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Spotlight on Applications

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Polythiophene-Based Optical Sensors for Small Molecules

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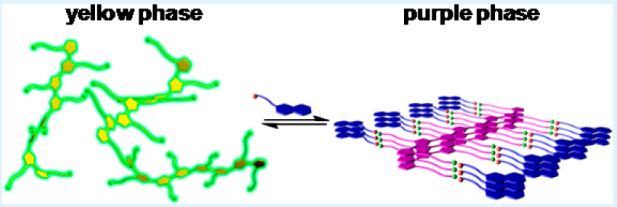
ABSTRACT: Water-soluble, regioregular polythiophene (PT) derivatives are conformational sensitive to external stimuli, and their spectral responses are determined by conformation changes, $\pi-\pi$ interactions and scattering of visible lights originated from PT aggregates. In this paper, we review the synthesis of water-soluble PTs and their photophysical properties, and then highlight our efforts toward the development of PT-based optical sensors for small molecules. Mechanism studies indicate that the interplay between side-chain steric/electrostatic repulsive and interchain attractive interactions is responsible for the assembly and disassembly of water-soluble PTs in aqueous media. Consequently, the planarization/deplanarization of PT backbones provides the possibility for colorimetric and fluorescent dual detection of small bioanalytes and chemical species.



KEYWORDS: *water-soluble polythiophene, sensor, colorimetric, fluorescent, small bioanalytes, inorganic ions*

INTRODUCTION

Conjugated polyelectrolytes (CPEs) are polymers featured with hydrophobic π-conjugated backbones and hydrophilic ionic side groups.[1,2] These structure characteristics endow CPEs with versatile properties including good water solubility, unique photophysical properties inherited from the chemical and electronic structures of their conjugated backbones, and abundant self-assembly behavior due to their inherent amphiphilic structures.[2] Thus, they provide a unique platform for the development of chemo- and biosensors in aqueous media.[3−11] The activity of this area has been spurred since a paper published by Whitten and co-workers in 1999,[12] in which they presented the first example of superquenching of a CPE, poly(2-methoxy-5-propyloxy sulfonate phenylene vinylene), by dimethyl viologen in an aqueous medium with a Stern−Volmer quenching constant (K_{SV}) as high as 1.7×10^7 M^{-1}. The strikingly amplified quenching effect was attributed to an effective electron transfer process, in which one bound quencher dimethyl viologen is sufficient to trap nearly the total exciton energy along one π-conjugated backbone.[13] Over the past decade, CPE-based optical chemo- and biosensors have attracted a considerable interest because of their simplicity, signal amplification effect (sensitivity), and selectivity toward diverse analytes including DNA, protein, small bioanalytes, metal ions, and surfactants.[3−11]

Most of CPE-based chemo- and biosensors rely on the changes in their fluorescence intensities upon binding analytes,[3−5,7−11] whereas few of them can be used for colorimetric detections.[6,14] The fluorescent approach is favored due to its high sensitivity and potential for in vivo imaging of living cells,[15,16] whereas the colorimetric strategy has inherent merits including visual detection and instrument-free signal output.[6,14] Thus the development of colorimetric and fluorescent dual probes based on CPEs has been becoming an attractive topic. Water-soluble polythiophenes (PTs) are of special importance for this purpose since their chain conformations and photophysical properties are sensitive to external stimuli including thermal- or phototreatment, the change of solvent composition, and the introduction of chemical and biochemical targets.[17] Especially, a variety of biomacromolecules, such as DNA and protein, can bind strongly with PT chains, providing efficient colorimetric and fluorescent signal outputs.[6] However, up to now, PT-based sensors for small molecules have not yet been well explored, possibly because of their weak optical outputs caused by the relative weak interactions between analytes and PT chains.

The detection of small molecules, such as inorganic anions, heavy metal ions, surfactants, and small biomolecules is of great importance in environment concern, clinical diagnosis, biological reactions, and metabolic processes. This Spotlight on Applications endeavors to highlight the work by our group on colorimetric and fluorescent sensors based on water-soluble PTs for detecting small molecules. The principles of designing this type of sensors will be discussed. Some relevant work from other groups will also be included to give a full picture of this field. More comprehensive reviews focused on CPE-based optical sensors can refer to the other recent authoritative articles.[3−11]

SYNTHESIS OF WATER-SOLUBLE PT DERIVATIVES

Water-soluble PTs can be synthesized by either oxidative polymerization or cross-coupling reactions. The first water-soluble PT was reported by Wudl, Heeger, and co-workers.[18] They synthesized the sodium salts of poly(3-thiophene-β-ethanesulfonate) (**1a**) and poly(3-(thiophene-δ-butanesulfo-

