Nanomedicine and Nanotoxicology

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Advanced Targeted Nanomedicine

A Communication Engineering Solution

Springer

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Preface

Molecular communication is an interdisciplinary subject that has become an interesting topic of discussion among scientists, engineers and lay commentators. This type of communication is defined on the principle of using biochemical signalling to achieve information exchange among naturally and artificially synthesised nanosystems. Among its envisaged application areas is the promising field of nanomedicine. The fundamental idea behind nanomedicine is to improve the efficiency of medical and healthcare systems, using the concepts, devices, tools, technologies and techniques of nanotechnology. Due to its ability to address disease challenges at the fundamental level of the cell, nanomedicine has become a promising tool in the diagnosis, therapy and monitoring of numerous chronic diseases, such as cancer, cardiovascular disease, Alzheimer's disease and diabetes.

Many studies on nanomedicine have been widely discussed and reported in the literature. However, several challenges have prevented the satisfactory translation of expectations and promises to clinical reality. To address these challenges, it is important to note that many chronic diseases are embedded in the fundamentals of biology; hence, uniting experts from a broad cross-section of related and unrelated fields would be of great benefit to solving these medical problems. To this end, the exploration of nanomedical applications and solutions on the platform of the interdisciplinary field of molecular communication engineering has been considered as an interesting option in the recent times. Molecular communication taps into the fundamentals of communication engineering, the gains of nanotechnology, the progress in tissue/molecular engineering and the outstanding results in the overall medical/natural science fields to proffer solutions to medical challenges. An offshoot of the application of molecular communication to nanomedicine is the concept of *advanced targeted nanomedicine*, which is the focus of this book. Advanced targeted nanomedicine is the term coined to define the exploration of medical challenges and their solutions by looking at them from the perspective of a communication engineer cum nanomedical scientist. Specifically, it provides practical knowledge, tools and functionality for designing and configuring nano, micro and macro communication/control devices to enhance their functionalities as nanomedical tools in order to address medical challenges.

The main objective of this book is to provide a motivation for engineers, scientists and lay commentators to explore the concept of molecular communication from the interesting application perspective of advanced targeted nanomedicine. This perspective considers, and rightly so, the occurrence of diseases as communication anomalies among biological entities in the human body. Consequently, communication principles and approaches can be employed to model, analyse and solve disease challenges, especially the chronic and indefatigable ones, such as cancer, Alzheimer's disease, HIV and cardiovascular disease.

This book is structured in a way that provides some understanding for beginners and idealistic insight to experts in molecular communication. In order to do this, we divided this book into seven chapters:

- Chapter 1 presents the role of communication principles, ideas and systems in understanding and treating diseases, and introduces the concept of advanced targeted nanomedicine.
- Chapter 2 presents some interesting discussions on the principles of communications among/between living and non-living systems as the basis for advanced targeted nanomedicine.
- In Chap. 3, the various components of the ATN systems are discussed.
- Chapter 4 explores the different modalities for administering nanosystems into the body, as well as the modelling, analysis and evaluation of nanosystems' delivery routes from the perspective of a communication engineering problem.
- Chapter 5 presents a case-driven classical framework for the design and development of ATN solutions.
- In Chap. 6, the concept of Internet of things as a tool in the delivery of effective ATN solution is discussed. The chapter also discusses some of the most poignant examples of the utility of nanomedicine in the detection and treatment of cardiovascular disease that have recently been reported.
- Chapter 7 presents exemplary suggestions to define possible ATN solutions to medical challenges such as cancer, Alzheimer's disease, HIV and cardiovascular disease.

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Chapter 1
Communication Engineering Meets Medical Science: *The Advanced Targeted Nanomedical Solution*

1.1 Introduction

With the rise in global population, the increase in the number of medically challenging diseases and the low number (as well as uneven distribution) of medical personnel, there is the need for a new approach to global healthcare delivery. In particular, the lack of clear-cut, permanent cures for cancer, Alzheimer's disease, human immunodeficiency virus (HIV), diabetes, cardiovascular diseases (such as severe coronary artery disease) and Ebola, as well as the projected increase in the proportion of the population at risk of some of these diseases [1, 2] means that everyone has something to worry about.

