition or mechanically communicate through moving components, like flagella, pili, or cilia [62].

B. Bio Nano Thing Communication

The idea behind IoBNT is that Bio-NanoThings must be able to communicate with one another and interact based on the information that is shared. The primary source of inspiration for researching communication strategies for IoBNT is the natural environment, as Bio-NanoThings are derived from the engineering of biological cells, as previously [60]said.

C. Molecular Communication in Nature

The synthesis, transformation, emission, propagation, and reception of molecules through biochemical and physical processes form the basis of information communication between cells in nature. Cell interactions and coordination of unicellular and multicellular organisms, populations, and multispecies consortia are made possible by this information exchange, which was recently categorised as MC in telecommunications engineering [62]. It also contributes to the majority of the main cellular functions, including cell growth and proliferation. The aforementioned signalling pathways—chains of chemical reactions that process information signals converted into chemical characteristics, such as molecule concentration, type, and energy state—are the foundation of MC in cells. These pathways convey signals from a source, or transmitter, to a destination or receiver [61]. Cell signalling pathways can be divided into four categories based on the distance between the source and the destination: endocrine (source and destination are far apart), paracrine (source and destination are close to one another but not in contact), juxtracrine (source and destination are cells in contact with one another), and intracrine (source and destination are within the same cell).

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Transporting molecules or molecule structures within cells via cytoskeletal molecular motors is an example of intracrine communication. Specialised intracellular proteins called molecular motors can transform the previously described ATP molecules into mechanical energy [62]. When a specific cargo, such as vesicles containing groups of molecules or entire cell organelles, is attached to the microfilament structures that make up the cell's skeleton, the cytoskeletal molecular motors can crawl along them to move the cargo from the nucleus to the cell membrane and vice versa [63]. The interchange of chemicals, like calcium ions Ca2+, between two cells that are joined by membrane-based communication junctions is an illustration of juxtacrine communication. Numerous natural examples, such as the signalling between muscle cells, or myocytes, during a heart contraction, demonstrate how a tiny number of chemicals can diffuse between nearby cells and be in charge of coordinating coordinated movements. Bacteria have a variety of natural communication mechanisms, including the paracrine communication that underlies a population's release of signalling molecules known as autoinducers [63]. Bacterial quorum sensing is a technique in which autoinducers diffuse throughout the intercellular space and, when received, enable the bacteria to assess the population density. They also have a linked response, such as the production of particular protein types [57]. Additionally, through a process known as conjugation, bacteria can exchange specific DNA molecules, or plasmids, by direct contact. Chemotaxis is the process by which bacteria travel along chemical trails to transfer the plasmids to other distant bacteria within the intercellular space. [58]Hormones, which are signalling molecules released from glandcomposing cells and travel through the circulatory system before reaching the cells of distant organs, are an example of endocrine communication in multicellular organisms. There, they cause particular reactions, like increased cell growth and reproduction [59]. Molecular communication (MC) is an emerging paradigm inspired by biological systems, where chemical signals (molecules) are used to encode, transmit, and decode information. This mode of communication is central to natural processes and is increasingly being explored for applications in nanotechnology, medicine, and bioengineering. Below is a comprehensive explanation of molecular communication [60]. Molecular communication mimics biological processes like hormone signaling or neural transmissions. Instead of using electromagnetic waves, it employs molecules as information carriers. This makes it suitable for environments where electromagnetic communication is impractical, such as inside the human body or underwater [63]. In addition to communicating with one another, Bio-NanoThings are anticipated to interact to form networks within the IoBNT, which will eventually connect to the Internet. To this aim, a crucial stage in the development of IoBNT is the definition of network topologies and protocols on top of the previously stated MC systems [64]. Another difficulty facing IoBNT is connecting heterogeneous networks, which are made up of various Bio-NanoThing types and based on various MC systems. Ultimately, the development of interfaces between the Internet's electrical domain and the IoBNT networks' biochemical domain will be the final step towards establishing a smooth connection between the biological environment and the modern cyberworld [64].

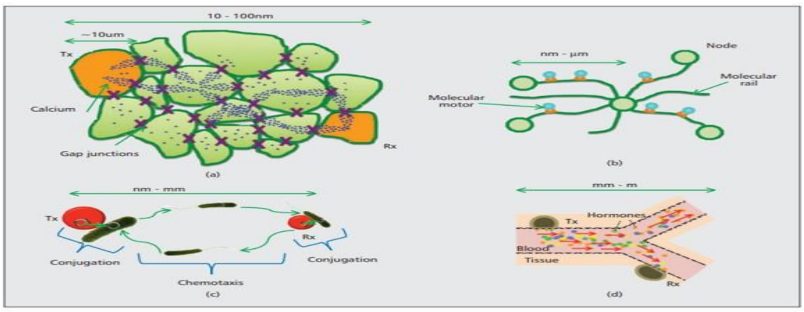

Figure 5: Shows several examples of molecular communication, including: a) Ca2+ communication, b) molecular motors, c) conjugation-chemotaxis in bacteria, and d) hormone communication. [63]

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Figure 6 depicts a potential scenario in which an entire Internet of Business Networks (IoBNT), consisting of multiple networks based on various MC systems, is installed inside the human body and communicates with a healthcare provider via a personal electrical device that is connected to the Internet. The device delivers intra-body status parameters and receives commands and instructions.
[65]

D. The concept of IoBNT for a medical application

Imagine an advanced medical therapy scenario in which a patient with a certain condition receives an injection of a specific set of nanodevices that penetrate specified tissues to carry out tissue repair, TDD, or diagnostic procedures. [64] Then, while the nanodevices silently carry out the assigned activities in the targeted system, the patient is free to return home and resume his or her regular responsibilities. Medical professionals at a distance then keep an eye on the actions and developments of the nanodevices [65]. Medical personnel use standard communication devices to send and receive signals and commands. Medical personnel may transmit commands in the form of sets of binary codes, each of which instructs a particular set of nanodevices in the patient's body to do tasks like replication, movement, sense, energy acquisition and expenditure, molecule release or synthesis, and decomposition [65].

However, the signals and information that the medical personnel receive typically originate from particular sets of nanodevices that function as nanosensors at the target nanonetwork within the patient's body [66]. The status of the targeted tissues' microenvironment and the nanodevices themselves will be disclosed by this data. It can determine the salinity, temperature, pH, and presence of specific biological substances at a given moment. The data obtained can be used, among other things, to determine when a group of devices should be removed from the system since they are no longer required. By delivering the right commands to start certain tasks, the medical staff can subsequently use this information to improve the performance of the nanodevice network [65].

