A Physical Channel Model and Analysis for Nanoscale Molecular Communications With Förster Resonance Energy Transfer (FRET)

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***Abstract*—In this study, a novel and physically realizable nanoscale communication paradigm is introduced based on a well-known phenomenon, Förster resonance energy transfer (FRET), for the first time in the literature. FRET is a nonradiative energy transfer process between fluorescent molecules based on the dipole–dipole interactions of molecules. Energy is transferred rapidly from a donor to an acceptor molecule in a close proximity such as 0 to 10 nm without radiation of a photon. Low dependence on the environmental factors, controllability of its parameters, and relatively wide transfer range make FRET a promising candidate to be used for a high-rate nanoscale communication channel. In this paper, the simplest form of the FRET-based molecular communication channel comprising a single transmitter–receiver nanomachine pair and an extended version of this channel with a relay nanomachine for long-range applications are modeled considering nanomachines as nanoscale electromechanical devices with some sensing, computing, and actuating capabilities. Furthermore, using the information theoretical approach, the capacities of these communication channels are investigated and the dependence of the capacity on some environmental and intrinsic parameters is analyzed. It is shown that the capacity can be increased by appropriately selecting the donor–acceptor pair, the medium, the intermolecular distance, and the orientation of the molecules.**

***Index Terms*—Förster resonance energy transfer (FRET), nanoscale communications.**

I. Introduction

NANOSCALE communication is a novel and quite interdisciplinary research area. Several potential approaches have been proposed in order to achieve communication in the nanoscale such as electromagnetic, acoustic, or molecular [1], [2]. In this paper, we introduce a novel and radically different method for the communication in the nanoscale by exploiting a well-known, physical controllable phenomenon, Förster (or fluorescence) resonance energy transfer (FRET).

FRET is a nonradiative energy transfer process between fluorescent molecules, and it is widely used in studies of biotechnological research including fluorescence microscopy, molecular biology, and optical imaging [3], [4]. The phenomenon yields a significant amount of structural information about the donor and acceptor pair; therefore, many methods based on FRET have been developed and used in these areas. For example, using its strong dependence on distance, FRET is exploited as a spectroscopic ruler [5] while determining the intramolecular and intermolecular distances and monitoring the conformational changes of proteins [6]. FRET is also used in molecular and quantum computing studies as a tool for creation of entangled quantum states [7], [8].

In this study, for the first time in the literature, FRET has been approached from the communication perspective and introduced as a novel molecular communication paradigm. There are many biologically inspired and theoretically modeled molecular communication techniques in the literature including the communication models devised based on intercellular calcium signaling [9], pheromones [10], flagellated bacteria and catalytic nanomotors [11], carbon nanotubes [12], pollen and spores [10], as well as morphogenesis [13] in order to encode, transfer, and decode information. The FRET-based communication method is based on a physically existing phenomenon, and unlike the other techniques, it provides significantly higher capacity communication. The excited-state energy of molecules that conveys the information is transferred in the nanosecond range so that FRET-based communication is incomparably faster than the already proposed nanoscale communication techniques. Furthermore, high-level controllability of almost all of the system parameters makes FRET-based channel more reliable. The abundance of both theoretical and practical studies about FRET in the literature and availability of its experimental setups provide the opportunity of making improvements, validating theoretical model based on experiments. Hence, unlike most of the existing approaches in the literature, we introduce an already analyzed and experimented, therefore, a physically realizable, and hence, clearly realistic solution to the problem of nanoscale communication.

In this paper, we have also extended our work in [14] by enhancing the FRET-based communication channel in order to realize nanoscale communication over distances longer than 10 nm with the integration of a relay node between the transmitter and the receiver. In the extended model, excited energy of the donor is transferred first to the fluorophore on the relay nanomachine; afterward, the excited relay transfers its energy to the acceptor on the receiver via FRET. This sequential energy transfer (also called multistep FRET in the literature) is achieved

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experimentally in some studies related to fluorescence spectroscopy such as [15], [16] locating several numbers of fluorophores in a linear order over several distances. This enhancement shows the potential of the FRET-based nanoscale communication in the sense that it can be extended further being a solution for long-range nanoscale communication and similar network schemes such as multiple access or broadcast.

The remainder of this paper is organized as follows. In Section II, we explain the basic concepts of FRET and underline the governing physical laws and its mathematical formulation. In Section III, we model the FRET-based communication channel with a single donor–acceptor pair. In Section IV, the extended version of the channel with an addition of a relay node is modeled to realize a longer range communication based on FRET. An information theoretical analysis of FRET-based channel is performed in Section V in order to determine the closed-form expression for the capacity of the channel. In Section VI, we analyze the dependence of the channel capacity on some environmental and intrinsic factors and demonstrate a selection strategy for these parameters to achieve higher communication capacity. Besides, we investigate the dependence of the capacity of the channel with a relay node on internodal distances. Finally, the concluding remarks are given in Section VII.

