Supporting Information for:

Amphiphilic Poly(disulfide) Micelle and Remarkable Impact of the Core Hydrophobicity on Redox Responsive Disassembly

*Dipankar Basak,[†] Raju Bej[†] and Suhrit Ghosh**

Indian Association for the Cultivation of Science, Polymer Science Unit
2A & 2B Raja S. C. Mullick Road, Kolkata, India-700032
Email: psusg2@iacs.res.in

Synthesis of **P1**:

P1a: The polymer **P1a** was synthesized by following literature reported protocol.[1] **M1** (0.867 g, 3.94 mmol) was taken in a reaction tube equipped with a magnetic stirrer, septum and gas inlet/outlet. After degassing for five minutes, 0.8 mL of dry and degassed dichloromethane was added and stirred for 10 minutes at room temperature (25 °C) to obtain a homogeneous solution. To this stirring solution 0.7 g (3.84 mmol) of **M2** and catalytic amount of acetic acid (10 µL) were added sequentially and the reaction mixture was stirred further at room temperature for 3 h. Afterwards the yellow suspension was dissolved in $CHCl_3$ (200 µL) and precipitated from excess of methanol. The yellow precipitate was re-dissolved in $CHCl_3$, and re-precipitated from methanol and dried under vacuum to obtain **P1a** as sticky light yellow liquid (0.57 g, 81%).

P1a: ^1H NMR ($CDCl_3$, 500 MHz) δ: 8.458 (d, g, J = 4Hz, 2H); 7.778 (bs, e, 2H); 7.684-7.649 (m, f, 2H); 7.108-7.084 (m, d, 2H); 3.82- 3.664 (m, b, 4H), 3.635-3.484 (m, a, 4H) , 3.014-2.878 (m, c, 4H) ,

P1b: Synthesis same as **P1a** (Yield 76%). ($CDCl_3$, 500 MHz) δ: 8.72 (bs, g, 2H); 8.20 (bs, e+f, 4H); 7.55 (bs, d, 2H); 2.75-2.64 (m, c, 4H), 1.77-1.71 (m, b, 4H), 1.49-1.42 (m, a, 4H).

P2a: To a glass ampule containing disulfide polymer **P1a** (0.184 g, 0.059 mmol) was added 0.5 mL of CH_2Cl_2. To this stirring solution one drop of acetic acid and 2-Mercaptoethanol (1.2 eq w.r.t the pyridyl sulfide group) were added and the resulting solution was stirred at room temperature under argon for 3 h. Afterwards, the polymer was precipitated from methanol, washed repeatedly with methanol and dried under vacuum to furnish **P2a** as colorless waxy material (0.14 g, 78%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 3.885 (t, *h*, J = 6.0Hz, 4H), 3.768- 3.724 (m, *b*, 4H), 3.644-3.635 (m, *a*, 4H) , 2.929-2.861 (m, *c*, 4H) ,

P2b: same as **P2a**, yield: 79%, ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 3.91 (t, *h*, J = 6.0 Hz, 4H), 2.87-2.68 (m, *c*, 4H); 1.78-1.71 (m, *b*, 4H), 1.52-1.43 (m, *a*, 4H).

P3a: The disulfide polymer **P2a** (0.137 g, 0.043 mmol) was taken in a reaction tube, equipped with a magnetic stirrer, septum and gas inlet/outlet and dissolved in 0.4 mL of dry and degassed dichloromethane. To this stirring solution triethylamine (119 μL, 0.853 mmol) was added drop wise and stirred for 10 min. A solution of 2-Bromoisobutyryl bromide (105 μL, 0.853 mmol, dissolved in 100 μL of CH_2Cl_2) was added drop wise for 10 min at 0 °C and the solution was allowed to come to room temperature and further stirred at this temperature for 12 h. After the course of the reaction, 0.4 mL CH_2Cl_2 was added and the organic layer was washed with aqueous solution of saturated sodium bicarbonate (3 x 0.5 mL). The organic layer was collected, dried over anhydrous sodium sulfate, and evaporated under vacuum. The resulting liquid was further dissolved in 200 μL of $CHCl_3$ and precipitated from methanol to yield **P3a** as solid powder (0.101 g, 68%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 4.44 (t, *h*, J = 6.5Hz, 4H), 3.74 (t, *b*, J = 6.5 Hz, 4H), 3.64 (s, *a*, 4H) , 2.97-2.88 (m, *c*, 4H) , 1.94 (s, *i*, 6H) .

