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Communication Theoretical Understanding of Intra-Body Nervous Nanonetworks

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ABSTRACT

Emerging nanoscale applications, e.g., nanoscale cooperative intelligent drug delivery or multiple intra-body nanosensors for health monitoring, mandate enabling nanomachines to communicate with each other, and hence, form nanonetworks to overcome the limitations of a single nanomachine. Indeed, the human body is a massive nanoscale molecular communications network composed of billions of interacting nanomachines, i.e., cells, whose functionalities depend on nanoscale molecular communications. In this paper, we first introduce the elementary models for nanoscale neuro-spike communication channels, and discuss its extensions to multi-terminal nervous system nanonetworks. Our objective is to learn from the elegant molecular communication mechanisms inside the human body to engineer practical communication techniques for emerging nanonetworks. Besides, we aim to pave the way for the advancement of revolutionary diagnosis and treatment techniques for neural diseases inspired from information and communication technologies (ICT), which is promising for future neuro-treatment and bio-inspired molecular communication applications.

INTRODUCTION

Recently, enormous improvements in the field of nanotechnology have enabled the realization of powerful and functional man-made tiny devices exploiting the behavior of atomic and molecular structures. *Nanomachine*s, composed of nanoscale components, are independently operating full-featured devices capable of tasks ranging from computing and data storing to sensing and actuation. However, their scarce memory and processing capabilities point out the need for establishment of *nanonetworks*, i.e., a number of nanomachines communicating to jointly execute application-specific tasks. Several communication paradigms are considered for intra-body applications of nanonetworks, however the most promising is *molecular communication*, where molecules are used to encode, transmit and receive information [1]. One main reason is that molecular communication of nanoscale entities is an existing natural phenomenon, and offers a field of study for developing solutions through modeling natural nanonetworks. Another reason is that artificial nanonetworks can be built upon such phenomena with appropriate tools, thus ensuring feasible engineering solutions.

To realize molecular nanonetworks, the foundations of molecular information theory should be established via identification of the existing molecular communication mechanisms, and development of networking techniques for nanomachines, which demand novel engineering efforts. Fortunately, these engineering skills and technology have been prepared within us by the natural evolution in the last several billions of years.

Indeed, the human body is a large-scale heterogeneous communication network of nanonetworks composed of interacting nanomachines, i.e., cells, whose functionalities primarily depend on nanoscale molecular communications [1]. Hence, the vital conditions of the human body directly depend on the performance, reliability, and continuous functioning of intra-body molecular nanonetworks. Furthermore, establishment of the information theoretical foundations of the existing intra-body molecular communication mechanisms will be a significant step towards the development of implementable architectures and communication techniques for emerging applications of nanonetworks. In addition, understanding potential disorders caused by communication failures ultimately paves the way for the development of ICT-inspired treatment techniques.

The most advanced and complex intra-body system is the nervous system, which is the ultra-large scale communication network of nerve cells, i.e., neurons. The nervous nanonetwork transmits the external stimulus to the brain and enables communication between different systems by conveying information with electro-molecular impulse signal known as *spike* or action potential (AP), where AP is a short-lasting event in which the electrical membrane potential of a nerve cell rapidly rises and falls, following a consistent trajectory [2].

The *hippocampus*, the part of brain that belongs to the limbic system, has an important role within nervous system in forming new memories and connecting emotions and senses [3]. Thus, research efforts focus on the investigation of the physiological principles of hippocampal neurons.

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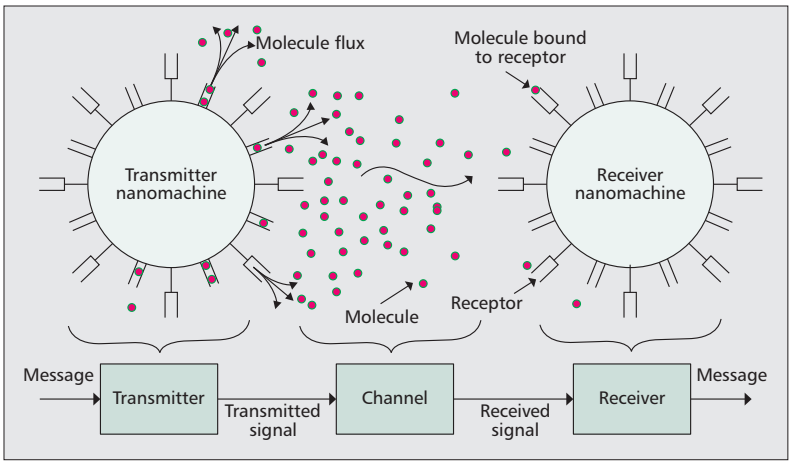

