
Recent method developments and applications in computational photochemistry, chemiluminescence and bioluminescence

Daniel Roca-Sanjuán,^a Ignacio Fdez. Galván,^b
Roland Lindh^b and Ya-Jun Liu^{*c}

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This review summarises and discusses the advances of computational photochemistry in 2012 and 2013 in both methodology and applications fields. The methodological developments of models and tools used to study and simulate non-adiabatic processes are highlighted. These developments can be summarised as assessment studies, new methods to locate conical intersections, tools for representation, interpretation and visualisation, new computational approaches and studies introducing simpler models to rationalise the quantum dynamics near and in the conical intersection. The applied works on the topics of photodissociation, photostability, photoisomerisations, proton/charge transfer, chemiluminescence and bioluminescence are summarised, and some illustrative examples of studies are analysed in more detail, particularly with reference to photostability and chemiluminescence. In addition, theoretical studies analysing solvent effects are also considered. We finish this review with conclusions and an outlook on the future.

1 Introduction

When the 2013 Nobel Prize in Chemistry was awarded to three theoretical chemists—Martin Karplus, Michael Levitt and Arieh Warshel—Chemical & Engineering reported “Theoretical chemistry doesn’t always get the respect it deserves”.¹ This has been also our feeling for many years. However, the situation seems to be changing nowadays, at least in the field of photochemistry, in which theoretical and computational researchers are better recognised as compared with those in other fields. We truly believe that science must take advantage of the synergy obtained when joining theory and experiments. And we gratefully appreciate journals, publishers and scientific organisations that facilitate approaches between experimentalists and theoreticians.

In the previous two volumes of this book series,² we already introduced the main concepts related to photochemistry (also called chemistry of the excited states), mainly focusing on those aspects that are relevant for the computational studies. Due to the complexity, diversity and short life of excited states, experiments by themselves cannot give the details of the reaction mechanism without assistance. However, computational

^a*Instituto de Ciencia Molecular, Universitat de València, València, Spain*

^b*Department of Chemistry—Ångström, Theoretical Chemistry Programme, Uppsala University, Uppsala, Sweden*

^c*Key Laboratory of Theoretical and Computational Photochemistry, Ministry of Education, College of Chemistry, Beijing Normal University, Beijing, China.
E-mail: yajun.liu@bnu.edu.cn*

photochemistry can assist. It can predict experimentally inaccessible information,³ interpret experimental observations, uncover the reaction mechanisms and ultimately be used to design novel photochemical systems with interesting properties.

With this review, we summarise the advances in computational photochemistry in 2012 and 2013 from the viewpoints of methodological developments and applications. The methodological development includes assessment studies, new methods to locate conical intersections (CIXs), tools for representation and interpretation, new computational approaches and studies introducing simpler models to rationalise the quantum dynamics near and in the CIX. The application works will be divided in the following topics: photodissociation, photostability, photoisomerisations, proton and charge transfer, solvent effects and chemiluminescence and bioluminescence. Two of them are especially highlighted. One is the photostability phenomenon, which provides certain biological molecules with photochemical channels for ultrafast release of the UV energy. The second one is chemi/bioluminescence, which is a hot topic in recent years and has been widely applied in various fields, such as biochemical analysis, gene expression, gene regulation and environmental monitoring. We finish this review by conclusions and an outlook on the future. If we have missed any important publication, the error is ours and we apologize.

2 Development of methodology (2012–2013)

The method developments over the period have been intense; a reflection of the significance that photochemistry has today in our quest to understand the nature of the chemical reactivity. While in the recent past, much effort was put into developing and understanding the pros and cons of various wave function models and density functional theory (DFT), to correctly describe, in both a qualitative and quantitative fashion, the CIX—a matter which to a large extent is settled now—the present period has seen scientific reports which are more of a general nature. In this respect the methods developments can be divided into five different categories. First, there are a number of interesting contributions which assess the quality and success of various electron structure models to describe CIXs and the usefulness and conditions which affect quantum dynamics simulations. Second, studies which analyse the quantum dynamics through the CIX or suggest simple models to rationalise the process. Third, reports which suggest novel methods to locate the CIX. Fourth, proposals to simplify or improve electron structure methods for the study of excited states and non-adiabatic processes. Fifth and final, scientific reports which suggest and propose tools related to the diabatic representation of potential energy surfaces (PESs). We will in some detail, but still very briefly, summarise these reports here, and for the curious we of course recommend reading of the original publications. Our purpose here is just to tease the reader's appetite for further reading or to present a compressed but informative list for the reader who just wants to stay in touch with the recent developments in the field.

2.1 Assessment studies

As mentioned above the use of single and multi-configurational wave function models and DFT in association with simulations of radiationless photochemical processes has been debated over the years. In particular, the ability of these methods to provide a qualitatively correct description of the CIX has been subject of intense debate. During 2012–2013 a number of assessment studies have been published which monitor this, in particular for the CIX of the retinal chromophore.^{4,5} In addition, one study⁶ focuses on the ability of obtaining molecular structures of CIXs using various DFT functionals. Moreover, the so-called occupation-restricted multiple-active-space (ORMAS) method⁷ has been studied with respect to the ability to compute non-adiabatic coupling (NAC) and the restricted active space spin-flip configuration approach (RASCI-SF) has been studied in cases of near degeneracy.⁸ Finally, it is worth mentioning two reports, which monitor the performance of frozen-width variational Gaussian product basis functions in association with non-adiabatic direct dynamics simulations⁹ and the wavepacket delocalisation due to the topology of the excited state PES during relaxation of polyatomic systems.¹⁰

The two studies by Gozem, Olivucci and co-workers^{4,5} on a retinal chromophore model (PSB3) have assessed the performance of DFT, equation-of-motion coupled cluster (EOM-CC) methods and multi-reference methods with respect to quantitative and qualitative accuracy to describe the PESs and the CIX. In the first study⁴ various DFT methods [generalised Kohn–Sham DFT (GKS-DFT), time-dependent DFT (TDDFT) and spin-restricted ensemble-DFT (REKS)] were benchmarked against multi-configurational reference results. In particular, the study focuses on the two important electronic configurations in the isomerisation process of PSB3—the diradical and the charge-transfer state. Here, Gozem and co-workers demonstrate that standard linear-response TDDFT has many shortcomings and that results are often qualitatively wrong and much dependent on the used functionals. It is concluded that only the so-called state-averaged REKS (SA-REKS) and state-interaction SA-REKS (SI-SA-REKS) give a reasonable agreement with the multi-reference configuration interaction singles, doubles plus quadruples (MRCISD + Q) reference values (see Fig. 1). This finding is in agreement with the study of Filatov⁶ who concluded that SI-SA-REKS reproduces accurate reference structures of CIXs for a number of organic molecules, that the crossing points had the correct dimensionality and that the model satisfied the sign-change theorem. In the second paper, Gozem, Olivucci and co-workers⁵ benchmark EOM-CC against MRCISD and multireference second-order perturbation theory (MRPT2) reference values for the same model system. Briefly, the authors conclude that EOM-CC methods, especially the spin-flip version of EOM-CC with second order perturbative corrections for triple excitations, provide an alternative in the study of the photochemistry of systems like PSB3, as compared to multireference methods.

In another study West and Windus⁷ assessed the ability of the ORMAS method to provide reliable gradients and NAC vectors around a CIX.

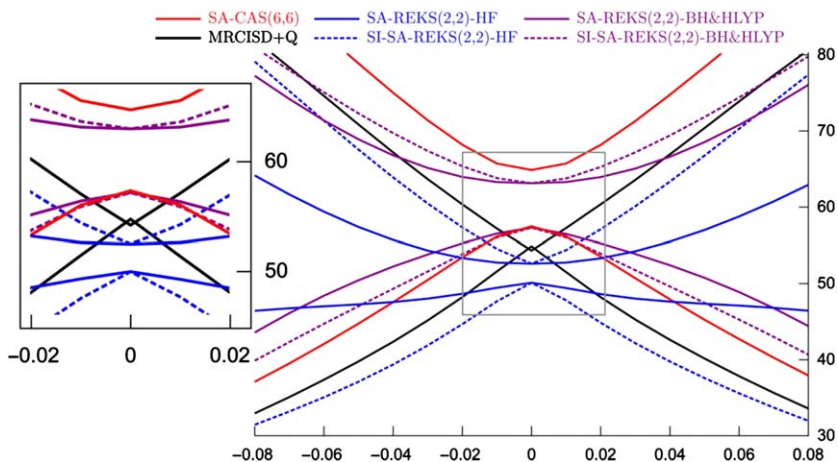


Fig. 1 SA-CAS(6,6), MRCISD and SA-REKS S_0 and S_1 energy profiles (in kcal mol⁻¹) along minimum energy path. [Reproduced from *J. Chem. Theory Comput.*, 2012, 9, 284.]

The development of the ORMAS method—a CI expansion size reduction method—has been initiated as an alternative to complete-active-space self-consistent-field (CASSCF) method when the latter gets computationally too expensive. However, for the ORMAS method to truly be an alternative it has to reproduce to a large degree of accuracy the CASSCF results. The benchmarking, based on SiCH₃ and butadiene, reveals that while the ORMAS and the ORMAS single excitation scheme can reproduce CASSCF geometries at the CIX, there is an issue with the integrity of the active space. The latter is a serious problem when using the method to explore PESs. Furthermore, the authors note that the CASSCF and the ORMAS methods do not provide a maximum magnitude of the NAC matrix elements for exactly the same molecular structures, additionally the gradients are different in the vicinity of the CIX. Similarly, Casanova⁸ benchmarked the reliability of the restricted space spin-flip CI approach (RASCI-nSF). The RASCI method is a single reference approach, in which the reference determinant is operated on by a general excitation operator to generate a linear combination of Slater determinants. In particular, the excitation operator can contain so-called spin-flip (SF) excitations. This facilitates the use of reference functions which do not have the same spin multiplicity as the target states. While the study shows that the RASCI-nSF is a reliable alternative to CASSCF, the lack of dynamic correlation can be an issue (just as for CASSCF). Moreover, the method needs to be further developed to include energy gradients with respect to the nuclear coordinates.