In his paper titled 'There's plenty of room at the bottom: An invitation to enter a new field of physics' [3], published in 1959, the physicist and Nobel prize winner Richard P Feynman stated that there would one day be nanotechnologies with associated possibilities. Recent advances in nanotechnology have triggered the exploration of advanced concepts in the field of medicine to address the abovementioned health challenges. This exploration gave birth to a highly specific medical intervention termed *nanomedicine* [4]. Fundamentally, nanomedicine focuses on the diagnosis, therapy, monitoring and control of diseases at the cellular levels of systems, with a high degree of specificity. This shift in thinking from contemporary medicine towards nanomedicine is motivated by the fact that diseases manifest from miniscule activities in the cells of living organisms such as humans. Typically, disorders in the activities of a cell or a group of cells result in uncoordinated communication among many other cells in the body. This is consequential to the pathological manifestation of subjective evidences such as headache, fatigue, fever and so on—*symptoms of diseases*. Hence, the fundamental concept of nanomedicine is that it is insightful and seemingly effective in tackling health challenges at the cellular level [5]. In nanomedicine, nanoparticles (usually 30–300 nm in diameter [6]) are designed and developed to deliver drug molecules to the disease cells (with minimal adverse effects to healthy cells), conduct highly precise in vivo disease diagnosis/analysis on specific cells and identify/mark disease agents in the body for elimination. It has

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found application in many disease therapies, such as in the treatment of cancer [7, 8], Alzheimer's disease [9], HIV [8], diabetes [10] and cardiovascular diseases [11].

Over the course of treatment for many of these diseases, it has been found that different individuals may respond differently when subjected to the same treatment. And even for the same individual with a particular ailment, physiological conditions often change with time, as is observable in cancer therapy [12]. For instances, intrinsic anticancer drug resistance appearing prior to chemotherapy, as well as acquired resistance due to drug treatment, remain the dominant impediments to curative cancer therapy [13]. The same applies to the treatment of Alzheimer's disease, where the vast heterogeneity in the disease aetiology involves very complex and divergent pathways [14]. Hence, there is the need for a personalised nanomedical approach to disease intervention that is based on the stratification of in-depth individual demographic and historical information. This personal nanomedicine is also termed *targeted nanomedicine*.

An important factor that must be noted at this point is the relationship between information exchange and diseases. Cells in our bodies are constantly sending and receiving signals, and many pathological conditions arise due to the breakdown in signalling/communication between or among cells. This is evident from diseases such cancer [15], Alzheimer's disease [16], multiple sclerosis [17], diabetes [18], stroke [19], etc. Hence, diseases and their treatments can be addressed using conventional communication paradigms, approaches, tools and devices. The targeted nanomedicine approach that relies heavily on the principle of information exchange/communication is termed *advanced targeted nanomedicine* (ATN). The rudimentary framework for ATN is molecular communication (MC) engineering. MC is a communication paradigm that uses biochemical signals to achieve information exchange among naturally and artificially created bio-nanosystems over short distances [20–24].

This chapter presents the role of communication principles, ideas and systems in understanding and treating diseases. The discussion is extended to concepts such as molecular communication, nanomedicine and ATN.

1.2 Communication Engineering and Medicine

From the standpoint of evolution theory, the idea that man evolved from molecules through single-cell and multicell organisms offers us a way of connecting communication principles to medical interventions. In the illustration presented in Fig. 1.1, molecules are the centre of the wheel of evolution. At that fundamental level, interactions (communications) exist between the molecules in the forms of covalent and non-covalent bonding. At the single-cell level, where viruses and bacteria reside, communications between these organisms are basically achieved by the interchange of signalling molecules such as in quorum sensing [25] and pheromonal signalling [26]. The last level is the multicellular level of evolution, where man exists. At this level, communications among organisms of the same species are achieved using their

Fig. 1.1 An illustration of molecules-to-human evolution

naturally equipped facilities such as auditory systems, olfactory systems, visual systems, chemoreceptor systems and mechanoreceptor systems. In the case of man and some animals, communication is achieved through a syntactically organised system of signals, such as voice sounds, intonations or pitch, gestures or written symbols that communicate thoughts or feelings.

