Introduction

The Nobel Committee's Report of 2016's Nobel Prize in chemistry[3] ends, "we are at the dawn of a new industrial revolution of the twenty-first century, and the future will show how molecular machinery can become an integral part of our lives. The advances made have also led to the first steps towards creating truly programmable machines, and it can be envisaged that molecular robotics will be one of the next major scientific areas."

There have been many advancements in the area of Nanotechnology and Biotechnology since then, leading to improvements in its Internet of Things (IOT) applications, New Ideas shift the horizons of the technology everyday.

One of the major reasons for quick progress and study in this field is the pre-existing natural framework of Bio-NanoThings (BNTs), Which offers a solid foundation for modelling artificial Nanonetworks composed of Nanomachines. Nanomachines are independently operating fully-featured devices theoretically capable of all tasks their Macro-Scale counterparts are, such as data-storage, sensing and actuation. However, at such a small scale, individual devices(Nodes) provide us with scarce capabilities, leading to the establishment of Nanonetworks.[2] Several nanonetworks are naturally occurring all of which have their own complexity and applications in Internet of Bio-NanoThings (IoBNT), and are reviewed in this paper. The ones proven to be useful for IoBNT applications are:

- Mammalian Nervous systems [1][4]
- Bacterial Networks [7][8][11][13][14]
- Plant and Fungal Networks

For the creation of any network, as with a Nanonetwork, a few requirements must be met, Namely: Communication between Individual Nodes, and Storage of Energy. In a biological environment, we must also make sure of compatibility with pre-existing biological systems. To fulfill the technical challenges some of the solutions proposed are:

1. **Communication and Interfacing Methods**

Developing better communication methods is one of the foremost technical challenges to be overcome, as conventional communication methods like Electromagnetic Transmission cannot be used at the Nano-Scale due to the size and energy constraints. The following technologies have emerged as the leading techniques for communication in nanonetworks.

- Molecular communication: it is already used by Natural BNT in an incredibly Energy Efficient Manner[5][9][15]
- High Frequency EM based methods: While conventional EM methods are not possible at the Nano-Scale, Graphene-Based antennas allow us to use the terahertz bands, proving promising for the high operating frequencies of BNTs
- Acoustic Communication: Ultrasonic Communication has been considered because of its advantages over its RF counterparts inside a fluidic environment like the human body.
- Optical based methods: Förster Resonance Energy Transfer (FRET) is non-radiative, high-rate energy transfer between fluorescent molecules, which promises a High rate of energy transfer in the order of Mbps.
- There are various other techniques as in Redox, Optogenetics and Fluorescence based techniques.

2. **Energy Issues**

Efficient supply, storage, and usage of energy is another necessary challenge to overcome for the realization of IoBNT as a practical technology. While living cells have evolved over Billions of years to use the biochemical energy in the most efficient way possible, artificial systems are missing a metabolism system for their energy management. Thus, following methods are discussed as a solution:

1. Energy Harvesting:
   - Harvesting from various Intrabody vibrations,
   - Ambient RF EM waves,
   - Active Wireless Power Transfer
2. Energy Storage
   - Nano-Scale Lithium Batteries

- Micro-super capacitors
- Conducting Polymers like PE-DOT/PSS and various polymer heterostructures.[6]

3. **Biocompatibility** concerns with the materials used in the physical architecture of BNTs, the energy solutions as well as the interfacing process. However it remains an unsolved issue as there is no standardised procedure for testing Biocompatibility yet.

We provide a comprehensive review of the these problems in a later section, along with a brief overview of the previously existing framework of BNTs. However, along with the technical challenges there are many social challenges to overcome which are also discussed.

