Journal of Materials Chemistry C



View Article Online

PAPER



Cite this: DOI: 10.1039/d0tc02721a

Simultaneous and visual detection of cysteamine based on Michael addition reaction with polydiacetylene liposomes[†]

Thanh Chung Pham, ^(b) ^a Seongman Lee,^a Ye Rim Son,^b Minseok Kwak, ^(b) ^{ab} Hyun Sung Kim ^(b) *^b and Songyi Lee*^{ab}

In this study, we report the fabrication of a highly sensitive colorimetric and fluorometric sensor comprising self-assembled polydiacetylene (**PDA**) liposomes for the measurement of cysteamine concentration. The *N*-maleimidomethanol (**HM**) moiety was used as the Michael addition acceptor, which reacts with the thiol groups in cysteamine to generate maleimide–thiol conjugation resulting in the conformational transition of the conjugated backbone. Furthermore, this chemosensor system displays a clear blue-to-red colorimetric transition in the presence of cysteamine among various biothiols with high selectivity and sensitivity owing to the structural specificity of cysteamine. The resulting **PDA** solutions were analyzed *via* FE-SEM, UV-vis, fluorescence and Raman spectroscopy, and chromoisomerism for naked-eye visualization. This chemosensor provides a convenient method for the detection of cysteamine in aqueous solution and in real samples.

Received 8th June 2020, Accepted 3rd August 2020

DOI: 10.1039/d0tc02721a

rsc.li/materials-c

Introduction

Intracellular thiols, such as cysteine (Cys), homocysteine (Hcy), glutathione (GSH) and cysteamine (Cyst), play a crucial role in cellular growth, metabolism, and the maintenance of biological systems.1 However, abnormal concentrations of thiols are implicated in a variety of health conditions, such as liver damage, skin lesions, delayed growth and edema.² Therefore, it is highly important to report changes in thiol concentrations via real-time monitoring. Cysteamine is an aminothiol compound (HS-CH₂-CH₂-NH₂) synthesized endogenously via the degradation of coenzyme A and converted to the neurotransmitter hypotaurine by cysteamine dioxygenase.³ Cyst has been used as a therapeutic agent for the treatment of cystinosis, cystic fibrosis, neurodegenerative disorders such as Huntington's disease and Parkinson's disease, and nonalcoholic fatty liver disease.⁴ Cysteamine hydrochloride (HS-CH₂-CH₂-NH₂· HCl) is also used in cosmetics as an antioxidant, a hair straightening agent, and a hair waving agent. However, recent studies in Europe and Japan reported that Cyst acts as an allergen affecting hairdressers.5 Biothiols have been analyzed

using several analytical techniques, including high-performance liquid chromatography (HPLC) with electrochemical,⁶ fluorescence⁷ and UV/Vis-absorbance detection,⁸ capillary electrophoresis,⁹ and gas chromatography with flame photometric detection.¹⁰ Generally, these techniques have been used in combination in order to increase the sensitivity and selectivity of the detection; however, this makes the procedure more complex and elaborate besides being time-inefficient and laborious. Recently, Singh et al. reported the detection of Cyst via UV/Vis spectroscopy using polydentate aromatic nanoparticles complexed with Cu2+.11 In addition, Pathak et al. and Kim et al. designed a N-doped carbon¹² and a three main component-containing long chain¹³ through one-photon and two-photon fluorescent probes for Cyst detection, respectively. However, most of these methods and materials were developed for the analysis of biological fluids with complicated sample pretreatments, such as derivatization. To our knowledge, no studies have performed the quantification of Cyst using a colorimetric sensor system.

Conjugated polymer systems are an enabling class of materials for various functions such as sensing matrices,¹⁴ organic semiconductors,¹⁵ microelectronics,¹⁶ and drug delivery systems (DDS).¹⁷ Polydiacetylenes (PDAs) are well-known conjugated polymers, which have been extensively investigated and utilized as an attractive platform in sensing applications due to their unique optical properties.¹⁸ The monomers of **PDA** easily self-assemble into liposomal structures in aqueous solution. PDAs can be generated *via* UV or γ irradiation, or by

^a Department of Industry 4.0 Convergence Bionics Engineering, Pukyong National University, Yongso-ro, Nam-gu, Busan 48513, Republic of Korea.

