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CONTENTS

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EDITORIAL

President's Letter

Dear EPA members
This is my second letter as president if this Association and I want to use this letter in order to account you on our activities for the Association.
We have several items to consider:
1. In our previous letter I asked your ideas to promote our Association in order to increase the EPA members: until now I do not receive any feedback and this not a good news for us.
2. We activated the first edition of the EPA awards for Young Scientist and for Service to the Photochemical Community. We received a significant number of applications for both the awards and the evaluation commissions created into the Executive Committee decided to assign the EPA awards for Young Scientist to Prof. Haining Tian, Associate Professor in Physical Chemistry at Uppsala University (Sweden), and to assign the EPA Award for Service to the Photochemical Community to Professor Silvia Braslavsky, Max-Planck-Institute for Bioinorganic Chemistry of Mülheim (Germany): congratulations to the winner.
3. We have to inform you that it is active on the website of the Association the procedure to present applications for the EPA Awards for PhD Thesis on Photochemistry. I think this is the best way to promote our Association to our young coworkers.
4. It is active the procedure to present applications for the Porter Medal. The Porter Medal is awarded every two years to the scientist who, in the opinion of the European Photochemistry Association, the Inter-American Photochemistry Society, and the Asian and Oceanian Photochemistry Association, has contributed most to the subject of Photochemistry. The Porter Medal, named for the late George Porter FRS, Nobel Laureate, is awarded biannually to the scientist who in the opinion of the judges, has contributed most to the science of photochemistry with particular emphasis on more physical aspects, reflecting George Porter's own interests.
5. Recently we have a meeting at Cambridge with the Royal Society of Chemistry to discuss the perspective of our journal, *Photochemical and Photobiological Sciences*. The impact factor of the journal was 2.9 in line

with those of the other journals in photochemistry. However, when you will read this letter, probably the new i.f. of *PPS* will be lower. Furthermore, in 2018 the number of submitted and accepted articles from European countries was not so high as we could expect. *Photochemical and Photobiological Sciences* is our journal and we have the duty to support it. In order to increase the number of open access articles in the journal, the previous Ownership Board meeting decided to reduce the open access fee for EPA members to £ 750. We hope that this decision can increase the open access articles on *PPS* form EPA members.

Maurizio D'Auria
Università della Basilicata, Potenza
Italy

THE PORTER MEDAL 2020 – CALL FOR NOMINATIONS

The Porter Medal is awarded every two years to the scientist who, in the opinion of the European Photochemistry Association, the Inter-American Photochemistry Society, and the Asian and Oceanian Photochemistry Association, has contributed most to the subject of Photochemistry. The Porter Medal, named for the late George Porter FRS, Nobel Laureate, is awarded biannually to the scientist who in the opinion of the judges, has contributed most to the science of photochemistry with particular emphasis on more physical aspects, reflecting George Porter's own interests.

To nominate European candidates for The Porter Medal 202', candidate's details should preferably be sent directly to the President of the European Photochemistry Association, Professor Maurizio D'Auria (maurizio.dauria@unibas.it). For nomination of candidates from other continents, see the Porter Medal webpage: http://www.portermedal.com. Nominations may also be sent to the Chair of the Porter Medal Committee, Professor James Durrant. The nomination package should include:

• Curriculum Vitae of the candidate

• A list of publications

• A citation for the award, not exceeding five pages

• Two letters of reference

Provisional closing date for the receipt of nominations (based on the guidelines from previous years) will be 3 Febraury 2020.

Previous winners:

1988 Lord Porter (George Porter), UK (Founding medal)
1990 Michael Kasha, USA
1992 Kinichi Honda, Japan
1994 Nicholas J.Turro, USA
1995 J.C."Tito" Scaiano, Canada (Special Medal for London ICP)
1996 Noboru Mataga, Japan
1998 Frans de Schryver, Belgium
2000 Vincenzo Balzani, Italy
2002 Josef Michl, USA
2004 Graham R.Fleming, USA
2006 Howard E. Zimmerman, USA
Hiroshi Masuhara, Japan
2008 Michael R. Wasielewski, USA
2010 David Philips, UK
2012 Thomas J. Meyer, USA
2014 Masahiro Irie, Japan
2016 Jim Barber, UK and Fredrick Lewis, USA
2018 Haruo Inoue, Japan

EPA PRIZE FOR BEST PHD THESIS IN PHOTOCHEMISTRY - CALL FOR NOMINATIONS

The EPA Prize for the best PhD thesis in photochemistry will be attributed during the 28th IUPAC International Symposium on Photochemistry in Amsterdam (12th-17th July 2020). The awardee will present his/her work at the Symposium. The Prize is 1000 Euros, plus travel costs to Amsterdam (within the limit of 300 €) and one free year of EPA membership. The candidate must have defended his/her PhD thesis in 2018/2019 and be nominated by an EPA member. Nominations should be sent (electronically only) to Maurizio D'Auria (maurizio.dauria@unibas.i). The nomination package should include:

- Curriculum Vitae of the candidate
- Copy of the thesis
- Abstract of thesis in English, no more than five pages
- List of publications arising from the thesis
- A letter of support.

Closing date for the receipt of nominations will be 31 December 2019.

Previous winners:

2008 Maria Abrahamsson (thesis supervisor: Leif Hammarström), Sweden, Alexandre Fürstenberg (thesis supervisior: Eric Vauthey), Switzerland
2010 Anne Kotiaho (thesis supervisior: Helge Lemmetyinen), Finland
2012 Karl Börjesson (thesis supervisior: Bo Albinsson), Sweden
2014 Giuseppina La Ganga (thesis supervisor: Sebastiano Campagna), Italy
2016 Tomáš Slanina (thesis supervisors: Petr Klán, Burkhard König), Czech Republic.
2018 Victor Gray (thesis supervisor: Kasper Moth-Poulsen), Sweden.

INTERNATIONAL FOUNDATION FOR PHOTOCHEMISTRY

The "International Foundation for Photochemistry" (IFP) is a non-profit foundation which provides financial support for the holding of scientific conferences in the field of photochemistry. Its operations are based on the following principle. Upon a written request by the conference Chair, IFP can advance a certain amount of money in order to facilitate organization of the conference. At the end of the meeting, the Chair pays back to IFP the conference budget surplus which will be retained for the organization of the next event.

For a considerable time, the IFP activities have been closely related to the IUPAC Photochemistry Symposia. In view of its favorable financial situation, IFP has decided to expand the financial support it can offer to other photochemistry meetings, in addition to IUPAC. A decision for funding support will be considered for each request made, after discussion and vote of the Executive Board.

The current composition of the IFP Executive Board is:

- Dimitra Markovitsi : Chair
  dimitra.markovitsi@cea.fr
- Kirk Schanze: Vice Chair
  kschanze@chem.ufl.edu
- Axel Griesbeck: Treasurer
  griesbeck@uni-koeln.de
- Werner Nau: Vice Treasurer
  w.nau@jacobs-university.de
- Ken Ghiggino: Member
  ghiggino@unimelb.edu.au
- Hiroaki Misawa: Advisory Member
  misawa@es.hokudai.ac.jp

PUBLICATIONS

Women in Photochemistry

Silvia E. Braslavsky
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During the writing of the article about the History of the IUPAC Symposia on Photochemistry,[*] I realized that the number of women invited to deliver plenary, invited and keynote lectures, or to organize workshops during the Symposia was not in agreement with the number (increasing number over the years) of women participating actively in the photochemical community, including assisting to the meetings. I decided then to analyze in more detail the participation of women in the field of photochemistry, in particular through the study of the programmes of the Symposia since the beginning in 1964, but also looking at the production of some prominent women that have contributed to our knowledge in the field but have not participated in the Symposia, in some cases because they lived before the starting of the Symposia in 1964.

An interesting woman was María Goeppert, a German physicist born in 1906 and educated in Goettingen in a school led by suffragettes. After getting her PhD in 1930 she moved to the US with her husband Mayer. In 1963 she was the first woman to be awarded a Nobel Prize in Physics. Since the widespread use of powerful lasers, several research groups measure by various methods the double-photon absorption coefficient with the unit that bears her name: Goeppert-Mayer.

A remarkable woman that contributed to the clarification of the quantitative evaluation of the photosynthesis efficiency in plants was Birgit Vennesland. She was Norwegian, studied in the US and became Professor at the University of Chicago; eventually she became

[*] Braslavsky, S. E. *Pure Appl. Chem.* (2015) **87**, 663-705. https://www.photochemistry.eu/wp-content/uploads/2018/03/2016_01_epanewsletter.pdf , page 100

Director at the Max Planck Institute for Cell Physiology in Berlin. From 1968 to 1970, she was Director of the special Section created for her (and called Vennesland Section) within the Max Planck Society structure.

In the very first IUPAC Symposium on Photochemistry organized by George Hammond in Strasbourg in 1964, Magdeleine Mousseron-Canet from Montpellier gave a plenary lecture on "Isomèrisation Photochimique de Quelques Systèmes Polyéniques". According to the review about photochemistry in French laboratories written by H. Bouas-Laurent and J. P. Desvergne, the group led by Magdeleine Mousseron and J. C. Canet was the first in France to explore aspects of molecular photochemistry.† In 1969 she authored, with J. C. Mani, a book called "Photochimie et réactions moléculaires" (Dunod, Paris).

The women invited to give plenary or invited talks, or to organize workshops within the frame of the IUPAC Symposia on Photochemistry are listed in the Table. Because in most cases the scientific chair of the Symposium did not work in the city chosen to host it (see list of scientific chairs in reference 1), a local photochemist as organizer has always been of central importance. Only in five cases the local co-organizers were women, their names are in green in the Table. Heinrike Döpp co-organized the symposium together with Dieter Döpp in Baden-Baden in 1972, Elizabeth Poquet co-organized with Henry Bouas-Laurent the Symposium in Pau in 1982, Silvia M. B. Costa chaired the local committee in Lisbon in 1986, and Carmen Brosa co-organized with a group of colleagues the Symposium in Sitges in 1998. Susan Quinn co-chaired the Dublin Symposium in 2018 together with Miguel García Garibay and chaired the local organizing committee.

It is interesting to analyze the number of women invited to talk about their work together with the number of women participating in the Symposia. In Seefeld in 1980 there were 27 women registered over a total of 318 participants (ca. 8%). Only one woman participated in a workshop (Irena Bronstein) and no woman gave an invited lecture, neither was any woman in the International Organizing Committee. Between 1982 and 1998 there were 1, 2 or 3 women invited to give Plenary or Invited lectures (see the Table), with the exception of the

† H. Bouas-Laurent, Jean-Pierre Desvergne, EPA Newslettre, **91**, Dec. 2016, p. 29.

Symposium in 1990 in Warwick, where no woman was among the invited speakers or as a member of the International Committee, although the number of women participants was ca. 54 over a total number of ca. 400.

One of the non-written traditions is to avoid repeated (especially consecutive) invitation to the same colleague for a plenary lecture. The various repetitions in general imply an invited lecture and next a plenary (or the other way around). Among those invited twice was Marye-Anne Fox who held an invited lecture in 1988 in Bologna and a plenary lecture in 1998 in Sitges.

I will mention three women that already in the '80s and '90s had produced very interesting work in the photosciences but did not have the opportunity, for whatever reason, of holding talks at the IUPAC Symposia. (i) Mary Archer from the University of Cambridge worked in photoelectrochemistry and was appointed already in 1970 to the Board of Directors of the International Solar Energy Society. Later on she became Chairman of the National Energy Foundation in the UK. (ii) Françoise Winnik from the University of Montreal has produced fundamental contributions to the structure of polymers using photophysical methods and is today Editor-In-Chief of the prestigious Journal *Langmuir*. (iii) Maria Elizabeth Michel-Beyerle from the Technical University in Munich up to 2000 (presently in Nanyang Technological University, Singapore) has contributed important work in the area of primary processes in photosynthesis and in other photobiological and photochemical processes.

For the Helsinki Symposium in 1996, I had the privilege of organizing a workshop on Photothermal Methods. While in Helsinki I was asked to Chair the Symposium in the year 2000, which was held in Dresden, thanks to the excellent work of the local organizing Committee chaired by Thomas Wolff. I was the first woman chairing an IUPAC Symposium on Photochemistry, and the only one until the co-chairing by Susan Quinn in 2018. In Dresden we were all very delighted by the excellent invited contributions in various areas of Photochemistry of 8 women scientists from 8 Countries (see the Table for the names). This represented about 20 % of the invited speakers, corresponding to 19 % of women registered in the Symposium.

Only two women were among the invited speakers in Budapest in 2002, whereas 11 women were invited lecturers (21 %) at the Symposium held in Granada in 2004. The list shown in the Table underlines the quality of the work presented in the Symposium.

Four women gave invited lectures in 2006 in Kyoto and 3 in Gotenburgh in 2008. One of them was Maria Abrahamsson, the EPA (European Photochemistry Association) awardee for best PhD Thesis in Photochemistry for the period 2006-7. Five women were invited to lecture in Ferrara in 2010, among them Anne Kotiaho, EPA awardee for the period 2008-2009. Seven women gave plenary or invited lectures in Coimbra in 2012 and five in Bordeaux in 2014 including Giuseppina La Ganga, EPA awardee for the period 2012-13. These numbers represent lower (in some cases much lower) percentage than those of the women registered at the respective Symposia.

Just one woman, Cornelia Bohne, was invited to contribute a Plenary Lecture at the Symposium held in Kyoto in 2016. We note that in the Asian and Oceania Countries, i.e., China, Taiwan, Hong-Kong, South Korea, Singapore, Australia, India and indeed in Japan, there are excellent women scientists that have actively participated in International Conferences and could, certainly should, serve as role models for the future generations of women scientists. Several of the Asiatic women photochemists have offered lectures in the IUPAC Symposia on Photochemistry held in Europe.

The organizers of the Dublin Symposium in 2018 made a special point of inviting a large number of women scientists. Thus, we could enjoy 9 excellent plenary and invited women lecturers in various aspects of the field (see Table). This represented ca. 37 % of the total number of those lectures and was even a bit larger than the percentage of women registered. And, in addition, there was my own special and well attended lunch-time lecture about "Women in the Photosciences". This paper is an extract of that lecture.

Since the institution in 1988 of the Porter medal, in honour of George Porter (1920-2002, Nobel Laureate 1967), the medal has been awarded during the IUPAC Symposium on Photochemistry, with the exceptions of the medal to J. C. Scaiano in 1995, awarded during the International Conference on Photochemistry (ICP) in London, and the very last one in 2018 to Haruo Inoue, awarded during the meeting of the Asian and Oceania Photochemistry Association held in Taipei in December 2018. So far, the Porter medal has never been awarded to a woman.‡ The analysis shown in the above demonstrates that there are several women that deserve the high award.

‡ http://www.portermedal.com/winners.html

Women have also been active in the Photochemical Societies and as editors in the various journals. As examples, Dimitra Markovitsi and Julia Pérez Prieto have been each President of EPA, whereas Olga Fedorova, Nina Gritsan and Sandra Monti have been several years members of the EPA Executive Committee. Claudia Turro and Cornelia Bohne have each served as President of the Inter-American Photochemical Society (I-APS), and at the moment Anna Gudmundsdotter is vice president and Carolina Aliaga, Ksenija Glusak, Elisabeth Harbron and Belinda Heyne are in the I-APS Executive Committee. Vivian Wing-Wah Yam, who has been for several years the first and only woman in the Executive Board of the Asian and Oceania Photochemistry Association (AOPA) was elected its President for the period 2017-2018.

Ana Moore has been in the Editorial Board of Advances in Chemical Research (as well as myself) and Cornelia Bohne has been one of the four main editors of ACS-Omega. Esther Oliveros, Monique Martin, and myself have been many years each Associate Editor of the *Journal of Photochemistry A and B*. Although the number of women as Associate Editors and in the Editorial Boards of the Journals has increased (see e.g., the list of Associate Editors in the webpages of the Journals *Photochemistry & Photobiology* and *Photochemical and Photobiological Sciences*) the number is still below the proportion of women working in the field.

Regarding the projects carried out within the frame of the Sub-Committee on Photochemistry (and within the former Commission on Photochemistry), which I chaired for several terms, several women contributed to various projects. Marta Litter was a main co-author of the "Glossary of Terms used in Photocatalysis and Radiation Catalysis"[§] and Esther Oliveros wrote an important comment about units in radiometry vs. units in photochemistry for the "Glossary of Terms used in Photochemistry".[**] Teresa Atvars, Cornelia Bohne, Marye-Anne Fox, Marta Litter and Sandra Monti contributed to the latter Glossary. Within the large project on Fluorescence Standards led by Enrique San Román and Fred Brouwer, Ute Resch-Genger and co-authors wrote fundamental technical documents useful for the daily application of photophysical

[§] http://iupac.org/publications/pac/pdf/2011/pdf/8304x0931.pdf
[**] https://www.degruyter.com/downloadpdf/j/pac.2007.79.issue-3/pac200779030293/pac200779030293.pdf

techniques. See e.g.[††] Sandra Monti has been in the Board of the International Photochemistry Foundation.

I want to add a paragraph about the participation of women in photochemistry in South America. Several women have contributed to the field and have been very active in the meetings organized in South America, such as the ELAFOT every two years and the Inter-American meeting of I-APS every five years. Some of the names in Argentina are Sonia Bertolotti, Sandra Churio, Lelia Dicelio, Rosa Erra-Balsells, Mónica González, M. Gabriela Lagorio, Marta Litter, Carolina Lorente, Alicia Peñéñory, Rita Rossi, in Chile Elsa Abuin (see the special issue of *Photochemistry & Photobiology* published in her honor),[‡‡] Carolina Aliaga, Ana Maria Edwards, and Maria Victoria Encinas, and in Brazil Teresa Atvars, plus a large number of younger women photochemists now very active, several formed in the groups led by the above mentioned women.

The analysis presented here shows that, in fact, over the years there has been an increase in the number of women contributing to our knowledge and to our organization in the field of Photochemistry. Women have become much more confident of their own possibilities, the society in general has slowly realized, through various facts and not without the enormous efforts of the women involved, that the large potential of women's contributions to all fields of human activities should not be neglected and several instruments have been created or expanded in various Countries and Institutions, to help make compatible family and work for women and men when children arrive in the family. However, not always the existence of women in the field is fully acknowledged by the organizers of scientific meetings, members of nominating and selection committees for various awards and even for positions, and academic bodies distributing grants and fellowships. According to press information, the Nobel Prize Committee recently sent a message to nominators for the prizes saying that they should remember that women exist!! Awareness is still missing and women should keep fighting for it.

I am very proud to be a woman, a scientist, and a mother of two great ladies, both academics and mothers themselves, one with a

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[††] https://www.degruyter.com/downloadpdf/j/pac.2013.85.issue-10/pac-rep-12-03-03/pac-rep-12-03-03.pdf

[‡‡] Special Issue dedicated to the memory of Elsa Beatriz Abuin Saccomano (1942-2012), *Photochem. Photobiol. (2013)* ***89***, 1270-1272.

PhD in Biology (plus husband and two children) and today an industrial scientist and the other with a PhD in Sociology (plus man and two children) and today University Professor. I am also very grateful to the women, and men, that could share with me the enthusiasm for science over many years in our laboratories and in the photochemical community and thank them for the joint work and joint learning that resulted in many interesting contributions to our field of science as well as in deep friendships.

IUPAC Symposium on Photochemistry, Dublin, 2018. (From left to right) Maria Luisa Marín García, Leticia González, Carolina Aliaga, Silvia Braslavsky, Julia Pérez Prieto, Susan Quinn, Stephan Landgraf, Anabel Lanterna, Raquel Galián, Liliana Jiménez.
With the only exception of Stephan, all women photochemists

Table. Women invited to give plenary, invited, or keynote talks or to organize or participate in workshops during the IUPAC Symposia on Photochemistry. In green are the names of women co-organizers of the Symposia. In red are women scientific chairs.

