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Conjugated Amplifying Polymers for Optical Sensing Applications

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ABSTRACT

Thanks to their unique optical and electrochemical properties, conjugated polymers have attracted considerable attention over the last two decades and resulted in numerous technological innovations. In particular, their implementation in sensing schemes and devices was widely investigated and produced a multitude of sensory systems and transduction mechanisms. Conjugated polymers possess numerous attractive features that make them particularly suitable for a broad variety of sensing tasks. They display sensory signal amplification (compared to their small-molecule counterparts) and their structures can easily be tailored to adjust solubility, absorption/emission wavelengths, energy offsets for excited state electron transfer, and/or for use in solution or in the solid state. This versatility has made conjugated polymers a fluorescence sensory platform of choice in the recent years. In this review we highlight a variety of conjugated polymer-based sensory mechanisms together with selected examples from the recent literature.

INTRODUCTION

The delocalized electronic structures of conjugated polymers confer on them attractive optical and electrochemical properties. In particular, the large extinction coefficients as well as the highly emissive properties provide great advantages for sensing applications. Indeed, the property that makes conjugated polymers a material of choice for chemical sensing is their ability to translate a binding (or unbinding) event into an easily measurable optical or electrochemical response. As a consequence of their conjugated nature, they display highly efficient intra- and interchain energy transfer. Specifically, when compared to small molecule sensors, conjugated polymers exhibit large signal amplification resulting from the collective response of many conjugated units. In optical transduction, the signal amplification is related to excited state (exciton) transport along a polymer backbone in solution, and to additional inter-polymer transport in aggregates or in thin films. The capture of the mobile (diffusing) exciton by the presence of an analyte is detected as changes in the fluorescence spectrum. The analyte can also promote color changes in the material, however direct absorbance changes do not benefit from the signal gain provided by exciton transport. Some sensing schemes allow the naked-eye detection of analytes by observing the sensory materials in visible (color change) or black (UV) light (fluorescence change). The synthesis of conjugated materials has been extensively studied and established methods (e.g. Sonogashira, Stille, or Suzuki couplings, or Gilch polymerization) can reliably produce functionalized materials in sufficiently high purity and yields. The present state of the field allows for the design of a diversity of polymers that can be tailored for different applications. For example, water solubility can be achieved by appending ionic and/or poly(ethylene)glycol side-chains, and sterically demanding groups such as iptycenes can give rise to optimal emission in the solid state, as will be demonstrated later. Using established design principles, the electronic properties can also be varied to match specific applications. An illustration of this is that most

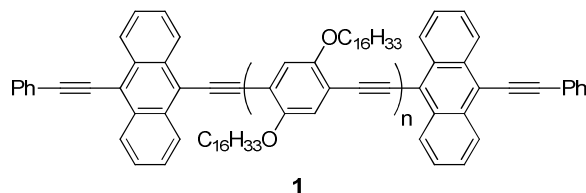
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3 conjugated polymers can be considered to have low electron affinities (electron-rich) and are
4 highly effective for the detection of electron-deficient analytes such as nitro-aromatic
5 explosives. However, it is possible to invert this axiom and produce electron-deficient
6 polymers that display strong sensory responses to electron-rich bioanalytes. Likewise,
7 complementary charges can play a role and polymer electrolytes that are highly positively
8 charged are effective in the sensing of polyanionic bioanalytes such as DNA. In summary,
9 tailor-made conjugated polymers are readily accessible, and the field is poised to
10 functionalize them with more sophisticated receptors for the development of selective
11 sensory schemes.
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24 In the first part of this review we describe the fundamentals of energy migration and a
25 selection of seminal articles. Then, we cover a series of analytes that have been investigated
26 by our laboratory, and by others. In particular, we mention sensory polymers for small,
27 electron-deficient molecules, as well as compounds designed for the detection of electron-
28 rich bioanalytes. We conclude by showing sensing assays for biomolecules such as DNA, or
29 for monitoring the activity of enzymes such as proteases. In order to keep this article to a
30 reasonable length and scope, we have mainly focused on selected key studies related to the
31 various mentioned analytes and sensing mechanisms, and on recent reports that have been
32 published since a previous comprehensive review of the field.¹
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45 ENERGY MIGRATION & AMPLIFICATION EFFECT

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48 Excited state (or exciton) migration along conjugated polymer chains to well-defined emissive
49 traps was initially investigated in photophysical studies of rigid-rod, soluble poly(*p*-
50 phenyleneethynylene)s (PPEs).² Specifically, upon excitation of anthracene-end-capped
51 poly(*p*-phenyleneethynylene) **1**, the resulting light emission originated predominantly (>
52 95%) from the anthracene end-groups. This observation was attributed to fast exciton
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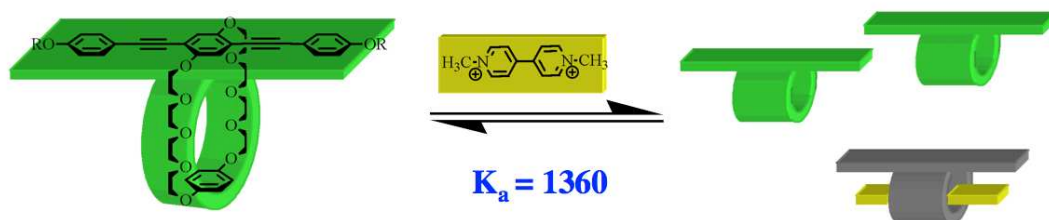
(electron-hole pair) transfer to the decreased band gaps (trapping sites) at the polymer's extremities. This antenna effect afforded by exciton migration within and between conjugated polymers is of primary importance to all of the emission-based sensing applications reviewed herein, and to applications that have been abundantly reviewed elsewhere, such as polymer-based organic solar cells,³⁻⁷ field-effect transistors,^{3, 8-9} and electroluminescent devices.¹⁰⁻¹¹



This energy migration facilitated by the π system of a conjugated polymer was subsequently shown to be the basis of signal amplification or superquenching phenomena, where a minority interaction between the polymer and another molecule (analyte) dominates the emission. This concept was demonstrated in poly(*p*-phenyleneethynylene)s adorned with cyclophane receptors (**2**) for paraquat (PQ^{2+}), a well-known electron transfer quenching agent (Figure 1).¹²⁻¹³ These studies focused on single isolated polymers in solution and carefully deconvoluted the role of binding and exciton transport as a function of the length of the polymer chains. These studies revealed that the exciton could diffuse over 65 receptors (130 -Ph-CC- units) and thereby produced a 65-fold amplification in sensitivity as compared to an equivalent single-receptor fluorescent molecule. In other words, for polymers isolated in solution that are up to 130 phenylene ethynylene units long, the binding of a single PQ^{2+} is sufficient to quench the emission of an entire polymer chain. This measurement also stands as perhaps one of the most direct measurements of the exciton diffusion length in these polymers. The finite nature of this diffusion length is clearly revealed by the fact that increasing the molecular weight beyond 130 phenylene ethynylene units does not provide an additional increase in efficiency, and is attributed to the finite excited state lifetime (≈ 0.6 ns),

the inefficient nature of one-dimensional diffusion processes and the conformational disorder in solution.

Monomeric Chemosensor: Sensitivity determined by the equilibrium constant



Receptor Wired in Series: Amplification due to a collective system response

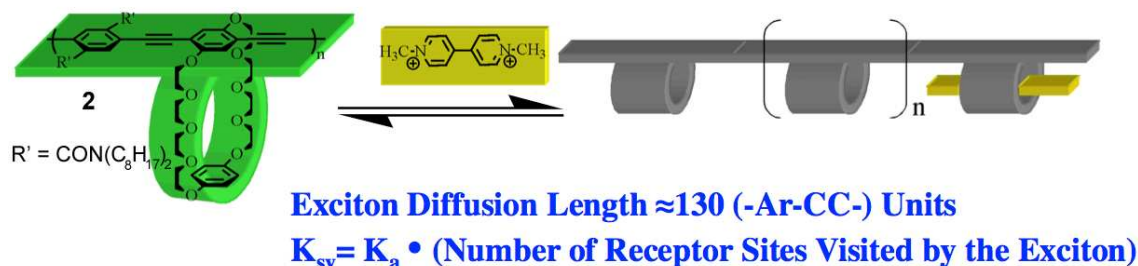


Figure 1. Schematic illustrating the comparative quenching of a monomer and of polymer **2** by PQ^{2+} .

Although the solution studies with **2** stand out as the most precise quantification of amplification of fluorescence sensing in conjugated polymers, the level of signal gain is limited by the fact that exciton diffusion is constrained to a one-dimensional random walk process. In this process, the exciton effectively revisits the same sites many times because it is randomly diffusing along an isolated polymer chain. Based on simple random walk statistics, simply allowing the excitons more freedom to diffuse in three dimensions should allow for dramatic increases in signal gain. As a result, our laboratory hypothesized that higher-dimensionality polymer assemblies would afford further enhanced sensory properties, owing to inter-chain excitation transfer for the sampling of the largest possible number of repeating units.¹⁴ These processes were thoroughly studied in thin films of polymer **2**

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3 precisely deposited a monolayer at a time by the Langmuir-Blodgett deposition (LB)
4
5 technique. The power of this deposition method was critical, since not only are the films
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7 deposited a monolayer at a time, but the polymer chains are aligned as a consequence of the
8
9 fact that the monolayers at the air-water interface are liquid crystalline, and the flow induced
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11 in the deposition to a glass slide creates bulk alignment. In contrast, deposition by spin
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13 coating affords disordered films. Systematic studies on monolayer assemblies with low
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15 energy dyes on the outer surface allowed for the rates of energy transfer to be deduced both
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17 within each monolayer and between monolayers. Although intra-layer energy transfer is
18
19 highest along the direction of the polymer chains, energy transfer between monolayers
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21 (perpendicular to the polymer chains) also occurs at an extremely high rate ($k > 10^{11} \text{ s}^{-1}$), and
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23 through distances in excess of 10 nm. These results have been the foundation for the design
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25 of sensory polymer-based devices, since they prove that polymer films can be formed that
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27 possess superior amplification properties compared to the same polymers in solution.
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33 The generalization of these concepts is illustrated in Figure 2 for two different modes of
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35 signal transduction. The quenching mechanism involves the addition of an analyte that
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37 quenches the excited state of the polymer through electron transfer or energy transfer. The
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39 gain in this process is dependent on the exciton diffusion length and the form of the material,
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41 with continuous films displaying the optimal amplification. The un-quenching process,
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43 although a turn-on mechanism, tends to suffer from lower sensitivity because to obtain a
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45 highly quenched state, some of the quenching groups will inevitably be located within the
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47 exciton diffusion length. A sensing process that removes these groups will therefore have
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49 reduced sensitivity because the removal of a quencher that resides within the exciton
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51 diffusion length of another quencher will not restore all of potential fluorescence. We
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53 emphasize this point because we have found that it is a common misperception to equate all
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55 turn-on mechanisms to higher sensitivity. Clearly, chemiluminescence sensing is
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extraordinarily sensitive because there is no background fluorescence and single photon counting can be utilized in the signal detection.

