Simulation study of a mathematical model of molecular communication based on ligand-receptor binding

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ABSTRACT

Molecular nanomachines are artificial or biological components which are in need to communicate with each other to perform a specific task. For this purpose, we consider two nanomachines called as transmitter nanomachine (TN) and receiver nanomachine (RN). TN transmits molecules in environment and RN receives the molecules through receptors, thus enabling them to communicate each other. The mathematical model which is based on ligand receptor binding is simulated in matlab code. The simulation results show that concentration of molecules, threshold concentration, pulse duration and temperature of environment affect on the channel capacity and thus appropriate values are be selected to achieve for maximum capacity of communication.

Keywords: Nanomachines, Molecular communication, Ligand receptor binding.

1. INTRODUCTION

Nanomachines or Nanosystems are objects with overall dimensions at or below the micrometer range and are made of assemblies of nanoscale components with individual dimensions ranging approximately between 1nm to 100nm. These nanosystems are in need to communicate/coordinate each other to perform a specific task. However, these nanodevices could not be communicated with the existing interconnection systems. Molecular communication is a recent interdisciplinary research area including nanotechnology, biotechnology and communication technology using molecules as a communication carrier [Suda, et al., 2005, Albert et al., 1998]. In nature, molecular communication is observed in living organisms to enable biological phenomena to communicate with each other [Lodish et al., 2000, Whitesides, 2001]. Hiyama et al explains the possibilities and research challenges for molecular communication

[Hiyama, et al., 2005]. In one paper, Suda et al introduce the concept of molecular communication and made an attempt for design of molecular communication system [Suda, et al., 2005, Nakano et al., 2007]. A communication system called gap junctions is described to communicate between two cells in [Akyildiz, et al., 2008]. In another technique, message bearing molecules in a small container known as vesicle conveys them along a filament connecting two devices using molecular motor [Hiyama, et al., 2005, Rospars, et al., 2000]. Cavalcauti et al propose a technique in which molecules may propagate in free space via Brownian motion sending the information in the pattern of molecule [Cavalcanti, et al., 2006]. There are reports on molecular communication based on ligand receptor bindings [Lansky, 2001, Moritani, Hiyama, Suda, 2006, Atakan, Akan, 2007, Lacasa, 2009]. In this paper, the main concern is to study molecular communication based on ligand – receptor interaction and find the optimum parameters such as concentration of emitted molecules, amplitude and duration of pulse of TN, total number of receptors on RN and temperature of the environment. The paper is organized as follows; in section 2, we briefly present the mathematical model available, the computational and simulation is discussed in section 3. The results of the simulation and interpretations are discussed in section 4. Conclusion of the overall work is given in section 5.

2. MATHEMATICAL MODEL

In ligand receptor binding model, the molecules L encounter receptors R and constitute complexes C (bound receptors) as,

$$L + R \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} C$$

If [L] and [R] are the ligand and receptor concentrations, then the rate of change of bound concentration [C] can be obviously written as, [Lansky,2001, Moritani, Hiyama, Suda, 2006, Atakan, Akan, 2007, Lacasa, 2009,]

$$\frac{d[C]}{dt} = -\left(k_{-1} + k_1[L]\right)[C] + k_1[L][N_R] \qquad (1)$$

where k_1, k_{-1}, are the binding rate and release rate respectively and $[R]+[C] = [N_R]$ is the total concentration of receptors available in RN.

Now, equation (1) can be simplified as follows,

$$e^{\left(k_{-1}+k_1[L]\right)t}\frac{d[C]}{dt} + \left(k_{-1}+k_1[L]\right)e^{\left(k_{-1}+k_1[L]\right)t}[C] = (k_1[L][N_R])e^{\left(k_{-1}+k_1[L]\right)t}$$

$$\frac{d}{dt}\left[[C]\,e^{\left(k_{-1}+k_1[L]\right)t}\right] = (k_1[L][N_R])\,e^{\left(k_{-1}+k_1[L]\right)t}$$

$$\left[[C]\,e^{\left(k_{-1}+k_1[L]\right)t}\right] = (k_1[L][N_R])\frac{e^{\left(k_{-1}+k_1[L]\right)t}}{\left(k_{-1}+k_1[L]\right)} + A$$

$$[C] = \frac{k_1[L][N_R]}{\left(k_{-1}+k_1[L]\right)} + A\,e^{-\left(k_{-1}+k_1[L]\right)t}$$