Figure 1. *General molecular communication system with two nodes.*

The *axonal propagation*, impulse propagation down the nerve fiber when the charge of the nerve fiber reaches some threshold, in the hippocampal neurons and its reliability are investigated in [4]. Trial-to-trial variability of the vesicle release process is explained in [5]. A simple model of the response of a neuron to a periodic stimulus is given by the integrate-and-fire model [6]. The Hodgkin-Huxley model, in which the neuron membrane is modeled as a capacitor in parallel with an ionic current, is the most important model in the physiological literature [6]. These contributions mediate the analysis of nervous system from the perspective of communication theory.

As a complex network of nanonetworks spanning the whole body, the nervous system is the most vital communication network of human body, which coordinates the functionalities of different body systems, e.g., endocrine or cardiovascular systems. Many research initiatives worldwide are in place to understand the role of the nervous nanonetwork. As part of the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) initiative, the Defense Advanced Research Projects Agency (DARPA) aims to understand the human mind and reveal new ways to prevent and cure brain disorders, such as Alzheimer's, schizophrenia, autism, and epilepsy. This project focuses on finding out how individual brain cells and neural circuits work together. Furthermore, the Human Brain Project (HBP), a European Flagship, aims to develop an ICT infrastructure to understand the brain, and translate this knowledge into new computing technology. The ICT community can contribute them in achieving their objectives, which makes our motivation in this study.

Our research starts with the pursuit of bringing groundbreaking molecular communication solutions out by observing and understanding the neurological processes we have. Thus, by introducing the models for elementary nanoscale neuro-spike communication channels and identifying few of vital intra-body nervous system nanonetworks to pave the way for the development of innovative communication theoretical solutions for future medicine and bio-inspired techniques for realization of nanonetworks are main objectives of this article.

In the remainder of this article, we focus on the point-to-point communication links between neurons, and then, the multiple-access neuro-spike communication channel. We look at the entire nervous system as a heterogenous nanonetwork, and identify some challenges. We focus on the neuronal disorders from a communication theoretic perspective, and provide modeling challenges with possible research directions.

Intra-Body Communication Channels

Molecular nanonetworks are inspired by communication networks among natural living entities. Single-input single-output (SISO) intra-body molecular communication channels are captured by the molecular nanonetwork model with two nanomachines as in Fig. 1.

We explore the foundations for molecular information transfer in nanoscale neuro-spike communication channel, with the functional blocks described next.

Nanoscale Neuro-Spike Communication Channel

Communication between neurons occurs via transmission of neural spike trains through junctional structures, either electrical or chemical synapses, connecting nerve terminals. Since neural communication is achieved at synapses, the process of neurotransmission is called synaptic communication.

Nervous system nanonetwork, composed of nerve cell bodies as the network nodes, is a distributed network over the entire body and extends up to extremities [3]. It is responsible for gathering information from different parts of the body, processing it and generating the required response for the body.

Neurons, electrically excitable cells capable of storing, processing and transmitting information through chemical and electrical signaling mechanisms, are considered as nanotransceivers of the nervous system nanonetwork. They receive signals, i.e., spikes, from other neurons or sensory cells, which changes the membrane electrical polarization.

The performance of neuro-spike communication depends on the AP transmission characteristics through neurons, where the neuro-spike communication channel is mainly exposed to axonal and synaptic noise sources. In fact, the realistic model for neuro-spike communication between single presynaptic neuron and single postsynaptic neuron includes three phases, which are the axonal propagation, the synaptic transmission and AP generation phases, as illustrated in Fig. 2 [2].

Axonal propagation is the first stage of the neuro-spike communication, in which APs are transmitted through the axon and arrive to its terminal branches, where the neuron makes an interface with other neurons through *synapses*, i.e., conductive links where cell-to-cell signals are produced [3]. The axonal channel is exposed to noise due to random opening and closing of ion channels [2].