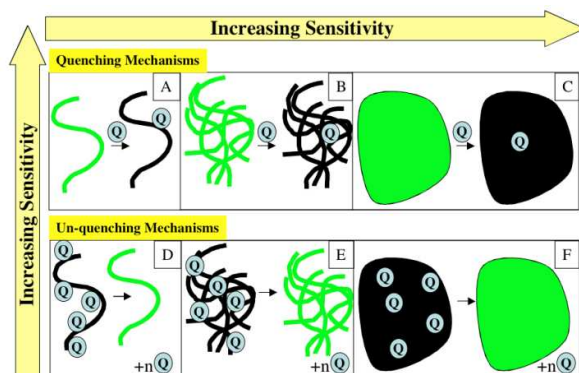


Figure 2. Effect of dimensionality on (un)quenching mechanisms. Quenching mechanisms are by nature more sensitive than unquenching mechanisms (a single quencher can affect the properties of a larger fluorophore), whereas higher-dimension materials display higher sensitivity relative to 1-dimension, or isolated, polymer wires. Reprinted with permission from ref. 1. Copyright 2007 American Chemical Society.

An alternative approach to the use of solid-phase polymers for signal amplification is represented by analyte-induced aggregation of polymers in solution. As an example, the anionic conjugated polymer **3** is highly responsive to polycationic biogenic amines (spermine, spermidine, putrescine, and the antibiotic neomycin) in ethanol/water solutions (Figure 3).¹⁵ The signaling mechanism in this scheme utilizes the tight aggregation that is induced between the anionic polymer chains by the presence of polycationic analytes. This analyte-induced aggregation dramatically increases the efficiency of exciton transfer to minority low-energy anthracene-based traps in the polymer chain, thereby giving a blue to green change in the emission color. The degree of aggregation is critically dependent on the number of charges on the analytes, and for example, analytes with three or more ammonium ions were required to induce aggregation. It is also noteworthy that **3** contains perfluorinated

side-chains which appear to assist the polymer to undergo organization in the aggregate that enhances energy migration. Similar aggregation-induced sensory schemes have been developed for polyanionic molecules, as will be detailed later.

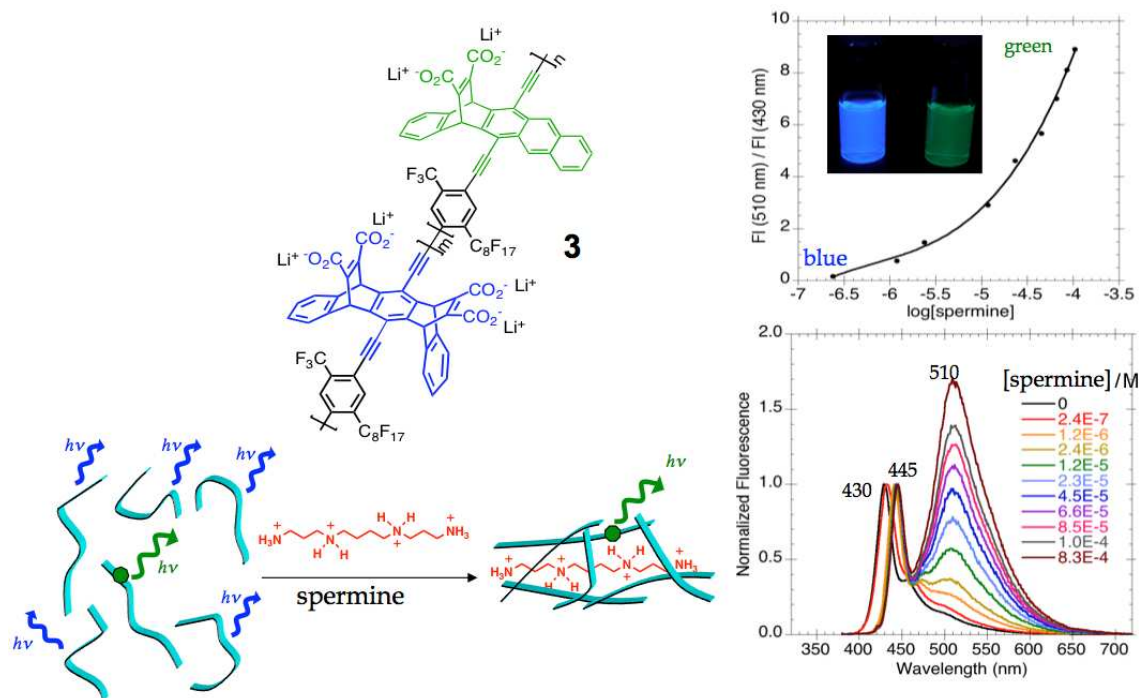
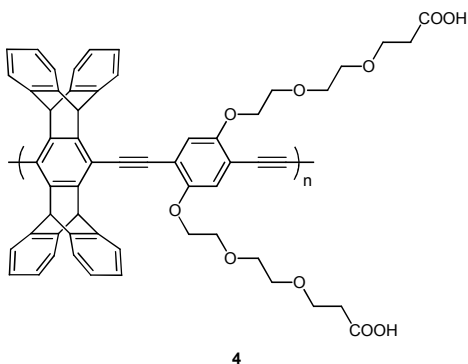


Figure 3. Schematic showing how spermine-induced aggregation of anionic polymer **3** triggers enhanced energy transfer to the minority anthracene emitter. As shown in the associated spectra and plots, sub-micromolar detection was established.

It is desirable to have detection assays that can be performed in solutions wherein mixing can allow for rapid diffusion of the analyte to the sensory polymer. However, as mentioned earlier, relying only on intrapolymer energy transfer restricts exciton diffusion and limits the degree of amplification observed in sensing schemes. To achieve higher sensitivity in a solution scheme, polymer layers can be deposited onto silica- or polystyrene-based microspheres.¹⁶⁻¹⁷ Care is needed to minimize polymer aggregation and self-quenching, and

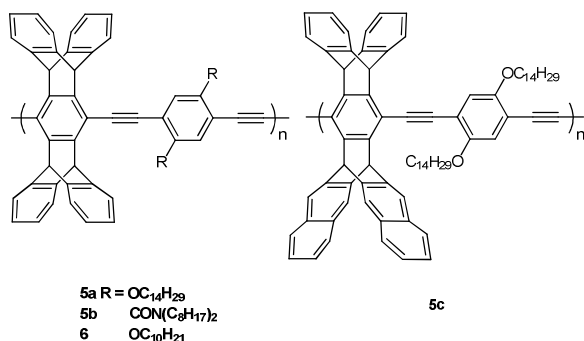
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3 pentiptycene groups were incorporated in the anionic PPEs (4) in order to prevent π -stacking.
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5 The microspheres were coated by layer-by-layer deposition with the polycationic polymer
6 poly(diallyldimethylammonium) chloride (PDAC),¹⁶ as well as by direct adsorption.¹⁷ The
7 emission properties of the polymer-coated microspheres were very similar to that of polymers
8 in solutions (owing to the absence of π -stacking). In sensing applications, these polymer-
9 coated microspheres displayed optical properties similar to that of solutions of the same
10 polymers, but with an enhanced sensitivity (up to 200-fold) to electron-deficient nitro-
11 aromatics or to PQ^{2+} -based quenchers. As a result of the amphiphilic character of the
12 polymers, hydrophobic interactions with the quenchers were also found to play a significant
13 role in the interaction mechanism.
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SENSING APPLICATIONS – SELECTED EXAMPLES

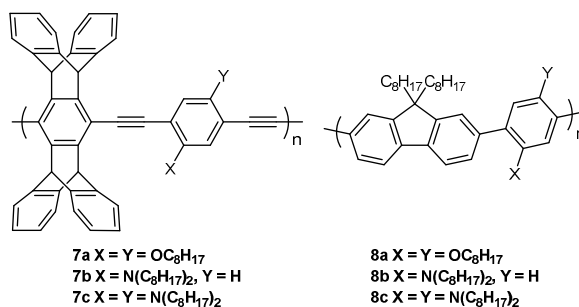
Detection of Explosives. Perhaps the most successful application of conjugated polymer sensors is in the detection of nitro-aromatic explosives.¹⁸⁻¹⁹ This work represented an early example of thin film sensors and a series of poly(*p*-phenyleneethynylene)s were developed (5a – 5c) that first introduced rigid iptycene moieties into a conjugated polymer backbone. These designs create materials that display solution-like (non- π -aggregated) optical properties in thin films by preventing quenching interactions that can limit exciton migration. The structures also produce free volume in the films that facilitate diffusion of small molecules