II. Theory of FRET

FRET is nonradiative energy transfer process observed among fluorescent molecules (fluorophores), i.e., the molecules with the ability of absorbing energy at a specific range of wavelength and emitting that absorbed energy at a different wavelength [17]. Quantum dots, organic dyes, and polymers are the most frequently used fluorophores in FRET studies. This electrodynamic phenomenon is based on long-range dipole–dipole interaction between a donor fluorophore in its excited state and an acceptor fluorophore in its ground state which are in a close proximity. When the donor is excited by an incident light, it may transfer its energy to an acceptor molecule through FRET and relaxes to its ground state, if certain conditions are satisfied. First of all, donor and acceptor must be located in a close proximity like 0–10 nm. In addition, the spectral characteristics of donor and acceptor must have significant similarity, i.e., the overlapping area of the emission spectrum of donor and the absorption spectrum of acceptor must be large enough. If these conditions are not satisfied, FRET does not occur, and in the case of donor excitation, donor relaxes to its ground state by releasing a photon.

In 1948, Förster postulated the governing equations in the theory of nonradiative energy transfer in his well-known article [18]. The first parameter that characterizes the donor–acceptor pairs is the Förster radius; the distance between donor and acceptor when the efficiency of the energy transfer is 50% and given by

$$R_0^6 = \frac{9000\ln(10)\kappa^2 Q_D}{128\pi^5 N n^4}\int_0^\infty F_D(\lambda)\epsilon_A(\lambda)\lambda^4 \mathrm{d}\lambda \tag{1}$$

where the κ^2 is the orientation factor, Q_D is the quantum yield of the donor, n is the refractive index of the medium, and N is

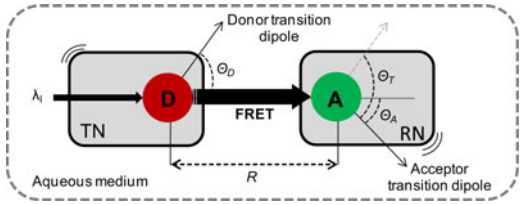

Fig. 1. Point-to-point FRET-based molecular communication channel model with single TN and RN communicating via FRET.

Avagadro's number. The integral part of (1) yields the degree of the overlap of the emission spectrum of the donor and the absorption spectrum of the acceptor and denoted by $J(\lambda)$:

$$J(\lambda) = \int_0^\infty F_D(\lambda)\epsilon_A(\lambda)\lambda^4 \mathrm{d}\lambda \tag{2}$$

where $F_D(\lambda)$ is the normalized fluorescence emission intensity and $\epsilon_A(\lambda)$ is the acceptor molar absorptivity. Here, the orientation factor (κ^2) is the most problematic, i.e., with the highest uncertainty, parameter given in [19] as

$$\kappa^2 = (\cos\theta_T - 3\cos\theta_D\cos\theta_A)^2 \tag{3}$$

where θ_T, θ_D, and θ_A are the angles determined by the emission and absorption transition dipoles of the fluorophores as shown in Fig. 1. It is not possible to determine the exact relative orientation of donor and acceptor, i.e., the exact value of κ^2; however, it ranges between 0 and 4. In most studies, donor and acceptor are supposed to randomly rotate and κ^2 is assumed to be $2/3$ which is the mean value [17].

The efficiency of energy transfer as a function of intermolecular distance and Förster radius R_0 is formulated as

$$E(R) = \frac{R_0^6}{R_0^6 + R^6} \tag{4}$$

where R is the distance between the donor and the acceptor [17].

The rate of the energy transfer is given by

$$k_T(R) = \frac{1}{\tau_D}\left(\frac{R_0}{R}\right)^6 \tag{5}$$

where τ_D is the donor lifetime, i.e., the average time the donor remains in its excited state [17]. Normally, in the absence of any nonradiative relaxation process, it is determined by only the radiative emission rate k_R and given in [17] as

$$\tau_D = \frac{1}{k_R}. \tag{6}$$

In the case of FRET, the energy transfer to the acceptor causes a reduction in donor's excited state lifetime, and it can be formulated as

$$\tau_{DA} = \frac{1}{k_R + k_T} \tag{7}$$

where τ_{DA} is the donor's excited state lifetime before it releases the energy through FRET [17].

III. FRET-Based Nanoscale Communication Channel

We constructed our communication model with a single-donor fluorescence molecule (D) bound to a transmitter nanomachine (TN), and a single-acceptor fluorescence molecule (A) bound to a receiver nanomachine (RN), at fixed locations separated by a reasonable distance R in an aqueous medium considering FRET as the communication channel with the system exciton, i.e., the combined state of electron and hole, being a carrier as shown in Fig. 1, where θ_T is the angle between the emission transition dipole of donor and the absorption transition dipole of the acceptor, θ_D and θ_A are the angles between these dipoles and vector joining the donor and the acceptor, respectively. The arrow between D and A shows the FRET direction. Other arrows show the transition dipoles of D and A as well as the direction of incoming photon with a wavelength of λ_i. Assuming the molecules are properly selected, i.e., they have sufficient spectral overlap $J(\lambda)$, in the case of a donor excitation, FRET occurs with probability of P_{FRET}.

