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The Analyst

Recent Evolution of Luminescent Photoinduced Electron Transfer Sensors*

A Review

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The photoactive supermolecule 'lumophore–spacer–receptor' is shown to be capable of considerable tuning and growth to satisfy the requirements of a versatile sensing system.

Keywords: *Luminescence; fluorescence; sensors; switches; photoinduced electron transfer; supramolecular photophysics*

Modularity brings multiple advantages to any functional system. While this truth has been appreciated by engineers for many decades, chemical designers are only beginning to exploit the possibilities that arise. We and others find that the field of chemical sensing can be considerably enriched by designing molecules which combine lumophores and receptors in a modular fashion.[1–7] Since this paper in intended to review the results from our laboratory, we apologize to those in other laboratories who have produced much good work and we hope to redress the balance on a separate occasion.

The photonic signalling of a host–guest recognition event can be easily arranged by coupling a receptor to a lumophore. However, the supramolecular nature of the system can be best preserved by interposing a spacer between the original units.[8,9] Then, the components or modules, each with its characteristic attributes, are clearly recognizable. If the components were completely isolated, the system would be unable to transduce the guest recognition event into a photonic signal. Hence we need a lumophore–receptor interaction which can transcend the spacer. Photoinduced electron transfer (PET) fits the bill admirably since it is an enduringly long-range process.[10,11] PET brings with it another appealing property, straightforward thermodynamic planning with excited state energies and redox potentials.[12] Kinetic analyses are also possible.[13,14] Our design relies on the fact that the redox potentials of a receptor module would be significantly perturbed on binding a guest, especially if the guest was ionic, whereas the excited state energy and the redox potentials of the lumophore module would be much less affected. Hence the PET thermodynamics can be arranged to switch from favourable to unfavourable (or *vice versa*) on guest binding. Emission from the lumophore is a constant competitor with PET as a means of excited state deactivation. Hence guest binding can cause switching of luminescence between 'off' and 'on' states.

This simple sensor design has proved to be reliable for two decades.[15–17] In ideal cases (of which there are several[18–25]), the UV/VIS absorption spectra remain virtually untouched by the guest, as do the emission spectra except for their quantum yield. The experimental guest binding isotherm can be quantitatively predicted from conventional mass action and from the binding constant of the receptor module. Failure to meet these high standards is usually due to lumophore–receptor interactions (other than PET) crossing the spacer.[26–29] Nevertheless, even these systems are perfectly useful for practical sensing purposes. Lumophore modules with excitation wavelengths from ultraviolet to green and emission wavelengths from violet to orange have been incorporated into PET sensors. Receptor modules targeting protons (pH), calcium, magnesium, sodium, phosphate and glucose in concentration ranges of physiological relevance have also seen service in PET sensing systems. The schematic design and two examples are shown in Fig. 1. The thermodynamic planning for sensor **2** proceeds as follows.[25] *N,N*-Dimethyl-2-anisidine has an oxidation potential of 0.82 V (*versus* SCE). This can serve as a model for the metal ion-free receptor module of **2** as far as one-electron oxidation is concerned. The oxidation potential of the lumophore module of **2** can be estimated from model rhodamine dyes as 1.44 V. Therefore, the photoexcited lumophore will receive an electron from the receptor with a thermodynamic driving force of about −0.62 eV (a spontaneous process). On the other hand, the Ca^{2+}-bound receptor module of **2** can be estimated to have an oxidation potential of about 1.76 V, which corresponds to a thermodynamic driving force of about +0.32 eV (a non-spontaneous process) for PET in Ca^{2+}-bound **2**.

Electron transfer is naturally subject to control by electric fields. The sensitivity of receptor redox potential to ionic guests, so necessary for the success of PET sensing, is an aspect of this

