An Intra-body Molecular Communication Networks Framework for Continuous Health Monitoring and Diagnosis

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***Abstract*— Intra-body communication networks are designed to interconnect nano- or micro-sized sensors located inside the body for health monitoring and drug delivery. The most promising solutions are made of implanted nanosensors to timely monitor the body for the presence of specific diseases and pronounce a diagnosis without the intervention of a physician. In this manner, several deadly health conditions such as heart attacks are avoided through the early in vivo detection of their biomarkers. In reality, nanosensors are challenged by the individual specificities, molecular noise, limited durability, and low energy resources. In this paper, a framework is proposed for estimating and detecting diseases and localizing the nanosensors. This framework is based on molecular communication, a novel communication paradigm where information is conveyed through molecules. Through the case study of the shedding of endothelial cells as an early biomarker for heart attack, the intra-body molecular communication networks framework is shown to resolve major issues with in vivo nanosensors and lay the foundations of low-complexity biomedical signal processing algorithms for continuous disease monitoring and diagnosis.**

I. Introduction

The vast majority of successful devices that report for vital signs are placed outside the body, and sense for mechanical (e. g. blood pressure) and electrical signals (e.g. electroencephalogram). The recent advances in nanotechnology have recently allowed the design of micro- and nano-scale implants that sense for specific molecules in vivo [11][12]. These implanted biochemical sensors have not been designed yet as elements of a large network due to the nature of the signals they process. Communication techniques are needed to enable the coordinated sensing and actuation of biochemical implants, extract information about deep tissues and cells, and export it through a gateway to the Internet.

The new generation of medicine is characterized by personalized and continuous monitoring, sensor-generated data, and algorithm-based diagnoses transmitted to electronic devices. The networking abilities of the current real-time sensors such as for blood pressure, glucose, and brain waves remain limited to communication outside of the body, due to the high attenuation of radio-frequency (RF) signals within a few centimeters inside the body. Novel communication techniques exploit higher frequency bands and other components of RF signals [9] to extend the communication range of intra-body sensors and reduce the size of antennas. The energy resources of these devices are also limited by battery sizes and power transfer constraints.

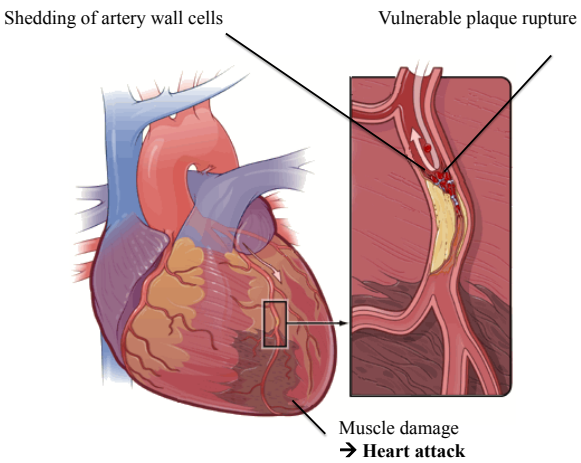

Fig. 1. Myocardial infarction caused by the rupture of plaque during coronary artery disease (atherosclerosis).

Molecular communication (MC) [2], a novel paradigm in communication theory where information is conveyed through molecules, is a promising alternative approach to enable intra-body communication networks. Inspired by the hormonal [6] and immune systems [4], MC enables the analytical modeling approach of how molecules propagate in the body and harnesse their potential to transfer information over long ranges (mm-m). MC has been proposed as an efficient and safe technique for enabling the Internet of Bio-Nano-Things (IoBNT) [1] to exchange information within the biochemical realm and interfacing it with the electrical realm of the Internet.

In this paper, a framework based on the MC paradigm is developed for estimating and detecting diseases, localizing the source of the disease, encoding and decoding genomic information, and predicting the hydrodynamic energy sources from the blood flow inspired by electrical engineering and communication concepts. Specifically, the shedding of endothelial cells in arteries as an early biomarker for a heart attack [7] is modeled through this framework (cf. Figure 1). The case study provides insights about the feasibility and