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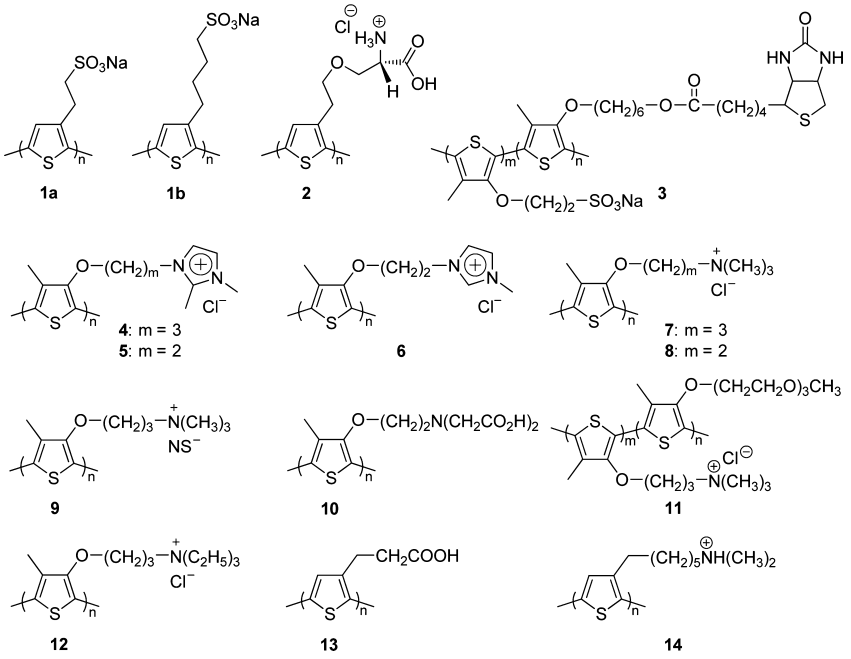
Chart 1. Chemical Structures of Typical Water-Soluble PTs



nate) (**1b**) in 1987 by electropolymerizing the corresponding methyl sulfonate monomers followed by converting the polymers into their sodium salts with sodium iodide in acetone. Inspired by this work, various water-soluble PT derivatives were designed and synthesized. In 1991, a zwitterionic PT derivative, poly (3-[(*S*)-5-amino-5-carboxyl-3-oxapentyl]-2,5-thiophene hydrochloride) (**2**) with a free L-amino acid side chain, was synthesized by chemical oxidative polymerization with $FeCl_3$.[19] This PT derivative is polyampholytic, having anionic or cationic charges depending on the pH value of its aqueous solution. Therefore, it is suitable for forming complexes with negatively or positively charged polymers through electrostatic interaction and hydrogen bonding. This unique structural feature has been applied to construct biosensors for monitoring DNA hybridization, and the conformation changes of certain peptides and proteins.[20−22]

In early 1990, Leclerc and co-workers designed and synthesized a series of poly(3-alkoxy-4-methylthiophenes), which featured with simple synthetic route by chemical oxidative polymerization with $FeCl_3$ in chloroform, regioregular structure, and intriguing optical properties including thermochromic, ionochromic, and photochromic effects in both solutions and solid states.[17] Required by the compatibility with aqueous environment for sensing biological targets, in 1996, a biotinylated copolymer of water-soluble poly(3-alkoxy-4-methylthiophenes) (**3**) was reported.[23] As expected, the interaction of avidin with biotinylated PTs resulted in dramatic color changes in aqueous solutions, realizing affinitychromic detection of avidin, indicating the promise for the development of novel colorimetric biosensors based on water-soluble PTs. Following similar procedures, a series of cationic water-soluble poly(3-alkoxy-4-methylthiophenes) have been prepared (**4**−**12**).[24−28] These polymers exhibited sensitive conformational change and/or aggregation of PT backbones upon interaction with DNA, protein, polysaccharide, or small analytes that can be conveniently monitored by using absorption or emission spectroscopy.

On the other hand, McCullough and co-workers synthesized regioregular water-soluble PTs by cross-coupling reactions. For example, 2,5-poly(thiophene-3-propionic acid) (**13**) with a head-to-tail regioregular chain structure was synthesized using a CuO-modified Stille coupling reaction followed by deprotonation in aqueous NH_4OH solution.[29] It was found that partially protonated PT **13** underwent protein-like hydrophobic assembly to form aggregates with purple color in aqueous solution caused by hydrogen bond stabilization. In a subsequent work, a cationic regioregular PT, head-to-tail 2,5-poly(3-(6-*N*,*N*-dimethylhexylammonium thiophene) (**14**), was synthesized via $Ni(dppp)Cl_2$ catalyzed cross-coupling followed by postpolymerization functionalization.[30]

OPTICAL PROPERTIES OF WATER-SOLUBLE PT DERIVATIVES

The optical properties of water-soluble PTs are highly dependent on their regioregularity, backbone conformations, and aggregation states in solutions or solid states. Generally, their photophysical properties are dominated by the chemical and electronic structures of π-conjugated backbones. Therefore, PTs with the same backbone structures and different side groups (either alkyl/alkoxy or ionic groups) usually exhibit similar optical properties. Water-soluble PTs tend to form aggregates in aqueous media because of their inherent amphiphilic structures. The formation of aggregates lowers the fluorescence quantum yields of PTs due to $\pi-\pi$ stacking and self-quenching, and thus decreases the sensitivities of fluorescent sensors. However, the color changes of their solutions can be optimized for the applications in colorimetric sensors. As early as the 1990s, Leclerc and co-workers performed a comprehensive study on the structure−property relationships in alkoxy-substituted PTs, which exhibited intriguing thermochromic, ionochromic, and affinitychromic effects.[17] These optical phenomena were found to be controlled by a delicate balance between side-chain steric repulsive and interchain attractive interactions.