Finally, some comments on two recent studies^{9,10} on methods for quantum dynamics simulations. In the first study, by Mendive-Tapia *et al.*,⁹ the convergence of non-adiabatic direct dynamics in conjunction with frozen-width variational Gaussian product basis functions is evaluated. The simulation of non-adiabatic dynamics can be subdivided into two groups: semi-classical methods (like the trajectory surface hopping approach) and wavepacket methods (for example, the

multi-configuration time-dependent Hartree method, MCTDH). While the former can be applied to arbitrarily large system, the approach does not allow for a systematic improvement towards convergence, however, the latter can provide numerically correct results but are limited to systems with just few degrees of freedom. The direct dynamics-variational multi-configuration Gaussian (DD-cMCG) wavepacket approach has been suggested as a method to bridge this gap. In the study by Mendive-Tapia *et al.*,⁹ the convergence of the DD-cMCG method was investigated in association with a study of fulvene, on the two lowest states and the corresponding radiationless decay. The study primarily explores the nature of convergence, based on the extent of spatial sampling of the CIX seam, the timescale and the populations of the states, with respect to the number of coupled Gaussian product basis functions. The authors demonstrate, in the case of fulvene, a convergence for 24 GBFs, but also indicate that this is just a single molecule conclusion. However, the preliminary results of the use of the DD-vMCG method are promising and indicate that the method has a significant potential for the future. The effect of surface topology (see Fig. 2) on the wavepacket delocalisation has been monitored by Krause and collaborators.¹⁰ This study reported the non-adiabatic relaxation for several molecular systems. In particular,

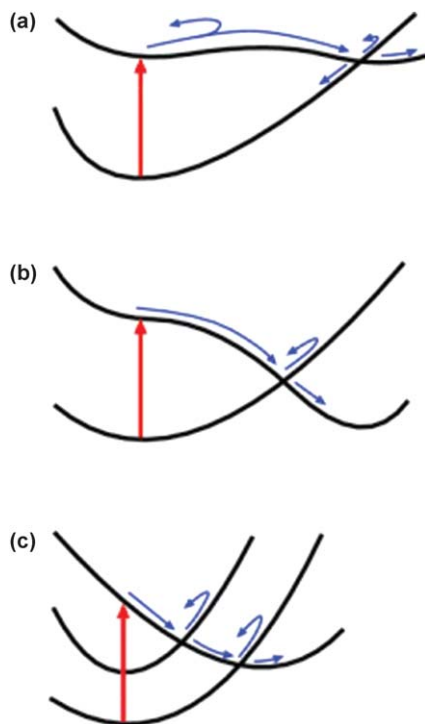


Fig. 2 Cartoons of PESs illustrating different cases of how the wavepacket can move and delocalise. Panel (a) shows an excited state with a barrier which can lead to delocalisation. Panel (b) shows an excited state that is steep and leads to localised dynamics. Panel (c) shows a case where CIXs between excited states can lead to delocalisation. [Reproduced from *J. Chem. Phys.*, 2012, **137**, 22A537.]

using a small 2D-model and the MCTDH approach, they report on how the topology of the excited state surfaces induces local or non-local relaxation. Additionally, the relaxation rate is determined to be another key factor which impacts the localisation of the relaxation.

2.2 Quantum dynamics in the conical intersection

To assist in the analysis of the quantum dynamics in internal conversion (IC) processes a number of papers have been presented which analyse the process in terms of perturbation theory, in terms of effective modes and quadratic coupling, careful analysis of the geometric phase effects near the CIX, or propose simple models to bring in a clearer picture of the fundamentals of the process.^{11–15}

In an elegant paper, by Molesky and Moran,¹¹ a fourth-order perturbative model is suggested and developed for the study of photoinduced IC. The authors stress that in case of a similar timescale for the electronic and nuclear motions, a second-order perturbation scheme, *à la Fermi*, will fail. Additionally, the model, as suggested here, in the case of a dominant promoting mode, can exclusively be parameterised from experimental data. The method is based on a three-way partition of a model Hamiltonian—system, bath and system–bath interaction. Subsequent use of a time correlation function approach facilitates the evaluation of rate formulas. This analysis is applied to a three-level model system containing a ground state, an optical active excited state and an optical dark state, the latter two share a CIX. In their paper the model is used to analyse the initial photoinduced process of alpha-terpinene. The primary conclusion of the study is that the most important influence on the population decay (Gaussian *versus* exponential) is the rate at which the wavepacket approaches the CIX of the two excited states.

The quadratic vibrational coupling (QVC) model has recently been suggested as an extension of the linear vibrational coupling (LVC) model. Vibok *et al.*¹² extend the QVC model applicability to larger systems by introducing a partitioning, similar to the one of Molesky and Moran,¹¹ *i.e.* a system and a bath part. Again, using time autocorrelation techniques Vibok and co-authors derive intensities, the centre of gravity and the width of the spectrum. The new QVC model, in association with a three-effective mode model, is benchmarked against a 3- and 5-effective mode LVC model and an exact 18-mode MCTDH model for the butatriene molecule. The authors report that the 3-mode QVC approach reproduces the short-time dynamics (0–14 fs) and the overall shape of the spectra. Additionally, the diabatic populations are in good agreement with the MCTDH results for up to 75 fs (see Fig. 3).

Effects due to the geometric phase (GP) have been reported by Joubert-Doriol, Ryabinkin and Izmaylov.^{13,14} In particular they report on symmetry breaking and spatial localisation,¹³ and on GP effects studied with the multi-dimensional LVQ model. In the first study by Ryabinkin and Izmaylov¹³ the ground state dynamics is considered of a two-state system approximated by (a) a Hamiltonian of a two-state CI model, (b) the Born–Oppenheimer (BO) model and (c) a BO model augmented with an explicit GP dependence in the kinetic energy operator. It is demonstrated that

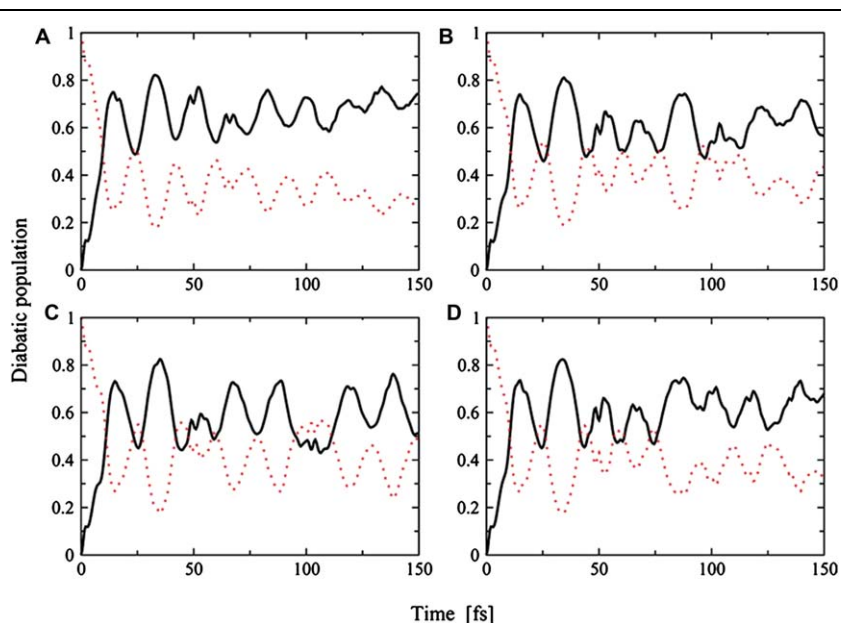


Fig. 3 Diabatic-state populations for the butatriene as a function of time. The D_1 state is initially excited. Population for the lower state D_0 (solid line) and for the upper state D_1 (dashed line) are presented. Panel A: exact 18-mode model. Panel B: linear vibronic coupling model (5-mode). Panel C: three-effective-mode approach. Panel D: quadratically extended three-effective-mode approach. [Reproduced from *J. Phys. Chem. A*, 2012, **116**, 2629.]

while for the BO model the ground state solution is delocalised both the two-state CI Hamiltonian model and the BO-GP approach mandate localised ground state wave function—a localisation which is attributed to the GP. Furthermore, on lifting the degeneracy the localisation in the BO-GP and the two-state CI Hamiltonian model persists for a range of the energy separation. Moreover, the authors demonstrate that the BO nuclear dynamics breaks down even in regions far away from the CI, especially low-energy dynamics as tunnelling between two wells is reduced or even blocked due to GP effects. In the second paper, by the same group,¹⁴ the GP effect is studied for the nuclear dynamics of a multi-dimensional LCV model and the authors stress that proper modelling of the nuclear dynamics requires that both non-adiabatic coupling and GP effects have to be included. In the model study the effective modes are partitioned into the subspace governed by the GP and the complementary $N - 2$ dimensional environment. The paper focuses on how the GP effects are affected by the subspace–environment interaction, a matter of some controversy. The authors demonstrate that while the branching space–environment interaction might make the nodal line in the branching space density disappear—a sign of GP effects (see Fig. 4)—the overall population dynamics are quite different with or without GP effects included in the model.

