Polydiacetylenes – recent molecular advances and applications

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Polydiacetylenes (PDAs) comprise a class of chromatic polymers which have attracted significant interest over the past 40 years as a promising platform for chemo- and bio-sensing. Specifically, the unique colorimetric and fluorescent transformations of PDA, induced by varied external stimuli, are a core property of these polymers, and have been widely exploited for diverse applications. In this review, we focus on recent developments in PDA chemistry, materials, and practical applications. We summarize the progress in development of new synthetic routes and assembly methods resulting in enhanced chromatic properties and interesting molecular configurations. We further outline the challenges that still exist for practical utilization of PDA technology, and possible future directions.

Introduction

Since the first reports on polydiacetylene (PDA) synthesis appeared at the end of the 1960s from the laboratory of Wegner,1,2 these molecules have captured the imagination of scientists and technologists alike due to their unique chromatic properties. Specifically, it has been shown that certain diacetylene monomers can be aligned in solutions and polymerized through ultraviolet (UV) irradiation, producing a conjugated PDA network3,4 (Fig. 1). The unique feature of PDA systems has been the observation that the conjugated PDA networks often absorb light in the visible spectral region, thereby exhibiting color, in most cases blue.5,6 Moreover, conjugated PDA can undergo phase changes, induced by varied environmental stimuli, leading to dramatic colorimetric transformations that are visible to the naked eye (Fig. 1). Another attractive feature of PDA systems in the context of sensing applications has been the fluorescence properties; blue phase PDA is non-fluorescence while the red-phase configuration exhibits high fluorescence with minimal bleaching.7–9

Beside the intriguing chromatic properties of PDA, the diverse physical configurations of the PDA have attracted broad research interest. PDA systems have been shown to organize in vesicles,10,11 Langmuir monolayers,12–14 self-assembled films,15,16 and single crystals.17,18 PDA has been also assembled as components within other “host” matrixes, including inorganic matrixes,19–21 other polymers,22,23 and even living cells.24 Remarkably, it has been shown that PDA generally retains its...
chromatic properties in these configurations, thus opening the way to construction of varied sensing assemblies.

This review aims to summarize recent innovative developments in PDA research. We do not cover here the broad PDA literature since the inception of the field, nor discussing the basic structural and physical properties of PDA systems. Several reviews on PDA properties and applications have been published in the past several years.\(^{25-27}\)

Due to space limitations, we discuss below only selected reports, designed to present the main aspects of the field, with particular emphasis on recent developments that open new scientific and technological horizons. Thematically, the Review is divided into four parts: we begin with a brief overview on the basic molecular properties of PDA. This is followed by sections depicting synthetic routes for modification of the diacetylene monomeric units, often giving rise to polydiacetylene assemblies exhibiting distinct physico-chemical properties; new PDA-based composite materials of PDA-based materials; and practical applications emanating both from the development of new synthesis schemes as well as overall materials designs and properties. Overlap naturally exists between these topics, as many publications span more than one of the above general topics.

**Basic molecular properties of PDA**

The unique chromatic properties of PDA systems arise from the molecular properties of the polymer. PDA is formed through 1,4 addition of aligned diacetylenic monomers, initiated by ultraviolet (UV) irradiation (Fig. 1). The diacetylene monomers do not absorb light in the visible region, while polydiacetylene appears intense blue (absorption peak at around 650 nm) due to electron delocalization within the linear \(\pi\)-conjugated framework, and corresponding to a \(\pi-\pi^*\) transition.

As indicated above, the colorimetric transformations of PDA, induced by a variety of external stimuli, have likely been the most interesting and technologically-attractive feature of PDA systems. The significant shift of the absorption peak from around 640 nm (the blue phase) to around 500 nm (the red phase) is ascribed to disruption of the conjugated network, resulting in shorter electronic delocalization lengths. The red phase of PDA is accompanied by intense fluorescence, which further exhibits negligible bleaching, contributing to utilization of the fluorescence properties in varied sensing applications.