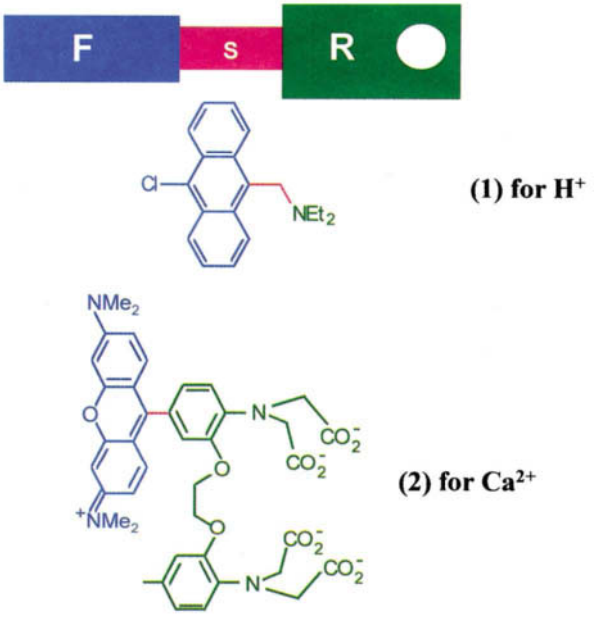

Fig. 1 Design and realization of fluorescent PET sensors. F = Fluorophore; S = spacer; R = receptor. Note that the two adjacent π-electron systems lie perpendicular to each other about the σ-bond shown in red for structure **2**.

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general truth. However, this also means that any photoinduced electric fields, such as those found in internal charge transfer (ICT) excited states of push–pull fluorophores, can seriously interfere with the simple thermodynamic planning of PET sensing, which remains innocent of such transient effects. Such interference can be either constructive or destructive, depending on whether the local electric field accelerates or retards the transiting electron. Hence one regioisomer, *e.g.*, **3**, can be a well behaved PET pH sensor, whereas the other, *e.g.*, **4** is not (Fig. 2). While this can be taken as a note of caution to sensor designers keen on mining the rich seam of push–pull fluorophores,[27] this also allows us to mimic some aspects of the unidirectionality of PET seen in the photosynthetic reaction centre[30] with much simpler supermolecules.[28]

Although the sharp 'on–off' switching of luminescence induced by the guest without any other spectral effects is ideal for chemical sensing under well defined conditions in the laboratory, more technical uses in hospitals or inside living cells require some method of internal referencing. Current sensors for use in these fields achieve such internal referencing either by ratioing intensity signals at two wavelengths, for systems that show guest-induced spectral wavelength shifts,[31] or by using emission lifetime rather than steady-state intensity as the sensory channel.[32–35] In wavelength ratioing, one population of sensor molecules (say, guest-bound) can be imagined to be serving as internal reference for the other population of guest-free sensors. We have recently shown how an internal referencing module can be 'added on' to the basic PET sensing scheme.[36] This system is distinguished by the fact that internal referencing is achieved at the level of single molecule rather than a large population. Hence, these systems are true single molecule devices which are ready for the challenges of molecular information handling in the future.[37] Fig. 3 outlines such a case (**5**) for pH sensing where one fluorophore (anthracene) is chosen to be PET active with the amine receptor whereas the second fluorophore (3-aminonaphthalimide) is chosen to be weakly PET active at best. When the anthracene module is preferentially excited, emission is observed from anthracene and 3-aminonaphthalimide in clearly distinguishable spectral regions. The former emission is sharply switched off at basic pH while maintaining the anthracene band shape. In complete contrast, the 3-aminonaphthalimide band shows a much smaller pH effect. This band serves as an internal reference for the anthracene emission sensory signal and wavelength ratioing is easily achieved. The fact that the sensory and the reference signals can be accumulated over very wide wavelength bands is appealing. As a bonus, these triad systems allow an insight into electronic energy transfer (EET) across intervening electron pairs which can be ionically switched in or out of the EET path.

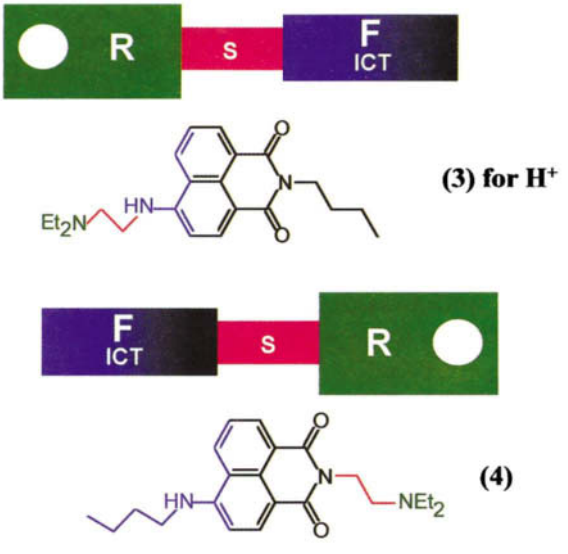

Fig. 2 Regiocontrol in fluorescent PET sensors. F(ICT) = Push–pull fluorophore with internal charge transfer excited state. Note that the two cases employ different connectivities to the fluorophore.