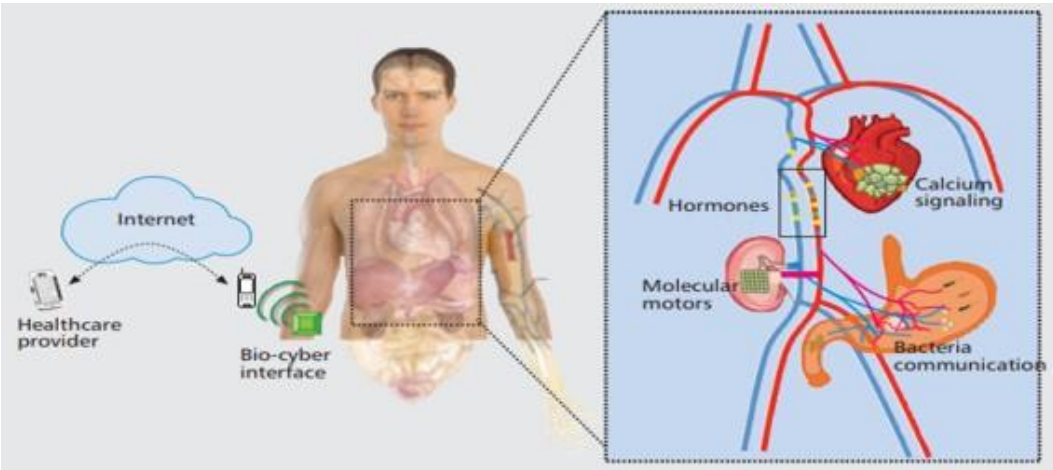

Figure 6: Shows the network architecture for intra-body applications of the Internet of Bio-Nano Things.[64]

In Figure 5, the medical personnel uses the Internet or another suitable network to send out the relevant signal in order to start a certain command. On the patient's body, such as on the wrist, a biocyber signalling system receives and relays this signal. When the bio-cyber system reacts, it sends the right signal via the body channel which may be the blood vessels to the specified group of devices in the target nanonetworks [66]. A specific nanotransmitter in the intended nanonetwork receives the biocyber signal, decodes it, and then transmits the proper biochemical signals to the targeted nanodevices. The targeted nanodevices react in a special way by carrying out the intended task. We have included an access point that transmits the command obtained from the Internet to enable the

patient's unrestricted mobility and improved signal reception. [67] Figure 5 shows that nTR1 is a liposome-based nanocarrier that is stimulated; nTR2 and nTR3 are nanodevices that can produce various chemicals in response to external signals. Therefore, nTR1, nTR2, and nTR3 can be referred to as nanotransceiver [65]. From here on, we will refer to the nanosensor and nanotransceivers as nanodevices. In the following scenario, a patient receives an injection of a nanosensor along with a set of therapeutic nanodevices, nTR1, nTR2, and nTR3 [66]. After that, the patient is free to return home while the nanodevices reach the targeted area via his blood vessel network. Complementary receptors that are only expressed at the targeted areas can be bound by the ligands that are attached to the nanodevices [67]. The nanodevices remain anchored at the location due to the high-affinity binding. Afterwards, particular enzymes that are expressed at the targeted sites—like matrix metalloproteinase
(MMP) [64] in the case of a malignant site increase nTR1's release of therapeutic molecules, such as GA, that they enclose. When nTR1 releases chemicals into the targeted environment, the nanosensor picks them up. In response to GA, the nanosensor releases a specific chemical called GB, which travels throughout the bloodstream and is picked up by the bio-cyber interface on the patient's wrist or any other handy location on the body [65]. After decoding the chemical information specified by GB, the bio-cyber interface sends forth the proper electromagnetic signal.

The access point receives the signal that is sent and transmits it to the medical staff over the Internet [66]. The initial therapeutic drug molecule GA has usually been delivered to the intended site, according to the information that the medical staff receives. The medical staff uses this information to instruct nTR2 to synthesise and release the upcoming medicinal medication GC [67]. The bio-cyber interface receives this command via the Internet and reacts by sending a certain concentration of the chemical GD into the blood network. After passing through the circulatory network, the molecules arrive at their intended location, where they cause GC to be synthesised and released. It is ideal for the nanodevices to be removed from the human system when the drug delivery process is completed. Therefore, following the drug delivery procedure, nTR3 receives a death command that causes all of the network's nanodevices to initiate self-annihilation [68]. The nTR3 sends out a death signal upon receiving the death command, and the corresponding nanodevices receive it and proceed to self-annihilate. [69]

E. First Description of a Practical hybrid Bio -Nano Thing

A design solution in the literature is given in this part, along with a discussion of the necessary characteristics of BNTs for infection detection applications. A sensor-interface chip, a coil/antenna, and a bio-nanosensor make up the three primary components of a BNT device [66].

BNTs can be used to wirelessly transmit the infection data to a wearable hub outside the body, as shown in Fig. 6, and to detect the quorum sensing signals of infectious bacteria. In the body, the tiny BNT can be used as a wearable or implanted device.In this section, we concentrate on the design and construction of a new sub-millimeter bio-nanosensor, as well as its interface chip and coil/antenna, which are the BNT components shown in Fig. 6. First, we outline the several sensing modules and describe how to put the bio-nanosensor into practice [66]. After that, we design highefficiency wireless power transfer circuits with an associated coil and antenna, as well as ultra-low power interface circuits with a variety of sensing properties.