Last in this subsection we would like to mention a report by Fermanian-Kammerer and Lasser on a surface hopping approximation

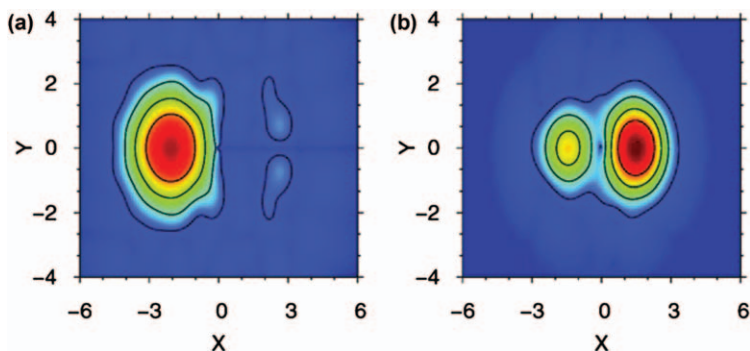


Fig. 4 Snapshots of $\sqrt{|x_1^{\text{adi}}|}$ at $t = 100.0$ a.u. for the same parameters: (a) with GP and (b) without GP. The square root is used to make a nodal line legible. [Reproduced from *J. Chem. Phys.*, 2013, **139**, 234103.]

for quantum dynamics.¹⁵ Despite the trivial nature of the model, a two-state system with a CIX in association with a single switch algorithm, it might have some merits in understanding the fundamentals of non-adiabatic processes at a CIX or an avoided crossing.

2.3 Conical intersection optimisations

Tools to find the CIXs in an efficient and robust way are instrumental in the simulations and computations of radiationless decay. During 2012–2013 three interesting reports^{16–18} dedicated to this craft were published. The first two present new approaches: the seam space nudged elastic band method (SS-NEB)¹⁶ and the double Newton–Raphson algorithm using composed steps (DNR-CS).¹⁷ The third report describes an automated search method to find minimum energy CIXs,¹⁸ the so-called SMF/ADDF approach.

The SS-NEB method, reported by Mori and Martínez, combines the nudged elastic band method with the gradient projected minimum-energy conical intersection (MECIX) optimisation approach to explore the minimum energy seam path (MESP). While the nudged elastic band method approach was originally developed to trace reaction paths, the projected gradient method implies a constrained optimisation. The combination of the two techniques allows for the generation of MESPs, which the authors suggest may be important in the understanding of radiationless decay. The so-called double Newton–Raphson (DNR) algorithm using composed steps (DNR-CS), a quasi-second order method, is proposed by Ruiz-Barragan, Robb and Blancafort.¹⁷ Here the authors combine an initial Newton–Raphson (NR) optimisation, in redundant coordinates to reach the seam, with a second NR optimisation using the branching space Hessian. The latter is obtained by the standard BFGS quasi-Newton update method using the branching vectors. While standard methods seem to suffer from the fact that the complementary vectors of the branching space are not uniquely defined the composed step approach avoids this. Ruiz-Barragan *et al.* report (see Fig. 5) that the new approach is 30% and 15% more efficient as compared to the

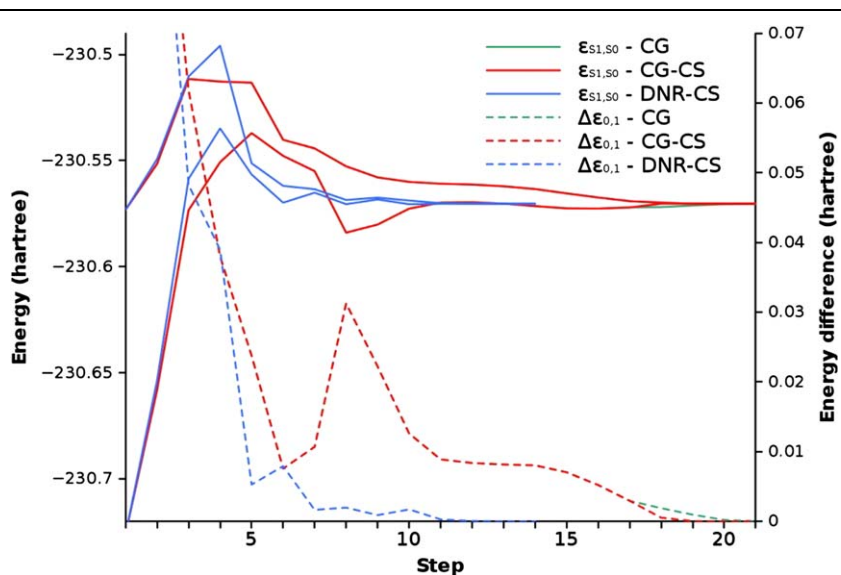


Fig. 5 Course of MECIX searches with the CG, CG-CS and DNR-CS algorithms for benzene (green, red and blue lines, respectively). Full lines, S_1 and S_0 energies (left y axis); hashed lines, S_1S_0 energy difference (right y axis). Energies in hartree. [Reproduced from *J. Chem. Theory Comput.*, 2013, 9, 1433.]

composed gradient (CG) and the CG-CS hybrid methods, respectively. The authors attribute the nature of the quasi-second order approach for geometry optimisation in the seam to be a vital part of the improvement represented by the DNR-CS method as compared to earlier methods.

Since most CIXs are located through chemical intuition one might worry that non-trivial and essential CIXs might be missed in standard simulations. Harabuchi and co-workers offer a solution to this potential problem.¹⁸ In their report they combine the anharmonic downwards distortion following method (ADDF) with a model function, a seam model function (SMF), which restricts the search to the intersection seam. The ADDF method has been developed to explore reaction paths in an automated way. While it can become prohibitively expensive for larger systems, additional variations of the method, as the large ADDF (l-ADDFn), make the approach more economical. The seam model function is based on a model function with two components: the average energy of the two states and a penalty function depending on the energy gap between the same two states. In their report Harabuchi *et al.* apply the SMF/l-ADDF3 approach to the location of S_0/S_1 CIXs of ethylene and 1,3-butadiene in association with spin-flip TDDFT. The new approach found automatically all previously reported minimum energy CIXs and some new, which subsequent calculations confirmed was relevant to the photochemistry of the studied systems.

2.4 Novel and simplified electronic structure methods

The quest to make simulations of photochemical processes simple and effective is limited to that only expensive and complicated

multireference and multi-configurational methods are today the standard reference method. It has been showed that for example the SI-SAREKS style of DFT or spin-flip EOM-CC in association with perturbative triplets corrections can be a leaner way for such simulations without any or significant loss of accuracy. However, these are not the only avenues toward reduced computational expenses in photochemical simulation techniques. Below we will mention three reports,^{19–21} which suggest some new approaches that could be part of the future standard tools for computer simulations. The first two reports^{19,20} are due to Lu and Matsika and are dedicated to the use of high-multiplicity natural orbitals in multireference CI models, whereas the third deals with a remedy to unphysical symmetry breaking for multireference methods. One of the more time consuming steps in the CASSCF/complete-active-space second-order perturbation theory (CASSCF/CASPT2) (or MRCI) approach is the generation of the self-consistent field orbitals. An alternative approach is to skip the orbital optimisation and simply do a CASCI. Could this be reasonable? Well, the use of SA-CASSCF orbitals—generated in an average way and not specifically for an individual state—indicates that there might be some truth in this. However, the SA-CASSCF orbitals are also expensive to compute and are not an alternative. This question has concerned Lu and Matsika who suggest that high-multiplicity natural orbitals (HMNO) might be an alternative.^{19,20} This approach is first developed in their initial report,¹⁹ where they test it for excitation energies. In the subsequent paper²⁰ they explore the approach more in general by studies on the accuracy of the PESs of excited states, which the new approach produces. The suggested recipe to produce starting orbitals, for the CASPT2 or MRCI calculation, is the generation of natural orbitals from a single reference CISD calculation with high-multiplicity (usually a triplet or quintet state). Additionally, Lu and Matsika noted that the use of natural orbitals allows for a systematic truncation of the virtual space in the CASPT2/MRCI treatment which shows a smooth convergence behaviour. To this purpose they developed an occupation criterion to facilitate a consistent convergence pattern for molecular systems of different numbers of electrons. With this approach they showed that singlet excitation energies of the HMNO/MRCI approach exhibit a difference to reference CASSCF/MRCI values of less than 0.1 eV while truncating a large part of the virtual space in the MRCI step. The small loss of accuracy comes with an attractive substantial reduction of the computational cost, as compared to the reference calculations. Additionally, they demonstrated that accuracy increases as the one-particle basis set is increased. In the subsequent paper,²⁰ comparing PESs rather than vertical excitation energies, Lu and Matsika note that errors can be between 0 and 1 eV. However, with a prudent approach the average error is as small as 0.2 eV. Furthermore they report that the regions of CIXs are faithfully reproduced by the HMNO/MRCI approach. One important observation is that the success of the method depends strongly on that the reference function does not itself experience any CIXs or weakly avoid crossing. Finally, they report that some care has to be taken in the selection of the active space and that standard selections in some cases can cause problems.