As mentioned above, emission lifetimes can also be used for sensing when internal referencing is desired. Of course, such methods become more convenient if the lifetimes are significantly longer than nanoseconds. Sensors with long lifetimes can bring out another and more important advantage with regard to medical or biological contexts. The presence of matrix autofluorescence and light scattering can contribute substantially to the background noise associated with the fluorescence signal from the sensor. If the sensory emission is long-lived, the sensor signal can be time-resolved out from the background noise (Fig. 4). While we have previously achieved this goal with 'message in a bottle' sensing systems utilizing organic phosphorescence,[38] we have also examined lanthanide lumophores as PET sensors components, especially because of their superior insensitivity to molecular oxygen. We modified a known luminescent label[39] by building-in tertiary amine receptors for protons (**6**).[40] The luminescence emission features due to the complexed terbium ion are switched on by a factor of 16 as protonation of the amine receptors takes place. Most important, the lifetime of the metal luminescence in acidic solution is 0.16 ms. In general, systems such as **6** will raise interesting issues regarding the initial reduction site during PET and the competition between EET and PET.

Most molecular sensors target one chemical species or one environmental property. However, there are situations of

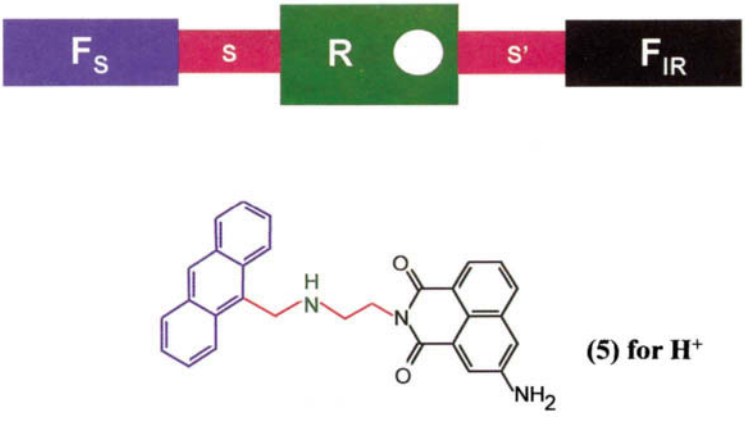

Fig. 3 Internally referenced sensing. F_S = Sensory fluorophore; F_{IR} = internal reference fluorophore.

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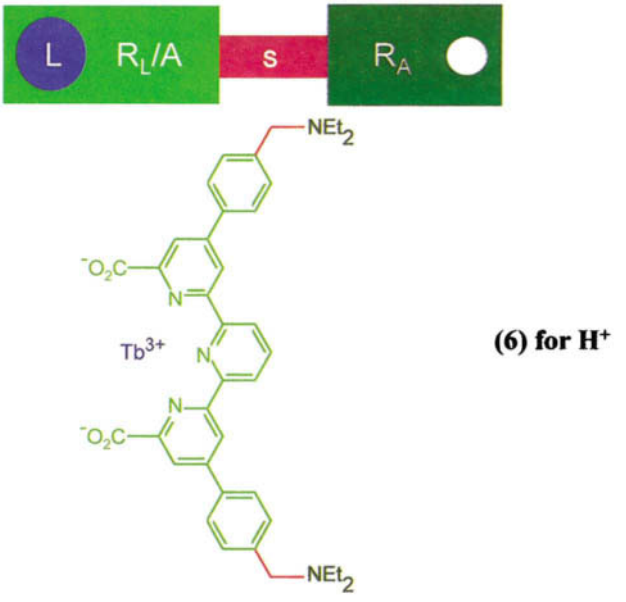
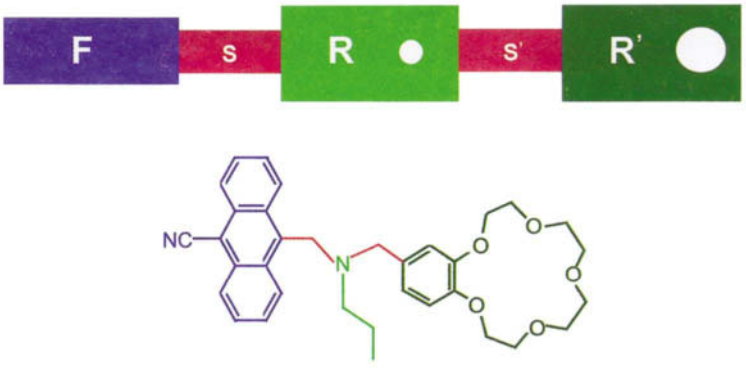


