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Review

Resonance energy transfer between FMN molecules in the presence of dimers: A review☆

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ABSTRACT

This review describes theoretical and experimental methods used to study nonradiative energy transport (NET) occurring between molecules both in solid and in liquid solutions.
In particular, the methods mentioned are applied in studying energy transport between FMN molecules playing the role of chromophores in blue light photoreceptors in many living organisms.
The application of the Bojarski theory of multistep energy transfer and SCDM theoretical model as well as Monte Carlo simulations to analyze spectroscopic data of fluorescence quantum yield and emission anisotropy of FMN allows to understand the paths of energy transfer in the set of FMN monomers and dimers in liquid, viscous and rigid solutions (energy transfer from M* to D, energy migration between monomers and dimers as well as reverse energy transfer).
Evidence is provided for the "blue" and "red" monomer and dimer species, which lead to dispersive energy transfer taking place from more to less energetic FMN luminescent centers.
The parameters characterizing energy transport are calculated and provided. The explained complex character of energy transport in the system studied may be important for analyzing processes occurring in biological systems containing FMN or other photobiological molecules connected with light-harvesting proteins.

Contents

Abbreviations: NET, nonradiative energy transfer; FET-HM, Hopping Model of Forward Nonradiative Energy Transfer; RET-HM, Hopping Model of Reverse Nonradiative Energy Transfer; SCDM, self-consistent diagrammatic model; IOBEL, inhomogeneous broadening of energy levels; M, monomer; D, dimer; SBC, Smoluchowski boundary condition; RBC, reflecting boundary condition.

☆ In memory of Professor Czesław Bojarski, the author of the first successful model of multistep energy migration and trapping.

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1. Introduction

Flavins are biologically important molecules which are omnipresent in living organisms. They take part in many biochemical processes in which flavin mononucleotide (FMN), as well as flavin adenine dinucleotide (FAD) and riboflavin (RF) (Fig. 1) play extremely important biological roles in redox reactions of the respiratory chain, Krebs cycle, pirogronian dehydrogenase system and other reactions. As chromophores in photoreceptors flavins also take part in a variety of photobiological processes, among others in photodynamic effect, phototropism, phototaxis and chloroplast translocations [1–5], modulation of the circadian clock and regulation of flowering [6–13]. The research on flavoprotein photoreceptors has been discussed in many reviews [1,2,6,8, 14–16]. Rapid progress can be observed in the characterization of photoreceptors, their structure [6,16–21] and photochemistry, as well as in their functioning. Extensive studies have been carried out on structural and conformational changes of photoreceptors induced by blue-light excitation [1,6,22–24], on signal transduction pathways [1,6,9,10, 13,23,25–27], photocycles [1,4,22,28] and thermodynamic functions of transformations occurring during photocycles [29–32].

In the last decade flavin dimers were shown to occur in several biological systems. Bieger et al. [33], relying on crystallographic studies, demonstrated the presence of six riboflavin dimers in dodecin, a flavoprotein from archeal *Halobacterium salinarium*. The biological function of these dimers is not fully understood. The authors speculate that dodecin and their riboflavin dimers could participate in some sort of redox reactions. Other potential functions might be light harvesting or protection against UV radiation by aromatic tetrade which is formed by sandwiching of the six riboflavin dimers [33]. Recently Staudt et al. [34] showed that riboflavin forms antiparallel stacked dimers in archeal dodecin in which the distance between the two isoalloxazine moieties is 3.5 Å. Exactly the same distance between the monomer units in flavin dimers was obtained by Grajek et al. in solutions (3.5 ± 0.3 Å in water [35] and 3.2 ± 0.3 Å in PVA [36,37]). The x-ray structures of bacterial dodecin from *Thermus thermophilus* revealed the binding of FMN staking dimers in a novel *si–si*-orientation [38]. Muralidhara and Wittung-Stafshede [39] found for the first time parallel plane FMN dimers in flavodoxin from *Desulfovibrio desulfuricans* expressed in *Escherichia coli* in which FMN is a co-factor. They confirmed the structure of stacking FMN dimers obtained by Grajek et al. [35] on the basis of calorimetric studies of isothermic titration, NMR as well as absorption and fluorescence spectroscopy. In the paper [40] Muralidhara et al. showed the conditions under which FMN binds to apoflavodoxin as a dimer or as a monomer. Also Kitizing et al. [41], relying on crystallographic measurements of the flavoprotein YqjM, showed that this is a tetrameric enzyme organized as a dimer of two active dimers containing FMN.

Noteworthy, the compounds which play key roles in photosynthesis take the form of dimers. Among them are chlorophylls acting as dimers in photosynthetic centers of both green plants [42,43] and photosynthetic bacteria [44].