When a laser source excites the donor at a proper wavelength, basically there are two ways of relaxation for the donor: the first one is through radiative emission, i.e., fluorescence, and the second one is through FRET, disregarding the other low-probability nonradiative relaxation pathways such as dissipation as heat or collision with another molecule, i.e., collisional quenching as well as intersystem crossing to an excited triplet state which can actually result in phosphorescence.

In FRET spectroscopy, the FRET efficiency is determined by continuously exciting the donor and calculating the proportion of the number of FRET relaxations to the number of total relaxation processes in a specified time interval [20]. Therefore, for a single cycle of excitation and relaxation of the donor, the efficiency can be considered as the probability of the excited donor to relax via FRET. Thus, using (4), for a single exciton, the probability of FRET as a function of intermolecular distance can be given by

$$P_{\mathrm{FRET}}(R) = E(R) = \frac{R_0^6}{R_0^6 + R^6} \tag{8}$$

where R_0 is the Förster radius and it is calculated according to (1). In [21], in a medium of water with a refractive index of 1.3342 at 25 °C, assuming rapid randomization of relative orientation of molecules, i.e., $\kappa^2 = 2/3$, for a pair consisting of enhanced cyan fluorescent protein (ECFP) as donor and enhanced yellow fluorescent protein (EYFP) as acceptor, the Förster radius is calculated as 4.92 nm. Both ECFP and EYFP are the variants of green fluorescent protein (GFP) and widely used in various fluorescence spectroscopy applications for their similar spectral characteristics, photostability, high extinction coefficients, and high quantum yields [22]. At the same time, the pair ECFP–EYFP is a good candidate for communication purposes due to the relatively large value of R_0.

In the FRET-based communication model, donor excitation is realized by a pulsed laser which has a wave shape approximated in Fig. 2. The duration of pulses can be selected very short compared to the lifetimes of the fluorophores used because of energy saving concern. The laser is considered as the main information source of the communication system and is not considered to be a part of TN at present due to energy and size limitations. Vast number of photons released by the laser with wavelengths near to the excitation maximum of the donor guarantee the donor excitation in femtoseconds duration, since the absorption probability of the donor is almost 1 for that wavelengths. Therefore, in the subsequent probability calculations, the probability of donor excitation at any instant of laser pulse duration is assumed to be 1.

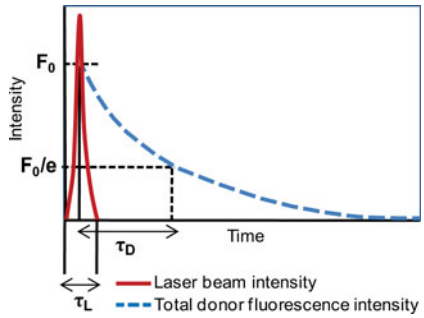

Fig. 2. Approximated laser pulse shape and lifetime determination.

Excited state lifetime is determined by measuring and recording the fluorescence times of many fluorophores of the same kind after an excitation by a very small duration pulsed laser and calculating the mean of these records as shown in Fig. 2. Therefore, it is very possible for the employed donor and acceptor not to have the anticipated lifetimes. The lifetime of a fluorophore is a critical parameter in determination of the laser excitation period T_H in the sense that an excited fluorophore cannot be re-excited until it relaxes to the ground state [23]. For example, the donor molecule cannot transfer the excited state energy to the acceptor through FRET if the acceptor is still in its excited state as a result of the preceding FRET process. Therefore, we consider the worst—with the longest duration—case while determining T_H.

In the model, we implemented ON–OFF keying (OOK) modulation with two bits available as in the traditional digital communications. The excitation of the donor by the information source at the beginning of a time interval T_H corresponds to bit 1, and no-excitation at the beginning of a time interval corresponds to bit 0. The RN is assumed to have the ability of checking whether the acceptor is excited through FRET or not during the corresponding time interval. If it is excited through FRET, it decides that the TN transmitted bit 1; otherwise, it decides that the TN transmitted bit 0. With further investigations on nanoscale system design, such RN designs can be potentially realizable. At current FRET studies, acceptor fluorescence is observed with a system comprising a photomultiplier tube and a near-field scanning optical microscope in order to detect whether or not FRET occurs [24]. This mechanism is considered to be used as the ultimate destination of information in the future studies aiming to validate the FRET-based communication channel experimentally.