Considering the initial condition: t = 0 and [C(0)] = 0

$$A = -\frac{k_1[L][N_R]}{\left(k_{-1}+k_1[L]\right)}$$

$$[C] = \frac{k_1[L][N_R]}{\left(k_{-1}+k_1[L]\right)}\left[1-e^{-\left(k_{-1}+k_1[L]\right)t}\right]$$

Then, $$[C(t)] = [C(\infty)]\left[1-e^{-\left(k_{-1}+k_1[L]\right)t}\right] \quad (2)$$

Here [C_∞] is the steady state concentration of bound receptors,

$$[C(\infty)] = \frac{k_1[L][N_R]}{\left(k_{-1}+k_1[L]\right)}$$

3. COMPUTATIONAL AND SIMULATION

We assume TN emits molecules with concentration [L(t)] in the form of pulses with amplitude [L] (μmol/liter) during t_o seconds with probability P_L of releasing ligand molecule

[L(t)] = [L] ; $n\,t_o \le t \le n\,t_o + t_o$ (n = 0, 1, 2, 3, ...)

and [L(t)] = 0 with probability ($1-P_L$) otherwise. (3)

During the pulse time, concentration of [C(t)] (μmol/liter) rises exponentially and at time t_o when the pulse duration ends, [C(t)] starts to decay accordingly

$[C(t)] = [C_\infty]\,(1 - e^{-t(k_{-1}+k_1[L])})$ for $0 \le t \le t_o$
$[C(t)] = [C_{to}]\,e^{-k_{-1}(t-to)}$ for $t \ge t_o$ (4)

In molecular communication paradigm, during the interval t_o, TN can emit either molecules (L) or transmit no molecule resulting in two molecular bits called MB1 and MB0. Consequently, if RN sense a concentration of molecules which is greater than a prescribed concentration [S] (μmol/liter), RN decides TN has transmitted molecular bit MB1 during t_o. Conversely, if that concentration is less than [S], RN decides TN transmitted molecular bit MB0. The concentration of delivered molecules within t_o, [N_L] is given by

$$[N_L] = \int_0^{t_o}[C(t)]\,dt$$

$$[N_L] = \int_0^{t_o}\frac{k_1[L][N_R]}{k_{-1}+k_1[L]}\left(1-e^{-t(k_{-1}+k_1[L])}\right)dt \quad (5)$$

Since TN is continuously emitting every t_o, the previous delivered bits affect the concentration of molecules in the current interval. Hence, the concentration of complexes coming from the previous interval that still remain in the current interval can be given as follows

$$[N_{LP}] = P_L[N_L]\int_0^{t_o} e^{-k_{-1}t}dt \quad (6)$$

Therefore, the expected total concentration of delivered molecules during t_o, will be $[N_T]= [N_L] + [N_{LP}]$. Consequently the maximum probability of having success in transmission of a MB1 can be written as $p_1 = [N_T]/[S]$ and $(1-p_1)$ is the probability for receiving the erroneous MB0. Thus TN achieves to deliver MB0 successfully with probability, $p_2 = [S]/[N_{LP}]$ and it does deliver it incorrectly with probability $(1-p_2)$. It is also possible to detect erroneous molecular communication bits at RN side, by detecting MB1 when TN intended to transmit MB0 or vice versa. Thus the molecule delivery capacity is defined as the maximum number of non-erroneous molecular bits which can be delivered within specific time duration. According to P_L, p_1 and p_2, the channel can be modeled as a symmetric channel and then transition matrix M, is given by

$$M = \begin{pmatrix} P_L p_1 & (1-P_L)(1-p_2) \\ P_L(1-p_1) & p_2(1-P_L) \end{pmatrix} \quad (7)$$

Based on the transition matrix, the mutual information (MI) which states the number of distinguishable molecular bits, is as follows

$$MI = -\left[P_L\frac{[N_T]}{[S]} + (1-P_L)\left(1-\frac{[S]}{[N_{LP}]}\right)\right]\log\left[P_L\frac{[N_T]}{[S]} + (1-P_L)\left(1-\frac{[S]}{[N_{LP}]}\right)\right]$$

$$-\left[P_L\left(1-\frac{[N_T]}{[S]}\right) + (1-P_L)\frac{[S]}{[N_{LP}]}\right]\log\left[P_L\left(1-\frac{[N_T]}{S}\right) + (1-P_L)\frac{[S]}{[N_{LP}]}\right]$$

$$-P_A\left[\frac{[N_T]}{[S]}\log\left(\frac{[N_T]}{[S]}\right) - \left(1-\frac{[N_{LP}]}{[S]}\right)\log\left(1-\frac{[N_T]}{[S]}\right)\right]$$

$$-(1-P_A)\left[\frac{[S]}{[N_{LP}]}\log\left(\frac{[S]}{[N_{LP}]}\right) - \left(1-\frac{[S]}{[N_{LP}]}\right)\log\left(1-\frac{[S]}{[N_{LP}]}\right)\right] \quad (8)$$