Strassbourg, 1964
Magdeleine Mousseron-Canet (Montpellier)

Baden-Baden, 1972
Heinrike Döpp, co-organizer

Seefeld, 1980
Irena Bronstein-Bonte (Workshop)
27 women / 318 part., ca 9 %

Pau, 1982
Elisabeth Poquet, co-organizer

Interlaken, 1984
Silvia E. Braslavsky
Silvia M. B. Costa
Irene Kochevar

Lisbon, 1986
Silvia M. B. Costa, Organizer
T. B. Truong

Bologna, 1988
Mary-Anne Fox

Warwick, 1990, none
53 w/400 partic., 13 %

Leuven, 1992
Sandra Monti
A. (Fanny) Kirsch-de Mesmaeker
Esther Oliveros

Prague, 1994
Linda Johnston
Nanda Sabattini

Helsinki, 1996
Workshop organizers:
Silvia E. Braslavsky
Esther Oliveros

Sitges, 1998
Carmen Brosa, co-organizer
Mary-Anne Fox

Dresden 2000
Silvia E. Braslavsky, Chair
Jacqueline Barton
Regina de Vivie-Riedle
Judit Fidy
Lucia Flamigni
María García Parajó
Gudrun Hermann
María Nowakowska
Vivian Wing-Wah Yam
91 w/ 481 participants

Budapest, 2002
Silvia E. Braslavsky
O. A. Fedorova

Granada, 2004
Teresa Atvars
Paula Bosch
Luisa De Cola
Nina Gritsan
A. (Fanny) Kirsch-De Mesmaeker
Virginie Lhiaubet
Dimitra Markovitsi
Manuela Merchan
Sandra Monti
Ana Moore
Alice Ting

Kyoto, 2006
Mireille Blanchard-Desce
Silvia E. Braslavsky
Rachel Evans
Monique Martin

Gotenburgh, 2008
Linda Johnston
Dimitra Markovitsi
Maria Abrahamsson (EPA PhD Thesis Prize 2006-7)

Ferrara, 2010
Luisa De Cola
Cristina Flors
Elena Galoppini
Esther Oliveros
Anne Kotiaho (EPA PhD Thesis Prize 2008-9)

Coimbra, 2012
Dimitra Markovitsi
Constanza Miliani
Thuc-Quyen Nguyen
Julia A. Weinstein
Danielle Wilson
Li-Zhu Wu
Vivian Wing-Wah Yam

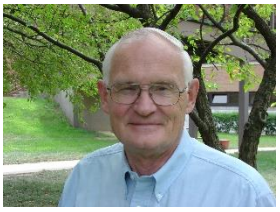
Bordeaux, 2014
S. E. Braslavsky
Lucia Flamigni
Marina Kuimova
Marta Litter
Giuseppina La Ganga
(EPA PhD Thesis Prize)

Osaka, 2016
Cornelia Bohne

Dublin, 2018
Susan Quinn – co-Chair
Leticia González
Anna Gudmundsdottir
Laura Herz
Tia Keyes
Ana Krylov
M. Gabriela Lagorio
Julia Pérez Prieto
Hongmei Su
Julia Weinstein
33 % women participants

Photomasking Groups to DNA Photo-manipulation, 50+ Years of Light Chemistry *I-APS 2019* (part 1)

R. Marshall Wilson
Center for Pure and Applied Photosciences, Bowling Green State University, Bowling Green, Ohio, USA

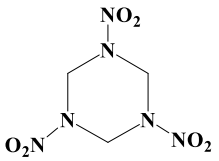


This document summarizes my presentation at the 2019 Inter-American Photochemical Society meeting in Sarasota, Florida where I was inducted as a Fellow of the Society.

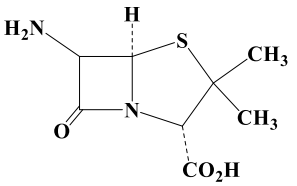
I grew up in an army family, attended 16 schools and lived in many locations in my youth including Sinjuku a suburb of Tokyo, Japan immediately following WWII and Orleans, France where I attended high school. I sailed across the Pacific twice and the Atlantic once causing me to miss up to three months of grade school. Many parents would say that this situation would adversely affect their child's education. However, I disagree. In these cases, that of my brother (future vice president of J. P. Morgan) and Waldemar Adam (*vide infra*), the constantly changing environment taught us how to adjust to many new situations. I attended college majoring in chemical engineering at The Pennsylvania State University from 1957-1961. My industrial experiences in summer jobs convinced me that an academic career was most desirable. Consequently, I applied and was accepted into the chemistry Ph.D. program at the Massachusetts Institute of Technology with the proviso that I minor in business administration in the Sloan School of Management, since I did not have enough liberal arts courses in my undergraduate program.

Professor John C. Sheehan

One of the most important aspects of any person's career is the significant people with whom they come into contact over the years. The first of these was Professor John C. Sheehan in the Chemistry Department at MIT who was my Ph.D. advisor. Professor Sheehan was a most impressive individual who in his younger years developed an improved synthesis of the high explosive RDX.[1] This explosive made battle ships obsolete. It had a much higher brisance (shattering power) than TNT (trinitrotoluene) and could blow its way through the 16 inches of case hardened stainless steel hulls of battleship making them obsolete since they were easy targets for submarines. These vessels were replaced by aircraft carriers in WWII as the strategic weapons of naval warfare. Another of his significant achievements was the synthesis of penicillin V with Kenneth Henery-Logan.[2] This is the basic structure of penicillin, but when he attempted to get MIT to patent this synthesis they declined since the synthesis was too many steps to be commercially viable. So Professor Sheehan personally completed a composition of matter patent on this unusual ring system. Two years later, an English company, British Drug Houses, found a mold that made penicillin V in large amounts and penicillin became available to the world at affordable prices and Professor Sheehan



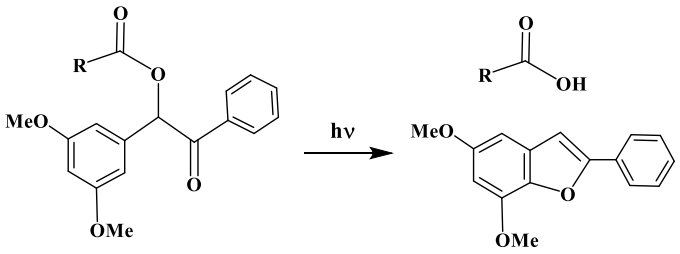
RDX



6-Aminopenicillanic Acid
Penicillin V

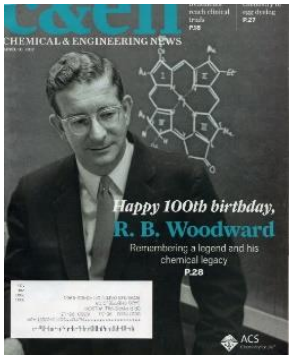
bought a Frank Loyd Wright house and had his own large personal yacht.

Professor Sheehan suggested to me when I entered the chemistry graduate program that we find a way to mask biologically important molecules and quickly release them in their biological environment with light. Photochemistry was an obscure area of chemistry at that time (1961), but we managed to find an excellent photomasking group in benzoin esters that released their biological cargo in nanoseconds in high yields with long wavelength UV light.[3] This was the first family of photomasking groups. However, the methoxy derivative, shown below, that provides the best release yields require some synthetic skill to synthesize and is not widely used for that reason.



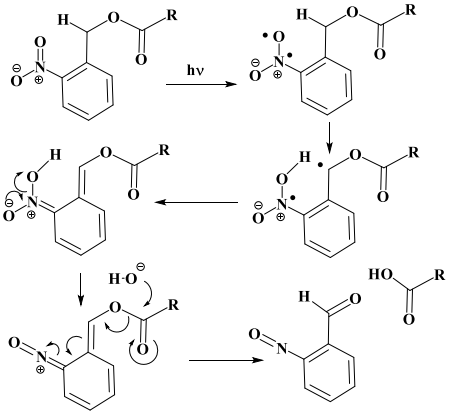
Following his Ph.D. degree, he joined the research group of Professor R. B. Woodward at Harvard University on the day that he won the Novel Prize in October 1965.

Professor R. B. Woodward smoking a cigarette and Abraham Patchornik in background.



In those days, people used to smoke cigarettes in class and lectures. Sometimes it was hard to see the blackboard the smoke was so thick. Woodward smoked constantly and flicked his cigarette butts across the room into the waste can. Woodward could give a one hour seminar that lasted three hours and nobody would leave. When E. J. Corey tried to do it, people would leave after an hour and a half. Woodward was a phenomenal chemist. His memory lives on today as demonstrated by the cover of a C&E NEWS in April 2017.

Coincidentally, during my postdoctoral time in the Woodward group another postdoc in the group was Abraham Patchornik who was developing the *o*-nitrobenzaldehyde photoremovable masking group.[4] This type of masking group is very easily prepared, but does not release the masked group quickly (micro and milliseconds). However, it is widely used today.

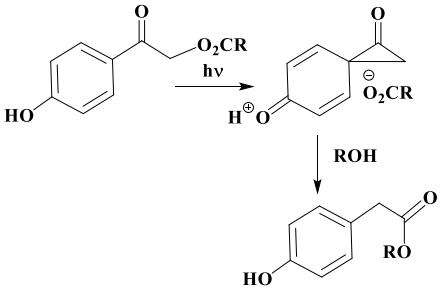


O-Nitrobenzaldehyde Masking Group

Abraham Patchornik

Some years later, Richard Givens introduced the *p*-hydroxyphenacyl masking group.[5] This masking group is both easily prepared and releases the masked group very rapidly. The release mechanism might be called a photoFavorsky mechanism as shown above. The history of photoremovable masking groups is best summarized in a review article published recently in Chemical Reviews published by a group of authors among which I knew well Richard Givens, Jakob Wirz and Vladimir Popik.[6]

Professor Richard S. Givens



PhotoFavorsky mechanism

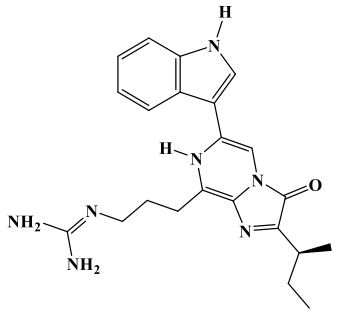
Professor Jakob Wirz

Professor Vladimir Popik

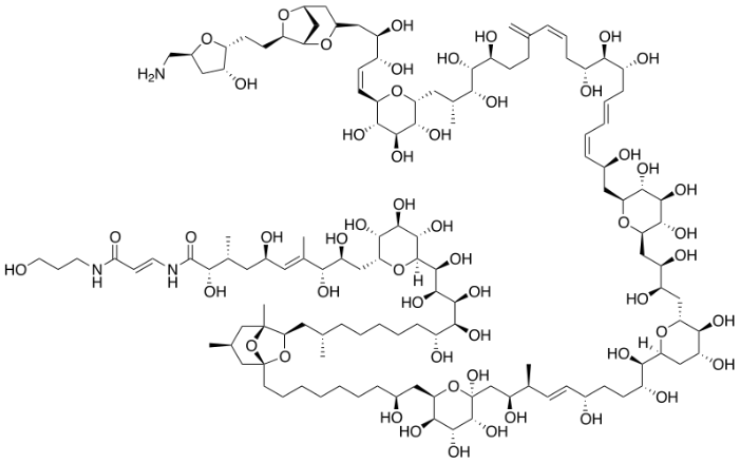
While postdocing at Harvard, I had the great honor of working next to one of the best synthetic organic chemists of that time, Yoshito Kishi. Yoshi could run 40 reactions in a single day and his skill in the laboratory made possible the synthesis of many very complex, important organic molecules such as palytoxin, the puffer fish toxin,[7]

and vargulin, the cypridina luciferin one of the first bioluminescent compounds studied in detail.[8]

Yoshito Kishi
Morris Loeb Professor
of Chemistry
Harvard University



Cypridina Luciferin.



Palytoxin

During these six years in Cambridge, Massachusetts, I lived in a different environment where the upstairs bathroom toilet flushed into our kitchen (we did not eat home often), Joan Baez and Tom Rush would sing in that upstairs apartment on Saturday nights, and I kept my car (a 1957 Corvette) in a garage on Massachusetts Avenue. When

I would wash the car on Saturdays, hundreds of thousands of dollars would be

1957 Corvette

1957 Volkswagen Square-backed Sudan

stacked on the hood of other cars in the garage. In those days lotteries were not legal and the illegal numbers were run by the garage owner (name unsaid). During those six years, my Corvette was stolen five time, but "garage owner" always got it returned to me. One must learn how to live in whatever environment is available. At the end of my stay in Cambridge, I traded my beautiful Corvette for a serviceable Volkswagen and a beautiful wife, Antonia Gigliello

Antonia Gigliello to Antonia Wilson

Following my postdoctoral studies at Harvard, I moved to a faculty position at the University of Cincinnati. The attraction of this position was the publication of the book "Theory and Application of Ultraviolet Spectroscopy" by Hans H. Jaffe and Milton Orchin. At the time this was the best text with application to photochemistry (624 pages, designed to facilitate the understanding of electronic absorption spectra. An organized empirical knowledge of ultraviolet spectra

within a framework of theoretical concepts, December 1962). In all they authored five important text books:

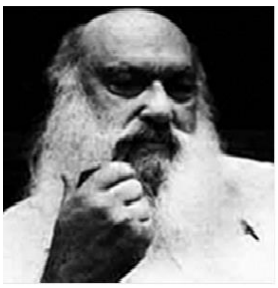
1. *Theory und Applications of Ultraviolet Spectroscopy,* John Wiley and Sons, Inc., New York, 1962. With M. Orchin.

2. *Symmetry in Chemistry,* John Wiley and Sons, Inc., New York, 1963. With M. Qrchin.

3. *The Importance of Antibonding Orbitals,* Houghton Mifflin Company, Boston, 1967. With M. Qrchin.

4. *Symmetry, Orbitals and Spectra,* John Wiley and Sons, Inc., New York, 1971. With M. Orchin

5. Answer Book for *"Symmetry, Orbitals and Spectra",* John Wiley and Sons, Inc., New York, 1971. With M. Orchin. H. H. Jaffé and Milton Orchin



Professor Hans H. Jaffe

Professor Milton Orchin

In addition, the University of Cincinnati was in the process of building a new chemistry building, Crosley Tower. In due course, this building was regarded as one of worst designed chemistry buildings in the United States.

The University of Cincinnati campus has disgusted design enthusiasts for years now with its envelope-pushing architecture. The Crosby Tower is a single pour of concrete, and the Vontz Center, designed by Frank Gehry, has no right angles. Both of these buildings should be studied as feats of engineering and architecture, but their historic value is no excuse for their total disfunction. Crosley Tower is 16 stories high so no fire ladders can reach the upper floors in case of emergencies, and laboratories are positioned on top of 10 floors of

offices. So when the laboratories flooded they wipe out 10-20 faculty offices below!

Crosley Tower, University of Cincinnati

50. University of Cincinnati
Location: Cincinnati
Year Built: 1893, Notable New Construction: 1994 - 2008 (Founded: 1819)
Key Architects: Various, including: Frank Gehry, Michael Graves, Peter Eisenman, Pei Cobb Freed and Partners, Gwathmey Siegel & Associates Architects, Moore Ruble Yudell, Bernard Tschumi, and STUDIOS Architecture.

Jaffe and Orchin initiating construction of Crosley Tower

ARCHITECTURE
The 8 Ugliest University Buildings in America.
Though not reflective of the caliber of the schools that built them, these campus façades are undeniable eyesores

However, Hans Jaffe was certainly one of the most influential chemists of his time who had a very significant impact on the science of photochemistry.

"Hans H. Jaffe, a former head of the UC chemistry department whose work is cited in chemistry textbooks around the world, died Sept. 17, 1989 at his home in Faywood Avenue in Western Hills. Jaffe, 70, retired in June after 35 years on the UC Faculty.

Jaffe was born in Marburg, Germany in 1919 and immigrated to the United States in 1940. He received a bachelor's degree in chemistry at the University of Iowa in 1941, earned his master's degree at Purdue in 1942, then earned this doctoral degree under Oscar Rice at the University of North Carolina.

Jaffe served as the director of graduate studies in the chemistry department from 1962-1966 when he became department head. Jaffe held that post until 1971.

His work in physical chemistry is known throughout the world. The Science Citation Index list him as one of the most cited authors in all of chemistry. He was a Fulbright Scholar and received numerous awards, including the Bronze Medal from the University of Helsinki, the American Chemical Society's Morley Medal, and UC's George Rieveschl Award.

As an educator, Jaffe supervised the dissertations and theses of 45 graduate students. He co-authored five books and published 165 articles and technical papers. One of those books, The Theory and Application of Ultraviolet Spectroscopy, went through five printings and was translated into all the languages used to teach advanced chemistry. Nobel laureate George Porter called it the "Bible of Ultraviolet Spectroscopy"."

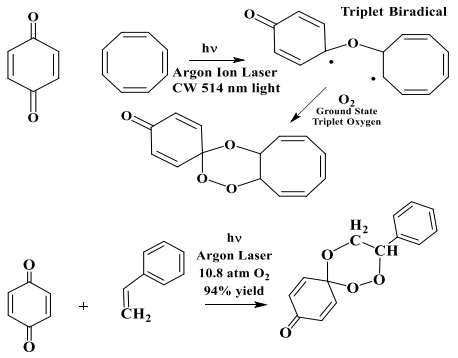
My first significant observation from his laboratory in Cincinnati was that triplet biradicals could be trapped by molecular oxygen in quinone-initiated trioxane reactions.[9] This work was best conducted with a continuous argon ion laser beam of 514 nm light and was made possible by the availability of such lasers in the laboratory of Leon Goldman at the University of Cincinnati Medical Center. Goldman was extremely generous in making his expensive lasers available to young faculty member like myself (http://articles.latimes.com/1997/dec/06/news/mn-61106).[10]

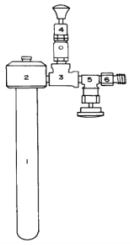
Dr. Leon Goldman: Pioneer in Laser Mdicine

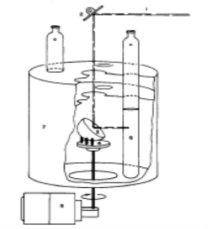
"Dr. Leon Goldman, a dermatologist and surgeon who pioneered laser medicine and was the founding president of the American Society of Laser Medicine, has died (December 6, 1997). He was 91. Goldman, who most recently practiced at the San Diego Naval Medical Center, died Tuesday of heart failure at a retirement home in Pacific Beach, Calif. He was officially designated the Father of Laser Medicine in 1979 at the Opto-Elecktronic Conference in Munich, Germany. The author of six books

on laser medicine, Goldman was quick to snare the innovative laser beam for medical applications. In 1960, only a year after lasers were invented, he began his research at the University of Cincinnati and later established a laser technology laboratory at the school's Medical Center. Bloodless surgery using laser greatly aids medicine, Goldman told The Times in 1973, particularly for such purposed as repairing livers and removing damaged tissue from burn wounds. But surgeons at that time remained reluctant to try lasers, he said, because of a fear of new methods. "It's a pity," he said, "as it interferes with progress." For years, Goldman advocated teaching laser surgery in medical schools with little success. "We just should have kicked out the old medical school chiefs and gotten some new blood," the told the Times in 1985. As medical uses for laser expanded, Goldman in off-duty moments experimented with laser art. "I think it has unlimited potential," he told Senior World six years ago. "We can use an argon laser to get a white etching in red plastic. That was not possible before lasers." He also pioneered other concepts in dermatology, including treating warts as a contagious virus. Born in Cincinnati, Goldman completed his medical education and residency and the taught and practiced at the University of Cincinnati Medical Center until 1980. He then became head of the Laser Treatment Center of the Jewish Hospital in Cincinnati. In addition to being founder and president of the American Society of Laser Medicine, Goldman was editor of its newsletter since 1980. He was also president of the American Society of Dermatological Surgery, which in 1985 named it Leon Goldman Medal in his honor. Goldman wrote more than 100 articles in medical journals as well as his books, including "The Biomedical Laser" and "Laser Medicine and Surgery in Dermatology."

The oxygen-biradical trapping chemistry shown below began with the lasers in Goldman's laboratory was made most efficient under high oxygen atmosphere pressures in special thick-walled Griffon-Worden tube laser reactors.[11]

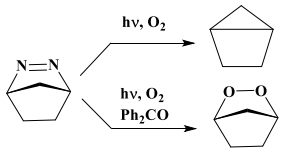


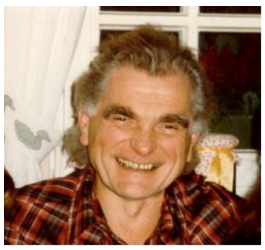




Griffin-Worden Tube irradiation vessel with pressure fittings (Kontes). Lighthouse photochemical reactor.

It was subsequently observed that biradicals generated in the photochemistry of azoalkanes could also be trapped by molecular oxygen. However, the singlet biradicals generated by the direct excitation of the azoalkanes were not trappable. In order to form trappable biradicals, it was necessary to generate long-lived triplet biradicals in the photosensitized decomposition of the azoalkanes.[12,13]

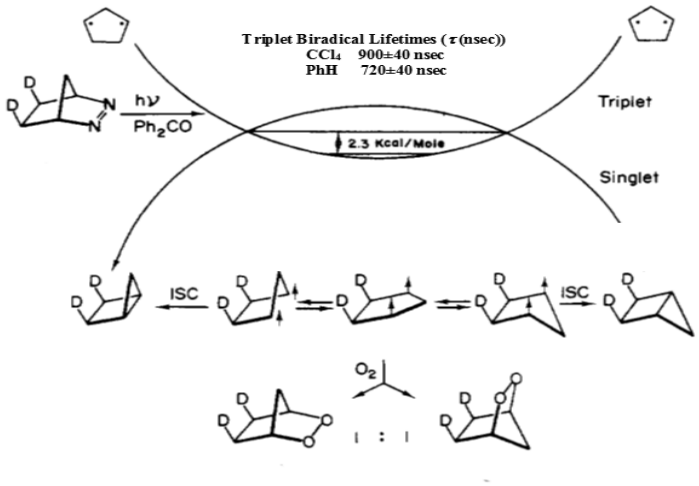


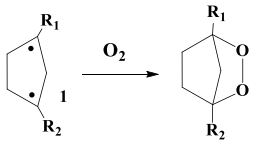


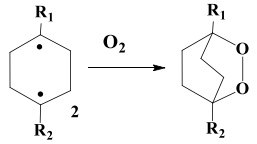
Professor Waldemar Adam

This work was extended to characterizing biradical lifetimes in collaboration with Waldemar Adam on a sabbatical at the University of Würzburg in Germany and Jacob Wirz in Basel, Switzerland.[14,15] Waldemar Adam constitutes another example of how people with complex childhoods learn to deal with adversity and succeed very well in later life. Waldemar was born in the Ukraine where his relatives moved from Germany five generations before. At the end of WWII, the Russian displaced all peoples of German extraction back to Germany. His mother would have to strap him to machinery in factories while she went out to look for food in Berlin. In this chaotic environment, he

did not pass the precollege test and was going have to go to trade school to become an auto mechanic or some such profession. So when it was time to go to college he came to the United States and went to the University of Illinois for his B.S. Degree and MIT for his Ph.D. degree. He married a woman from Puerto Rico and taught at the University of Puerto Rico where his students had to go to the airport every morning to get dry ice. Nevertheless, he did such creative research with chemiluminescent organisms that he was offered the directorship at the University of Würzburg in Germany, which may have been the best German university in organic chemistry at that time. Wait a minute, he didn't pass the test to go to college when he was nine years old, truly an amazing individual. Finally, dinner at Waldemar's house was a linguistic experience. His children would ask a question in German. He would answer in English and his wife in Spanish. By the time dinner was done one did not know what language to use.