In Fig. 3, conceptually, we demonstrate the different cases for data transmission. For the case in Fig. 3(a), a laser

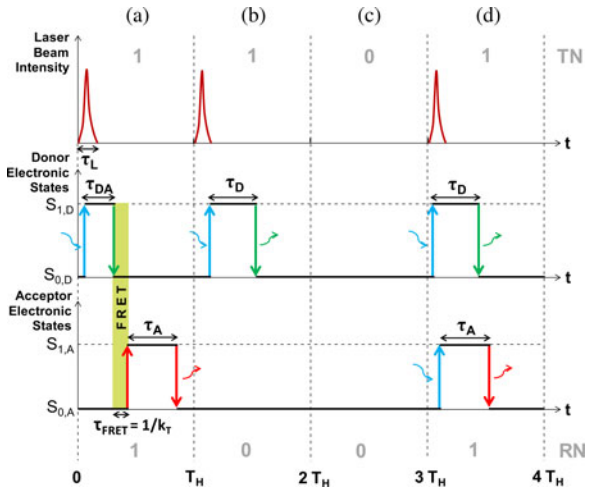

Fig. 3. Example data stream demonstrating pulsed laser beam intensity. Donor and acceptor state transitions for different cases. (a) FRET case: bit 1 is transmitted by TN, bit 1 is detected by RN. (b) No-FRET case: bit 1 is transmitted, bit 0 is detected. (c) No-excitation case: bit 0 is transmitted, bit 0 is detected. (d) Direct excitation case: bit 1 is transmitted, bit 1 is detected.

directed to the donor releases a pulse which has a duration of τ_L. The wavelength of photons released by laser is near to the excitation maximum of the donor in order to guarantee the donor excitation. During τ_L, donor absorbs a photon and becomes excited. In the excited state, after an average time τ_{DA}, i.e., the lifetime of donor in the case of FRET, donor succeeds in transferring the excited energy to the acceptor through FRET with the probability of $P_{\mathrm{FRET}}(R)$. Therefore, acceptor on RN also becomes excited through FRET. The time required for FRET to be completed is the reciprocal of the FRET rate, i.e., $\tau_{\mathrm{FRET}}(R) = 1/k_T(R) = \tau_D(R/R_0)^6$. Acceptor stays in the excited state for an average time of τ_A, and then, it relaxes by emitting a photon. RN detects the excited state of acceptor in the time interval $0 - T_H$ and decides bit 1. In the figure, excitation and fluorescence durations are neglected, since they are too small compared to the lifetimes and FRET duration which are approximated according to the measured values for previously mentioned fluorescent protein pair ECFP–EYCP. The measured lifetimes are 2.68 ns for the donor ECFP and 2.88 ns for the acceptor EYFP [25].

In Fig. 3(b), again the donor is excited to transmit bit 1; however, this time donor fails to deliver its excited energy to the acceptor molecule of RN with the probability of $1 - P_{\mathrm{FRET}}(R)$ in the time interval $T_H - 2T_H$. Therefore, RN cannot detect an excited state during this time interval and decides bit 0. The probability of failure for this case can be minimized by decreasing the intermolecular distance.

In Fig. 3(c), the laser source does not release pulse in order for TN to transmit bit 0; therefore, the donor is not excited in the time interval $2T_H - 3T_H$. As a result, the acceptor also is not excited and RN decides the correct bit, i.e., bit 0.

In Fig. 3(d), the laser excites both the donor and the acceptor directly. This situation is known as direct excitation and can be problematic for FRET applications in fluorescence microscopy. Direct excitation occurs when donor is excited by a laser at a wavelength that belongs to excitation spectrum of both donor and acceptor. Although direct excitation can be minimized by using a laser with a small excitation volume and appropriately directing the laser source to the donor molecule in TN, it is seen in Fig. 3(d) that direct excitation does not result in any confusion for RN to detect the correct bit.

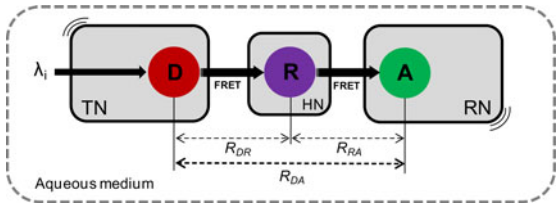

Fig. 4. Long-range FRET-based communication model with multistep FRET.

The case in Fig. 3(a) can be extended to the worst—with the longest duration—case for data transmission to determine minimum excitation period, i.e., $T_{H-\min}$. Since the fluorophores with lifetimes longer than the determined average lifetime constitute a small portion of the entire as seen in Fig. 2; in order to ease the calculation, we assume that the maximum values of lifetimes are the same as the mean values, i.e., $\tau_{D-\max} = \tau_D$ and $\tau_{A-\max} = \tau_A$ as well as $\tau_{DA-\max} = \tau_{DA}$. Assuming that the donor excitation occurs with the absorption of the last photon released by laser and neglecting the excitation time of the donor and disregarding direct excitation, in order to prevent intersymbol interference, the minimum value of the excitation period T_H is given as

$$T_{H-\min} = \tau_L + \tau_{DA} + \tau_{\mathrm{FRET}} + \tau_A. \tag{9}$$

T_H must be reasonably greater than the minimum value considering the weakness of the assumptions made.