Fig. 4 Time-resolved sensing. L = Lanthanide ion lumophore; R_L/A = receptor for lumophore which also serves as a photon antenna; R_A = receptor for analyte guest.

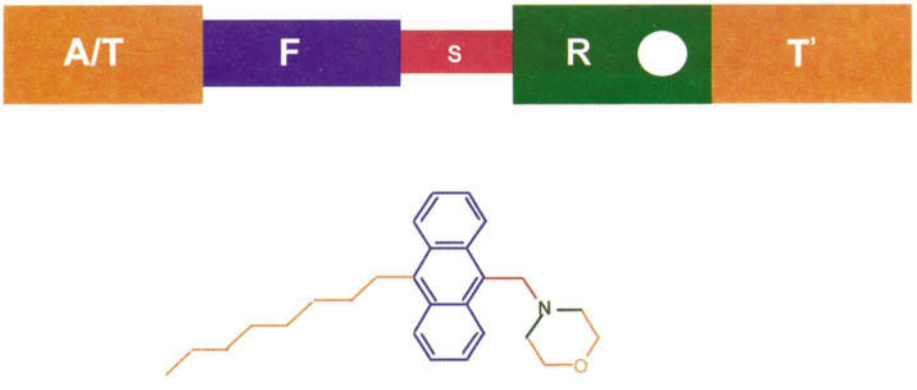
interest which involve two species coincident in space–time, *e.g.*, an enzyme and its cofactor are both required before a substrate can be processed. While two sensors separately targeted to each chemical species can deliver the necessary information, it is more elegant if a single sensor can perform the same task. Also, the use of a single sensor eliminates any registration difficulties possible in the two-sensor experiment, *i.e.*, the accurate overlapping of the data from each sensor for a given point in space–time. Such difficulties can be particularly serious when molecular-scale microenvironments are being addressed. If a PET-active receptor selective to a second guest is added on to the basic PET sensor as shown in Fig. 5, we can develop the idea of coincidence sensing. Radiation physicists have used the related method of coincidence counting for many years. In the chemical arena, we have examined the related but distinct idea of two separate spectral parameters.[41,42] Case **7** requires the simultaneous presence of protons and sodium ions at sufficient concentration in its locality before a fluorescence signal is generated. Although such systems are important as molecular AND logic gates[43] for future information processors,[37] we must not lose sight of their more immediate applications as coincidence sensors; **7** would give a direct visual indication of regions where both protons and sodium ions congregate.

To round off this short review, we draw attention to the possibilities raised by truly molecular sensor systems. With their subnanometre spatial resolution, molecular sensors can



(7) for coincident H^+ and Na^+

Fig. 5 Coincidence sensing. Note that the two receptors R and R′ have mutually exclusive selectivity characteristics towards incoming guest species.



(8) for H^+ near membranes

Fig. 6 Targeted sensing. A/T = Anchoring and targeting unit; T′ = targeting unit for fine positioning of receptor.

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penetrate to the very heart of biological action. When we fit transport modules to the basic PET scheme (Fig. 6), we can drive the sensor to a microlocation. On parking there we can receive space-selected information. For instance, **8** can be anchored in a membrane while its receptor module samples the membrane-bounded protons in the manner of a submarine periscope.[44] Different regions near the membrane can be examined by structurally tuning the hydrophobicities of the targeting modules. These systems can aid studies in bio-energetics where protons gradients near membranes are all-important.

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