Prognosis of Infection Spread Deploying Internet of Bio-NanoThings

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***Abstract*—Internet of Things(IoT) is an embryonic field having interdisciplinary linkages; one such terrain is Bio-medical Technology. Early detection of infection is a predominant priority for better care and treatment of patients. In the current epitome system application of the Internet of Bio-Nano Things(IoBNT), the communication between the Quorum Sensing Molecule is perceived to deduce the infection level. The nano device implanted in body sends signal to the station outside the body which can reach to health service providers for further supervising the treatment with the help of backbone networks like the internet or cellular communication. The work formulates the functioning of the Bio-Nano Things(BNTs) and the issue of localization of anomaly for a reliable, swift and responsive infection detection system with an overall effective system architecture. This paper uses COMSOL simulation to show that the detection could be done between [1000,1500] seconds for the case of multiple infection outbreaks.**

***Index Terms*—Bio-Nano Sensors, Quorum Sensing, Anchor Nodes, Molecular Communication, Localization, COMSOL**

I. Introduction

A. Background

The present state-of-art diagnostics of disease depends mostly on reactive methods of diagnosis, where once the symptoms arise, the diagnosis is carried out and then precautionary measures are taken. The accurate treatment is limited by the imprecise nature of external devices and elongation in the diagnosis process. Hence, there arises the need of automation in the field of diagnostics. By leveraging contemporary approach combining interdisciplinary techniques like Internet of Things(IoT), Bio-medical Technology and Nano Technology to forge the Internet of Bio-Nano Things(IoBNT), the face of future curative can be revolutionized. This novel technology has gained popularity in past few years; first coined as a paradigm-shifting concept for communication and network engineering in [1], that deals with networking among bio-chemical molecules and electrical domain through Bio-cyber interface [2] as shown in Fig. 1.

The IoBNT conceptualizes the network of nanoscale machines [3] that has the ability to sense even the minor change in different factors distinguishing itself from conventional technologies. The in-body mobile devices can be fabricated with

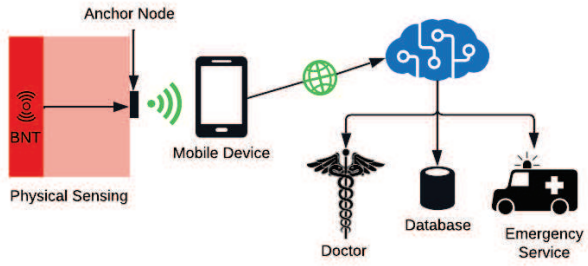


Fig. 1: Conventional Bio-cyber Interface with BNT, wearable hub and mobile device

the help of neoteric nano-materials called Bio-Nano Things. These motile devices implanted within the body, interprets the bio-chemical information and transmits the information to stations outside the body called anchor nodes; which are hooks for collecting information. Further information is passed onto the health care officials or emergency services, so the required steps for treatment can be taken care of and virulence of the infection spread can be decreased. Hence, the infection can be detected even before the symptoms arise; without even visiting the laboratory. The infection can be treated with appropriate therapy reducing the treatment timing and in turn the cost of healthcare and fatality among specific diseases. The framework not only focuses on the infection spread, in case of epidemic or pandemic it can also be useful to track the spread and time of quarantining infected for specific period; remotely accessing the in-body data of the infected noting at a peculiar time interval.

Molecular communication plays a very crucial role in such type of systems at infinitesimal level. Every infection bacterium communicates with others and within themselves. The communication takes place with the help of Quorum Sensing, based on gene regulation for detecting bacterial population and density within the area. Eventually they adapt to the environment making them resilient to antibiotics, leaving the immune system of the host weak and making it difficult for health care officials to treat them. Receptors decipher the bacteria produced Quorum Sensing Molecules(QSM) or auto-