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3 into the film, but also give rise to size exclusion properties and insensitivity to larger
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5 analytes.¹⁹ The decreased interchain interactions were also found to impart enhanced
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7 solubility compared to other poly(*p*-phenyleneethynylene)s, whereas thin films displayed
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9 high fluorescence quantum yields and stabilities. Taken together, these properties allowed the
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11 development of powerful sensory devices responsive to electron-deficient small nitro-
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13 compounds such as 2,4,6-trinitrotoluene (TNT). The high electron affinity of TNT results in
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15 highly efficient electron transfer quenching reactions with the excited state of the polymers.
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17 A detailed study¹⁸ identified the influence of polymer properties (electronic structure, film
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19 thickness and morphology) as well as of analyte characteristics (vapor pressure, quenching
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21 ability, binding strength with the polymer and diffusion rate through the film) on the
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23 sensitivity and selectivity of several polymers towards small organic molecules. In particular,
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25 thin film of polymer **5a** was found to be able to detect TNT at a 10 ppb concentration after a
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27 few seconds exposure (passive diffusion), underlying the extraordinarily high sensitivity
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29 imparted by energy migration through polymer films. When placed in designed sensory
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31 devices, these materials enabled for the real-time vapor detection of trace explosives and
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33 commercial sensors based on this technology have been used in the detection of buried
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35 landmines, roadside bombs, detection of suspected bomb makers, and a variety of other
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37 homeland security-related tasks.²⁰ An interesting expansion of this work was reported in
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39 2008²¹ wherein multiphoton irradiation was used to excite polymer **6**. Specifically, compound
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41 **6** was found to have large two-photon cross-section, and its response in solution to the
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43 presence of low millimolar amounts of TNT was found to be in qualitative agreement with
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45 that reported under single-photon excitation conditions for similar polymers. Using
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47 multiphoton excitation allows the use of infrared irradiation, which is advantageous from a
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49 safety point of view, but also to reduce scattering and absorbance by the medium and
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51 improve penetration depth for stand-off (remote) sensing.
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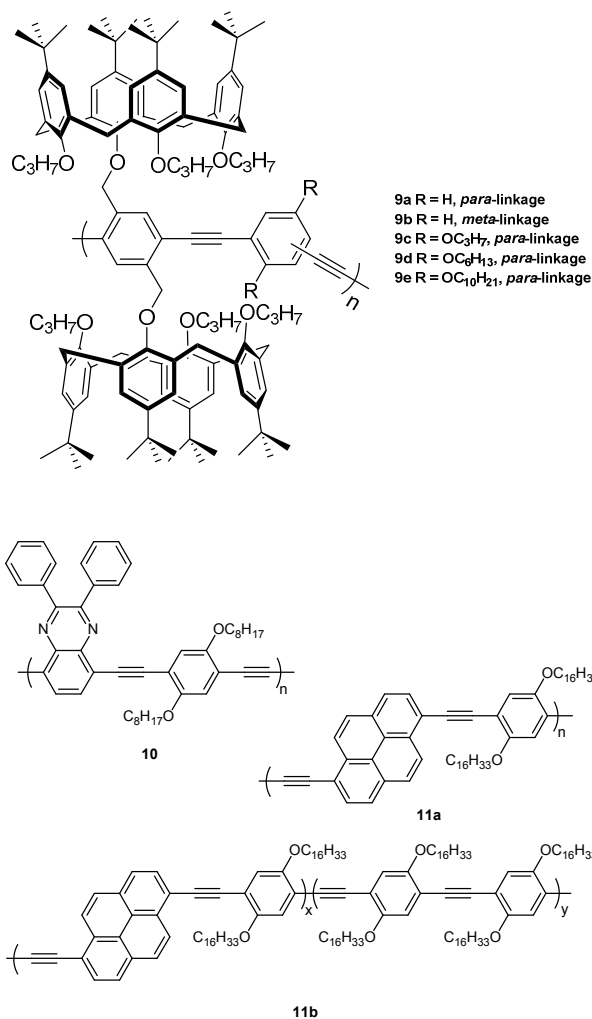
In addition to the direct detection of explosive materials, it is desirable to detect taggants, which are higher-volatility materials added to explosives to facilitate detection. The most widely used taggant is 2,3-dimethyl-2,3-dinitrobutane (DMNB), which is a required additive in all legally manufactured plastic explosives. Rigid poly(*p*-phenyleneethynylene)s similar to those presented above (**7a** – **7c**) were found to be relatively inefficient for the vapor detection of DMNB. This fact is the result of the lower electron affinity of DMNB (relative to nitroaromatics), and the band energies of the polymers lacked the necessary thermodynamic potentials to display photoinduced electron transfer quenching. Indeed, the LUMO levels of PPEs were found to be too low, even after attempted optimizations, to allow efficient electron transfer to the LUMO of DMNB and result in a quenching of the emission of the PPEs. As a consequence, a series of poly(phenylene)s (PPs), which display larger band gap, and as a consequence, higher-energy LUMO orbitals, were prepared (**8a** – **8c**). This rationale allowed for the elaboration of polymers that were able to detect DMNB at sub-ppm levels.²² The detection limits for DMNB are higher than those previously observed for TNT as a result of its physical properties. Indeed, the strong π -associations between TNT and surfaces lead to its intrinsically low vapor pressure, which causes it to preconcentrate in the films. As a result, with long exposure times most materials will be able to detect ppb levels of TNT, and the sensitivity must take into account the response time. Alternatively, DMNB was chosen as a taggant because of its higher vapor pressure that is related to its lack of planarity. As a

result, DMNB doesn't tend to preconcentrate in polymer films and displays fast absorption/desorption kinetics. A combination of electronic structure and photochemical stability result in **8a** being a superior DMNB sensory material with sub-ppm detection limits.



Considering the interest for the detection of explosives, it comes as no surprise that several research groups have been continuing investigations in this field, and there have been recent reviews of this area.²³⁻²⁵ Recent examples of PPE-based sensory materials for electron-poor nitro-aromatics involve calixarene-functionalized polymers (**9a – 9e**), as well as quinoxaline- and pyrene-incorporating PPE skeletons (**10** and **11a-b**, respectively). The calixarene substituents of polymers **9a – 9e** prevent π -stacking in the solid state, thus preserving the optical properties of the material.²⁶ Further, the bulky, bowl-shaped building block helped form porous materials, and allowed to create films that were highly sensitive to explosives such as TNT or DNT: in the presence of 10 ppb TNT, a 50 % emission quenching was recorded in 10 seconds. In comparison, PPE films not carrying calixarene receptors displayed very limited sensing capacities. The optical properties of films of polymer **10** were indicative of strong interchain interactions (both absorbance and emission were substantially red-shifted going from solution to solid state).²⁷ Nevertheless, **10** was able to interact with TNT in both solution and the solid state, resulting in a nearly complete quenching of the fluorescence. The relatively limited sensitivity of this system (in the low ppm range) is likely a consequence of strong π -stacking of polymer chains that results in shortened excited state lifetimes and trapping. Thin films of the pyrene-containing polymers²⁸ (**11a** and **11b**) were found to be

responsive when immersed in aqueous solutions containing low micromolar amounts of TNT. The pronounced emission quenching was attributed to the formation of nonfluorescent complexes between the polymer and TNT, which is promoted by the matching polymer's orbital energies with those of the analyte. The presence of pyrene units was found to be essential, and provided selectivity for TNT over the usual interferent analytes such as DNT (dinitrotoluene), nitrobenzene, and trinitrophenol.

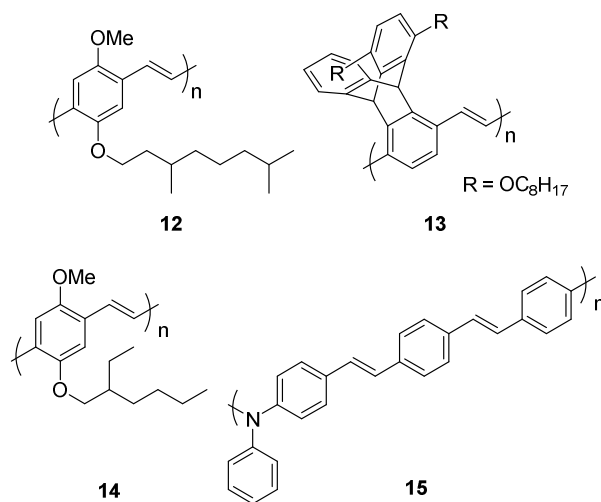


In addition to PPEs, numerous classes of conjugated polymers have been investigated for the sensing of explosives. Poly(*p*-phenylene)vinylenes (PPVs) have been reported as efficient quenchers for viologen-type fluorophores and to act as amplifying polymers,²⁹ and hence