To conclude this subsection we would like to briefly report on a study by Shu and Levine.²¹ The multi-configurational SCF procedure can in some instances produce unphysical symmetry breaking—this is not something unheard of before. Usually it manifests itself in that the symmetry of the wave function does not follow the symmetry of the molecular nuclear structure. Shu and Levine report on several such cases and suggest the origin of the feature and a remedy. The presence of off-diagonal Hamiltonian elements, similar to what is observed in pseudo-Jahn–Teller effects, is assigned as the origin of the unphysical behaviour. Shu and Levine propose a singly excited active space CASCI approach to eliminate the dependency of these off-diagonal Hamiltonian elements. However, in their conclusion they state that while the new approach reduces the artefact it does not completely eliminate the effect. But, they also report that for a number of model systems used in their study the optimised SEAS-CASCI structures were nearly identical to the CASSCF reference structures.

2.5 Diabatisations

For an accurate quantum dynamical description of nonadiabatic processes analytic representation of adiabatic potential energies and non-adiabatic coupling are required. However, the singular nature of the nonadiabatic coupling in the CIX and the related large variation close to it makes them inconvenient for studies of the dynamics. This problem can to a large extent be removed by the use of a diabatic representation—a representation which is not uniquely defined. In this section we briefly mention two recent studies,^{22,23} which report different procedures to generate (quasi-)diabatic representations. In the first report Yang and co-workers²² report on a variation of the so-called fourfold-way diabatisation scheme by Nakamura and Truhlar. The attractive feature of this approach is that it is “direct”—the potential and nonadiabatic coupling of the diabatic states are geometry unique—and the diabatic electronic states span the same space as the original adiabatic states. The scheme is based on the density matrix. In the original implementation this density matrix was evaluated at the correlated level of theory, while in the new report the density matrix includes only static electron correlation at the multi-configuration SCF level of theory. In particular, the scheme uses diabatic molecular orbitals (DMOs) generated at the CASSCF level of theory rather than at the multi-configuration quasi-degenerate perturbation theory (MC-QDPT) level of theory, a simplification which has both practical and computational advantages. In the former case, the use of CASSCF DMOs over MC-QDPT DMOs relieves the diabatisation of some of the known problems that some perturbation theories experience close to a CIX. In conclusion, Yang *et al.* report that the quality of the MC-QDPT diabatic states is not compromised by the use of the CASSCF DMOs rather than the MC-QDPT DMOs. In the second paper, Zhu and Yarkony propose a new quasi-diabatic fitting scheme based on a vibronic coupling model, that is, no explicit considerations of the wave function is included as in the fourfold-way diabatisation approach. This diabatisation approach is of a least-square fitting nature, but is designed such that

the fit is exact for some points which are considered to be of high significance, for example, for points in the conical seam. This approach is hence purely numerical but of high precision. In the paper Zhu and Yarkony describe in some detail the numerical details of the approach, including the use of an approximate Newton–Raphson method and polynomials with flexible origins. The accuracy and improvement of the method is demonstrated by an example of the photodissociation of ammonia.

3 Applications (2012–2013)

In the presently reviewed period of time, 1662 publications appear in the Web of Science by using the topic keywords “theoretical” and “excited state”.²⁴ This may give a rough idea of the impact of theoretical and computational chemistry of the excited states. Among the theoretical studies on photochemistry, the target systems range from small-size isolated molecules to large molecules in proteins, and middle-size molecular systems are often studied reporting predictions for the gas phase and/or solution. Theoretical works on the dynamics are found, although electronic structure computations aimed to report mechanisms using a static approach are more common. One important trend is towards the understanding of photochemistry in complex systems. In this section, we will summarise relevant topics in the studies published in 2012 and 2013. As for the methodological developments, our purpose here is to update the reader interested in the field of applications of computational photochemistry with some illustrative examples rather than providing him with a detailed description of the complete list of application works.

3.1 Photodissociation

“Photodissociation, photolysis or photodecomposition is a chemical reaction in which a chemical compound is broken down by photons”.²⁵ Studies on molecular photodissociation reactions aim at understanding the chemistry of bond cleavage induced by irradiation with light. More than 500 papers with photodissociation (or photolysis, or photodecomposition) in the title have been published in 2012 and 2013. Theoretical calculations play an important role in most of these publications. The studied systems are carbonyl compounds, aromatic compounds, water, aliphatic and aryl halides, ozone and so on. The theoretical study on the photodissociation of NO_3 is impressive, and it is selected here as an example.

Morokuma and co-workers systematically studied the photodissociation mechanism of $\text{NO}_3 \rightarrow \text{NO} + \text{O}_2$ by calculating the global PESs, quasiclassical trajectory dynamics simulations and all possible photocatalytic channels.^{26–28} A series of joint theoretical and experimental studies firstly demonstrate an excited-state roaming mechanism on the visible light-induced reaction $\text{NO}_3 \rightarrow \text{NO} + \text{O}_2$. In NO_3 photolysis there are two roaming pathways involved. One is that, after a N–O bond cleavage, the dissociated fragments ($\text{NO}_2 \cdots \text{O}$) of the molecule do not have sufficient energy to escape, and the dissociating O atom orbits the

remaining NO₂ fragment until encountering a reactive site to form the products NO + O₂ *via* intramolecular abstraction. The other is *via* a CIX between the first excited and ground states in the region of the dissociating O atom orbiting the remaining NO₂ fragment, which mediates the decay to the ground state, and finally the abstraction of another O atom takes place to give the products NO + O₂. The roaming mechanism is different from that obtained with the traditional transition-state theory, and entirely bypasses the saddle point. In general, roaming is discussed exclusively for reactions on the ground electronic state. Morokuma's group firstly declared that the roaming pathways of NO₃ photolysis take place on an excited electronic state, as illustrated in Fig. 6. They also reported analytical global PESs for the three low-lying doublet states of NO₃ based on multistate CASPT2 (MS-CASPT2) calculations and invariant permutation principle. Furthermore, Bowman's group in cooperation with Morokuma's group carried out hundreds of thousands of quasi-classical trajectory calculations relying on the modified new PESs, and compared with the experimental information including two roaming pathways, products NO + O₂ vibrational state, rotation state, translational energy distributions, and so on. The theoretical results are in a good agreement with the experimental ones in the NO₃ system.

3.2 Photostability, ultrafast non-radiative decay

The term "photostability" (as it is employed here) refers to the photochemical property of those molecular systems in which the most efficient decay channel after light irradiation is the ultrafast decay toward the original equilibrium structure on the ground state surface. Experimentally, sub-picosecond or picosecond lifetime signals are typically measured in the photostable molecules. Meanwhile, from a mechanistic point of view, the ultrafast energy deactivation process takes place by means of a barrierless or almost barrierless path from the bright excited state at the equilibrium structure of the ground state to the very same original geometry *via* a CIX which transfers the excited-state population back to the ground state (see Fig. 7a). Out of the group of photostable molecules, we can find molecular systems which spend long time on the

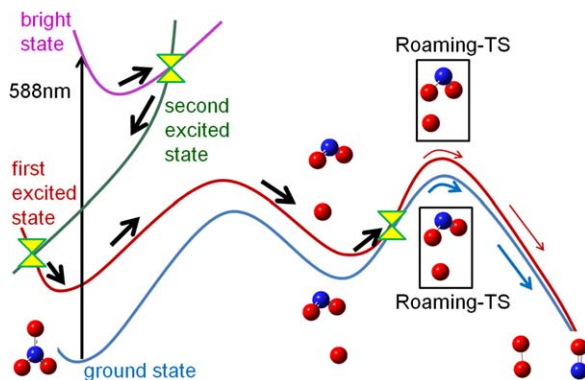


Fig. 6 PESs and proposed reaction pathways for photodissociation of NO₃ → NO + O₂.

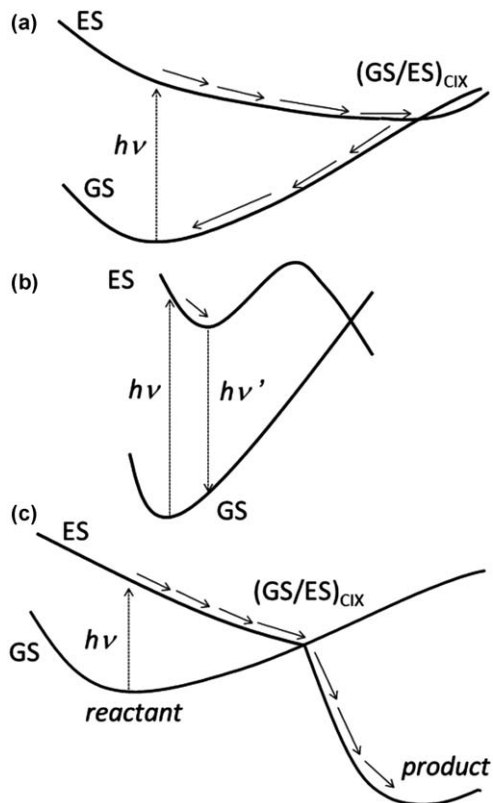


Fig. 7 Scheme based on PESs of different types of decay mechanisms: (a) non-reactive non-radiative, (b) non-reactive radiative and (c) reactive non-radiative.

excited state after photoexcitation (see Fig. 7b) and other molecules that decay to a new equilibrium structure on the ground-state PES (see Fig. 7c). Isomers or degradation (decomposition) products are typically produced in the latter process.

The naturally-occurring DNA nucleobases are examples of molecules featuring photostable properties against the UV radiation (see ref. 29 and references therein). During the last decades, great efforts have been dedicated by many well-recognised theoretical groups in the field to decipher different aspects of the mechanism for ultrafast decay. We have reviewed relevant studies published in the periods 2007–2011 in our previous contributions to the Photochemistry series.^{30,31} Three distinct theoretical approaches can be distinguished: geometry optimisations of several minima on the excited-state PES and determination of the minimum-energy CIXs between the excited and the ground states (approach A), minimum energy path (MEP) computations from the FC region on the brightest excited state (approach B) and dynamics simulations (approach C). Only the latter can produce a complete description of the decay channels, with the percentage of molecules that follows each possible route and the associated life times. However, highly accurate dynamics simulations are nowadays still very time- and CPU-demanding.