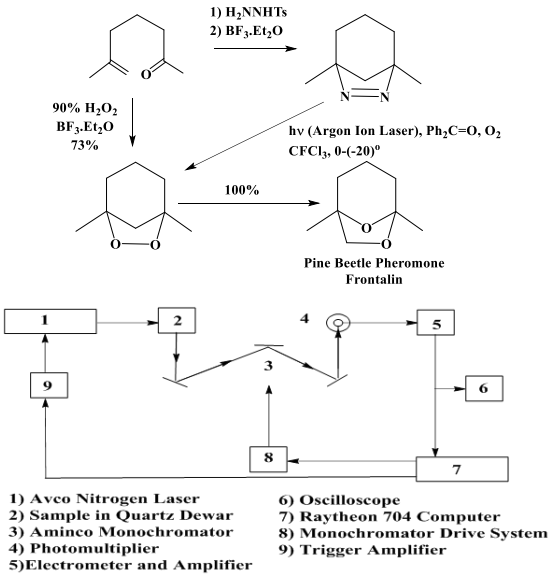


a) R_1 and R_2 = H
b) R_1 = Ph, R_2 = H
c) R_1 and R_2 = Ph

Triplet Biradical	Solvent	Biradical Lifetime (nsec)
1a	$CFCl_3$	<0.1
1b	Benzene	275±15
1c	Benzene	265±20
2a	Benzene	115±20
2b	Benzene	390±50
2c	Benzene	30000±4000

Professor Nicholas J. Turro

This azoalkane biradical trapping chemistry created some problems that illustrate how the world does not always behave as one expects. Following publication of this work, Nicholas Turro called me to tell me that this chemistry did not work in his laboratory. A truly disturbing evaluation from the godfather of photochemistry. However, after a bit of experimentation, it was found that the success of the biradical trapping experiment depended upon how one prepared the azoalkane starting material. If one purified the azoalkane by sublimation, the trapping worked very well. However, if one purified the azoalkane by recrystallization the peroxide could not be isolated. The azoalkane was prepared by copper metal oxidation of the hydrazoalkane, and if one recrystallized the product azoalkane in the usual fashion, traces of copper metal remained that destroyed the peroxide product. Purification by sublimation removed all copper metal and the peroxide product was stable and could be isolated. All parties finally agreed with this evaluation and this example illustrates how all experiments may not be fully characterized at the time of publication.



In a different approach to computerized kinetic luminescence spectrometry, a pulsed nitrogen laser apparatus was constructed to measure the emission decay at individual wavelengths over the spectrum of emitting molecules and reconstructing the emission spectra of these molecules at different times following the exciting pulse.[18] Today this same technique, albeit on a much shorter time scale, (30 fsec (10^{-15} sec)) is used for ultrafast transient absorption spectroscopy.[18]

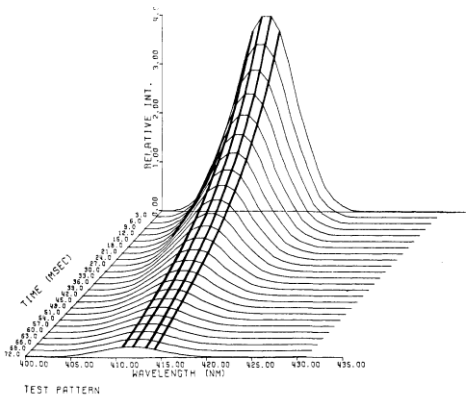
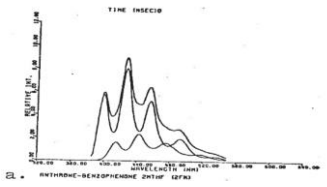
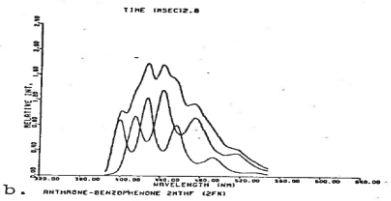


Figure 1. Luminescence life history assembled from decay data

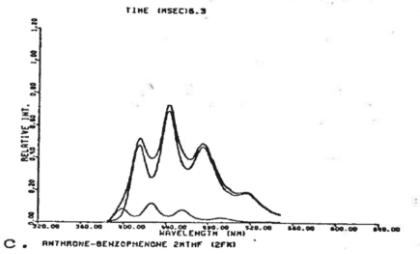
0 msec



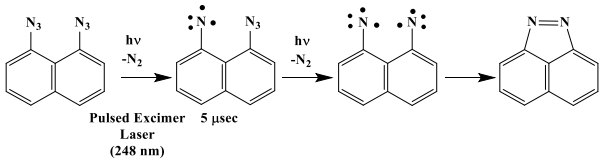
2.8 msec



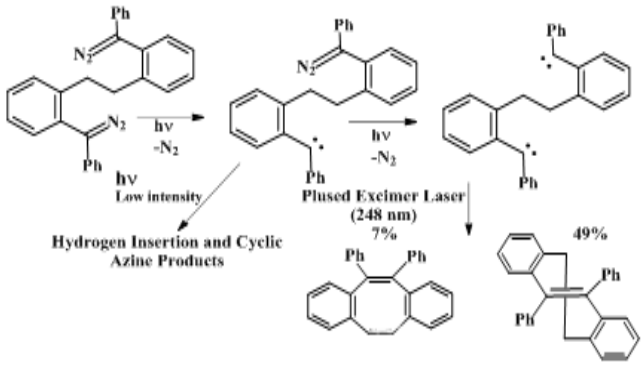
6.3 msec



Another aspect of pulsed laser photochemistry that was developed in the 1980's was multiphoton photochemistry. Thus, Akihiko Ouchi[19] in Japan and Jakob Wirz[20] in Switzerland developed pulsed laser techniques for double photon absorption and generation of dinitrenes and dicarbenes followed by their dimerization.



Jacob Wirz implemented similar carbene dimerizations with high intensity laser pulses.[20]



Professor Alan Pinhas

We developed a special apparatus for initiating very high intensity laser photochemistry using a cw. argon ion laser.[21, 22] In this apparatus, the cw. argon ion laser is focused on a microjet of solution that is ejected from a capillary gas chromatography column nozzle. Jet dimeters of 50-100 microns can be obtained in this fashion and the jet streams are freely suspended in space without contact with glass surfaces. This apparatus was developed in collaboration with Professors Alan Pinhas of the Cincinnati Chemistry Department and Leon Goldman of the Medical School. The alignment and focusing of the laser beam on the microjet is critical

and must be done with high precision. This same type of apparatus is used today to weld detached retinas back into place. It was used on my eye in 1991 when I was shot in the eye 300 times to reattach the retina of my left eye.

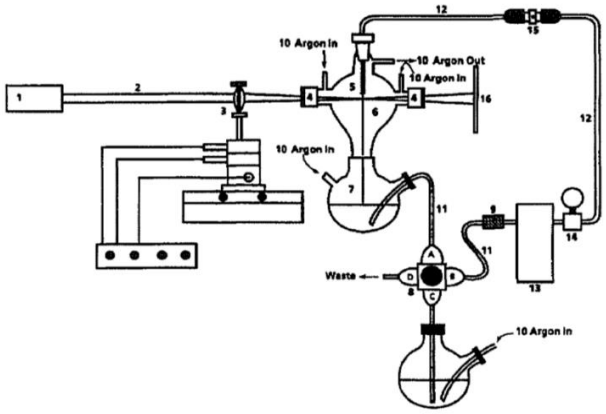
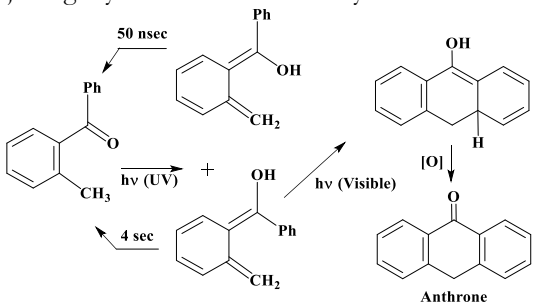


Figure 2. Laser-jet apparatus: (1) argon ion laser, (2) laser beam, (3) lens on motorized micropositioner, (4) demountable reaction chamber windows, (5) capillary nozzle, (6) reaction chamber, (7) reservoir receiving flask, (8) 4-way valve, (9) filter, (10) inert atmosphere ports, (11) low-pressure tubing, (12) high-pressure tubing, (13) HPLC pump, (14) pressure gauge, (15) shut-off valve, and (16) projection screen.

Some examples of multiphoton photochemistry were observed using multiple light beams of different wavelenths.[23] Thus, anthrone can be formed by first exciting 2-methylbenzophenone with UV light to form the photoenol which absorbs visible light and then exciting the jet slightly downstream with very intense beam of visible light.

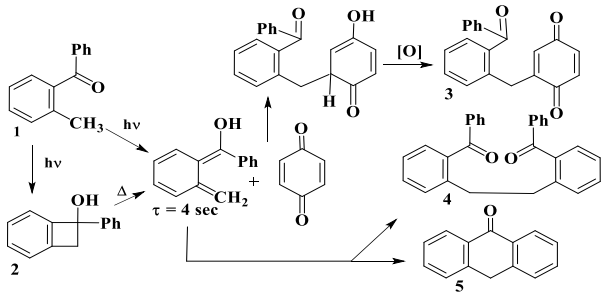


Laser-Jet (Argon Ion Laser) UV lines (333-364 nm) Watts	Irradiation time (min)	Yield of Anthrone (%)	Rayonet Photoreactor
0.55	45	11	
1.30	45	22	
2.85	45	24	
2.85*	45	34	
	20 hours	0.5	350 nm lamps

*UV beam 2.85 Watts, Visible beam (458-514 nm) (9 Watts) focused 0.1 mm below UV beam

Professor William R. Heineman

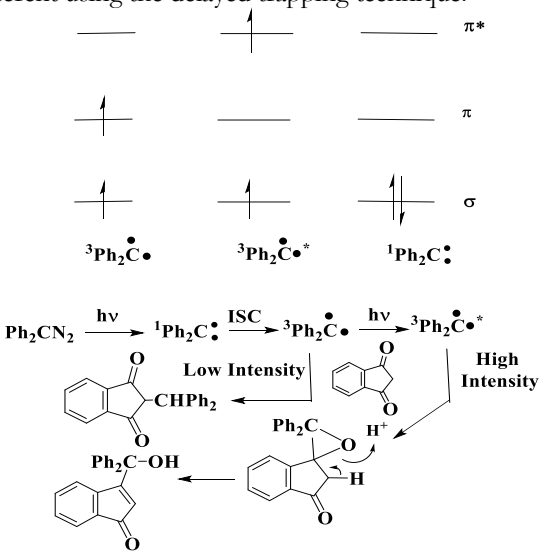
The microjet velocity is so fast, 4.25 m/sec, that it can be irradiated and quenched in the receiving flask before reactive photointermediates return to their original ground states. Thus, the photoenol of 2-methylbenzophenone that has a lifetime of 4 seconds can be trapped by benzoquinone by delayed trapping in this microjet apparatus.[24] This work was done in collaboration with Professor William R. Heineman of the University of Cincinnati.



Nozzle diameter = 100-50 mm. Velocity of jet = 4.25 m/sec. Residence time in laser focal region = 25 msec. Delay time between irradiation and quenching in trapping solution = 1 msec.

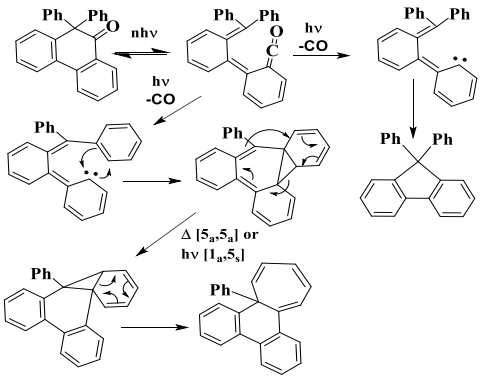
Structure Number	Laser-Jet (14% Conversion of 1)	Thermal Conversion of 2
3	60%	47%
4	6%	5%
5	19%	0%
2	-	15%

This same delayed trapping technique was used to study the Lewis acid properties of excited carbenes. Thus, the chemistry of ground state triplet carbenes and exited triplet carbenes were shown to be quite different using the delayed trapping technique.[25,26]



Other examples of multiphoton photochemistry include decarbonylation of ketene intermediates.[27,28] This work was done in collaboration with Cornelia Bohne of the University of Victoria, British Columbia.

Professor Cornelia Bohne



The second and final instalment of this article will appear in the December issue of the EPA Newsletter.

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Temperature Dependence of Primary and Secondary Fluorescence Quantum Yield Standards

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Fluorescence quantum yields (QY) are still an increasing topic in photochemistry and photophysics. The number of articles in the literature is gradually increasing (approx. 5% per year). Most authors did not give precise experimental conditions when using relative fluorescence standards. Especially the temperature is not given or even not controlled. Inside a compact fluorescence spectrometer the temperature is far from constant and far from room temperature when no controlled cuvette holder is applied. State-of-the-art QY measurements need a temperature control during the experiment. However, this is not a standard equipment and has to be bought and installed separately.

This gives rise to two experimental errors [1]: First, the refractive index, which depends slightly negatively on temperature (together with the density). In the main equation for calculating the fluorescence quantum yield the refractive index enters as n^2. For all commonly applied solvents, this error is presented in a range from 10 to 40 °C in Fig. 1. As the temperatures of reference (R) and sample (S) are not necessarily the same, this error can duplicate in the worst case.

$$\emptyset_f(S) = \emptyset_f(R) \cdot \frac{1 - 10^{-A_R}}{1 - 10^{-A_S}} \cdot \frac{n_S^2}{n_R^2} \cdot \frac{\int I_S(\nu) d\nu}{\int I_R(\nu) d\nu}$$

Equation 1. Calculation of the QY of the sample S in comparison to the standard R. A is the optical density at the focal point, n is the refractive index of the solvent used, the integral is the total corrected emission as a function of ν (or λ).

Secondly, all fluorescent molecules with a QY of less than 1 should be temperature dependent. The reason is the non-radiative decay, which is an activated process. In fact, the results are more complicated as there are positive and negative deviations from zero. Therefore, all

primary and secondary standards recommend by the IUPAC [2] are investigated for their temperature dependence in a range of 20 to 35 °C. Again, this error can duplicate.

Temperature dependence of the refractive index

The refractive index of all solvents used for the IUPAC standards have been plotted relative of the values at 25 °C. The slope varies from -0.015 %/K for water to -0.09 %/K for cyclohexane [3]. As a result, the quantum yield tends to change slightly negative with temperature independent from the properties of the fluorophores. The overall error might be around ±1% in the absence of temperature control in the spectrometer during a working day.

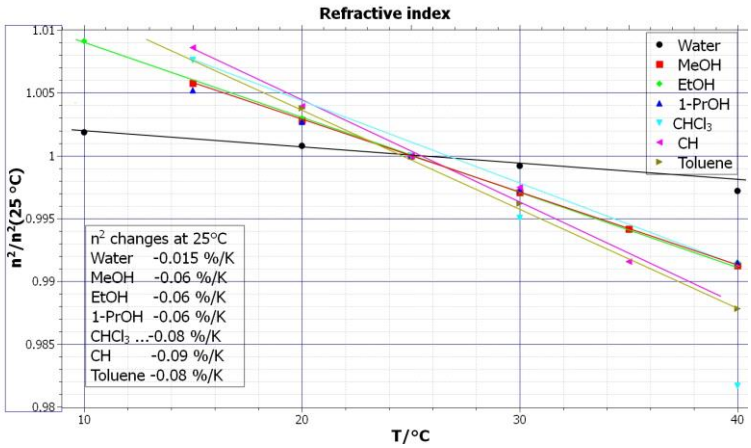

Figure 1. Temperature dependence of the n^2 value from Eq. 1. The solvents used are water, methanol (MeOH), ethanol (EtOH), 1-propanol (1-PrOH), chloroform ($CHCl_3$), cyclohexane (CH), and toluene.

Temperature dependence of the measured fluorescence intensity

According to the influences mentioned above, it was expected to have a negative temperature dependence on the QY for all fluorophores. In order to measure the temperature dependence of the QY experiments in a completely renewed and updated fluorimeter (FluoroMax-2, Horiba) have been performed in the kinetic mode over a 3h period. Exact values for the temperature have been measured with a digital sensor in the cuvette holder which is connected to a water bath from the back of the fluorimeter and thermally isolated from the environment. As shown in Fig. 2, the stability of the measurements is very high and therefore the resolution is less than 0.02 %/K.

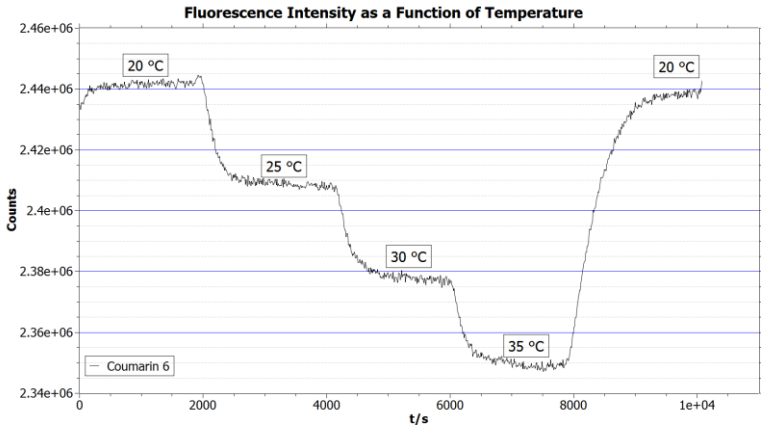

Figure 2. Temperature dependent fluorescence signal (S/R) of coumarin 6 in EtOH. S is the PMT signal in counts and R is the internal reference from a silicon diode detector. S/R is independent from the excitation intensity. The value of R is about 0.05 in this experiment.

Table 1. Temperature dependence of the primary (P) and secondary (S) fluorescence standards used by IUPAC. For absolute QY values please refer to [2].

Fluorophore	Solvent	P/S	Temperature coefficient of luminescence, %/K
p-Terphenyl,	CH	P	-0.20
PPO	MeOH	S	almost zero
Quinine sulfate	0.1 M $HClO_4$	P	-0.30
9,10-DPA	CH	S	-0.04
Coumarine 102	EtOH	S	-0.02
Coumarine 153	EtOH	P	-0.70
$[Ru(byp)_3]^{2+}$	Water	S	-0.04
Coumarine 6	EtOH	S	-0.25
Fluorescein	0.1 M NaOH	P	almost zero
DCM	EtOH	S	-1.6
Perylene orange	$CHCl_3$	S	-0.40
Rhodamin 6G	EtOH	P	-0.13
Erythrosin B	Water	S	+0.75 §
Erythrosin B	MeOH	S	-0.37
Zn TPP	Toluene	S	-0.20
Rhodamin 101	EtOH	P	+0.22
Perylene red	$CHCl_3$	S	-0.30
Cresyl violet	EtOH	P	-0.013
Oxazine 170	EtOH	S	+0.19
Oxazine 1	EtOH	P	-2.5
Zn Ph	Toluene	S	-0.44
Zn Ph	1-PrOH	S	-0.20

DPA: Diphenyl-anthracene, TPP: Tetraphenylporphyrine, Ph: Phthalocyanine, relative experimental error: ±10%, absolute experimental error ±0.02 %/K, detection limit <0.01 %/K. § depends weakly on concentration.

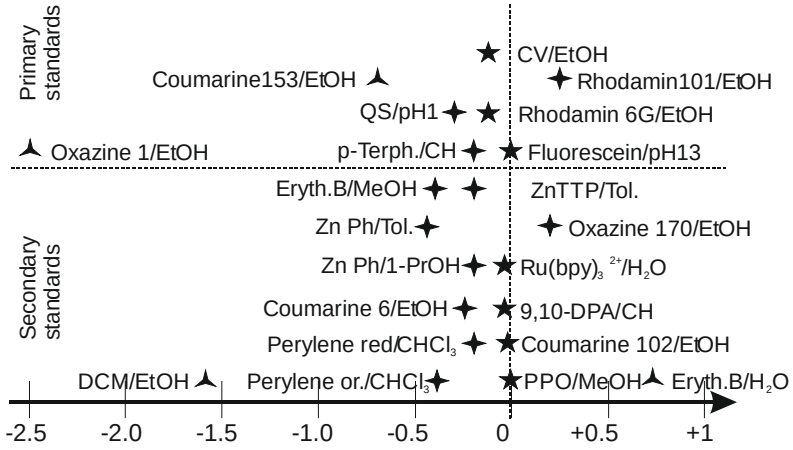

Figure 3. Temperature dependence (%/K) of the primary (P) and secondary (S) fluorescence standards used by IUPAC. The measured results are a combination of the n^2 effect and the QY itself.