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3 they similarly function in the detection of electron-poor nitrated aromatics. PPV derivative **12**
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5 was found to be responsive to TNT, both in solution and in the solid state.³⁰ In solution,
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7 fluorescence quenching by TNT is observed together with a slight to moderate red-shift of the
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9 emission maximum, suggesting that TNT changes the polymer's conformation. Interestingly,
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11 compound **12** was found to be responsive enough to allow detection of TNT on surfaces, and
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13 the authors report a color change when the polymer is sprayed on traces of TNT. Similarly to
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15 polymer **6**, PPV compound **13** was found to have large two-photon cross-section, and could
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17 be employed for the multiphoton detection of TNT.²¹ As was described for the above-
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19 mentioned PPE polymers, large triptycene moieties prevent interchain interactions and dense
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21 packing in the solid state. Nevertheless, PPV **13** was found to be less responsive to TNT than
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23 the PPE reported in the same study (**6**), which was attributed to the advantageous rigidity
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25 displayed by PPEs, that results in enhanced exciton transport as compared to that of more
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27 flexible PPVs. Other recent uses of PPVs for the detection of explosives have focused on
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29 systems where the sensory polymer was deposited onto porous materials or nanoparticles.
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31 The adsorption of the commercially available MEH-PPV (**14**) on porous silica creates a
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33 composite material responsive to vapor traces of TNT, as evidenced by fluorescence and
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35 reflectance measurements.³¹ The benefit of using a porous substrate was reflected in the
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37 wavelength-dependence of the fluorescence quenching, which was modulated by the
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39 resonance of the microcavities.
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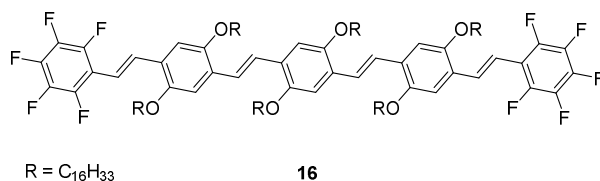
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46 Building on the demonstration that under certain conditions, PPVs can efficiently act as
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48 lasing materials and therefore act as superior sensory substrates,³² the sensing abilities of
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50 polymer **15** were evaluated after deposition onto titania nanoparticles.³³ Compound **15**
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52 displayed lasing emission that was 20 times more sensitive to explosive vapors than
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54 spontaneous emission. As a result, TNT vapor was detected at 10 ppb concentrations by
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56 observing the induced cessation of the lasing emission. An alternative, PPV-based scheme
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3 involves the formation of unsubstituted PPV inside mesoporous silica nanoparticles, which
4 were functionalized by amines.³⁴ When dispersed in ethanol these particles display the
5 expected PPV emission. Upon addition of TNT, Meisenheimer complexes are formed
6 between TNT and the amines inside the pores. These charge-transfer complexes are highly
7 absorbing, and therefore able to quench the PPV emission *via* a FRET process, as opposed to
8 the electron-transfer quenching mechanism. DNT displays a much lower response owing to
9 its decreased electron accepting properties and lower propensity toward Meisenheimer
10 complex formation.
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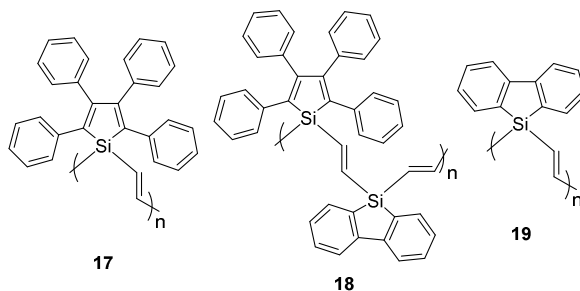


Oligo(*p*-phenylenevinylene) **16** is a fluorescent organogelator that forms fibrous structures when coated onto glass or paper substrates. Solution-based experiments showed a weak quenching of the fluorescence in the presence of sub- and low millimolar concentrations of TNT. However, exposure of fluorescent xerogels of **16** to vapors of nitro-aromatic compounds resulted in a very efficient emission quenching. X-ray diffraction studies revealed that the presence of absorbed nitro-aromatics in the interstitial space of **16** has a negligible impact on the packing, and the fluorescence quenching was attributed to excited-state phenomena and fast exciton migration within the self-assembled structures.³⁵ Exploiting the solid-state behavior, a simple filter paper-based assay was developed, that was able to detect

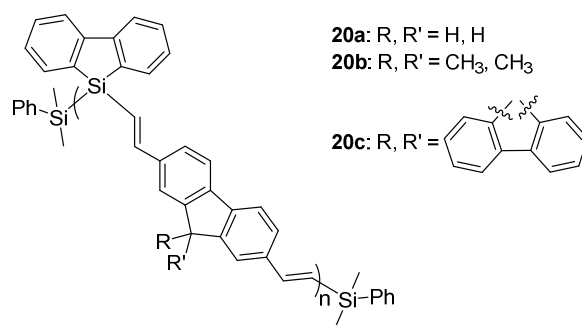
attograms of TNT by simple contact with a contaminated surface. Alternatively, the same paper strips were demonstrated to respond to aqueous solutions containing ppq concentrations of TNT.



Polymers incorporating silicon-based units have been widely investigated for their sensory properties. Polysiloles are effective in the detection of nitro-aromatic explosives³⁶ thanks to characteristic low-lying LUMO orbitals that result from mixing of the π^* and σ^* orbitals to give delocalized excited states that promote exciton diffusion.^{24,37} A series of poly(silole)vinylenes (**17** - **19**) was prepared, and vinylene linkers were found to promote additional ground-state σ^* - π or excited-state σ^* - π^* mixing to give delocalized electronic states.³⁸ The solid-state fluorescence of polymers **17** and **18** was quenched in the presence of nitro-aromatic explosives, and the open structure of polymer **19** allowed for a less selective response to a wide array of explosive molecules and a detection limit of 200 pg cm⁻² for Tetryl (i.e. 2,4,6-trinitrophenylmethylnitramine). Lewis acid-base interactions between the silicon centers and the nitro groups of the analytes were proposed as the driving force for this sensing scheme.



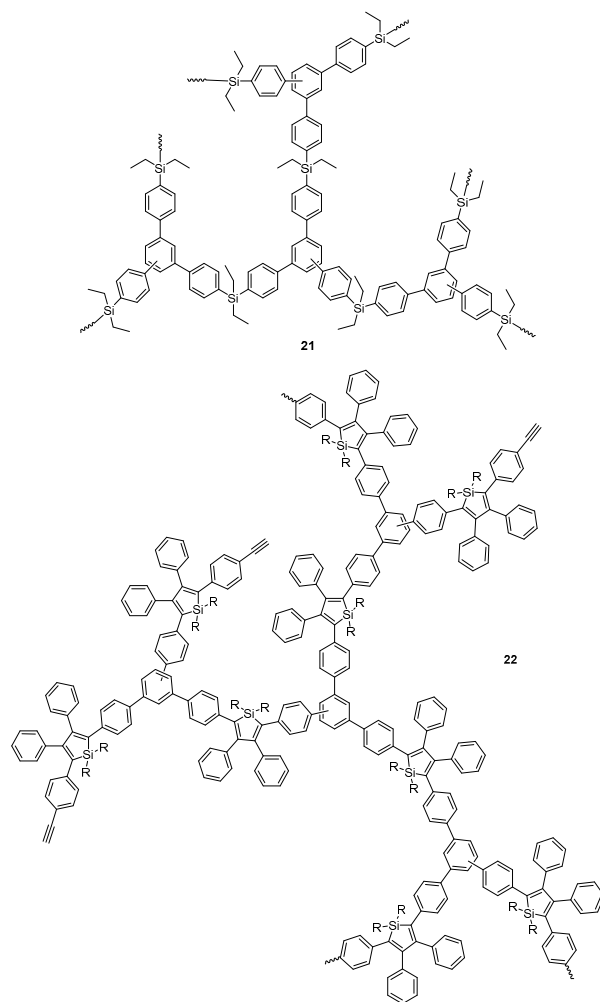
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3 Polymers **20a** -**20c** contain fluorenyl building blocks that are conjugated to the silicon centers
4 through vinylene bridges.³⁹ Both fluorene and silafluorene proved necessary to confer
5 improved processability and optical properties on the polymers, and efficient fluorescence
6 quenching of thin films of polymers **20a** – **20c** was observed in the presence of trace
7 explosives. This response was attributed to excited-state electron transfer from the polymer to
8 the LUMO of nitrated aromatics captured at the silacycle rings. The same type of polymers
9 linked to silica gel plates display more efficient quenching, thereby allowing lower visual
10 detection limits (down to 4.5 pg mm⁻² for the detection of TNT with **20c**).⁴⁰



34 Polymer **20b** was also integrated into silica nanoparticles⁴¹ that were suspended in aqueous
35 solutions and displayed a pronounced quenching of the emission when treated with dissolved
36 explosives TNT or RDX (cyclotrimethylenetrinitramine). These water-dispersible **20b**-coated
37 nanoparticles possess a 35-fold increase in sensitivity for the detection of TNT (200 ppb), as
38 compared to solutions of **20b** in toluene. Under the same conditions, an 800 ppb detection
39 limit was determined for RDX, an explosive compound rarely targeted by conjugated
40 polymer-based sensing schemes. These enhanced sensing abilities were attributed to the close
41 proximity between explosive analytes and polymers induced by the strong affinity of the
42 analytes for the silica nanoparticles.