IV. Long-Range FRET-Based Communication Channel With Multistep FRET

In the literature, there are several studies that achieve multistep FRET for transmission of excited energy over distances longer than 10 nm [15], [16]. Multistep FRET is realized by employing relay molecules between donor and acceptor. These relay molecules act like both donor and acceptor at the same time. A long-range version of FRET-based communication comprising sequential FRET channels can be realized using a multistep method.

In Fig. 4, the simplest form of the multistep FRET-based communication model with one TN with a donor fluorophore (D), one RN with an acceptor fluorophore (A), and one relay nanomachine (HN) with a relay fluorophore (R) is demonstrated. The arrows between D, R, and A show the FRET direction. Other arrow shows the direction of incoming photon with a wavelength of λ_i. The nanomachines are located linearly to improve the energy transfer range; therefore, the intermolecular distance between the donor fluorophore on TN and the acceptor fluorophore on RN, i.e., R_{DA} is given by

$$R_{DA} = R_{DR} + R_{RA} \tag{10}$$

where R_{DR} is the distance between the donor and relay and R_{RA} is the distance between the relay and acceptor.

The overlap between the emission spectrum of donor and the absorption spectrum of the relay as well as the overlap between the emission spectrum of relay and the absorption spectrum of the acceptor must be significantly large to allow multistep FRET to occur between these molecules. The probability of direct FRET between TN and RN is ignored assuming R_{DA} is significantly greater than $R_{0,DA}$, i.e., the Förster distance of donor–acceptor pair. As a consequence, the direct communication between TN and RN is assumed to be disabled. Therefore, the multistep channel is considered as a series of two independent channels. Therefore, the overall transfer efficiency between the donor and acceptor via multistep FRET, i.e., E_{DA} is given by

$$E_{DA} = E_{DR} \times E_{RA} \tag{11}$$

where E_{DR} is the FRET efficiency between the donor and relay fluorophore and E_{RA} is the FRET efficiency between the relay and acceptor fluorophore [16]. Using (4), (8), and (11), the probability of FRET between the donor and acceptor for a single exciton in terms of R_{DR} and R_{RA} is given by

$$P_{\mathrm{FRET,DA}}(R_{DR}, R_{RA}) = \frac{R_{0,DR}^6}{R_{0,DR}^6 + R_{DR}^6} \times \frac{R_{0,RA}^6}{R_{0,RA}^6 + R_{RA}^6} \tag{12}$$

where $R_{0,DR}$ is the Förster distance of donor–relay pair and $R_{0,RA}$ is the Förster distance of relay–acceptor pair. As is seen in (12), if $R_{0,DR}$ and $R_{0,RA}$ are not equal, $P_{\mathrm{FRET,DA}}$ is not directly related to $R_{0,DA}$ as in the case of single-pair FRET-based communication.

In order to demonstrate the dependence of $P_{\mathrm{FRET,DA}}$ on R_{DR} and R_{RA}, we theoretically construct a multistep communication model using the previously mentioned fluorescent proteins in linear arrangement and in a medium of water at 25 °C, assuming rapid randomization of relative orientation of molecules. We select ECFP as the donor, EYFP as the relay, and enhanced green fluorescent protein (EGFP) as the acceptor molecule. The Förster distances between these molecules under given constraints are measured in [21] as $R_{0,\mathrm{ECFP–EYFP}} = 4.92$ nm and $R_{0,\mathrm{EYFP–EGFP}} = 3.25$ nm. The dependence is shown in Fig. 5. As is seen, in order to optimize this two-step channel for high FRET efficiency and long communication range, it would be a wise decision to set R_{DR} greater than R_{RA}, because $R_{0,DR}$ is greater than $R_{0,RA}$.

The idea of multistep can be applied to realize longer communication with more than one relay in the same manner. For example, in the experimental study [15], a relatively high FRET efficiency of $\sim$68% is achieved with five flurophores over a distance of $\sim$13 nm. We believe, with the discoveries of high-efficiency FRET pairs and further improvements on locating and orienting techniques of fluorophores, nanoscale communication can be realized over longer internodal distances with less relay nodes by using a multistep FRET technique and the advantages of this communication paradigm over wiring the nanomachines together such as mobility and minimizing energy and budget become more clear.

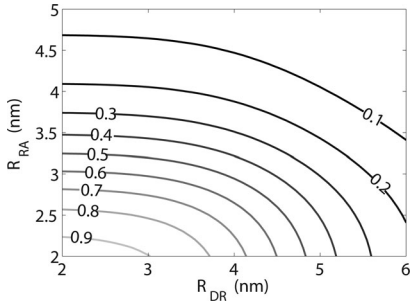

Fig. 5. $P_{\mathrm{FRET,DA}}$ with varying R_{DR} and R_{RA} for ECFP(D)–EYFP(R)–EGFP(A) arrangement.