Despite decades of studies, elucidating the exact mechanisms responsible for the chromatic transformations of PDA has not been fully accomplished. It has been recognized that the shifts in spectral absorbance are closely linked to structural modifications of the conjugated polymer framework.\(^{14}\) Early models accounting for the spectral/structural modulations proposed transformation of the polymer backbone from the ene-yne to a butatriene conformation.\(^{28}\) Recent crystallographic and theoretical investigations have illuminated intimate structural aspects pertaining to the chromatic properties. In particular, it has been established that the pendant side-chains of PDA play a prominent role in affecting the chromatic transformations. Specifically, the interactions between the functional groups of the side-chains are believed to significantly affect the overall conformation of the polymer chain, primarily rotations around the C–C bonds (Fig. 1) affecting the planarity of the backbone and concomitant overlap between adjacent \(\pi\) orbitals.\(^{14}\) Indeed, theoretical calculations suggested that even rotation of a few degrees of the side-groups around the C–C bond would give rise to a significant change of the \(\pi\)-orbital overlap and resultant blue-red transition.\(^{29}\)

The realization that PDA side-chains exhibit significant effects upon the chromatic properties of the polymer has led to intense research aiming to modulate PDA spectral response through synthetic modifications of side-chain functional groups. Efforts have been directed, for example, to alter the crystal packing of the individual monomers – the essential precondition to photo-polymerization and the resultant linear polymer chains – via side-chain modification. A notable consequence of the close links between crystal packing and pendant side-chain orientation is the achievement of color reversibility. While most of the early work on supramolecular PDA assemblies demonstrated irreversible color transformations, there have been an increasing number of reports depicting color-change reversibility via chemical modification of the PDA side-chains, thus altering the molecular packing and topochemical transformations within the polymer modules.\(^{30,31}\)

**Synthetic pathways**

Early work in the field has predominantly focused upon the “standard” diacetylene monomers 10,12-tricosadynoic acid and 5,7-pentacosadynoic acid (Fig. 2). These monomers, currently commercially available, can be aligned in aqueous solutions and the hydrogen bond network maintained among the carboxylic headgroups enable the occurrence of ene-yne
transformation and formation of the polymerized conjugated backbone system.

Recent years have witnessed a proliferation of synthesis schemes producing novel diacetylene monomeric units. Numerous examples have been presented in the literature, and some examples, by no means exhaustive, are presented in the following. Interesting peptide–diacetylene monomers in which the diacetylene backbone is flanked by peptide moieties have been reported (Fig. 3). Some members of the peptide–diacetylene family could be polymerized using UV irradiation, although the chromatic properties were generally different compared to native PDA. Polymerization times, for example, were significantly longer (around 30 minutes) and pH-dependent, and the colorimetric transformations in the PDA derivatives were not readily induced. The peptide–PDA assemblies, however, displayed both unique nano-structured configurations (nanowires, “nano-mesh” morphologies), as well as macroscopic organization – producing potentially-useful hydrogel networks.

Other PDA–peptide conjugates have been synthesized, bestowing interesting properties to the resultant materials. Vesicles comprising a PDA–histidine derivative and PDA–pentathylene which further contained a fluorescent moiety, constituted vehicles for binding and detection of lipopolysaccharides (LPS) – the prominent recognition units displayed on bacterial surfaces. Specifically, the organized positively-charged amino residues in the synthetically-modulated PDA vesicles mimicked the recognition surface of polymyxin-B, a natural antibiotic which specifically binds to LPS primarily through electrostatic attraction.

While that work presents a nice example of diacetylene monomer derivatization enabling distinct recognition capabilities, the modified vesicles in that case also exhibited photophysical properties that were different from “conventional” PDA systems. Specifically, the PDA assembly displayed an interesting fluorescence “turn-on” mechanism: the initial state of the vesicles, which were in the fluorescent “red” phase, was non-fluorescent due to energy transfer between the PDA network and a surface-displayed fluorescent dye; binding of LPS-presenting bacteria to the vesicles prevented the energy transfer and gave rise to enhanced fluorescence. A similar study depicted the use of peptide-displayed PDA for detection of trinitrotoluene (TNT), the common ingredient in explosives. The peptide moiety in that system served as the recognition element for the TNT molecules.

