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Review article

Molecular communication for drug delivery systems: A survey

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ABSTRACT

Drug delivery systems (DDS) are engineered methods to enable the targeted delivery of therapeutic agents at the right rate and location while minimizing the undesired side effects. The recent advances in bioengineering and nanotechnology make it possible to design molecular compounds with specific sizes, shapes, structures and chemical properties to improve the drug uptake and minimize its side effects. Despite all of this progress, overcoming the biological barriers to drug delivery remains challenging. Observing the parallels between the delivery of drugs and the delivery of data, a new paradigm in communication systems research, called molecular communication (MC), has been devised to approach this problem. This paper presents the state-of-the-art, challenges and research opportunities in studying DDS through the MC paradigm. First, the constituting elements of a DDS are presented, highlighting the contributions from MC research. Second, an overview is given of the novel modeling approaches based on communication theory and several simulation platforms applicable to the study of drug delivery systems are presented. Finally, lessons are drawn from the efforts of the MC community on this research topic and future research opportunities and challenges are discussed.

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1. Introduction

Drug delivery systems (DDS) are therapeutic techniques at the forefront of pharmacology aiming to deliver drugs to their desired location at a controlled rate and dosage while minimizing the effect on the health parts of the body. The continuing advances in nanotechnology, biotechnology and biomedical engineering enable a better understanding of the physical and biological barriers for drug delivery and the design of molecular compounds with highly customized layouts, content, and physiochemical properties. In addition, the improvements in microelectromechanical systems promise to create micro-sized machines operating in the human body to deliver drugs. Many of these advances have attained the clinical stages and are approved for commercialization.

Despite this progress, many diseases remain challenging to manage due to the undesirable side effects and the poor efficacy and limited patient compliance. Drug delivery systems promise to tackle these hurdles to achieve a controlled rate of drug release with precise location. In conventional medical practice, drugs may be delivered to treat only the diseased part, by using ointment on infected tissue through the skin for example or by injecting drugs directly in the inflamed area of the body. However, some drugs may only be delivered through the circulation in the body.

In parallel with experimental work on DDS, modeling methods have been developed for decades to elucidate the underlying biological and physiochemical mechanisms and enable predictions about future DDS methods, which minimizes the need to perform time-consuming costly in vitro and in vivo experiments. The existing models include analytical models, numerical methods and discrete-event simulations [1,2] that capture the drug release and transport mechanisms. In the face of the complexity of the human body and the countless phenomena affect DDS, a major remaining challenge is to combine the physics-based models of drug release, transport and take-up in a realistic way with a small number of system parameters, validating the results against experimental results, extending the applicability to various types of DDS and accounting for patient variabilities. This is necessary to achieve the goal of creating patient-tailored DDS.

Researchers with a communication theory background have taken up the challenge of DDS complexity. Owing to the numerous similarities between the delivery of therapy and the delivery of information, a new paradigm emerged under the name of molecular communication (MC) where the information is encoded in molecules instead of the electromagnetic signals in classical wireline and wireless communication. MC provides a systems approach for elucidating the principles of multi-scale molecular and biological phenomena. MC brings abstractions traditionally used to characterize the functions of networking and computing systems. Also, MC can formulate DDS problems in a way to be tackled with the mathematical tools used in communications, such as stochastic analysis, information theory and control theory.

Health applications and intra-body communication are one of the major motivations behind MC. Medicine applications of MC are reviewed in general in [3]. There, applications for disease diagnosis and treatment are surveyed, mechanisms for interfacing with non-molecular signals are listed and visionary applications are discussed. Various DDS techniques are discussed, such as virus-based, bacteria-based, antibody-based and nanoparticle-based DDS. Possible transmission mediums for MC networks inside the human body are reviewed in [4]. These include neuronal communication, calcium signaling and hormones. The interactions between these channels are discussed to create heterogeneous MC intra-body networks. A review of nano-scale electromagnetic communication for healthy applications is available in [5] with potential interfacing with MC networks.

In this paper, the focus is put on surveying the existing work on MC for DDS and discussing challenges and future perspectives. First, in Section 2, major target diseases for DDS are presented, the challenges that they pose to therapists are highlighted and relevant MC works on each of these diseases are briefly introduced. Second, in Section 3, the main elements that constitute a DDS, namely routes of administration, release mechanisms, vehicles, cargos, transport processes, take-up and activation, are presented with a review on the available biochemical and biomedical techniques to achieve them. Third, in Section 4, the existing modeling methods relevant to DDS, mainly from the MC field, are presented. Fourth, in Section 5, the research opportunities and challenges to apply MC for DDS are discussed. Finally, Section 6 concludes the paper.

2. Applications

In this section, a few target applications for advanced DDS are described in terms of mechanism, treatment challenges and therapeutic solutions. Relevant work from the communication theory perspective on analyzing these application scenarios are mentioned.

2.1. Cancer therapy

Cancer is a disease characterized by the abnormal proliferation of cells (tumors) inside tissues, threatening the survival of the organism. These abnormal cells all derive from the same initial cancer cell which has developed the ability to divide indefinitely. The migration of these cells from the location of their production is possible, which is a process named metastasis, causing the rapid spread of cancer. Cancer cells may exhibit behaviors such as becoming irresponsive to cellular growth and division stimuli, survival under low nutrient conditions, insensitivity to mechanisms against cell proliferation, the lack of ability for programmed cell death (apoptosis), the ability to construct blood vessels (angiogenesis), tissue invasion and metastasis. At the genetic level, the mutations that lead to cancer cells are either