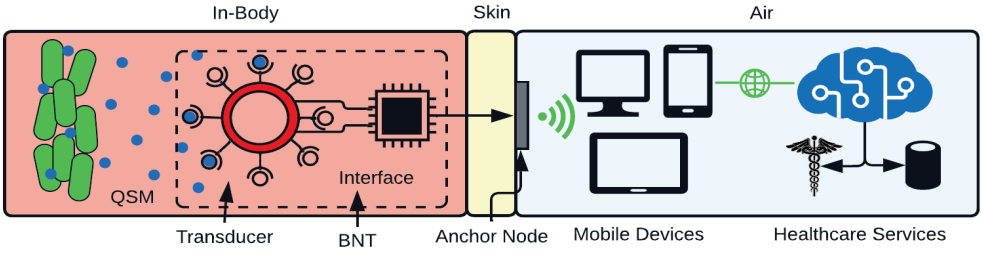


Fig. 2: Overview of Architecture

inducers for cell-to-cell communication, causing a shift in gene regulation. It can be said that,'Drug makers can now listen while bacteria talks'. With accurate treatment we can reduce the fatality rate almost five folds [4]. The infection can spread by any mean through air, water, laceration, or even by touch; we can not predict the location outbreak and its severity ourselves. There are chances of infection being spread to a certain region and causing fatal infection. Moreover, there is a probability of organ failure or permanent deformation or demise. The present detection technology is based on culture of microbial organisms from collected samples of patients using polymerase chain reaction(PCR). Hence, by utilizing Molecular Communication, we can detect premature infection spread and mitigate the disease. Further application could be advancement in the drug delivery channel [5]. There are two types of delivery; active and passive. Passive drug delivery requires human intervention and their decision to inject the drug. While in case of active drug delivery, the BNTs or the station discharges the drug into blood. Moreover, Quorum Quenching can be used to inhibit the bacterial communication by disrupting the production of auto-inducers and prevents Quorum Sensing. The following sub-section discusses the incentives for future progression.

B. Motivation

Early detection in the case of infection is necessary. In order to minimize detection time, by designing a realistic solution. Finding an optimal location for the receiver; as restricted by their number. The system should have high sensitivity and be optimal enough to detect small concentration changes. The detection time of infection, studied in laboratory with help of heavy machinery which takes around 1-2 hours [6] to detect RNA. By optimally configuring, we can significantly reduce detection time by continuously monitering physical parameters. Despite of studies of IoBNT paradigm, there are certain validation points that are yet to be identified. Hardship of bringing a multi-disciplinary expertise makes it a frightful task for researchers. Need for overall architecture for early detection arises for implementation of system in real life.

C. Contributions

Based on the above motivation, this work mainly focuses on decreasing the detection time for the multiple case of infection junction, and developing a simulation of infection spread so contributions of the work can be justified.

Firstly, an effective overall architecture is proposed. Present work focuses more on individual (in-body and on-body) communication channels, however this work incorporates both aspects. BNT performs vivo continuous monitoring of QSM, but we have to incorporate the scenario of multiple stations to transfer information and allow the station to communicate among themselves, so delay in transmission can be alleviated. Including the real-time case of multiple wound (infection nodes) could complicate the prediction of optimal location of anomaly and give better results due to large input concentration. The work optimizes the architecture in terms of infection detection time, studying an efficient and simple method for on-body communication.

Secondly, a simulation framework is considered for understanding the above results and getting a better perspective of the problem. We have generated multiple transmission sites, recorded the change in concentration with respect to time, shown the simulation of QSM through skin. We have tried to demonstrate the considered architecture using substantial scalable values of the human body and using P. Aeruginosa, a Gram negative bacteria using COMSOL. The data generated from the simulation is presented in pictorial form for justifying the results proposed in the work.

II. Proposed Model

The system consists of four troupe parts; Bio-Nano Sensors for detection, Anchor Nodes for data processing, the end-to-end communication channel and Anomaly localization approach. Fig. 2 shows architecture of the system.

A. Bio-Nano Things

The cognizance of IoBNT starts with the concept of embedding nano-scale devices called Bio-nano Things within the body. The BNT within themselves is a large area of study; miniaturizing the mobile devices with effective interface, power management system and wireless data transfer with help of coil or antenna. For detecting the breach of infection in human tissues by pathogenic bacteria BNTs are used for sensing and communicating with anchor nodes. There are sensors monitoring different physical parameters as shown

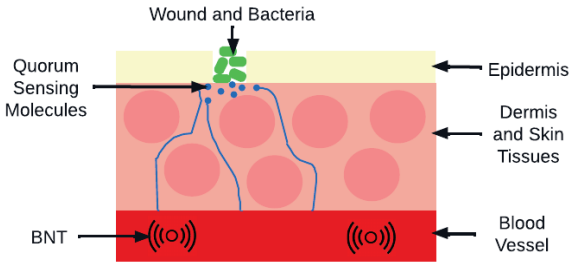


Fig. 3: Diffusion of QSM through tissue on skin level model

in Fig. 3, and noting position at time of detection [7] [8] [9] [10]. The architecture is simple, but the challenge is to make a compact structure with antenna; small enough that they can be transfused within the body. The advancements in Nano-Technology are useful for fabrication of nano things like graphene and its derivatives [11].

