Optimal Deployment of Multiple Transmitter Drug Delivery System: A Spatial Sampling Theorem Approach

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ABSTRACT

This paper considers a multiple transmitter approach to implement targeted drug delivery (TDD). This approach permits a distributed method of confining drug in irregular shapes of diseased tissue, as well as distributing the released rate among transmitters. A multiple transmitters TDD system is formulated as an image processing problem to derive the minimum number of transmitters, which is required to treat an arbitrary tumor of a given size.

1. INTRODUCTION

Molecular communication (MC) is considered as a key enabling technology for future health related applications due to bio-compatibility, where targeted drug delivery (TDD) stands as one of the most notable applications [2, 3]. Unfortunately, given the small size of nano-transmitters, it is unlikely for a single transmitter to have enough accumulated drug to cover an entire diseased area. A multiple transmitter-based TDD system allows a more efficient synthesis of a desired concentration, hence minimizing potential side effects, as well as distributing the required drug among multiple devices.

Having a large amount of deployed transmitters may, however, increase the complexity of the MC network to a level that nano-transmitters cannot afford. This paper proposes the use of image processing tools that permit transmitters to decide the drug release rate upon their local information. It is also a method that enables fast computation and prediction during the study of such networks. We leverage these tools to optimize the number of transmitters that best approximate the desired drug concentration.

2. SYSTEM DESCRIPTION

Nano-transmitters release medication over an extended period of time to ensure prolonged treatment of the diseased area. In this regimen, the drug concentration needs to be maintained between a minimum referred as Least Effective Concentration (LEC), where drug does not provide the sufficient therapeutic effect, and a maximum referred as the Maximum Tolerated Concentration (MTC), where the drug results in harmful effect for the rest of the body.

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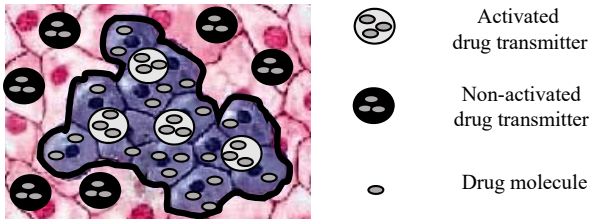

Figure 1: System description

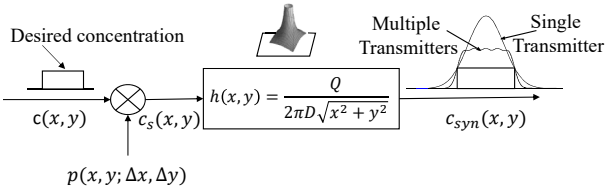

Figure 2: Image processing abstraction

To achieve this, we consider a network of drug transmitters previously distributed throughout the body. These transmitters can be either active or inactive. A generic demonstration of this scenario is shown in Fig. 1.

Nano-transmitters release molecules in a duty cycled manner. This has been demonstrated to approach a constant release rate of molecules [3], which in steady state and with assumption of no absorption, produces the concentration $h(x, y)$ given by [1]:

$$h(x,y) = \frac{Q}{2\pi D\sqrt{x^2+y^2}} \tag{1}$$

where Q is the release rate and D refers to the diffusion coefficient. Provided that the diffusion channel is an LTI system [4], the drug concentration at each point can be calculated as the superposition of concentration of each transmitter at that point.

3. SPATIAL SAMPLING AND RECONSTRUCTION

We have formulated the multiple transmitter TDD problem as an image processing problem. This approach simplifies the system model through which the computations can be done more efficiently. The block diagram of the equiva-