Spectroscopy and photochemistry of flavins have been the subject of intensive studies for about eighty years [45–58] in view of the wide biological function that they play in living organisms, particularly as chromophores in blue light photoreceptors [1,6,14]. Since the sixties of the 20th century every few years the symposia devoted to flavins: "Flavins and Flavoproteins — International Symposium" have been organized. The survey of spectroscopic examinations of flavins can be found in numerous review articles [37,53,57,58].

The absorption spectra of FMN, FAD and RF are similar. FMN possesses characteristic absorption maxima at 445 nm, 370 nm, 265 nm and 220 nm (Fig. 2) and it exhibits fluorescence with the maximum at around 520 nm in PVA and 530 nm in water solutions and a phosphorescence band at around 605 nm at low temperatures (below 150 K) in ethanol. At high concentrations flavins form dimers. The examinations showed that FMN in aqueous solutions [62,63] and in rigid solutions (PVA) [61,37], even at extremely high concentrations, does not form aggregates higher than dimers. The absorption spectra of dimers (Fig. 2) possess a characteristic shoulder at about 480 nm [35,37,64].

Until the eighties, the dimerization process of FMN and its influence on absorption spectra has not been studied, although the suggestions that flavins might form dimers had appeared earlier in literature [50, 51,65]. Song et al. [57] suggested extremely weak fluorescence of riboflavin (and its derivative) dimer based on the phosphorescence excitation spectra at T = 77 K. The mentioned studies have not been, however, oriented towards the determination of dimerization constant and investigation of dimerization process. In 1968 Sarma et al. [66] followed by Kainosho & Kyogoku [67] proposed the models of FMN dimer based on NMR studies, in which FMN monomers were aligned "face to face" one above the other and slightly shifted. These models differ by the shifts of isoalloxazine rings.

For the first time typical studies of the FMN dimerization process were carried out for FMN in water and in a glycerol–water solution in 1984 [64,35]. In these works the effect of dimerization on the absorption spectrum of flavins was studied. The next FMN dimerization process was examined in rigid PVA [61]. These investigations were performed very carefully and with high accuracy. The limit of solubility was not exceeded and not approached. In water, the solubility of FMN reaches 8×10^{-2} M, but in investigations of FMN in water the following range of concentrations was used: from $C = 1 \times 10^{-5}$ M to 1.8×10^{-2} M (in publications [62,64,35,68]). However, the solubility of FMN in the glycerol–water (GW) solution and in PVA is higher, so C_{max} =

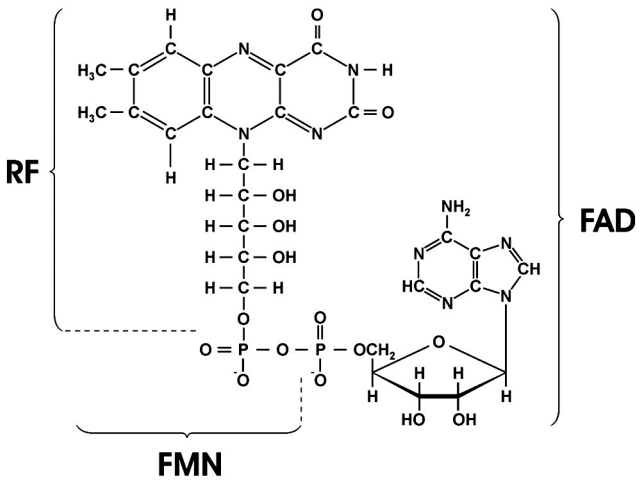

Fig. 1. Structural formula of some common flavins: riboflavin (RF), flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD).

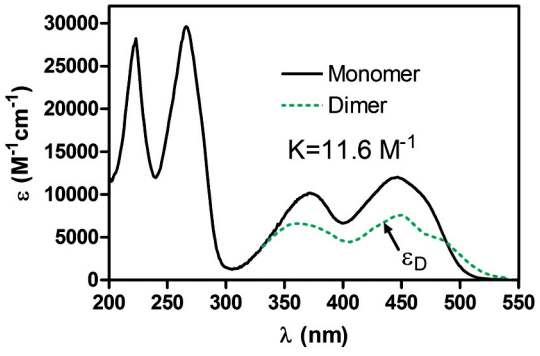

Fig. 2. Absorption spectrum of flavin mononucleotide (FMN) in aqueous solution (——) and dimer spectrum (– – – –). Dimer spectrum and the dimerization constant K were calculated on the bases of modified Förster and Levshin methods. [50–52]