In addition, the results are extremely sensitive to the level of theory used for the PES, which make low-level methodological approaches non reliable. On the other hand, the static approach provides plausible photochemical mechanisms and discards others. In this context, single determinations of excited-state minima and CIXs with the ground state (approach A) are not safe procedures. Instead, the photochemical reaction path approach must be used (approach B). It corresponds to the determination of the most probable evolution of the molecule after light absorption to the brightest excited state towards a minimum or a state crossing by means of MEP computations and the location of the most relevant CIX points for surface hopping.

In 2013, the first MEP at the CASPT2//CASPT2 level for cytosine was computed by Nakayama *et al.*³² The findings are in agreement with previous CASPT2//CASSCF results and support the presence of a minimum along the main decay path, which is in contrast to the scenario described by MEP computations at the CASPT2//CASSCF level for thymine and uracil.³³ The presence of the barrier in cytosine is also supported by recent experimental studies that have reported a dependence on temperature of the fluorescence.³⁴ In any case, the energy barrier height is estimated to be very small, thus preserving the photostable properties of the molecule.

The MS-CASPT2 method was earlier used within the approach A by Yamazaki and Taketsugu³⁵ to study thymine and uracil, pointing out to the importance of taking into account the dynamic electron correlation in the geometry optimisation method to properly determine the geometries of the critical points on the PESs of the low-lying excited states of the nucleobases. The hypothesis of a direct path to the crossing with the ground state involving only the lowest-lying $^1(\pi\pi^*)$ [and not both $^1(\pi\pi^*)$ and $^1(n\pi^*)$ states, as described in other studies],^{36–38} is supported. However, MEP computations (approach B) or highly-accurate dynamics simulations (approach C) would be required to determine the most relevant decay paths taking place in thymine and uracil.

Regarding theoretical studies on the dynamics (approach C), it is worth mentioning the work by Barbatti *et al.*³⁹ carried out in order to find the reason for the discrepancies obtained in previous studies^{40–44} on the dynamics of adenine in the gas phase concerning the predominant decay mechanism. The work highlights (as described above) the fine dependence of the data obtained from the dynamics simulations on the topography of the PESs. The TDDFT method employing different functionals was shown to fail to predict the ultrafast decay, whereas simulations with the semiempirical OM2 and *ab initio* MRCI methods predicted similar timescales, although through different IC channels.

The relaxation mechanisms of modified or derivative nucleobases are also very helpful to understand the peculiar photochemical properties of the canonical nucleobases. In 2012, Bakalska and Delchev⁴⁵ compared the decay paths of cytosine and isocytosine. In 2013, Engler *et al.*⁴⁶ focused on the differences between 9*H*-adenine and 9-acetyladenine by carrying out a study combining data obtained from resonant two-photon ionisation spectroscopy of the laser-desorbed molecules and DFT/MRCI

and CC2 results. The authors ascribed the different experimental signals to the fact that the excitation process in the derivative nucleobase involves a partial charge transfer from the chromophore to the acetyl group not present in the canonical nucleobase.

The intersystem crossing (ISC) process in the canonical and substituted DNA nucleobases has also been studied during the 2012–2013 period by the groups of Borin^{47,48} and González.^{49–51} By means of adding aza- or thio-substituents to the natural molecular structure of the DNA nucleobases, the quantum yield for the population of the triplet state increases significantly. Hence, these new compounds can be used as photosensitisers in photodynamic therapy. Gobbo and Borin determined the mechanisms for triplet excited states population of 6-aza-2-thiothymine⁴⁷ and 8-azaadenine⁴⁸ by using the photochemical reaction path approach based on MEP computations and the determination of the most relevant ISC points. Meanwhile, González and co-workers focused on the dynamics of the ISC process in the keto and enol tautomers of cytosine^{49,50} and the 6-thioguanine⁵¹ molecule.

Besides the intrinsic properties for ultrafast decay of the isolated nucleobases, other photochemical channels might be activated in the DNA *via* excited state proton/hydrogen transfers (ESPT/ESHT) in the guanine–cytosine and adenine–thymine base pairs. As explained in our previous review³¹ and by Gobbo *et al.*⁵² in the study of the latter dimer, the new decay routes can provide additional photostability to the DNA, although they can also produce tautomers of the nucleobases. In 2013, Sauri *et al.*⁵³ performed an extended quantum mechanics (QM) and QM/molecular mechanics (QM/MM) study on the guanine–cytosine base pair in which first, the most relevant decay channels for photostability and photoinduced tautomerism *via* ESHT was determined for the gas phase with the CASPT2 method, second, the plausibility of the *in vacuo* mechanism was analysed in the DNA by means of the CASPT2/MM hybrid methodology, and finally, some aspects on the dynamics of the ESHT process in the base pair were considered using *ab initio* molecular dynamics based on the CASSCF method. Figure 8 shows all the possible

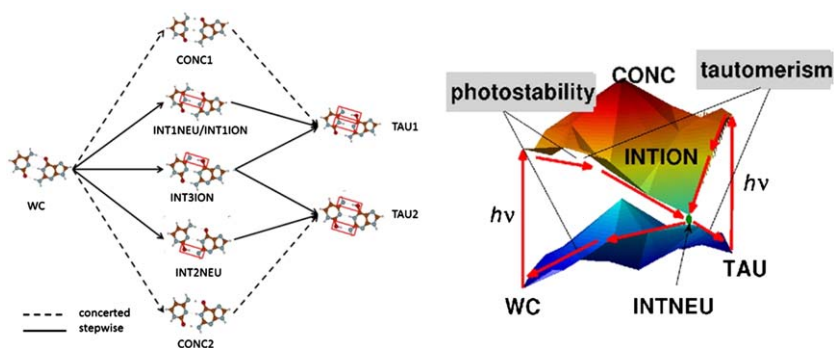


Fig. 8 Mechanisms for the excited-state double proton/hydrogen transfer in the guanine–cytosine base pair (left) and PESs of the ground and excited states along the corresponding reaction coordinates (right). [Reproduced from *J. Chem. Theor. Comput.*, 2013, 9, 481–496.]

mechanisms for ESPT and ESHT between the two nucleobases in the base pair and the shape of the PESs of the ground and excited states for the relevant mechanisms. According to the findings, concerted double ESPT can be discarded as relevant route for photostability and photo-tautomerism since the ground and excited state do not cross along the corresponding reaction coordinate (right; Fig. 8). Similarly, stepwise double ESPT through the transient ionic structures INT1ION and INT3ION gives rise always to a considerable energy separation between the ground and excited state although lower than that for the concerted mechanism. Finally, when the proton transfers are accompanied by electron transfers in the same direction (resulting therefore in hydrogen transfers), the molecular structure produced after the first hydrogen transfer appears in a region of near-degeneracy between the PES of the ground and excited state (INT1NEU and INT2NEU). A second ESHT of the same hydrogen atom in the opposite direction will regenerate the canonical base pair (photostable channel). On the other hand, if the second ESHT takes place in another hydrogen atom, the tautomeric forms TAU1 or TAU2 might be produced (phototautomerism). Yamazaki and Taketsugu⁵⁴ also studied the photo-induced hydrogen transfer process in the guanine–cytosine base pair together with the intrinsic decay of guanine by means of the TDDFT method. The results suggest that both channels may be possible in the base pair and therefore will compete for releasing the extra energy.

Hydrogen bonds may also provide photostability to other biological systems such as proteins. Guglielmi *et al.*⁵⁵ studied and compared the photodynamics of the partially and fully hydrated Lys(+)-Trp dimer in the Human Serum Albumin protein by means of the TDDFT/MM hybrid methodology. Whereas photodissociation of a charged amino group was found in the former case, photostability was maintained in the latter. Finally, other molecules such as mequinol (4-methoxyphenol),⁵⁶ iso-indigo,⁵⁷ the antihypertensive drug nifedipine⁵⁸ and the herbicide asulam⁵⁹ have been the target of theoretical studies in which the photostability (in some cases *vs.* the photodegradation) is fully or partially analysed.