Communication

The goal of a communication system is to transfer information across space and time. To achieve this, a signal needs to be generated by a transmitter in accordance to the information that is intended to be transferred to a receiver. This signal then propagates to a receiver, where the intended information is decoded from the received signal. Therefore, any communication system can be broken down into three major components. The Transmitter, the receiver, and the channel. On December 29, 1959, Richard Feynman gave a lecture at American Physical Society meeting in Caltech titled, "There's Plenty of Room at the Bottom" [16]; In which he asked, How Much can we shrink a communication system? While we haven't found the lower limit for it yet, we do have technologies which can work at the nano scale. The reason why we even need new methods for communication is that the conventional methods, i.e. Electromagnetic(EM) Communication cannot be used due to a large amount of noise being generated at the scale, a large energy requirement not suitable for the nano devices, and the miniaturized antennas being highly inefficient and hard to design. [17][18] The Three methods discussed in this papers are used in contemporary nanotech.

1. **Molecular Communication Framework**:

Molecular Communication is a Biomimetic technology, inspired from Communication in bacteria using chemical signals at Nano and Micro-scale and in the social-insect populations at Macro-Scales using Pheromones; Since it a very new technology, it does not benefit from the preexisting theory of communication. However, it is very bio-compatible for our applications, It also has better Energy Efficiency and Very Low Heat Dissipation in comparison to EM based communication methods. MC is also employed in Humans in neurotransmitters, they use free diffusion (Passive Transport) to communicate over short range. Inside cells, Motor Proteins Actively Transport cargo over mid-range.

In MC, small particles called information particles act as chemical signals conveying the information. The Channel for communication is any environment in which the particles can freely propagate. Information particles are typically a few nanometers to a few micrometers in size. These could be biological compounds, such as proteins, or synthetic compounds, such as gold nano particles or any mixture of the two. The structure and size of these information particles affects how they propagate in the environment; For Example, Increasing the particle size may change the diffusion coefficient, which changes the diffusion process. Along with that, to make the MC more reliable Information particles need to be chemically robust against the environmental noise. The particles may also degrade over time. Along with the channel for communication, There needs to be a transmitter and a receiver. As for the transmitter- it should contain the following components

- Power Source - It may contain the power source, or harvest power from the environment
- Processing Unit - It may operate chemically, electrically, or through other means.
- Information Particle Generator/Container
- Information Particle release mechanism

After the Information Particles are generated, there needs to be some mechanism to get the particles to the receiver. This can be diffusion based, flow based, or an engineered solution using Molecular motors. some of these are discussed in the following section.

1. **Free Diffusion:** Also known as Brownian motion, refers to the random motion of a particle as it collides with other molecules in its vicinity. Through this random motion. The information particles can propagate from the transmitter to the receiver by utilizing the thermal energy of the channel. This can be accurately modeled through a Monte-Carlo simulation [20].

2. **Diffusion with First Hitting:** Since MC creates a lot of noise in the channel environment, a lot of Information Particles may hit the receiver at the same time, causing a sort of race-condition. To prevent this, in Nature, most receptors remove the information molecules from the environment through various means [21]. Another way is to make sure that each signal contributes to the receiver only once.
3. **Flow Assisted Propagation:** While Diffusion is great, it has the disadvantage of being incredibly slow. One of the ways to increase it's speed is to introduce flow into the environment. The most effective way would be, from the transmitter to the receiver. An Example of all three combined in the human body is when certain organs secrete hormones that propagate using the blood-flow and diffuse into other, more distant parts of the body.
4. **Molecular Motors:** Another way of Propagation is to transport the Information Particles actively using molecular motors, over microtubules. They're Naturally Occurring in cytoskeletons found throughout the cytoplasm, involved in maintaining the structure of the cell and providing platforms for a number of intracellular processes.

Propagation Scheme	**Method**	**Information Carrier**	**Energy Requirement**
Free Diffusion	Diffusion	Molecules	0
Diffusion with First Hitting	Diffusion	Molecules	0
Flow Assisted Diffusion	Diffusion + Flow	Molecules	for Flow
Motor Protein over MT	Motor Protein	Vesicle	1 ATP for 8 nm
MT over Motor Protein	Motor Protein	Vesicle	1 ATP for 8 nm
Bacteria Assisted	Bacteria Motility	Bacteria	for Bacteria Motility
Gap Junction	Diffusion + Gates	Molecule	for Triggering Gates
Neurochemical	Diffusion + Enzyme	Molecule	0

Table 1: A Comparision of Various Methods of Propagation[15]