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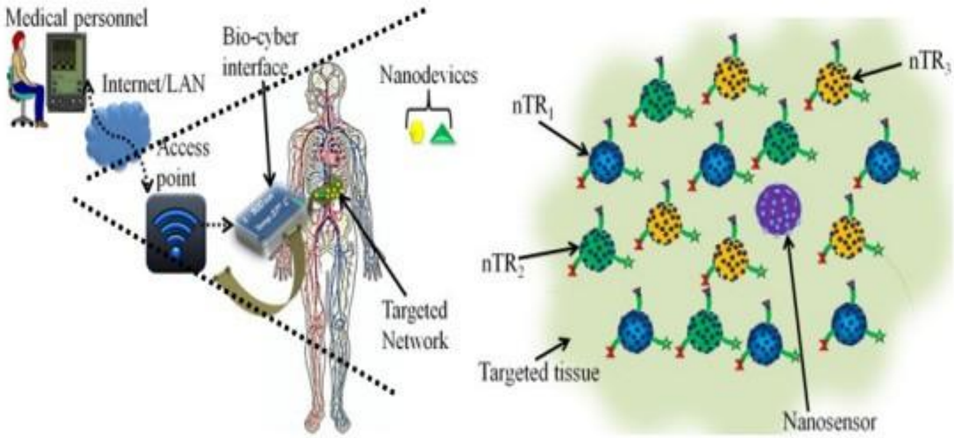

Figure 7: Illustration of the concept of IoBNT for a medical application[65]

- BIO-NANOSENSOR:
  When pathogenic bacteria invade different healthy human tissues, they grow, disrupt tissue function, and cause diseases. This is known as an infection. We create BNTs that take use of the quorum sensing communication of bacteria that infect humans and are picked up by bionanosensors in order to detect it with IoBNT [67]. The primary method of communication between cells is quorum sensing, in which bacteria create and release chemical signal molecules whose external concentration rises in response to an increase in cell population density. Thus, the density of the pathogenic bacterial population can be estimated by measuring the concentration of its quorum sensing molecules. The BNT biosensor can be designed in a variety of ways. An other technique is the direct detection of the target bacteria's QS molecules using antibodies [66] coupled to a transducer, as shown in Fig. 7.a. Other techniques involve using a different kind of bacteria as the sensor's detector. As shown in Fig. 7.b, the bio-nanosensor's engineered bacteria detect MC signals produced by the infectious bacteria and catalyse a chemical reaction to produce an electro-active product, or they produce light that is detected by the transducer, which transforms light into electrical current, as shown in Fig. 7.c. Bacterial sensors with engineered synthetic pathways are frequently used by researchers for molecular sensing [67]. Bacterial sensors' primary benefit is that they have membrane receptors that have evolved to engage with the target of interest with high specificity and sensitivity. A human-harmless genetically modified strain of E. coli K12 can be used in the bacterial sensor to attach to QS molecules and generate an optical signal in the form of bioluminescence/fluorescence or molecular signals that are simple for electrochemical sensors to detect [65].
- SENSOR-INTERFACE CHIP: In order to improve the infection detection system's dependability in the decision-making process, we think about using multiple strategies. Thus, it is recommended to use a multimodal sensing paradigm that optimises the sensitivity and specificity of BNTs by combining optical (florescence/bioluminescence) and electrochemical sensing mechanisms [66]. A low µW-level sensor-interface chip is required to reduce the heat produced in the wireless power delivery and management blocks and avoid potential tissue damage in accordance with regulatory standards, such as particular electromagnetic power absorption limitations [68]. The sensor-interface chip is composed of four primary parts in order to meet these requirements.
- ANALOG FRONT-END (AFE)
  The AFE circuit, which communicates with bio-nanosensors, needs an impedance and/or current detection circuit that can sense a wide range of frequencies and performs well in terms

of linearity [68]. To reduce the impact of in-body noise on the sensed data, the AFE circuit should have very low noise in addition to low power sensing and long integration capability [69].

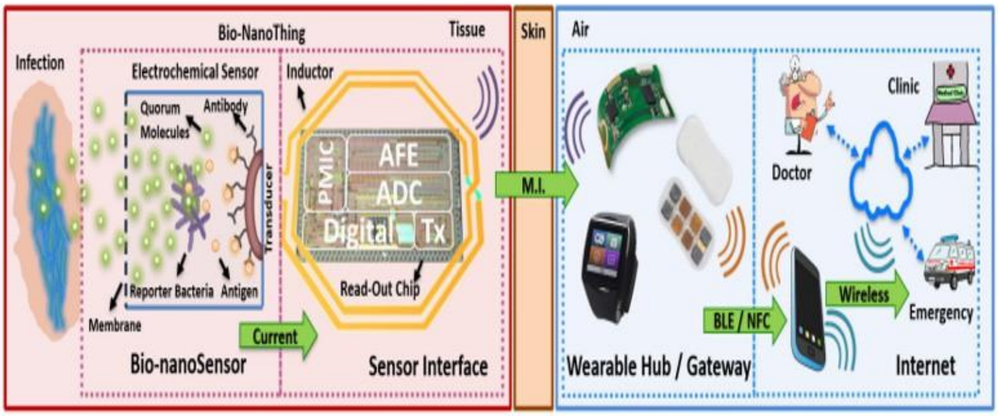

Figure 8: PANACEA System Overview[66]

- ANALOG-TO-DIGITAL CONVERTER (ADC)
  Among the least power-intensive architectures are specific absorption rate (SAR) ADCs, which have an astoundingly low 0.88 pJ per conversion level but in order to accomplish both low power and great resolution, they take up a lot of space on the semiconductor [67]. High resolution can be attained by delta-sigma ADCs with comparatively low power levels and tiny footprints. Existing ADC circuits must balance low power consumption with big area occupation [64].
- POWER MANAGEMENT IC
  An extremely efficient charging mechanism can be built in an adaptive heavily duty-cycled architecture to harvest the low incoming electromagnetic energy from the wireless power link, store it in very small off-chip capacitors with a high charge density, raising the voltage level [65], and use it over a brief period of time when the bio-nanosensors are activated. The AFE pre-processes and conditions the acquired signals, the ADC samples and digitises them, and the back telemetry link transmits the resulting data to the wireless wearable hub outside the host body [66].

- WIRELESS DATA TRANSMITTER
  Digital optical and biochemical signals are compressed, packetized, and wirelessly sent from the host body to the external wearable Internet hub and to enhance data security and integrity, the data communication block also has forward data modulation, encoding, and encryption (if required) in addition to the back telemetry switch [68].
- COIL/ANTENNA WPT is becoming more and more crucial in powering IMDs that are inefficient or too small to run on primary batteries. Researchers have looked into using ultrasonic, laser, and ultra-high frequency (UHF) fields to power smaller IMDs, but WPT to IMDs is still thought to be the safest and most dependable method for creating a power/data link between one or more transmitter (Tx) and one or more receiver (Rx) coils that are electromagnetically coupled in the near field. One of the main challenges with magnetic induction-based wireless communication networks and power-efficient, dependable energy harvesting is the need for a properly engineered miniaturised coil to connect BNTs to the wearable hub [68].