3.3 Photoisomerisations

Some of the most studied photochemical reactions are photoinduced isomerisations, particularly when they are reversible. The species suffering the isomerisation often contains a formal double bond which can adopt two configurations (*cis* or *trans*, *Z* or *E*) in the electronic ground state. Typically, after the initial excitation the system structure relaxes on the excited-state PES, to reach a rotation around the double bond close to 90°, where it can access the ground-state surface through a CIX, resulting in an ultrafast relaxation and, depending on the specific features, an isomerisation. However, this description is only a simplification, there are many different subtleties that can affect the behaviour of each system. In biological systems, photoisomerisation reactions play a key role in the interaction of organisms with the light. A significant example is the retinal molecule, which in a more or less modified form is the responsible for the process of vision in all animals, and participates in other

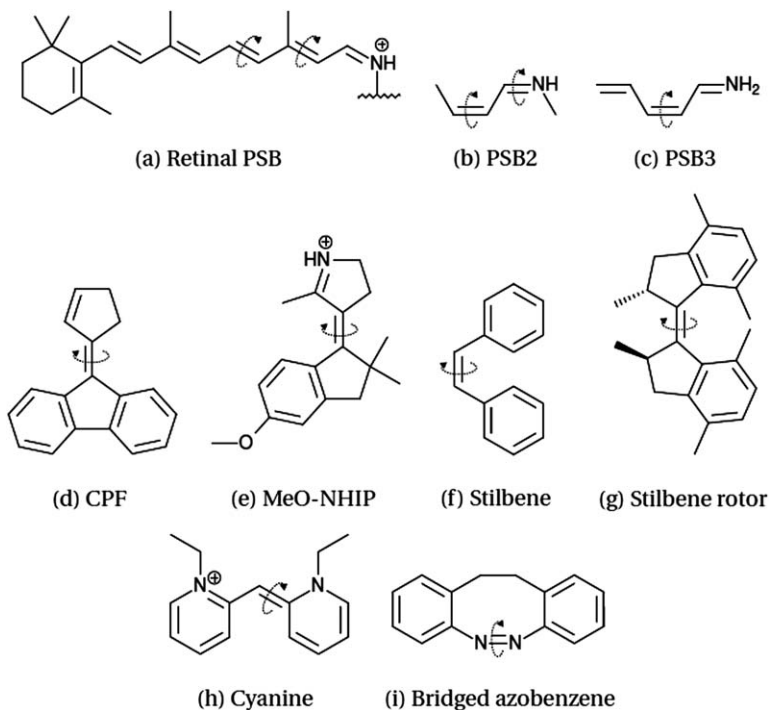


Fig. 9 Some examples of molecules suffering photoisomerisation on the indicated bonds.

light-activated processes in some algae and archaea. In its active form, the retinal molecule is covalently bonded to a protein forming a protonated Schiff base (PSB, Fig. 9a), and the isomerisation of one of its double bonds determines a conformational change in the protein, which ultimately triggers the biological response. The photophysics and photochemistry of retinal and many smaller model molecules have appeared profusely studied in the literature. One of the smallest possible models, containing two double bonds (PSB2, Fig. 9b), has been simulated with *ab initio* molecular dynamics.⁶⁰ The authors analysed how the initial conditions on the excited state (after an initial photon absorption) determine which one of the double bonds is twisted and whether an isomerisation is produced or the initial configuration is recovered. The results show that an appropriate pre-twisting can lead to a preferential rotation of one of the bonds and increase the probability of a successful isomerisation. Meanwhile, Gozem *et al.*⁶¹ have performed a mapping of the excited-state PES of a slightly larger retinal model (PSB3, Fig. 9c), at both CASSCF and CASPT2 levels. The study addresses the photoisomerisation of the central double bond, where a single CIX-seam is reached by following a minimal energy path from either the *cis* or *trans* isomer. A significant difference is that while the CASSCF pathway is barrierless from the Franck–Condon point to the CIX, at CASPT2 level the initial path leads to a minimum on the excited-state surface, from which an energy barrier must be surmounted to reach the CIX. The authors also

compared the performance of several MRPT2 and EOM-CC methods along the obtained paths, both in terms of relative energies (energy gaps or energy barriers) and “parallelity” of the surfaces.

Photoisomerisations have been used to design artificial molecular switches or motors that can be activated by light. A class of compounds based on an indanylidene–pyrroline framework (Fig. 9e) has been found to undergo photoisomerisation with a speed and efficiency reminiscent of those found in the biological retinal-containing systems. Theoretical QM/MM semiclassical simulations suggest that these properties are a consequence of the molecular framework, and are not very sensitive to solvent or counterion effects.⁶² Another widely studied molecular switch is the stilbene molecule (Fig. 9f). Despite its apparent simplicity, this system still poses a serious challenge for any electronic structure computation method, as demonstrated by Ioffe and Granovsky in a thorough study of the different electronic PESs relevant for the *cis*–*trans* photoisomerisation. In this work the authors likewise discuss a series of computational strategies in relation with multiconfigurational methods, and extended multiconfiguration quasi-degenerate second-order perturbation theory (XMCQDPT2) in particular, such as the active space selection, the broadness of the state averaging, or the need for avoiding intruder states.⁶³

It is often the case that molecular motions orthogonal to the primary rotation coordinate are needed in order to reach the CIX region. This can be exemplified in a theoretical study of a rotary motor with cyclopentene and fluorene moieties (CPF, Fig. 9d),⁶⁴ where it was shown that the details of these orthogonal motions can define the direction of the rotation and the outcome of the reaction. If a unidirectional rotation is desired, some chirality must be introduced in the system. A derivative of stilbene has been shown to work as a unidirectional rotor (Fig. 9g). The planar *cis* and *trans* conformations are not stable, and the chiral substitutions on the five-membered ring determine that the minima obtained by torsions in one or the other direction are not specular images and therefore have different stabilities. Thus, four distinct minima are found in a 360° rotation around the central double bond (A → B → C → D → A), where the steps A → B and C → D are photoactivated, while B → C and D → A are thermally activated. In a CASPT2//CASSCF analysis of the full rotation cycle,⁶⁵ including three electronic states, Liu and Morokuma proposed a preferred pathway for the process and explained the unidirectionality of the rotation by considering the topology of the PESs and the crossing points between the different states.

3.4 Proton/charge transfer

Proton transfer processes in the excited state are one of the most important photochemical deactivation routes in biological systems.⁶⁶ It has been shown that an intramolecular proton transfer can suppress the double-bond isomerisation that would normally be expected in the excited salicylideneaniline (Fig. 10a).⁶⁷ A similar effect was found in an analogue for a recently synthesised green fluorescence protein (GFP) chromophore, 4-(2-hydroxybenzylidene)-1*H*-imidazol-5(4*H*)-one (OHBI,

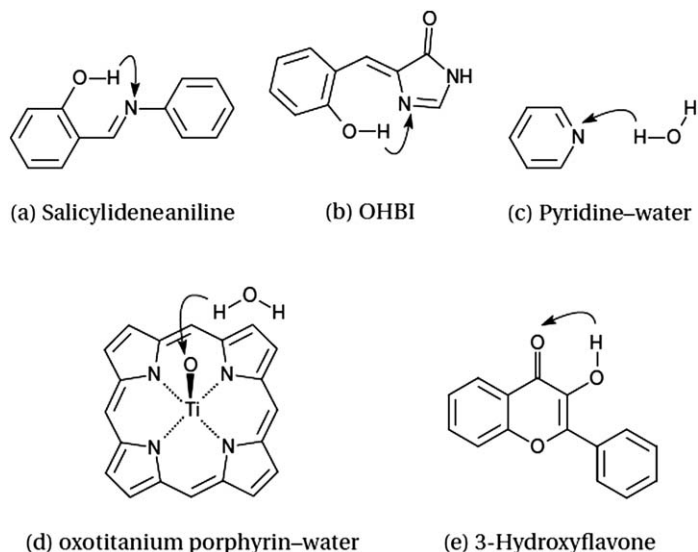


Fig. 10 Excited-state proton transfers.

Fig. 10b),⁶⁸ where an ultrafast intramolecular excited-state charge-induced proton transfer occurs in tens of femtoseconds after the vertical excitation of the ground state. The proton transfer alters the energy landscape and IC to the ground-state surface takes place with no *cis-trans* isomerisation, unlike other chromophores, where the intramolecular proton transfer is not possible.

Photoactivated proton or hydrogen transfers can be used as a means of capturing solar energy into chemical energy. For example, the homolytic dissociation of water in a pyridine–water complex (Fig. 10c) upon excitation was investigated with multireference and approximate coupled-cluster methods.^{69,70} The transfer of a proton stabilises electronic states with charge transfer character, thus giving rise to diradical products, which can potentially be harnessed in further useful reactions. A similar process was studied by Sobolewski and Domcke, who proposed an oxotitaniumporphyrin complex (porTiO, Fig. 10d) as a model system potentially suitable for direct photochemical water splitting.⁷¹ The authors computed with TDDFT methods the feasibility of the photochemical reaction $\text{porTiO-H}_2\text{O} \rightarrow \text{porTiOH}\cdot + \cdot\text{OH}$ and the subsequent regeneration of the catalyst: $\text{porTiOH}\cdot \rightarrow \text{porTiO} + \text{H}\cdot$. The results suggest a possible mechanism for the process, but they also show that a rich dynamics is to be expected, involving a number of electronic states, and additional calculations with multi-configurational methods are required to better understand the system.

3.5 Solvent effects

Useful photochemical processes rarely take place in gas phase. Most of experimental and applied chemistry occurs in condensed phase, generally in solution, as do practically all biologically relevant processes. Although *in vacuo* calculations are extremely important for the

understanding and interpretation of these processes, the effect of the solvent or the surrounding environment is often introduced qualitatively and *a posteriori*. This has been a successful approach in many cases, but it is clear that sometimes the molecular environment plays a crucial role in the outcome of the process, and this is particularly true in biological systems, where proteins have evolved with very specific tasks.