A classification can be been done in the following way:
Five stars: $< \pm 0.2$ %/K is negligible, effect mainly from n^2
Four stars: $< \pm 0.5$ %/K has already a significant influence on the results
Three stars: $> \pm 0.5$ %/K not useful without temperature control, error
can be really large

Preliminary explanation of positive and negative temperature dependence

It is worth mentioning that there is a sign inversion for Erythrosin B in water (+) and methanol (-). The two solvents seem to be not so much different (highly polar, H-bonding ability). This means that the temperature dependence is not only a function of the molecule but also on the solvent applied. In order to get a first idea about the nature of the positive temperature effect concentration dependent measurement for the system Erythrosin B in water has been performed. In fact, there is a significant influence (2.3 μM +0.70%/K, 4.5 μM +0.75%/K, and 9 μM +0.83 %/K) which is larger than the experimental error.

So, the basic scheme for negative temperature effect is the activated non-radiative decay for QY less than 1 (Φ_F<0).

$$F + h\nu \rightarrow F^*$$
$$F^* \rightarrow F + h\nu_F + \Delta$$

The formation of heat (Δ) is controlled by k_{nr} (T) which increases with temperature. So, even if k_f is constant, the overall QY decreases.

For the positive effect a pre-equilibrium of the fluorophore with negative enthalpy can describe the results.

$$F + F \leftrightarrow 2F \qquad \Delta H < 0$$
$$F + h\nu \rightarrow F^* \qquad 2F + h\nu \rightarrow 2F^*$$
$$F^* \rightarrow F + h\nu_F + \Delta \qquad 2F^* \rightarrow 2F + \Delta$$

The equilibrium shifts to the left side at higher temperatures. If $2F^*$ has no or lower QY of fluorescence compared to F^*, but similar optical absorption, the overall measured intensity increases with temperature due to the higher concentration of F. Using Eq. 1 Φ_F depends positive on temperature.

Summary and Outlook

As shown in Table 1 and Fig. 3 the influence of the temperature on the measured signal intensity is far more complex than expected. Deviations can be negative and positive. The solvent can change sign and size of the temperature effect. Further investigations are absolutely necessary to understand better the fundamentals of fluorescence.

For quantitative fluorescence measurements it is necessary that the cell is temperature controlled. Without values of quantum yields should not be published even if one uses the five star standards. The effect of the molecule under investigation is not known and cannot be predicted up to now without measurements.

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Determination of Reaction Quantum Yields: LED Based Setup with Better 5 % Precision

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Introduction

With the increasing awareness of green and energy efficient chemistry and the rapidly developing availability of LED light sources, photochemistry and in particular photocatalysis are developing on a seemingly exponential rate. The reaction quantum yield (QY) is one of the paramount characteristics of these light induced processes. It describes how many product molecules are generated from one absorbed photon. The higher the yield, the lower the cost of the photoinitiated reaction.
Chemical actinometers still remain as a widely used method for the determination of the quantum yield.[1] Standardized chemical reactions are used to effectively measure the amount of light absorbed under given experimental conditions. Just for liquid solutions 67 different reactions are suggested, partially with rather complicated detection schemes. The use of photometric procedures is strongly discouraged, since it is claimed that photodiodes can age dramatically – a book chapter from 1974 is cited.
Times have changed since the 2004 report on Chemical Actinometry, luckily providing great improvements. If one just looks at silicon based detectors, the quoted decrease in efficiency would not allow the widespread solar panels now found even under the harshest conditions. In contrast, some of the actinometer substances are not anymore available due to retirement of older chemists that have synthesized them.
Most importantly, the experimental result of actinometry relies on the known quantum yield of the individual substances that are specified as a standard. The excitation wavelengths are restricted to the absorption range of the actinometer substance and this leads to severe limitations in the choice of excitation wavelength. In particular there are no chemical actinometers in the red and NIR range with many new interesting reactions being initiated there. Last but not least, one has to

remember that all existing chemical actinometer quantum yields were determined through photometric measurements with typically the equipment available in the fifties and sixties of the last century.[2,3]
We have now worked for nearly ten years on establishing an alternative procedure that enables a rapid, facile and reproducible determination of the quantum yield without any significant restrictions. We combine controlled illumination by high power LEDs with a precise measurement of the absorbed light power by a commercially calibrated thermopile or a readily calibrated large area solar cell detector. The procedure is augmented by PC assisted data recording, evaluation and modelling used to extract the QY values. This article summarizes the large range of improvements made to the original Quantum Yield Determination Setup (QYDS) published in 2010 by Megerle et al.[4]

Basic Principle

The quantum yield $\phi(\lambda)$ of a photochemical reaction is defined as the number of formed product molecules N_{prod} in ratio to the number of absorbed photons $N_{ph,abs}$ of a particular wavelength:[5,6,7]

$$\phi(\lambda) = \frac{N_{prod}}{N_{ph,abs}}$$

For a precise determination of the QY both of the above quantities have to be exactly quantified. The amount of created reaction products can be measured via standard spectroscopic techniques, e.g., NMR spectroscopy[8,9], UV/Vis spectrophotometry[10] or other well established and accessible chemical methods. To determine the number of photons absorbed by the chemical system, actinometry uses a comparison with the actinometer substance. In this way the complete illumination geometry and operating conditions are included. Even a small change leads to the need for a recalibration. We want to argue that it is much easier, precise and controllable to relate the photon flux to a commercially available NIST traceable calibrated thermopile powermeter.
According to our experience the main challenge for the exact determination of the quantum yield is the determination of the number of product molecules rather than the number of photons. For instance, in the measurement of molecular switches, the main limiting factor for precise measurement of the concentration is the weighing of the

substance and preparation of the solution to specify the molar absorptivity. As the concentration and volume of solution irradiated renders the number of molecules, any relative determination of the product mixture will only determine the number of product molecules as precise as the starting conditions. This challenge is the same for the chemical actinometry and our new setup and procedure. We therefore will not include it in the further discussion. For any given use of the QYDS it has, however, to be considered carefully.

Experimental Setup

The scheme of the QYDS is shown in Fig. 1. As light source high power LEDs are used. To control the amount of light precisely, a lens system is used to image the LED die (emitting semiconductor chip) into the cuvette holding the investigated solution. The illumination time is precisely regulated by a mechanical shutter that is electronically controlled. In principle one is tempted to just switch the driving current of the LED, but we find that this does alter the power and spectrum of the light for some initial period.

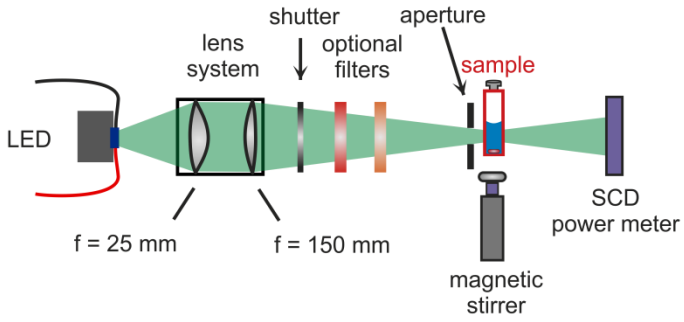

Figure 1. Schematic of the experimental setup.

Filters can be placed into the beam path to further control the amount of light. For typical photochemical measurements hundreds of µW of light are sufficient since the substrate is identical to the photosensitizer. In a photocatalytic system a large excess of substrate should be converted and tens to hundreds of mW can be applied. In any case the duration of the illumination and even individual steps to determine the temporal reaction profile should not be chosen shorter than about a minute. We have to bear in mind that the sample is never illuminated

homogeneously and only rapid stirring will lead to the quasi-equilibrium condition needed for a simple evaluation. Experimentally, we find that complete mixing by stirring is rather slow.
We prefer to hold the sample in a 10x10 mm^2 spectroscopic cuvette. This allows a controlled experiment, unlike round or irregularly shaped vials or flasks. For some experiments also cuvettes with a smaller optical path are used. In order to be sure that all applied light is indeed going into the solution, we place a carefully centered 8x8 mm^2 mechanical aperture right in front of the cuvette. A magnetic bar on an electrically driven motor stirs the small bar inside the cuvette.
The power of light transmitted through the cuvette is constantly monitored. Great care is taken that all of the light is indeed imaged onto the sensor area of the powermeter. Measuring the power of the transmitted light with sample in the cuvette in comparison to the transmission with a solvent cuvette renders the absorbed illumination power.

High power LEDs are a cost effective and efficient light source[11] for the QYDS. They are now available without gap in the full spectral range between the UV-C up to the NIR. We use LEDs from 265 to 1050 nm from various manufacturers, see Fig. 2 for representative spectra. It can be seen that the output spectrum of each LED is fairly narrow compared to molecular absorption bands in solution. For most investigations no further filtering is needed. However, modern dielectric short pass, long pass and band pass filter can be added easily in the beam path.
The power of the incident light can be changed by about a factor of ten through the driving current of the LED and for larger changes by a neutral density filter. The possibility to control the applied light power at will without significant change in spectrum or beam propagation is unique to LEDs. Any classical lamp combined with a monochromator cannot compete in this respect.

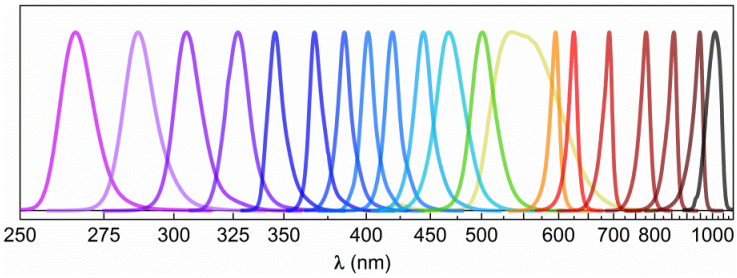

Figure 2. Selection of high power LEDs available as excitation light.

A dedicated **lens system** is used for imaging of the LED die into the cuvette. We started by using a photographic lens with an f-number of 1.4.[4] This is a good choice for tens of mW light at the sample in the visible. For UV light and better light collection we switched to fused silica best form lenses.[12] Typically we use an f=25 mm lens to collimate a sizable fraction of the LED and an f=150 mm lens to image into the sample. The nominal magnification of 6 allows passage through the 8x8 mm^2 aperture without problem. This is, however, only true for LEDs with a plane output window. For LEDs with a silicone lens for collimation, this lens leads to an effective enlargement of the die and we turn to an f=100 mm second best form lens. For the highest light throughput we resort to aspheric lenses now readily available both in the visible and in the UV. These allow an unprecedented f-number of around 0.65 and a collection efficiency of the LED light above 50 %.

The power arriving at the sample is around 100 mW for the best form lenses and around 500 mW for the aspheric lenses. This is not to be confused with the electric power driving the LED of typically a few Watt – quoted by most authors in the field. If a large power is needed in restricted space and at low budget, Fresnel lenses can also be used quite successfully. All these power levels are just guiding values as the power depends rather strongly on the wavelength. The quoted values are for the UV-A and blue and also the red part of the spectrum. In the green and particular the UV-B and –C the values are down by up to one order of magnitude.

The light emitted from a LED originates from the die within the SMD chip (see Fig. 3 left). The light is imaged in a controlled fashion into the sample. The imaged light can be observed on a screen placed at the

position where the cuvette is during the actual measurement. As can be seen from Fig. 3 right, we find a clear image that is magnified by the above mentioned factor. The fine structure deposited on the die can easily be recognized as sign of the proper imaging. With the chosen optics and geometry, this is the smallest image possible. Contrary to a classical lamp the image and hence the area where light is absorbed in the cuvette is well defined and allows for the precise determination of the amount absorbed.

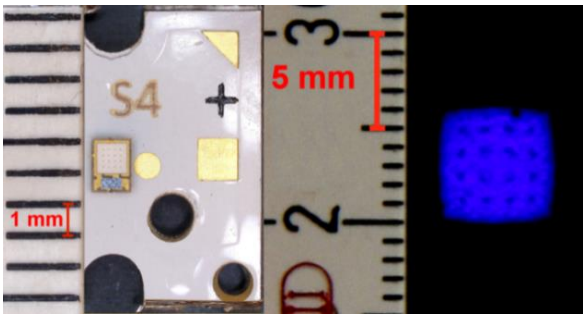

Figure 3. Detailed view on the 1x1 mm² die in the SMD chip Luxeon LHUV-0415-0600 with a nominal wavelength of 415 nm (left). The imaging of the LED light into the sample plane leads to a fine pattern originating from the structure of the die (right).

The most important part of the QYDS is the detector used to record the light power after the sample. With the reference measurement already discussed, it allows for the precise determination of the number of photons absorbed by the sample. With commercially available thermopile power heads, powers of tens to hundreds of mW can be measured with an accuracy of better than 3 %. Typically, the calibration is NIST traceable, i.e. it can be traced back to the most accurate calibrations known. We routinely use a PowerMax USB - PS19Q from Coherent, Inc. with an aperture of 19 mm. This ensures that all light is caught even in the diverging part of the beam behind the sample position. The head has a stated wavelength range of 300 to 3000 nm, but we were able to certify, that it is usable at least down to 250 nm. As all of our LEDs deliver at least 10 mW to the sample, we have a secondary standard with this power head. In particular for photocatalytic measurements the head is used directly.
A solar cell detector (SCD) of our own design serves as an alternative

to the powermeter for light levels in the μW to single digit mW range. The SCD is made from a 27x45 mm² piece of UV sensitive solar cell without any coating. We characterized the SCD and found that the quantum efficiency is 50 % or higher for the whole range of 265 – 900 nm. To convert the photocurrent into a voltage that can be read into the PC controlling the measurements, we designed a large dynamic range IU converter according to ref. 13. With a well stabilized voltage supply we measure the light power with a residual noise of less than 100 μV at 0.1 to 10 V levels. So the electronic noise does not enter into the measurement accuracy.
To calibrate the SCD for any selected wavelength (LED), we first set the light level into the 10 mW regime and measure this level with the thermal powermeter. Then we substitute the SCD and record its output level. In auxiliary measurements we found the linearity of the SCD to be better than 0.1 %. Now the LED level can be turned down to levels in the range of 200 μW or even lower and this amount of light still be measured to better than 3 % accuracy. The use of the SCD overcomes the errors associated with thermal drift of the powermeter at low light levels. Tests over more than a year show that the SCD does not age appreciably in office and laboratory air and with the relevant illumination levels. The later are always below the solar irradiation encountered by solar panels.

Figure 4 shows the **implementation of the QYDS** that we use and have supplied to about 15 other laboratories so far. Its footprint is 580x190 mm² and it is normally covered by black PVC shields to avoid any spurious light input or output that could falsify the measurement or endanger the operator. In addition to the optical setup, a precise power supply for the range up to 1 A and a laptop for experimental control and data recording is used. A digital scope (Picoscope 2204A, Pico Technology Ltd.) reads in the power level recorded by the thermopile or the SCD. The IU converter and the control electronics for the shutter are both contained in the QYDS box.
As the system is set up fully modularly, it can very easily be adjusted to changing needs. For some measurements the sample has to be degassed and more space is needed at the sample location. In addition the housing has to be enlarged in this region. Lately, we even combined 2 LEDs and shutters to perform fatigue measurements on molecular switches.

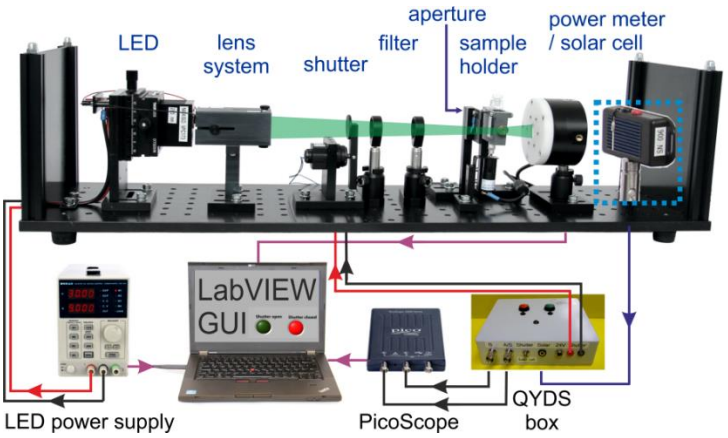

Figure 4. Schematic view of the Quantum Yield Determination Setup **QYDS**. The light from the LED is imaged into the sample by a lens system consisting in this case of fused silica best form lenses (f=25 mm and 150 mm). The transmitted light is detected either by a calibrated powermeter or a calibrated UV sensitive solar cell.

Validation and Measurement Example

For a new method like our QYDS that is proposed to replace an established method in chemical analysis a sound validation is needed. Already in our earlier report we showed that the new concept of controlled LED illumination and photometric measurement of the absorbed light amount is reproducing the QY values of the most frequently used chemical actinometer, the potassium ferrioxalate system.[4]

We subsequently searched for further test grounds with the focus on spectroscopically determinable systems. The azobenzene isomerization seems ideal. However, even the list of selected publications suggested by the IUPAC report[1] gives QY values that vary by about a factor of 2 between different authors reporting the same excitation wavelength, solvent and reaction direction.[14,15,16] So the azobenzene cannot be used for a validation aimed at sub-5 % accuracy. We still measured the various processes in ethanol and find values within the range reported. Repetition on different days, by

different students and a range of ten in the illumination level confirmed these new values.

A further actinometric system that seems well suited for validation with spectroscopic detection of the photoinitiated process is the *o*-nitrobenz-aldehyde → *o*-nitrosobenzoic acid photoisomerization.[17] The substrate spectrum can be seen in the left part of Fig. 5 (purple line for 0 min). We performed measurements with 325 and 340 nm excitation. We used 0.507 mW for 2 mL of 135 μM solution in MeCN. Particularly for 325 nm there are clear signs of degradation as the reaction is driven into the photostationary state. We assign this to absorption of another photon by the product and subsequent reaction. This has also been proposed by ref. 9. As the reaction proceeds, the UV-C absorption decreases and a new band around 300 nm grows in. Initially a clear isosbestic point is found, that gets lost at later times.

For the determination of the temporal evolution of the substrate and product concentration, we need the product molar absorption spectrum. This is not available in the literature and the product cannot be purchased. We therefore used the dataset for 340 nm and chose the last spectrum, which still confirms to the isosbestic point, to determine the product spectrum. We have to make an assumption on the ratio of product to remaining substrate. This is done by varying the value in the range from 10 to 5 % and finding the lowest value where the decomposition of all measured spectra does not lead to a formally negative concentration of the substrate. The value of 7 % then renders the value for the QY of 41.2 % with the procedure explained below. Only a minute change in the QY value results if we vary the remaining substrate concentration by a few percent.

The right hand side of Fig. 5 shows the measured product concentration profile together with the modelling fit (grey line). The residuum (green dots) shows a minor deviation from zero due to the decomposition. Our value matches the two newer values reported by Galbavy et al.[18] and Gescheidt and coworker.[10] We therefore support their suggestion to replace the established value of 0.5.[1,17,19]

On passing we want to mention that the original value of around 0.5 was measured with a homebuilt thermopile of 1934, with no newer measurements referenced in ref. 1.

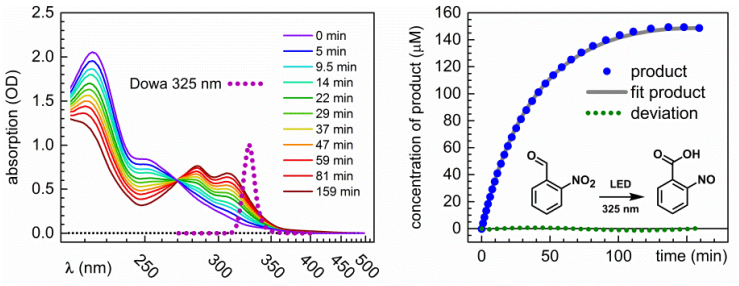

Figure 5. Investigation of *o*-nitrobenzaldehyde → *o*-nitrosobenzoic acid photoisomerization. The left panel shows the evolution of the UV/Vis spectra under 325 nm illumination. The right panel shows the temporal evolution of the product concentration.

There are good arguments to use molecular switches for actinometry.[20] Many of them are known to be very fatigue resistant and can be switched back and forth many times. Particular switches with well separated optical spectra for the two isomers look appealing. Surprisingly only azobenzene - see discussion above - , stilbene with its complicated ultrafast dynamics and the fulgide Aberchrome 540 are recommended.[1] The latter is not any more commercially available.
We chose a model system from the diarylethene family in accord with recent work.[20] The molecular photoswitch 1,2-Bis(2,4-dimethyl-5-phenyl-3-thienyl)-3,3,4,4,5,5-hexa-fluoro-1-cyclopentene undergoes cyclization upon irradiation with UV-B light.[21] The cycloreversion process can be initiated by orange light. The molar absorptivity in n-hexane as well as the spectrum of the excitation light used for the determination of the quantum yield are shown in Fig. 6. Since the spectra of the open and the closed form of the substance overlap, the generated product starts to absorb the incident light as soon as a significant amount of conversion is reached. Therefore, it is important to carefully choose the excitation LED. We recommend to select an irradiation wavelength that results in a photostationary state (PSS) with a dominance on the product side.