E-mail: slee@pknu.ac.kr

^b Department of Chemistry, Pukyong National University, Busan 48513, Republic of Korea. E-mail: kimhs75@pknu.ac.kr

Republic of Korea. E-mail: kimhs75@pknu.ac.kr

 $[\]dagger$ Electronic supplementary information (ESI) available. See DOI: 10.1039/ d0tc02721a

Paper

plasma treatment of self-assembled diacetylene monomers.¹⁹ No catalysts or initiators are required for the polymerization, which ensures that the PDAs are produced with a high degree of purity. PDA undergoes a color shift from blue to red upon environmental stimulation, accompanied by fluorescent transition. The stimulus-induced blue-to-red transition and the fluorescence enhancement of PDA facilitate the development of various chemosensors using the polymer. The dual signal generation is mainly attributed to the interfacial perturbation of PDA caused by external stimuli, which subsequently induce a conformational change in the PDA-conjugated backbone. To date, a variety of PDA-based sensors have been developed for the detection of changes in temperature²⁰ and mechanical force,²¹ as well as various analytes.²² Moreover, the PDAcontaining sensing systems have been adapted to various architectural constructs such as liposomes, fibers, films, and organic-inorganic hybrids, which are used as matrices in biosensing applications.²³ A popular strategy to promote ideal sensing properties has been to introduce special receptors into the PDA system. In this approach, the receptor moiety is covalently linked to a monomeric diacetylene acid, followed by direct self-assembly. Recently, Kim et al. have designed a colorimetric and fluorometric polydiacetylene sensor based on the decomposition of a pyridine-mercury complex.²⁴ However, the PDA impregnated paper undergoes a blue-to-red color change in the presence of alkyl-, aryl- and bio-thiols, which has not been expected for selective sensors.

In the current study, we developed a simple and effective analytical method for the selective and sensitive quantification of Cyst using a conjugated **PDA-HM** sensor system carrying the receptor for cysteamine. The reaction of Cyst and the **HM**moiety in the polymer network based on Michael addition reaction and the structural specificity of Cyst play an important role in the color change from blue to red as well as in the spectral results of **PDA-HM**. To the best of our knowledge, this study reports an unprecedented Cyst sensor with simultaneous and visual detection.

Experimental

Materials and methods

We purchased 10,12-pentacosadiynoic acid (PCDA), oxalyl chloride, maleimide, and formaldehyde from TCI, South Korea. All organic solvents used in the synthesis were obtained from Sigma-Aldrich and used without further purification. Real samples were purchased from a drugstore, including 'Biomed – Aloe moisture protein BB PER', BVI – Ceramide Clinic Perm', 'Nico Nico – Blue smart wave', and 'Nico Nico – Red smart wave', all of which contain cysteamine, and 'Biomed – Amino acid L.P.P. Perm' that does not contain cysteamine. Flash chromatography was carried out on silica gel (230–400 mesh), followed by the determination of ¹H and ¹³C NMR spectra using a Bruker Advance 400 MHz and 600 NMR spectrometer. Mass spectra were obtained using a maXis HD (Bruker). UV absorption spectroscopy measurements were conducted using a V-730

UV-Visible spectrophotometer (Jasco) at room temperature. Fluorescence emission spectra were obtained using an F-7000 fluorescence spectrophotometer (Hitachi High-Tech). The structures and morphologies were analyzed with a field emission scanning electron microscope (FE-SEM, CX-200, COXEM, Republic of Korea; JEM-2100F, JEOL).

Synthesis of *N*-(2-hydroxymethyl)maleimide (HM). Maleimide (1.0 g, 10.30 mmol) and 36% aq. formaldehyde (3.16 mL, 41.20 mmol) were dissolved in 10 mL deionized water. The mixture was stirred and heated to reflux for 4 h. The solution was cooled to room temperature, then extracted with EtOAc, dried over Na₂SO₄, and concentrated in a vacuum to obtain a white residue (yield: 59.2%) with the following spectral details: ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.07 (s, 2H), 6.29 (s, 1H), 4.77 (s, 2H); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 171.16, 135.46, 60.13. ESI HRMS *m*/*z* = 150.0163 [M + Na]⁺, calc. for C₅H₅NO₃ = 127.03.