Synaptic transmission is the next step, which is composed of vesicle release, diffusion, and generation of Excitatory PostSynaptic Potential

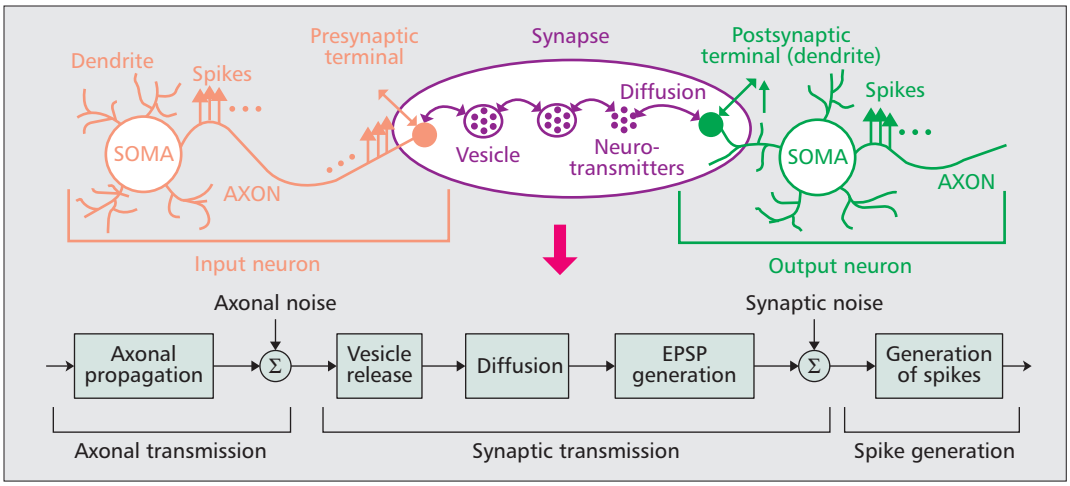

Figure 2. *Channel model for nanoscale neuro-spike communication [2].*

Molecular nanonetworks are inspired by communication networks among natural living entities. Single-input single-output (SISO) intra-body molecular communication channels are captured by the molecular nanonetwork model with two nanomachines.

(EPSP), i.e., the excitation due to the vesicle release. An arriving spike, i.e., nerve impulse or AP, to a synaptic interface yields an influx of calcium ions through voltage-dependent calcium ion channels. Calcium ions then bind to the proteins found within the membranes of the synaptic vesicles. Vesicles then release their contents, *neurotransmitters*, i.e., *information molecules*, to the synaptic cleft, which occurs through an unusually rapid process of cellular secretion, which is shaped by the rate of AP generation. Hence, we consider and model the neuro-spike communication channel as series of electrical and molecular channels. The synaptic noise, which is due to extreme synaptic effect from thousands of other synapses, affects the communication performance within neurons [2].

Generation of the spikes, which is the final step in the neuronal communication model, is caused by the spread of electrical potential along the cell body and then, its accumulation at the base of the axon. When the electrical potential exceeds the threshold for AP generation, spikes are generated. Spikes carry information from one neuron to the others through propagation along the axon to its terminal extensions. In [7], we employed the linear-nonlinear-Poisson (LNP) model of spike generation to model the neuro-spike communication channel. LNP has been successfully used to describe the neuronal response characteristics. It comprises a linear weighting block to model the empirical characteristics of the axonal low-pass filtering process, a point nonlinearity due to the saturation of the presynaptic neurons, and a Poisson encoding stage, which determines the spike generation rate.

There has been some research focusing on the limits on information transmission over synaptic terminals. In [2], authors investigate the communication behavior of neurons as a new nanoscale communication paradigm and model the end-to-end neural communication channel. A synaptic communication model is suggested in [8]. It involves the fundamental events during the synaptic transmission as different blocks, namely the vesicle release in response to a spike, EPSP due to the vesicle release, and trial-to-trial variability of this potential. The authors derive the theoretical lower bounds on the capacity of a simple model of a cortical synapse by signal estimation and signal detection paradigms. Although the hybrid structure of neuronal communication is investigated, extensive communication models for neuro-spike channels need to be derived to build the analogies between communication theory and biomedicine aspects of neuro-spike terminology, and to realize revolutionary treatment alternatives inspired by communication aspects as also pointed out later.

Multi-terminal Neuro-Spike Communication Channels

In this section, we extend the SISO channel model to multi-input single-output (MISO), that is, the multiple-access neuro-spike communication channel, in which the neural signal (i.e., the AP) is transmitted through multiple synaptic paths directed to a common postsynaptic neuron terminal. Synaptic transmission is initiated with random vesicle release process from presynaptic neurons to synaptic paths. Each synaptic channel is characterized by its impulse response and available postsynaptic receptors. We modeled the multiple-access synaptic communication channel, and investigated the information rate per spike at the postsynaptic neuron, and how the rate is enhanced compared to single-terminal synaptic communication channel in [7]. A hypothetical model with a block diagram for a multiple-access synaptic communication channel is shown in Fig. 3, which incorporates four important stages determining the performance of the neuro-spike communication that are the LNP filtering, the stochastic vesicle release, the variable quantal amplitude and the EPSP shape characteristics.