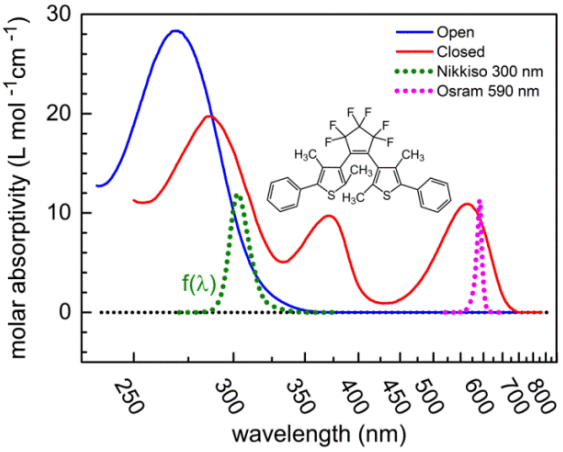

Figure 6. Molar absorptivities of the diarylethene based molecular switch dissolved in n-hexane. The spectral distribution of the LEDs used for the quantum yield determination is shown by the dotted lines.

The evolution of the UV/Vis spectrum with 156 µW illumination at 300 nm of a 95 mM solution of the switch in n-hexane is shown in Fig. 7. It can be seen that the total irradiation of 2 hours leads to the PSS. For the determination of the quantum yield the full range of the experimental data are evaluated - from start of the isomerization up to the PSS. With the predetermined spectra of the molar absorptivity of both the open and closed form, we can perform a unique spectral decomposition. This analysis enables us to determine the concentration of both species at each temporal data point (see Fig. 8 left). With 590 nm light the closed form can again be converted to the open form (see Fig. 8 right). As the efficiency for ring opening is much lower, 2.935 mW for 760 µL of 200 µM solution in a 10x4 mm Semi-Micro-cuvette were used.

It should be noted that we do not try to use the "linear regime" like often described in the literature. For one we think that without an explicit observation of the whole process up to the PSS one can not tell how far the process is "linear". Secondly, working only with data at small conversion, the evaluation loses precision and the enormous wealth of information contained in the full conversion is neglected.

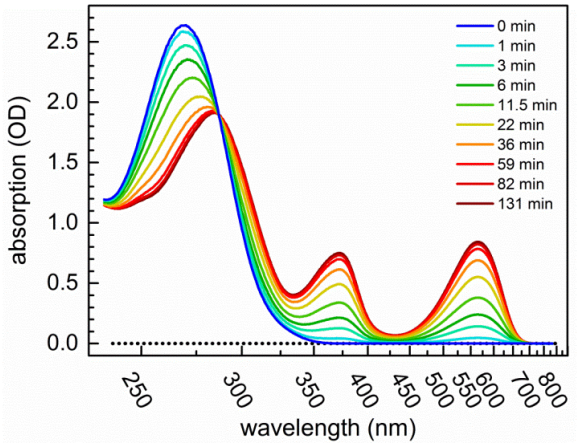

Figure 7. UV/Vis spectra of the ring closing process measured during the irradiation of 2 mL of a 95 µM solution in a 10 mm absorption cuvette. Illumination by a 300 nm LED with an applied power of 156 µW.

The number of photons absorbed by the sample per second and wavelength interval is given as

$$N_{Ph}(\lambda)\left[\frac{1}{s}\right] = \frac{P_0 \cdot f(\lambda)}{E_{Photon}(\lambda)} \cdot Abs(\lambda) = \frac{P_0 \cdot f(\lambda) \cdot \lambda}{h \cdot c} \cdot Abs(\lambda)$$

Here P_0 is the incoming power, $f(\lambda)$ is the spectral distribution of the LED light (see dotted line in Figure 6), h the Planck's constant, c the speed of light. $Abs(\lambda)$ is the absorbance of the sample with

$$Abs = 1 - Transmission.$$

The absorbance depends on the cuvette thickness d, the concentration c of the isomers A and B and the molar absorptivity ε:

$$Abs(t,\lambda) = 1 - 10^{-d\cdot[c_A(t)\cdot\varepsilon_A(\lambda)+c_B(t)\cdot\varepsilon_B(\lambda)]}$$

The following system of differential equations characterizes the change in the number of the isomer molecules per illumination time interval:

$$\frac{dN_A(t)}{dt} = -\phi_{A\to B}\int \frac{c_A(t)\varepsilon_A(\lambda)}{c_A(t)\varepsilon_A(\lambda) + c_B(t)\varepsilon_B(\lambda)} \frac{P_0 \cdot f(\lambda)\cdot\lambda}{h\cdot c} Abs(t,\lambda)\, d\lambda$$

$$+\phi_{B\to A}\int \frac{c_B(t)\varepsilon_B(\lambda)}{c_A(t)\varepsilon_A(\lambda) + c_B(t)\varepsilon_B(\lambda)} \frac{P_0 \cdot f(\lambda)\cdot\lambda}{h\cdot c} Abs(t,\lambda)\, d\lambda$$

$$\frac{dN_B(t)}{dt} = -\phi_{B\to A}\int \frac{c_B(t)\varepsilon_B(\lambda)}{c_A(t)\varepsilon_A(\lambda) + c_B(t)\varepsilon_B(\lambda)} \frac{P_0 \cdot f(\lambda)\cdot\lambda}{h\cdot c} Abs(t,\lambda)\, d\lambda$$

$$+\phi_{A\to B}\int \frac{c_A(t)\varepsilon_A(\lambda)}{c_A(t)\varepsilon_A(\lambda) + c_B(t)\varepsilon_B(\lambda)} \frac{P_0 \cdot f(\lambda)\cdot\lambda}{h\cdot c} Abs(t,\lambda)\, d\lambda$$

The fundamental quantities of interest are the forward and backward quantum yield $\phi_{A\to B}$ and $\phi_{B\to A}$. As we model the complete sample conversion, both of them enter the calculation. Consequently we can also extract not only the forward QY, but also the backward QY from the measurement.

The numerical integration of the equations is fitted to the experimentally determined concentrations with the quantum yields as fit parameters. The measured QY of 0.476 ± 0.024 for ring closing at 300 nm and 0.0179 at 590 nm for ring opening corresponds within the experimental error to those reported by Irie et al. (0.45 ± 0.02 for cyclization at 313 nm and 0.0166 at 590 nm for the cycloreversion process.[22]

It is interesting to note, that Irie and coworkers used a Shimadzu QYM-01, Photoreaction Quantum Yield Evaluation System. It relies on an integral NIST traceable actinometer, indeed a calibrated photocell. Unfortunately, the instrument is not available for Europe and some other countries.[23]

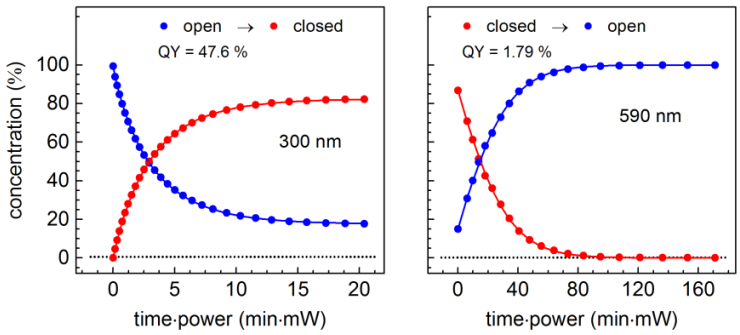

Figure 8. Time evolution of the concentrations during the illumination. A volume of 2 mL of the ring open form was irradiated with 300 nm in a 10 mm cuvette (left). For the cycloreversion process 760 µL at a concentration of 200 µM was illuminated at 590 nm in a 10x4 mm Semi-Micro-cuvette (right).

LED Pulser – A Novel "Rotating Slit" Setup

Free radical chain reactions are one of the most important product pathways in visible-light photoredox catalytic synthesis.[24] A radical chain can make extremely good use of the illumination. In radical-mediated synthetic transformations knowledge about such properties as the radical lifetime and the chain length are of uttermost importance for the understanding and optimization. The former can in principle be measured with transient absorption, the latter is rarely measured due to a lack of suitable experimental protocols. The "rotating sector" (RS) method[25] used to be popular but has lost attention. In RS the light is modulated by a mechanical chopper and the influence of the modulation frequency is analyzed.

A simple extension of the QYDS turns it into a modern version of the RS method which can be easily applied in chemical labs. By an extra electronic circuit (pulse generator), the sample can be irradiated intermittently, which enables us to control the concentration of the free radical generated by light absorption. By combining the measurement with a chemical kinetic model, the intermittent illumination allows to measure the temporal propagation length of the chain.

A schematic diagram of the LED pulser combined with the QYDS is shown in Fig. 9. The pulser is able to generate a well-defined electric

pulse that is gated by a logic signal (pulse input) and whose amplitude is set separately. For the input pulse we use the arbitrary waveform generator (AWG) of the PicoScope. According to the pulse input, the LED pulser establishes the drive current sent to the high power LED in the QYDS. Since different kinds of LEDs have distinct current limits, a current limit is used to prevent damage of the LED. For initial analysis the light pulses are monitored by a ns photodiode (ET-2020, Electro-Optics Technology). The LED light is imaged onto the photodiode with a large aperture aspheric lens. For power measurements the photodiode is replaced by a Coherent USB19Q powermeter head.

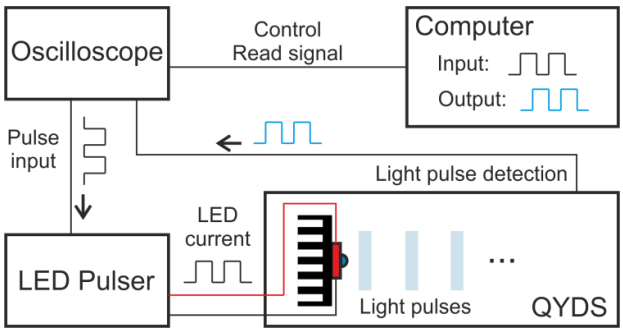

Figure 9. Schematic diagram of the LED light pulse generation.

The characteristics of a representative blue LED (470 nm, Osram) are presented. The pulse repetition frequency is set to 10 kHz. In order to change the pulse duration of the light pulse, the duty cycle of the input pulse is adjusted. The relationship between the light power and drive current of the LED is established, as shown in Fig. 10 and Table 1. The results show that the peak power increases with the increase of the drive current. With 4 A supplied to the LED, the integrated light power is 142 mW and the peak power 1.4 W. The reported peak power is available for spectroscopic experiments in a standard 10x10 mm^2 cuvette in an area that can be made smaller than 2x2 mm^2. Driving high power LEDs with peak currents much higher than the nominal 1 A current limit has been shown before.[8] Within the relevant times of a series of spectroscopic experiments we see no degradation of the LED.

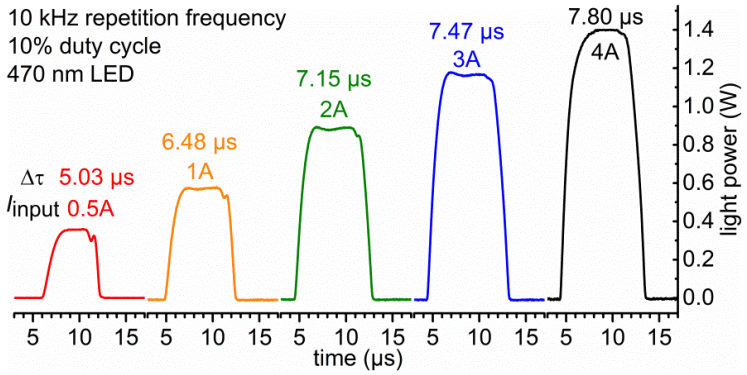

Figure 10. Relationship between the light power and the drive current.

The FWHM light pulse duration is weakly dependent on the drive current (see Table 2). By tweaking the electrical pulse length the desired optical pulse length can be adjusted. Also the rise and fall time of the light pulse are current dependent. Table 2 shows that the pulse rise time drops first and then rises with the increase of the drive current. This is an intricate interplay between the current/voltage curve of the LED and the finite slew rate of the OPA 548 OpAmp used in the pulser.

Table 1. Power of 470 nm LED light pulse generated by different LED drive currents.

Input parameters			Light power [mW]	Peak Power [W]
Pulse frequency	**Duty cycle**	**LED drive current**		
10 kHz	13% electrical 10% optical	1 A	53.4	0.5
		2 A	88.7	0.9
		3 A	117.7	1.2
		4 A	142.3	1.4

The pulse fall time rises more strongly with the increase of the drive current. With 4 A peak current supplied to the LED, the fall time of the light pulse is 3.5 times higher than that with 0.5 A. This slowing of the turn-off is due to the large capacitance of the LED and the resulting "after-glow" when the current is turned off. With just a

transistor used to switch the LED, we see about a 50 µs after-glow. To avoid this, the charge is actively drawn from the LED. By optimizing the electrical input pulse, a light pulse as short as 2.3 µs can be generated. This leads to a maximum frequency for RS of above 100 kHz.

Table 2. Characteristics of 470 nm LED light pulses generated by different LED drive currents.

Pulse frequency	LED drive current [A]	Duty cycle [%]	Pulse rise time [ms]	Pulse fall time [ms]	Pulse duration [ms]
	0.5		1.00	0.33	5.03
	1		0.94	0.50	6.48
10 kHz	2	10	0.90	0.78	7.15
	3		0.95	1.02	7.47
	4		1.07	1.15	7.80

Summary and Outlook

The IUPAC definition of an actinometer is "A chemical system or physical device which determines the number of photons integrally or per unit time."[5] In the first actinometer built by Herschel in 1825[26], an absorbing liquid in a thermometer like geometry was used for the light absorption. The expansion due to the heating was measured in a calibrated fashion. Subsequently other devices like calibrated thermopiles were used, but only available from national laboratories for very few laboratories. Consequently, the chemical actinometers were introduced as secondary standards that were thought to be easily available to chemists and precise.

The need for such a transfer standard has since vanished. Thermopiles far better than the ones used in determining the QYs of the actinometer substances are now commercially available at moderate price. They can regularly be recalibrated to NIST standards. Due to the availability of such detectors there is no longer any requirement to perform an additional spectroscopic measurement only for the determination of the illumination power. The additional evaluation of such data can at best be cumbersome, it might even lead to errors. With high power LEDs, light sources superior to classical lamps - combined with filters or even monochromator - are already in wide use in most laboratories performing photochemistry or

photocatalytic research.[27,28] The combination can readily replace chemical actinometry as shown in this work. The main focus should be on the precise preparation of the sample, the determination of the absorbtivity spectra, and the careful evaluation.

We hope that through this development the efforts in enhanced illumination power in the photocatalytic reactions, as demonstrated in the McMillan photoreactor[29] will be augmented by precise QY determinations. The call of Maschmeyer and Che to establish a device with highly reproducible results independent on experimental boundary conditions, i.e. a setup that will enable direct comparison of photocatalytic performance, can now be fulfilled.[30]

We are quite willing to support the efforts of other groups trying to implement or just use a system built according to the principles outlined above. Hopefully, the widespread use will lead to further validation and dissemination of the principle for the better of photoinitiated chemistry.

Acknowledgements

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Photons and Molecules: Basic Concepts of Photochemistry in Video Tutorials

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Five open access video tutorials concerning photochemistry for science education are presented. They especially address teachers and students, but can also serve for making photochemistry accessible to the general public. The common format of the five tutorials is the dialogue between the young layman Niklas and a young scientist who introduces him to different topics of photochemistry. These topics correspond to three common core concepts chemical education: structure/property-relationships, equilibria, and energy.

Purpose of the video tutorials

Each tutorial focusses on one relevant aspect of photochemistry and presents it in a didactically reduced way. The protagonist, a young layman Niklas, is accompanied on his journey into different areas of photochemistry by laypersons, students, and scientists. The entertaining travels into Niklas' scientific *terra incognita* last approximately five minutes.

The videos have been produced for two main reasons. First of all, teachers can use the tutorials for their science lessons, as many of the discussed photochemical concepts overlap greatly with core concepts within science education syllabi. They can, for example, be used as starting points into an understanding of everyday phenomena, as further research input into scientific fields that have been dealt with before, or as tools with certain gaps which, in turn, can be filled by students' own research projects. Second, there is the entertaining yet scientifically correct presentation of expert knowledge in the field of light-involving chemical processes.

Five video tutorials - generic features

The five tutorials are available on
http://chemiemitlicht.uni-wuppertal.de/en/movies-videos/fascinating-photochemistry.html
https://www.beilstein.tv/categories/Photochemistry/
They cover the following aspects of photochemistry:

- "Light turns ON and OFF: A photoactive molecular switch."
- "What is a photon? Particle-wave duality."
- "Unequal equilibria: Thermodynamic equilibrium vs. photo-steady state."
- "A chemical chameleon: Molecular environment and solvatochromism."
- "Underground miniature golf: Colour by light emission."

All of them follow the same generic pattern: At the beginning of each clip, Niklas, who takes a keen interest in everyday phenomena and who has a comparably great urge to find out the scientific explanations behind them, presents a current everyday phenomenon. In a second step, he embarks on a journey into the world of photochemistry. He is always guided by a peer, a young photochemist from the Wuppertal-Groups of Professors Claudia Bohrmann-Linde and Michael W. Tausch, who takes his questions seriously and who explains the science background of the phenomenon to him. This main part of the clips provides a reasonable theoretical background explanation, some experiments, and a conversation at eye-level. Additionally, energy models, molecular models, animations, and diagrams contribute vitally to the explanation process. Finally, Niklas rounds off the tutorial by establishing a proper frame for the entertaining, yet scientific narrative.

Tutorial 1 – "Light turns ON and OFF: A photoactive molecular switch."

In this clip, Niklas wants to take a look behind the scenes of photochromic glasses. It is Nuno who guides Niklas into the world of *photoactive molecular switches*. He explains to Niklas that - even though there is no photoactive

molecular switch in his glasses - there are photosensitive molecules such as spiropyrane, which change their structure when exposed to light of a certain wavelength. In this case, the colourless spiropyrane probe switches by irradiation with violet light into a coloured probe containing the isomer merocyanine. This process is a reversible one as thermal energy or light of a different wavelength, in this case green light, can switch the merocyanine isomer back into the spiropyrane isomer. Nuno employs an 'intelligent' foil in order to visualize the process: He "draws with nothing but light", as Niklas puts it, turning the embedded molecular switch on, only to turn it off by means of a green light torch, for one thing, and hot water, for another. Furthermore, Nuno uses molecular models of the aforementioned photoactive molecular switch in order to show Niklas what scientists understand by *isomerism* and how this gives rise to a new molecular structure with new properties. Additionally, they talk about how the new shape of molecules brings about a change in the chromophore, resulting in a different light absorption and, consequently, in a different colour of the probe. All of this again leads Niklas to a higher level of understanding.

Switching on the photochromic glasses

Nuno and Niklas in the lab

Corresponding key terminology: photoactive molecular switch, photosensitive molecules, photochromic substances, switching with UV light and green light, drawing with light, 'intelligent' foil, light absorption and perceived colour, isomerism, chromophore, spiropyrane, merocyanine.

Tutorial 2 – "What is a photon? Particle-wave duality."

In the introductory part of this video, Niklas raises the question how photons interact with molecules. He uses the beautiful phenomenon of a rainbow to introduce the viewer to his questions about this topic. Most interestingly, the setting of this video tutorial is not a laboratory, but the *Waldfrieden Sculpture Park Wuppertal*, founded by the renowned British artist Tony Cragg, who uses this location to exhibit his artwork, among them a sculpture called "Photon". Here Niklas meets Claudia, who presents to him the idiosyncratic nature of a photon, that is, a quantum object, which she pragmatically defines as "the smallest indivisible energy package of light." In order to discuss the particle quality of a photon she refers to a reflection experiment. To highlight the fact that a photon also comprises wave properties, Claudia explains the outcome of a diffraction grating experiment to Niklas. A joint visit to the sculpture "Photon" then helps Niklas to apply his newly gained knowledge when he interprets the sculpture, which seemingly combines both *wave and particle properties* in an artistic way. The discussion then centres around what happens when *a photon is absorbed by a molecule*, for example when a spiropyrane molecule is promoted to an excited state. Even though Niklas has now accepted the complex nature of a photon, some questions remain, as it is quite complex to comprehend the properties of these tiny energy packages. Or, as artist Tony Cragg has put it: "The world we see around us is only the tip of the iceberg. How are we supposed to imagine a photon […]? We can only see an object, if light bounces off it and goes into our eye. But we are always attempting to see underneath the surface". It remains to be seen to what extent future technological developments will do away with the last remaining uncertainties and provide both, teachers and students, with satisfactory answers as to what is "underneath the surface".


Niklas and Claudia follow the light: Scientific discussions and the joint interpretation of art

Corresponding key terminology: photon, particle-wave-duality, the nature of a quantum object, artistic interpretation, electronically excited state, ground state, photon absorption.

Tutorial 3 – "Unequal equilibria: Thermodynamic equilibrium *vs.* photo-steady state."