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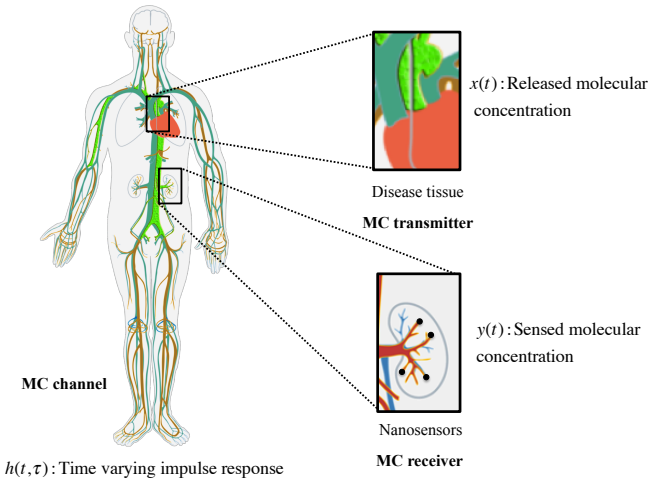


Fig. 2. Scheme of the intra-body molecular communication network for health monitoring and diagnosis.

limitations of the MC-based framework for intra-body communication.

The paper is organized as follows. In Section II, the system model of intra-body molecular communication is presented. In Section III, molecular signal processing techniques for biochemical sensor estimation and detection, and localization are presented. In Section IV, the case study for heart attack biomarkers is analyzed through numerical evaluations stemming from the developed framework. Section V concludes the paper.

II. System Model

As shown in Figure 2, the monitoring and diagnosis of a disease is abstracted through three elements of an MC system. Namely, the the MC transmitter for the *release process* of molecules, the MC channel for the *propagation process*, and the MC receiver for the *reception process*. In the following, we present the mathematical models for each of these elements.

A. Release Process

The release process abstracts the release of biomarker molecules from the location of the disease. For example, these molecules can be released due to the shedding of endothelial cells from the arterial wall in the case of the rupture of an atheroma [7]. In that case, the biomarker release process depends on the matrix structure of the arterial wall. The Weibull function is frequently used in the literature as a generic mathematical model for the molecular release concentration from a matrix structure [10]. The Weibull function will be used here as an MC transmitter signal, and allows to express the biomarker release concentration analytically as follows

$$x(t) = x_0 \left(1 - e^{-kt^b}\right) , \tag{1}$$

where x_0 is the released biomarker concentration at infinity ($t = +\infty$), b is the unitless biomarker power-law coefficient, which depends on the mass transport in the medium where the biomarker is released, and k is the biomarker release coefficient with a unit that depends on the unitless biomarker power-law coefficient $[s^{-b}]$, which depends on the structure of the arterial wall.

B. Propagation Process

The propagation process abstracts the transport of molecules from the location of the disease to the nanosensor. The transport model enables the prediction of the propagation of molecules in the blood vessels and tissues. The time-varying impulse response $h(t,\tau)$ is obtained by combining the time-varying impulse responses of each blood vessel located between the disease location to the nanosensor location, as follows

$$h_V(t,\tau) = h_1(t,\tau) * \dots h_i(t,\tau) \dots * h_L(t,\tau) , \tag{2}$$

where $*$ is the notation for the operation of cascading time-varying impulse responses as presented in [6], $h_i(t,\tau)$ is the time-varying impulse response of the i-th blood vessel, and L is the number of blood vessels located between the disease location and the nanosensor location.

The time-varying impulse response $h_i(t,\tau)$ for each blood vessel is expressed based on the generalized Taylor dispersion equation and can account for complex interactions such as absorption and adherence as follows

$$h_i(t,\tau) = \frac{1}{\sqrt{2\pi\sigma_i^2(t,\tau)}} \exp\left(-\frac{(l - m_i(t,\tau))^2}{2\sigma_i^2(t,\tau)}\right) , \tag{3}$$

where:

- The mean biomolecule velocity $m_i(t,\tau)$ is a function of the average blood velocity as follows:

$$m_i(t,\tau) = \int_\tau^t u_i(t')\, dt' , \tag{4}$$

  where $u_i(t)$ is the average blood velocity in a blood vessel as a function of time, where t and t' are time variables.
- The variance of the biomolecule is a function of the effective diffusivity as follows

$$\sigma_i^2(t,\tau) = 2\int_\tau^t D_i(t')\, dt' , \tag{5}$$

where $D_i(t)$ is the time-varying effective diffusivity of a biomolecule. $h_i(t,\tau)$ depends on the properties of the biomolecules, the dimensions of the cardiovascular network, and the blood flow.

C. Reception Process

The reception process abstracts the detection of biomolecules by the nanosensors. This process is stochastic in nature and depends on the detection capabilities of the sensors characterized by a sensing probability p_r and a background noise η. Stemming from the derivations in [5],

the number of biomarkers detected by the nanosensors is an inhomogeneous Poisson process as follows

$$y(t) \sim Pois\left(\int_{-\infty}^{+\infty} h(t,\tau)p_r x(\tau)d\tau + p_r\eta\right), \quad (6)$$

where $x(t)$ is the MC transmitter signal from the release process expressed in (1) and the the MC channel from the propagation process expressed in (2).