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F. COMMUNICATION NETWORKS AMONG BIO-NANO THINGS

It is the aim to be identified using BNTs in light of this, we examine bacterial quorum sensing (QS) as a sign of infection [66]. QS is a technique for communication between cells in which bacteria create and release chemical signalling molecules whose concentration corresponds to the density of bacterial cells [68]. A network of submilimeter-sized BNTs placed in tissues in vast quantities can measure the spatiotemporal concentration of QS molecules specific to target bacteria, allowing us to estimate the number of infectious bacteria present and track the infection's progression [67]. Molecular communication theory, which examines the exchange of information through the emission, propagation, and reception of molecules, can be used to abstract QS communication in bacteria. The main focus of MC theory is on the molecular transport-based biological communication systems that allow information to move between biological cells, tissues, and naturally occurring organisms [70].Diffusion-based, flow-based, and molecular motors are some of the several channel models that can be developed based on the transport media [69]. Our earlier research on bacterium-based molecular communication focused on using bacteria as active message carriers, and as bio transceiver devices for MC. With the MC paradigm, the principles of multi-scale molecular and biological processes can be properly modelled without the drawbacks of experimental methods or the excessive complexity of system biology models. We can estimate the initial position and quantity of bacteria at the infection site by modelling and analysing the propagation of QS molecules from the infection site to BNTs using MC abstraction of QS [70].

- MC CHANNEL FOR INFECTION

  It is possible to think of the quantity of infectious bacteria as the message that is conveyed by the concentration of QS molecules that diffuse through tissue and reach BNTs. Figure 8 illustrates how an end-to-end model resembling might be used to depict this channel [68]. The initial process in this MC channel is the transmission process, which is when infecting bacteria produce and release QS molecules. One of the numerous QS models that see a population of bacteria as a single entity and abstract away all of the intermediate biological reactions to reduce the system to a set of linked nonlinear differential equations can be used to represent this QS mechanism [69]. The random spatial distribution of bacteria and the variations among individual bacteria within a population can be introduced as noise sources during the transmission process [70].The propagation process, or the movement of QS molecules through the tissue where they permeate the cells and the fluid between them, comes next. Initially, only local infections that do not yet include pathogenic microorganisms entering the bloodstream are taken into consideration [71]. Small molecules, like QS molecules, move through the interstitial space (the tiny gaps between biological structures) by diffusion and convection, which is modelled by the general mass transport balance. This balance depends on the interstitial fluid's flow velocity, the diffusion coefficient, and the reaction rates that take into consideration cell binding, consumption, and degradation [71].QS molecules must move around cells and diffuse both inside and outside of cells, which is similar to channel models with multipath, shadowing, reflection, and refraction in a crowded environment. This makes the transport in interstitial space more complex than in previous studies on diffusionbased MC models [69]. In the final stage, known as the reception phase, QS molecules approach BNTs and have the potential to be picked up by bio-nano sensors [70]. The MC receivers are bacterial bio-nano sensors, which use bacterial receptors to sense the concentration of QS molecules in conjunction with photodiode-detected fluorescence and/or bioluminescence. The time needed to create electroactive proteins, fluorescence, or bioluminescence limits the pace of this signal transduction (reporter). [68] One reporter protein can be detected by a particularly sensitive photodiode, which can compensate for the delay caused by this phenomenon [69]. Analysing the delay, attenuation, and noise of each of these three processes is necessary in order to calculate the number of bacteria based on the concentration determined by BNTs. In order to maximise infection detection, the delay and attenuation models recommend the design of the sensor and receiver. The accuracy of the infection estimation is represented by the MC

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channel's capacity, which was calculated using the models that describe these processes and the corresponding noises [70].

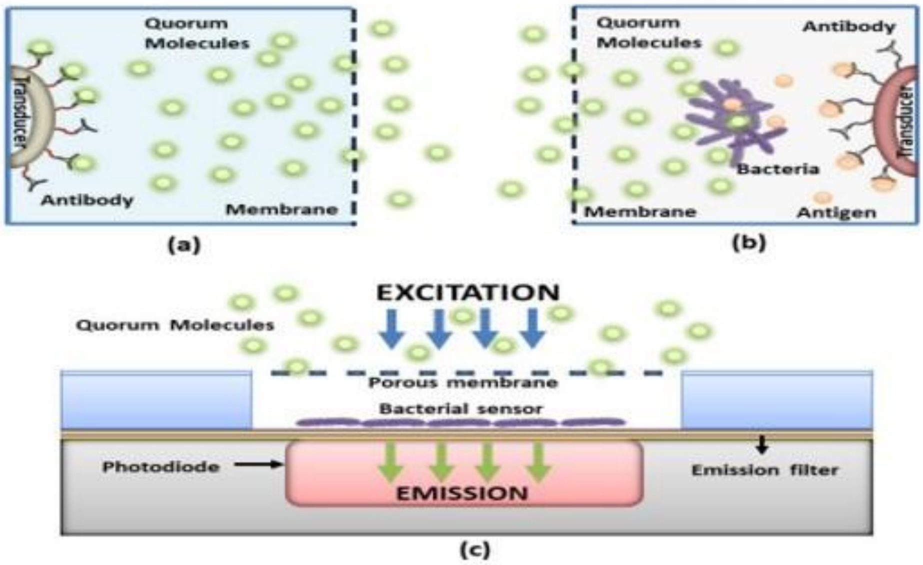

Figure 9: There are several approaches to create the BNT biosensor[67]

- MC CHANNEL FOR DRUG DELIVERY
  An actuator mechanism built in either an active or passive drug delivery form can be incorporated into the suggested IoBNT application to produce a closed loop system. Incorporating healthcare practitioners' viewpoints into the delivery logic allows for the inclusion of humans in the decision-making process for passive drug distribution. An external device that transmits the pre-programmed drug recipe or notifies patients to take the customised medication may be set up in accordance with that. The wearable hub or BNTs can both release a medication directly for active drug delivery [71].Quorum quenching, or stopping quorum sensing by interfering with the signalling, is a further actuator mechanism that extends the idea of QS eavesdropping. Infectious bacteria may be stopped from invading healthy tissues by disrupting their quorum sensing communication and blocking quorum sensing-controlled virulence pathways [71].

