Current Developments in Fluorescent PET (Photoinduced Electron Transfer) Sensors and Switches


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Following a brief introduction to the principle of fluorescent PET (photoinduced electron transfer) sensors and switches, the outputs of laboratories in various countries from the past year or two are categorized and critically discussed. Emphasis is placed on the molecular design and the experimental outcomes in terms of target-induced fluorescence enhancements and input/output wavelengths. The handling of single targets takes up a major fraction of the review, but the extension to multiple targets is also illustrated. Conceptually new channels of investigation are opened up by the latter approach, e.g. ‘lab-on-a-molecule’ systems and molecular keypad locks. The growing trends of theoretically-fortified design and intracellular engineering design and of its visual appeal. After all, Weller decades ago, we were convinced of its semi-quantitative difficulties.

1. Introduction

When we established the generality of the fluorescent PET (Photoinduced Electron Transfer) sensor/switch principle three decades ago, we were convinced of its semi-quantitative engineering design and of its visual appeal.1–3 After all, Weller had given us a strong thermodynamics basis for the intermolecular PET process since the 1960’s. He had also recognized the competition between fluorescence and PET for the deactivation of the excited state.4,5 The kinetic aspects had received Marcus’ crucial input.5,6 So our role had been to apply the competition scenario twice under intramolecular conditions - once when the sensor/switch was devoid of the analyte/target species and once again when the latter was present – so that the fluorescence signal would alter between the two situations. Such a change in a fluorescence signal would be easily observable by people, with or without instrumental augmentation. However, it would have been foolhardy in the 1980’s to predict the wide and sustained uptake of the principle by laboratories worldwide that we see today (Figure 1).5–9 The circumstances of the early days has been reported in two reviews.10,11

Figure 1a and 1b. Approximate world maps of sources of fluorescent PET sensors and switches aimed at single targets. Only the names of corresponding authors from the literature are given.

The week goes by without a fluorescent PET sensor being reported’ was our observation in 2009,11 and the situation is no different in 2014. Indeed, 59 references from 2014 are specifically cited in this review, with a substantial fraction coming in for detailed
discussion, subject to space limitations. Of course, older references are cited in strength, so that the historical threads are
fully exposed, theoretical foundations are suitably developed, and adequate contexts are set out from the viewpoint of our
experience in establishing the generality of the field.

Binary possibilities arose from instances where the fluorescence signal change was large enough to be considered as
‘off-on’ or ‘on-off’. These took on added significance in a world which was increasingly conscious of information technology.
Thus, molecular information processors became possible in 1993.12 Although a myriad ways became available for molecules
to be interrogated like semiconductor devices, the fluorescent PET sensor/switch principle provided the first approach and still
remains a very profitable avenue.13-18

In this review, we concentrate on fluorescent PET sensors and
switches which have appeared during the last year or so, while
offering some context from the past. The emphasis of this review
is on small-molecule sensors.

2. The fluorescent PET sensor/switch principle
It might be prudent to give a brief summary of the principle at the
outset. In its commonest manifestation, a fluorophore is weakly
coupled electronically with a receptor so that the two modules
quantitatively maintain their individual properties in the
photochemistry and supramolecular chemistry spheres. The two
modules are chosen so that the excited fluorophore has sufficient
energy to transfer an electron, say, from the receptor to the
fluorophore. This means that the excited state energy is larger
than the sum of the moduli of the oxidation and reduction potentials of the receptor and fluorophore respectively. If the
experimental redox potentials are unavailable, modern quantum
chemistry software can supply adequate estimates of the energies
of the frontier orbitals of the two modules, and these can do the
job almost as well. When the analyte/target species was bound to
the receptor module, the oxidation potential would be
significantly increased,19 so that the PET process fails and
fluorescence re-asserts itself.

While electrochemical experiments and frontier orbital energy
calculations are very useful as design tools, experimental proof of
fluorescent PET sensor/switch behaviour requires the observation
of radical ion species following fast laser photolysis. While
Weller provided such evidence in intermolecular PET,4
intramolecular PET sensor/switch systems have been studied
rarely.20,21 The laboratories of McClenaghan and Jonusauskas
join forces to provide a timely example 1.22 A broad absorption
between 520 and 570 nm, which corresponds to the previously
known radical anion band of the borodipyromethene (BODIPY)
fluorophore, appears and decays within 1 ns in THF solution. The
radical cation of the receptor also appears, though less
unequivocally, at 330 nm. The radical ions recombine at longer
times to produce the fluorophore’s triplet excited state. A very
fast PET rate of 3.3x10^{11} s^{-1} could be calculated under these
conditions.