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Self-assembly of water-soluble PTs in aqueous solutions with different pH values has also been studied for elucidating their conformational changes. It was demonstrated that PT **13** chains were able to be switched from an aggregate state to a random coil phase in aqueous media by increasing the concentration of a base, NH_4OH.[29] The introduction of excess NH_4OH (>5 equiv) can efficiently break hydrogen bonds among PT chains that direct aggregational ordering and consequently destroy the aggregates. This phenomenon has also been observed by Osada and co-workers from the aqueous solution of poly(3-thiophene acetic acid), in which the polymer chains underwent an abrupt conformational change at pH 6.[31]

In 1997, McCullough and co-workers reported that the colorimetric response of PT **13** could be modulated by tuning the size of its countercation.[29] Upon addition of Bu_4NOH, a base with larger cation than NH_4^+, into the aqueous solution of PT **13**/NH_4OH, the absorption maximum of PT **13** was blue-shifted by 130 nm. As a result, the solution exhibited a dramatic color change from purple to yellow. It was proposed that small cations favored the self-assembly of PT **13** in aqueous solution, facilitating the formation of aggregated phase, whereas large cations can completely disrupt the aggregated phase. These findings paved a way for visual sensing small analytes with water-soluble PTs.

Recently, several groups including us have found that the absorption and emission spectra of water-soluble PTs could be dramatically altered in aqueous media containing surfactants because of the formation of ionic complexes through ionic self-assembly.[28,32−34] Subtle differences in the surfactant structures (e.g., chain length, headgroup, and charge density) resulted in marked variations in complex types and sizes, which can be directly correlated to unique colorimetric and fluorescent fingerprints. The pH value, surfactant, and counterion are therefore important factors to regulate optical properties of water-soluble PTs, and they need to be considered for designing colorimetric and fluorescent sensors.

ANALYTE-INDUCED AGGREGATION MECHANISM FOR SENSING SMALL MOLECULES

Water-soluble PTs are conformation sensitive to external stimuli and thus can be applied as colorimetric and fluorescent dual probes, providing advantages over the other CPEs by considering the balance between sensitivity (fluorescent mode) with simplicity (colorimetric mode). In 2003, Leclerc and co-workers demonstrated that the introduction of iodide anions into aqueous PT **4** solution led to a distinct solution color change from yellow to red-violet and a red-shift in its absorption peak from 406 to 543 nm.[25] The absorption spectrum of the violet form is similar with that of a PT **4** solid film, indicating that a more-planar conformation and a strong intermolecular interaction were induced upon noncovalent binding with iodide anions. Moreover, the emission of PT **4** at 550 nm (λ_{ex} = 420 nm) was quenched upon addition of iodide, signifying the possibility for constructing colorimetric and fluorescent dual mode chemosensor for the detection of iodide anion. To further demonstrate that iodide is not responsible for the quenching effect, they used PT **5** with a shorter side chain for comparison. It was found that both absorption and emission of PT **5** were scarcely affected by halogen anions, demonstrating that iodide-induced optical properties are strongly dependent on the nature of the PT side chain.

In 2005, Shinkai and co-workers reported a colorimetric and fluorescent dual probe based on a cationic PT derivative (PT **7**) for the detection of adenosine triphosphate (ATP) in aqueous solution at physiological pH.[35] In this assay, titration of PT **7** with ATP in water led to a remarkable red-shift of absorption peak from 400 to 538 nm together with solution color change from yellow to pink-red (Figure 1). They proposed that the

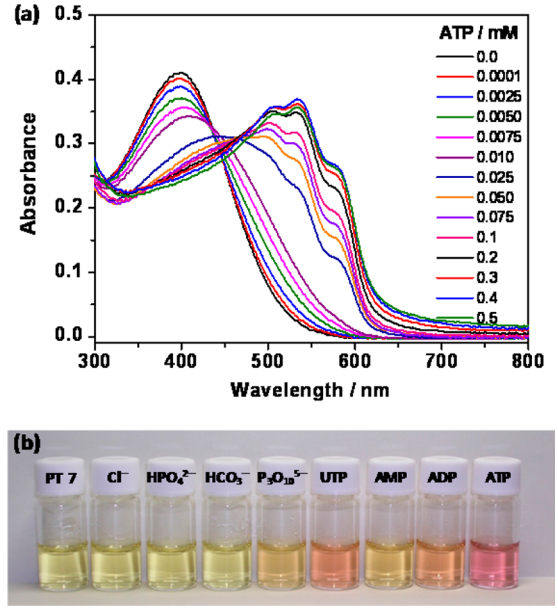

Figure 1. (a) Absorption spectra of PT **7** (0.1 mM) in water with increasing concentrations of ATP as indicated. (b) Photograph of PT **7** aqueous solutions in the presence of equimolar amounts of various anions. Reprinted with permission from ref 35. Copyright 2005 Wiley-VCH.