- LNP stage specifies the AP generation rate, and the neuron response characteristics for each presynaptic terminal.
- *Stochastic vesicle release* is the second stage where the presynaptic terminals independently release vesicles with an average probability of p upon arrival of the spike train. In multiple-access neuro-spike communication channel, the released vesicles are directed to a common postsynaptic terminal through distinct synapses.
- *Variable quantal amplitude* at each synaptic channel is characterized by a random amplitude determined by a Gamma distributed

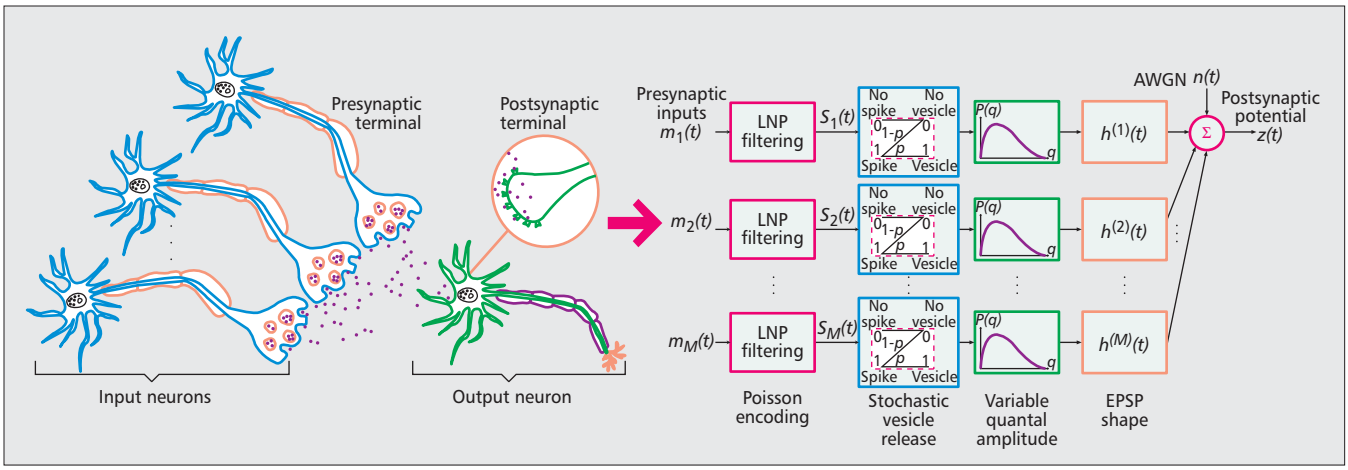

Figure 3. *Multiple-access channel model between presynaptic and postsynaptic neuron terminals [7].*

variable q. Hence, the synaptic channels can be independently characterized.

- *EPSP shape* is another factor that determines the synaptic response characteristics. Summation of the EPSPs at the postsynaptic terminal enables the generation of APs. Therefore, synchronization of EPSPs are required so that the postsynaptic cell reaches the threshold to fire an AP.

At the end of the synaptic transmission, voltage seen at the postsynaptic terminal is stochastically determined by the random spike generation and vesicle release processes at each input terminal, and the variability at each synaptic channel.

Performance of the synaptic MISO channel is affected by:

Learning and Memory — Learning and memory processes are based on the changes in strength and connectivity of neural networks which usually contain multiple synaptic connections. Synaptic channels have variable conductances. Neural learning algorithm can be explained through synaptic weight modification. These weights, i.e., conductances, are adjusted through spike-timing-dependent plasticity (STDP).

Spike-timing-dependent plasticity (STDP) is a biological process that adjusts the strength of connections between neurons in the brain. The process adjusts the connection strengths based on the relative timing of a particular neuron's output and input APs (or spikes) [9]. The STDP process explains the development of the human's brain with regards to long-term potentiation (LTP) and long-term depression (LTD).