3. Proton targets
It is apt that protons represent the first target to consider. Their
binding to appropriate receptors (Bronsted bases) is less complex
than those of larger ions. Also, their role near membranes22,23 in
bioenergetics is disproportionately important24 given their small
size.

A first-generation dendron containing a tertiary amine is
employed as a receptor by Bojnow’s team within 2.25 When
excited at 302 nm, the emission at 397 nm shows a H+-induced
fluorescence enhancement (FEH+) of 7.6 with an associated pKa
of 9.5. Research on related naphthalimide fluorophores is
available.27 Interestingly, transition metal ions do not interfere
significantly with 2’s performance perhaps because they would
be held rather distant from the fluorophore.

Emission in the redder regions of the spectrum is preferred for
intracellular studies, owing to less scattering and better
penetration. Sun, Ge and co-workers provide an easily
synthesized example 3,28 where x-ray crystallographic proof is
available for the substantial rotation of the plane of the aniline
ring with respect to the xanthene tricycle. Thus, PET across a
virtual spacer from the aniline to the xanthene fluorophore
becomes feasible, especially because the calculated HOMO of the
aniline lies higher in energy than the HOMO of the xanthene.
Thus, excitation of an electron from the xanthene HOMO would
leave a vacancy into which another electron can be transferred
from the aniline HOMO. Protonation of the aniline removes this
PET process and indeed, the fluorescence at 592 nm gives FEH+=
400 (pKa = 4.7) when excited at 535 nm. Many other cell
determinants do not interfere and acidic lysosomal regions of
HeLa cells show up nicely in fluorescence microscopic
experiments.

We return to the blue region where sensor 4 responds in an
‘on-off’ (or NOT logical) manner to H+, following protonation of
one pyrimidine and the diethylamino group. The second
pyrimidine, which is nearby, does not protonate owing to
electrostatic considerations.1H nmr evidence is offered for this
double protonation. An H+-induced blue shift of 70 nm in the
ultraviolet spectrum is also suggestive. Frontier orbital energy
calculations show that, upon protonation of the diethylamino
group, the fluorophore HOMO falls in energy below the HOMO
of the unprotonated pyrimidine ring. Thus PET can occur from
the protonated pyrimidine to the protonated aminocoumarin.
The fluorescence at 460 nm indicates FEH+= 0.025 (pKa = 2.1)
when excited at 385 nm. E. Coli grown in media as acidic as pH
6.0 shows appropriately weak fluorescence from 4 within.

4. Alkali and alkaline earth ion targets
The next logical step would be to consider light metal ions. Since
the McClenaghan-Jonusauskas case12 carries the famous Tsien
receptor for Ca^{2+}, it is no wonder that a FE_{Ca^{2+}} value of 122
(log_{10} FE_{Ca^{2+}} = 6.3) is found by monitoring the fluorescence at 514
nm while exciting at 475 nm. As is the trend these days, frontier
orbital energy calculations produce the appropriate HOMO
energy ordering, i.e. the HOMO energy of the receptor lies higher
in energy than the HOMO of the fluorophore.

K+ is the target for a strong team assembled by Holdt.29 They
construct 5, which interestingly shares the diethylaminocoumarin
motif with 4.29 However, this unit is clicked onto a
phenylazacrown receptor and results in an excellent selectivity for the target over several potential interferents like Na⁺ and H⁺ at their normal intracellular levels. This is a very positive result for such a simple receptor and therefore it is not surprising that sensor 5 succeeds inside NRK cells. The fluorescence at 493 nm gives F_EK⁺ = 3.0 (LogβK⁺ = 1.5) when excited at 420 nm, due to K⁺-induced arrest of PET across the virtual spacer.