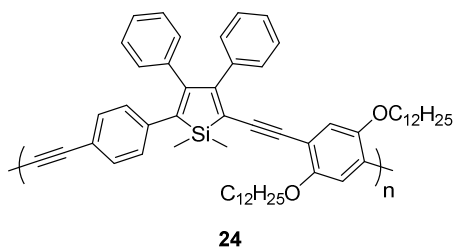
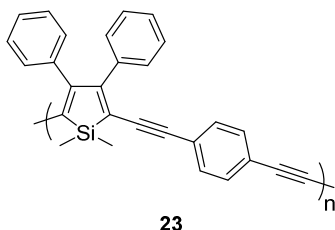
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55 Hyperbranched conjugated polysiloles⁴² and poly(silylene)phenylenes⁴³ have limited
56 fluorescence in solution as a result of fast non-radiative transitions mediated by
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3 intramolecular rotation of the phenyl rings. Their fluorescence is enhanced by addition of a
4 “poor” solvent (*e.g.*, water) which produces aggregation-induced emission (AIE).⁴⁴ The
5 aggregates of these hyperbranched polymers, **21** and **22**, responded to picric acid (PA) with a
6 1 ppm limit in solution through emission quenching.⁴²⁻⁴³ The authors point to the combined
7 roles of the aggregates, the expanded conjugation with Si-containing fragments, and Lewis
8 acid-base interactions as producing the necessary recognition process.
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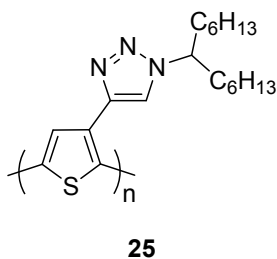


51 Recently, poly(arylene)ethynylene silols have also been reported for the solution-based
52 detection of electron-deficient explosive compounds. The aggregation-induced emission of
53 compounds **23**⁴⁵ and **24**⁴⁶ was quenched in the presence of nitrated aromatics (PA, TNT,
54 DNT) in organic solvents, allowing detection of such compounds in the low ppm
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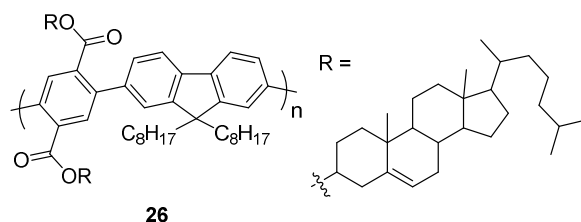
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3 concentration range. As in formerly described silicon-containing polymer sensors, the
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5 recognition relies on Lewis acid/base interactions between the nitro groups of the explosives
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7 and the silacycle cores, whereas the emission quenching results from excited-state electron
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9 transfer.
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31 Polythiophenes have been relatively rarely investigated in the context of small molecule
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33 fluorescence sensing applications. It was demonstrated that polymer **25** with long alkyl side-
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35 chains did not display aggregation-induced emission quenching in the solid state.⁴⁷ When
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37 exposed to vapors of TNT or DNT, thin films of polymer **25** displayed a strong, fast and
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39 reversible response. The very polar triazole groups were proposed as the basis of a strong
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41 interaction between the polymer and nitro-aromatic compounds, resulting in an efficient
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43 fluorescence quenching. The intensity and kinetics of the response were slightly below those
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45 that were determined for PPE **5a**.
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3 In addition to poly(phenylene)s **8a** – **8c**, that have been mentioned earlier for their ability to
4 interact with taggant DMNB,²² other poly(phenylene)s have been investigated in the context
5 of nitro-aromatics sensing. In particular, it was reported that polymer **26**, with bulky groups
6 (alkyl chains and, interestingly, cholesteryl moieties) along a poly(fluorene)phenylene
7 backbone,⁴⁸ displayed limited interchain interactions in thin films that were porous to allow
8 DNT vapor molecules to penetrate them. As a result, the emission of the polymer was rapidly
9 quenched, and at sufficiently long exposure times the emission was completely extinguished.
10 Polymer **26** was further incorporated in an optic-fiber probe allowing remote detection of
11 explosive compounds.
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33 **Detection of Hydrazine.** Contrary to the “turn-off” response of conjugated polymers **5** - **8** to
34 vapors of electron-deficient small molecules (TNT, DNT, DMNB), hydrazine’s reducing
35 power was found to create *increases* in the emission intensity in thin films of polymer **6**, **7b**
36 or **7c**.⁴⁹ These polymers are electron rich and are readily photo-oxidized to give a few
37 quenching sites that dramatically lower the polymer’s emission. Trace vapors of hydrazine
38 are able to reduce these oxidized defects, resulting in an “unquenching” mechanism. It was
39 found that the polymer that is the most readily oxidized (**7c**) gives a larger on-off ratio upon
40 exposure to hydrazine. Hence, this unique, alternative mechanism makes it possible to detect
41 a very toxic compound such as hydrazine at a 100 ppb concentration (10% of its permissible
42 exposure limit).
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3 **Detection of Electron-Rich Small Molecules.** As a complement to the common electron-
4 rich conjugated polymers, electron-poor (high electron affinity) polymers **27 - 31**⁵⁰⁻⁵¹ were
5 developed for the detection of electron-rich analytes. These PPEs contain [2.2.2] bicyclic ring
6 systems structurally related to ipitycene-based fragments in order to prevent π -stacking,
7 increase solubility and enhance emission intensity in the solid state. The electron-
8 withdrawing substituents increase the ionization potential (HOMO level) of the polymers,
9 such that they have sufficient excited state oxidation power to undergo electron transfer
10 quenching with electron-rich species. A unique effect in these types of materials is the
11 homoconjugation between the bridging electron-poor alkene in the [2.2.2] ring system and
12 the polymer backbone that allows an additional mechanism for the tailoring of the electronic
13 energy levels. In accord with these designs, the emission of thin films of polymer **30c** are
14 quenched by indole vapor, whereas no change was observed in the presence of the electron-
15 poor DNT, which broadly quenches most conjugated polymers' emission. The electron-poor
16 nature of polymers **29b** and **30c** resulted in the formation of excited-state charge-complexes
17 (exciplexes) with electron-donating analytes such as indole, dimethylaniline, 1,4-
18 dimethoxybenzene, and *N,N*-dimethyl-*p*-toluidine. The new long wavelength emission from
19 these exciplex species suggests new modes for the selective detection of electron-rich
20 aromatic analytes.
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44 The utility of these electron-deficient polymers for biological sensing was demonstrated with
45 the water-soluble polymer **31**, and electron-donating bioanalytes (amino acids, proteins, or
46 neurotransmitters) could be detected at trace concentrations through amplified quenching of
47 the polymer's fluorescence (Figure 4).⁵⁰
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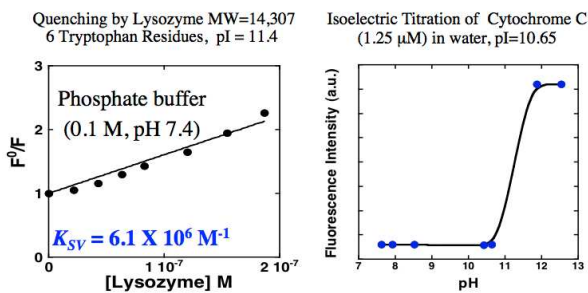
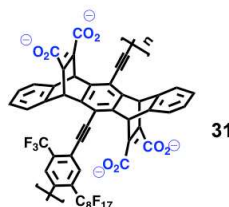
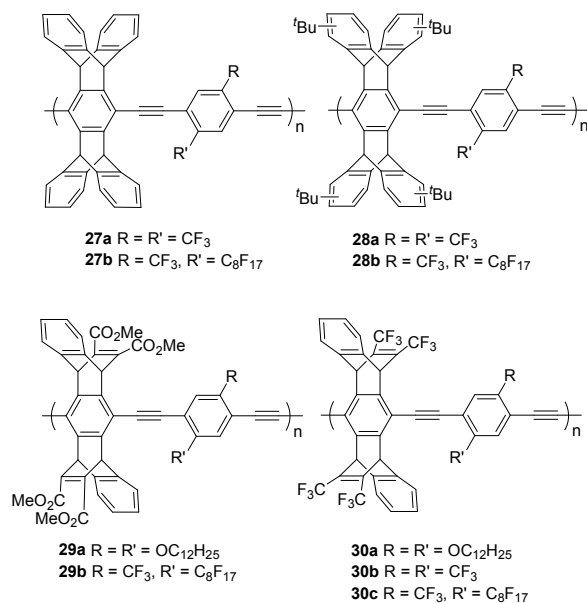
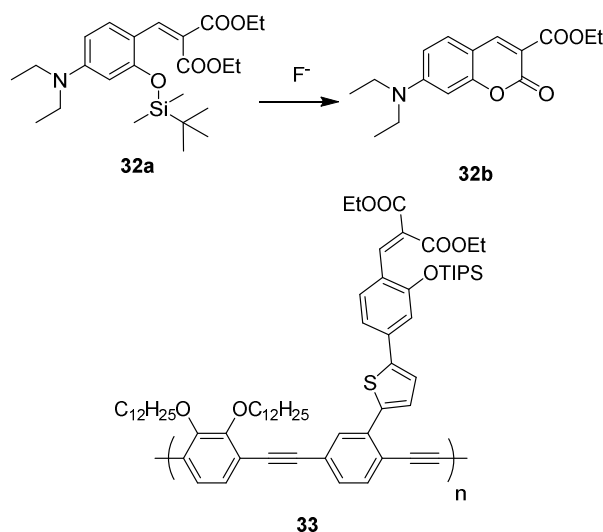


Figure 4. Polymer **31** is a powerful photo-oxidant that is quenched by tryptophan units in cationic (high pI) proteins. Note that the electrostatic assembly allows for the direct measurement of the pI of the analyte.