red-shift of the absorption maximum and the appearance of characteristic vibronic bands were associated with the changes in the conformation and aggregation mode of PT backbones. Indeed, the absorbance spectrum of aqueous PT **7** solution upon addition of an equimolar amount of ATP was similar to that of a solid film casting from PT **7** solution, suggesting the formation of interchain π-stacking aggregates induced by ATP. To address the molecular mechanism beyond this observation, the authors examined the influences of the nucleotides that bear different nulceobase moieties and different numbers of phosphate groups (negative charges) on the polymer aggregation.[35,36] It was found that the nucleobase adenine with a larger aromatic plane facilitated the polymer aggregation through hydrophobic effects, whereas smaller spectral changes were observed upon exposure of PT **7** to uridine triphosphate (UTP), triphosphate, pyrophosphate, and phosphate. The amount of negative charge on the analyte is another dominant factor. The distinct solution color change and the largest absorbance response of aqueous PT **7** solution was observed upon addition of oligoanionic ATP, whereas unconspicuous change occurred upon blending with adenosine diphosphate (ADP) or adenosine monophosphate (AMP). Moreover, PT **7** was selective for ATP detection over other simple anions such as Cl^-, HPO_4^{2-}, and HCO_3^-, and this assay was also scarcely interfered by the presence of alkali and alkali-earth metal cations. In addition to red-shifted absorbance, the addition of ATP to an aqueous solution of PT **7** also resulted in fluorescence quenching. The fluorescence response was most sensitive to ATP over ADP or AMP. The detection limit, based

on fluorescence quenching, for ATP was reported to be approximately 10^{-8} M (Figure 2).

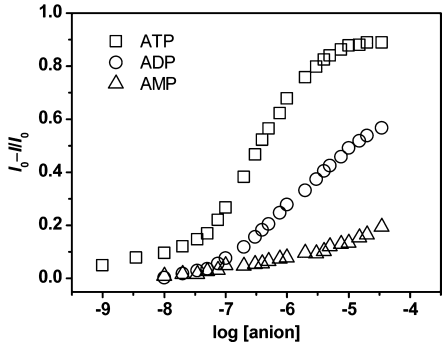

Figure 2. Fluorescence quenching of PT 7 (5.0 μM) by AMP, ADP, and ATP in HEPES buffer (10 mM, pH 7.4). I_0 and I are the fluorescence intensity of PT 7 solution in the absence and the presence of different amounts of analytes, respectively. Reprinted with permission from ref 35. Copyright 2005 Wiley-VCH.

In a subsequent work, our group further studied the supramolecular chiral complex formation between folic acid and PTs (PT 7 and PT **8**), in which the amphiphilic nature of PT derivatives was tuned by changing the length of hydrophobic alkyl moieties.[37] The binding mechanism was proposed based on several evidence including temperature- and solvent composition-dependent absorption, circular dichroism (CD) spectra, and ^{1}H NMR spectra of the complexes. It was confirmed that the interplay of hydrophilic and hydrophobic interactions between cationic PTs and bioanions accounts for the formation of PT aggregates with different molecular ordering as revealed by different CD patterns and intensities. PT **8** with shorter alkyl moieties is more hydrophilic and selectively response to folic acid over ATP; whereas more hydrophobic PT 7 is easy to aggregate upon the interaction with either folic acid or ATP, lacking selectivity between both targeting molecules. These results indicate that a tiny and subtle adjustment of the structure of PTs can efficiently improve the selectivity toward a special analyte.