K⁺ was also the target, though not so selectively, for our very old work with 6. This work, along with that of Desvergné, Bouas-Laurent and Lehn32 launched fluorescent PET sensors and switches as an important branch of supramolecular chemistry. Now, Wang and co-workers33 support the outcome of Madhu and Ravikanth’s earlier studies.46 and the emission disappears again. The final outcome is probably due to electronic energy transfer (EET) from the fluorophore to the Cu²⁺ centre, if we go by the conclusions of earlier studies.47

Zn²⁺-induced arrest of PET from an amine to the quinoline fluorophore is responsible for the fluorescence of 11 at 382 nm giving a F_EZn²⁺ of 34 (LogβZn²⁺ = 4.5) when excited at 311 nm in MeCN.48 Importantly, Cd²⁺ has virtually no effect. However, the receptor property of the quinoline fluorophore is responsible for the ICT (internal charge transfer) aspects of the sensor behaviour, e.g. Zn²⁺-induced changes in the absorption spectrum. The bispicolylamine moiety hiding within 11 also needs to be highlighted.

12 due to Yang’s team, including He and Chen,49 is a careful modification of Gunnlaugsson’s previous Zn²⁺ sensor,50 where attention is paid to parameters such as wet storage which only hardened industrialists would realize. The fluorescence at 550 nm, when excited at 470 nm, gives F_EZn²⁺ = 50 (LogβZn²⁺ = 4.6). The glutamate side chain aids cell permeability in its diester form and later in its dicarboxylate form, helps retention in the cytosol of HeLa cells. Gunnlaugsson’s design components of the aminonaphthalimide fluorophore, the N-phenyliminodiacetate receptor and the PET switching mechanism itself are maintained.

Though equipped with only pyridyl and alcohol units as potential receptors, the fluorescence of 13 at 375 nm gives F_EZn²⁺ = 0.06 (LogβZn²⁺ = 3.2) when excited at 272 nm in water, with PET and/or EET from the fluorophore to the bound Fe³⁺ being responsible. Like Ihmels’ sensing of DNA-bound Hg²⁺,52 Zeng et al measure Ag⁺ near DNA with 14.53 14’s fluorescence at 590 nm, when excited at 455 nm, gives F_EAg⁺ = 28 (LogβAg⁺ = 4.6). Like Finney’s 8,37 the PET donor of 14 is based on sulfur. The polyamionic nature of DNA concentrates Ag⁺ in 14’s vicinity. Although, the intercalation of cationic 14 within DNA suppresses rotation around the styryl alkene linkage, the drop of fluorescence intensity indicates that PET is accelerated at this stage.

6. Anion targets

This review would be lacking unless some reports on anion targets are considered from the past year. Like 1,27 75 and 9,41 Madhu and Ravikanth’s 15 focuses on the BODIPY fluorophore. However, 15 has an appended benzimidazole which engages in N-H…F hydrogen bonding with the two fluorines on the boron centre. X-ray crystallography shows that this hydrogen bonding also leads to planarization of the entire structure (except the two fluorines). There is a large F⁻-induced alteration in the absorption spectrum which causes a pink-to-blue colour change. The fluorescence at 592 nm in MeCN, when excited at 550 nm, gives F_EF⁻ = 0.11 (LogβF⁻ = 6.4, 1.2 15-F⁻), though the absorbance changes need to be borne in mind. The F⁻-induced
fluorescence quenching is caused by deprotonation of the benzimidazole so that the latter anionic unit can rotate out of the BODIPY plane. Now PET can take place from the benzimidazole anion to the BODIPY unit. The HF side-product picks up an additional F\textsuperscript{-} to give FHF\textsuperscript{-}. Addition of H\textsuperscript{+} reverses the above effects.

A similar PET process from a deprotonated receptor to a BODIPY fluorophore is implicated in the case of \textsuperscript{16} due to Rurack and coworkers.\textsuperscript{55} In this case, F\textsuperscript{-}-induced deprotonation of a N-(4-nitrophenyl)thiourea is involved. The fluorescence of \textsuperscript{16} at 513 nm gives F\textsubscript{E0cl\textsuperscript{-}} = 0.47 (LogF\textsubscript{E0cl\textsuperscript{-}} = 4.7) when excited at 482 nm in 1:1, DMSO:water at pH 6.8. Test strips containing \textsuperscript{16} can be used to measure F\textsuperscript{-} in lateral-flow readers, which augurs well for the future. Older F\textsuperscript{-} sensors which share some structural features and operate in mixed aqueous solution are known.\textsuperscript{56,57}