The device consists of mainly four parts: Bio-nano Sensor, Inertial Measurement Units, Sensor interface chip and a coil/antenna. Firstly, the receptors monitor the concentration of infection. The antigens get attached to the antibody of the transducer and a small amount of current is passed to the interface, E. coli bacteria; harmless to human can be used as transducers, producing molecular signals can be easily encountered by electro-chemical sensors giving high sensitivity and specificity. The marking of location of anomaly is done by Inertial Measurement Units (IMUs); further application in Localization. The transducers on receiving the auto-inducers pass current to the sensor interface having an Analog front end which is then converted into digital form with the help of analog-to-digital converter (ADC). The Specific Absorption Rate (SAR) ADCs are among the lowest power consuming architectures with amazingly low 0.88 pJ per conversion levels reported in [12]. Mostly the power is transmitted from hub outside via multi-coiled Wireless Power Transmission. The data transmission ID is carried out using impulse-radio based transmission, which eliminates the carrier signal to save power. They are allowed to flow in random motion at certain rate (10-20 cm/s in the arteries over 0.1 cm/s in the arterioles to $5\text{x}10^{-3}$ cm/s in the capillaries [13]) for favorable outcomes.

Considering the real-time growth of bacteria, it is difficult to study the stochastic behavior as the sensor also is a type of chemical transducer, so there are chances that it too replicates itself. Moreover, there is a bacterial noise present in the background as they interact with the environment and evolve themselves. Absorption of bacteria can affect the results and bio-distribution of drugs. To eliminate the errors due to false detection high specificity is incorporated, only the molecules specific to the interest can be considered. The main challenge behind designing BNT is making it power efficient, nano-scaled and reliable with a miniaturized coil or antenna bridging it with the wearable hub outside the body.

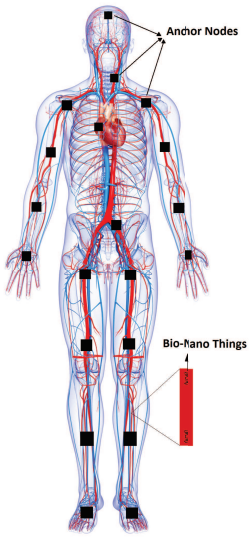


Fig. 4: Silhouette of the human Cardiovascular System, Bio-Nano Things floats in blood and nodes anchored to the skin

B. Anchor Nodes

Transferring data perceived to healthcare official is important, but the raw data have to be processed before passing to mobile device. The linkage in between is done by anchor nodes fit on the skin similar to insulin patch as shown in Fig. 4. Anchor Nodes are IoT devices interconnected with a base station via multi-hop communication as described in [14]. The anchor nodes are connected with other nodes and mobile devices outside the body with a standard wireless personal area network IEEE 802.11 or 802.15 [13]. The anchor node constantly emits THz signals which encapsulates the data and BNT reflects back to node. The anchor node maintains the data in the form of columns gathered from Bio-Nano Sensors, passed on to mobile device where it is managed and updated. Nodes integrate collected time stamp and location stamp from BNT for receiving data packets. For simulation of human cardiovascular system, [13] uses ns3 module BloodVoyagerS [15], to observe the time frame at which BNT move through the nodes.