Finally, the capacity of molecular channel between TN and RN that is the maximum number of non erroneous molecular bits delivered within t_o, is max (MI) [Atakan, Akan, 2007, Lacasa, 2009].

4. NUMERICAL RESULTS AND DISCUSSION

For starting numerical calculation, we take the initial simulation parameter from the literature [Lansky,2001, Moritani, Hiyama, Suda, 2006, Atakan, Akan, 2007, Lacasa, 2009]. First, we calculate MI varying with probability P_L for different prescribe concentration [S] to fix appropriate concentration of molecules (threshold concentration) that must be delivered to RN within time interval t_o for a successful delivery of MB1. For this simulation, k_1=0.1 µmol/liter/sec, [L]=1 µmol/liter, $[N_R]$=0.001 µmol/liter, k_{-1}=0.0001 1/sec, t_o=1 sec are used. In figure 1, MI is shown with varying P_L for different values of [S]=0.0001 µmol/liter, 0.00001µmol/liter, 0.000001 µmol/liter.

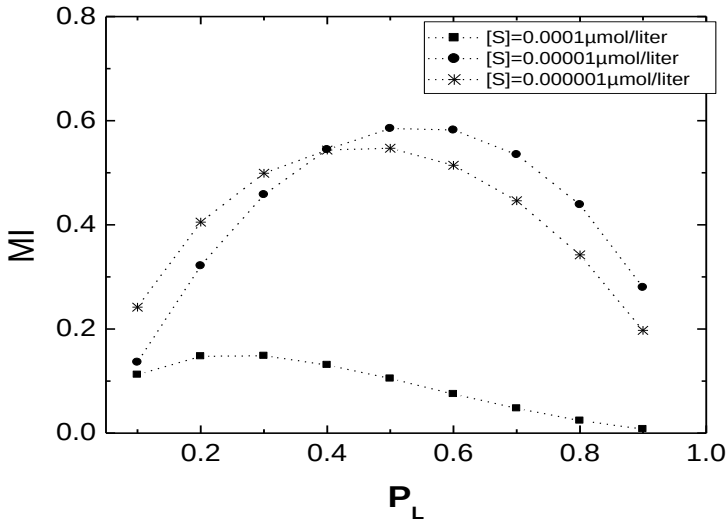

Figure 1
MI verses P_L for different concentrations [S].

It shows that for lower concentrations [S]=0.00001 µmol/liter and 0.000001 µmol/liter, max(MI) increases with appropriate P_L. It indicates that there is possibility to deliver non-erroneous MB1. However, for the higher concentration [S]=0.0001 µmol/liter, max(MI) is small and in the lower side of the probability P_L. From this analysis, we consider [S] in between $1.0*10^{-6}$ µmol/liter to $9.0*10^{-6}$ µmol/liter for further simulation. Figure 2 shows the plot of MI with variation of P_L for different pulse amplitude [L]=0.5 µmol/liter to 3 µmol/liter. It is required to find appropriate amplitude such that TN can deliver sufficient concentration to RN. For this simulation we have taken [S] =1.0e-6 µmol/liter. It is found that [L] smaller than 0.5 µmol/liter cannot give maximum MI. However [L] greater than 0.5 µmol/liter is sufficiently high to achieve maximum MI. Therefore, appropriate value of [L] must be selected to achieve maximum molecular communication capacity.