7. Reactive oxygen targets

The fluorescent PET sensor/switch principle can also be applied in the form of fluorescent PET reagents when the target reacts irreversibly as in the case of various thiols.\textsuperscript{68-63} Some of these improve selectivity towards cases like glutathione versus simpler thiols by cleverly employing AND logic involving connected chemical inputs.\textsuperscript{64} However, we choose to focus on reactive oxygen species (ROS) at this time.\textsuperscript{65-68} Hypochlorite oxidizes the aminophenoxy unit to a quinoneimine and leaves a naphthalimide with a carbamate in the 3-position which emits at 460 nm when excited at 340 nm (F\textsubscript{E0cl\textsuperscript{-}} = 71). This partly decarboxylates to yield a 3-aminonaphthalimide which emits at 570 nm (F\textsubscript{E0cl\textsuperscript{-}} = 63). Only the 460 nm component of this dual emission is found when peroxyxinitrite is the ROS. Other ROS like hydrogen peroxide produce no emission at all. Even 7x10\textsuperscript{-4} M hypochlorite can be detected in this way, even inside HeLa cells.

Kim and Kim’s \textsuperscript{18} is non-fluorescent because of PET from the catechol moiety to the BODIPY unit.\textsuperscript{64} Hypochlorite oxidizes the catechol unit to a o-quinone. Apparently, the possible PET to the latter group from the BODIPY unit does not occur. Though further analysis of this issue would be welcome, the experimental upshot is a rather selective F\textsubscript{E0cl\textsuperscript{-}} value of 80 with a limit of detection of 3x10\textsuperscript{-7} M.

8. Physicochemical property targets

A consortium of Xu, Cui, Qian, Spring and colleagues\textsuperscript{20} exploit the fl axing rotatory motion inherent in the generation of twisted intramolecular charge transfer (TICT) excited states\textsuperscript{21} and the configuration-dependent PET to develop the viscosity sensor \textsuperscript{19} and apply it to intracellular microscopy studies. Fluorescence intensity and lifetime are both put to use. Nice viscosity maps with organelle-level resolution are produced. The thermodynamics of TICT states\textsuperscript{22} and PET processes\textsuperscript{23} are very similar since a radical ion pair is produced in each case, though there are subtle differences in a sensor context.\textsuperscript{73} Structurally, \textsuperscript{19} contains two fluorophores - aminonaphthalimide and anthracene - and an electron donor aniline. The latter shows no metal binding ability and displays a pK\textsubscript{a} value of 3.1. So, protonation-based interference would not be expected even in some of the most acidic regions, i.e. lysosomes with pH values around 5. However, a word of caution would be advised here since organelle membranes can easily concentrate H\textsuperscript{+} at nanometric distances near them by several orders of magnitude, thus encroaching on \textsuperscript{19}'s pK\textsubscript{a} value of 3.1. Such effects are known from model membrane studies.\textsuperscript{23,24} Classical optical microscopy images would not be able to resolve such effects. The presence of two fluorophores leads to electronic energy transfer (EET) effects too, and almost exactly this pair has been studied in a ratiometric PET/EET-based pH sensor context before.\textsuperscript{74} The presence of the anthracene emission serves as an internal reference for the viscosity-dependent emission of the aminonaphthalimide moiety.

As seen in other PET sensors,\textsuperscript{75,76} the fluorescence of \textsuperscript{19} has a substantial polarity effect, i.e. the total quantum yield goes from 0.004 in water to 0.14 in toluene, though the viscosity effect is clearly present too, as seen in the corresponding value of 0.36 in glycerol. Therefore, another word of caution would be that organelle membranes can have polarities at least as low as toluene, so that nanoenvironments nearby (which are unresolvable by conventional optics) would cause switching ‘on’ at any available aminonaphthalimide emission. Indeed, such polarity-related interference has led to the failure of rather hydrophobic pH sensors to operate correctly inside cells, by remaining switched ‘on’ at whatever pH value.\textsuperscript{77}

An aniline electron donor is also found in Tsien’s PET sensor \textsuperscript{20} for membrane potential\textsuperscript{78,79} in live cells. The relatively large fluorescence intensity response shown by \textsuperscript{20} when cells are depolarized allows it to produce images of membrane potential with submicrometer and microsecond resolution. Thus it forms a nice complement to classical electrophysiology. \textsuperscript{20} positions itself in cell membranes owing to its hydrocarbon chains and general hydrophobicity. The oligoalkene section acts as a molecular wire to facilitate the PET process.\textsuperscript{80} However, the hydrophilic ionized fluorescein fluorophore sticks out into the aqueous environment. Because of its depth of penetration of the membrane, \textsuperscript{20} can respond to the electric field caused by a large fraction of the membrane potential. Molecular-scale electric fields are known to control PET rates very strongly.\textsuperscript{81}