Synaptic Input Correlation — Learning occurs through cooperation between synaptic inputs, and the plasticity rules select inputs that have a strong correlation with other inputs. Synaptic plasticity contributes to memory storage, and the activity-dependent development of neuronal networks. In [7], we investigated the postsynaptic throughput for synaptic MISO channel for both uncorrelated and correlated firing of neurons, where the neural spike trains generated at each presynaptic terminal are independent, and have a first order correlation, respectively. According to our analysis, the total communication rate is reinforced in the same way as the correlation amount among the APs generated at the input neurons. Multi-order correlations should be incorporated into the model for a more realistic analysis of synaptic rate region.

Interference — Synaptic channels adjust their conductances depending on the AP characteristics, called as neural plasticity (NP) in the neuroscience literature [9]. NP aims at building stronger connections among neurons so that actively transmitting neurons are sustained to carry information. On the other hand, other connections, which we call interfering connections, and usually not correlated with most of the transmitted information, fade away. To enable the reduction of interference caused by uncorrelated synapses, neurons manage to adjust the synaptic weights through feedback mechanisms. In [10], we investigated the optimality of this adaptive interference canceling. To the best of our knowledge, the interference among a bunch of neurons has not been investigated yet.

Before moving to the entire network model discussion from earlier, we focus on the multi-hop neuro-spike communication. In a multi-hop neuro-spike communication link, the neuronal response decays in time since firing of a single neuron is not sufficient to generate a postsynaptic response, but a miniature EPSP, and multiple miniature EPSPs are simultaneously required to fire the postsynaptic terminal. Other multi-terminal communication channel extensions, such as the relay, broadcast or the MIMO channel generalizations can be implemented based on the point-to-point and multiple-access channel models for the communication via neuro-spikes as studied in [2] and [7]. Development of these channel models is promising for future nanoscale and molecular communication applications, and considering the essential role that neurons and synaptic connections play in memory and learning, more analysis is needed to characterize neuro-spike communication.

Nervous System Nanonetwork

Nervous system nanonetwork is intrinsically a large-scale network of nanotransceivers, i.e., neurons, spanning the overall body. It is divided into two main subnetworks, namely central (CNN) and peripheral (PNN) nervous networks.

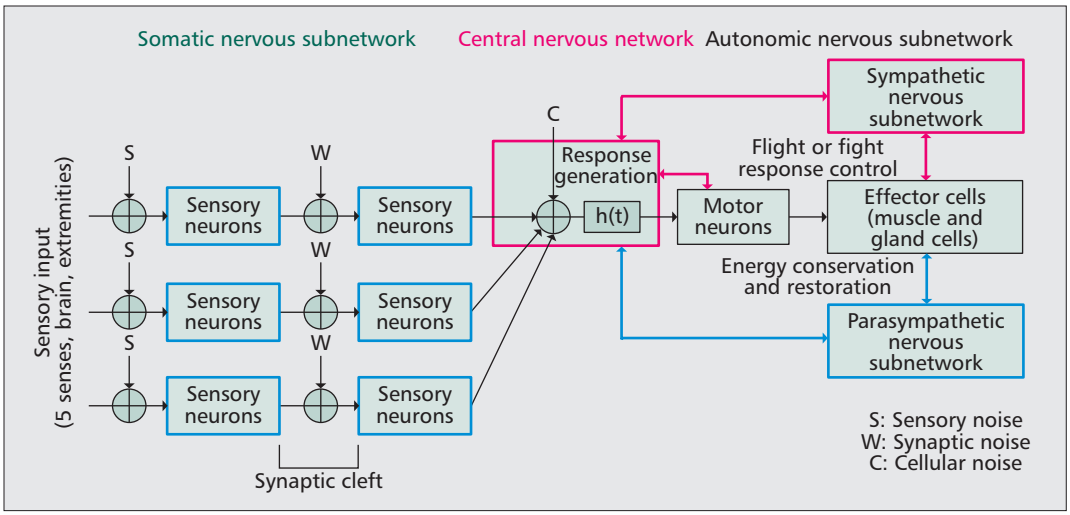

Figure 4. *Communication architecture for overall nervous network.*

CNN integrates the sensory input information and provides the motor output to gland cells [3]. It is the main processor of the body. PNN is grouped into two parts, which are somatic (SoNS) and autonomic (ANS) nervous subnetworks. SoNS collects information from the receptors of five-senses and heads through sensory neurons to convey to CNN. ANS transports the motor outputs generated by CNN to smooth muscles, cardiac muscles and glands through motor neurons. Hence, the main function of the PNN is to connect the CNN to the systems [3]. Thus, we consider PNN as the gateway network for CNN to reach the rest of human Internet. ANS is composed of two subnetworks, i.e., sympathetic (SNS) and parasympathetic (PSNS) nervous subnetworks. SNS controls neural and hormonal stress, i.e., flight-or-fight responses. Complementary to SNS, PSNS is the energy conservation and restoration center of the body [3].