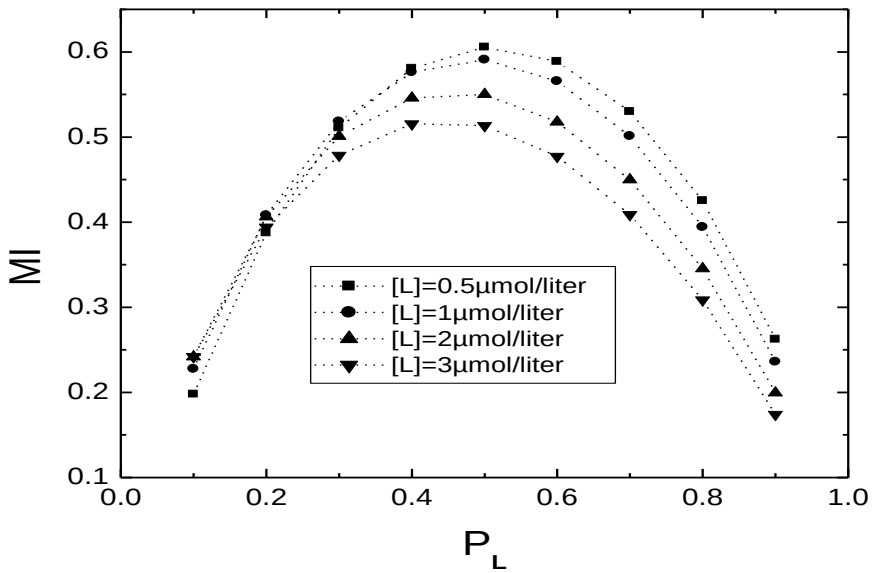

Figure 2
MI verses P_L for different pulse amplitude [L].

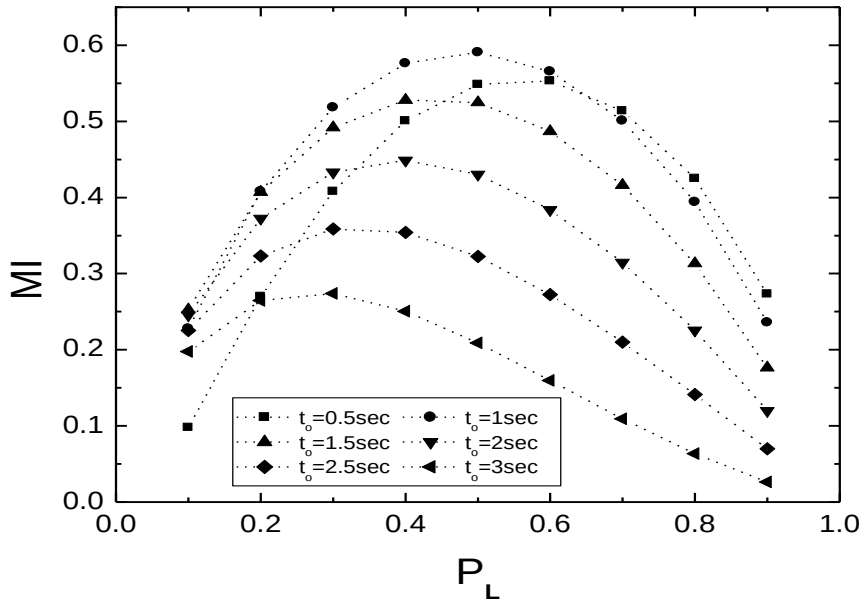

Figure 3
MI verse P_L for different pulse duration t_o.