C. Molecular Communication Channel

Molecular Communication is based on transmission of information molecules between biological cells, tissues and organisms. The molecular channel consists of three elementary processes; transmission, propagation and reception. As discussed in the previous section, the QS molecules are produced and propagated considering the case of dermal wound, the QSMs have to propagate through tissue to reach the blood vessels shown in Fig. 5. Tissue has interstitial fluid among the biological cells; that hinders the transmission making situation similar to diffusion of particles in porous medium with random motion. There are three basic properties of molecules; growth, production and propagation. The propagation of quorum sens-

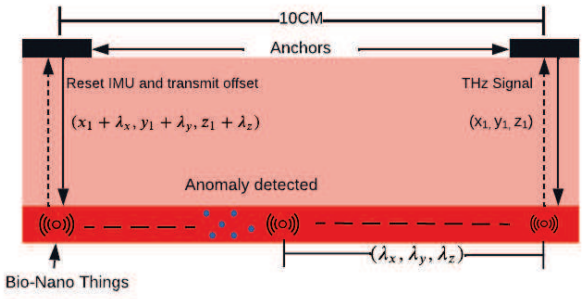


Fig. 5: Transmission of information from traversing BNT.

ing molecule concentration in tissues is described by mass transport equation in porous media as;

$$\frac{\partial C}{\partial t} = \frac{D}{\lambda^2} \cdot \nabla^2 C + \frac{Q}{\alpha} - \frac{f(C)}{\alpha} - v \cdot \nabla C \qquad (1)$$

where C is the concentration of the QSM, D is the diffusion coefficient, λ is the tortuosity, Q is mass of molecules passing given volume in unit amount of time, α is the volume fraction and v is velocity of interstitial fluid . The term f(C) represents the clearance, loss, and uptake [16] here $f(C) = 0$ as the loss is negligible.

This communication is complex and can later be studied with the Boolean modelling [17], to understand over-complicated biological anatomy and system view of virulence network to gain insights for pathogenicity of bacteria. The bigger challenge here is localizing BNT by placing at a distance of few millimeters for optimal communication and reduced the detection time. As in [18], the BNTs are placed just above the blood vessel in dermis. While in [13], they are allowed to flow in blood. Placing it inside dermis would make the position fixed so to cover maximum region of the body we have to maximize the number of BNTs to be injected. Moreover, injecting it to a certain depth would also require more of expertise and human trust. Certain type of infection spread via blood or transmitted through transfusion; like Dengue, Hepatitis, COVID-19, etc. such spread cannot be efficiently diagnosed. We can minimize the number of BNT; but the challenge is to localize hubs outside the body. Work [15] shows simulation with 20 anchor nodes. Allowing them to flow makes it more compelling due to various factors, but it gives rise to noise due to the random movement of molecules in medium and other influential properties of the medium. Determining the position of hub is also important in identifying the anomaly position.

D. Localization Approach

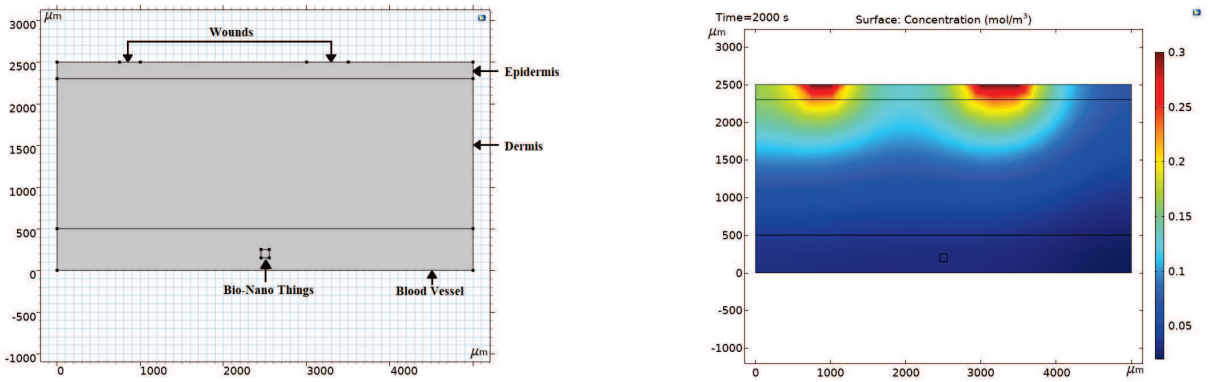
As discussed in the previous section, we need to stabilize anchor nodes. In order to reduce the infection detection time we have to use multi-nodal approach, as placing them at finite distance reduces the travelling time in between. There are IMUs placed in BNT to record the location of anomaly and reset to its initial state in order to eliminate accumulation errors. There are various possible types of errors in accelerometer and gyroscope measurement due to Gaussian noise and biases. Placing the anchor node on the region with a thin layer of skin in order to reduce the distance in turn reduces chances of error. The preeminent flaw by using a sensor is false reading so we need to cultivate position through sensors. The nodes are placed approximately 10 cm from each other; as shown in Fig. 4 such that BNT has less distance to travel between nodes. Consider the location of the first node be (x_1, y_1, z_1) as in Fig.5 and location marked by BNT is $(\widehat{x_1}, \widehat{y_1}, \widehat{z_1})$. So, $\widehat{x_1} = x_1 + \lambda_x$, $\widehat{y_1} = y_1 + \lambda_y$, and $\widehat{z_1} = z_1 + \lambda_z$. Here, ($\lambda_x$, λ_y, λ_z) is distance traversed noted by accelerator as it considers g(gravitational acceleration) with time and non-uniform velocity. So, distance the λ can be calculated simply by the kinematics equation;