Synthesis of PCDA-HM^{22b}. Oxalyl chloride (0.7 mL, 5.51 mmol) was added dropwise to a CH₂Cl₂ (20 mL) solution containing 10,12-pentacosadiynoic acid (PCDA) (0.5 g, 1.34 mmol) under N₂ at room temperature. After 1 h of stirring, DMF (0.1 mL) was added to the solution. The resulting mixture was stirred for 4 to 6 h, followed by concentration under reduced pressure to obtain PCDA-Cl, which was used directly without any purification by dissolving in THF (30 mL). To this mixture was added a solution containing 125 mg (0.98 mmol) of HM and 0.4 mL (4 mmol) of triethylamine in 10 mL of THF. The resulting solution was stirred overnight at room temperature under N2. After evaporating the liquid, the crude product was dissolved with H₂O, extracted with EtOAc and purified via silica gel column chromatography (hexane-EtOAc: 1-1) to obtain a white solid (yield: 29.2%) with the following spectral data: ¹H NMR (400 MHz, chloroform-d) δ 6.80 (s, 2H), 5.52 (s, 2H), 2.27 (t, J = 7.5 Hz, 2H), 2.24-2.17 (m, 4H), 1.57 (p, J = 7.5 Hz, 2H),1.52–1.43 (m, 4H), 1.40–1.31 (m, 4H), 1.23 (d, J = 4.9 Hz, 24H), 0.88-0.83 (m, 3H); ¹³C NMR (101 MHz, chloroform-d) δ 169.04, 134.89, 60.26, 33.89, 32.01, 29.74, 29.72, 29.71, 29.58, 29.45, 29.20, 29.11, 29.01, 28.95, 28.82, 28.44, 28.37, 24.65, 22.79, 19.29, 19.27, 14.23. ESI HRMS $m/z = 484.3420 [M + H]^+$, calc. for $C_{30}H_{45}NO_4 = 483.33$.

Preparation for the diacetylene assembly and photopolymerization²⁰. The PCDA-HM monomer (9.67 mg, 0.02 mmol) was dissolved in DMF (1 mL) and injected into 19 mL of deionized water while shaking the mixed solution to yield a total monomer concentration of 1 mM. The sample was then sonicated at 80 °C for 40 min. The resulting solution was filtered through cotton, yielding a filtrate that was cooled down to 4 °C for 12 h. Polymerization was carried out at room temperature by irradiating the solution with 254 nm UV light (1 mW cm⁻²) for 10 min.

Characterization of PDA-HM liposomes. Before and after treatment with Cyst, the morphologies of **PDA** liposomes were characterized *via* FE-SEM. Samples were freshly prepared and dropped on small fragments of silicon wafers, which were dried at room temperature overnight. The samples were then coated with 3–4 nm-thick Pt for 40 s before FE-SEM examination at an accelerating voltage of 15 kV. The Raman spectra were recorded

using an NRS-5100 (Jasco) Raman microscope with 785 nm radiation.

Results and discussion

Design and synthesis of the monomer and preparation of the polymer

The chemosensor was designed according to the following principles: (1) the chromatic transition of polydiacetylene is very sensitive to terminal perturbations, and (2) maleimide-thiol conjugation *via* Michael addition occurs under mild conditions. The synthetic route of the monomer **PCDA-HM** is depicted in Scheme 1. The reaction of maleimide and formal-dehyde afforded a detection group **HM** with a 59.2% yield.²⁵ In addition, the **HM** moiety reacted with **PCDA** to yield **PCDA-HM** as a white solid with a 29.2% yield, followed by column chromatography with hexane : EtOAc = 50 : 50 and further treatment using Sephadex-LH 20 with chloroform : MeOH = $60: 40.^{22b}$ The synthesized **PCDA-HM** monomer was characterized using ¹H NMR, ¹³C NMR and ESI HR-MS (ESI[†]).