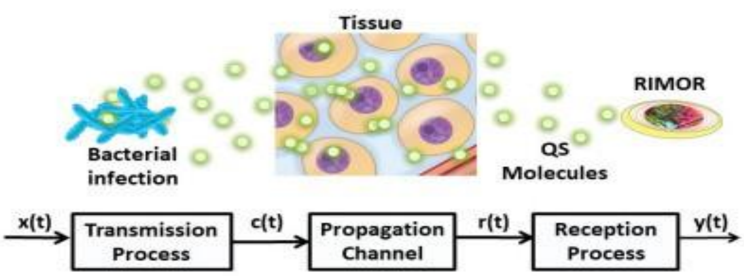

Figure 10: MC channel for infection in an end-to-end model[68]

The MC paradigm has been used to model drug delivery systems (DDS), which can be used to mitigate infection by providing antibiotics, in addition to bacterial infections. DDS is an abstraction of the propagation of drug particles throughout the body [65]. MC can define DDS problems in a way that can be addressed with mathematical methods used in communications, such as stochastic analysis, information theory, and control theory, by introducing abstractions that are traditionally used to characterise the functions of networking and computer systems [66]. Particle advection and diffusion, in conjunction with additional physicochemical processes including adhesion, reactivity, and absorption, are used to describe the biodistribution of medications across blood arteries [67].But this model just looks at the medication that is injected into blood vessels. From an MC perspective, other passive drug administration techniques, including oral antibiotics, necessitate the abstraction of drug absorption through the gastrointestinal tract and blood mixing. The MC paradigm should include regulated medication release for active drug delivery systems like dressing/patch and implanted drug delivery. [69]

G. COMMUNICATION OF BNT NETWORKS WITH INTERNET

BNT networks are made up of a variety of devices, including electrical and cell-based ones, and communication methods, including MC and near field communication [70]. Realising interfaces across many domains is crucial to enabling IoBNT functionality. The ultimate goal of "cell-connected-toInternet" will be achieved through the smooth integration of cyberspace and the biological environment [70]. The most difficult interface in IoBNT is the conversion of MC signals into electrical signals, which BNTs can accomplish. In this scenario, the sensor bacteria receive MC signals in the form of QS molecules and produce bioluminescence and/or fluorescence, which photodiodes then capture to create a current [71]. The intrinsic noisy behaviour of biological systems is being acquired by this interface since it depends on the sensor bacteria. Further compounding the already significant propagation delays in MC, this interface adds delay since sensor bacteria require time to create bioluminescence and/or fluorescent proteins [71].The next task for diverse IoBNT networks is to figure out how to combine these protocols with traditional network protocols on the IoBNTs' cyber side. For IoBNT networks, it is essential to create new protocols that meet the demands of both the electrical and molecular network domains [72]. BNTs use near-field communication techniques to transmit the data from MC channels to a wearable hub after it has been transformed into electrical impulses. Delivery of data and power to the implanted BNTs can be ensured by magnetic-induction, ultrasound, or radio frequency [72]. This wearable and wireless controller hub is in charge of sending data to the Internet from BNTs. Data communication is possible using common protocols like BLE or NFC. A small, flexible printed circuit board (Flex-PCB) that is easily affixed to the body in the abdomen region. For example, as a patch near the site of BNT implantation or a gadget resembling a smart watch might serve [69] as the wearable hub.

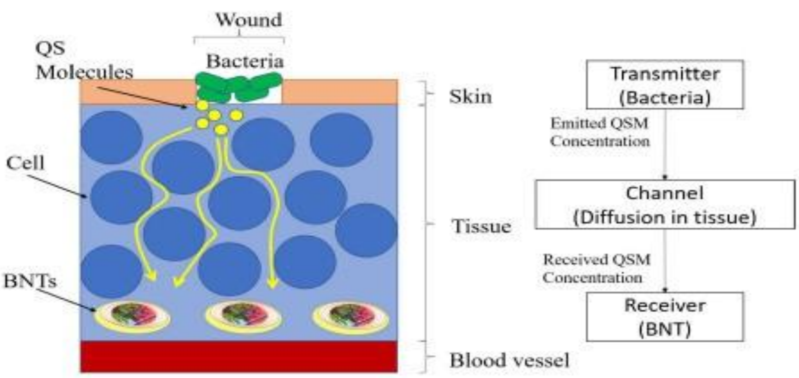

Figure 11: MC channel for the detection of infections[69]

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H. Application of Molecular Communication in Natural and Artificial Health Settings

The MC theory is used to model information flows at three different scales in the natural system direction: 1) body system, where organs and tissues work together to accomplish a particular task; 2) cellular, where cells communicate and process information; and 3) molecular, where information is encoded into substances and transferred through chemical reactions and molecule transport [69].In the direction of synthetically constructed systems, the following are engineered using the MC theory: MC devices, which are engineered biological systems, ranging from microbes to human cells, capable of preprogrammed MC behaviours; 2) MC components, which use genetic programming tools from synthetic biology and technologies to interface with classical electronics; and 3) MC networks, in which engineered biological systems connect to one another to ubiquitously monitor and control human health parameters and interface to the wider Internet. [70]

As shown in Fig. 10, we distinguish between two primary approaches to applying MC theory to human health: those of naturally occurring systems and those of artificially created ones.

- Application to Natural Systems System/Organ/Tissue Scale-The human body is made up of several systems, with organs and tissues working together to carry out particular physiological tasks. From the optimisation of drug molecule delivery and propagation within the body to the utilisation of intrabody communication channels for body area network infrastructures, the MC theory is used to model and characterise the information flow in these systems for a variety of applications
  [72].
  Cardiovascular System: With the long-term objectives of maximising the drug delivery rate at the target tissue and reducing the harmful dissemination of the drug in healthy tissues, MC theory has been used to describe the propagation of nanoscale and microscale drug molecules [73]. This model is based on an MC abstraction, in which the target tissue, connected by MC linkages, is the destination and the medicine to be injected into the system is the source of information [73].Based on the dispersion of drug molecules and fluid flow via the network of blood vessels, these connections are made. The blood velocity is calculated analytically by considering the heartbeat, the blood's physical characteristics, and the vessel walls' elasticity. The drug injection rate and location are used to accurately represent the rate at which drug molecules are delivered to the target tissue and other parts of the body. This information can then be optimised for the previously described objectives. [74]
  Nervous System: The MC literature has modelled, described, and experimented with the transmission of information-carrying electrochemical impulses through neurones and their interconnections as a communication system [74].Specifically, communication theoretical characteristics have been determined, including the error rate and latency of the propagation of a nonlinear active spike via many successive neurones and the frequency response of a passive quasi-linear propagation of inputs through a single neuron [75].
  Microbiome Gut Brain: Using MC theory, usable communication channels are modelled on top of the biological mechanisms that underlie the microbiome gut brain axis (MGBA), which is made up of the enteric nervous system, gut tissues, the gut microbial community, and their interactions [74]. The goal is to create electrical/MCs between biological and electrical devices that are externally accessible, diverse, and minimally intrusive [75].These communications involve the source or sources modifying natural communication parameters at specific MGBA locations or through ingestion, such as gut microbial community composition, mechanical muscular activity, concentration of chemical compounds (e.g., hormones, metabolites, and neurotransmitters), and neural electrical activity (enteric and autonomic) at other MGBA locations, such as the muscular system [74].
  Cellular Scale:The fundamental structural and functional building blocks of life are cells, which interact and work together to form the tissues and organs that make up the previously described systems. For applications ranging from cancer diagnosis and classification to the sensing and regulation of the gut microbial community, MC theory is used to model and