In this clip, the protagonists Niklas and Yasemin elaborate on the idea of a specific equilibrium - the photosteady state. Before exploring the content matter, the idea of different balances in certain everyday situations is brought up by Niklas. "But is there also a *chemical equilibrium that is linked to the presence of light*?" Having raised this question, he seeks help with Yasemin. By means of the spiropyrane-merocyanine-equilibrium from tutorial 2, the two of them carry out a sequence of experiments. First, they irradiate spiropyrane solutions at different temperatures and find out that they all turn from colourless to blue in an equally fast way. However, the hotter the solution, the faster the blue colour fades. Now Niklas wonders why the colour vanishes at all - and why at different rates. Based on the experiments, Yasemin explains the concepts of the two influences affecting the equilibrium to Niklas. The *photo-steady state* is reached when the light-driven reaction that promotes the formation of merocyanine, and the thermal back reaction from merocyanine to spiropyrane occur simultaneously. This is emphasized by a further experiment in which a spiropyrane solution is irradiated at − 16 °C. This answers Niklas´ question. A more detailed explanation of the photo-steady state by an interactive model animation can be found at

http://chemiemitlicht.uni-wuppertal.de/en/models-animations/fluorescence-and-phosphorescence-in-the-energy-level-model.html.

Irradiation of a spiropyrane-solution at −16 °C

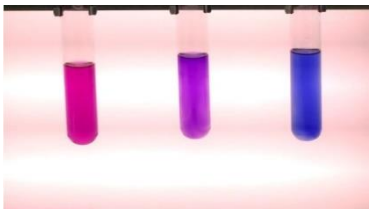
Yasemin and Niklas conducting an experiment.

Corresponding key terminology: ground state, excited state, thermodynamic equilibrium (chemical equilibrium), photo-steady state, spiropyrane, merocyanine, molecular switch, Le Châtelier's principle.

Tutorial 4 – "A chemical chameleon: Molecular environment and solvatochromism."

Here Niklas establishes a bridge between a living animal, a chameleon, which allegedly changes its colour based on its surroundings and a chemical 'chameleon', which does so indeed. It is Sebastian, who sheds some light on this topic by dissolving the compound spiropyrane in *three different solvents*. Having irradiated the three different solutions and switched the colourless spiropyrane into the coloured isomer merocyanine, the two of them now observe three different colors (red, purple, blue). Niklas wonders: "Why's that? I thought you've only put *one kind* of molecule into all of these test tubes?" Sebastian explains the effect of *solvatochromism* to Niklas, using an absorption diagram and an energy level diagram. The same molecule generates differently coloured solutions depending on the surrounding solvent molecules. The solvent molecules´ influence on the energy gaps between the

respective highest occupied energy level and the lowest unoccupied energy level of the merocyanine molecule is responsible. Finally, Niklas has found a scientific answer to his question about the three different colours.

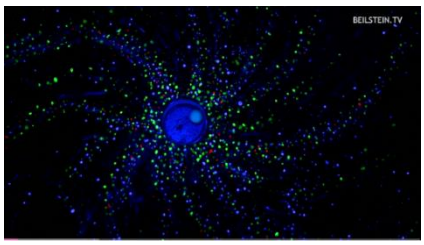


Merocyanine in three different solvents

Sebastian and Niklas discuss the effect of different solvents

Corresponding key terminology: solvatochromism, molecular environment, light absorption and perceived colour, molecular switch, highest occupied energy level (highest occupied molecular orbital HOMO), lowest unoccupied energy level (lowest unoccupied molecular orbital LUMO), spiropyrane, merocyanine.

Tutorial 5 – "Underground miniature golf: Colour by light emission."



The context of this tutorial is an underground miniature golf course. Accordingly, this clip takes its point of origin in Niklas wondering how the light from the dark violet tubes can "create all of these bright colours" that he perceives on a fashionable Wuppertal miniature golf course. In this case, Nico helps Niklas understand the underlying concepts of *fluorescence* and *phosphorescence* by employing a model animation. In connection with a parallel luminescence experiment, the animation comprises detailed explanations concerning the *Stokes Shift* and the additional bathochromic shift by phosphorescence. It becomes evident that the emitted photons are less energetic than the absorbed ones.

However, Nico challenges Niklas' newly-acquired knowledge by showing him in another experiment, how he can turn the aforementioned principle upside down: The cognitive conflict is created by Nico pointing a laser beam on a small snap-on glass containing a seemingly ordinary solution – however, most astonishingly, the *green* of the laser beam turns immediately into a *blue* fluorescent track in the solution. That is, the energy of the emitted photons now contains more energy than the energy of the absorbed photons (*Anti-Stokes Shift*). The experiment is followed by a discussion between Niklas (who, unfortunately, fails with his intelligent guess that the extra energy could stem from a hot solution) and Nico, who uses a didactically reduced energy diagram so Niklas can understand how the blue colour appears.

From green to blue: Anti-Stokes Shift

Nico and Niklas discussing a seemingly illogical experimental observation

Corresponding key terminology: colour by light emission, fluorescence, phosphorescence, invisible UV light, visible light, model animation, ground state, electronically excited state, vibrational states, triplet triplet annihilation, photon down- and upconversion, Stokes Shift, Anti-Stokes Shift.

SUNRISE - Solar Energy for a Circular Economy. A preparation action for a new European Research and Innovation large-scale Initiative in the Energy Area

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SUNRISE Coordination and Support Action

SUNRISE is one of the six Coordination and Support Actions (CSA) selected by the European Commission to address key European challenges.[1] Within the Energy, Environment and Climate Change area, SUNRISE received a €1M grant for one year, starting in March 2019. The action aims at preparing a new scientific and technological large initiative to be potentially supported in the next European research and innovation framework programme, Horizon Europe.[2]

SUNRISE relies on artificial photosynthesis as a sustainable alternative to the fossil based, energy-intensive production of fuels and base chemicals. The energy required will be provided by sunlight and the raw materials will be molecules abundantly available in the atmosphere, such as water, carbon dioxide and nitrogen (H_2O, CO_2 and N_2).

During the one year CSA, the SUNRISE action will focus on three main objectives:

(i) Develop the Science and Technology (S&T) roadmap of a future European large scale research initiative;
(ii) Build the community for carrying out the roadmap including scientific, industrial, policy and general public stakeholders;
(iii) Establish an effective large-project governance scheme.

SUNRISE large-scale initiative: Challenges, Goals and Approaches

Recent IPCC (Intergovernmental Panel on Climate Change) reports[3] underline the need to reduce anthropogenic CO_2 emissions to below zero within 50 years in order to reach the ambitious goals of the 2015 Paris agreement. Technologies enabling such a transition are still in their infancy. Therefore, to reach these ambitious goals large-scale research and development efforts (from the megawatt scale onward) and massive investment are crucial.

Fossil fuels dominate transport and heating, with huge existing infrastructure. The chemical industry, which supplies a variety of indispensable bulk chemicals, is dependent on fossil-based feedstock. Proposing alternative energy carriers and sustainable raw materials is a real game changer for today's energy system and the chemical industry.

The enormous increase of wind and photovoltaic capacity in the EU and worldwide shows that a consolidated alternative to the use of fossil fuels already exists for electricity production.[4] The situation is much less advanced for the conversion of solar energy into fuels and chemicals. Sunlight is a free, widely available and infinite source of energy with the potential to completely replace fossil fuels, as the flux of photons hitting the Earth is far in excess of modern civilization's energy requirements. However, the energy of incoming solar radiation must be harnessed and converted into a storable and transportable form, i.e. storing energy in chemical bonds for the production of solar fuels and solar chemicals.

SUNRISE proposition will contribute to reach a sustainable CO_2 cycle, aiming for a decrease in the concentration of CO_2 that can be then maintained at a level compatible with climate stability. Moreover,

sustainable use of natural resources and land will be key to start the transition **from a linear fossil fuels-based economy towards a solar-powered circular economy**. This strategy is fully aligned with the European Commission plans for the transition to a circular economy[5] and a climate neutral Europe by 2050.[6]

The SUNRISE community is already working to prepare a strategic long-term research roadmap and a consolidated vision of a future large research project, based on the following goals:

- The use of H_2O, CO_2 and N_2, as feedstock to deploy solar energy converters that produce fuels (e.g. CH_4, methanol, ethanol), synthesis gas (CO and H_2), commodity chemicals (e.g. ethylene, ammonia) and high-value chemicals at a groundbreaking level of over 100 ton/ha per year.

- The conversion of up to 2500 ton/ha per year of CO_2, depending on the molecular species and latitude, into the cyclic economic system.

- The enabling of CO_2 reduction in the atmosphere, long-term goal, when direct solar energy converters with a 300% energy gain over the current industrial practice will be deployed worldwide on the tera-watt (TW) scale for a negative-emission Earth system.

SUNRISE will facilitate the transition to a circular economy and a carbon neutral society. Artificial photosynthesis technologies will be developed as part of a large research initiative, based on three approaches:

1 - Electrochemical Conversion with renewable power: photovoltaics (PV) and wind renewable electricity generation technologies have grown fast offering competitive price expectations. SUNRISE will build on the current MW demonstration plants for power-to-hydrogen, power-to-gas and power-to-liquid fuels, analysing bottlenecks and exploring new opportunities, such as the direct electrocatalytic conversion of CO_2 with earth abundant metals. Selected robust technologies will be scaled in a final SUNRISE demonstrator plant flexible to operate with intermittent energy supply.

2 - Direct conversion via integrated artificial photosynthetic systems: SUNRISE aims to develop integrated photoelectrocatalytic arrays to enable disruptive renewable fuel and chemical synthesis from photoexcited states of materials, thus directly driving catalytic transformations. An integrated approach, although more challenging, is potentially more efficient and could lead to higher performance and lower materials and systems costs. SUNRISE aims at optimising and upscaling current artificial devices, at laboratory scale, by engineering semiconductor/catalyst surfaces and improving control of light-harvesting, charge separation, and catalysis between the different components of the devices.

3 - Direct conversion via Biological and Biohybrid systems: photosynthetic microbial cell factories will be designed and tailored with advanced synthetic biology tools to enable high efficiency and selectivity, allowing also growing them on fresh, saline, and wastewaters, thus promoting a circular economy and ensuring a low impact on agriculture and arable land use. In addition, biohybrid systems, relying on human-made solar energy conversion systems

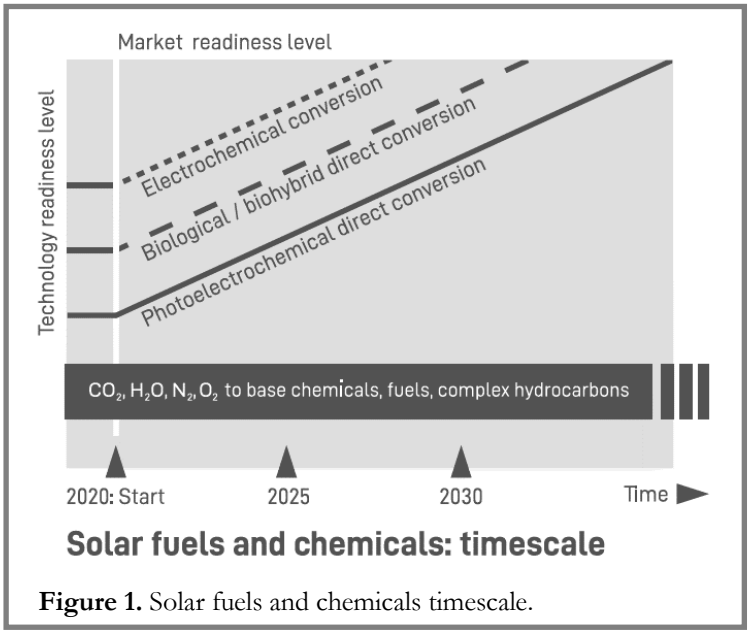

Figure 1. Solar fuels and chemicals timescale.

coupled to non-photosynthetic microorganisms, will be maximized for CO_2 reduction and the production of high-density, complex carbon products, focusing on the construction of optimized interfaces between living systems and materials.

Continuous analysis of research advances, mapping barriers and opportunities will be carried out, as well as exchanges between the three approaches to accelerate process development, taking into account key constraints such as the EROI (Energy Return On Investment)[6] and availability and durability of critical materials. Catalyst and material optimization together with HPC (High-Performance Computing) for multi-scale modelling will be key in the three approaches to lead to enhanced technologies that can be upscaled, achieving also pilot prototypes for approaches 2 and 3.

SUNRISE LARGE RESEARCH INITIATIVE

IN THE SHORT TERM. SUNRISE aims at providing value chemicals using renewable electricity sources and waste CO_2 from industrial processes as raw material for the circular production of chemicals and fuels.

IN THE LONG TERM. Final targets are sustainable high-value products produced by technologies going beyond the natural photosynthesis process, with higher efficiency and a wider selection of target molecules.

THE KEY ENABLERS. Information technology and bottom-up engineering of new advanced materials will enhance this ambitious paradigm shift.

Figure 2. Summary of the goals of the SUNRISE large-scale research initiative

The growing SUNRISE community

SUNRISE is coordinated by Prof. Huub de Groot from Leiden University (the Netherlands) and brings together a multidisciplinary consortium of 20 partners from 13 European countries.

The SUNRISE consortium includes:

- **seven universities**: Leiden University, University of Uppsala, Imperial College London, University of Turku, University of Warsaw, Norwegian University of Science and Technology and Université Catholique de Louvain;
- **eight research centres**: French Alternative Energies and Atomic Energy Commission (CEA), Italian National Research Council (CNR), Swiss Federal Laboratories for Materials Science and Technology (Empa), IMDEA Energy Institute, Fraunhofer Gesellschaft, Forschungszentrum Jülich GmbH, J. Heyrovský Institute of Physical Chemistry and Institute of Chemical Research of Catalonia (ICIQ);
- **two large European associations**: European Energy Research Alliance (EERA), Energy Materials Industrial Research Initiative (EMIRI);
- **three companies**: Siemens AG, Johnson Matthey and ENGIE.

In addition, **SUNRISE action counts with around 200 supporters** including companies from the energy and gas&oil sectors, chemistry and materials sectors and also non-governmental organisations, strategic networks, educational associations, funding bodies, universities and research centres.

Building a strong and actively growing "SUNRISE ecosystem", gathering players from academia, industry, policy-making and society is one of the main aims of the CSA. A multidisciplinary and intersectoral approach will be key to set the basis of a large visionary, science-driven, long-term research project focused on addressing one of the major European societal challenges, the transition towards a non-fossil dependent circular economy, and to turn scientific advances into concrete innovation opportunities, growth and jobs.

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From SFLM (Francophone Society of Medical Lasers) to SFPMed (Francophone Society of Medical Photonics)

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The French Society of Medical Lasers, SFLM, was founded in 1981.Originally, SFLM sets itself the target of promoting and coordinating all actions allowing the development of the use of lasers in medicine. This society which, since the beginning, brought together doctors, scientists and industrialists was able to successfully fulfill the mission that it had set itself, in particular by organizing every year one or more congresses and by writing books, notably "*l'encyclopédie des lasers en Médecine et en Chirurgie*", published in 1995 and chapters in "*Les lasers en Dermatologie*" 2017. The European Interuniversity Diploma of Medical Lasers was created by several founding members of the society, thus contributing to the laser training of many doctors. The SFLM was successively chaired by Prof. Maurice Bruhat✞ (1981-1988), Prof. Jean-Marc Brunetaud (1989-1999), Dr. Frédéric Laffitte✞ (2000-2006), Pr. Bertrand Devaux (2007–-2010) and Prof. Serge Mordon (2011-2018).

Lasers have been used for medical applications shortly after their discovery in the 60's. Their fantastic technological developments, with a large spectrum of sources, wavelengths, emission modes and power levels, expanded their use in many medical and surgical specialties.. Most applications of lasers in medicine are based on photothermal and photochemical laser-tissue interactions. Their main use is in dermatology, with broad applications for skin diseases, hair and tattoo removal, and ophthalmology with retinal photocoagulations and refractive surgery. Lasers are also used for tumors, precancerous and benign lesions removal, in gastro-enterology, pneumology, gynecology, neurosurgery and head & neck surgery. Interstitial therapies using lasers are mainly performed in oncology. Photoablative and mechanical interaction have more limited

applications, in ophthalmology, urology and cardiology. Medical lasers compete today with other devices, including radiofrequency or ultrasonic instruments.

Today, technological developments and the needs of medicine have led us to expand our field of action by adding two new themes in real expansion: PhotoDynamic Therapy (PDT) and Medical Optical Imaging.

Medical optical imaging (acquisition and display of human body images, at various scale) is undergoing rapid growth thanks a huge amount of technological progress, particularly with the advent of optical fibers, lasers, miniaturized cameras, display screens and image processing algorithms. The most outstanding recent achievements include among others: fluorescence imaging, OCT (optical coherent tomography), confocal endomicroscopy, photo-acoustic imaging, polarimetric imaging, Raman spectroscopy, DRS (diffuse reflectance spectroscopy), multiphotonic imaging, DOT (diffuse optical tomography), hyperspectral imaging ...Based on its numerous advantages (selective, non-invasive, cost effective and compactness ...) optical imaging technics have become a major player in the field of medical imaging. Optical biopsy has become a reality in numerous medical fields.

Optical imaging is now a major component of image guided surgery and "theragnostic" development. Augmented reality and deep learning are today's technological advances, which lead and continue to lead to improved images and perceptions.

Photodynamic therapy (PDT) is an effective anticancer treatment modality, which has a long-standing history and a widespread field of application. Basically, three components are needed for PDT: oxygen, photosensitizer and proper wavelength of light. Cells (primarily the rapidly proliferating ones, but tumor stroma cells as well) accumulate the photosensitizer in subcellular organelles, which is then excited by light, resulting in the release of ROS, oxidizing biomolecules, which leads to tissue destruction and elimination of the damaged tissue by apoptosis, necrosis or autophagy. As an indirect effect, PDT induces vascular shutdown by destroying endothelial cells and the vascular basement membrane, resulting in oxygen deprivation. Moreover, acute

local inflammatory and immunological reactions, involving the innate and adaptive immune system, are induced, which contribute not only to control the growth of the primary tumor but also to prevent the development of a second one.

The SFLM has therefore decided to change its name to become in 2019 the French Society of Medical Photonics, SFPMed (www.sfpmed.org, see Figure 1). SFPMed is a non-profit association that brings together academic researchers, medical professionals and manufacturers . It is a place of exchange between these stakeholders who wish to work for the knowledge, the promotion and the evolution of Photonics in the medical field. SFPMed is now chaired by Dr. Céline Frochot.

Figure 1. The "Francophone Society of Medical Photonics" Logo

Its main fields of action are:
- Organization of an annual congress at the beginning of each year,
- Participation to the organization of conferences dedicated to Medical Lasers, Medical Optical Imaging and PDT,
- Creation of a website: www.sfpmed.org, with an agenda of upcoming events (congress, workshop ...), scientific and industrial news, useful links, industry information and reports (reserved for members),
- Information to members via email on a regular basis,
- Active interlocutor with public authorities (HAS, ANSES, ANSM ...) professional authorities (SNITEM, Photonics France, ...) and national or international companies (SFD, SFO, ELA, IPA, GFP2P, SFPB ...).

ABSTRACT OF THESIS ON PHOTOCHEMISTRY

Benchmarking and applications of a computational photobiology tool for design of novel and highly fluorescent rhodopsin proteins

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In recent years, world economy and technological advancement have been transformed by *Genomics*, which allows us to study, design and build biologically relevant molecules. Genomics is already deeply embedded in industries as diverse as pharmaceutical, food and agricultural, environmental and bio-tech in general. Fast and cheap tools for gene sequencing, protein expression and analysis are commonly used for high-throughput genomic-related studies. However, due to experimental difficulties and long time scales (*e.g.*, protein crystallization), protein structure determination, and thus the fundamental structure function rationalization, cannot presently be performed at the same fast pace: a fact that is slowing down the discovery of proteins with new features, as well as *ex novo* design. These difficulties are particularly felt in the field of **photobiology**, where the crystal structure of Bovine rhodopsin (Rh, retina dim-light visual photo-receptor), still remains the only structure of a vertebrate **photo-receptor** sensor available for **photobiological studies** since the year 2000. Rhodopsin proteins constitute a class of light-triggered proteins that can be found throughout the whole spectrum of living organisms, and represent the perfect blue-print for building light-activated bio-molecular machines.

In principle, the problem of not having a sufficient number of rhodopsins molecular structures could be circumvented and overcome with the construction of accurate atomistic computer models of the set of studied photoreceptors, which would allow: (i) *in silico* fundamental structure-function characterization, (ii) thorough and

detailed screening of mutant series, and even (iii) *ex novo* design. Nevertheless, such models should also be constructed using a fast, relatively cheap, reliable and standardized protocol, of known accuracy.

Encouraged with the experimental difficulties presented and the new research topics focused on computational building of rhodopsins models; in my Ph.D. thesis, **I refine and test the Automatic Rhodopsin Modeling (ARM) computational protocol (developed in 2016 by Olivucci's research group at the University of Siena, Italy), which I demonstrate as being capable of helping to address the above issues**. Such protocol has the primary target of generating congruous quantum mechanical/molecular mechanical (QM/MM) models of rhodopsins (Fig. 1a), with the aim of facilitating systematic rhodopsin-mutants studies. The cornerstone of my thesis is the validation of the ARM protocol as a successful attempt to provide a basis for the standardization and reproducibility of rhodopsin QM/MM models, aimed to study the behaviour of **photoactive molecules**.