SENSING BASED ON MODIFICATION OF ANALYTE STRUCTURE AND INDUCED AGGREGATION MECHANISM

Some small bioanalytes with simple structures, such as amino acids and peptides, cannot bind strongly with CPE chains to induce distinct conformational changes and aggregation. Thus, CPE probes were scarcely applied for sensing small bioanalytes with respect to biomacromolecules (DNA and protein).[3−11] Recently, our group reported the colorimetric and fluorescent dual detection of glutathione (GSH) through an in situ premodification technique by using PT 7 and a derivatization agent, *o*-phthalaldehyde (OPA), which can selectively react with GSH to form an isoindole derivative in borate buffer at pH 9.0−9.5 (Figure 3a).[38] In the case of the absence of OPA, exposure of PT 7 to GSH in borate buffer (20 mM, pH 9.0) resulted in a small red-shift by 12 nm in absorption spectrum. In this system, PT 7 chains adopt a random-coiled conformation with yellow color. When a premixed GSH and OPA mixture was introduced into a PT 7 solution, the absorption maximum of PT 7 is red-shifted to 545 nm together with a color change from yellow to pink-red (Figure 3b, c). This large shift (by 126 nm) and the appearance of two vibronic bands at 512 and 588 nm are characteristic of the aggregation of PT backbones, indicating that the introduction of an aromatic moiety into GSH greatly improved its ability to induce aggregation of the PT 7 backbones from a random-coiled conformation to an ordered phase. In addition to distinct color change, the addition of GSH/OPA to PT 7 aqueous solution also resulted in fluorescence quenching, and the detection limit can be extended to be as low as 10 nM. By optimizing the ratio of OPA to GSH, this approach is applicable for sensing GSH at physiological pH featured with rapid response, visual detection, excitation and emission in the visible

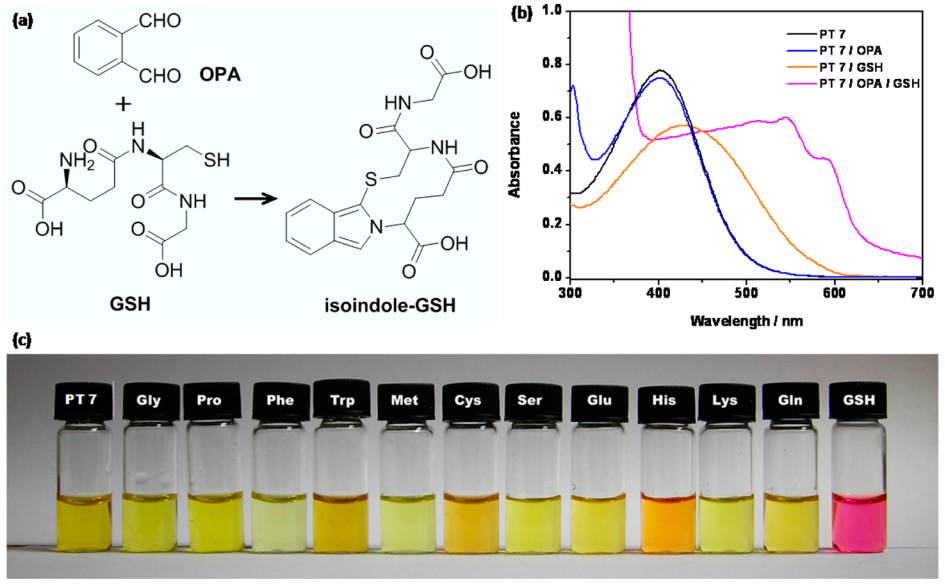

Figure 3. (a) Schematic illustration of the in situ premodification reaction GSH with OPA. (b) Absorption spectra of PT 7 in the absence and the presence of OPA, GSH, and the mixture of OPA and GSH in borate buffer (20 mM, pH 9.0) at 25 °C. (c) Photograph of PT 7 solutions in borate buffer (pH 9.0) induced by addition of various OPA-amino acids and OPA-GSH. [PT 7] = 0.15 mM; [OPA] = 0.75 mM; [amino acids] = [GSH] = 0.5 mM. Reprinted with permission from ref 38. Copyright 2009 Royal Society of Chemistry Publishing.

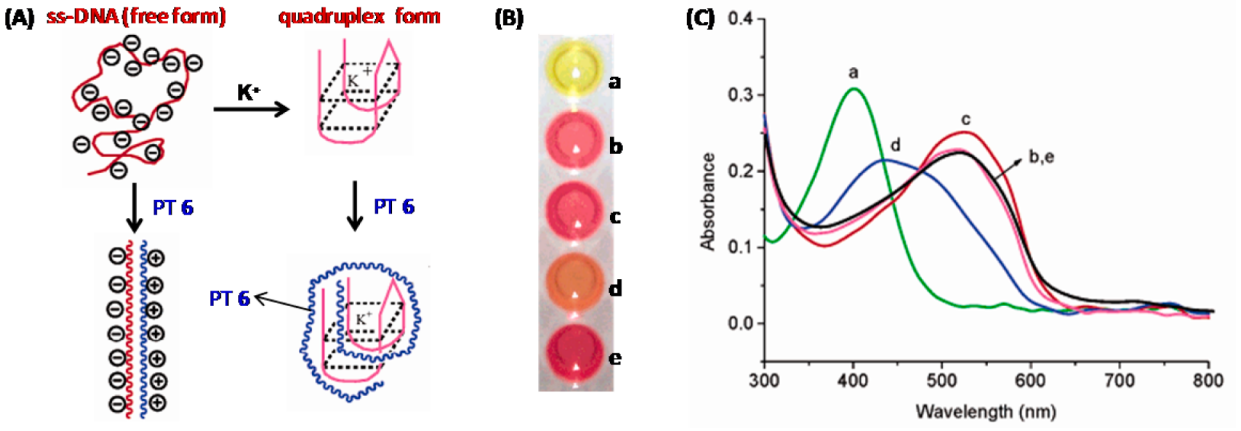

Figure 4. (A) Schematic illustration of the principle of specific detection of K^+ ions. (B) Photograph and (C) absorption spectra of PT **6** in the presence of ss-DNA and different alkali cations in water at 25 °C. a, PT **6** alone; b, Li^+; c, Na^+; d, K^+; e, Rb^+. Reprinted with permission from ref 41. Copyright 2004 American Chemical Society.