$$\lambda = v_0.t + \frac{1}{2}at^2 \qquad (2)$$

Here, v_0 is the velocity of interstitial fluid that is considered discontinuous, t is time passed and a is acceleration calculated by accelerometer. There are also uniformly distributed errors determined by backscattering communication. The expected outcome given by BNT for location of anomaly is $(\widehat{x_1}, \widehat{y_1}, \widehat{z_1})$, which includes all the above mentioned errors. Whenever anomaly is encountered, transducers sends current by induction to interface. It triggers the IMU to mark the location and pass it in form of packets; each data packet of BNT possess unique ID and location readings which are then reset to initial state. In case of Radio Frequency Identification (RFID) some Radio Frequencies are not suitable for in-body communication. So, in recent times the Tera Hertz (THz) band has gained attention and it is yet un-utilized for Body Centric Network purposes. The main idea is to create energy efficient and light weight technique to reduce power consumption [19]. The transmission channel is also in the range of a few milimeters(2.5mm), but there can be lots of disturbance due to absorption of water molecules, causing path loss and noise factor [20]. System also suffers from scattering loss, Backscattered power decreases due to forward and backward link; channel capacity significantly decreases as shown in [13].

III. Simulation and Results

The section shows the outcome of the work and helps visualize the scenario with the help of Pseudomonas aeruginosa; a gram negative bacteria with a large repertoire of virulence factors. COMSOL, the tool used in this work, is the multiphysics simulator capable of both simulating the growth of the bacteria and the propagation of QSM in the given simulation geometry.



(a) Domain for Simulation

(b) Concentration of QSM at t=2000 seconds

Fig. 6: COMSOL Simulation Framework

TABLE I: Simulation Parameters

Parameter	Value	Unit
Diffusion Coefficient(D_f)	4.3x10^{-11}	m^2/s
Carrying Capacity(K)	3x10^9	cells/ml^{-1}
Bacterial Growth Rate(r)	0.6	h^{-1}
Production Rate(k)	74000	h^{-1}
Volume Fraction(α)	0.25	1
Degradation Rate(β)	600	h^{-1}
Cell Density(ρ)	1010	kg/m^3

A. Simulation Analysis

COMSOL domain is developed, considering the skin layers; epidermis is 200 μm, dermis is 1800 μm and blood vessel is 500 μm summing total separation of 2500 μm. The BNT is placed in the blood vessel and wound represents the transmission site. As tissue contains interstitial spaces hence physics used is Transport Diluted Species in 2D that is modelled with Darcy's Law depicting the flow through porous medium and propagation through (1). Effective Diffusion coefficient is shown as;

$$D_e = \frac{\epsilon_p}{\tau_f} D_f \tag{3}$$

Here, $\tau_f = \epsilon_p^{-1/2}$ as per Bruggeman Model for Effective medium approximations in porous medium, D_e is effective Diffusion Coefficient, D_f is Diffusion Coefficient of fluid and ϵ_p is porosity. The parameters considered for the simulation are shown in Table 1;