V. Information Theoretical Analysis for FRET-Based Communication

The FRET channel is modeled similar to Z-channel with OOK modulation assuming the excitation period i.e., T_H, is large enough to prevent ISI.

Every time when the laser excites the donor at the beginning of the interval T_H, i.e., it intends to transmit bit 1 with probability P_F, the probability of FRET occurrence during that interval determines the success of transmission of bit 1. Thus, using (8), TN achieves to deliver bit 1 with probability of p_1 given in terms of intermolecular distance R as follows:

$$p_1[R] = \frac{R_0^6}{R_0^6 + R^6}. \tag{13}$$

Therefore, the probability of failure of transmitting bit 1 when the donor is excited is $(1 - p_1[R])$.

When the donor is not excited at the beginning of an interval, the probability of FRET abstinence during that interval gives the success probability of bit 0. The only noise source for that transmission might be an external laser source exciting the acceptor molecule and causes the acceptor to fluorescence randomly. In our model with one information source, assume there is no noise factor that affects the channel and the receiver is reasonable. Hence, the successful transmission probability of bit 0 is unity, i.e., $p_0 = 1$. Therefore, in this case, the failure probability of transmitting bit 0 becomes $(1 - p_0) = 0$.

Although we disregard the external noise factors, the channel acts like a noisy channel since the probability of FRET occurrence is intrinsically not equal to 1. According to the transmission probabilities, the transition matrix of the Z-channel considering *X* as the transmitted bit by TN, and *Y* as the received bit by RN is given as

$$P(Y|X) = \begin{bmatrix} (1-P_F)p_0 & (1-P_F)(1-p_0) \\ P_F(1-p_1[R]) & P_F\, p_1[R] \end{bmatrix}.$$

The simplified form for $p_0 = 1$ can be given by

$$P(Y|X) = \begin{bmatrix} (1-P_F) & 0 \\ P_F\left(\frac{R^6}{R_0^6+R^6}\right) & P_F\left(\frac{R_0^6}{R_0^6+R^6}\right) \end{bmatrix}.$$

Consequently, the mutual information *I(X;Y)* between *X* and *Y* can be inferred from the transition matrix as

$$I(X;Y) = H(P_F p_1[R]) - P_F H(1 - p_1[R]) \tag{14}$$

TABLE 1
SIMULATION PARAMETERS

Donor - Acceptor pair	EBFP - DsRed ECFP - EYFP EGFP - EYFP ECFP - EYFP - EGFP (relayed case)
Intermolecular distance (R)	$(3-6)\ nm$
Refractive index (n)	1 (vacuum) 1.3342 (water at 25 °C) 1.5185 (silicon oil at 25 °C)
Orientation factor (κ^2)	2/3 (rapid randomization) 4 (parallel dipole moments)

where *H(.)* denotes the binary entropy. Therefore, the capacity of the FRET channel C_F can be given by maximizing the mutual information as follows:

$$C_F = \max[I(X;Y)]. \tag{15}$$

It is possible to increase the channel capacity that varies in accordance with some external and intrinsic parameters by selecting appropriate excitation probabilities, i.e., P_F.

VI. NUMERICAL ANALYSIS

In this section, we present the numerical analysis performed over the mutual information expression given in (14) to show how the FRET-based communication capacity varies according to some environmental parameters and some intrinsic parameters that are specific to the employed FRET pair. The aim of this analysis is to determine the appropriate configuration of FRET-based communication parameters, which can achieve high communication capacity according to changing environmental parameters. We perform the numerical analysis using MATLAB. The simulation parameters can be seen in Table I.

A. Effect of Intermolecular Distance

For the first analysis, we investigate the effect of the intermolecular distance (R) on the capacity of FRET-based communication channel. The analysis is carried out with single-donor and single-acceptor configuration using ECFP–EYFP as the FRET pair assembled on the nanomachines, assuming rapid randomization of the relative orientation of the molecules as well as the nanomachines in a medium of water at 25 °C.

Selecting the medium and orientation parameters as specified previously, the Förster radius for ECFP–EYFP pair is calculated as $R_0 = 4.92$ nm [21]. In Fig. 6(a), mutual information ($I(X;Y)$) given in (14) is shown with varying excitation probability of the donor (P_F) for different R. For R values higher than the R_0, the probability of FRET in the case of donor excitation, i.e., p_1, significantly decreases. As a result, the transmission of bit 1 can be erroneous when the distance between TN and RN is large. Therefore, the capacity decreases for higher R. On the other hand, when R is less than R_0, p_1 increases. Therefore, the capacity increases with decreasing internodal distance. Consequently, it is necessary to select appropriate R and P_F according to the assembled donor–acceptor pair to achieve higher communication capacity. The capacity is maximized for $R = 3$ nm by $P_F = 0.474$. We find $C_{\max} = 0.86$ bit. Hence, we can communicate more information by using input symbol 0 more frequently than 1 with intermolecular distance of 3 nm.

