

# Chapter 1

## Short History of Energy Transfer Theory Before Förster, At The Time of Förster, and After Förster

This chapter gives a brief introduction to the historical development of energy transfer. In this chapter, we are not dealing with a detailed review of applications, nor a review of modern theoretical development; instead, we outline some of the ideas, experiments and theories that formed the scientific background that culminated in the Förster resonance energy transfer (FRET) theory. A more detailed description of the historical events regarding to FRET can be found in a review [1] and references within.

FRET is a physical process where the excited state energy of the “donor” can be transferred to the “acceptor” in the ground state. This can take place whenever the donor and the acceptor are close enough, usually less than 10 nm at room temperature, and under certain other conditions.

FRET is one of the major experimental methods for discovering whether two interacting particles are in close proximity, or for determining the distance between two specific locations in a complex micro/nano structure. It has become a major experimental technique in the field of single particles, since the efficiency of energy transfer is measured via fluorescence tools. The energy transfer is typically detected relatively easily and it is used to show interactions between two particles. It is a powerful technique since FRET measures dynamics on a spatial scale that is unique (in nanometers range). It is fairly simple and can be studied in most of the laboratories. FRET has been used since early 1950s, however, its use has been exploded in the last decades mainly because of instrumentation improvements and innovations and the great number of commercially available synthetic fluorophores, which can be featured with particular chemical groups for specific purposes.

In the following section we briefly discuss the historical events that led to the understanding and modeling of FRET. First, the concept of electromagnetism and quantum mechanics as well as the concept of energy transfer previous to Förster are discussed. Next, we shortly review the experiments and concept of energy transfer

during the Förster time. Finally, we summarize the concept of energy transfer after Förster.

## 1.1 Brief Review of Scientific Achievements Before Förster Theory

The notion that electricity and magnetism are related were suspected before 1800 because of the formal similarities between static electricity and magnetism. Hans Christian Oersted in 1820 was the first to demonstrate the interrelationship of electricity and magnetism. He reported that a magnet's needle held next to a current-carrying wire was deflected and oriented itself perpendicular to the line of current. This discovery, easy to reproduce, was repeated by André-Marie Ampère and others (e.g., Jean-Baptiste Biot and Félix Savart). In 1822, Ampère published a theory of electromagnetic interactions involving currents. He found that current-carrying wires attract or repel each other depending on whether the currents is in the same direction or opposite.

Faraday who discovered that changing magnetic fields produce circulating electrical fields, known as "Faraday induction", introduced in 1821 an intuitive pictorial representation of lines of forces. Faraday pictured these lines of forces as the mechanism by which electrical and magnetic objects interact with themselves and with each other, where these lines of forces serve as "the carries" of forces through space. The first field theory was introduced by James Clerk Maxwell in 1864. His equations describe electromagnetic fields where the objects (electrical or magnetic) enter only through boundary conditions. Using the ideas and experiments of Faraday, Maxwell created a complete mathematical representation of Faraday's descriptions of electricity and magnetism. He understood Faraday's lines of force as a line passing through any point of space representing the direction of the force exerted giving the vector representation of the electromagnetic field. In addition to Faraday's ideas, Maxwell introduced the notion of displacement current, that is, the circulatory magnetic field caused by a time-varying electric field. Maxwell's equations describe all classical electrodynamic phenomena and settled the theoretical basis to predict electromagnetic radiation, which is the starting point for describing the classical theory of energy transfer.

Maxwell's equations predicted the identity of electromagnetism and light and the quantitative properties of light (interference, refrangibility and polarization as well as the speed of light). This was confirmed by the experiment of Heinrich Hertz with his famous Hertzian oscillating dipole. Hertz carried out the experiments in 1888 and in 1889 he published the theory to explain the electromagnetic fields surrounding this electric oscillator. These theory was derived from Maxwell's equations. Hertz experiments were performed by producing high frequency repetitive sparks in an air gap of a primary oscillating circuit. The electrodynamic disturbance was detected at a distance by a secondary circuit, resonance with the first,

with similar air gaps. Sparks were observed in the secondary receiving circuit when it was resonant with the primary circuit. Hertz calculated a graphic field-line representation of the electromagnetic field of an oscillating dipole in the near field (shorter than a wavelength of the emitted radiation), in an intermediate zone, and in the far field (at distances farther than a wavelength) where the electromagnetic energy escapes as radiation. Hertz graphical and mathematical descriptions of the oscillating electric field emanating from his Hertzian dipole, in particular in the near field, played a critical role in understanding of the energy transfer theory.