The self-assembled monomers of **PCDA-HM** were converted to **PDA** polymers (**PDA-HM**) *via* exposure to 254 nm UV irradiation for 1 min, resulting in a clear blue-colored solution (Scheme 2).²⁰ The individual **PCDA-HM** monomer self-assembled and was polymerized easily because of the extra π - π interaction and the less steric hindrance associated with the relatively small head group.

As illustrated in Scheme 2, after the self-assembly of **PCDA-HM** into liposomes, the suspension showed a blue color. Furthermore, Cyst treatment of the blue **PDA** liposomes directly restored the fluorescence accompanied by a clear color change from blue to red. Finally, to demonstrate the practical application of our chemosensor, the **PDA** system was successfully used to detect Cyst in aqueous solutions with high sensitivity and selectivity.

Characterization of PDA-HM liposomes

The prepared **PDA** liposomes were characterized *via* FE-SEM and Raman spectroscopy. The SEM images of PDAs revealed



Scheme 1 Synthesis of the monomer PCDA-HM.



Scheme 2 Self-assembly and polymerization of PCDA-HM and the schematic illustration of Cyst analysis using PDA liposomes.

spherical particles with a diameter of ~ 200 nm (Fig. 1a and Fig. S8, ESI[†]). The addition of Cyst (100 µM) induced structureless images, possibly due to the aggregation, as presented in Fig. 1b. The conjugated backbone of PDA-HM liposomes was subjected to Raman spectroscopy, since the chromatic transition of PDA from blue to red is highly related to the conformational change of the PDA backbone. To obtain an insight into the polymer backbone of PDA-HM liposomes in response to Cyst, Raman spectra were then recorded before and after the treatment with Cyst at room temperature (Fig. 1c). The characteristic C = C and C = C stretching frequencies of blue phase PDAs appear at 2120 and 1516 cm^{-1} , which shift to 2079 and 1452 cm⁻¹, respectively, after treatment with Cyst. This result indicates that the conjugated backbone in the red phase was twisted after the Cyst treatment, and the conjugation in the blue phase at room temperature was greater than that in the red phase.

Cysteamine detection using PDA-HM liposomes

The detection of Cyst among various thiols (Fig. 2) using the PDA-HM sensor system was investigated via colorimetric changes and altered UV absorption and fluorescence emission in HEPES buffer (10 mM, pH 7.4). As shown Fig. 3a and b, we investigated the colorimetric responses of PDA-HM (400 µM) with Cyst (1 eq.) and other thiols (10 eq.), such as GSH, Cys, Hcy, sodium pyrosulfate (Na_sS₂O₇), potassium thiocyanate (KSCN), thioglycolic acid, 2-mercaptoethanol and hydrogen sulfide (H₂S) (10 eq.). Among the various analytes, only Cyst immediately induced the blue-to-violet color transition at 1 eq. An extremely imperceptible change was detected with H₂S (10 eq.), but no changes with other reagents. Cyst penetrates into the polymer network of PDA-HM easily and rapidly, probably due to its small size and flexible structure, leading to a reaction with the C=C double bond of the maleimide moiety via Michael addition to generate maleimide-thiol conjugation,²⁶ which might



Fig. 1 SEM images of (a) 100 μ M PDA-HM after 254 nm UV irradiation and (b) PDA-HM following treatment with 100 μ M of Cyst. (c) Raman spectra of PDA-HM liposomes at room temperature (the blue line) and after treatment with Cyst (the red line).



Fia. 2 Chemical structures of various thiols



of Cyst (1 eq.) and other thiols (10 eq.), and Na_sS₂O₇ (10 eq.), and KSCN (10 eq.) in HEPES buffer (10 mM, pH 7.4). (b) Colorimetric responses of PDA-HM (400 µM) in the presence of various amounts of Cyst in HEPES buffer (10 mM, pH 7.4).

