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RESONANCE ENERGY TRANSFER IN MEMBRANE SYSTEMS II. EFFECT OF SURFACE CURVATURE

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The model of resonance energy transfer (RET) in lipid particles and small lipid vesicles is presented. It is shown that RET in lipid particles becomes independent of surface curvature when particle radius threefold exceeds Förster radius. For small lipid vesicles containing two donor and one acceptor spherical array the contribution of curvature effects to the RET efficiency is found to increase with decreasing Förster radius and increasing the separation between donor arrays.

KEY WORDS: resonance energy transfer, membrane systems, surface curvature

Resonance energy transfer is currently regarded as one of the most appropriate physical methods providing information on the spatial relationships in biomembranes. Correct application of this method requires taking into account peculiar geometric conditions occurring in membrane systems. These conditions are determined by dimensionality of fluorophore distribution, curvature of lipid-water interface, separation of donor and acceptor arrays, organization of acceptor assemblies, *etc.*[1-3]. Relative contributions of the above factors to the RET efficiency have been evaluated in a number of theoretical studies considering the systems of different geometries [4-9]. Our previous paper has been focused on characterizing the RET dependence on the dimensionality of donor and acceptor distribution in a membrane [10]. As a next step of theoretical analysis, in the present study it seems of interest to assess the extent to which RET efficiency is affected by the curvature of membrane surface.

THEORY

Model of resonance energy transfer in small lipid particles

Let us consider lipid particle of radius R_s containing spherical arrays of donors and acceptors separated by a distance d (Fig. 1). In terms of the formalism described in more detail previously [6,10] relative quantum yield of a donor (Q_r) can be written as:

$$Q_r = \frac{Q_{DA}}{Q_D} = \int_0^{\infty} \exp[-\lambda](I(t))^N d\lambda \tag{1}$$

$$I(t) = \int_0^{\theta_d} \exp\left[-\lambda(R_0/R)^6\right] W(\theta)d\theta = \int_0^{\theta_d} \exp\left[-\lambda\left(R_0/\sqrt{R_s^2+(R_s-d)^2-2(R_s-d)R_s\cos\theta}\right)^6\right] W(\theta)d\theta \tag{2}$$

where Q_D, Q_{DA} are the donor quantum yields in the absence and presence of acceptors, respectively, R is the distance between donor and acceptor, θ_d is the half-angle corresponding to spherical segment containing N acceptor molecules involved in energy transfer, R_0 is the Förster radius, $\lambda=t/\tau_d$, τ_d is the lifetime of an excited donor in the absence of acceptors. The probability of finding acceptor within the spherical layer between the angles θ and $\theta+d\theta$ is given by:

$$W(\theta)d\theta = \frac{\sin\theta d\theta}{1-\cos\theta_d}; \qquad \theta_d = \arccos\left(\frac{R_s^2+(R_s-d)^2-R_d^2}{2(R_s-d)R_s}\right) \tag{3}$$

where R_d is the radius of the sphere beyond which energy transfer is becoming negligibly small. By denoting the surface acceptor concentration C_a^s and the area of spherical segment S_{seg} one obtains:

$$N = S_{seg}C_a^s; \; S_{seg} = 2\pi(R_s-d)^2(1-\cos\theta_d) \tag{4}$$

When acceptors reside in the particle interior deeper than donors the following relationship holds:

$$C_a = \frac{N_A B}{4\pi(R_s-d)^2 N_v} \tag{5}$$

where N_V is the number of lipid particle per litre, related to molar concentration of lipid (L) and volume of lipid molecule (V_L) as: $N_V = \frac{3N_A L V_L}{4\pi R_s^3}$, B is molar concentration of bound acceptor, N_A is Avogadro's number.