One of the difficulties when including solvent effects in photochemical calculations is how to consider the solvent relaxation after an electronic change in the solute. The two extreme situations are keeping a “frozen solvent” that remains static, or assuming the solvent is at every moment in equilibrium with the solute. The most realistic description would be somewhere between these two extremes. For example, in a joint experimental and theoretical study of the photoisomerisation of a cyanine dye (Fig. 9h)⁷² it was shown that an equilibration of the solvent with the excited-state electronic structure is required for permitting an efficient IC to the ground state, possibly leading to an isomerisation. The theoretical calculations used polarizable continuum model (PCM) to model the solvent effect, both in equilibrium and non-equilibrium regimes, obtaining the PES along the isomerisation coordinate on the excited states. The computational results helped the authors interpret the experimental data obtained from several techniques and propose a detailed mechanism for the reaction. The necessary solvent reorganisation implies a slower reaction rate than could be expected from the PES alone. A significant solvent reorganisation is expected when there are large geometric changes in the solute, as steric hindrance would simply prevent the reaction to occur otherwise. But even when the geometric changes are minimal, a strong electronic reorganisation in the solute can induce large changes in a surrounding polar medium, which in turn can affect the reaction itself. This effect can be seen, for instance, in electron and proton transfers between Watson–Crick pairs of DNA bases, where the overall structure of the pair remains largely unchanged, but the charge distribution changes significantly. In a TDDFT/PCM study of such a process,⁷³ it was shown that an equilibration of the solvent response with the changing electronic structure of the solute is needed to allow a proton transfer and a deactivation of the system, leading to the conclusion that dynamical solvent effects (not included in the work) would play a key role in determining the reaction rate. In addition, the authors also note that the linear-response variant of the PCM model (see ref. 74 for a discussion in the context of coupled-cluster theory) should not be considered appropriate whenever these charge transfer processes are involved. Continuum methods such as PCM are very useful to include the “bulk” solvent effect, but they cannot describe specific interactions like hydrogen bonds or π – π stacking, which are ubiquitous in biological systems. Therefore theoretical studies of proteins often employ discrete QM/MM methods that use an atomistic description (through MM) to represent the environment. Falklöf and Durbeej studied the performance of different DFT functionals and QM/MM strategies in the modelling of a phytochrome absorption spectrum.⁷⁵ They showed that, although a continuum model can yield results comparable with the experiments,

this is due to a cancellation of errors. They also analysed the relative importance of geometry relaxation in the chromophore and in the environment, and the sensitivity of the results to the size of the QM region. Even for describing “static” properties, such as absorption spectra, it may be necessary to include the solvent dynamics in the theoretical model. In an investigation of the solvent and counterion effects on the photophysical properties of retinal model,⁷⁶ using the averaged solvent electrostatic potential from molecular dynamics (ASEP/MD) method to describe the solvent, the authors found that the thermal agitation of a non-polar solvent determines the average solute-counterion distance, which significantly affects the absorption band position. It is perhaps needless to state that when solvent dynamics becomes most important is when dynamical processes are involved. Boggio-Pasqua *et al.*⁷⁷ provided an overview of their recent works on the photoactive yellow protein, both in solution and in the protein environment, using QM/MM methods. They describe their simulations of the photoisomerisation process and, more importantly, discuss the advantages and shortcomings of the QM/MM simulation approach, as well as suggestions to overcome the latter. Another QM/MM study of the photoisomerisation of an azobenzene derivative⁷⁸ (Fig. 9i), including explicit solvent molecules, could explain the high quantum yields observed experimentally, while previous simulations *in vacuo* gave inconsistent results. In this case the solvent viscosity (resistance to reorganisation) or its ability to “cool” down the excited solute can affect in different ways the *cis-trans* or *trans-cis* isomerisation. Bellucci and Coker⁷⁹ applied an empirical valence bond parametrisation to study the excited-state intramolecular proton transfer in 3-hydroxyflavone (Fig. 10e) in different solvents, modelled with classical MM force fields. When solvent molecules can form hydrogen bonds with the solute, the intramolecular proton transfer is significantly hindered. *Ab initio* molecular dynamics simulations have also been used to study photochemical reactions such as photoisomerisations or excited-state proton transfers, including the solvent or protein environment.^{80,81}

3.6 Chemiluminescence and bioluminescence

Chemiluminescence and bioluminescence are phenomena in which a thermally-activated chemical reaction produces a product in an excited (singlet or triplet) state which subsequently emits light. Whereas the former word is more general, the latter applies only for the chemiluminescence in living beings where the emitting chromophore is embedded in an enzyme. As for the photochemical phenomena, excited-state and non-adiabatic (IC or ISC) chemistry is crucial in the study of the chemi/bioluminescence phenomena. Hence, they are worth to review here as we did in the previous contribution.³¹

To highlight the particular meaning of bioluminescence, the studies in which the interactions between the luciferin (chromophore) and the luciferase (enzyme) or the effects of the latter on the reaction and light emission properties are studied will be separated from those merely focusing on the chromophore.

3.6.1 Chemiluminescence. Several theoretical studies on chemiluminescence have been performed in the period 2012–2013. Among them, the most popular molecule has been the firefly luciferin/oxyluciferin system, with many studies having focused on the parent molecule in one or several protonation forms^{82–90} and also on some derivatives⁹¹ and analogues bearing an amino group, such as the aminoluciferin, quinolylaminoluciferin, naphthylaminoluciferin, coumarylaminoluciferin, anthrylaminoluciferin and pyrenylaminoluciferin.⁹² Other target organic systems have been 1,2-dioxetane,⁹³ 1,2-dioxetanones,^{94–98} 1,2-dioxetanediene,⁹⁹ 2,3,5-trisubstituted pyrazine compounds,¹⁰⁰ the 3-(2'-spiroadamantyl)-4-(3''-phosphoryloxy)-phenyl-1,2-dioxetane,¹⁰¹ indolylmaleimide derivatives,¹⁰² 2-coumarones¹⁰³ and coelenteramide.^{104,105} It is possible to differentiate between works mainly focused on the molecular basis of the reaction which brings the population to the excited states and studies analysing the absorption and/or emission properties of the product of the chemiluminescent reaction or substituted compounds. Furthermore, it is worth noting that DFT and TDDFT prevail when researchers address theoretical studies on the topic. The TDDFT method can produce relatively accurate values for the fluorescence emission energies. However, much more care must be taken when the DFT and TDDFT (or single-reference methods) are applied to study the reaction mechanism of the chemiluminescence. IC and ISC processes take a part in the mechanism, which requires methods able to properly compute CIX and ISC state crossings (see Section 2.1). In addition, biradical intermediates might be present in the mechanism. These biradical structures correspond to open-shell electronic configurations and are difficult to be accurately determined with computational methodologies in which state functions of different spin multiplicity are allowed to mix (spin contamination).⁹⁷ The CASSCF/CASPT2 method is particularly useful in these situations because it accounts for both static and dynamic electron correlation, for an accurate determination of CIX and ISC points, and does not suffer from spin contamination problems. Hence, among the whole list of works on chemiluminescence, we would like to briefly describe here some of the high-level studies that despite being performed in small models provide accurate predictions and important clues on the molecular basis of the chemiluminescent mechanism. In particular, the new results on the decomposition mechanism of 1,2-dioxetane and the dilemma on the chemiluminescence of dioxetanone will be reviewed below.

1,2-Dioxetane and 1,2-dioxetanone are key chemical structures in many chemiluminescent and bioluminescent systems. The molecular structure of these systems bears the chemiluminophore properties of the chemi/bioluminescent molecules based on them, providing a channel for a thermally activated chemical reaction that produces a compound in an electronically excited state.^{106,107} The efficiency of the chemiluminescent process in 1,2-dioxetane and dioxetanone is however low and requires an electron-donor group to increase the quantum yield of luminescence. In addition, it is observed experimentally that the triplet emission is significantly more favourable than singlet emission in these small systems. From a theoretical standpoint, the general aspects of the

chemiluminescent mechanism have been determined.^{106,108,109} However, finding the reason for the higher quantum yield of triplet emission with respect to singlet emission observed experimentally shows more difficulties. Recently, Farahani *et al.*⁹³ have pushed to the limit the level of theory to revisit the decomposition mechanism of 1,2-dioxetane which produces two formaldehyde molecules, one of them in the excited state. On the basis of the previous findings from De Vico *et al.*¹⁰⁸ obtained with the MS-CASPT2//CASSCF method and the triple- ζ quality basis set (Fig. 11), larger basis sets have been analysed (ANO-RCC-VQZP profile; Fig. 11), improvements of the geometries have been carried out by performing geometry optimisations at the MS-CASPT2 level (MS-CASPT2//MS-CASPT2 profile; Fig. 11) and the zero-point vibrational energy corrections (ZPVE profile; Fig. 11) and entropy effects (Gibbs profile; Fig. 11) have been added. The general mechanism arisen from the previous and recent works^{93,108} implies a stepwise process in which first, the O–O bond is broken, second, the molecule enters in a biradical region and third, the C–C bond cleavage takes place. From the latter bond breaking, three channels are possible: ground-state dissociation (thermal decomposition) or singlet or triplet excited-state dissociation (chemiluminescence decomposition). The recent findings⁹³ provide further details on the mechanism and allow rationalizing the experimental observations related to the ratio of triplet to singlet dissociation products.

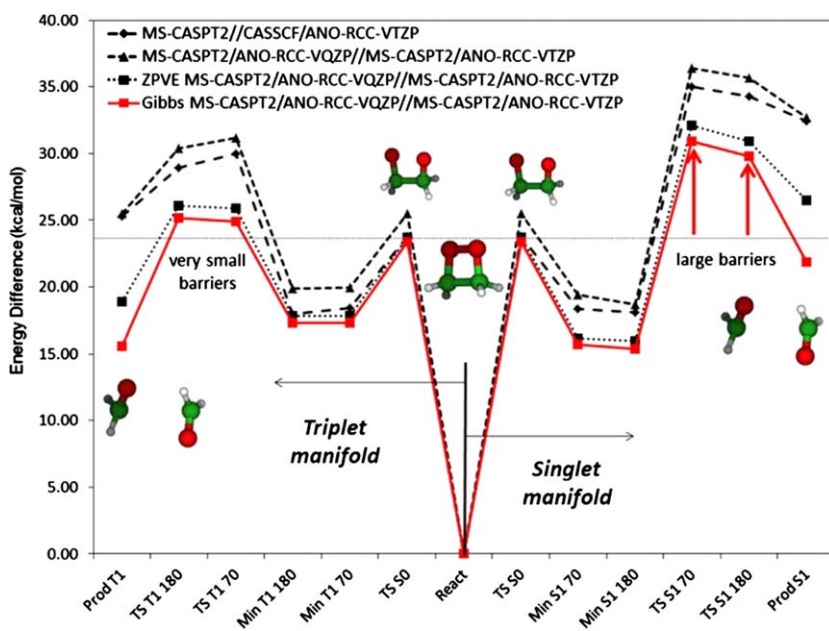


Fig. 11 Chemiluminescence singlet and triplet mechanisms of 1,2-dioxetane. The relative energies of the stationary points obtained at different levels of theory are shown. The energy barrier heights for the TS of the C–C bond dissociations ($TS_{S1(70)}$, $TS_{S1(180)}$, $TS_{T1(70)}$ and $TS_{T1(180)}$) are highlighted relative to the TS of the O–O bond breaking (TS_{S0}). See text and ref. 93 for further details. [Reproduced from *J. Chem. Theor. Comput.*, 2013, 9, 5404–5411.]