then perturb the backbone of the PDA polymer, allowing the release of the strain on the alkyl side chains generated during polymerization. The release of the side chain strain induces the partial distortion of the arrayed p-orbitals, which leads to the observed changes in optical properties.²⁷ Thiol groups play a significant role in the blue-to-red phase transition in response to Cyst. When PDA-HM solutions are treated with ethylenediamine, which is similar to Cyst in structure but lacks the thiol groups, the blue color of PDAs remains unchanged (Fig. S9, ESI†). Despite the presence of the -SH functional group, due to the larger structures of GSH, Cys, Hcy and thioglycolic acid, it is hard for them to penetrate into the supramolecular system, and hence they do not react with the densely packed PDA-HM polymer. H₂S reacts with the alkene bond of the maleimide moiety; however, it is not large enough to completely induce configurational disorder of the polymer backbone. Furthermore, the -NH₂ groups act as nucleophiles, leading to a reaction of maleimide with Cyst via Michael addition. It is also demonstrated that 2-mercaptoethanol



Scheme 3 A suggested mechanism for the production of maleimidethiol conjugation

could not change the color of PDA-HM from blue to red even though it has a similar structure to Cyst. A reaction mechanism that generates maleimide-thiol conjugation is suggested in Scheme 3.28 This phenomenon suggests that PDA-HM can be used in the detection of Cyst with high selectivity. Fig. 2b shows the colorimetric titration of PDA-HM in the presence of various levels of Cyst in HEPES buffer (10 mM, pH 7.4).

The analysis of the UV/Vis absorption spectra of an aqueous solution of PDA-HM suggests that the original 640 nm absorption band of PDA-HM decreased with a concomitant increase at 540 nm upon binding with Cyst (Fig. 4a and Fig. S10, ESI⁺). Furthermore, the presence of Cyst was also monitored by the increase in fluorescent emission because the color transition was accompanied by fluorescence emission (Fig. 4b). We measured the fluorescence of PDA-HM (200 µM) immersed in Cyst aqueous solutions at different concentrations. As shown in Fig. 4b, the emission intensity of PDA-HM increased gradually with the increase in the Cyst concentration from 0 to 600 µM.

Moreover, the detection limit represents a significant parameter for molecular recognition. The limit of detection was calculated according to a procedure reported in the literature.²⁹ The linear calibration curve assumed that the response y is linearly related to the concentration x for a limited range of concentration and expressed as y = a + bx. This model was used to determine the sensitivity (b) and the LOD value. The limit of detection (LOD) was estimated at 22.83 µM, which was calculated using the following equation:

$$LOD = 3 \times S_a \div b_a$$

where S_a is the standard deviation of the response and b is the slope of the calibration curve. The standard deviation of the



Fig. 4 (a) UV/Vis spectra and (b) fluorescence titration ($\lambda_{ex} = 540$ nm, slit: 5 nm/5 nm) of **PDA–HM** (200 μ M) in the presence of various amounts of Cyst (0–600 μ M) in HEPES buffer (10 mM, pH 7.4).

response was estimated using the standard deviation of either *y*-residuals or *y*-intercepts of regression lines (Fig. S11, ESI†). Recently, Kim *et al.* designed a colorimetric and fluorometric polydiacetylene biothiol sensor and the LOD values for the respective Cys, Hcy and GSH were 2.97, 20.5 and 30.0 μ M, respectively.²⁴ However it did not show the selective quantification of the sensor. Therefore, the LOD of 22.83 μ M is considered as a low value in polydiacetylene biothiol sensors.

To confirm the binding stoichiometry of the sensor PDA-HM with Cyst, a Job's plot was obtained (Fig. S12, ESI[†]). The maxima with a mole fraction of approximately 0.5 indicated a 1:1 stoichiometry. To quantify the extent of the color transition, the colorimetric response (CR) (%) was calculated using the following equation:^{19b}

$$CR = \frac{PB_0 - PB_1}{PB_0} \times 100,$$

where PB = $A_{\text{blue}}/(A_{\text{blue}} + A_{\text{red(violet)}})$, with *A* denoting the absorbance at either the blue or the red (violet) component in the UV/Vis spectrum. In the presence of 200 μ M Cyst, **PDA-HM** (200 μ M) yielded a CR value of 19.33% (Fig. S13, ESI[†]).