region, and good selectivity relative to amino acids (Figure 3c). Following this strategy, we subsequently reported PT **7**-based assays for the colorimetric and fluorescent detection of taurine,[39] cysteine, and homocysteine.[40]

METAL CATION SENSING BASED ON TARGET-INDUCED CONFORMATIONAL CHANGE OF OLIGONUCLEOTIDES AND PT DERIVATIVES

Similar with small bioanalytes, metal cations alone can scarcely induce distinct conformational changes or aggregation of water-soluble PTs, thus a mediator is required to enforce interaction with PTs for giving sufficient optical signal output. With the help of the target-specific oligonucleotides, water-soluble PTs have been applied for the detection of metal cations with biological importance. In 2004, Leclerc's group developed a label-free method for the detection of K^+ ion using PT **6** and single-stranded DNA (ss-DNA: 5′-GGTTGGTGTGGTTGG-3′), which can specifically bind K^+ ions and undergo a conformational transition from an unfolded to a folded structure (Figure 4A).[41] In the absence of K^+ ions, cationic PT **6** readily forms a stoichiometric complex with unfolded anionic ss-DNA, which adopts a planar conformation with red-violet color (λ_{max} = 527 nm). Upon the introduction of K^+ ions into the above solution, the solution color and the optical properties of PT **6** were changed. This phenomenon is independent of the halogen counterions, indicating the specificity of the assay toward K^+ ions (Figure 4B, C). The authors proposed that the formation of a quadruplex structure of ss-DNA induced and stabilized by K^+ ions allowed PT **6** chains to wrap the folded structure through electrostatic interactions, leading to a random-coil conformation of PT **6** and a dark orange solution color. Similarly, Fan, Wang, and co-workers reported the colorimetric detection Hg^{2+} ions by using an ionic complex of PT **12** and mercury-specific oligonucleotide (5′-CATTTCTTTCTTCCCCTTGTTTGTTTCA-3′) as probe.[42] More recently, the detection of Pb^{2+} ions was realized through the same approach.[43]

SURFACTANT SENSING BASED ON DISASSEMBLY OF PT AGGREGATES

Surfactants have been becoming a major component of the environmental pollutants because of their wide applications in household cleaning products and manufacturing processes. Thus, it is important to develop simple, selective, and sensitive method to monitor the concentration of surfactants in water. Recently, our group designed and synthesized three kinds of PT derivatives (PTs **9**−**11**), which are water-soluble in the aggregated forms, and display colorimetric changes in the presence of a variety of surfactants.[28] PT **9** in HEPES buffer (10 mM, pH 7.4) exhibits two major peaks at 543 and 589 nm, and a broad shoulder around 504 nm, being characteristic of the formation of a π-stacked aggregate. Exposure of sodium dodecylbenzenesulfonate (SDBS) into aqueous PT **9** solution, the absorption maximum is blue-shifted to 368 nm along with a solution color change from purple to light yellow, implying the dissociation of PT **9** aggregates. Moreover, a good linear relationship between A_{589}/A_{422} and the concentration of SDBS (R = 0.998 from 0.001 to 0.04 mM) is observed, indicating that this approach is applicable for ratiometric detection of SDBS (Figure 5).

Most notably, PT **9** exhibits satisfied specificity toward anionic surfactants (with benzenesulfonate, sulfonate, sulfate, carboxylate, and phosphate ionic groups) over cationic surfactant (CTAB, cetyltrimethylammonium bromide), non-ionic surfactant (Triton X-100), and simple ions including Cl^-,

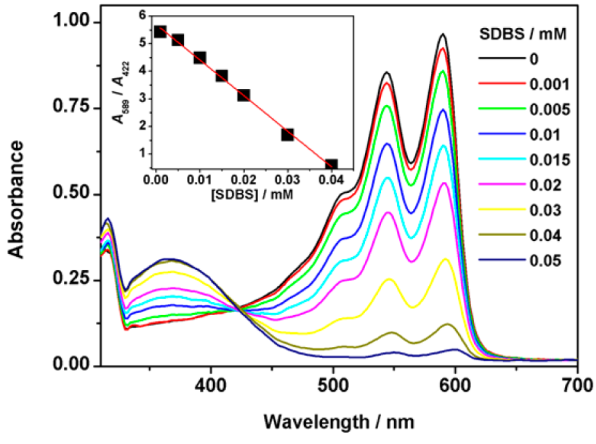

Figure 5. Absorption spectra of PT **9** (0.1 mM) in HEPES buffer with increasing concentrations of SDBS. Inset: the relationship between (A_{589}/A_{422}) and the concentration of SDBS from 0.001 to 0.04 mM. Reprinted with permission from ref 28. Copyright 2009 Royal Society of Chemistry Publishing.