III. Molecular signal processing

In this section, a signal processing method is presented to estimate information about the disease (location, intensity, release process, etc.) using the signals experienced by the nanosensor, assuming some knowledge about the release, the propagation, and the reception processes presented in the previous section. Based on (6), the signal received by the nanosensors is an inhomogeneous Poisson process. In order to estimate system parameters, the likelihood ratio test is used. This test enables to find the set of system parameters that is more likely to provide the observed sensor data. Therefore, the maximum likelihood ratio of the received signal $y(t)$ for observation times $t \in \{t_1, \ldots, t_N\}$ during a total observation time of ΔT is expressed as follows

$$\Theta\left(y(t); t \in \{t_1, \ldots, t_N\}\right) = e^{\theta}\frac{\theta^N}{N!}\prod_{n=1}^{N}\frac{y(t_n)}{\theta}, \quad (7)$$

where the parameter θ is equal to

$$\theta = e^{-\int_0^{\Delta T} y(t)dt}. \quad (8)$$

Therefore, the log-likelihood ratio to be maximized is expressed as

$$\begin{aligned}\Lambda(y(t)) = &-\int_0^{\Delta T}\left(\int_{-\infty}^{+\infty} h(t,\tau)p_r x(\tau)d\tau + p_r\eta\right)dt \\ &+\sum_{n=1}^{N}\log\left(\int_{-\infty}^{+\infty} h(t,\tau)p_r x(\tau)d\tau + p_r\eta\right).\end{aligned} \quad (9)$$

Therefore the timing and pattern of the biomarker release can be estimated through a joint optimization procedure as follows

$$\begin{aligned}&(t_0^0, x_0^*, b_0^*) = \\ &\arg\max_{t_0, x_0, b_0 \geq 0}\Lambda\left(\int_{-\infty}^{+\infty} h(t,\tau)x_0\left(1 - e^{-k(\tau - t_0)^b}\right)d\tau\right).\end{aligned} \quad (10)$$

Other parameters of the systems such as the distance between the source of the disease and the nanosensors, the blood flow conditions, and the biomarkers kinetic processes can be estimated using a similar procedure.

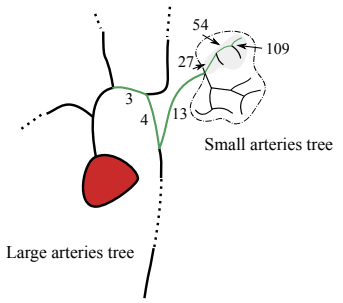
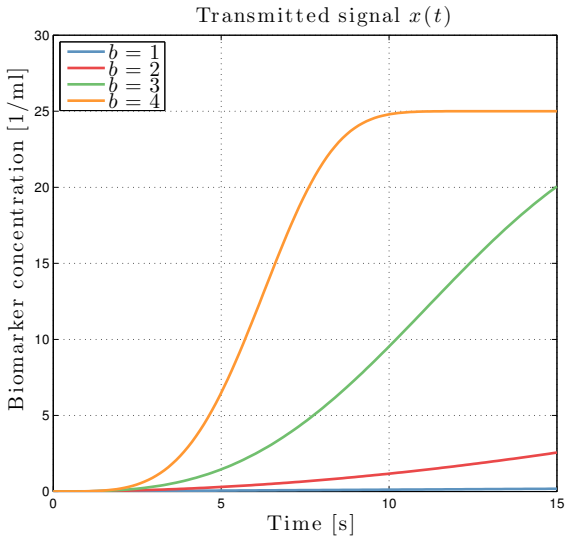


Fig. 3. Path between the MC transmitter and the MC receiver.