To investigate the reaction between **PCDA-HM** and Cyst, ¹H NMR experiments of **PCDA-HM** (5 mM) following the addition of Cyst were performed in DMSO (d_6) (Fig. S14, ESI[†]). When the Cyst was added to the **PCDA-HM** solution, the intensities of H_a (7.17 ppm) and H_b (5.40 ppm) proton peaks decreased and a new peak observed at 5.36 ppm was assigned to the H_c proton. Together with the ESI HRMS, the result of $m/z = 583.3535 [M + Na]^+$, calc. for $C_{32}H_{52}N_2O_4S$ (Fig. S7, ESI†), confirmed that **PCDA-HM** reacted with Cyst *via* Michael addition. All these results indicate that **PDA-HM** meets the sensitive and selective requirements for Cyst detection. Furthermore, **PDA-HM** was applied for detecting the presence of Cyst in commercial hair dyes and hair conditioners (Fig. S15, ESI†). It can rapidly recognize the presence or absence of Cyst in real samples *via* color change, which can be confirmed by fluorescence spectra. Additionally, the anti-interference ability of the detection method was demonstrated *via* the detection of Cyst and/or H₂S in commercial 'Biomed – Amino acid L.P.P. Perm', which does not contain cysteamine (Fig. S16, ESI†).

Conclusions

In the current study, we designed and synthesized a novel **PCDA-HM** sensor derived from the reaction between **PCDA** and **HM**. The **PDA-HM** polymer was prepared in aqueous solution. Upon treatment with Cyst, **PDA-HM** displayed a selective colorimetric shift from blue to red, as well as enhanced fluorescence among various biothiols. The conjugated backbones of **PDA-HM** were efficiently disrupted by the interaction between the **HM** receptor and the thiol groups in Cyst. The mechanism of Michael addition ensures the higher selectivity of **PDA-HM** toward Cyst compared with other thiols due to the structural specificity of Cyst. Such a dramatic change facilitated visual detection with an LOD as low as 22.83 µM. The reaction between **PCDA-HM** and Cyst was confirmed by NMR and mass spectroscopy. The Cyst detection of **PDA-HM** was confirmed in real samples and the anti-interference ability of the detection method was demonstrated.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

This research was supported through the Basic Science Research Program of the National Research Foundation of Korea (NRF) funded by the Ministry of Education (No. 2017R1A6A3A04004954) to S. L. and Performance Advancement & Foundation Construction (2020 Program 01-4 at Pukyong National University) funded by Ministry of Science and ICT to M. K.

Notes and references

 (a) L. Y. Niu, Y. Z. Chen, H. R. Zheng, L. Z. Wu, C. H. Tung and Q. Z. Yang, *Chem. Soc. Rev.*, 2015, 44, 6143–6160;
 (b) S. Y. Zhang, C. N. Ong and H. M. Shen, *Cancer Lett.*, 2004, 208, 143–153; (c) M. H. Lee, J. H. Han, P. S. Kwon, S. Bhuniya, J. Y. Kim, J. L. Sessler, C. Kang and J. S. Kim, *J. Am. Chem. Soc.*, 2012, 134, 1316–1322.