P3b: same as **P3a**, yield: 67%, ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 4.43 (t, *h'*, J = 6.8 Hz, 4H), 2.73-2.66 (m, *c*, 4H); 1.95 (s, i) 1.69-1.67 (m, *b*, 4H), 1.43-1.39 (m, *a*, 4H).

P4a: PTEGMA-*b*-PDS-*b*-PTEGMA block copolymers were synthesized using standard ATRP technique. In a typical polymerization run, Cu(I)Br (2.45 mg, 0.017 mmol) was taken in a glass ampule equipped with a septum and gas inlet/outlet. After degassing for 5 min, **M4** (0.397 g, 1.708 mmol) and a solution of PMDETA (7.2 μL, 0.034 mmol; a stock solution of PMDETA was prepared by adding 36 μL PMDETA in 100 μL of dry and degassed anisole, from which 20 μL was added) in dry and degassed anisole were added to the glass ampule and stirred for 10 min at room temperature to allow catalyst formation while the solution (total volume 100 μL) turned into light green color. To it a homogeneous solution of **P3a** (0.03 g, 0.0085 mmol) dissolved in 100 μl of degassed anisole was added and the resulting mixture was transferred to a pre-heated oil bath at 90 °C and stirred for 3 h at this temperature under argon atmosphere. Polymerization was rapidly quenched after dipping the reaction ampule into liquid nitrogen and then the green viscous product was dissolved in 0.2 mL of $CHCl_3$ and precipitated from diethyl ether. The precipitate was centrifuged and dried in vacuum to obtain **P4a** as slightly bluish sticky polymer (0.145 g, 52%).

^{1}H NMR ($CDCl_3$, 500 MHz) δ: 4.088 (bs, *d*, 2H), 3.757 (t, *b*, *J* = 6.5Hz, 4H) 3.665-3.651 (m, *a+e+f,* 12H), 3.558 (s, *g*, 2H) , 3.384 (s, *h*, 3H) , 3.00-2.953 (m, *c,* 4H) , 1.897-1.801 (m, polymer backbone), 1.631 (s, j, 2H), 1.032-0.86 (bs, *i,* 3H)

P4b: same as **P4a**, yield: 41%, ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 4.09 (bs, *a*, 2H), 3.66-3.57 (bs, *c*+*d*, 8H), 3.57 (bs, *h*, 2H), 3.39 (bs, *b*, 3H), 2.79-2.73 (m, *e*, 4H), 1.91-1.74 (m, *f*, 4H), 1.61 (bs, *j*, 2H), 1.56 (bs, *g*, 4H), 1.25-0.87 (b, *i*, 3H)

Additional Figures:

Table S1: Solubility tests of **P4a** (*c* = 1.0 mg/mL) in different solvents at room temperature (25 °C)

Solvent	Observation
water	insoluble
methanol	insoluble
ethanol	insoluble
^{t}butanol	insoluble
chloroform	soluble
tetrahydrofuran	soluble
acetone	soluble
1,4-dioxane	soluble
DMF	soluble
diethyl ether	partially soluble

Table S2: Comparative physical parameters of **P4a** and **P4b** obtained using pyrene as a hydrophobic probe

Entry	CAC(M)	Encapsulation efficiency/1.0mg polymer	I_{373}/I_{384}
P4a	$1x10^{-5}$	0.0046 mg	1.36 CH_2Cl_2(1.37) 8.93ε_o at 20ºC
P4b	$7.5x10^{-6}$	0.0061 mg	1.31 $CHCl_3$(1.28) 4.8ε_o at 20ºC