Monomeric diacetylene units have also been derivatized with non-peptidic residues. An interesting scheme was recently reported in which “diacetylene macrocycle” units have been synthesized, producing “columnar structures” upon polymerization (Fig. 4). The thrust of that study has been the assembly of porous “molecular columns” enabled through the polymerization process of the diacetylenic macrocycles. In essence, the polymerized diacetylene network in this case provided the “scaffolding” for the columns, rather than the means for optical/spectroscopic transformations.

A systematic study has recently investigated the crystalline organizations of diacetylene monomers functionalized with different phenyl-containing units. The goal of that work was to assess the polymerization pathways of the materials, particularly the effect of the substituted moieties upon the packing of the monomeric diacetylenic units and feasibility of the concurrent topochemical polymerization. Specifically, the experiments revealed that despite the bulky phenyl-substituted headgroups, aromatic perfluorophenyl–phenyl interactions facilitated efficient polymerization and formation of the conjugated PDA backbone. This study highlights an important aspect of PDA chemistry, specifically the effect of monomer modification upon polymerization and photophysical properties. Indeed, while diacetylene monomers can be readily manipulated via diverse synthetic routes, in many cases the resultant molecules do not undergo topotactic polymerization to the polymer phase since...
the structural modifications disrupt the monomer alignment essential for the ene-yne transformation.\textsuperscript{39,40}

Another recently-reported synthetic pathway has focused upon modification of diacetylene monomers with a fluorescent coumarin headgroup.\textsuperscript{41} The display of the dyes gave rise to interesting structural and optical properties upon polymerization. Somewhat unexpectedly, the relatively bulky coumarin moieties did not prevent polymerization. Moreover, Langmuir–Blodgett films of coumarin–PDA exhibited remarkable reversibility of temperature-induced color change. Also noteworthy, the polymerized film assemblies were chiral even though the coumarin–diacetylene monomers were achiral, confirming the distinct ordering of the functionalized diacetylene units in the polymer configuration.

Attaining reversibility of PDA chromatic changes has been among the most remarkable achievements in this field. In that regard, synthetic progress has often gone beyond establishing a firm understanding of the molecular mechanisms pertaining to color reversibility in PDA systems. It is generally accepted that reorganization of the hydrogen bond network through synthetic manipulations of the diacetylene headgroups is the core factor making possible reversible blue-red transformations of PDA. Accordingly, most reported reversible PDA systems have employed varied schemes for manipulating the polar headgroups of the polymer.

Almost all examples of reversible PDA-based systems have focused upon thermally-induced transformations, i.e. blue-red changes brought about by heating, while the reversible red-blue transformation occurring following cooling. Among the diacetylene units shown to affect color reversibility following polymerization were monomers displaying 2,2,2-trifluoro-N-(4-hydroxyphenyl)acetamide,\textsuperscript{42} 3-carboxypropylpentacosa-10,12-dynamide,\textsuperscript{43} azo chromophore-functionalized diacetylene,\textsuperscript{44} secondary amine salts,\textsuperscript{45} naphthylmethylammonium carboxylate,\textsuperscript{46} and non-polar benzyl moieties.\textsuperscript{47}

Intriguing reversible thermochromism has been demonstrated in a supramolecular system in which PDA was not derivatized (\textit{i.e.} the conventional 10,12-pentacosadiynoic acid has been used).\textsuperscript{48} In that system, temperature-induced reversible color transitions were traced to a hierarchical organization in which the PDA domains were encapsulated within a poly(vinylpyrrolidone) (PVP) matrix (Fig. 5). The intercalation of PVP domains within the PDA framework was the likely factor enabling reorientation of the PDA headgroups affecting reversibility of the conjugated polymer network length (and consequent reversible chromatic transitions).