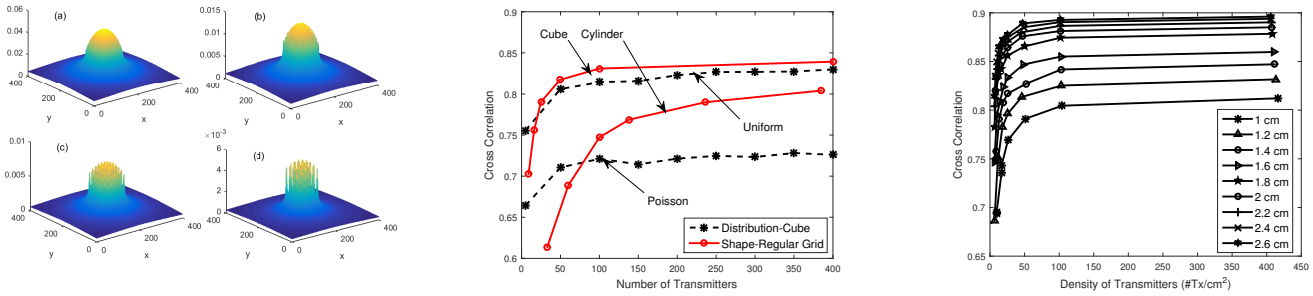

Figure 3: from left to right (i) Synthesizing a cube with 100, 49, 25 and 16 transmitters (ii) Cross correlation of different shapes and different deployment distributions (iii) Cross correlation as function of density of transmitters for several realistic tumor diameters

lent system is shown in Fig. 2. The ideal concentration is set as the 2D input signal, $c(x, y)$. This is sampled by a 2D impulse train $p(x, y; \Delta x, \Delta y)$, which represents the location of the deployed transmitters. This is given by:

$$p(x, y; \Delta x, \Delta y) = \sum_{m=-\infty}^{+\infty} \sum_{n=-\infty}^{+\infty} \delta(x - m\Delta x, y - n\Delta y). \quad (2)$$

Hence, the sampled concentration is given by:

$$\begin{aligned} c_s(x, y) &= c(x, y)p(x, y; \Delta x, \Delta y) \\ &= \sum_{m=-\infty}^{+\infty} \sum_{n=-\infty}^{+\infty} c(m\Delta x, n\Delta y)\delta(x - m\Delta x, y - n\Delta y). \end{aligned} \quad (3)$$

The molecule release of each transmitter operates as the low-pass reconstructing filter in the image processing discipline. This is characterized by (1). The output signal of the equivalent system corresponds to the synthesized concentration, $c_{syn}(x, y)$, given by:

$$\begin{aligned} c_{syn}(x, y) &= c_s(x, y) * h(x, y) \\ &= \frac{Q}{2\pi D} \sum_{m=-\infty}^{+\infty} \sum_{n=-\infty}^{+\infty} \frac{c(m\Delta x, n\Delta y)}{\sqrt{(x - m\Delta x)^2 + (y - n\Delta y)^2}}. \end{aligned} \quad (4)$$

4. SIMULATION RESULTS

In this section, we evaluate the proposed model and the accuracy of the synthesized concentration as a function of the number of transmitters (i.e., sampling rate of the equivalent image processing based system). We consistently consider the cross correlation between the ideal and the synthesized shapes as the basic metric to evaluate their similarity.

We first show in Fig. 3(i) the synthesis of a cubic-shaped concentration for different number of employed transmitters. As shown, the drug molecules are confined to the desired area and their propagation throughout the body is avoided through local deployment of the drug transmitters. In the latter case of 16 employed transmitters, a great deal of fluctuations in the synthesized concentration can be seen; an emphasis on inability of the limited number of transmitters in achieving an accurate estimate of LEC.

Fig. 3(ii) shows the cross correlation between the ideal and synthesized shapes as a function of the number of transmitters. In the figure, we compare the achieved similarity by considering different deployment distributions and shapes. It is observed that the cross correlation increases with the increase of the number of transmitters, for any shape, until it becomes saturated. i.e., there is a minimum number of transmitters for an arbitrary shape after which the similarity does not increase significantly. To calculate the effect of the deployment distribution the simulation has been performed 1000 times for a cubic shape. The uniform distribution outperforms Poisson distribution.

We show in Fig. 3(iii) the cross correlation as a function of density of transmitters, for several realistic tumor diameters. We show that a sampling rate of 100 transmitters per cm^2 is required for an accurate synthesis of desired concentration. It also shows the minimum diameter of a tumor for which we can synthesize a desired concentration with a given accuracy.

5. CONCLUSIONS

A multiple transmitter drug delivery system is proposed in this paper in order to confine drug molecules to the area of tumor. Through a local drug delivery system it is possible to avoid the side effects of propagation of drug molecules to adjacent nearby regions. We formulated the problem as an image processing problem for simplicity and ease of computation. The distribution and the minimum number of transmitters to treat an arbitrary tumor of a given size are investigated.

6. ACKNOWLEDGMENTS

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