9. Multiple targets

Given the molecular engineering backdrop to the fluorescent PET sensor/switch principle, chemical emulation of physical devices was an associated discipline from the early days. While logic devices receive a lot of airtime,\textsuperscript{16} some attention has to be given to their components. The triode,\textsuperscript{82} which is one of those, is a three-electrode assembly where the input to one electrode influences the output from another. We arrange something similar by using a ‘fluorophore-spacer-receptor-spacer:-receptor’ system \textsuperscript{21,83} where receptor\textsubscript{1} and receptor\textsubscript{2} target H\textsuperscript{+} and Na\textsuperscript{+} respectively. However, only receptor\textsubscript{1} is PET-active. The upshot is that a sigmoidal fluorescence intensity – pH profile is tuned by altering Na\textsuperscript{+} concentration. Electrostatic repulsion between the receptor-bound H\textsuperscript{+} and receptor-bound Na\textsuperscript{+} is responsible for this tuning by influencing the pK\textsubscript{a} value of the sensor. It is only fair to note that Gust, Moore, Moore and their colleagues published an all-photic triode emulsion in 2010.\textsuperscript{84} AND logic gate \textsuperscript{22,85} due to Farrugia and Magri, contains an
amine moiety to interact with H+ and a ferrocene moiety to respond to redox inputs. Both moieties are PET-active and fluorescence is weakened as a result. Arrest of both these PET pathways by the provision of H+ and an oxidizing equivalent leads to switching ‘on’ of fluorescence. However there is a residual PET process from the fluorophore to the ferricinium moiety (in the oxidized form of 22), which puts an upper limit on the FEH+-redox value. 22 is logically extended to 23 by Margulis and his colleagues. They do it by the addition of a PET-active benzocrown ether receptor to interact with Na+ inputs. A H+, redox, Na+-driven AND gate is the result, which would become a ‘lab-on-a-molecule’ for direct detection of some cancers which possess elevated H+, Na+ and free iron.

The original approach to a ‘lab-on-a-molecule’ exploited a small set of selective receptors which communicated intramolecularly with a fluorophore, which then provided a binary readout to a human observer. At least conceptually, this approach can be modified to contain a set of relatively nonselective receptors, e.g. phenylboronic acids to tackle a set of sugar-based drugs. In compensation, a set of fluorophores can be built into the supermolecule so that the fluorescence intensities at several wavelengths serve as readouts. The intensity patterns can be chemometrically analyzed for further sharpening of the results so that the drugs become distinguishable with confidence. Margulis’ 24 is the first successful case of this kind, showing that several of the imaginable pitfalls due to the complexity of the structures do not arise. Though the design is broad enough to embrace multiple photochemical mechanisms, PET remains at its heart since several arylmethylamine 25 units are present within 24. The binding of sugar-based drugs to aminomethyl-phenylboronic receptors will then affect fluorescence intensities at a primary level. An internal charge transfer (ICT) mechanism 26 also affects fluorescence intensities at some wavelengths at a primary level due to the presence of a fluorophore with push-pull groups. Electronic energy transfer (EET) between the different fluorophores serves to modulate the fluorescence intensity pattern at a second level.

As found in several cases within section 5, the bispicolylamine moiety also stars within Akkaya’s 25 where PET is arranged to occur from the bispicolylamine unit to the BODIPY fluorophore. However, the special feature of this work is that Zn2+ is supplied to 25 by a photo-uncaging procedure. 26 Zn2+ is held within the ‘cage’ of 26 and is only released when a 360 nm light dose decomposes 26 to 27 and N-methylpicolylamine. The mechanism here is a rather classical bit of organic photochemistry. The nπ* triplet excited state of the nitroaryl unit causes an intramolecular hydrogen abstraction via a six-membered ring intermediate. This work has the wider vision of physically integrating molecular logic gates by using metal ions as the linker species. In this context, the 360 nm light dose is input. The powerful general complexant EDTA is input. Since EDTA would swallow up any Zn2+ to prevent the fluorescence activation of 25, it serves as a disabling input. Thus 26 is a light dose; EDTA-driven INHIBIT (EDTA) gate where EDTA is the disabling input. Its output of Zn2+ then feeds the YES logic gate 25 whose own output is its fluorescence. Similar physical concatenation of logic gates aided by H+ was known previously. 94, 95