Researchers have reported the use of synthetic derivatives of diacetylene monomers for assembly of other functional species. Fig. 6 depicts a microfluidic scheme in which PDA microbubbles were prepared for potential use in biomedical imaging.\textsuperscript{49} The diacetylene monomers in that assembly were functionalized with varied headgroups, particularly polyethylene-glycol (PEG), designed to achieve efficient embedding of gas molecules (used as imaging contrast agents), and minimize bubble aggregation. Indeed, the PDA framework in this system was not aimed to achieve sensing capabilities through the colorimetric/fluorescence properties of the polymer, but rather was employed as a resilient and stable gas-encapsulating shell aimed at achieving a better stability of the microbubbles in physiological environments. Accordingly, these polymerized shell microbubbles might function as contrast agents in ultrasound imaging.\textsuperscript{50}

### PDA-based composite materials

Composite materials comprising PDA mixed with or coupled to other molecular species have been pursued, yielding in many cases advanced materials exhibiting interesting properties. PDA–carbon nanotubes (CNTs) are a case in point.\textsuperscript{51,52} In such systems, the surfaces of single-walled CNTs (SWCNTs) have been used as a “template” upon which organization and polymerization of the diacetylene units occurred. The resultant composite materials exhibited intriguing properties.

In one study, “ring-shaped” polydiacetylene structures formed upon the SWCNT surface were capable of solubilizing...
and stabilizing highly hydrophobic substances, such as membrane proteins and dyes, through interactions with the pendant side-chains of the polymer. Accordingly, such PDA–SWCNT constructs might find uses as “smart detergents” in cosmetics, membrane proteins structure determination, and others.

While that work concentrated on the structural/functional features of PDA–SWCNT systems, it should be emphasized that SWCNTs are also expected to affect the photophysical properties of the nanotube-associated PDA. Significantly, a recent study has demonstrated that CNTs not only provided a physical framework upon which polymerization could be carried out, but also constituted a source of fluorescent energy, transferred to the PDA via Forster resonance energy transfer, giving rise to intense emission of the material in the near infrared (NIR) spectral region. The PDA–CNT assemblies could also take advantage of the known “stealth” properties of CNTs, thus particularly employed in cellular imaging applications.

A conceptually-similar PDA–nanostructure system has utilized magnetic nanoparticles (NPs) as a template for assembly of the chromatic polymer. The organized PDA layers in this case were formed upon the surface of magnetic Fe₂O₃ NPs through non-covalent hydrogen bonds between the diacetylene moieties and the polar surface of the MNPs. Remarkably, the magnetic particles not only enabled the topotactic polymerization of the monomers into the extended polymer network, but experiments demonstrated that the blue-red transformation in this case could be induced by application of a magnetic field (Fig. 7), presumably associated with localized heating of the NP surface through alternating magnetic field. This unusual “magnetochromic effect” might find uses in sensing and electro-optic applications.

Modulation of the diacetylene headgroups has led to preparation of self-assembled species displaying remarkable structural and functional properties. A diacetylene monomer composed of a long alkyl chain and bulky hydrophilic nitrotriacetate (NTA) headgroup (Fig. 8) was shown to undergo unique self-assembly processes and, furthermore, exhibit potentially useful biological imaging functionalities. The researchers have discovered that self-assembly of these diacetylenic monomers can be modulated through the pH conditions of the solution. Indeed, remarkable morphologies could be attained through alteration of the solution acidity, including ribbons, twisted ribbons, spirals, micelles, and others. That work underscored both the fundamental roles played by the diacetylene headgroups in shaping the self-assembly properties of the polymer, as well as the sophisticated synthetic means available to modulate PDA structures and associated functionalities.

Conjugation of PDA with inorganic, porous materials has been a major route in PDA technology development. In general, porous materials constitute attractive targets for practical applications involving PDA. This is due to the large (internal) surface areas of porous matrixes useful for immobilization of high polymer concentration, and transparency – making possible exploiting the optical/spectroscopic properties of PDA within the inorganic framework. An example of this concept has been the incorporation of PDA within templates of anodized aluminum oxide (AAO) – a popular porous matrix employed for “template-synthesis” applications. AAOs contain ordered porous “tubes” which dimensions can be tuned via control of the synthesis conditions. A recent study has demonstrated that PDA “nano-fibers” could be assembled within an AAO template. That work underscored important facets of what can be referred to as “template-directed PDA synthesis”.

