Communication via FRET in Nanonetworks of Mobile Proteins

Jakub Kmiecik
Department of Telecommunications, AGH University of Science and Technology
Al. Mickiewicza 30
30-059 Krakow, Poland
jkmiecik@agh.edu.pl

Pawel Kulakowski
Department of Telecommunications, AGH University of Science and Technology
Al. Mickiewicza 30
30-059 Krakow, Poland
kulakowski@kt.agh.edu.pl

Krzysztof Wojcik
Division of Cell Biophysics, Faculty of Biochemistry, Biophysics and Biotechnology, Jagiellonian University
7 Gronostajowa St.
30-387 Krakow, Poland
krzysztof.wojcik@uj.edu.pl

Andrzej Jajszczyk
Department of Telecommunications, AGH University of Science and Technology
Al. Mickiewicza 30
30-059 Krakow, Poland
jajszczyk@kt.agh.edu.pl

ABSTRACT
A practical, biologically motivated case of protein complexes (immunoglobulin G and FcRII receptors) moving on the surface of mastcells, that are common parts of an immunological system, is investigated. Proteins are considered as nanomachines creating a nanonetwork. Accurate molecular models of the proteins and the fluorophores which act as their nanoantennas are used to simulate the communication between the nanomachines when they are close to each other. The theory of diffusion-based Brownian motion is applied to model movements of the proteins. It is assumed that fluorophore molecules send and receive signals using the Förster Resonance Energy Transfer. The probability of the efficient signal transfer and the respective bit error rate are calculated and discussed.

CCS Concepts
•**Applied computing~Biological networks**•*Networks~Network performance evaluation*•*Networks~Mobile networks*•Computing methodologies~Molecular simulation.

Keywords
Molecular communication; nanocommunication; FRET; nanonetworks; communication channel; MIMO.

1. INTRODUCTION AND FRET BASICS
As the nanotechnology is rapidly expanding, there is an urgent need for designing communication schemes for nanodevices. One of the most promising communication techniques is Förster Resonance Energy Transfer (FRET), which is a physical phenomenon where an excited molecule, called donor, non-radiatively passes its energy to another molecule, called acceptor, located in its vicinity. Both molecules must be spectrally matched, i.e., the donor emission spectrum should overlap the acceptor absorption spectrum. Such a pair of molecules may be seen as a wireless communication system: the donor is a transmitter antenna and the acceptor plays the role of the receiver antenna. The probability of successful transmission may be increased if there are more molecules involved, i.e., more donors and acceptors at both sides of the communication channel. Having all the donors excited at the same time, it is enough that one of them passes its energy to an acceptor, then the signal is successfully sent via the communication channel. On the basis of our previous work [7], we may calculate the probability that at least one FRET process occurs in a channel with n donors and m acceptors:

$$E_{n,m} = 1 - \prod_{k=1}^{n} \left(1 - \frac{R_0^6 \sum_{i=1}^{m} \frac{1}{r_{ki}^6}}{1 + R_0^6 \sum_{i=1}^{m} \frac{1}{r_{ki}^6}} \right) \quad (1)$$

The variable r_{ki} is the separation between the k-th donor and the i-th acceptor and R_0 is the so-called Förster distance which is a parameter characteristic for each pair of two molecules, depending on their emission/absorption spectra.

Adopting, like in [1], the ON-OFF modulation scheme, we may send bit '1' exciting all the donors at once; the transmission is then successful with the probability $E_{n,m}$. Bit '0' is sent just by keeping all donors in the ground state, i.e., not exciting them; such a transmission is always successful. Assuming that transmissions of '0' and '1' are equally probable, the bit error rate is equal to:

$$\mathrm{BER} = 0.5\left(1 - E_{n,m}\right) \quad (2)$$

FRET for the nanocommunication purposes was proposed a few years ago [4, 1] and studied both theoretically and experimentally [2, 5, 7]. FRET is characterized by small propagation delays, usually few dozens of nanoseconds, and allows for transmissions of data streams with bit rates of several Mbit/s.

2. THE MOBILE FRET NETWORK
We consider a scenario of a mobile nanonetwork motivated by a real biological situation. We analyze antibodies moving on the surface of a mast cell. These cells, having the average diameter of about 10 micrometers, are covered by a lipid membrane. There are, on average, 40 thousand of antibodies (immunoglobulin) on the surface of each mast cell. Each antibody is attached to an Fc receptor, which can, however, float freely in the lipid membrane.

Antibodies are very well suited to act as nanomachines. They may perform several functions in living organisms, recognizing and binding other molecules. Smaller molecules called fluorophores may be mounted on the antibodies (*antibodies are labeled*). The fluorophores serve as nanoantennas and communicate with other fluorophores mounted on other antibodies via FRET.

NANOCOM'16, September 28 - 30, 2016, New York, NY, USA

ACM 978-1-4503-4061-8/16/09 …$15.00
DOI: http://dx.doi.org/10.1145/2967446.2967477

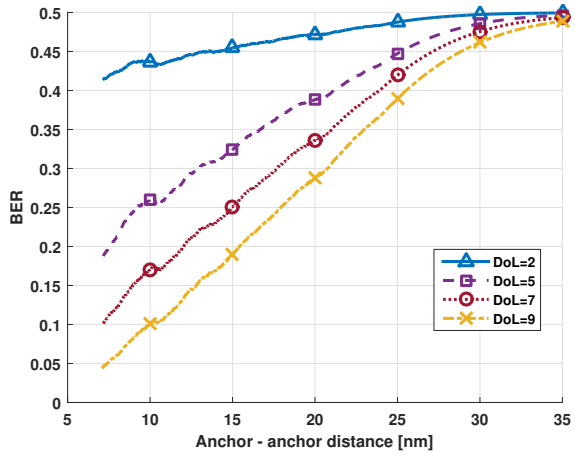

Fig. 1. Bit error rate for two communicating nanomachines as a function of their separation.