To begin with, I validate the **ARM protocol,**[1,8] which employs a CASPT2//CASSCF/AMBER scheme, for a benchmark set of rhodopsins from different biological kingdoms (Fig. 1b). We show that ARM is able to reproduce and predict absorption trends in rhodopsin

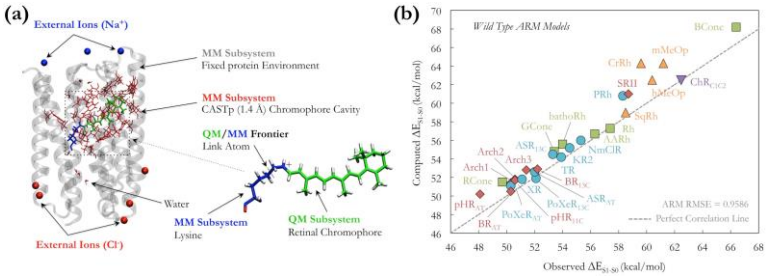

Figure 1. (a) General structure of the QM/MM model constructed using ARM protocol displaying the protein environment in grey with external counterions in blue and red, cavity with residues in red, and Lys-QM system, in green and blue, respectively. (b) Observed -vs- computed values for vertical excitation energies ($\Delta E_{S1\text{-}S0}$) of wild type rhodopsins. Each point represents the average of $\Delta E_{S1\text{-}S0}$ values (N=10). The colours and symbols refer to: vertebrate (green squares), invertebrate and non-visual (orange triangles), *Bacteria* (blue circles), *Archaea* (red diamonds) and *Eukaryotic* (purple inverted triangle).

protein sets, with blue-shifted values not much displaced (a few kcal/mol) from the observed data.[1-3,5-9] This is encouraging when we consider that the set includes evolutionary distant organisms with different physiological functions. We have also shown that a similar level of accuracy is also preserved when the *Bacteria* rhodopsin mutants[2,3,5] trend is predicted. ARM constitutes the first step towards a fast and computational low-cost tool filling the gap between slow experimental structure determination, fast protein expression and characterization achieved by genetic engineering techniques. The standardization of the tool reduces the accidental/user errors during the building of the QM/MM models for **photobiological studies** of rhodopsin proteins, including their vertical excitation energy calculations. It is translates into an improvement of the reproducibility and quickness of the results, with a better control, faster production and a minimization of the manual errors.

Secondly, I present how to get the most out of ARM protocol to prepare effective **Optogenetic tools** for *in vivo* applications to further expand the wild type benchmarking set and to explore the possibility of colour tuning specific microbial rhodopsins through different rounds of mutations. **Optogenetics** is an innovative biological tool aimed to visualize and control neuron signals though light. Another target of an *in silico* mutant screening would be the tuning of the chemical reactivity properties. This thesis reports the first detailed computational study on one aspect of the spectroscopy of *Anabaena* sensory rhodopsin (ASR)[3,5] and *Krokinobacter eikastus* rhodopsin 2 (KR2)[7]: the effect of point mutations on the excited state decay and the isomerization reaction times of mutants. The adopted strategy is to pursue both experimental and theoretical searches together, which would provide a detailed and robust understanding of the mutation effects on the retinal protonated Schiff base (rPSB) protein interactions.

The ground state absorption spectra of ASR mutants, involving amino acid replacements in the chromophore binding pocket, are all blue-shifted with respect to ASR wild type. The quantum chemistry computations show that electrostatic interactions of the pocket residues with rPSB are responsible for the colour tuning in the mutants. The specific biological function of ASR, as a sensor for light-intensity levels, requires differences in the absorption spectra of the ASR isomers (all-*trans* and 13-*cis*) and differences in their isomerization quantum yield, so as to allow for considerable changes of the isomer

content upon light- or dark-adaptation. It will be therefore relevant in the future to determinate experimentally and understand theoretically the effect of the mutations on the ASR reaction quantum yield.

On the other hand, the ground state absorption spectra of KR2 mutants, screened around the beta-ionone ring, are red-shifted with respect to KR2 wild type and the QM/MM simulations demonstrate that the mutations affect the distortion of the retinal chromophore. The modeling suggests that the change in retinal structure contributes to the increase of the energy gap between ground and first excited state. However, the change in the electrostatic protein environment achieved through the dipole changes due to specific mutations makes the energy gap smaller. This implies the rational design of red-shifted proteins by modifying the dipole moments of other residues and/or introducing other types of mutations to recover the retinal planarity. The role of the protein rigidity/flexibility in the colour tuning is not well understood compared to the role of amino acid polarity, and it should be more comprehensively studied in future work.

Lastly, I **explore the fluorescence of ASR mutants**, particularly useful for the **visualization of neuronal activity**. The goal of this work is to use QM/MM simulations to understand the opposite behaviour observed in two blue-shifted ASR mutants (Fig. 2, top), where one presents a negligible fluorescence, while the other displays one order of magnitude enhanced fluorescence, with respect to the wild type protein.[3,5] Our QM/MM models show that specific electrostatic and steric interactions control the character mixing of different electronic states, opening a path to the rational engineering of highly fluorescent rhodopsins.

By exploring the fact that multi-configurational quantum chemistry (MCQC)-based QM/MM models are able to reproduce the observed absorption and emission trends (Fig. 2, bottom) we have used such models for mechanistic studies. Accordingly, as documented above, scans along the reaction path and the corresponding Franck-Condon (FC) trajectories how, consistently, that the observed change in excited state lifetime (ESL) is due to opposite changes in the charge transfer character of the first excited state of the mutants. Namely, an increase in the charge transfer character leads to a shorter ESL. The residue replacements in the two investigated mutants appear to operate via dramatically different effects: single mutation (L83Q) is dominated by an electrostatic effect while the double mutation (W76S/Y179F), which enhanced the fluorescence with respect the wild type, is

controlled by steric effects. These findings point to an undeniable intrinsic complexity of the regulation of a basic spectroscopic property such as light emission. Even if the studied mutations represent a minimal set, the consistence with the experimental data have a direct impact in the **engineering of microbial rhodopsins with enhancement fluorescence**.

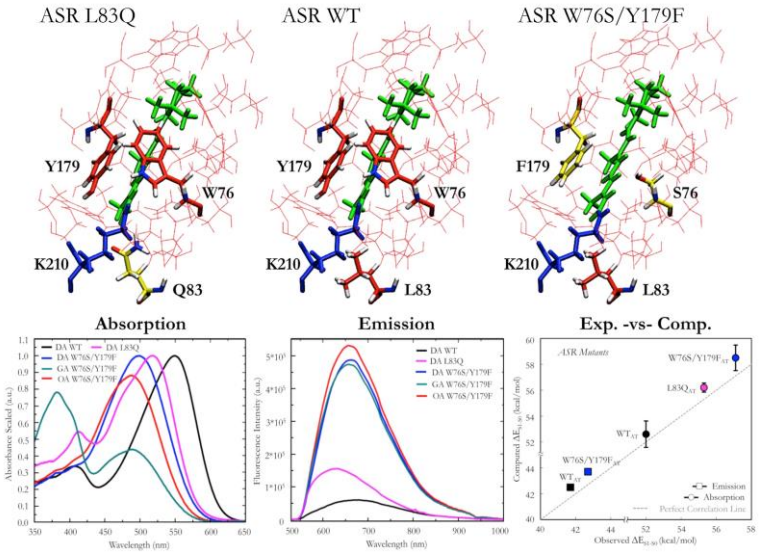

Figure 2. (Top) Cavity residues (red) of all-*trans* ASR ARM models. The variable cavity residues are shown in tube representation (red for WT and yellow for mutants). Retinal chromophore and lysine linker are shown in green blue, respectively. (Bottom) Absorption and emission light- and dark-adapted spectra of WT and its mutants, and comparison of observed and computed vertical excitation energies.

In conclusion, within the limits of its automation, the ARM protocol allows the study of ground and excited states of specific **photoactive proteins: rhodopsins**. This opens the way to an improved molecular-level understanding of rhodopsin **photochemistry** and **photobiology**. The results obtained highlight the importance of having a standardized, effective and automatic protocol, which renders this kind of studies more efficient and accessible, by drastically shortening the time required to produce accurate and congruous QM/MM models. For the above reasons I

believe that ARM stands as an important cogwheel in the virtuous cycle between experimental and theoretical work, aimed to prepare the **photobiological tools** for tomorrow's needs. Future research will be focused on making the ARM protocol more robust on exploring new mutations, making it a fully-fledged predicting tool for production of rhodopsins with enhancement functions, such as fluorescence. If such research line will be proven to be fruitful, our ultimate goal would be the extension of the same methodologies to protein domains other than rhodopsins, with the objective of making it applicable to any protein-chromophore complex, so that ARM could eventually become a general tool in computational photobiology

My Ph.D. was supervised by Prof. Massimo Olivucci. Nine articles from this PhD work has been published in peer scientific journals (5 Journal of Chemical Theory and Computation, 1 Journal of the American Society, 1 Faraday Discussions, 1 Nature Communication and 1 Proceeding of the National Academy of Sciences of the United States of America). The results were disseminated in 12 national and international conferences: 8 posters and 4 oral contributions.

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Photochemistry of 1,3-Dicarbonyl Compounds: DNA Photodamage vs. Photoprotection

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The 1,3-dicarbonyl functional groups are present in a wide range of compounds. Their photochemistry displays interesting features due to the presence of a hydrogen at α position allowing the keto-enol equilibrium to take place and therefore various isomers can exist exhibiting particular spectroscopic properties or photoreactivity [1,2]. In this context, the large UVA absorption of the chelated enol isomer of dibenzoylmethane has been widely used in cosmetic industry for photoprotection purposes. [3, 4 ,5] However, the β-dicarbonyl compounds are also found in the structure of photoreactive thymidine or uridine derivatives bearing a pivaloyl [6, 7, 8] or formyl [9, 10, 11] group at C5 position.

The main goal of this thesis is to contrast the role of these 1,3-dicarbonyl compounds as DNA damaging agents to their photoprotective potential (figure 1). Thus, on the one hand the properties of β-dicarbonyl compounds as part of the DNA structure have been addressed through the study of C5-pivaloyl substituted dihydropyrimidines as photolabile precursors of carbon centered radicals, but also through the assessment of the DNA oxidatively generated damage, 5-formyluracil, as a potential intrinsic DNA photosensitizing agent. On the other hand, the diketo isomer of the most representative UVA filter ie. 4-*tert*-butyl-4'-

methoxydibenzoylmethane, the so-called avobenzone, contains two well-established photoremovable phenacyl groups [13]. This has led to the development of a new strategy for photoprotection based on the photorelease of a photosensitizing topical drug together with this protecting UVA filter.

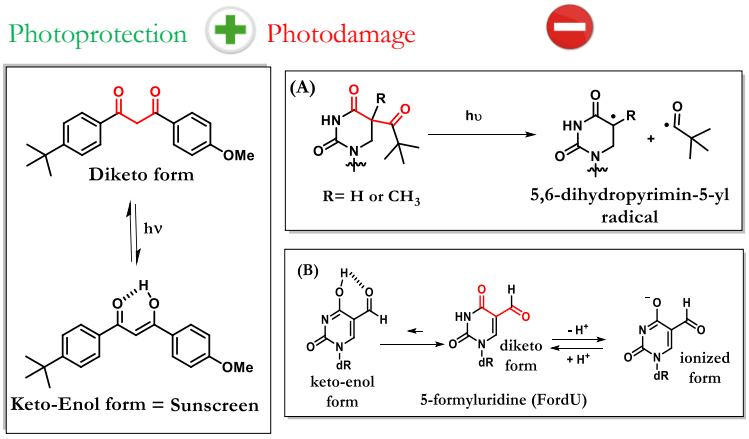

Figure 1. In photoprotection, chelated enol of avobenzone has large UVA absorption properties; which is exploited in this thesis to bring protection to photosensitizing topical drugs. After UV light absorption, an extensive photoisomerization to the β-diketone occurs giving rise to a new band absorption 260-280 nm. In photodamage (A), the photoremovable protecting group (PPG) methodology has been used on pyrimidine nucleobases to perform photophysical and photochemical study of radicals involved in DNA damage. And in (B), the oxidatively generated DNA damage 5-formyl-2'-deoxyuridine (FordU) exhibits higher resonance possibility, meaning a possible extension of the active fraction of sunlight.

Firstly, 5,6-dihydropyrimidines have been derivatized using a *tert*-butyl ketone photolabile group [6, 7, 8] in order to study the generation of C5-centered radicals in non aqueous media. This is of particular importance as the microenvironment provided by DNA structure and its complexes with proteins such as histones may not be fully reproduced by aqueous media, and the pyrimidine-derived radical would be embedded into the complex DNA/RNA system, which constitutes a hetereogeneous environment. Thus, laser flash photolysis study in acetonitrile of the designed 1,3-dicarbonyl derivatives gives

rise to the formation of the purported 5,6-dihydropyrimidin-5-yl radicals. Their photophysical characterization shows long lived transient species, which do not decay in the μs range and are centered at 400-420 nm or 350-400 nm. Moreover, radical generation has also been evidenced by steady state fluorescence experiments by using a profluorescent radical trap [13] (figure 2, AAA-TEMPO). This probe has been especially designed to fulfill principally two requirements: (*i*) be excited at wavelengths higher than 350 nm, where DNA does not absorb and (*ii*) show little if any absorption in the 260-330 nm range in order to not interfere with the absorbance of the *tert*-butyl ketone moiety. Thus, irradiation of the photolabile nucleic acid derivatives in the presence of AAA-TEMPO results in an increased fluorescence emission, in agreement with the trapping of the C5 radical by the paramagnetic probe. Formation of the resulting adduct has been confirmed by UPLC-HMRS. Finally, experimental data have been corroborated with ab initio CASPT2//CASSCF theoretical calculations.

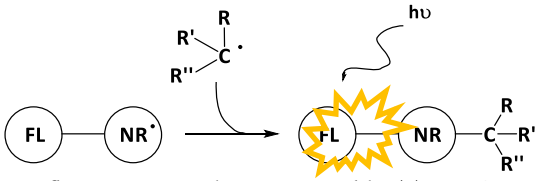

Figure 2. Profluoroscent probe composed by TEMPO paramagnetic specie (NR) which is covalently attached to a fluorophore (FL), 9-anthraceneacetic acid (AAA).

In a second chapter, another 1,3-dicarbonyl derivative of pyrimidine has been investigated. Indeed, the oxidatively generated damage 5-formyluracil (ForU) presents interesting features as a potential intrinsic DNA photosensitizing agent due to the presence of a formyl substituent at C5 position that could affect the distribution and nature of excited states [11] if compared with those of the methyl group of the unaltered thymine. Thus, spectroscopic studies reveal that ForU has not only an absorption in the UVA/UVB range, where canonical bases barely absorb, but also a triplet excited state (^{3}ForU*) with a lifetime of some μs and with an energy high enough to behave as an appropriate energy donor and photosensitize the well-known cyclobutane pyrimidine dimers (CPDs) through triplet-triplet energy transfer (figure 3A). This process has been confirmed by means of the

synthesis of two model Thy-Thy and Cyt-Cyt dyads, which after irradiation in the presence of ForU have demonstrated by HPLC-UV (figure 3B), UPLC-MS and NMR analysis to produce new signals assigned to CPDs with the help of a photochemically synthesized standard. Finally, the study, extended to plasmid DNA combined with gel agarose electrophoresis experiments, allowed establishing the ability of ForU to produce single strand breaks and CPDs by means of the T4 endonuclease V, the enzyme revealing DNA damage in pyrimidinic bases.

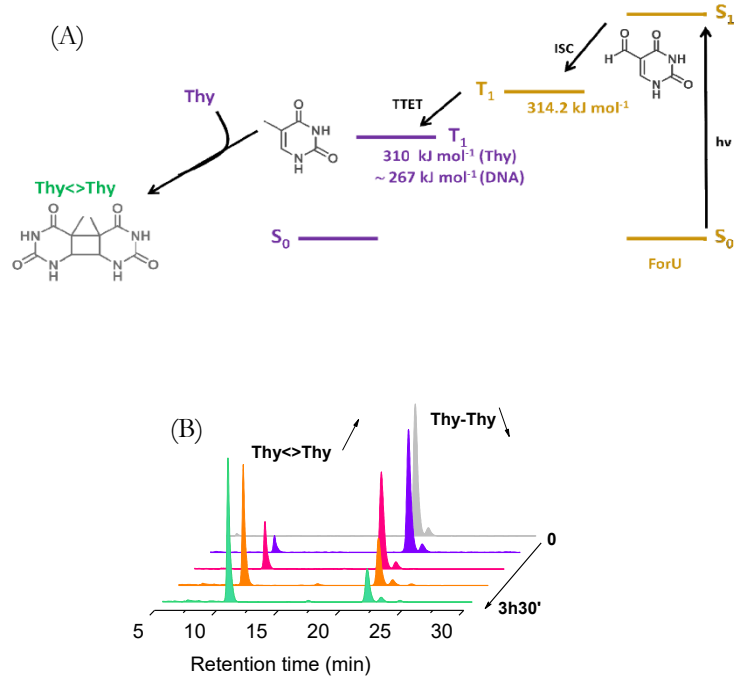

Figure 3. (A) Excitation of ForU and the feasible TTET process to pyrimidine, as for example thymine. (B) Chromatogram of the photosensitized photocycloaddition reaction between Thy-Thy model dyad and ForU as photosensitizer.

Next, the attention has been focused on the development of a new strategy for photoprotection of bioactive molecules taking advantage of the photochemical reactivity of the 1,3-diketo tautomer of the UVA filter avobenzone (AB).[14, 15] The selected bioactive compounds are two

photosensitive topical non steroidal anti-inflammatory drugs, [16, 17] namely (S)-ketoprofen (KP) and diclofenac (DF). In this context, the diketo tautomer of avobenzone contains two phenacyl moieties, which are well-known photoremovable protecting groups.[13] Thus, a judicious design and synthesis of a pro-drug/pro-filter dyad allows the photorelease of the drug and its protecting shield, avobenzone (figure 4). In this context, avobenzone was brominated at α position of the carbonyl groups and subsequently a nucleophilic substitution with the respective drug salt afforded the desired dyads as a diasteomeric or enantiomeric mixture for AB-KP and AB-DF, respectively. The viability of this controlled release of the active ingredients was checked by simulated sunlight irradiation combined with UV-Vis spectrophotometry in different solvents of different H donating properties and viscosity to simulate topical formulation. It appeared that the viability of the photorelease uniquely happened under H donating conditions, being ethanol under anaerobic conditions and propylene glycol and diethylene glycol under aerobic conditions, the solvents that better afforded the photorelease. In addition, laser flash photolysis studies in ethanol allow characterization of a transient absorption band at 400-420 nm assigned to the triplet excited state of the dyad by comparison with that of the diketo form of AB.

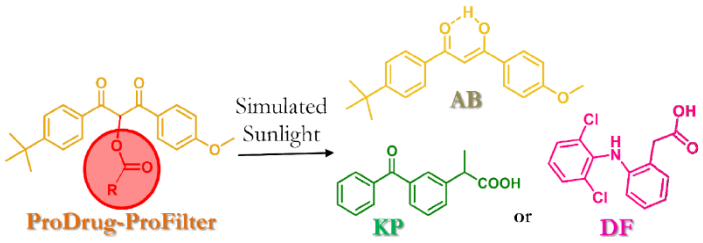

Figure 4. Design of photoactivable dyad containing a drug and a solar filter.

Finally, the photosafety of this pro-drug/pro-filter compound (AB-KP photoactivatable dyad) has been assessed by studying its photosensitizing potential on key biomolecules such as fatty acid, as model of membrane components, [18, 19] or DNA [20] by in chemico and in vitro tests, respectively. An interesting result is obtained from the transient absorption spectra of the AB-KP dyad in cyclohexane where,

by contrast with ethanol, the observed species is the triplet excited state of KP and not that of the AB in its diketo form. This is of paramount importance in terms of phototoxicity and photogenotoxicity in connection with the widely studied photosensitizing properties of KP. The impact on the cellular membrane has been addressed by UVA irradiation of linoleic acid solutions in the presence of the dyad. Phototoxic potential of the dyad has been evidenced by UV-Vis spectrophotometry through the formation of the conjugated dienic hydroperoxides derived from linoleic acid which exhibit a band absorption at 233 nm. However, AB-KP does not exhibit a photogenotoxic potential as demonstrated by comet assay experiments performed with fibroblast epidermis cells, where by contrast with KP, the non damaged round shape of the DNA cell is still observed after UVA irradiation (figure 5).

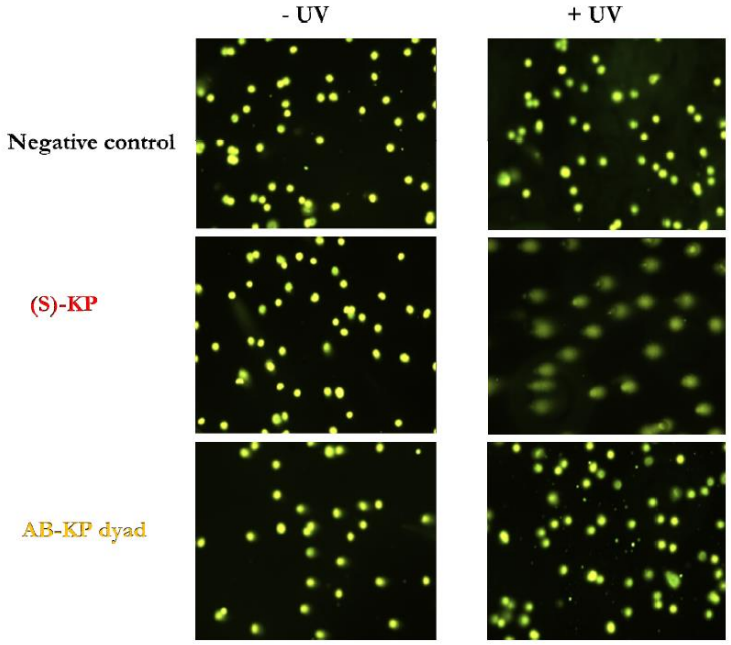

Figure 5. UV-induced direct strand breaks in nuclei of fibroblast detected by comet assay technique.