B. Effect of Medium

In this analysis, we investigate the channel capacity for different media. The analysis is carried out with single ECFP–EYFP pair as the donor and the acceptor assembled on TN and RN, respectively. The nanomachines are located in different mediums and separated by a distance of 4 nm, assuming rapid randomization of relative orientation of the molecules.

For ECFP–EYFP pair, the Förster radius calculated in [21] changes in accordance with the refractive index of the medium. In Fig. 6(b), mutual information $I(X;Y)$ given in (14) is shown for varying excitation probability of the donor (P_F) for different media and different refractive indexes. As the refractive index of the medium decreases, the Förster radius given in (1) increases. Therefore, the probability of FRET, i.e., successful transmission probability of bit 1 increases. As a consequence, the capacity of the channel increases with decreasing refractive index. The capacity is maximized for vacuum by $P_F = 0.43$. We find $C_{\max} = 0.57$ bit.

C. Effect of Relative Orientation Factor

Here, we investigate the effect of relative orientation factor (κ^2) on the channel capacity using ECFP–EYFP as the donor–acceptor pair assembled on the nanomachines. The nanomachines are located in a medium of water at 25 °C and separated by a distance of 4 nm.

The relative orientation factor is a measure of the relative orientation of the donor emission dipole moment and the acceptor absorption dipole moment. Determining the exact orientations of donor and acceptor molecules is impossible at this point. However, many of the studies in the literature about FRET assume rapid randomization of the relative orientation of the dipole moments. The orientation factor is 2/3 in the case of rapid randomization. In addition, we investigate the mutual information when the orientation of the dipole moments of the molecules are parallel. In this case, the orientation factor reaches its maximum value, i.e., $\kappa^2 = 4$. The result of the analysis seen in Fig. 6(c) reveals that the parallel orientation can significantly increase the capacity of FRET-based channel compared to rapid randomization. When further advances in the nanotechnology make it possible to control the orientation of molecules, orienting the dipole moments of the donor and the acceptor molecules in parallel will be a wise strategy to achieve higher communication capacities. For parallel orientation, the capacity is $P_F = 0.47$. We find $C_{\max} = 0.70$ bit.

D. Capacity Analysis for Different FRET Pairs

In this analysis, we investigate the communication capacity for various donor–acceptor pairs with different spectral properties, assembled on TN and RN, respectively. The nanomachines are located in a medium of water at 25 °C and separated by a distance of 4 nm. The molecules that constitute the FRET pairs are selected among the variants of GFP. The selected

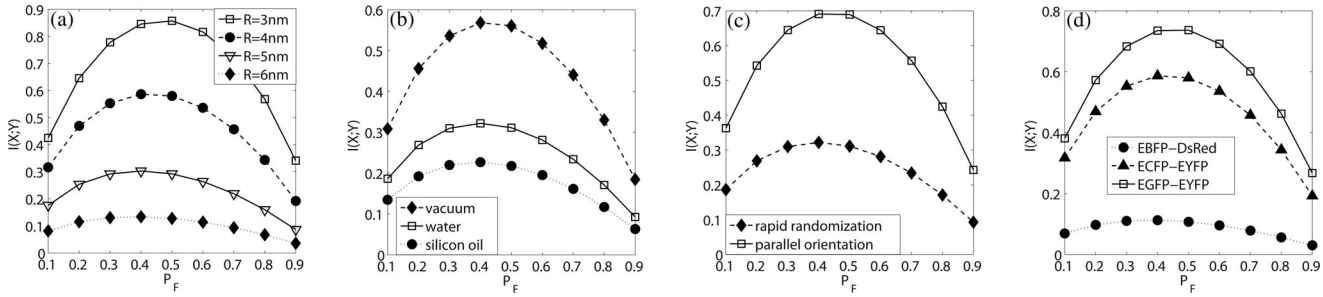

Fig. 6. $I(X;Y)$ in bits/symbol for several (a) internodal distances (R), (b) media, (c) relative orientations, and (d) FRET-pair selections with varying P_F.

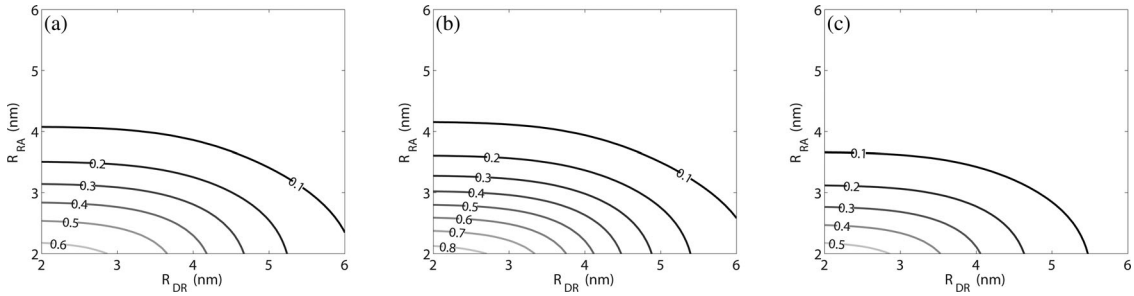

Fig. 7. $I(X;Y)$ in bits/symbol for (a) $P_F = 0.2$, (b) $P_F = 0.5$, and (c) $P_F = 0.8$ with varying R_{DR} and R_{RA} for ECFP(D)–EYFP(R)–EGFP(A) configuration.