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3 **Detection of Fluoride Anion.** Selective detection of fluoride anion by compound **32a** was
4 achieved by exploiting the unique reactivity of fluoride with silicon.⁵² Specifically, a
5 fluoride-triggered removal of the silyl protecting group resulted in the formation of a highly
6 emissive coumarin fluorophore (**32b**), that was integrated into a polymeric structure (Figure
7 5). To optimally implement this polymer-based amplifying scheme, polymer **33** was prepared
8 with the goal of creating a strongly electronically-coupled coumarin unit. As expected,
9 fluoride-induced formation of coumarin residues along the PPE polymer chain acts as local
10 band gap traps for the mobile excitons and gives an amplified signal. As a result, the presence
11 of sub-micromolar amounts of fluoride translates into a highly enhanced emission (up to 100-
12 fold) compared to single molecule-based detection. In addition to increased fluorescence
13 quantum yield, the fluoride-induced cyclization translates into red-shifted absorbance and
14 emission bands compared to those of original polymer **33**.
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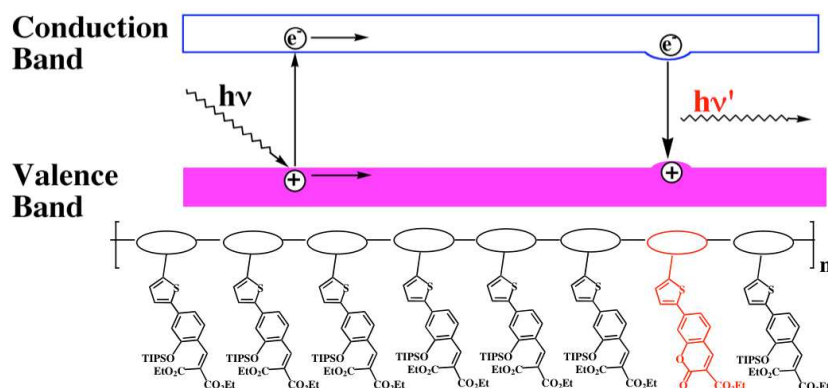
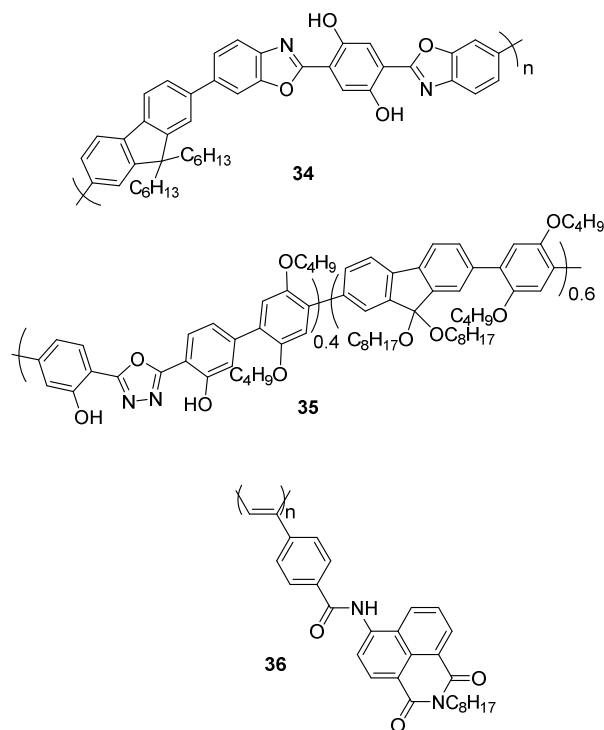


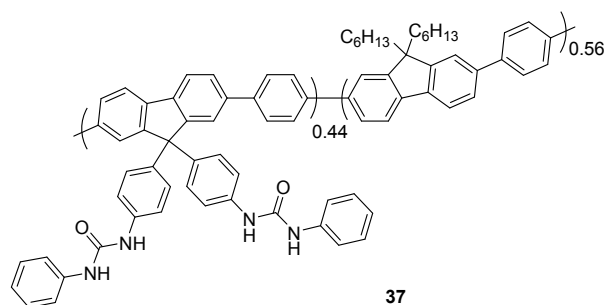
Figure 5. Schematic band diagram showing how an exciton migrates along polymer **33** until it reaches a trap created by the presence of a coumarin unit produced by the fluoride-triggered lactonization reaction. As a result, a new, amplified emission is observed. Reproduced with permission from ref. 52. Copyright 2003 Wiley-VCH publishers.

Recent conjugated polymer-based fluoride sensing schemes have relied on alternate mechanisms. The polymer **34** exhibits a low fluorescence quantum yield as a result of the presence of bis(hydroxyphenylbenzoxazole) groups. However, in the presence of anions (such as fluoride, acetate or hydroxide), the fluorescence is enhanced by as much as a factor of 20, and undergoes a slight red shift. This behavior is attributed to deprotonation of bis(hydroxyphenylbenzoxazole) by the basic anions.⁵³ The resultant anionic chromophore is then unable to undergo the efficient nonradiative processes that quenched the fluorescence. Polymer **35** also contains acidic OH groups and responds to fluoride in a selective fashion (only dihydrogen phosphate also showed a minor response). Contrary to the response of polymer **34**, a 380-fold *reduction* of the emission of polymer **35** is observed in the presence of fluoride. H-bonding between fluoride anions and the highly acidic phenolic protons are proposed as the basis of this selective sensing scheme. The polymer also displayed greater sensitivity as compared to small molecules for the detection of fluoride, and the proportion of oxadiazole units in the structure proved critical in order to achieve optimal performance.⁵⁴

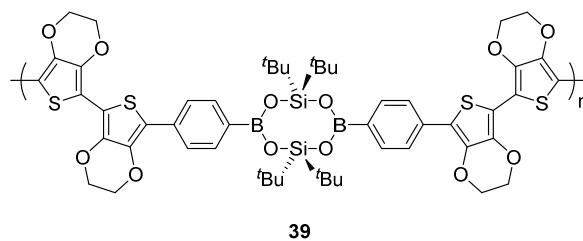
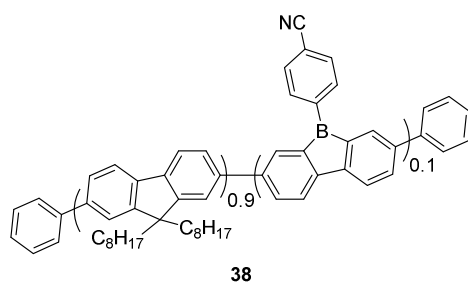


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In polyacetylene **36**, the naphthalimide side-chains are isolated from the polymer backbone. In the presence of fluoride, the amide is deprotonated, which results in extended conjugation connecting the polymer's π -system with that of the naphthalimide groups. Sub-millimolar concentrations of F^- are detected by polymer **36**, which displays a transition from blue-to-orange in its emission color.⁵⁵ Fluorescence quenching of random copolymer **37** in the presence of fluoride, acetate or dihydrogen phosphate was reported,⁵⁶ and was attributed to an enhanced photoinduced electron transfer (PET) process when anions were complexed by urea protons through H-bonding, thus increasing the electron density on the polymer side-chains.



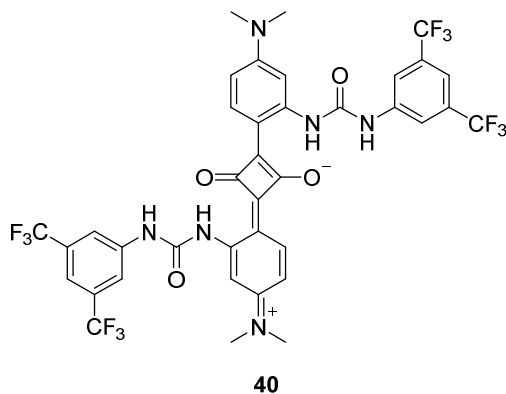
Approaches based on Lewis acid-base interactions have also been devised. For example, random copolymer **38** bearing acidic borane groups was reported and its response to fluoride, iodide and cyanide was studied.⁵⁷ Although it lacked selectivity, **38** could detect F⁻ in the sub-millimolar concentration range in THF by a fluorescence quenching mechanism induced by notoriously strong boron-fluoride interactions. Fluoride and cyanide were found to quench the fluorescence via static quenching mechanisms, whereas iodide induced collisional quenching. Organoboron polymer **39** displays a through-space electronic coupling between polythiophene fragments with a UV-vis spectrum that is noticeably red-shifted compared to that of monomeric fragments.⁵⁸ In the presence of fluoride, a reversible quenching of the fluorescence was observed that was attributed to the formation of B-F bonds. Upon reaction with fluoride, the p_z orbital of the boron center is removed from the conjugated system, which results in an increased band gap and a blue-shifted absorbance band that can be visually detected when a thin film of polymer **39** is exposed to F⁻.



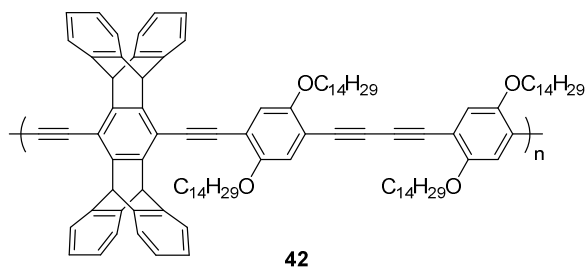
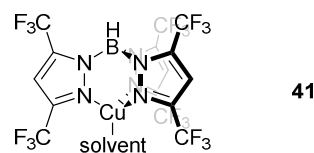
Sensing of Cyclic Ketones. The detection of simple alkyl carbonyl compounds is challenging as a result of their low basicity and high band gaps. Cyclohexanone is an analyte

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3 of interest since it is used to recrystallize the highly explosive compound RDX and can be a
4 vapor signature of explosive compositions. The detection of cyclic ketones was accomplished
5 by the non-covalent association of a light-collecting polymer and a receptor containing a
6 fluorescent dye.⁵⁹ The green emitting PPE **5a** possessing pentiptycene units has the molecular
7 porosity that allows the diffusion of cyclic ketones into the bulk, and the associated free space
8 allows for some mobility of the embedded red-emitting squaraine-based sensing units **40**.
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10 Dye **40** also has an integrated urea unit for hydrogen-bonding interactions with cyclic
11 ketones. A unique aspect of these sensors is that the squaraine dye's absorption has
12 negligible overlap with the emission of the polymer and therefore, the Förster energy transfer
13 to the low energy dye is minimal. Nevertheless, only a few percent of the low energy
14 squaraine dye is required to dominate the emission, and efficient energy transfer is mediated
15 by an electron exchange mechanism. Hence, in contrast to Förster energy transfer that can
16 occur over long distances, the dominating energy transfer to the squaraine dye is highly
17 dependent on very short-range orbital overlap. This mechanism allows for large fluorescence
18 changes to be induced by small changes in the interactions of the dyes with the polymer
19 backbone. Consequently, exposure of the dye/polymer composite to cyclic ketone vapors
20 (cyclopentanone, -hexanone and -heptanone) produced ratiometric emission responses with
21 the emission of the squaraine dye decreasing and the polymer's emission increasing. Studies
22 of a number of different ketones as well as parallel quartz crystal microbalance studies
23 unraveled several effects that contributed to the unique sensitivity to cyclic ketones. In
24 particular, the steric hindrance around the ketone functionality could limit the binding with
25 the urea-containing dyes, larger ketones partition more effectively into the sensory films, and
26 there can be commensurate swelling of the film which can reduce self-quenching of the
27 polymer. Remarkably, this scheme allows sensitive detection of analytes possessing no
28 electronic states capable of interacting with the electronic properties of either the polymer or
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of the dye. These sensors are particularly effective for cyclohexanone and a vapor phase detection limit of 4.76 ppm was determined.