1.2.1 Diseases as Breakdown in Communication

Communication at the various level of the evolution wheel is crucial to the continuous and harmonious existence of each species, especially at the single-cell level and beyond. These organisms communicate in a network format among themselves to spread knowledge, establishing/improve relationships so as to achieve cohesive organisation, attain greater productivity, search for food and mates and avoid dangers. Figure 1.2 illustrates the different levels of communication networks associated with humans and other multicellular animals. Here, the *social communication network* involves person-to-person interactions, which enable humans to spread knowledge, establish relationships, build cohesive organisation, increase productivity and ultimately ensure survival. For a human to be able to establish a social communication network, it is required that the network of body organs (brain, liver, heart, lung, kidney, etc.) must be established and working. In this sense, the entropy required to work, walk, talk, see, think, live, etc., must be properly 'exchanged/communicated' among the organs. These organs are primarily made up of cells, which themselves communicate over the *cellular network*. Different organs have different cells that work collaboratively to achieve the primary task of the particular organ. And each

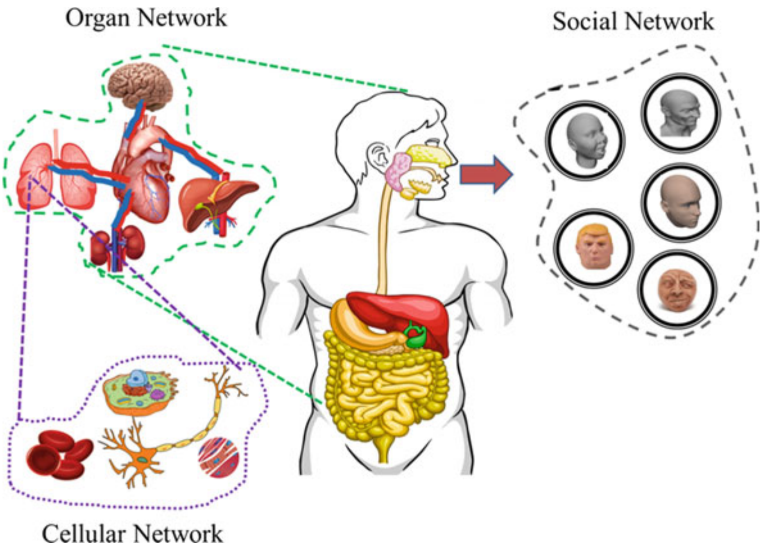

Fig. 1.2 Illustration of the different levels of communication networks associated with humans (and other multicellular animals)

organ works collaboratively with the other organs to keep the host alive in order to communicate with other humans to build a more progressive and resilient society.

Typically, any breakdown in the communication among the organs renders the host organism ineffective and may lead to the death of the host. Implicitly, the breakdown in communications at the cellular level affects the effectiveness of the host organs to perform their primary tasks, which invariably affect communication in the entire organ network and the human at large. The breakdown in communication results in diseases that usually manifest as observable symptoms. For instance, defects in pancreatic cells make them unable to produce enough insulin to signal to the muscle, fat and liver cells the presence of glucose in the blood, resulting in the Type I diabetes with its attendant symptoms [27]. In Type II diabetes, while the pancreatic cells are properly functioning, the muscle, fat and liver cells do not respond appropriately to the insulin signalling [27]. Cell growth and death are strictly controlled by signalling, and when there is a breakdown in the ability of a cell to respond appropriately to growth or death signalling, cancer results [15]. Indeed, a large number of diseases are caused by defective communication within the cellular network.