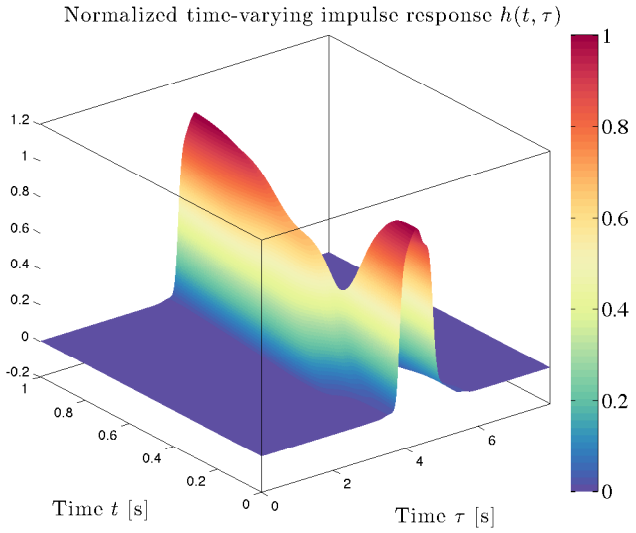
IV. Real-time heart attack prevention

For the numerical evaluation of the framework, the case of real-time heart attack prevention is considered. Figure 1 shows how the sudden rupture of plaque that has accumulated during coronary artery disease (atherosclerosis) can cause direct heart muscle damage leading to a heart attack (Myocardial infarction). The nanosensor has a reception probability $p_r = 0.05$. The nanosensor is assumed to be $90\ \mu m$ in size, which allows it to remain in the capillary area. It is located in the capillary bed of the small artery 109 as shown in Figure 3, and can sense the circulating endothelial cells shedding from the aortic arch (Large artery 3). The physiology of the patient is the same considered in [6]. The diffusion coefficient of the biomarker (circulating endothelial cells) is equal to $10^{-8}\ m^2/s$. Figure 4(a), Figure 4(b), and Figure 4(c) show the biomarker concentration, in the release process, the propagation process, and the reception process, respectively. In Figure 4(a), different release profiles are considered with different power-law coefficients b and a fixed release coefficient $k = 0.48 \cdot 10^{-3} s^{-b}$. The resulting transmitted signals $x(t)$ have different kinetics, the higher the power-law coefficient, the faster is the concentration to reach the saturated value x_0. In Figure 4(b), the time-varying impulse response is shown. It is normalized with respect to its maximum value. In this scenario, the dispersion of the molecular signals is not high in comparison with the blood flow period and is consistent for various injection times t, however, the attenuation varies significantly as a function of the injection time. The delay is around $4\ s$ to traverse the 5 blood arteries. In Figure 4(c), the values measured by the nanosensors are shown for the same transmitted signals in the release process shown in Figure 4(a). The number of biomarkers is highly attenuated due to the branching of the arterial tree and the dispersion in the channel. The noise is multiplicative to the concentration level. The lower concentrations have less noise than the higher concentrations, and the signals appear to be around $6\ s$ delayed from the transmitted signals $x(t)$.

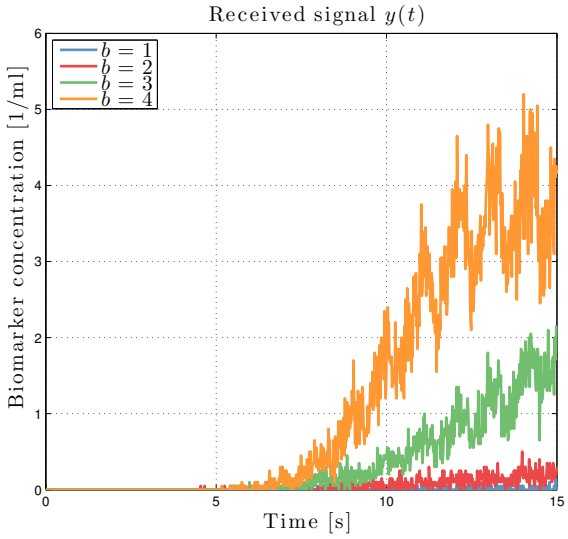
The sensed data illustrated in Figure 4(c) can be used to deliver a diagnosis to prevent a heart attack that would otherwise occur within hours. The data can also be used to estimate unknown system parameters such as the distance between the location of the endothelial cell shedding and the nanosensors and the kinetic parameters of the shedding using



(a) Release process.



(b) Propagation process



(c) Reception process.

Fig. 4. Response of the intra-body molecular communication network between the source of the disease and the nanosensors.

the method described in Section III. Since the expressions involved in the MC model are analytical, the numerical evaluation and the optimization are more efficient than using finite-element methods.

V. Conclusion

In this paper, the molecular communication (MC) paradigm has been utilized to enable intra-body communication for health monitoring and diagnosis. Based on the model of drug release, propagation, and reception by nanosensors, a framework has been developed for estimating the timing and pattern of disease biomarkers, the location of the disease, among other parameters. The case study of circulating endothelial cells as early indicators of myocardial infarction has been studied using this method. The advantage of MC is the a priori knowledge about the release, propagation, and sensing processes which reduces the dimensionality of the system, allowing to apply efficient optimization techniques for disease estimation and diagnosis.

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