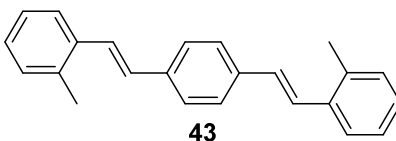


Detection of Ethylene. As a turn-on fluorescence sensing scheme for the plant hormone ethylene, a conjugated polymer was developed that could bind to a copper(I) scorpionate complex (**41**) which displays strong albeit labile interactions with ethylene.⁶⁰ Reversible copper(I) coordination to the polymer is observed and results in the emission being quenched. However, a small concentration of ethylene shifts the equilibrium to the ethylene-copper(I) complex and thereby restores the polymer's emission.⁶¹ Quantum calculations revealed that the planarity and conjugation of the Ar-CC-Ar linkages in a PPE would be strongly disturbed by the steric demand imposed by complexation of the alkynes with **41**. Therefore, polymer **42** (poly(*p*-phenylene butadiynylene)) was prepared in order to allow sterically more accessible dialkyne linkages to interact with copper complex **41** and thereby minimize the disruption of the π system. This scheme also provides some molecular level porosity as a result of the shape-persistent pentiptycenes for rapid gas diffusion in the film. As a result, this system works both in solution and in thin films, and was able to detect ethylene in the micromolar range (solution-based measurements) and at 1000 ppm concentration (vapor-phase measurements).



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Ag(I) salts embedded in polymeric or oligomeric matrices have also been found to function as sensory systems for ethylene.⁶² Ethylene, ammonia and propylene induced fluorescence quenching, and a system made of oligomeric 1,4-bis(methylstyryl)benzene (BMSB, **43**) impregnated with AgBF₄ was responsive to ethylene vapor at a pressure of 50 Torr. The presence of silver ions is essential in this mechanism, as they serve as recognition units for ethylene, and transduce the binding event to the fluorescent oligomers.



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Sensing of DNA. Considerable efforts have been devoted to the use of conjugated polymers for biosensing purposes, and we restrict our overview to only a few significant contributions. Cationic conjugated polyelectrolytes were first utilized over a decade ago for the detection of polyanionic bioanalytes.⁶³⁻⁶⁴ A diverse array of detection schemes have since been developed, and we focus here on label-free techniques (*i.e.*, where the target *analyte* is label-free). FRET-based schemes have proved to be very effective for the detection of DNA single strands (ssDNA). In such a scheme, a polycationic poly(fluorene)phenylene (**44**) is paired

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3 with a probe peptide nucleic acid (PNA) that is labeled with a fluorescent indicator
4 (fluorescein). The high spectral overlap of the fluorescein and cationic polymer **44** (Figure
5 6a) is critical. In the absence of complementary DNA, the PNA strand, which is electrically
6 neutral, does not interact electrostatically with **44** and no FRET is detected. However, upon
7 hybridization of the PNA strand with a complementary ssDNA (the target analyte), the
8 resultant duplex is negatively charged and binding of the cationic polyelectrolyte **44** produces
9 a FRET signal.⁶⁵ Detection limits of 10 pM were determined, and exciting the polymer
10 resulted in a 25-fold amplification of fluorescein emission, compared to a direct excitation of
11 the fluorophore. Interestingly, a fluorescein-labeled, negatively charged, ssDNA could also
12 be used as a probe instead of a PNA strand. In this case, the detection mechanism relies on a
13 stronger binding of **44** to the larger negative charge of the hybridized dsDNA (Figure 6b).⁶⁶
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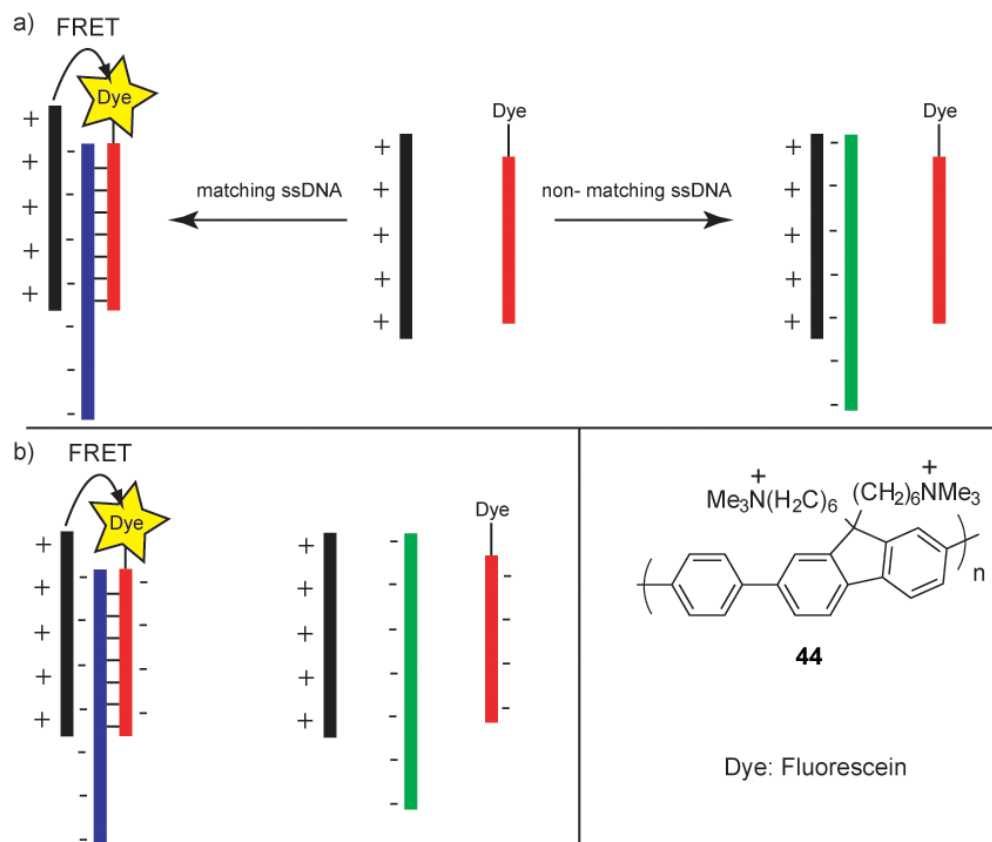
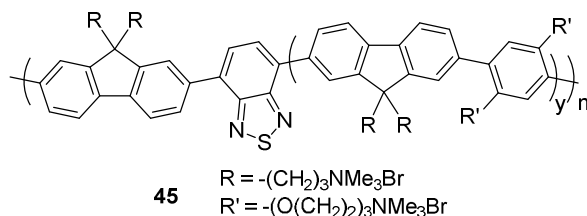


Figure 6. Schematic description of the use of water-soluble cationic conjugated polymer (black, **44**) with specific a) Fluorescein-labeled PNA reporter (red), or b) Fluorescein-labeled ssDNA reporter (red), to detect a complementary ssDNA sequence (blue). The green strand represents a non-complementary ssDNA strand.

A variety of sensing schemes have been elaborated based on the electrostatic assembly scheme, and using conjugated cationic polymers with minority low band gap emitters in their structures eliminated the need of a fluorescent label (**45**). The approach in this case is similar to what was previously described for anionic polymer **3**, and has allowed for the detection of dsDNA in pM concentrations with a dynamic range spanning nearly 7 orders of magnitude.⁶⁷ Polymer **45** contains a fraction of 2,1,3-benzothiadiazole (10 – 20%), and in the presence of negatively charged DNA strands, higher emission is observed from the benzothiadiazole fragments.



Other efforts enabled the naked-eye detection of dsDNA in the low nM range with the covalent incorporation of DNA intercalators in the side chains of **44**.⁶⁸ The DNA intercalator approach allows a strong selectivity for dsDNA against ssDNA, and the FRET mechanism from the conjugated polymer to the dye is strongly enhanced in the presence of dsDNA. Further, a two-step FRET scheme between cationic polymer **44** and a dye appended to a probe ssDNA strand and a DNA intercalator was reported.⁶⁹ In the presence of the target ssDNA, the intercalator can insert into the newly-formed dsDNA. A subsequent cascade of

FRET events from the polymer to the labeled probe and finally to the intercalator indicates hybridization. The molecular-beacon nature of this sensing scheme improves the selectivity for the desired ssDNA target against targets possessing mismatches (Figure 7).

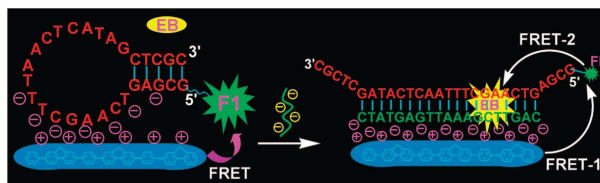


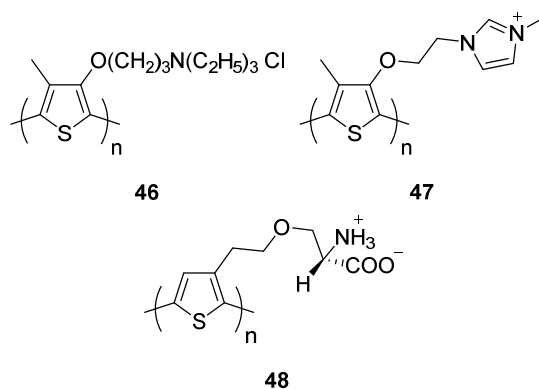
Figure 7. Schematic representation of a double-FRET, molecular-beacon mechanism for the detection of ssDNA. The conjugated polymer is compound **44**, F1 and EB indicate fluorescein and ethidium bromide dyes, respectively. Reproduced with permission from ref. 69. Copyright 2008 American Chemical Society.