Specifically, the AAO template enabled fabrication of highly uniform, crystalline PDA structures (Fig. 9). Furthermore, the

![Fig. 7](image1.png) **Fig. 7** PDA–magnetic nanoparticle conjugates. Schematic illustration of the preparation of “magnetochromic NPs” comprising Fe₃O₃ cores coated with diacetylene moieties. Reprinted with permission from X. Chen et al., Angew. Chem., Int. Ed., 2011, 50, 5486–5489. Copyright (2011) John Wiley and Sons.

![Fig. 8](image2.png) **Fig. 8** Diacetylene–nitrotriacetate (DA–NTA) monomers. Top: molecular structure of the monomer; bottom: polymerization through UV irradiation – the bulky headgroup did not adversely affect the polymerization process. Reprinted with permission from E. Gravel et al., Chem.–Eur. J., 2011, 18, 400–408. Copyright (2011) John Wiley and Sons.
crystalline PDA fibers could be released from the AAO host matrix without adversely affecting their structural integrity. Particularly noteworthy is the fact that PDA could retain its chromatic properties – polymerization and chromatic changes induced by external stimuli.

In some experimental setups, PDA has not been used as a signal-generating component but rather as “smart scaffolding”. A pertinent example has been the assembly of “nano-containers” for controlled drug release comprising PDA and a cyclodextrin (CD) derivative. The vesicular particles in that system could be triggered to release their molecular cargo through two externally-applied stimuli. Specifically, light illumination (e.g. photo-activation) was accomplished through coupling of the CD moieties to photo-switchable azobenzene. Furthermore, pH-induced release could be achieved via the known sensitivity of the PDA network to pH changes. Altogether, such PDA-based nano-containers point to potential applications of PDA systems in drug delivery, taking advantage of their high stability, on the one hand, and intrinsic structural triggering mechanisms, on the other hand.

Several studies have examined the structural and chromatic consequences of association of guest species with PDA host matrixes. Unlike most PDA investigations focusing upon vesicular PDA assemblies or thin films, a recent report described the effect of alkylamine guest molecules upon the organization and properties of PDA crystals. Fig. 10 depicts the impact of an alkylamine molecular guest upon the organization of the PDA host. Specifically, the researchers have found that intercalation among the alkyl chains of the guest molecules affected both the crystal structure of the resultant supramolecular assembly, as well as extent and dynamics of the chromatic transitions of the PDA crystallites following addition of the alkylamines.

**Applications of PDA systems**

Historically and up to the present, the main drawing point of PDA systems have been their remarkable chromatic sensing capabilities. In particular, the incorporation of diverse molecular recognition elements within PDA assemblies has made PDA a highly versatile sensing platform. Importantly, since the PDA headgroups are intrinsically negatively-charged, many reported biosensing applications have focused on detection of positively-charged amphiphilic molecules. Inclusion of positive units within PDA assemblies, however, can bestow sensing capabilities of negative molecules as well. A recent example has been the use of liposomes comprising diacetylenic units covalently displaying positive NH₃⁺ moieties for colorimetric detection of heparin, an important polyanionic biological molecule. Interestingly, that study indicates that chromatic transformations did not occur in all cases in which positive units were displayed on the liposome surface; rather, color transitions were recorded only when the positive residues were attached to distinct molecular “arms”. Furthermore, the most pronounced chromatic response was induced when sizeable anionic polymers (i.e. heparin) were present in the tested solution, highlighting sensitivity of PDA systems to intimate variations even in electrostatic interactions between the analyte and vesicle surface.

The significance of steric factors in affecting the chromatic transformations of PDA vesicles induced by molecular recognition events was further analysed. That study utilized a micro-array liposome-based system to investigate the fluorescence changes induced by interactions between peptide components of the influenza virus (as well as the viral particles themselves) and their respective antibodies. Based upon the experimental data, the researchers have concluded that steric repulsion between vesicle-bound ligands play more significant
roles in affecting the structural/chromatic transformations of PDA as compared to the binding strength between the analyte and vesicle-displayed recognition element (Fig. 11). This interpretation, if proven to be universal for PDA systems, is important, since it could shape the design of PDA-based sensors aiming to achieve optimal sensitivity.

