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Synthetic protocols for nano sensor transmitting platforms using enzyme and DNA based computing

Frank Walsh, Sasitharan Balasubramaniam *, Dmitri Botvich, William Donnelly

Telecommunication Software and Systems Group, Waterford Institute of Technology, Carriganore Campus, Waterford, Ireland

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ABSTRACT

The ability to create communication networks of biological nanoscale devices has the potential to open up new opportunities and applications, particularly in areas such as health care and information processing. Inspired by recent developments in molecular communication and biomolecular computing, we present in this paper a biological cell based molecular communication transmitting platform using synthetic molecular computing techniques. We investigated two protocol solutions which include DNA based computing coupled with viral particles and enzyme based computing coupled with calcium signaling. Each of these solutions is designed for different applications and environments. For each of these approaches we demonstrate how elements from various layers in the communication stack are developed using the molecular computing mechanisms. Simulation results are also presented to illustrate the functionality and performance of each solution.

1. Introduction

In recent years, advancements in nanotechnology have attracted tremendous attention, particularly in the field of medicine. These developments have ranged from advances in materials for nano devices, to improved capabilities (e.g. self-assembling) as well as applications (e.g. diagnosis, drug delivery). While these developments have increased application opportunities for nano devices, a specific aspect that is still in its infancy is communication capabilities. This has led to new research opportunities of nanoscale communication and networking, which is being currently pursued by communication network researchers [2]. Improving the communication capabilities of nano devices can greatly impact not only the current applications of nano devices, but also open new opportunities for uses of nanotechnology (e.g. networked nano sensors). Molecular communication is one research field that has investigated communication capabilities between nano devices, particularly in biological environments [29,2,16]. Over the years, development of communication systems has evolved from fixed infrastructure to wireless communication for mobile and sensor devices, where the design paradigms have remained the same. Similar to design paradigms used in conventional communication systems, molecular communication aims to encode information into biomolecules and diffuse this through the biological medium to nano device receivers, which in turn will decode this information.

However, developing molecular communication systems with the same design paradigms of conventional communication systems brings new challenges. Firstly, nano machines, unlike computing devices, have limited capabilities for incorporating dedicated physical communication systems. Therefore, any communication mechanism must be developed using components within biological environment. Secondly, information would have to be transformed into biomolecules in order to be passed to the underlying biological environments. Thirdly, biological environments as a physical media are very different in nature to conventional physical communication media, where propagation of molecules is usually based on diffusion and are very slow. Therefore, acknowledgements

* Corresponding author. Tel.: +353 051 302912.
E-mail address: sasib@tssg.org (S. Balasubramaniam).

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of messages may not be suitable in ensuring the reliability of message transmissions. Based on these challenges, communication protocols designed for nano devices will need to be modular, flexible and highly dependent on applications. In this paper, we propose solutions for communication protocols for nano devices, based on the original TCP/IP protocol stack design paradigm. While various attempts have been made to improve communication network performance by adopting mechanisms from biology, we have taken an opposite approach [9,10]. The functionalities of each layer of the protocol stack are realized through existing molecular computing approaches [32,30]. In particular, we focus on two molecular computing approaches, which includes DNA and enzyme based computing solutions. Each approach is tailored to suit different physical layer molecular communication mechanism, which includes calcium signaling as well as viral particle biomolecule approach. We have designed the two protocols as a communication platform that can target various nano device applications, but mainly focusing on synthetic nano sensors.

The paper is organized as follows: Section 2 presents related work on molecular communications and molecular computing. Section 3 presents a high level overview of applications of molecular communication network that can exploit our proposed protocol design. Section 4 presents the enzyme based computing approach that is coupled with calcium signaling, while Section 5 presents the DNA computing approach that is coupled with viral particle biomolecules. Section 6 presents the discussion, and finally, Section 7 presents the conclusion.

2. Related work

The related work is divided into two sections, which includes current research work in molecular communications and molecular computing.

2.1. Molecular communication

In our previous work [43] we reviewed molecular communication as a communication mechanism for biological nano and BioMEMS (Biological Microelectromechanical Systems) devices. In [29], Nakano et al. showed through both experiments and simulation, that distant nano devices can communicate by encoding information through the temporal and spatial properties of intercellular calcium waves. Intercellular waves are shown to propagate through a multicellular environment via connexons, where two connexons form gap junctions between the cells allowing exchange of molecules and ions. In [28], Moritani et al. define a molecular communication interface that uses vesicles embedded with gap junction proteins to transport encoded molecules. The vesicles encapsulate the information molecules (e.g. this could be represented as metabolites, or small nucleotides) and are used as signal carriers between the sender and receiver nano devices. In [8], Bush et al. investigates the impact of topology sensitivity, information capacity, and latency on carbon nanotube (CNT) networks for bio-nano applications, drawing comparisons to cell based microtubule structures. The author examines effects such as isotropy and persistence length on CNT performance and also proposes autocorrelation and persistence area as design metrics for CNT bio-nano networks. Eckford [11] addresses molecular communication from an information theoretic context, formulating an abstract model for molecular communication applicable to both communication and information theorists. In all these research work, the focus of investigation has largely been at the physical layer, which can be complementary to the solution of upper layer protocols that we propose in this paper.

2.2. Biomolecular computing

Biomolecular computing (from here on we will just use the term *molecular computing*) uses biomolecules, biochemistry and molecular biology to perform computation. In the context of the solution proposed in this paper, molecular computing provides a programmable mechanism to implement communication protocols in bio-nano devices. This section examines two common biomolecular computing methods; DNA and enzyme based computing. A summary and the characteristic differences between the two types of computation are also described.

2.2.1. DNA based computing

DNA molecules have a number of advantages for biomolecular computation, such as encoding information as sequence of biochemical symbols as well as using these symbols to perform computing operations. In [33], Rinaudo et al. use RNA interference (RNAi) in biological cells to implement generic Boolean logic. This solution forms the basis for a bio-nano device that can respond to and make decisions based on incoming, extracellular inputs. This work extends Benenson et al.'s work in [5] that investigated a programmable autonomous finite state automaton consisting entirely of biomolecules. The autonomous finite state automaton consists of a long double stranded DNA input molecule that is processed repeatedly by a restriction nuclease *FokI*, where short DNA "rule" molecules control the operation of *FolkI*. These concepts can form the core of programmable bio-nano devices that can be designed to carry out several tasks such as *in vivo* disease detection and the release of treatment based on several disease-indicating inputs.

2.2.2. Enzyme based computing

In [38], Stetter et al. uses the bistable nature of biochemical enzymatic reactions to create a reusable architecture that forms the basis of several Boolean logic functions such as AND, and OR gates. This small enzyme based circuit can act as a sub-component in composing more complex functions. A key requirement of enzyme based Boolean functions is the sinusoidal, "*switch-like*" response to inputs. For example, in [26] Markevich et al. describe a bistable switch using a cell based Kinase–Phosphatase signaling cascade that is highly conserved in eukaryotic cells. In doing so, the authors demonstrate the use of ultrasensitive cell based enzyme signaling pathways to perform digital logic computation. Similarly, in [32] Prasanna de Silva et al. demonstrate the potential for