donor–acceptor pairs are commonly used in FRET studies and there is a wide variety of studies about GFP variants in the literature.

There is a direct relationship between the spectral overlap of molecules and R_0 as well as FRET efficiency, i.e., the transmission probability of bit 1 (p_1). As the overlap of the spectra increases, R_0 as well as p_1 increases. For the pair of enhanced blue fluorescent protein (EBFP) and red fluorescent protein (DsRed), the spectral overlap is the minimum among the selected pairs. Therefore, R_0 for EBFP and DsRed is the minimum and calculated as 3.17 nm [21]. Conversely, the overlap between the emission spectrum of EGFP and the absorption spectrum of EYFP is the maximum. As a result, R_0 for EGFP–EYFP pair is the maximum and calculated as 5.64 nm [21]. For ECFP–EYFP pair, R_0 is previously given as 4.92 nm [21].

Fig. 6(d) demonstrates the mutual information, $I(X;Y)$, given in (14) for varying excitation probabilities (P_F). As expected, the capacity is higher for the pair EGFP–EYFP because of the higher transmission probability of bit 1 (p_1) as the consequence of higher spectral overlap. As the spectral overlap decreases, the capacity also decreases. Therefore, for the pair EBFP–DsRed, the capacity is the minimum among the others. The selection of the donor and acceptor pair with larger spectral overlap is the key strategy in order to achieve higher communication capacity. The capacity is maximized for EGFP–EYFP by $P_F = 0.45$. We find $C_{\max} = 0.74$ bit.

E. Capacity Analysis for Long-Range FRET-Based Communication Channel With Multistep FRET

Here, we analyze the multistep FRET-based communication channel information theoretically for the simplest form with only one relay in a similar manner with the single-pair analyses. The main difference of the multistep case is the determination of p_1. Assuming that a proper selection for excitation period (T_H) is made, neglecting direct excitation and using the fact that $p_1 = P_{\mathrm{FRET}}$, p_1, i.e., the probability of successful transmission of bit 1 between TN and RN for the linear two-step donor–relay–acceptor arrangement can be expressed as the same as the right-hand side of (12) in terms of the intermolecular distances. With the same assumption for T_H, the probability of success in transmission of bit 0 between TN and RN ($p_{0,DA}$) is 1. Therefore, the multistep channel also shows the Z-channel characteristics.

For a linear arrangement of the previously mentioned triplet ECFP–EYFP–EGFP on TN, HN, and RN, respectively, which are located in a medium of water at 25 °C and assuming rapid randomization of relative orientation of the molecules on the nanomachines, i.e., $\kappa^2 = 2/3$, the dependence of mutual information ($I(X;Y)$) on R_{DR} and R_{RA} is analyzed using (14) and the results are demonstrated in Fig. 7.

As seen in Fig. 7, the dependence of the reliability of the channel on internodal distances is in parallel with the results obtained for efficiency dependence in Fig. 5. Particularly, we conclude that using bit 0 more frequently than bit 1, i.e., decreasing P_F, results in an increase in the mutual information and the capacity for the same arrangement.

VII. Conclusion

In this study, we propose a novel molecular communication technique exploiting a well-known phenomenon FRET for the first time in the literature. We define a realistic communication channel model for a single transmitter–receiver pair (point-to-point) within the scope of FRET theory. Succeeding that, the capacity of the newborn channel is formalized information

theoretically, and the variation in the communication channel capacity is analyzed for different environmental and intrinsic parameters. The result of analysis reveals that the capacity of the channel can be increased significantly by appropriately choosing the parameters in accordance with each other.

Throughout this paper, we show that with the relatively low dependence on the environmental factors, high-level controllability of the parameters, and simplicity, FRET-based molecular communication model stands as a promising solution to high-rate nanoscale communication between nanomachines. Furthermore, we show the potential of the model for long-range nanonetworks by serially connecting the channels using relay nanomachines. In parallel to the FRET studies in the fluorescent spectroscopy area and with further investigations over this model, broadcast and multiple access methods and more reliable communication as well as new modulation techniques can be realized over this channel.

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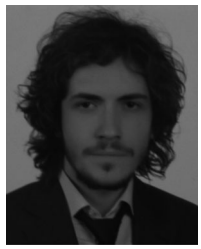

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