Complete architecture for the nervous system nanonetwork can be established using the connections and communication relations among its subnetworks, i.e., SoNS, CNN and ANS. Furthermore, nervous nanonetwork is susceptible to noise. Sensory noise (S) limits the amount of information available to other areas of the CNN. Cellular noise (C) contributes to neuronal variability. Finally, synaptic noise (W) results from the noisy biochemical processes that underlie synaptic transmission. Adding up these noise sources can account for the observed postsynaptic-response variability. Incorporating the noise sources, communication architecture for overall nervous nanonetwork is established, as depicted in Fig. 4.

Overall, regulating different human body mechanisms, the nervous nanonetwork works towards achieving and preserving the stable state, i.e., homeostasis, of the human body. Many of the neurological disorders are closely related with the degraded communication capability of neurons or certain parts of nervous nanonetwork. Multiple sclerosis (MS) is a nervous disease resulting from the destruction of myelin sheath, affecting the ability of nerve cells to communicate. *Alzheimer's disease*, which leads to loss of cognitive functions and death, even though the exact mechanism behind it is unknown, is caused by degeneration of neurons in the brain. *Spinal cord* injuries are due to the damaged neurons in the spinal cord, which disconnects the brain and spinal cord neurons leading to paralysis of the body. Thus, sustaining effective communication capabilities in the nervous nanonetwork is imperative for the functional and metabolic efficiency of the human body. Besides, understanding disorders caused by communication failures paves the way for the possible development of a new generation of ICT-inspired treatment techniques.

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Synaptic Communication Disorders

Neurons are susceptible to electrochemical and structural disruption. Disorders of neuromuscular transmission are due to a wide variety of agents, such as genetic disorders, systemic diseases, drugs, environmental health problems, infections, lifestyle, hormones, some are genetically determined, many are of unknown etiology [11]. All such disorders interfere with the events in the sequence whereby a nerve impulse excites an AP. Here, we reveal the potential relations between neuronal coefficients, synaptic communication problems and the neuronal disorders, focusing on the disorders characterized by pre- and postsynaptic and synaptic abnormalities.

Disorders Characterized by Presynaptic Abnormality

Impairments in AP generation, vesicle fusion and release processes are the main causes for presynaptic abnormalities.

Action Potential and Neurotransmission — APs get amplified and degraded depending on outside factors. For example, nicotine enhances neurotransmission rate by causing more APs in the presynaptic neuron [11]. Alcohol, on the other hand, blocks neurotransmission by inhibiting the excitatory channels on the postsynaptic neuron, and then lowering the rate of APs from the presynaptic neuron. As a result, fusion rate decays, and hence, the synaptic performance drops.