- 2 (a) J. M. Estrela, A. Ortega and E. Obrador, *Crit. Rev. Clin. Lab. Sci.*, 2006, 43, 143–181; (b) C. Hwang, A. Sinskey and H. Lodish, *Science*, 1992, 257, 1496–1502; L. A. Herzenberg, S. C. De Rosa, J. G. Dubs, M. Roederer, M. T. Anderson, S. W. Ela, S. C. Deresinski and L. A. Herzenberg, *Proc. Natl. Acad. Sci. U. S. A.*, 1997, 94, 1967–1972.
- 3 R. M. Coloso, L. L. Hirschberger, J. E. Dominy, J. I. Lee and M. H. Stipanuk, *Adv. Exp. Med. Biol.*, 2006, 583, 25–36.
- 4 M. Besouw, R. Masereeuw, L. van den Heuvel and E. Levtchenko, *Drug Discovery Today*, 2013, **18**, 785–792.
- 5 (a) K. Nishioka, A. Koizumi and Y. Takita, *Contact Dermatitis*, 2019, 80, 174–175; (b) W. Uter, L. Bensefa-Colas, P. Frosch, A. Gimenez-Arnau, S. M. John, J. P. Lepoittevin, C. Liden, I. R. White and J. Duus Johansen, *Contact Dermatitis*, 2015, 73, 69–81.
- 6 (a) Y. Kim and D. H. Na, *Toxicol. Res.*, 2019, 35, 161–165;
 (b) K. Kusmierek, G. Chwatko, R. Glowachi and E. Bald, J. Chromatogr. B: Anal. Technol. Biomed. Life Sci., 2009, 877, 3300–3308.
- 7 (a) S. Lee, J. Li, X. Zhou, J. Yin and J. Yoon, Coord. Chem. Rev., 2018, 366, 29–68; (b) C. Yin, W. Zhang, T. Liu, J. Chao and F. Huo, Sens. Actuators, B, 2017, 246, 988–993; (c) H. S. Jung, X. Chen, J. S. Kim and J. Yoon, Chem. Soc. Rev., 2013, 42, 6019–6031; (d) C. Yin, F. Huo, J. Zhang, M.-M. Ramón, Y. Yang, H. Lv and S. Li, Chem. Soc. Rev., 2013, 42, 6032–6059; (e) C.-X. Yin, K.-M. Xiong, F.-J. Huo, J. C. Salamanca and R. M. Strongin, Angew. Chem., Int. Ed., 2017, 56, 13188–13198; (f) N. Zhao, Q. Gong, R. X. Zhang, J. Yang, Z. Y. Huang, N. Li and B. Z. Tang, J. Mater. Chem. C, 2015, 3, 8397–8402; (g) B. Shi, N. Ren, L. Gu, G. Xu, R. Wang, T. Zhu, Y. Zhu, C. Fan, C. Zhao and H. Tian, Angew. Chem., Int. Ed., 2019, 58, 16826–16830; (h) Q. Wang, F. Ta, W. Tang, S. Zhao, C. Li and Y. Xie, Dyes Pigm., 2018, 148, 437–443; (i) Q. Wang, X. Wei, C. Li and Y. Xie, Dyes Pigm., 2018, 148, 212–218.
- 8 I. Sanskriti and K. K. Upadhyay, New J. Chem., 2017, 41, 4316-4321.
- 9 K. Kusmierek, G. Chwatko, R. Glowacki, P. Kubalczyk and E. Bald, *J. Chromatogr. B: Anal. Technol. Biomed. Life Sci.*, 2011, **879**, 1290–1307.
- 10 H. Kataoka, Y. Imamura, H. Tanaka and M. Makita, *J. Pharm. Biomed. Anal.*, 1993, **11**, 963–969.
- 11 G. Singh, D. Bains, H. Singh, N. Kaur and N. Singh, ACS Appl. Nano Mater., 2019, 2, 5841–5849.
- 12 S. Konar, B. N. P. Kumar, M. Kr. Mahto, D. Samanta, M. A. S. Shaik, M. Shaw, M. Mandal and A. Pathak, *Sens. Actuators, B*, 2019, 286, 77–85.
- 13 A. R. Sarkar, C. H. Heo, E. Kim, H. W. Lee, H. Singh, J. J. Kim, H. Kang, C. Kang and H. M. Kim, *Chem. Commun.*, 2015, **51**, 2407–2410.
- 14 (a) Y. K. Choi, S. Y. Lee and D. J. Ahn, J. Mater. Chem. C, 2019, 7, 13130–13138; (b) B. Yoon, J. Lee, I. S. Park, S. Jeon, J. Lee and J.-M. Kim, J. Mater. Chem. C, 2013, 1, 2388–2403;

(c) Y. Ding, W.-H. Zhu and Y. Xie, Chem. Rev., 2017, 117, 2203–2256.