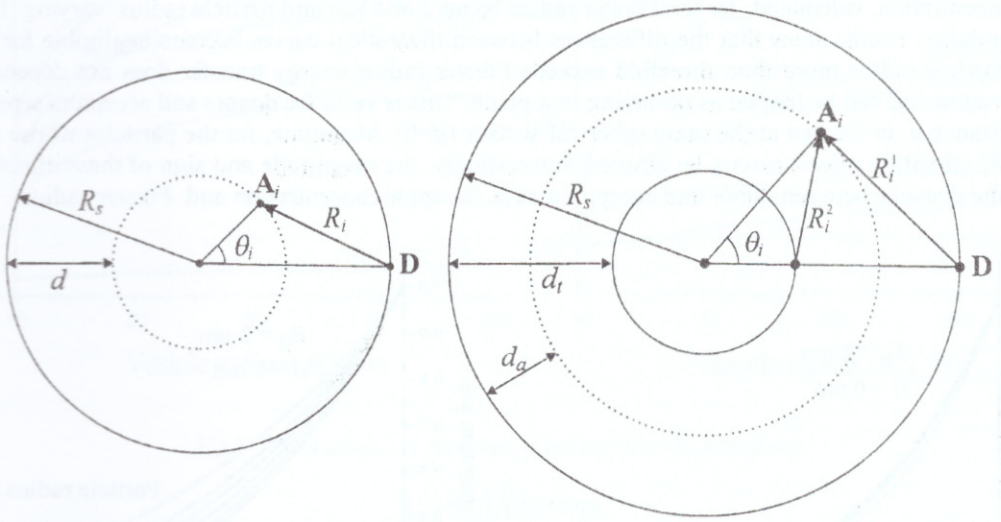

Fig.1. Diagram of parameters used in the model of energy transfer in small lipid particles and vesicles.

In the case where donors are located deeper than acceptors eqs. (4,5) become:

$$S_{seg} = 2\pi R_s^2(1-\cos\theta_d); \quad C_a^* = \frac{N_A B}{4\pi R_s^2 N_V} \tag{6}$$

Note that R_d values taken as $3R_o$ for the majority of donor-acceptor pairs are greater than 5 nm [1]. Therefore, for small lipid particles (micelles) whose diameter does not exceed 5 nm, it appears that $(2R_s - d) < R_d$, *i.e.* $\theta_d = \pi$ and parameter N can be regarded as corresponding to the number of acceptor molecules per lipid particle.

Model of resonance energy transfer in small unilamellar lipid vesicles

In a similar manner one can treat the case when the donors and acceptors are uniformly distributed on the surface of concentric spheres in the bilayer of small lipid vesicles. Two possibilities must be considered – acceptor spherical array resides between two donor arrays and donor spherical array is situated between two acceptor arrays. The fractions of donors or acceptors on the outer or inner spheres can be calculated as follows:

$$f_e = \frac{R_s^2}{R_s^2 + (R_s - d_t)^2}; f_i = \frac{(R_s - d_t)^2}{R_s^2 + (R_s - d_t)^2} \tag{7}$$

When acceptor sphere resides between two donor spheres energy transfer can be described by the following relationships:

$$Q_r = f_e \int_0^\infty \exp(-\lambda)(I_1(\lambda))^{N_1} d\lambda + f_i \int_0^\infty \exp(-\lambda)(I_2(\lambda))^{N_2} d\lambda \tag{8}$$

$$I_1(\lambda) = \int_0^{\theta_{d1}} \exp\left[-\lambda(R_o/R_1)^6\left(\frac{\sin\theta}{1-\cos\theta_{d1}}\right)\right] d\theta; \quad \theta_{d1} = \arccos\left(\frac{R_s^2 + (R_s - d_a)^2 - R_d^2}{2(R_s - d_a)R_s}\right) \tag{9}$$

$$I_2(\lambda) = \int_0^{\theta_{d2}} \exp\left[-\lambda(R_o/R_2)^6\left(\frac{\sin\theta}{1-\cos\theta_{d2}}\right)\right] d\theta; \quad \theta_{d2} = \arccos\left(\frac{(R_s - d_t)^2 + (R_s - d_a)^2 - R_d^2}{2(R_s - d_t)(R_s - d_a)}\right) \tag{10}$$

$$R_1 = \sqrt{R_s^2 + (R_s - d_a)^2 - 2(R_s - d_a)R_s\cos\theta}; R_2 = \sqrt{(R_s - d_t)^2 + (R_s - d_a)^2 - 2(R_s - d_a)(R_s - d_t)\cos\theta} \tag{11}$$

$$N_{1,2} = S_{seg_{1,2}} C_a^*; \quad S_{seg_{1,2}} = 2\pi(R_s - d_a)^2(1-\cos\theta_{d1,2}) \quad C_a^* = \frac{N_A B}{4\pi(R_s - d_a)^2 N_V} \tag{12}$$

DISCUSSION

Using the above equations we made an attempt to assess the curvature effect on the energy transfer efficiency. Shown in Fig. 2 are theoretical dependencies of the relative quantum yield of a donor on the surface acceptor concentration, calculated for the Förster radius being 2 or 5 nm and particle radius varying from 2 to 20 nm. Simulation results show that the differences between theoretical curves become negligible for $R_s>3R_o$, *i.e.* when particle radius more than threefold exceeds Förster radius energy transfer does not depend on the surface curvature and can be treated as occurring in a plane. This is valid for donors and acceptors separated by a certain distance d or located at the same spherical surface (d=0). Meantime, for the particles whose radius is less than $3R_o$ curvature effects cannot be ignored. Interestingly, the magnitude and sign of these effects clearly depend on the distance between donor and acceptor arrays, acceptor concentration and Förster radius.