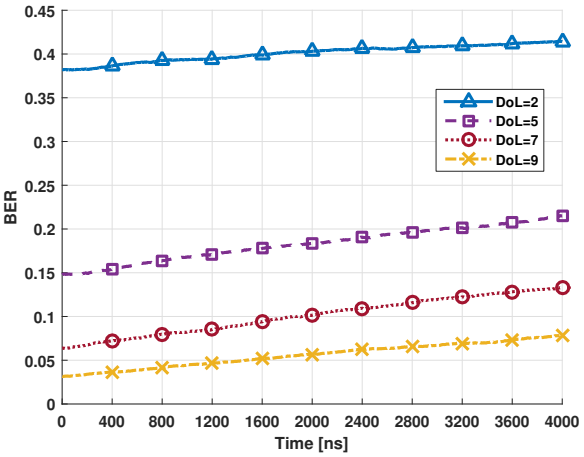

Fig. 2. Bit error rate for two communicating nanomachines moving via Brownian motion.

The antibodies together with Fc receptors move over the surface of the lipid membrane fueled by Brownian motion. As Brownian motion is a random process, it cannot be exactly predicted if two specific antibodies approach each other during their movement. Having in mind the high density of antibodies on the membrane, about 30 molecules per square micrometer, we can, however, assume that antibodies are frequently very close to each other. Here, we focus on a pair of antibodies located close enough to each other that the FRET communication is possible. Because of the randomness of the antibodies movement, we cannot predict the exact moment of the closeness. Instead, we track their movement when they are already in a close distance and they move freely, which finally makes them separated. We calculate the efficiency of the FRET transmission and the channel BER.

3. SIMULATION SCENARIO

Computer simulations have been performed using suitable structural models of all the network components. The molecular structures of antibodies, immunoglobulin G, have been taken from Protein Data Bank (available online). These antibodies are about 15 nm long, with a characteristic shape of 3-element airscrew. As fluorophores, we have chosen Atto 610 dyes as donors and Atto 655 dyes as acceptors. The Förster distance between chosen dyes is quite large, i.e., 7.6 nm, which is very advantageous for efficient FRET transmission. Fluorophores are much smaller particles, with the diameter of about 1.5 nm; their models are available at PubChem database. The degree of labeling (the number of donors/acceptors per antibody) for Atto dyes ranges from 2 to 9 and these values were simulated. The exact fluorophores positions and nanomachines orientations were chosen randomly in each of 1000 simulation runs. The movements of the Fc receptor and the antibody with Atto fluorophores were simulated according to the formula of Brownian motion [3]:

$$B(t_2) - B(t_1) \sim N\left(0, \sigma^2(t_2 - t_1)\right) \quad (3)$$

In the formula above, $B(t_1)$, $B(t_2)$ represent positions of an antibody at times t_1, t_2 respectively, so $B(t_2) - B(t_1)$ is a shift of the antibody in the time interval $t_2 - t_1$. The shift is a Gaussian random variable with 0 mean and $\sigma^2(t_2 - t_1)$ variance. The variance is dependent on the free diffusion coefficient D of the considered particle and equals $\sigma^2 = 2D$. The rotational diffusion has been neglected because of the small value of its diffusion coefficient [6].

4. BIT ERROR RATE RESULTS

First, we measured how the BER depends on the average distance between the communicating nanomachines. The results are presented in Fig. 1. Second, we investigated *how long* the communication might take place. Assuming that two antibodies were already very close to each other (just 1 nm of surface-to-surface separation), we simulated their movements with Brownian motion and calculated how the BER depended on time. The simulation results for different degrees of labeling (DoL) are given in Fig. 2. The results show that the transmission may be maintained over a few thousand of nanoseconds, especially when the transmitting and receiving nanomachines (proteins) are equipped with large number of nanoantennas (fluorophores).

5. REFERENCES

[1] M. Kuscu, O.B. Akan, A Physical Channel Model and Analysis for Nanoscale Communications with Förster Resonance Energy Transfer (FRET), IEEE Trans.on Nanotechnology, vol. 11, no. 1, pp. 200-207, January 2012.

[2] M. Kuscu, A. Kiraz, O.B. Akan, Fluorescent Molecules as Transceiver Nanoantennas: The First Practical and High-Rate Information Transfer over a Nanoscale Communication Channel based on FRET,Nature Scientific Reports, vol. 5, no. 7831, January 2015.

[3] T. Nakano, A.W. Eckford, T. Haraguchi, Molecular Communication, Cambridge University Press, 2013.

[4] L. Parcerisa, I.F. Akyildiz, Molecular Communication Options for Long Range Nanonetworks, Computer Networks (Elsevier) Journal, vol. 53, pp. 2753-2766, 2009.

[5] K. Solarczyk, K. Wojcik, P. Kulakowski, Nanocommunication via FRET with DyLight Dyes using Multiple Donors and Acceptors, IEEE Trans. on NanoBioscience, vol. 15, no. 3, pp. 275-283, April 2016.

[6] M. M. Timbs, N. L. Thompson, Slow rotational mobilities of antibodies and lipids associated with substrate-supported phospholipid monolayers as measured by polarized fluorescence photobleaching recovery, Biophys J., vol. 58(2), pp. 413-428, Aug., 1990.

[7] K. Wojcik, K. Solarczyk, P. Kulakowski, Measurements on MIMO-FRET nanonetworks based on Alexa Fluor dyes, IEEE Trans. on Nanotechnology, vol. 14, no. 3, pp. 531-539, May 2015.