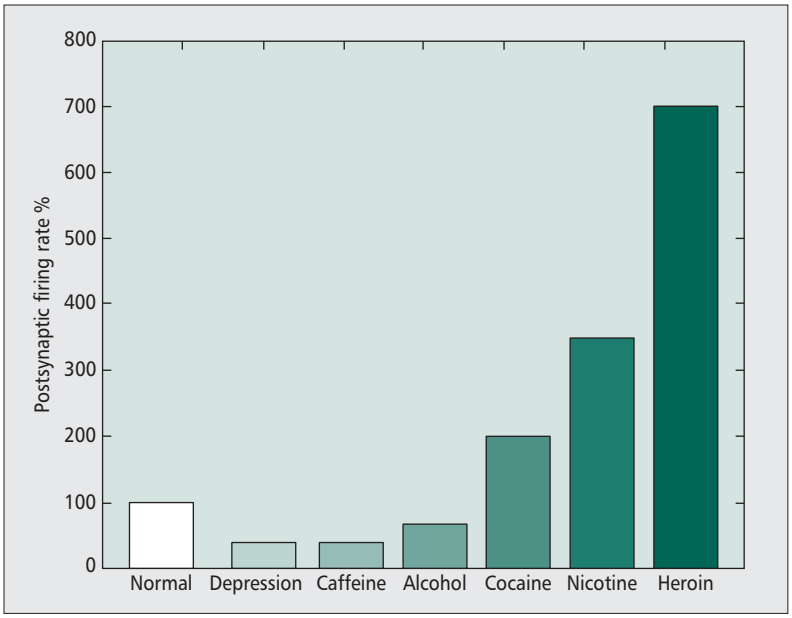

Figure 5. *The effects of drugs and diseases on synaptic transmission [11].*

Vesicle Fusion Rate and Neurotransmission — Diminishing neurotransmitter release is directly linked to neurological syndromes. Depression is associated with fewer neurotransmitters released per vesicle [11]. Cocaine blocks the reuptake of dopamine by the presynaptic neuron. This leads to a higher dopamine concentration in the synapse, which increases neurotransmission in *brain reward system*, i.e., the brain circuit that reinforces behavior by inducing pleasurable effects, hence more postsynaptic firing [11]. Heroin increases the rate of vesicle fusion in the presynaptic neurons that use dopamine as a neurotransmitter. Figure 5 depicts the deteriorating effect of drug use and depression on postsynaptic firing of neurons.

Disorders Characterized by Synaptic Abnormality

Synaptic transmission is the most crucial part of neuronal signaling, which is vulnerable to many kinds of disruption.

Synaptic Depression — Depletion of the readily releasable vesicles causes significant drop in postsynaptic firing rates, leading to synaptic fatigue and depression.

Abnormal Synaptic Plasticity — Plasticity is the ability of the synapse to change in strength in response to either use or disuse of transmission over synaptic paths. Quantal variations of neurotransmitters released into a synapse and the postsynaptic response variability cooperate to achieve plasticity. Variations in quantal amplitude affect the communication performance by modulating the postsynaptic voltage levels.

Disorders Characterized by Postsynaptic Abnormality

Excessive postsynaptic firing and postsynaptic receptor saturation are the factors attributed to postsynaptic abnormalities.

Postsynaptic Firing Rate and Neural Disorders — High postsynaptic firing rates could lead to sleepiness at synapses where adenosine is the primary transmitter. Caffeine inhibits sleepiness by inhibiting adenosine receptors [12]. Hence, available neurotransmitter amount at synapses decreases, yielding to decrement in postsynaptic firing rates.

Postsynaptic Receptor Saturation — Neurodegenerative disorders including schizophrenia, epilepsy, Alzheimer's and Huntington's diseases are associated with increased and decreased stimulation of a special type of postsynaptic receptor, i.e., NMDA receptor [3], which causes alterations in EPSP amplitudes, affecting neuronal communication performance.

Future Research Avenues

To pave the way for the advancement of ICT-inspired neuro-treatment and bio-inspired molecular communication applications, we focus on the nanoscale neuro-spike communication channels and nervous nanonetworks to engineer practical communication techniques for emerging nanonetworks.

Nanoscale Neuro-Spike Communication Channels

Although there exists preliminary research on diffusion-based molecular communication commonly for generic frameworks, main molecular communication directions for biological systems and specifically, communication pathways in human nervous system are not explored yet. Thus, open issues include the communication models and extensive performance analyses for intra-body neuro-spike communication channels.

- The information capacity of the single- and multi-terminal neuro-spike communication channels, and the noise, error probability, rate and delay performance together with feedback regulation and signaling mechanisms need to be analytically investigated to reveal their fundamental limits and potential communication failures.
- Fundamental communication parameters and metrics, such as interference, channel access, collision probability over multi-neuron connections should be analyzed.
- Network information theoretical analysis of the realistic multi-terminal neuro-spike channels should be performed to find the corresponding achievable rate regions.
- A bio-compatible nanoscale artificial synapse should be designed inspired by nervous communication channels to replace the damaged neurons and communicate two disconnected neurons, and to establish a connection between two disjoint neurons primarily observed in neural disorders such as Spinal Cord Injury (SCI), in which sensed information cannot be communicated to brain and brain cannot send commands to muscles.
- Carbon NanoTubes (CNTs), which are biocompatible materials that are capable to release molecules [13], can be utilized to receive and to transmit electrical neuro-spikes. Furthermore, CNT-based drug delivery methods could be exploited to realize diffusion-based molecular communication channel for synaptic transmission.

Nervous System Nanonetwork

Many studies on molecular nanonetworks concentrate on developing new modulation scenarios and molecular sensing mechanisms without considering intra-body molecular pathways. However, inspired from nervous nanonetworks, novel ways of synchronization among nanonodes can be achieved. Hence, foundations of nanoscale neuro-spike communication channels will contribute to the extension of single- and multi-terminal channel models to intra-body nervous nanonetworks.