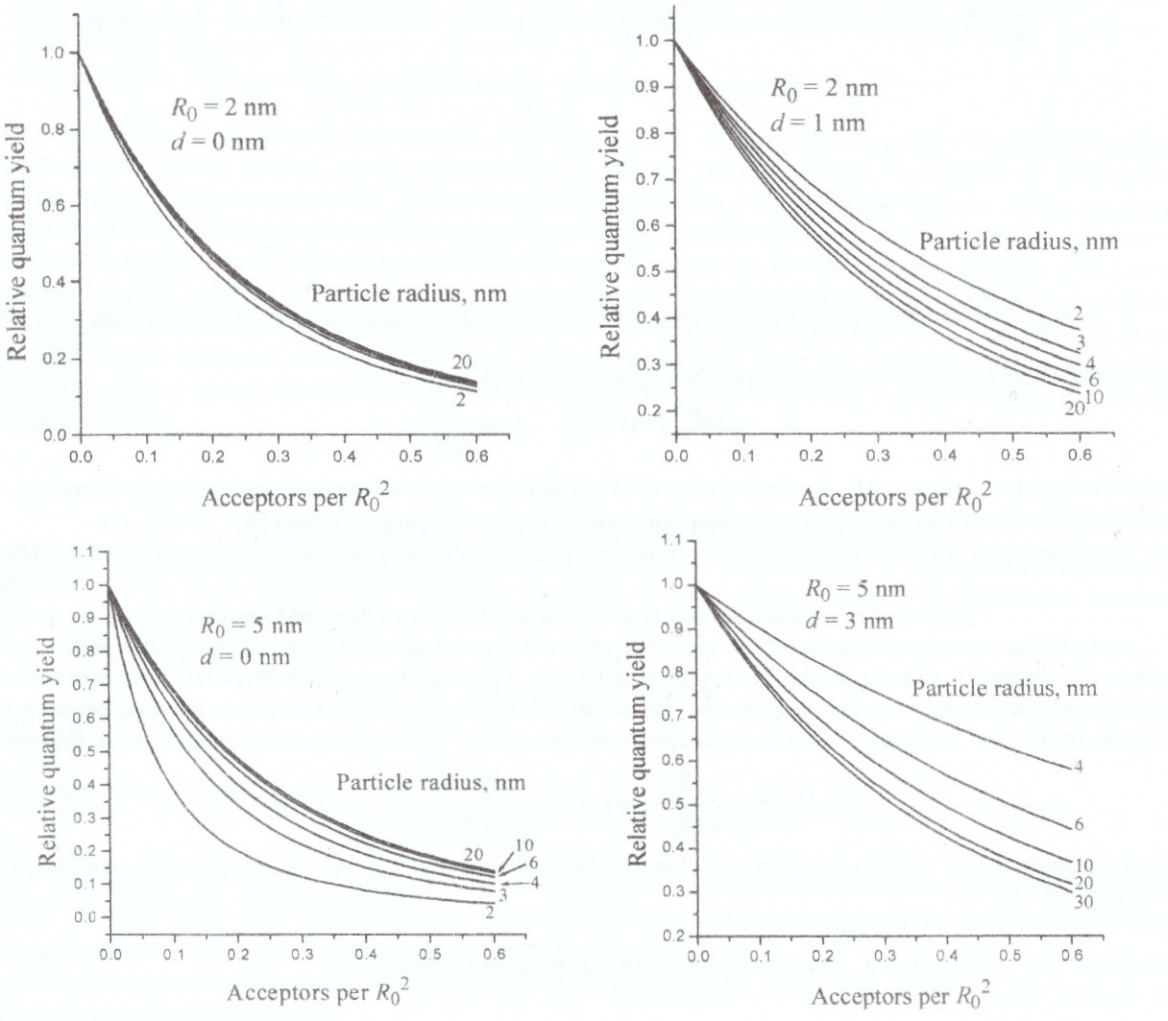

Fig.2. Quenching profiles calculated according Eqs. (1)-(6) for lipid particles.