Cationic polythiophenes are able to detect ssDNA without the need of any external signaling unit.⁷⁰⁻⁷¹ When polymer **46** is mixed with an ssDNA probe, the initially yellow solution turns red, indicating the formation of electrostatically bound duplex wherein the polymer is in a more planar conformation that promotes extended electronic delocalization. The addition of complementary DNA target produces dsDNA, and a triplex structure forms with a change in color from red back to yellow. These processes are modulated by the charge density, by the rigidity of the assembly, and by hydrophobicity, and are best monitored through the emission of the polythiophene, which is sensitive to the conformation. This approach made it possible to detect ssDNA at an attomole concentration (10^{-18} M) and with excellent selectivity utilizing polymer **47**.⁷¹

Approaches where the ssDNA probe is labeled with a fluorescent dye have also been developed, and the FRET intensity was weak when the labeled ssDNA probe and the cationic polythiophene **47** were mixed in solution. However, upon addition of target ssDNA, the

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3 formation of dsDNA resulted in the formation of triplex structures (dsDNA-polymer) that
4 display an enhanced FRET emission intensity.⁷²
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8 The use of conjugated polythiophenes for the sensing of DNA has also been reported making
9 use of interactions between DNA and a zwitterionic polythiophene (**48**).⁷³ The structural
10 changes experienced by the polymer in the presence of a probe ssDNA and upon
11 hybridization of the probe ssDNA with a target ssDNA translated into emission changes.
12 Interestingly, these responses persist in the solid state, allowing the fabrication of microchips
13 for sequence-selective DNA sensing.
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37 **Detection of Proteases.** Protease activity can be correlated with several diseases and cancers
38 and as a result, there is considerable interest in the monitoring of their presence/activity.
39 Schemes for the detection of protease activity often include molecular constructs that are
40 substrates for the enzyme, and these activity assays have been implemented with fluorescent
41 conjugated polymers. Initial examples⁷⁴⁻⁷⁵ take advantage of this mechanism by employing
42 the activity of an enzyme to modify the assembly with quenchers of water-soluble PPE
43 polymers. Covalent attachment of the enzymatic substrate has advantages for immobilization
44 on surfaces, and was accomplished using PPEs containing long oligo(ethyleneglycol) side-
45 chains,⁷⁶ some of which were terminated by carboxylic acid functionalities. The carboxylic
46 acid groups afford conjugation to polypeptide substrates that were terminated by
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3 An alternative approach to protease detection has recently been reported that makes use of
4 changes in the physical properties of polymers as a function of peptide crosslinking.⁷⁸ This
5 method also represented a dramatic expansion in the polymer architectures used in sensing by
6 employing pentablock “ABCBA” copolymers to produce structured nanoparticles. The cores
7 of the particles are based on PPEs with rigid pentiptycenes as well as a small fraction of a
8 highly emissive low band gap perylene fluorophore (**50**). The conjugated backbone is an
9 efficient antenna that captures and transfers energy to the perylene dyes. Hence, direct
10 irradiation at the absorbance maximum produced dual emission from the majority PPE and
11 the minority perylene groups for ratiometric sensing. The sensing nanoparticles are produced
12 when THF solutions of the ABCBA pentablock polymer **50** are added to water. The core (C
13 block) of the nanoparticles contains the PPE bearing the red-emitting chromophores
14 (perylene), whereas the outer shells were made of two blocks, one containing functional
15 groups (succinimidyl ester groups, Figure 8), and the other based on a hydrogel. The
16 succinimidyl ester containing blocks are then cross-linked by oligopeptides that are substrates
17 for proteases. Cross-linking compresses the particles, and the emission intensity of the
18 nanoparticles was reduced, owing to a tighter packing of the fluorescent core. The
19 fluorescence is then recovered in the presence of proteases. The mechanism is described as a
20 strain-release process, because the nanoparticles are effectively being squeezed by the
21 crosslinking peptides, and cleavage of these linkages by a protease under physiological
22 conditions allows for an observable expansion in the size of the nanoparticles and a 15-fold
23 increase in emission intensity.
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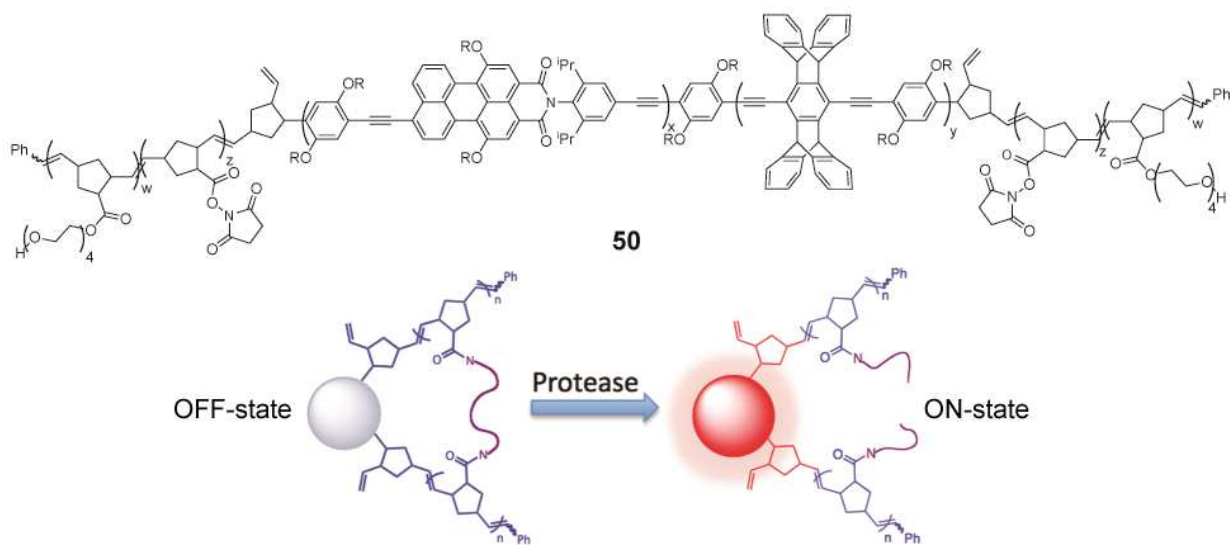


Figure 8. Top: copolymer **50** used for the protease assay; bottom: protease-induced emission turn-on scheme.

CONCLUSION AND FUTURE PERSPECTIVES

In this review, we emphasized some fundamentals of conjugated polymers for sensing applications, and demonstrated how they have been implemented in a large variety of detection schemes. Since the initial reports dating from the mid-1990s, which featured PPEs for the sensing of electron-deficient aromatic analytes, much progress has been made in order to tune the polymers' properties to the analytes to be detected, and to the conditions under which the sensing events have to happen. Hence, detection can now be achieved in the liquid or in the solid state, in aqueous or in organic environments, and even in a complex matrix such as blood serum. Analytes as varied as nitro-aromatic explosives, cyclic ketones, plant hormones, short peptides, DNA strands, or enzyme substrates have been successfully detected by schemes relying on the properties of conjugated polymers. New insights in detection mechanisms have led to improvements in sensitivity, selectivity and transduction of sensing events, that in some cases led to systems where naked-eye detection of desired analytes could be performed in extremely diluted conditions.

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3 We identify two main avenues for future progress in the field of sensory conjugated
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5 polymers. First, one of the most attractive features of these systems relies on their simplicity:
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7 the polymers are in principle easily accessible (some of them are even commercially
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9 available), and their colorimetric or fluorescence behaviors can be monitored with simple
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11 instrumentation, when not just with the naked eye. A challenge is therefore to keep improving
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13 the sensitivity and selectivity of these assays, such as to decrease detection limits and
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15 increase response intensity, while maintaining their ease of preparation and use. It appears
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17 clear that a fundamental understanding of the mechanisms and interactions that are at the
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19 origin of the sensory behaviors is necessary in order to be able to improve the polymers
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21 involved in these detection schemes. A second research avenue that is being pursued (albeit
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23 not covered in this review) is the incorporation of sensory polymers in more sophisticated
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25 devices and on surfaces. Developments along these lines lead to more practical applications
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27 of such materials. For example, sensory materials can be incorporated into microfluidic
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29 devices or adsorbed on responsive surfaces (such as microcantilevers or quartz crystal
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31 microbalances). Although the sophistication level is higher in these cases and applications
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33 probably require more highly-trained users, important improvements in sensitivity and
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35 reliability are at stake. Further, the need for high-throughput screening assays, in particular
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37 for the detection of bioanalytes, emphasizes the need for economically viable detection
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39 schemes, leading to multiple-use or recyclable sensory devices, which are generally easier to
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41 build upon solid-state-based technologies, as opposed to solution-based detection schemes.
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43 Finally, progress still has to be made in order to implement polymer-based sensing schemes
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45 working in “real-world” conditions (humid and/or polluted air, biological fluids or “as-
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47 collected” water samples), and that can operate in the presence of potentially interfering
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49 species and with minimal sample pre-treatment.
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3 In summary, the field of conjugated polymers for sensing applications has been flourishing in
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5 the last decades, but we believe it still has to reach its full potential. Research efforts are still
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7 needed in order to broaden the scope of analytes that can be detected, as well as the
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9 sensitivity, selectivity and practicality of the detection schemes.
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46 47 KEYWORDS

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49 Conjugated Polymers; Fluorescence; Chemical Sensing; Fluorescence Quenching; Explosive
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51 Detection; Biosensing.
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