## 12.1. <u>FÖRSTER RESONANCE ENERGY TRANSFER</u>

Förster resonance energy transfer (FRET) refers to the nonradiative transfer of an electronic excitation from a donor molecule to an acceptor molecule:

$$D^* + A \rightarrow D + A^* \qquad (12.1)$$

This electronic excitation transfer, whose practical description was first given by Förster,[*] arises from a dipole-dipole interaction between the electronic states of the donor and the acceptor, and does not involve the emission and re-absorption of a light field. Transfer occurs when the oscillations of an optically induced electronic coherence on the donor are resonant with the electronic energy gap of the acceptor. The strength of the interaction depends on the magnitude of a transition dipole interaction, which depends on the magnitude of the donor and acceptor transition matrix elements, and the alignment and separation of the dipoles. The sharp $1/r^6$ dependence on distance is often used in spectroscopic characterization of the proximity of donor and acceptor.

To describe FRET, there are four electronic states that must be considered: The electronic ground and excited states of the donor and acceptor. We consider the case in which we have excited the donor electronic transition, and the acceptor is in the ground state. Absorption of light by the donor at the equilibrium energy gap is followed by rapid vibrational relaxation which dissipates the reorganization energy of the donor λ_D over the course of picoseconds. This leaves

the donor in a coherence that oscillates at the energy gap in the donor excited state $\omega_{eg}^D (q_D = d_D)$. The time-scale for FRET is typically nanoseconds, so this preparation step is typically much faster than the transfer phase. For resonance energy transfer we require a resonance condition, so that the oscillation of the excited donor

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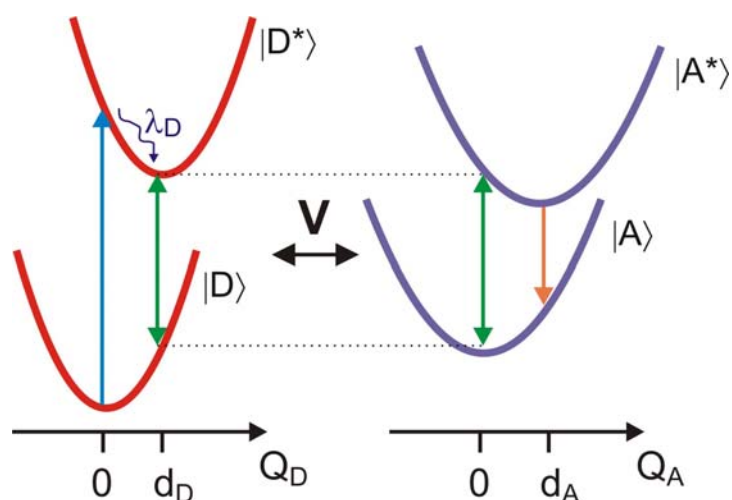
[*] Th. Förster, "Experimentelle und theoretische Untersuchung des zwischenmolecularen Uebergangs von Electronenanregungsenergie," *Z. Naturforsch*, **4a**, 321 (1949); "Zwischenmoleculare Energiewanderung und Fluoreszenz," *Ann. Physik* **2,** 55 (1948); "Transfer Mechanisms of Electronic Excitation," *Discussions Faraday Soc.* **27**, 7 (1959).

coherence is resonant with the ground state electronic energy gap of the acceptor $\omega_{eg}^{A}\left(q_{A}=0\right)$. Transfer of energy to the acceptor leads to vibrational relaxation and subsequent acceptor fluorescence that is spectrally shifted from the donor fluorescence. In practice, the efficiency of energy transfer is obtained by comparing the fluorescence emitted from donor and acceptor.

Since the donor and acceptor are weakly coupled, we can write our Hamiltonian for this problem in a form that can be solved by perturbation theory

$$H = H_0 + V$$

$$H_0 = \left|D^*A\right\rangle H_D \left\langle D^*A\right| + \left|A^*D\right\rangle H_A \left\langle A^*D\right|$$

(12.2)

Here H_D is the Hamiltonian of the system with the donor excited, and H_A is the Hamiltonian with the acceptor excited. $\left|D^*A\right\rangle$ represents the electronic and nuclear configuration for both donor and acceptor molecules, which could be more properly written $\left|d^*n_{D^*}a\,n_A\right\rangle$. The interaction between donor and acceptor takes the form of a dipole-dipole interaction:

$$V = \frac{3\left(\bar{\mu}_A \cdot \hat{r}\right)\left(\bar{\mu}_D \cdot \hat{r}\right) - \bar{\mu}_A \cdot \bar{\mu}_D}{\bar{r}^3}\,,$$