Molecular keypad locks 96 are interesting examples of logical molecules which are history-dependent, i.e. the output signal value depends on the order of addition of the inputs. One way of arranging this history-dependence is to exploit multivalent interactions so that the full disconnection of complexed species becomes sluggish. Then, several kinetically stable states may appear for a given system. Being replete with aminomethyl-phenylboronic acids, Margulis’ 24, 97, 98 can engage in such multivalent interactions with inputs chosen from a set of many sugars as well as the catechol derivative 28. Thus it can also serve as a molecular keypad lock with new features which are more reminiscent of semiconductor-based counterparts. One of these new features is that inputs can be repeated to result in passwords such as 333. In the present instance, this means that the intensity pattern obtained by reading at several wavelengths (following chemometric analysis, if necessary) is dependent on the input species concentration, i.e. when the latter is doubled or trebled. Another of these new features is that multiple passwords can be declared as being valid to open the lock. Of course, this requires a separate definition of ‘open’ and ‘closed’ states, which is best done from a Boolean standpoint. 10

10. Conclusions and perspectives for future research

The work surveyed above reveals several trends. One of these is that many fluorescent PET sensor/switch laboratories are augmenting their research with frontier orbital energy calculations conducted through general software. This move to appreciate the physicochemical design aspects is to be applauded, especially because the fluorescent PET sensor/switch principle started off as an exercise in molecular engineering. 3 Dedicated papers on calculations are also being published, 99, 100 so that additional insights can be gained. Another of these trends is that a large fraction of the publications are including intracellular evaluations. This move to be involved in the physiological application aspects is important because fluorescent PET sensors are tools. Tools are meant to be used so that they shed light on cellular processes involving the analytes. Tsien’s pioneering work along this line remains inspirational. 101 Just as fluorescent PET sensors are being associated with cells, they can also be anchored on polymer particles of various kinds. 102, 103 Though there is no room for detailed discussion, we cite additional references to the fluorescent PET sensing/switching literature from 2014, 105-138 where a few cases concerning mechanisms which closely related to PET are also included.
As noted in the previous paragraph, Tsien’s work\textsuperscript{101} still has much to guide future developments in the field of fluorescent PET sensors and switches. For instance, he showed how real-time fluorescence PET sensors/switches. It is clear that the fluorescent PET sensors and switches. For instance, he showed how real-time fluorescence sensing studies in real time. Currently, most studies are reporting single fluorescence micrographs in the presence of the target species. If these can be extended to a set of images in time sequence as the cell goes about its business, the value of the results will be greatly enhanced. During this process, challenges with respect to sensor photostability, sensor survival in the face of cellular processes and calibration of target species concentrations will need to be faced.

Further exploitation of fluorescent PET sensors and switches in the future will also benefit if they can operate deeper within tissue. Such multi-cell monitoring can produce important information about cell-cell communication. Two-photon fluorescence versions of fluorescent PET sensors should be able to achieve this by employing red or near-infra red photons for excitation. Once the excited state is produced, the usual PET criteria and arguments would apply. It is a delight to note that sensor photostability, sensor survival in the face of cell-cell communication and other advantages of such sensors/switches will prove attractive to those who want their information about cell-cell communication to be useful to others.

It is our hope that this review will provide added impetus to research on fluorescence PET sensors/switches. It is clear that the examples published very recently which caught our attention, and which formed the bulk of this review, cover a broad range of targets. This breadth will draw new adherents. When coupled with the continuing commercial success of fluorescent PET sensors for blood electrolytes and gases,\textsuperscript{38,39} it is also clear that this general field will prove attractive to those who want their science to be useful to others.

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Notes and references

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**Table of Contents Graphic**

**Table of Contents Entry**
Fluorophores can be combined with receptors according to a molecular engineering design to yield fluorescent sensing and switching devices.

**Group photograph**

**Biography**
The authors came to study for their PhD at Queen’s University Belfast, Northern Ireland, from places as far apart as Zhenjiang, Belfast and Colombo. Besides the chemistry day jobs, Brian (left) brings up his two daughters, Jue (centre) plays basketball and AP (right) plays percussion with an Irish traditional band.