As mentioned above, the incorporation of recognition elements within PDA-based vesicles has been the most widely-used vehicle for sensing applications using the conjugated polymer, and diverse systems have been reported. A recent study has demonstrated detection of apoptotic cells using PDA vesicles.64 That sensing scheme was based upon the well-recognized phenomenon in which increased exposure of phosphatidylserine (PS) occurs on the surface of apoptotic cells.65 Accordingly, the researchers succeeded to achieve specific response to apoptotic cells through covalent attachment of a Zn$^{2+}$-stabilized complex onto the PDA network (Fig. 12). The binding between the complex and PS units in that system was the recognition event triggering the colorimetric transformations of the vesicles. An interesting construct has been reported in which PDA vesicles comprising antibodies against the H5N1 strain of influenza virus were embedded upon the surface of polystyrene beads.66 The antibody was covalently attached to the bead–PDA system, enabling detection of viral particles. The bead–PDA constructs were stable in different solution conditions, enabled naked-eye detection of viral particles, and might be implemented in microfluidic device applications through placing the beads within device microchannels.

Another example of the versatility and sensing power of PDA assemblies derivatized with recognition units is a recent report describing colorimetric detection of gaseous compounds by PDA-based vesicles comprising oxime functional groups.67 The significance of this work lies in the remarkable specificity attained by the oxime–PDA vesicles towards toxic volatile species that might be employed in chemical warfare scenarios.

An interesting vapor sensing application accomplished through a PDA-based approach has been recently reported.68 In that study, the researchers combined several notable features generating a potentially powerful sensing platform. First, they succeeded to couple diacetylene monomers to a filter paper, without adversely affecting the polymerization (and chromatic) properties of the PDA framework. Second, the coupled PDA–paper system exhibited sensitivity to vapors of volatile organic compounds (VOCs), undergoing visible colorimetric transformations in the presence of the compounds in the gas phase. Moreover, to achieve specificity, the researchers prepared a matrix in which each component comprised a diacetylene monomer displaying a different headgroup. Together, the array of distinctly-functionalized PDA units produced colorimetric “fingerprints” for different VOCs, akin to “artificial nose” detection concepts.69

In few cases, displayed functional units can bestow chromatic response to diagnostically-important anionic species. An example of such a system has been the construction of thin films comprising PDA derivatized with imidazolium units, and the use of such films for sensing anionic surfactants.70 Interestingly, the imidazolium-functionalized PDA exhibited unusual blue-yellow and blue-orange transformations (besides the more conventional blue-red changes), as well as reversibility of thermoehromic transitions.

In some instances, the sensitivity of PDA detection schemes has been enhanced through more complex, hybrid detection schemes in which the PDA detector was coupled to orthogonal signal enhancement mechanisms. An example of such an approach has been a system for detection of the cancer marker prostate-specific antigen (PSA) through PDA chromatic response.71 The basic sensing approach relied on conjugating anti-PSA monoclonal antibodies (mAbs) onto the PDA vesicle surface. However, to amplify the chromatic signal magnetic beads coupled to polyclonal antibodies (pAbs) against PSA were further added to the reaction mixture. The consequent binding of the pAb–beads to the vesicles produced a significant

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Fig. 11  Significance of steric repulsion vs. analyte binding for PDA chromatic transitions. Effects of different stimuli upon the mechanical perturbation and concomitant color transformations of PDA vesicles. Reprinted with permission from S. Seo et al., Macromol. Rapid Commun., 2013, 34, 743–748 Copyright (2013) John Wiley and Sons.

Fig. 12  “Turn-on” fluorescence detection of apoptotic cells based upon phosphatidylserine (PS) recognition. Principle of “turn-on” fluorescence detection of apoptotic cells through binding of Zn(PDA) to PS displayed upon the cell exterior. Reprinted with permission from Y. S. Cho et al., Chem.–Asian J., 2013, 8, 755–759. Copyright (2013) John Wiley and Sons.
mechanical perturbation giving rise to enhanced chromatic response of the PDA.