The initial concentration entering is considered to be 3x10^{-1} mol/m^3 which gradually reaches to the BNT. The BNT moves with blood flow; the effect of blood flow is neglected as our focus is concentration of QSM. As shown in Fig. 6(a) there are three main domains; wounds, BNT and skin layers. The BNT here is fixed at (2450,150)μm and wounds at (750,2500)μm and (3000,2500)μm on epidermis. No flux condition has been considered, so there is negligible loss of molecules during diffusion. The initial concentration of molecules in body i.e.

$$\frac{\partial C}{\partial t} = 0, \ at \ t = 0 \ seconds \tag{4}$$

is considered. Fig. 6(b) shows the concentration plot of QSM entering the wound at time t=2000 seconds. With the increase in time, the concentration increases and spreads towards BNT. The plot helps us understand the porous diffusion within the tissue and impact of different parameters on it.

B. Detection Time

The key intention behind IoBNT is early detection of infection spread. By using the proposed approach we can reduce the detection time to significant rate. As in [13], in 80% of simulations carried out the BNT required 10 seconds window to reach one node to another; the worst case being 80 seconds in 20 anchor setup. So, for a complete round it takes close to 200 seconds and that is the time taken by QSM to reach BNT. If the infection is in blood the detection time is still less. The sensing of Bio-Nano Sensors takes place every 5-10 seconds, the sampling rate of 0.25 seconds are evidently achieveable [7] [9].

There are practical sensors having sensitivity upto 10^{-3}mol/m^3. Anything above that can be measured by BNT [21], so here the threshold is assumed to be 2x10^{-3} mol/m^3. Fig. 7 represents the change in concentration of QSM reaching BNT for varying value of porosity of the tissue, the one with higher porosity corresponds to more pores resulting in swift diffusion of molecules anticipating higher concentration. Now, considering the location of BNT to be static at $\lambda = 5cm$ anomaly can occur anywhere between $\lambda = 1cm$ to $\lambda = 10cm$; $\lambda = 1cm$ being anomaly has occurred at the location that BNT has already traversed, $\lambda = 5cm$ is location exactly above BNT and $\lambda = 10cm$ is location BNT will traverse after sometime. Fig. 8 shows concentration plot for different values of λ. It is observed that threshold can be sensed between [1000,1500] sec. for almost all scenarios except one, but in that case the BNT will be traversing through location after some interval of time; in case of [18] it was [6000,7000] sec. while in case of laboratory it stretches up to 16-24 hours attaining better detection time.

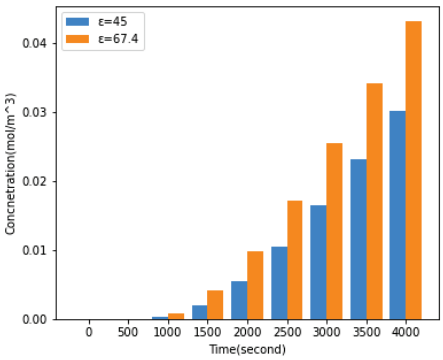


Fig. 7: Variation in concentration with porosity (ϵ_p)

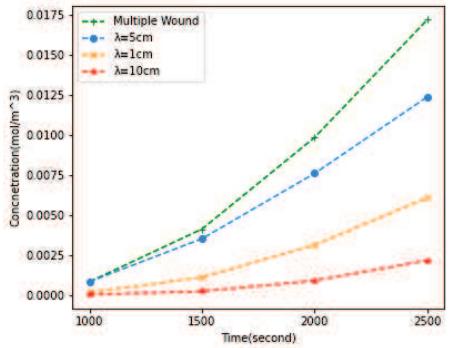


Fig. 8: Variation in Concentration with the occurrence of anomaly.

IV. Conclusion and Future Works

For eavesdropping on bacterial communication, this work has proposed an approach that combines the development of BNT, localization and communication to give optimal output. IoBNT aims to predict the infection spread even before the ailment emerges. The approach carries forwards the discussion on communication outside the body and determines the position of anomaly within body. The explanation of the proposed architecture, if put into execution could be a break through in the field of Bio-medical Technology, developing the system to depict human behavior of detection of disease. The scope of this work can be expanded to the use of multiple BNTs and predicting multiple breaches simultaneously. More emphasis can be laid on THz communication and interface the BNT for detecting other types of diseases autonomously. The interdisciplinary aspect of the IoBNT shows spectacular potential for human health and better disease prediction.

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