The first recorded measurements of energy transfer over distances larger than collision radii were made by Cairo and Franck in 1922 [2–4]. Cairo observed emission from thallium in a mixture of mercury and thallium vapor, when the vapor mixture was excited at wavelength of 253.6 nm, which can only excite the mercury atoms. This fluorescence emission from thallium was named “sensitized fluorescence”. The importance of resonance between energy levels of the sensitizer (the donor) and the sensitize (the acceptor) atoms was explicitly shown by further experiments, especially by the experiments of Beutler and Josephi [5, 6], who studied the sensitized fluorescence of sodium vapor in the presence of mercury vapor. The sensitized fluorescence increased in intensity when the energy differences are smaller between the states of the two participating atoms. Many of these experiments were interpreted in terms of collision theory. The number of collisions per time could be calculated from gas theory and the fraction of collision that was effective could be determined. If the rate of collisions is smaller than the calculated one, then only a certain percentage of the collisions are effective. If the rate of collisions is larger than the calculated, then there are interactions between the two collision partners that extend beyond their encounter radius. This discovery that energy transfer could take place over distances longer than the encounter radii showed that hard physical collisions were not required for atoms to interchange energy.

In 1928, Kallmann and London [7] proposed a quantum mechanical theory to explain the transfer of energy between atoms at longer distances compared to the collisional radii. This theory assumed *almost resonance* between the energy levels of the interacting atoms. They found that, provided that the corresponding transitions between the energy states of the two atoms were *dipole-allowed*, the effective cross-section  $q$  of the two interacting atoms increases as  $\sigma^{-2/3}$ , where  $\sigma$  is the difference between the excitation energies of the two interacting systems. As  $\sigma \rightarrow 0$ , the cross-section approaches a limiting value much larger than the collisional radii.

The Perrins (the father and the son) were the first to attempt a quantitative description of nonradiative energy transfer in solution between an excited molecule and a neighboring molecule in the ground state. The Perrins reasoned that the depolarization decrease that occurs in a fluorophore solution of at higher concentrations resulted from the transfer of excitation energy between molecules with different orientations before a photon was emitted. The Perrins’ model involved a near-field energy interaction between the oscillating dipoles of two identical molecules, i.e., the oscillating dipoles are in resonance. Initially, J. Perrin (the

father) developed a classical model to explain the depolarization decrease in a solution of a single chemical species of the fluorophore [8, 9]. He hypothesized that the transfer of the excitation energy could hop from one molecule to the other through interaction between oscillating dipoles of closely spaced molecules. J. Perrin modeled the participating molecules classically as Hertzian dipoles under the assumption that, if the molecules were separated by a sufficiently small distance, the energy could be transferred to the acceptor molecule nonradiatively. He named this process “*transfert d’activation*” (transfer of activation). He calculated that the distance for this process to take place is approximately  $\lambda/(2\pi)$ , where  $\lambda$  is the wavelength of the free electric field oscillating at the frequency of the atomic electric field,  $\nu = c/\lambda$  ( $c$  is the speed of light). However, this value was 20-fold greater than the experimental results. Later, F. Perrin (J. Perrin’s son) extended J. Perrin’s theory of energy transfer by developing a quantum mechanical model [10, 11], similar to what had been suggested for the energy transfer between atoms in gases [7]. He estimated that the rate of transfer is proportional to  $1/R^3$ . This results in energy transfer at much longer distances than those found experimentally. Also later, F. Perrin considered collisions between the chromophores and the solvent molecules as well as Doppler effects. These reduced the distances to about 20–25 nm, which were still too long. Because of this discrepancy, the Perrin’s theory of energy transfer lay dormant for about 20 years.

## 1.2 Förster Energy Transfer Theory

Förster’s theory and his accompanying experimental work on the energy transfer are the most widely known, and most influential, of all energy transfer publications. His major papers are listed here [12–22]. T. Förster provided an accessible theory in a form that was practical for experimenters, commonly referred to as the Förster Resonance Energy Transfer (FRET) today. Because of this reason, FRET has been widely used in physics, engineering, chemistry, biology, and medicine.

T. Förster became interested in the energy transfer process because of the known effectiveness of photosynthesis. Experiments had shown that the capture and utilization of light energy by the plant’s leaves was much more effective than was expected if it were required that photons exactly hit the reaction centers. He reasoned that an efficient transfer of energy between the chlorophyll molecules must be responsible for the eventual diffusion of the energy, which was absorbed over the whole surface of the leaf, into the relatively sparse reaction centers. Förster assumed that this diffusion is because of the energy being rapidly hopping (resonating) between molecules.

In his first paper on FRET [12], he correctly developed the basic theoretical background of FRET. First, he reviewed the mechanisms proposed by the Perrins. Then, he proceeded to take three critical, important steps that allowed him to derive a quantitative theory of nonradiative energy transfer [14]: (1) Förster took into

account the broad spectral dispersion of the donor fluorescence and the acceptor absorption, i.e., the overlapping oscillation frequencies of the donor in the excited state and the acceptor molecules in the ground state. In his first paper [12], Förster treated this frequency overlap semi-classically and semi-quantitatively. However, shortly after [13, 14], he gave a full quantum mechanical treatment. (2) Förster was able to develop a quantitative theory of the rate of energy transfer from an excited donor molecule to a ground state acceptor molecule in terms of the *overlap integral*. The overlap integral represents the probability that the two molecular transition dipoles will have the same frequency. This was a major conceptual step because these spectroscopic transitions can be measured experimentally, independent of the FRET measurement, opening a way to quantitative interpretation of the experimental data. Förster also introduced helpful expressions for the orientation factor,  $\kappa^2$ , and included the effect of the index of refraction, which affects all electric interactions in condensed media at high optical frequencies. (3) Förster's model included quantitatively the  $1/R^6$  distance dependence of the dipole-dipole interaction. He calculated the distance  $R_0$  (known as the Förster radius) where the rate of the energy transfer was equal to the rate of fluorescence emission in terms of the overlap integral, the quantum yield of the acceptor, the lifetime of the donor in the absence of an acceptor and the effective index of refraction.