(12.3)

where r is the distance between donor and acceptor dipoles and $\hat{r}$ is a unit vector that marks the direction between them. The dipole operators here are taken to only act on the electronic states and be independent of nuclear configuration, i.e. the Condon approximation. We write the transition dipole matrix elements that couple the ground and excited electronic states for the donor and acceptor as

$$\bar{\mu}_A = \left|A\right\rangle \bar{\mu}_{AA^*} \left\langle A^*\right| + \left|A^*\right\rangle \bar{\mu}_{A^*A} \left\langle A\right| \qquad \hat{u}_A \qquad (12.4)$$

$$\bar{\mu}_D = \left|D\right\rangle \bar{\mu}_{DD^*} \left\langle D^*\right| + \left|D^*\right\rangle \bar{\mu}_{D^*D} \left\langle D\right| \qquad (12.5)$$
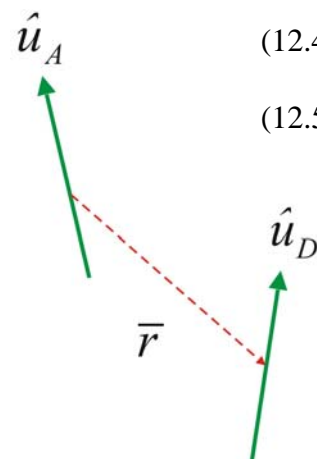
For the dipole operator, we can separate the scalar and orientational contributions as

$$\bar{\mu}_A = \hat{u}_A\,\mu_A \qquad (12.6)$$

This allows the transition dipole interaction in eq. (12.3) to be written as

$$V = \mu_A \mu_B \frac{\kappa}{r^3}\left[\left|D^*A\right\rangle\left\langle A^*D\right| + \left|A^*D\right\rangle\left\langle D^*A\right|\right] \qquad (12.7)$$

All of the orientational factors are now in the term κ:

$$\kappa = 3\left(\hat{u}_A \cdot \hat{r}\right)\left(\hat{u}_D \cdot \hat{r}\right) - \hat{u}_A \cdot \hat{u}_D . \tag{12.8}$$

We can now obtain the rates of energy transfer using Fermi's Golden Rule expressed as a correlation function in the interaction Hamiltonian:

$$w_{k\ell} = \frac{2\pi}{\hbar^2} \sum_\ell p_\ell \left| V_{k\ell} \right|^2 \delta\left(\omega_k - \omega_\ell\right) = \frac{1}{\hbar^2} \int_{-\infty}^{+\infty} dt \left\langle V_I(t) V_I(0) \right\rangle \tag{12.9}$$

Note that this is not a Fourier transform! Since we are using a correlation function there is an assumption that we have an equilibrium system, even though we are initially in the excited donor state. This is reasonable for the case that there is a clear time scale separation between the ps vibrational relaxation and thermalization in the donor excited state and the time-scale (or inverse rate) of the energy transfer process.

Now substituting the initial state $\ell = \left| D^* A \right\rangle$ and the final state $k = \left| A^* D \right\rangle$, we find

$$w_{ET} = \frac{1}{\hbar^2} \int_{-\infty}^{+\infty} dt \, \frac{\left\langle \kappa^2 \right\rangle}{r^6} \left\langle D^* A \left| \mu_D(t) \mu_A(t) \mu_D(0) \mu_A(0) \right| D^* A \right\rangle \tag{12.10}$$

where $\mu_D(t) = e^{iH_D t/\hbar} \mu_D e^{-iH_D t/\hbar}$. Here, we have neglected the rotational motion of the dipoles. Most generally, the orientational average is

$$\left\langle \kappa^2 \right\rangle = \left\langle \kappa(t) \kappa(0) \right\rangle . \tag{12.11}$$

However, this factor is easier to evaluate if the dipoles are static, or if they rapidly rotate to become isotropically distributed. For the static case $\left\langle \kappa^2 \right\rangle = 0.475$. For the case of fast loss of orientation: $\left\langle \kappa^2 \right\rangle \rightarrow \left\langle K(t) \right\rangle \left\langle K(0) \right\rangle = \left\langle \kappa \right\rangle^2 = 2/3$.

Since the dipole operators act only on $\left| A \right\rangle$ or $\left| D^* \right\rangle$, and the D and A nuclear coordinates are orthogonal, we can separate terms in the donor and acceptor states.

$$\begin{aligned} w_{ET} &= \frac{1}{\hbar^2} \int_{-\infty}^{+\infty} dt \, \frac{\left\langle \kappa^2 \right\rangle}{r^6} \left\langle D^* \left| \mu_D(t) \mu_D(0) \right| D^* \right\rangle \left\langle A \left| \mu_A(t) \mu_A(0) \right| A \right\rangle \\ &= \frac{1}{\hbar^2} \int_{-\infty}^{+\infty} dt \, \frac{\left\langle \kappa^2 \right\rangle}{r^6} C_{D^* D^*}(t) C_{AA}(t) \end{aligned} \tag{12.12}$$

The terms in this equation represent the dipole correlation function for the donor initiating in the excited state and the acceptor correlation function initiating in the ground state. That is, these are correlation functions for the donor emission (fluorescence) and acceptor absorption.