Comparison of the donor quenching profiles obtained using Eqs. (7)-(12) for small lipid vesicles also allowed to disclose some features of the RET dependence on surface curvature. Fig. 3 shows the increments of Q_r values calculated as a function of R_s for varying d_a and d_t.

Analysis of these simulation data indicates that curvature effects tend to enhance with i) decreasing R_o; ii) lowering d_a and iii) increasing d_t values. It is noteworthy that most pronounced dependence of RET efficiency on the vesicle radius is observed for R_s lying between 10 and 20 nm. By applying the above models in analyzing experimental results one could estimate the distances between the spherical arrays of donors and acceptors in the lipid monolayers or bilayers.

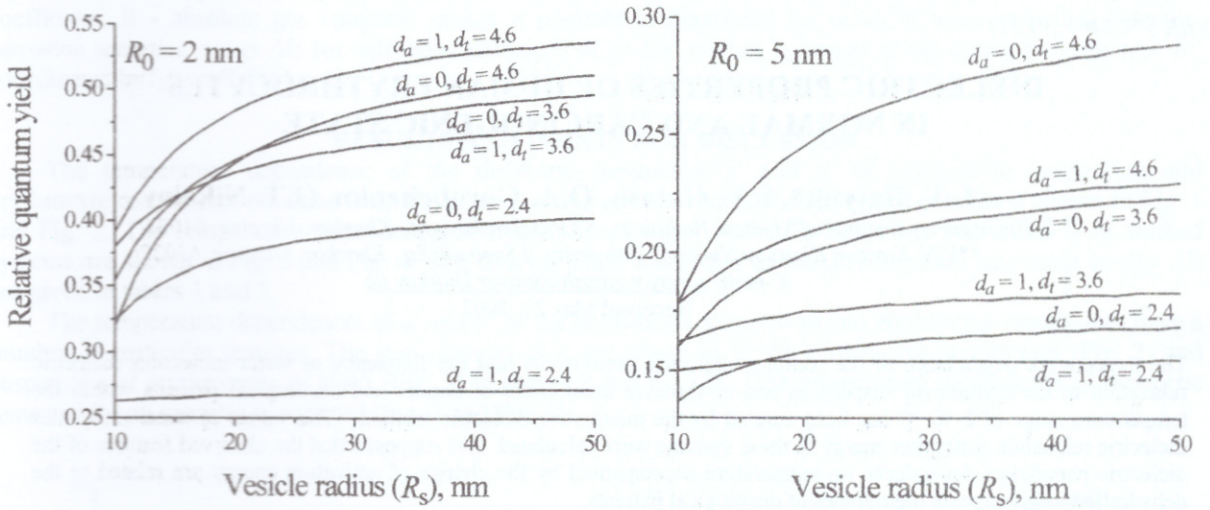

Fig.3. Effect of vesicle curvature on energy transfer efficiency.

CONCLUSIONS

Theoretical consideration of resonance energy transfer between donors and acceptors distributed in the interior of lipid particles or small bilayer vesicles suggests that contribution of curvature effects to the transfer efficiency becomes more significant with decreasing the particle (vesicle) radius to Förster radius ratio. In the cases where this ratio is less than ~ 3 obtaining adequate structural information requires the surface curvature to be incorporated as one of the parameters of theoretical model employed in analyzing experimental data.

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ІНДУКТИВНО-РЕЗОНАНСНИЙ ПЕРЕНОС ЕНЕРГІЇ В МЕМБРАННИХ СИСТЕМАХ
II. РОЛЬ КРИВИЗНИ ПОВЕРХНІ

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Запропоновано модель індуктивно-резонансного переносу енергії в ліпідних частинках та везикулах, що мають радіус, який не перевищує 50 нм. Показано, що ефективність переносу енергії в ліпідних частинках втрачає залежність від кривизни поверхні, коли радіус частинки більш ніж втричі перевищує радіус Ферстера. Встановлено, що вклад ефекту кривизни в ефективність переносу в ліпідних везикулах невеликого розміру, що містять дві сферичні поверхні локалізації донорів, між якими розмішені акцептори, підвищується при зменшенні радіусу Ферстера та при зростанні відстані між поверхнями донорів.

КЛЮЧОВІ СЛОВА: індуктивно-резонансний перенос енергії, мембранні системи, кривизна поверхні.