Coupling PDA with other functional materials could open avenues to intriguing novel applications. A recent study demonstrated that a solution of surfactants and diacetylene monomers could be used as ink. Application of the diacetylene-containing ink onto paper through conventional inkjet printing produced chromatic patterns (Fig. 13). Remarkably, upon selection of the appropriate diacetylene monomers, the thermochromic transitions of the PDA-based ink were reversible — e.g. from blue to red upon heating, back to blue following cooling.

Increasing the sensitivity of PDA chromatic properties to environmental stimuli through coupling to additional species has been a major driving force for research efforts aiming to create PDA-based sensing devices. Fig. 14 depicts a recent example of a PDA/sol–gel composite material for detection of bacterial biofilms. In that study, PDA/sol–gel films were assembled on glass substrates through a dip-coating technique. Microscopic analysis of the resultant films indicated that distinct PDA domains were formed within the glassy sol–gel matrix (Fig. 14). Remarkably, when the PDA/sol–gel films were placed in solutions containing biofilm-forming bacteria, they underwent gradual blue-red transformations.

The colorimetric transitions (and corresponding fluorescent emission) were ascribed in that case to the dense biofilm matrix forming upon the PDA domains, subsequently producing the localized mechanical stress inducing the structural modulation of PDA.

The conjugated network of PDA provides a useful means for fabricating rigid, stable supramolecular assemblies. A synthetic route has been recently presented in which diacetylenic amphiphile monomers were designed, subsequently forming micellar structures that could be used for gene delivery applications. Fig. 15 depicts the experimental scheme. The diacetylene surfactant monomers in this case displayed positive moieties, designed to anchor DNA moieties — thus forming lipoplex-type assemblies. The polymerized PDA–surfactant micelles were stable in physiological solutions, and, importantly, exhibited lower cytotoxicity compared to conventional surfactant-based lipoplexes. Notably, the cationic PDA micelles were shown to be effective gene delivery vehicles, and photopolymerization actually enhanced their gene transfection efficiency. This result is likely related to the high stability of the conjugated polymer framework, facilitating better transport of the gene cargo to the cell nucleus compared to more conventional non cross-linked lipoplexes.

**Summary and future directions**

Since their first appearance on Science stage more than 40 years ago, polydiacetylenes have evolved and branched into diverse fields and applications, both in basic research as well as technology. Recent years have witnessed a significant expansion in PDA research, from the “classical” applications of PDA in biosensing and chemosensing, towards new schemes demonstrating PDA-based materials as drug delivery platforms.
molecular carriers, and others. This review summarized the main aspects of current PDA research and recent developments in synthesis, materials design, and practical applications of this unique polymer.

Importantly, while tremendous progress and sophistication of PDA systems have been achieved in recent years, identifying definite mechanistic aspects pertaining to PDA chromatic properties and transitions is still somewhat “work-in-progress”. In particular, elucidation of the precise linkage between the colorimetric/fluorescence transitions and structural changes of PDA networks is still sought. In this context, the comprehensive synthetic “tool-box” currently available to researchers in the field should enable further testing of varied hypotheses pertaining to the relationships between changes of PDA crystal packing induced by external stimuli and corresponding structural/chromatic transformations. Such physico-chemical analyses are expected to constitute an active research area in the PDA field.

In conclusion, like many scientific disciplines before it, the “critical mass” of research groups and activities focused on PDA promise to greatly expand the impact and future promise of the field. New synthetic pathways will continue to modulate supramolecular PDA assemblies, and particularly the physical properties of the materials. While the unique colorimetric and fluorescent characteristics of PDA will likely continue to attract significant interest, it is expected that other molecular features of the polymer, such as enhanced stability in different solutions, morphological control, and macroscopic properties, will be increasingly exploited. Last but not least, after a long “gestation”, practical utilization of PDA systems is expected to appear in greater abundance in the technology and commercial arenas.

Notes and references