During the pre-doctoral period I have collaborated in two MINECO projects developing multidisciplinary works in the field of chemistry and biology. Five research works related to my Ph D have been published in prestigious science journals of the photochemistry and chemistry field. I have also collaborated in other international work which brought me the opportunity to publish an extra article in a well-regarded journal. The advances of my research have been presented in three national and international congresses as two poster sessions and one oral communication. In addition to this, chapter number 3 allowed me to be awarded with a national honorific mention by the XII Scientific-technical award of Algemesi town hall.

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Photoredox catalysis for environmental and chemical applications. A mechanistically-based approach.

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Supervisors: Prof. M. L Marin, Prof. M. A. Miranda

In the last decades, photoinduced-redox processes mediated through visible light have obtained great attention due to the generally mild operating conditions that they offer. As a result, they constitute a real alternative within the so-called Advanced Oxidation Processes (AOPs).[1] Besides, they are becoming an outstanding methodology in organic synthesis, which has opened the door to new synthetic and chemical routes. However, despite the growth of the field, little attention has been paid to the mechanistic pathways behind these processes.[2]

This thesis belongs to the field of photochemistry with environmental applications and its main objective was to gain deeper understanding of different photoredox processes carried out using organic photocatalysts. The thesis was divided in three main parts in which different mechanisms of photoinduced-redox processes were analyzed. More specifically, in *Part I,* oxidative electron transfer were studied; in *Part II*, competition between *Type I* and *Type II* mechanisms were analyzed; and finally, in *Part III,* the attention was paid to reductive electron trensfer mechanisms. As a result, the viability of several organic photocatalysts was studied, and besides, a careful mechanistic study, based on time resolved techniques, supported the postulated mechanisms (Fig. 1). With this information, a methodology determining the key points to consider in a photoredox system were established.

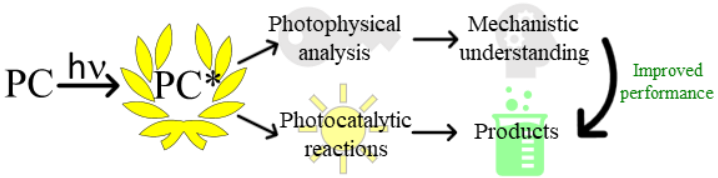

Figure 1: Schematic representation of the methodology.

In the next lines, a summary of each part can be read, including the most interesting results:

Part I: Oxidative electron transfer processes

In this part, two photocatalysts, pyrylium and thiapyrylium salts, which operate through an oxidative electron transfer, have been used with different objectives. In a first study, the viability of the photodegradation of two common pollutants from cork industry, gallic acid (GA) and 2,4,6-trichloroanisole (TCA), and the operating mechanism of the photodegradtion have been evaluated. As a result, both photocatalysts are able to remove GA easily, meanwhile TCA is more reluctant. Regarding to the mechanism, the main species involved in the degradation of GA are the triplets of both photocatalysts, and, in the case of TCA, the formation of ground-state complexes are the only detected species.[3] In the second study of this part, the direct detection of all the TPP^+ derived short-lived intermediates in the photocatalyzed oxidation of a mixture of pollutants using TPP^+ is proposed as a methodology to assess the photodegradation extent. The results point out that the oxidation of the selected pollutants is concomitant with the TPP^+ reduction, therefore with the formation of pyranil radical ($TPP^{\cdot}$). The detection of the reduced species of TPP ($TPP^{\cdot}$) by laser flash phoptolysis is a finger print of the redox nature of the photodegradation process.[4] Finally, in the last study of this Part I, $TPTP^+$ is used to establish the characteristics of an ideal photocatalyst. These characteristics are: i) to absorb in the visible region; ii) to have an appropiate redox potential from its exited states; iii) to have a high intersystem crossing quantum yield; and iv) to have a long triplet excited state lifetime. Besides, the study claimed the influence of the concentration of the target substances in the efficiency of the excited states or, in general, of the key short-lived intermediates.[5]

Part II: Type I vs Type II processes

In Part II, two different studies were carried out. In the fist one, rose bengal (RB), a typical photocatalyst used in wastewater remediation, known for working via Type II mechanism, was evaluated for the removal of two common drugs, acetaminophen and diclofenac. In addition, a second one, perinaphtenone (PN), which gives rise to even a higher singlet oxygen quantum yield than RB, was tested. The results

reveal that triplet excited states of both photocatalysts are efficiently quenched by the pollutants and also by oxygen (forming $^1O_2$) with diffusion-controlled constants. However, $^1O_2$ is inefficently quenched by the pollutants.[6] In the second study of this part, *N*-methylquinolinium (NMQ^+), a non-typical photocatalyst able of generate singlet oxygen from its singlet excited state, was used in the photooxidation of three different chlorinated pollutants. The photophyisical experiments show that in this case, $^1O_2$ is also inefficently quenched by the pollutants.[7] In conclusion, in both studies, the major contribution of Type I *vs* Type II mechanism was demonstrated.

Part III: Reductive electron transfer processes

Finally, in Part III, a study was devoted to the photocatalytic reduction of organic bromides, paying attention to both kintetics and thermodynamics. In this case, riboflavin (RF), a naturally occuring organic dye, was used as a photocatalyst and an amine as electron donnor in order to obtain the reduced species of RF ($RF^{\cdot-}$), which is the species responsible for the halides reduction. Analogously, careful attention was paid to the behavior of the intermediates, as well as to the thermodynamics of the steps involved in the photocatalytic cycle. In this study, time-resolved techniques provide useful data to analyse the kinetic feasibility of the thermodinamically allowed pathways in the photocatalytic reduction of several halides mediated by RF. Besides, the kinetices of the $RF^{\cdot-}$ in the presence of the bromides are in agreement with the themodynamic calculations and demonstrate the key role of this intermediate.[8]

In conclusion, this thesis claims the importance of the knowledge of the mechanistics details in a photoredox process and the employed procedures followed at each part may provide a methodology for futures studies.

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[1] AOPs are a set of chemical procedures in which hardly degradable matter is removed from an effluent through oxidative reactions. Among these procedures, photocatalysis is a widely used one.

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Model Studies on the Photorepair of (6-4) Dimeric Lesions of DNA

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Ultraviolet radiation is associated with the formation of certain lesions in the DNA that are at the origin of skin cancer. Among the most relevant are the damages that occur at pyrimidine bases: the cyclobutane dimers (CPD) and (6-4) photoproducts (6-4) (6-4PP). To obtain protection from DNA photolesions, living organisms have enzymes that restore the lesions to their original form, thus maintaining genetic integrity. In some organisms, CPD and 6-4PP show an additional repair process, which corresponds to photoreactivation and involves enzymes called CPD and (6-4) photolyases. In particular, there is currently a lively discussion about the mechanism of repair by (6-4) photolyase, being a possible hypothesis the formation and cycloreversion of a four-membered ring heterocycle through a photochemically induced electron transfer from the catalytic flavin-adenosine cofactor. Indeed, the study of this process is not straightforward due not only to the ultrashort (some picoseconds) lifetime of the excited flavin of the photolyases but also

to the unstable character of the four-membered ring intermediates. In this context, strategies based on the development of models to mimic the four-membered ring intermediate have to be developed to investigate the electron transfer step responsible for the photocycloreversion. Therefore, the objective of this Doctoral Thesis has been to study the cycloreversion of the proposed intermediate of 6-4PP lesions as a key to support one of the mechanisms proposed so far.

Here, a model of the highly unstable azetidine intermediate, proposed for the repair of 6-4PP at TC sequences, has been synthetized to investigate for the first time both the photoinduced reductive and oxidative process. First, stable azabipyrimidinic azetidine T_m<>$azaU_m$ (Figure 1) was obtained from a photosensitized intramolecular [2+2] cycloaddition reaction between thymine and a blocked imine moiety, the 6-azauracil, connected through a trimethylene bridge.

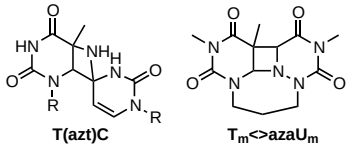

Figure 1. Structure of the azetidine model T_m<>$azaU_m$ studied related to the intermediate T(azt)C involved in the photorepair mechanism of 6-4PP at TC sequences.

Secondly, spectroscopic and photochemical studies showed that the injection or removal of one electron from photosensitizers in the singlet excited state into the azetidine can occur and leads to a clean cycloreversion that "repairs" the nucleobases. Parallel studies of time-resolved fluorescence and cyclic voltammetry on related cyclobutane and azetidine derivatives evidenced that the presence of a nitrogen atom in the four-membered ring does not affect the reduction process; however, it affects the oxidation potential being more favorable the electron transfer for the azetidine compounds than for the related cyclobutane thymine dimer. These findings have also been corroborated by DFT quantum chemistry, which have determined similar electron affinities and different ionization potentials between the azetidine compound and the related cyclobutane thymine dimer. Altogether, the experimental and theoretical findings represent an

important advance in the understanding of photoinduced cycloreversion of azetidines by electron transfer.

Moreover, the study was extended to the ability of the intrinsic photoreductant 8-oxoGuanosine, the main oxidatively generated DNA lesion, to act as an artificial photolyase. First, the photocycloreversion of four-membered model systems bearing an oxetane or a cyclobutane thymine dimer as electron accepting moiety, covalently attached to the photoreductant, were addressed through photochemical and photophysical studies. It has been proved that, after photoexcitation, the oxidized guanine, transfers an electron to the four-membered rings, which induces the splitting of the cyclobutane or oxetane ring and regeneration of 8-oxoGuanosine and thymine bases after a subsequent back electron transfer. Regarding to the efficiency splitting, a more efficient cycloreversion was observed for oxetane than cyclobutane ring, which is in agreement with the quantum yields reported for models where oxetane and cyclobutane are covalently linked to flavin. Interestingly, it was found a more efficiency splitting for 8-oxoGuanosine than for the flavin-systems, which agrees with its higher oxidation potential in the singlet excited state.

Secondly, the photocycloreversion of an azetidine using the photoreductant 8-oxoGuanosine within an oligonucleotide was performed. In this way, the azetidine ring was incorporated for the first time into an oligonucleotide through a photosensitized intramolecular [2+2] photocycloaddition between adjacent thymidine and 6-azauridine nucleotides. Photochemical studies revealed that electron migration is taking place between 8-oxoGuanosine inserted in the opposite strand to the azetidine, splitting the ring and yielding the restored 6-azauracil and thymine original bases. Therefore, it was shown that a DNA lesion, the oxidized guanine, has the capacity to repair another one, imitating the function of the flavin cofactor in (6-4) photolyase mechanism. Finally, the ability of (6-4) and CPD photolyases to recognize the azetidines derived oligonucleotide and achieve its repair is under study at this moment.

To summarize, this Doctoral Thesis has provided solid bases to develop the photochemical, photophysical, photobiological study of the oxidative and reductive photocycloreversion of an azetidine. The synthesized models show interesting characteristics as "mimic" of the unstable intermediates involved in the repair of 6-4PP damage by the

photolyase. This way, it has been established that these heterocycles can be "repaired" by photoreductants with a reduction potential in the excited state close to that of the reduced flavin, the active cofactor of photolyase. Therefore, photolyases must be capable to cyclorevert the azetidine proposed as a potential intermediate during the repair of (6-4) photoproduct at TC sequences. The study of the azetidine model inserted in an oligonucleotide using the real photorepair enzymes should provide more details about this mechanism. Altogether the obtained results are relevant to understand the process involved in of (6-4) photolyase and support the feasibility of the mechanistic pathway involving reductive splitting of an azetidine intermediate.

Smart and Highly Phosphorescent Asterisks for (bio)Sensors, Antennae and Molecular Imaging

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This doctoral work has been carried out in a joint agreement between the University of Bologna and the University of Marseille, under the supervision of Prof. Paola Ceroni and Prof. Marc Gingras
This work focuses on the synthesis and photophysical characterization of sulfurated materials, notably persulfurated molecular asterisks, in order to develop new sensors or new dyes for imaging, based on the Aggregation-Induced Emission (AIE) concept.[1,2]
An increasing attention has been devoted to highly emissive phosphorescent materials. The archetype of persulfurated asterisks is hexakis(p-tolylthio) benzene[3] (Fig. 1). This compound is not emissive in solution, but in the solid state, it is one of the strongest phosphorescent emitter with a phosphorescence quantum yield close to 100%.

The primary objective of this thesis was to synthesize some asterisk derivatives bearing carboxylic acids at their periphery to increase solubility in water and to exploit their ability to selectively coordinate metal ions in aqueous solution. (Fig. 2).

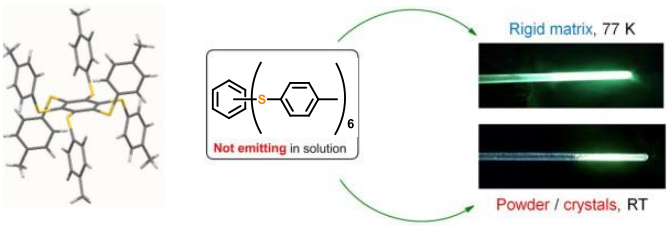

Figure 1. Structure of hexakis(p-tolylthio) benzene and emission in solid state or rigid matrix (MeOH/DCM 1:1) at 77 K.

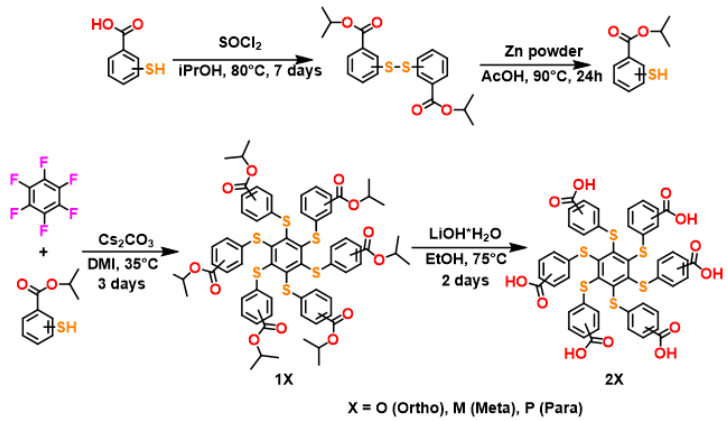

Figure 2. General synthetic scheme of carboxylic esters 1O (ortho-isomer), 1P (para-isomer), 1M (meta-isomer) and the corresponding acid isomers 2O, 2P and 2M.

Like all members of this family,[4] the hexacarboxylated asterisks are not emissive in solution, but are phosphorescent in the solid state or in a rigid matrix at 77 K, with a green-yellow emission. In the solid state, the meta (**2M**) and para isomers (**2P**) have a comparable phosphorescence quantum yield (0.10), while the ortho isomer (**2O**) has a much lower quantum yield. These hexacarboxylated asterisks were dissolved in basic aqueous solution and titrated with Pb(II) ions. A phosphorescence band identical to that obtained in the solid state was observed, with a maximum at 555 nm for the para isomer, and at 580 nm for the ortho isomer. The emission reaches a plateau at about three equivalents of Pb(II) ions per molecule. The addition of alkali,

alkaline earth and transition metal cations demonstrates good discrimination of the para isomer between the different ions, with phosphorescence appearance by selective complexation of Pb(II) and Cd(II) ions. (Fig. 3) with a detection limit as low as 6.0 x 10-7 M.[5]

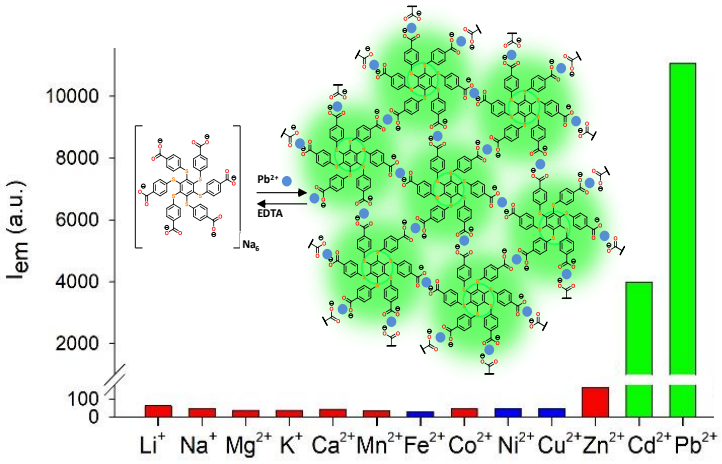

Figure 3. Relative phosphorescence quantum yields of **2P** in aqueous solution at pH=8 upon addition of different metal ions. Colored bars indicate: no strong complexation (red), complexation and luminescence quenching (blue), complexation and phosphorescence enhancement (green).

The second part of the thesis deals with the encapsulation of the carboxylated asterisks (**2P**) inside silica nanoparticles (NPs) capped with PEG chains,[6,7] to rigidify the structure and thus, to turn on the phosphorescence. These new phosphorescent silica NPs could then be tested for biological applications using two-photon excitation microscopy. The absorption spectra are similar to the original compounds and a phosphorescence emission with a quantum yield of 0.07 appears with a lifetime of 15 µs in an aerated solution. In the absence of oxygen, the lifetime time increases to 39 µs and the quantum yield to 0.17. The Stern-Volmer graph indicates that this system behaves like an oxygen sensor. In addition, the phosphorescence is observed also upon two-photon excitation at 700 nm. These new phosphorescent NPs can then be considered as oxygen sensors for two-photon excitation microscopy in a biological medium.

The last part of the thesis deals with the synthesis and the characterization of a thiospherulene (**BF0**), a polysulfurated and phosphorescent molecular ball, assimilated to a polysulfurated and chiral cyclophane. The structure was confirmed by X-ray diffraction of a monocrystal.

BF0 is phosphorescent in solution with a quantum yield of 0.10. In deoxygenated solution, phosphorescence increases by a factor of four with a quantum yield of 0.42 and a lifetime of 9.8 µs. Oxygen, thus quench the phosphorescence of **BF0** and the quenching constant by dioxygen is 3.1×10^7 $M^{-1}s^{-1}$
Compound **BF0** has a cavity between its two central benzene rings and its ability to encapsulate 2,5-dichloro-1,4-quinone was evaluated by a Stern-Volmer titration. The deactivation constant is 2×10^9 $M^{-1}s^{-1}$, a value close to the solvent diffusion constant. This result means that deactivation is dynamic, and there is no insertion inside the thiospherulene.

In conclusion we synthetized new families of persulfurated compounds and studied their AIE process for an application as sensor for metal ions or dioxygen in solution.

Acknowledgements
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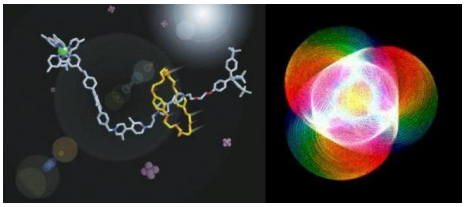

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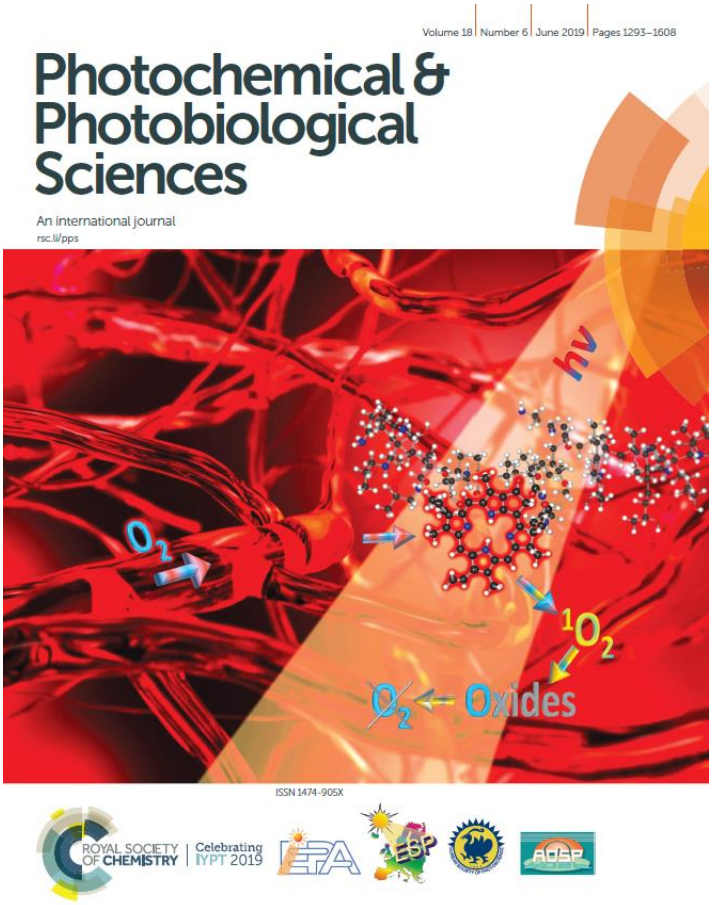

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