- (a) F. S. Melkonyan, W. Zhao, M. Drees, N. D. Eastham, M. J. Leonardi, M. R. Butler, Z. Chen, X. Yu, R. P. H. Chang, M. A. Ratner, A. F. Facchetti and T. J. Marks, *J. Am. Chem.* Soc., 2016, 138, 6944–6947; (b) J. Chen, X. Zhang, G. Wang, M. A. Uddin, Y. Tang, Y. Wang, Q. Liao, A. Facchetti, T. J. Marks and X. Guo, *J. Mater. Chem. C*, 2017, 5, 9559–9569; (c) H. Jiang, G. Hershtig, S. Richter and R. Jelinek, *J. Phys. Chem. Lett.*, 2016, 7, 1628–1631.
- 16 F. Wu, N. V. S. D. K. Bhupathiraju, A. Brown, Z. Liu, C. M. Drain and J. D. Batteas, *J. Phys. Chem. C*, 2020, **124**, 4081–4089.
- 17 E. Gravel, J. Ogier, T. Arnauld, N. Mackiewicz, F. Ducongé and E. Doris, *Chem. – Eur. J.*, 2012, **18**, 400–408.
- 18 (a) S. Lee, J.-Y. Kim, X. Chen and J. Yoon, *Chem. Commun.*, 2016, 52, 9178–9196; (b) B. Yoon, S. Lee and J.-M. Kim, *Chem. Soc. Rev.*, 2009, 38, 1958–1968; (c) X. Sun, T. Chen, S. Huang, L. Li and H. Peng, *Chem. Soc. Rev.*, 2010, 39, 4244–4257; (d) R. Jelinek and M. Ritenberg, *RSC Adv.*, 2013, 3, 21192–21201.
- 19 (a) O. Yarimaga, J. Jaworski, B. Yoon and J.-M. Kim, Chem. Commun., 2012, 48, 2469–2485; (b) S. Okada, S. Peng, W. Spevak and D. Charych, Acc. Chem. Res., 1998, 31, 229–239; (c) M. A. Reppy and B. A. Pindzola, Chem. Commun., 2007, 4317–4338; (d) S. Lee, Y. Cho, B. U. Ye, J. M. Baik, M. H. Kim and J. Yoon, Chem. Commun., 2014, 50, 12447–12449.
- 20 S. Lee, J. Lee, M. Lee, Y. K. Cho, J. Baek, J. Kim, S. Park, M. H. Kim, R. Chang and J. Yoon, *Adv. Funct. Mater.*, 2014, 24, 3699–3705.
- 21 L. Polacchi, A. Brosseau, R. Métivier and C. Allain, *Chem. Commun.*, 2019, **55**, 14566–14569.
- 22 (a) D.-E. Wang, L. Zhao, M.-S. Yuan, S.-W. Chen, T. Li and J. Wang, ACS Appl. Mater. Interfaces, 2016, 8, 28231–28240;
 (b) T. C. Pham, Y. K. Kim, J. B. Park, S. Jeon, J. Ahn, Y. Yim, J. Yoon and S. Lee, ChemPhotoChem, 2019, 3, 1133–1137.
- 23 (a) C. Kim and K. Lee, *Biomacromolecules*, 2019, 20, 3392–3398; (b) J. Lee, O. Yarimaga, C. H. Lee, Y.-K. Choi and J.-M. Kim, *Adv. Funct. Mater.*, 2011, 21, 1032–1039.
- 24 J. P. Lee, F. Jannah, K. Baea and J.-M. Kim, *Sens. Actuators, B*, 2020, **309**, 127771.
- 25 H.-Y. Duan, Y.-X. Wang, L.-J. Wang, Y.-Q. Min, X.-H. Zhang and B.-Y. Du, *Macromolecules*, 2017, **50**, 1353–1361.
- 26 B. H. Northrop, S. H. Frayne and U. Choudhary, *Polym. Chem.*, 2015, **6**, 3415–3430.
- 27 K. M. Lee, X. Chen, W. Fang, J.-M. Kim and J. Yoon, *Macromol. Rapid Commun.*, 2011, **32**, 497–500.
- 28 Y. Sun, H. Liu, L. Cheng, S. Zhu, C. Cai, T. Yang, L. Yang and P. Ding, *Polym. Int.*, 2018, **67**, 25–31.
- 29 A. Shrivastava and V. B. Gupta, *Chron. Young Sci.*, 2011, 1, 21–25.