Hence, whereas the previous MS-CASPT2//CASSCF profile shows energy barriers for the C–C bond breaking both on the singlet (TS_{S1(70)} and TS_{S1(180)}) and triplet (TS_{T1(70)} and TS_{T1(180)}) manifolds that are clearly larger than the one related to the O–O bond dissociation (TS_{S0}), the addition of the ZPVE corrections and entropy factor to the energies brings the triplet TS_{T1(70)} and TS_{T1(180)} structures almost degenerated with the TS_{S0}, which is not the case for the singlet TS_{S1(70)} and TS_{S1(180)} points. This is in agreement with the observation in the experiments of a larger triplet emission quantum yield for the chemiluminescence reaction with a measured activation energy of 22 kcal mol⁻¹.¹¹⁰

Regarding 1,2-dioxetanone, the CASPT2//CASSCF findings from Liu *et al.*¹⁰⁹ do not show significant differences for the accessibility from the ground state (S₀) to the two lowest-lying singlet (S₁) and triplet (T₁) excited states, which is in contrast to 1,2-dioxetane. In the last two years, theoretical studies performed by Da Silva and Esteves da Silva⁹⁶ proposed a concerted mechanism for the decomposition reaction of dioxetanone based on results obtained with the DFT and TDDFT methods. The S₁ state was found to have much higher energy than S₀ and T₁, which was used to explain the preference for triplet emission rather than singlet emission. However, the theoretical approach employed has been proved to be not correct.^{97,111} Similar high-level analysis as that carried out for 1,2-dioxetane described above might help to unveil the source of discrepancy between experimental and theoretical works.

3.6.2 Bioluminescence. Theoretical analysis on bioluminescence requires the treatment of the enzyme–substrate actually occurring in the biological organisms. Due to the size of the system, high-level quantum-chemistry methods cannot be used in the entire enzyme and other theoretical strategies must be applied. Hybrid QM and MM methodologies have shown to be successful to theoretically study the bioluminescence process inside the enzyme.¹⁰⁶

In the last two years, the QM/MM approach has been employed to analyse certain aspects of the bioluminescence phenomenon mainly in the firefly luciferase–luciferin and *Aequorea* obelin–coelenterazine system. Based on a previous CASPT2 study by Roca-Sanjuán *et al.*¹¹² on a small model of coelenteramide pointing at differences between fluorescence and chemiluminescence, Navizet *et al.*¹¹³ revisited the bioluminescence process in the firefly luciferase–luciferin. According to the results obtained, the excited-state structures reached along the decomposition reaction of the luciferin and along the photochemistry of the oxyluciferin are the same. From both studies, it can be pointed out that conjugation of the excited carbonyl moiety with the aromatic system might be important to reach the fluorescent emissive structure which accounts for a larger quantum yield of fluorescence.

Da Silva *et al.*¹¹⁴ performed a joint experimental and theoretical work giving support to a bioluminescence mechanism in which the reactive benzothiazole hydroxyl group of the firefly dioxetanone (reactant) is not deprotonated prior to the reaction. Instead, the deprotonation is suggested to take place through an excited-state proton transfer with the

active site molecules. This is in contrast to other studies showing that the deprotonation is needed to initiate the bioluminescence reaction by lowering the energy barrier of the decomposition process taking place. In another study,¹¹⁵ the most relevant interactions in the active site of the *Photinus pyralis* bioluminescence system are analysed.

Li *et al.*¹¹⁶ and Chen *et al.*¹¹⁷ studied the bioluminescence of coelenterazine. Whereas the former work focused only on the absorption and emission properties of the product of the reaction (coelenteramide), the latter study also analysed relevant aspects of the mechanism, particularly, the origin and differences among chemiluminescence, bioluminescence and fluorescence in aequorin. On the basis of the TDDFT/MM findings and the previous CASPT2 results¹¹² on a small model and TDDFT results of the chemiluminophore *in vacuo*,¹⁰⁴ the proposed mechanism (Fig. 12) has the characteristics described in the following:

(1) A transient excited state is immediately produced after the decomposition of coelenterazine in coelenteramide and CO₂. The excitation is localised in the carbonyl moiety which features an sp³ hybridisation. The emission efficiency of this species is however very low (dark state).

(2) The excitation delocalises over the aromatic rings conjugated with the CO₂, producing the neutral form of coelenteramide in the excited state (2H*).

(3) An excited-state proton transfer might occur to produce the anion coelenteramide 2O^{-*} species which is proposed as the actual aequorin blue-light emitter.

Even though the bioluminescence and fluorescence spectra in aequorin have nearly the same emission maxima, the theoretical study points to clear difference in the charge distributions and geometries of the structures responsible for both processes. This issue was already brought forth in the previous work on a small model of coelenteramide¹¹² and shall be taken into account as the possible source of spectroscopic differences in other bioluminescence systems in which both bioluminescence and fluorescence spectra differ.

4 Conclusion and outlook

As evidenced by the present review, the state-of-the-art developments and applications in computational photochemistry largely involve non-adiabatic processes. The recent advances in methodology have focused on different aspects related to the determination of the CIXs, which are the theoretical concept associated to the non-adiabatic IC phenomenon. In this context, the published works in 2012–2013 have dedicated great efforts to assess the applicability and accuracy of various electronic structure methods to determine CIXs, to analyse the dynamical aspects of the IC process through the CIX by means of quantum dynamics and to search novel, simple and faster methods and computational approaches to locate CIXs. Meanwhile, a large number of applied works have reported and analysed the details of photochemical mechanisms which are based on energy decays taking place through CIXs. The non-adiabatic chemistry is

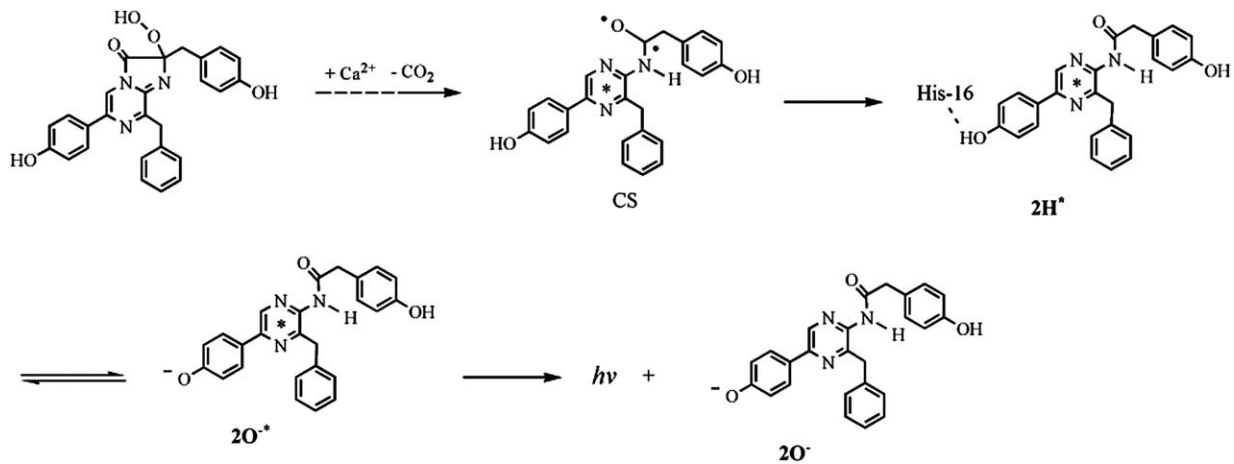


Fig. 12 Mechanism proposed for the bioluminescence of aequorin from TDDFT/MM results.¹¹⁷

behind many photoinduced processes, such as dissociations, isomerisations, tautomerisations and proton and charge transfers. Moreover, non-adiabatic processes provide certain molecules with photostability and are crucial in the chemi/bioluminescence mechanism. Analysis of solvent effects and interactions between chromophores and the surrounding biological environment (such as enzymes) has also been the aim of some theoretical studies in the years 2012–2013. Hence, they have also been briefly reviewed here.

Computational photochemistry is nowadays a powerful tool to determine mechanisms of photoinduced processes, establishing plausible decay channels (without or with small energy barriers) and discarding others. To improve this description, accurate predictions of efficiencies and life times among the plausible energy relaxation routes would be valuable. However, studies on the dynamics of the systems are still facing some difficulties derived in part from the fact that the outcomes are very sensitive to the topography of the PESs of the ground and excited states, and accurate dynamics computations are very time demanding. We feel that the developments of methodology in the recent future will be guided towards solving those problems, and applications will move to consider in a larger extent the dynamical aspects.

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