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Figure 6. Photograph of PT **9** (0.1 mM) in HEPES buffer (10 mM, pH 7.4) induced by addition of various analytes. [SDBS] = 0.05 mM; [SDS] = [SLS] = 0.1 mM; [CTAB] = [Triton X-100] = [simple ions] = 0.5 mM. Reprinted with permission from ref 28. Copyright 2009 Royal Society of Chemistry Publishing.

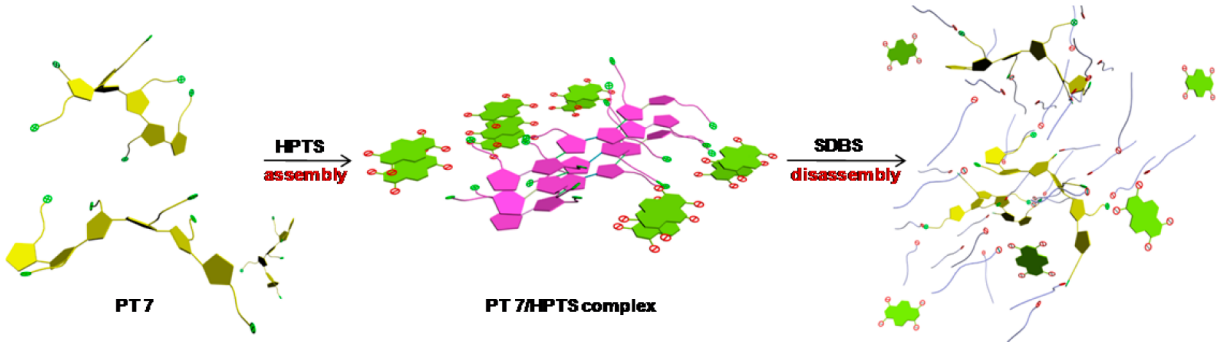

Figure 7. Schematic illustration of the assembly and disassembly processes of PT 7 in the presence of HPTS and anionic surfactant SDBS. Reprinted with permission from ref 33. Copyright 2009 Royal Society of Chemistry Publishing.

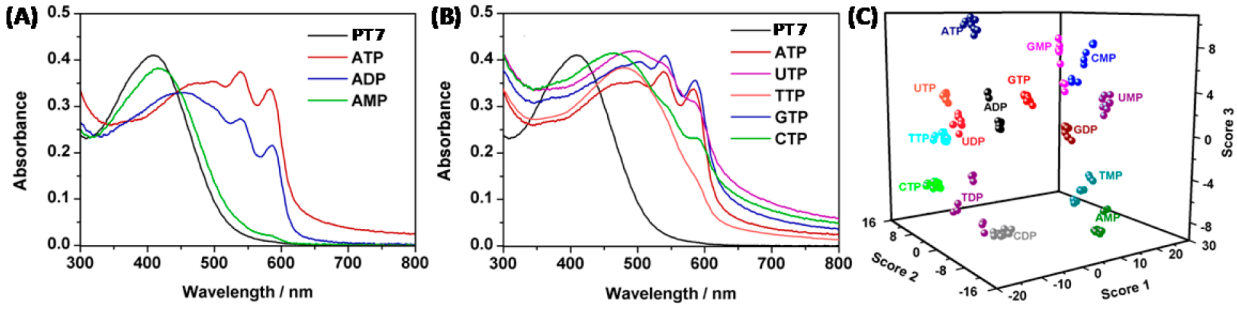

Figure 8. Absorption spectra of PT 7 (0.1 mM) in the absence and presence of an equimolar amount of (A) ATP, ADP, and AMP, and (B) ATP, UTP, TTP, GTP, and CTP in HEPES buffer (10 mM, pH 7.4). (C) Three-dimensional LDA score plot for the analysis of fifteen nucleotides. Reprinted with permission from ref 46. Copyright 2009 Royal Society of Chemistry.