Remembering that $\left|D^*\right\rangle$ represents the electronic and nuclear configuration $\left|d^* n_{D^*}\right\rangle$, we can use the displaced harmonic oscillator Hamiltonian or energy gap Hamiltonian to evaluate the correlation functions. For the case of Gaussian statistics we can write

$$C_{D^*D^*}(t) = \left|\mu_{DD^*}\right|^2 e^{-i\left(\omega_{DD^*}-2\lambda_D\right)t - g_D^*(t)} \tag{12.13}$$

$$C_{AA}(t) = \left|\mu_{AA^*}\right|^2 e^{-i\omega_{AA^*}t - g_A(t)}. \tag{12.14}$$

Here we made use of

$$\omega_{D^*D} = \omega_{DD^*} - 2\lambda_D, \tag{12.15}$$

which expresses the emission frequency as a frequency shift of $2\lambda_D$ relative to the donor absorption frequency.

The dipole correlation functions can be expressed in terms of the inverse Fourier transforms of a fluorescence or absorption lineshape:

$$C_{D^*D^*}(t) = \frac{1}{2\pi}\int_{-\infty}^{+\infty} d\omega \, e^{-i\omega t}\, \sigma_{fluor}^D(\omega) \tag{12.16}$$

$$C_{AA}(t) = \frac{1}{2\pi}\int_{-\infty}^{+\infty} d\omega \, e^{-i\omega t}\, \sigma_{abs}^A(\omega). \tag{12.17}$$

To express the rate of energy transfer in terms of its common practical form, we make use of Parsival's Theorem, which states that if a Fourier transform pair is defined for two functions, the integral over a product of those functions is equal whether evaluated in the time or frequency domain:
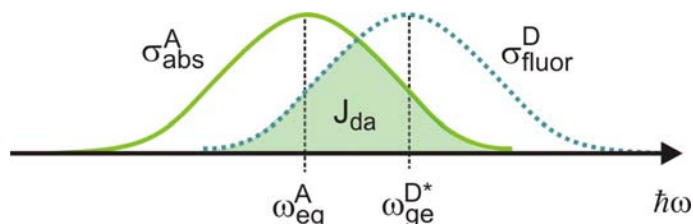
$$\int_{-\infty}^{\infty} f_1(t) f_2^*(t)\,dt = \int_{-\infty}^{\infty} \tilde{f}_1(\omega)\tilde{f}_2^*(\omega)\,d\omega. \tag{12.18}$$

This allows us to express the energy transfer rate as an overlap integral J_{DA} between the donor fluorescence and acceptor absorption spectra:

$$w_{ET} = \frac{1}{\hbar^2}\frac{\langle\kappa^2\rangle}{r^6}\left|\mu_{DD^*}\right|^2\left|\mu_{AA^*}\right|^2\int_{-\infty}^{+\infty} d\omega \, \underset{\sim}{\sigma}_{abs}^A(\omega)\underset{\sim}{\sigma}_{fluor}^D(\omega). \tag{12.19}$$

Here $\underset{\sim}{\sigma}$ is the lineshape normalized to the transition matrix element squared: $\underset{\sim}{\sigma} = \sigma/\left|\mu\right|^2$. The overlap integral is a

measure of resonance between donor and acceptor transitions.

So, the energy transfer rate scales as r^{-6}, depends on the strengths of the electronic transitions for donor and acceptor molecules, and requires resonance between donor fluorescence and acceptor absorption. One of the things we have neglected is that the rate of energy transfer will also depend on the rate of excited donor state population relaxation. Since this relaxation is typically dominated by the donor fluorescence rate, the rate of energy transfer is commonly written in terms of an effective distance R_0, and the fluorescence lifetime of the donor τ_D:

$$w_{ET} = \frac{1}{\tau_D} \left(\frac{R_0}{r} \right)^6 \qquad (12.20)$$

At the critical transfer distance R_0 the rate (or probability) of energy transfer is equal to the rate of fluorescence. R_0 is defined in terms of the sixth-root of the terms in eq. (12.19), and is commonly written as

$$R_0^6 = \frac{9000 \ln(10) \phi_D \left\langle \kappa^2 \right\rangle}{128 \pi^5 n^4 N} \int_0^\infty d\bar{\nu} \, \frac{\sigma_{\text{fluor}}^D \left(\bar{\nu} \right) \varepsilon_A \left(\bar{\nu} \right)}{\bar{\nu}^4} \qquad (12.21)$$

This is the practical definition which accounts for the frequency dependence of the transition-dipole interaction and non-radiative donor relaxation in addition to being expressed in common units. $\bar{\nu}$ represents units of frequency in cm^{-1}. The fluorescence spectrum $\underset{\sim}{\sigma}_{fluor}^D$ must be normalized to unit area, so that $\sigma_{\text{fluor}}^D \left(\bar{\nu} \right)$ is expressed in cm (inverse wavenumbers). The absorption spectrum $\varepsilon_A \left(\bar{\nu} \right)$ must be expressed in molar decadic extinction coefficient units (liter/mol·cm). n is the index of refraction of the solvent, N is Avagadro's number, and ϕ_D is the donor fluorescence quantum yield.