- Ultra-large scale and heterogeneous connections of various types of neurons, corresponding to multi-terminal channels should be realized, considering link, medium access, routing and reliable message delivery mechanisms.
- Network information theoretical analysis of the entire nervous nanonetwor*k* should be performed to reveal its information capacity based on known nervous nanonetwork connectivity results in the physiology literature. As the spinal cord serves as the wideband backbone link between the brain and the rest of the nervous nanonetwork, we should also explore approaches for applying our results to obtain communication theoretical model and information theoretical capacity of the spinal cord.
- A Nervous NaNoNetwork Simulator, N^4S, should be developed to evaluate the theoretical results, capture communication theoretical insights of neuronal diseases, e.g., multiple sclerosis, paralysis, Alzheimer's, related to potential communication failures, and pave the way for ICT-inspired diagnosis and treatment techniques.
- As the first step to provide ICT-inspired neuro-treatment approaches to neurological and spinal cord disorders, utilizing CNTs that are capable to release molecules to artificially realize molecular communication in synapses and neuro-transmitter molecules as in drug delivery applications, the first practical nanoscale bio-inspired communication system could be designed and developed.

Conclusion

The realization of bio-inspired artificial nanonetworks operating at the efficiency of nervous nanonetworks is still missing. Identifying the existing nervous molecular communication mechanisms, and establishing the communication and information theoretical foundations of these communication channels will be a giant step towards developing real implementable architectures, e.g., bio-inspired and ICT-based prosthetic systems with neural communication capabilities, and communication techniques for emerging applications of nanonetworks.

In brief, the investigation of the fundamentals of neuro-spike communication channels and their role in providing the integrity of all biological systems through nanonetwork relations broadens the contributions and promotes the development of the ICT field. Thus, with this background, ICT is anticipated to provide substantial contributions to the development of nanoscale molecular communication networks inspired by the human nervous system, and to pave the way for developing ICT-inspired curing strategies for neural diseases.

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References

[1] I. F. Akyildiz et al., "Nanonetworks: A New Communication Paradigm," *Computer Networks*, vol. 52, Aug. 2008, pp. 2260–79.

[2] E. Balevi and O. B. Akan, "A Physical Channel Model for Nanoscale Neurospike Communication," *IEEE Trans. Commun.*, vol. 61, 2013, pp. 1178–87.

[3] A. C. Guyton and J. E. Hall, *Textbook of Medical Physiology*, Philadelphia, W. B. Saunders, 2006.

[4] J. P. Meeks and S. Mennerick, "Action Potential Initiation and Propagation in CA3 Pyramidal Axons," *J Neurophysiol*, vol. 97, May 2007, pp. 3460–72.

[5] H. Markram *et al.*, "Physiology and Anatomy of Synaptic Connections Between Thick Tufted Pyramidal Neurons in the Developing Rat Neocortex," *J Physiol*, vol. 500, no. 2, Apr. 1997, pp. 409–40.

[6] J. Keener, J. Sneyd, *Mathematical Physiology*, Springer, New York, 1998.

[7] D. Malak, O. B. Akan, "A Communication Theoretical Analysis of Synaptic Multiple-Access Channel in Hippocampal-Cortical Neurons," *IEEE Trans. Commun.*, vol. 61, no. 6, June 2013, pp. 2457–67.

[8] A. Manwani and C. Koch, "Detecting and Estimating Signals over Noisy and Unreliable Synapses: Information-Theoretic Analysis," *Neural Comp.*, vol. 13, no. 1, Jan. 2001, pp. 1–33.

[9] S. F. Cooke, T. V. P. Bliss, "Plasticity in the Human Central Nervous System," *Brain*, vol. 129, no. 7, May 2006, pp. 1659–73.

[10] D. Malak, O. B. Akan, "Adaptive Weight Update in Cortical Neurons and Estimation of Channel Weights in Synaptic Interference Channel," submitted for publication, 2013.

[11] D. Muzzey, "The Effects of Drug and Disease on Synaptic Transmission," available at: http://outreach.mcb.harvard.edu/animations/synapse.swf.

[12] J. A. Ribeiro *et al.*, "Adenosine Receptors in the Nervous System: Pathophysiological Implications," *Prog Neurobiol*, vol. 68, 2002, pp. 377–92.

[13] M. M. De Villiers, P. Aramwit, and G. S. Kwon, *Nanotechnology in Drug Delivery*, Springer, New York 2009.

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