characterise their mutual information exchange as well as their information acquisition and release from/into the environment [74].Cells communicate with one another through a variety of interactions, such as diffusion or contact, and chemicals, such as hormones or signalling molecules. Although there aren't many abstract models that use MC theory to simulate and describe natural cell communication, we believe that current pharmacological and radiological research can help create a more comprehensive detailed model that connects internal signalling pathways and how they affect intercellular [74] communication.

Cell Information Processing: Through the processing of information from the external environment and the subsequent regulation of their behaviour through genetic programs, cells possess the innate ability to adjust to changing environmental conditions in order to maximise their chances of growing, reproducing, and/or maintaining the homeostasis of the multicellular body [75].This ability is quantified using MC theory, which estimates the flow of information from the external environment to the adaptation of cell behaviour. The objective is to provide a new metric for comparing and categorising various cells, which may be involved in disorders. Two other human gut bacterial species as well as the Escherichia coli (E. coli) bacterium have been the subject of studies on this estimation [76].

Molecular Scale: MC theory and all of its applications to human health, as discussed in this paper, are based on the modelling and characterisation of molecular structure, chemical reactions, and transport processes, which form the basis of the previously mentioned information propagation at all scales of the human body. [77]

Molecular Information Exchange: Fick's second rule is the most widely used mathematical model for free diffusion, which is the bulk effect of the inevitable Brownian motion forces on molecules and one of the basic transport processes taken into account in the MC theory. Several research have concentrated on describing the communication channel in terms of the transport mechanism of molecules, including collisions between molecules [75].

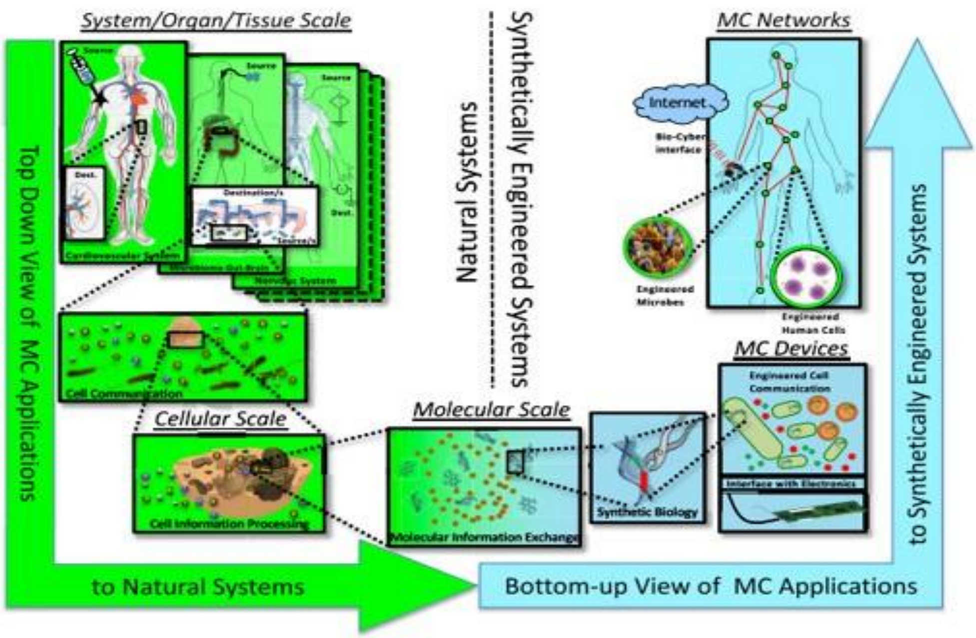

Figure 12: Shows how MC theory is applied to human health in both natural and artificially created settings[72]

• Application to Synthetically Engineered Systems

Molecular Scale: In theory, information encoding and exchange in an MC system can be engineered using a variety of the chemical compounds' properties [76]. The amount of material, such as the number of molecules, total mass, occupied volume, enthalpy, or entropy, does not affect the molecular composition and structure, concentration, density, pressure, or temperature [77].Some of these characteristics, including the chemical makeup of antigens to stimulate immune system antibodies, can be altered in vitro and subsequently transferred from the external environment to an intrabody natural MC system. However, synthetic biology is enabling the realisation of fully integrated in vivo MC systems by utilising the molecular sensing, processing, and actuation capabilities of cells [75].
Synthetic Biology: This multidisciplinary area of engineering offers a feasible route to the actualisation of MC-capable systems via genetic code programming in cells [76]. Specifically, biological circuit engineering, which is constructed by altering genetic regulatory networks found in biological cells, is accomplished by reassembling or modifying predetermined DNA segments into functional genes. These genes are then connected into cause-and-effect networks by mechanisms of mutual activation and repression that control the expression of these genes into proteins [76]. MC Components: The biochemical processes and synthetic biology components that could be used to engineer MC systems, much like amplifiers, encoders, filters, and antennas are being designed for electrical communication systems, are currently not thoroughly designed, analysed, and characterised computationally and experimentally in the field of MC theory [77].