SO_4^{2-}, CO_3^{2-}, HPO_4^{2-}, NO_3^-, K^+, Na^+, Ca^{2+}, and Mg^{2+} (Figure 6). The sensing mechanism was also explored by examining temperature-dependent absorption spectra of PT **9**, the effects of chain length of alkyl sulfonates on the absorption spectra and colorimetric response of PT **9**, and the influences of SDBS concentration on the emission intensity of PT **9**. We proposed that the synergistic effect of electrostatic and hydrophobic interactions between hydrophobic alkyl chains promoted the disassembly of PT **9** aggregates, shifting the $\pi-\pi^*$ transition to shorter wavelengths and leading to a color change from purple to light yellow. Based on the above disassembly driven colorimetric sensing mechanism proposed for anionic surfactants, colorimetric sensing of cationic (CTAB) and nonionic (Triton X-100) surfactants was also realized by using anionic PT **10** and methoxy triethylene glycol functionalized PT copolymer (PT **11**) as probes, respectively. This simple colorimetric approach is the first CPE-based colorimetric sensing system that can easily distinguish anionic, cationic, and nonionic surfactants in a 100% aqueous solution. More recently, a colorimetric assay based on the disassembly assembly of PT **10** in aqueous solution was reported for acetylcholinesterase activity detecting and inhibitor screening, in which the cooperative electrostatic and hydrophobic interactions between PT **10** and a cationic surfactant, myristoylcholine (the substrate of acetylcholinesterase), play decisive roles.[32]

The colorimetric approach described above has unique advantages of visual detection and real-time in situ responses, but usually at the cost of detection limit (1×10^{-6} M level) because of the much lower sensitivity of absorption technique with respect to fluorometric method. However, attempts to improve the sensitivity by fluorescent mode failed because of the low fluorescence quantum yield of PT derivative (Φ = 0.49%),[44] and the inherent sensing mechanism of conjugated polymers.[5] To extend the detection limits for surfactants, we reported an alternative fluorescent approach[33] by monitoring the fluorescence recovery of an anionic dye, 8-hydroxy-1,3,6-pyrenetrisulfonic acid trisodium salt (HPTS). This dye acted as

a component in the composite probe of PT 7/HPTS complex, and has high quantum yield of 0.82. HPTS with large aromatic plane and multiple negative charges can readily form a complex with cationic PT 7 through electrostatic and hydrophobic cooperative interactions, in which both PT 7 and HPTS were quenched efficiently due to the formation of aggregates and/or electron transfer between these two components. The disassembly of the complex due to the introduction of anionic surfactant (SDBS) can easily be monitored by recording fluorescence recovery of HPTS (Figure 7), and the detection limit can be extended to be as low as the order of 10^{-9} M.

CROSS-REACTIVE ARRAYS FOR THE DISCRIMINATION OF STRUCTURALLY SIMILAR ANALYTES

The multivalent nature of CPE probes facilitates the self-assembly and the formation of aggregate structure by binding analytes with respect to small-molecule probes, which can be utilized to construct cross-reactive CPE array to identify and classify structurally similar analytes.[45] PT 7 is cross-reactive and can bind with various nucleotides (XNPs: X = A, U, T, G, and C; N = mono, di, and tri) to form PT 7/XNP complexes with different molecular ordering, which can be clearly reflected in their absorption spectra (Figure 8A, B) and provides a specific signal transduction of the nucleotide binding. The unique response from PT 7 toward each XNP is assigned to the changes in the conformation and the aggregation mode of PT backbones, and the formation of an ordered phase of PTs, driven by ionic self-assembly between cationic PT 7 and anionic XNPs. Moreover, scattering lights at longer wavelengths from the small PT 7/XNP aggregates also provide an alternate transduction mechanism. The spectral variations for the different XNPs in the overall shape of the absorbance curve of PT 7 are responsible for the classification of 15 XNPs, as depicted in a three-dimensional score plot (Figure 8C), in which the data of all fifteen XNPs appear in well-separated groups and are visually distinguishable with 100% accuracy based on linear discriminant analysis (LDA).[46]

CONCLUSIONS AND PERSPECTIVES

Water-soluble PTs with regioregular structures are a kind of attractive CPE probes for applications in sensing small chemical and biological species including nucleotides, folic acid, glutathione, inorganic anions, metal ions, and surfactants. Both oxidation-coupling and metal-catalyzed cross-coupling polymerization methods have been developed for preparing these polymers. Especially, many water-soluble regioregular PTs can be easily prepared by chemically oxidative polymerization of PT monomer with regioregular structures. A key advantage of the water-soluble, regioregular PT-based assays is the colorimetric and fluorescent dual response toward chemically or biologically important targets due to the distinct conformational changes or the aggregation of their π-conjugated backbones induced by binding of small analytes.

In recent years, extensive effort has been devoted to the construction of PT-based assays for the detection of small molecules, and a considerable progress has already been achieved. Nevertheless, in our opinion, the following challenges still remain. First, fluorescence quantum yield of water-soluble PT derivative is low (several %) over other CPEs such as poly(phenylene ethynylene), limiting the improvement of sensitivity of the PT-based sensors. Synthesis of water-soluble PTs with high quantum yield is required. Second, in most cases, electrostatic interactions is the primary driving force for the binding of polymer probes with analytes, therefore, these assays are sensitive to ionic strength, preventing more practical applications in complex fluids. Third, water-soluble PTs are featured with amphiphilic structures, facilitating nonspecific interactions with analytes through both electrostatic and hydrophobic interactions. With these issues solved, water-soluble PTs will continue to lead the way to new practical sensory systems with improved performances.

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Notes

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