Förster's original theoretical description of energy transfer set the stage for all subsequent applications of FRET in many fields of research, and his theory is still used to interpret experimental results. His insight and great contribution were to provide the quantitatively correct and very practical description of the FRET process in terms of experimentally accessible parameters. By relating the rate of energy transfer to purely experimentally available parameters, he provided the general theoretical framework for all FRET applications.

It is worth mentioning that, before T. Förster, J.R. Oppenheimer reported the theory of FRET in 1941 at the American Physical Society meeting in a paper entitled "Internal Conversion in Photosynthesis" [23]. However, the full contribution of J.R. Oppenheimer and W. Arnold was published in 1950 [24]. In the 1941 abstract, Oppenheimer discussed that the high efficiency of the energy transfer from certain dyes to chlorophyll cannot happen due to light emission and re-absorption because the probability of this process is too small. However, the energy transfer can be enhanced if the chlorophyll molecules are much closer than the wavelength of chlorophyll fluorescence, that is, in the near field of a Hertzian dipole. In the 1950 publication, Arnold and Oppenheimer proposed a mechanism of the energy transfer from phycocyanin to chlorophyll in the blue-green algae. Here, they considered three ways for the energy transfer: (1) by direct collision, (2) by emission and re-absorption, and (3) by "internal conversion". They found that the probability for energy transfer by the first two mechanisms was too small. Therefore, they focused on the energy transfer in the near field zone of Hertzian dipole radiation, that is, "internal conversion". They calculated that the total energy transfer from phycocyanin to a randomly localized chlorophyll is proportional to  $1/d^3$ , which was the result of integrating  $1/r^6$  from  $d$  to infinity.

### 1.3 Developments After Förster

Following the pioneering studies of the Perrins and Förster, there have been many reports and reviews on FRET, both theoretical and experimental. A long literature list is available in several recent reviews [25–33]. There have been several extensions of the theory of energy transfer to other experimental conditions, by T. Förster, D. Dexter, and others. Dexter [34] made a very important contribution by generalizing and extending Förster’s energy transfer model to include the donors and acceptors with overlapping electron orbitals. This resulting energy transfer over a very small distance is called “Dexter transfer” or transfer by “electron exchange”. The distance dependence of the Dexter transfer is very different from the Förster transfer, and the rate of the Dexter process is only efficient for very short donor-acceptor separation ( $<1$  nm).

In Ref. [28], Medintz and Mattoussi provided an overview on FRET using semiconductor quantum dots (QDs) and the application of QD-based FRET in biology. They started by discussing some of the relevant conceptual elements of FRET, the unique QD optical properties, and the advantages and limitations of using QDs as exciton donors and/or acceptors. Then, they described representative examples where QD-based FRET has been used for biological applications, including the detection of hybridization using QD-nuclei acid conjugates, pH and ion sensing, and antibody-based sensing. Overall, they provided a good understanding of the most important parameters that govern FRET for the D-A pairs of QD-QD, QD-dye, dye-QD, QD-Au-NP, and bioluminescent substrate-QD. Another review by U.O.S. Seker and H.V. Demir presented a summary on FRET based systems and applications using material binding peptides [29]. This focused on the selection process, molecular binding characterization and utilization of peptides as molecular linkers, molecular assembles and material synthesizers for FRET applications.

Rogach et al. [30] reviewed energy transfer using semiconductor nanocrystals (NCs). This review semiconductors NC containing thin films, solution-based complexes, and bioconjugates. Here, the energy transfer involving metal nanoantennae and metal nanoparticles were discussed. In this review, it was concluded that energy transfer involving semiconductor NCs coupled to metal nanoparticles or dyes can be used for bio-imaging and sensing. And, the use of directional energy transfer in semiconductor NCs can provide a new approach for hybrid photovoltaics. Agranovich et al. [31] presented a review on FRET in hybrid organic-inorganic nanostructures. They reported several theoretical aspects of energy transfer and discussed how hybrid organic-inorganic nanostructures can be used for optoelectronic applications. A perspective on the recent understanding of the excitonic dynamics in the organic-inorganic composites of semiconductor NCs is given by Guzelurk and Demir [35]. In another review, Guzelurk et al. [32] discussed the use of colloidal quantum dots and quantum wires in FRET for the light generation and harvesting applications.

This chapter has covered mostly the work relevant to the understanding of energy transfer prior to Förster, leading up to the final, practical expression for FRET. In the following chapters we will discuss the process of energy transfer in detail.

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