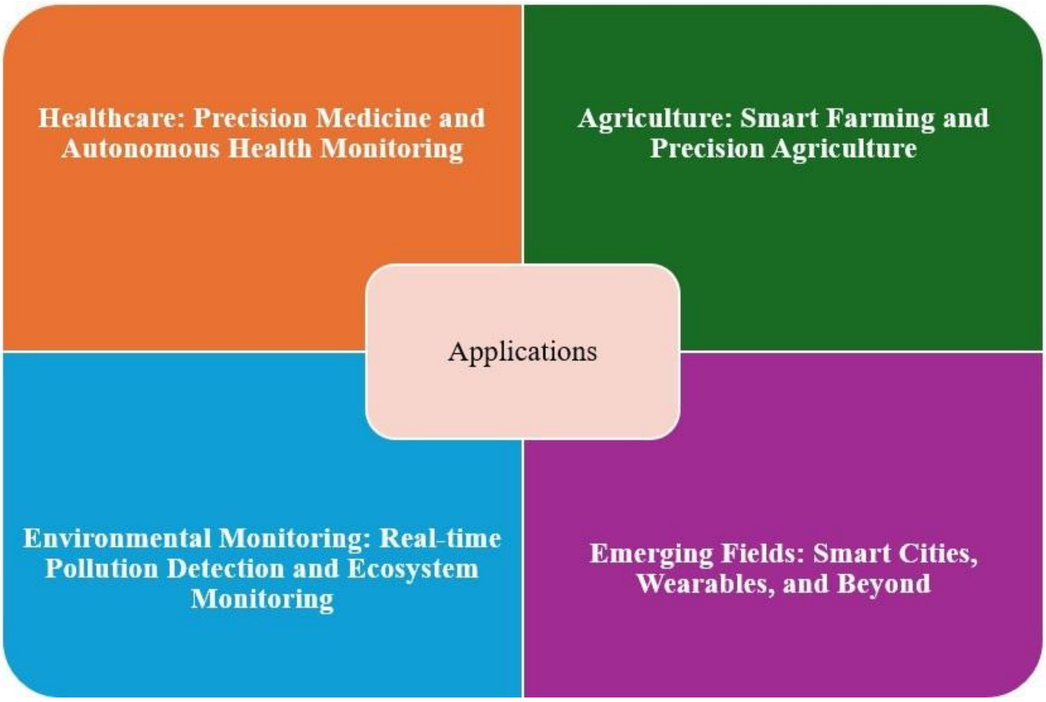

Figure 13: Applications of IoBNT[53]

Engineered Cell Communication: One of the most recent developments in synthetic biology is the engineering of cell communications based on the previously described programming of DNA biological circuits. This involves programming cells to act as transmitters and/or receivers of molecules that carry information [76]. By modelling and characterising the smallest subset of genetic circuit elements required to realise a basic MC link and establishing

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broad recommendations to optimise these systems, attempts have been made to create engineered cell communications [75].

Interfaces With Electronics: Technologies that connect the MC domain to traditional electronics are essential for the monitoring, data collection/analysis, and management of engineered MC systems for human health. In light of this, research is being done to harness biochemical processes where electron propagation is associated with the elements at the core of MC theory, as opposed to the common usage of fluorescent markers in synthetic biology [77].Redox (reduction–oxidation) processes, in particular, are chemical reactions in which electrons are transferred between molecules one that is reduced and the other that is oxidised. edox-based proof-of-concept device facilitates quick and dependable information transfer between the biological (molecular) and electrical domain [77].

MC Devices: Engineered Microbes:Since they are single-celled organisms, bacteria use MC to help their population endure and adapt to changes in their environment. Because it is simple to design new functions through the alteration and insertion of the genetic code, synthetic biologists use them frequently. Several methods that link synthetic biology to MC between cells have produced a variety of applications in the field of theoretical MC [78].Since they are singlecelled organisms, bacteria use MC to help their population endure and adapt to changes in their environment. Because it is simple to design new functions through the alteration and insertion of the genetic code, synthetic biologists use them frequently [79].

Engineered Human Cells:Human cells are frequently engineered using human pluripotent cells, which are candidate cells that can be trained into any type of cell in the body [77]. By using gene knockouts, which enable the inhibition of certain gene functions, these cells can be engineered. Programming human pluripotent cells to develop into tissue cells and produce immunological T-cells are only two of the many uses that have arisen from this technique. Although the creation of MC systems from human pluripotent cells has not been studied, it can undoubtedly offer fresh resources for human cell engineering [78].

MC Networks: The ability to network the many created systems and, eventually, network to the cyber-world via the Internet is crucial, even though engineering the cells can result in controlled MC performing unique roles [78]. This includes a bio cyber interface that converts molecular signals into electrical signals that can communicate with an external device, as well as artificial cells that are made to serve as gateways for translating between various molecule kinds [79]. Several methods can be employed to create artificial cell gateways that can translate molecules between various MC systems. These can be constructed from the metabolic engineering of cellular pathways to allow cells to produce a variety of chemical enzymes. Synthetic biology has made it possible for cells to produce a wide range of engineered molecules [79].

VII. APPLICATIONS OF IOBNT: REVOLUTIONIZING DIVERSE SECTORS

A. Healthcare: Precision Medicine and Autonomous Health Monitoring

IoBNT offers significant promise in healthcare, where the convergence of bio-nano technologies and IoT can enable personalized medicine, continuous health monitoring, and precision treatment. Some key applications include: Real-time Health Monitoring: Bio-nano sensors embedded in the human body could continuously monitor biomarkers, such as glucose, cholesterol, or hormone levels, allowing for early detection of diseases. For example, nano-sensors could detect glucose levels for patients with diabetes, providing real-time feedback to healthcare providers and enabling automated insulin delivery through nano-actuators [80]. Nano-Drug Delivery: Using nano-robots or nano-carriers, IoBNT could facilitate targeted drug delivery, where therapeutics are directly delivered to the affected tissues or organs in response to real-time biological data. This approach would enhance treatment efficacy while minimizing side effects, particularly for diseases like cancer, where precise targeting is crucial [79]. Biosensors for Disease Diagnosis: Nano-biosensors could revolutionize early disease detection, enabling the identification of diseases at molecular levels, such

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as the presence of cancer biomarkers or pathogens in the bloodstream. Early diagnosis allows for timely interventions and prevention strategies, potentially saving lives [79]. Wearable Bio-Nano Devices: IoBNT systems can integrate with wearable health devices that continuously monitor vital signs such as heart rate, blood pressure, and oxygen levels. These devices can transmit data to healthcare providers in real time, enabling remote patient monitoring and telemedicine solutions [80]. Technological Impact: These innovations will lead to smarter healthcare systems, reducing the need for frequent hospital visits, improving diagnosis accuracy, and enabling better disease management. The ability to remotely monitor and treat patients opens up opportunities for personalized healthcare [80]. Societal Impact: IoBNT's role in healthcare could significantly reduce healthcare costs, especially for chronic diseases, by providing continuous, low-cost monitoring and preventive care. It would also improve access to healthcare for people in remote or underserved areas [81].