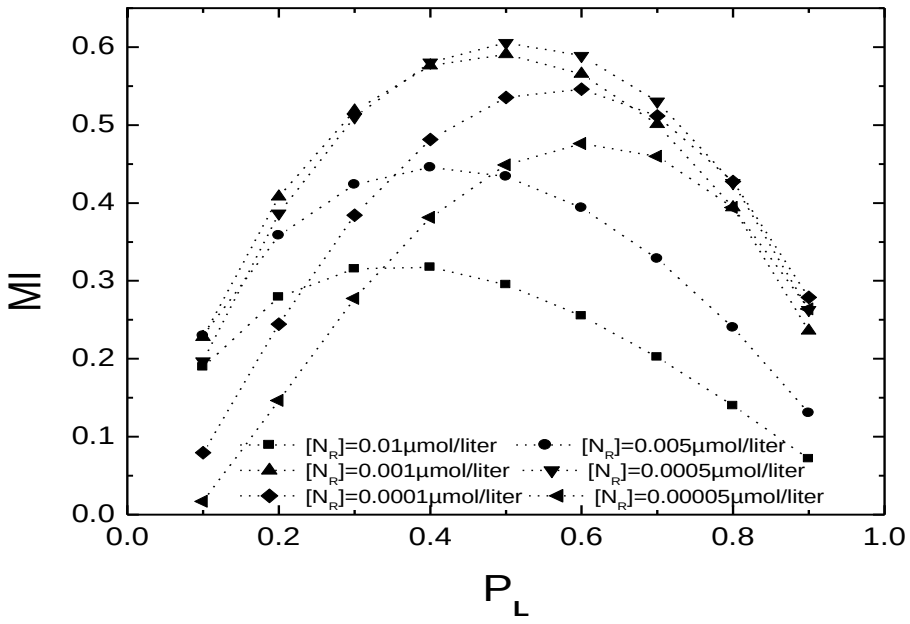

Figure 4
MI verses P_L for different concentration of receptors $[N_R]$ on RN

The pulse duration t_o is also an important simulation parameter. Figure 3 shows the plot of MI verses P_L for different values of pulse duration t_o. For t_o=0.5 sec and 1 sec, maximum MI is obtained. However, t_o greater than 1sec, maximum MI decreases at the lower side of P_L. It indicates that TN cannot deliver appropriate concentration of molecules to RN at higher pulse duration.

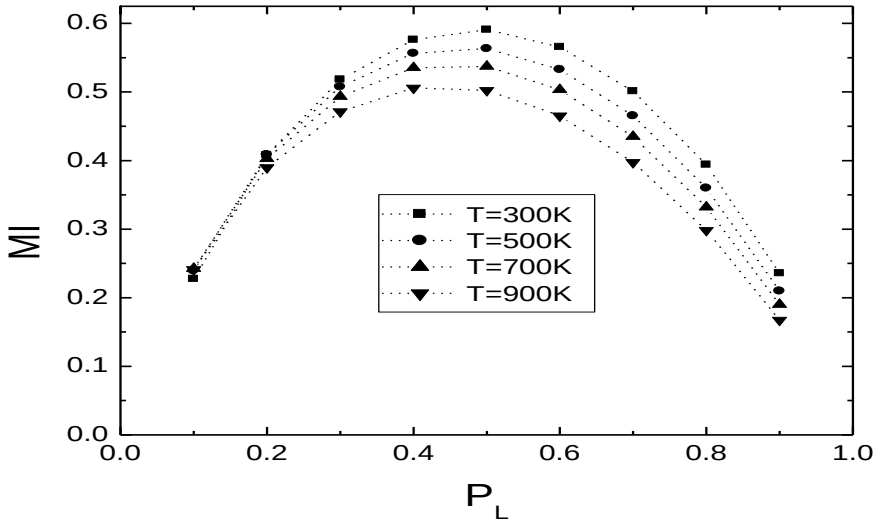

Figure 5
MI verses P_L for different temperature T of environment

For concentrations of receptors on RN, $[N_R]$=0.01 μmol/liter to 0.00005 μmol/liter, the plot of MI with varying P_L is shown in figure 4. It is seen that for lower values of $[N_R]$=0.00005 μmol/liter, and 0.0001 μmol/liter, the max(MI) is low at the higher probability. This is probable that although TN transmits sufficient number of molecules; there cannot be formed sufficient number of ligand receptor complexes on RN because of small concentration of receptors on RN. If we consider a higher concentration $[N_R]$=0.01 μmol/liter, the maximum MI is still low. It means that TN may transfer more than the prescribe concentration to RN for delivery MB0 results in an erroneous molecular MB1. In between the concentration in the range $[N_R]$=0.001 μmol/liter to 0.005 μmol/liter shows maximum MI at appropriate probability. Therefore, it is required to select appropriate range of $[N_R]$ to optimize communication capacity. Figure 5 shows the plot of MI with varying P_L for different temperatures T of environment. It is seen in the figure, for T= 300 K to 900 K, maximum MI can be achieved at an appropriate probability but as T increases, maximum MI decreases. It may be attributed due to increase of T, k_{-1} decreases and k_1 increases such that TN can transmit higher concentration of molecules. On the other hand, TN cannot deliver concentration smaller than [S] for transmission of MB1. So here is the erroneous transfer of molecular bit. Hence, temperature of environment in which molecular transfer takes place is also an important parameter to achieve higher communication capacity.

5. CONCLUSION

In this paper, we have studied a simplified mathematical model for the possibility of molecular communication in the light of ligand receptor model. The simulation results revealed that concentration of emitted molecules, amplitude and duration of pulse of the transmitter nanomachine, total number of receptors on the receiver nanomachine and temperature of the environment affect the molecular communication capacity. We conclude that appropriate values of the above mentioned parameters are to be selected so that maximum channel capacity may be achieved.

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