B. Environmental Monitoring: Real-time Pollution Detection and Ecosystem Monitoring

In environmental monitoring, IoBNT can be applied to track and address various ecological issues, such as pollution, biodiversity, and climate change. Some critical applications include: Pollution Monitoring: Bio-nano sensors could be deployed in air, water, and soil to detect toxic substances or pollutants at the nanoscale [84]. For example, nano-sensors embedded in water bodies could monitor heavy metals, pesticides, or microplastics, transmitting data in real time to alert environmental agencies about potential risks [83]. Wildlife Tracking and Ecosystem Health: IoBNT can be utilized to monitor wildlife populations and track ecosystem health through bio-nano devices that collect data on animal health, migration patterns, or habitat conditions. These systems could assist in conservation efforts, enabling better management of endangered species or ecosystems [82]. Climate Change Monitoring: With IoBNT, environmental data such as temperature, humidity, and air quality could be continuously monitored at localized levels, providing real-time insights into the impact of climate change on various ecosystems. This could improve climate resilience by enabling better preparation and response to extreme weather events [80]. Technological Impact: IoBNT will revolutionize environmental monitoring by providing real-time, high-precision data on pollutants, climate conditions, and ecosystem health, offering a more proactive approach to environmental protection [83]. Societal Impact: The ability to continuously monitor environmental conditions will facilitate faster response times to environmental crises, such as chemical spills or natural disasters. It could also foster more sustainable agricultural practices and improve public health by identifying and mitigating pollution sources [82].

C. Agriculture: Smart Farming and Precision Agriculture

In agriculture, IoBNT has the potential to optimize resource usage, increase crop yields, and promote sustainability [84]. Some impactful applications include: Soil and Crop Monitoring: IoBNT systems can deploy bio-nano sensors in the soil to continuously monitor moisture levels, nutrient content, and pH levels, allowing farmers to adjust irrigation, fertilization, and pest control strategies in real time. This could lead to more efficient use of resources and reduced waste in farming practices [82]. Precision Pest Control: Bio-nano sensors could also be used to detect early signs of pest infestations or crop diseases, enabling targeted interventions that minimize pesticide use and reduce environmental impact [83]. Automated Harvesting and Crop Management: With the help of nano-actuators and robotic systems, IoBNT could enable automated harvesting, monitoring, and management of crops, reducing labor costs and improving the efficiency of agricultural practices [84]. Technological Impact: IoBNT could help optimize agricultural productivity by providing real-time data on crop health and environmental conditions. This would enable farmers to make data-driven decisions, enhancing crop yields and sustainability while reducing costs [82]. Societal Impact: With smarter farming systems, IoBNT could contribute to global food security, reduce the environmental footprint of agriculture, and promote sustainable farming practices, particularly in areas experiencing water scarcity or soil degradation [83].

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D. Emerging Fields: Smart Cities, Wearables, and Beyond

Beyond traditional sectors, IoBNT is also poised to play a transformative role in emerging fields, including smart cities, wearable technologies, and autonomous systems. Smart Cities: IoBNT could enable smart infrastructure by integrating bio-nano devices into urban environments for continuous monitoring of air quality, energy use, and traffic patterns. Real-time data from these devices could be used to optimize urban planning, reduce energy consumption, and enhance public health [84]. Wearable Devices: The integration of bio-nano devices in wearable electronics could enable seamless health monitoring on a global scale. These wearables could track everything from biological signals to environmental conditions, providing a wealth of real-time data to consumers and healthcare providers alike [82]. Autonomous Systems: IoBNT could drive the development of autonomous bio-robots capable of performing complex tasks, such as navigating through the human body for medical diagnostics or delivering drugs in response to molecular signals [83]. Technological Impact: The integration of bio-nano devices into these emerging fields will create smarter, more efficient, and data-driven systems, where decisions can be made autonomously and in real time, based on insights gained from continuous, distributed sensing [84]. Societal Impact: These advancements will make everyday life more convenient, healthier, and sustainable, creating smarter cities that are better equipped to manage resources and improve the quality of life for citizens. They will also democratize access to advanced technologies such as real-time health monitoring and personalized medical treatments [84].

VIII. FUTURE CHALLENGES

The future of IoBNT-based molecular communication faces several critical challenges that must be addressed for its successful implementation. Scalability remains a significant hurdle, as molecular networks struggle with limited communication range, high latency, and interference in dense environments. Ensuring reliable and robust communication is difficult due to the variability of biological environments, where factors like pH, temperature, and molecular noise can disrupt signal propagation. Energy efficiency is another challenge, as powering nanoscale devices within living organisms requires innovative solutions like energy harvesting from biological sources. Biocompatibility is essential to prevent immune responses or cytotoxic effects, while maintaining stable integration with biological tissues. Additionally, molecular communication is constrained by low data rates and limited bandwidth, restricting its capacity for real-time applications. Security and privacy are also critical concerns, as molecular networks are vulnerable to eavesdropping and signal tampering, with limited encryption options at the nanoscale. The lack of standardization in protocols and interfaces further complicates the integration of IoBNT with existing IoT systems. Ethical and regulatory challenges, including privacy, safety, and potential misuse, must be addressed to ensure responsible deployment. Finally, advancements in synthetic biology and nanoscale manufacturing are necessary to develop reliable, scalable, and cost-effective bio-nano devices capable of operating in complex biological environments.

IX. CONCLUSION

The Internet of Nano Things aims to expand the boundaries of the Internet of Things (IoT) concept to include nanotechnology-enabled nanoscale devices that are easily hidden, implanted, and dispersed throughout the environment. The IoT is facilitating the ubiquitous connectivity of real-world physical elements to the Internet and to each other. In order to create things that are based on the control, reuse, modification, and reengineering of biological cells, we presented the further idea of the Internet of Bio-Nano Things in this article. This concept combines synthetic biology and nanotechnology. Using paradigm-shifting approaches for the domains of network engineering and communication, this essay described the difficulties that will be encountered in order to realise these Things and, more crucially, to facilitate their networking and communication. We think that although though IoBNT research is still in its early stages, it will produce a revolutionary technology for tomorrow's civilisation. A historical review from 2005 to 2024 illustrates IoBNT's journey from theoretical underpinnings in molecular communication to a rapidly evolving field with real-world applications. IoBNT continues to benefit from advancements in nanotechnology, synthetic biology, and AI, positioning it for transformative impacts in healthcare, environmental monitoring, and beyond.

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