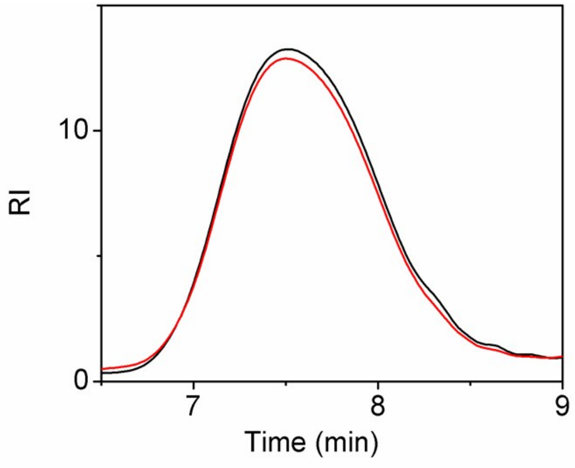

Fig. S1 GPC traces of **P1a** (in black) and **P2a** (in red) in THF

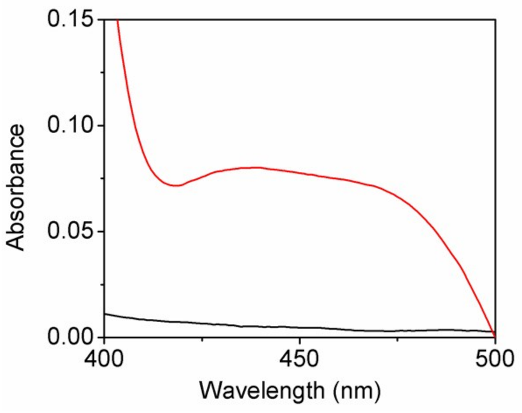

Fig. S2 UV-vis spectrum of **P1a** (black) and **M2** (red) after treating with Ellman's reagent (*c* = 0.1 mg/mL polymer/**M2**, 1.0 cm pathlength)

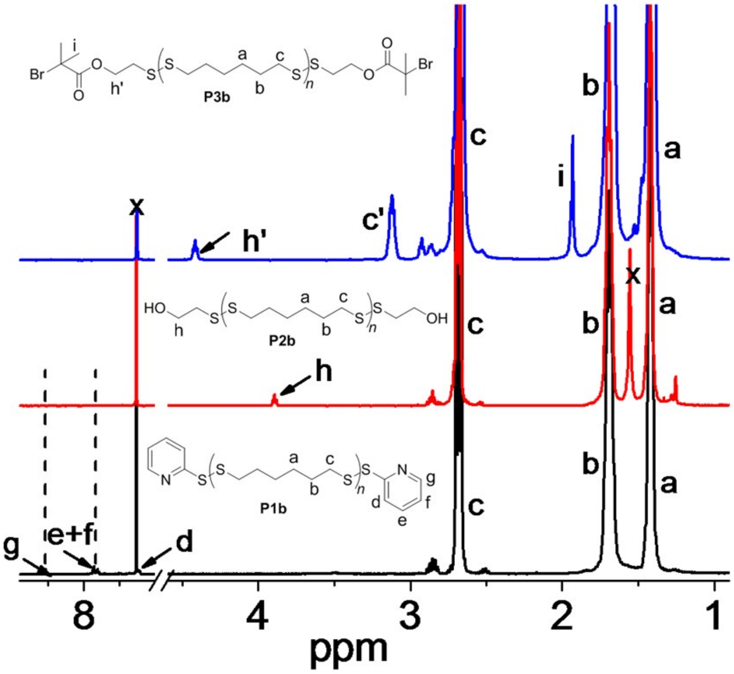

Fig. S3 ^{1}H NMR spectra of **P1b-P3b** in $CDCl_3$, X indicates peaks corresponding to residual $CHCl_3$ in $CDCl_3$

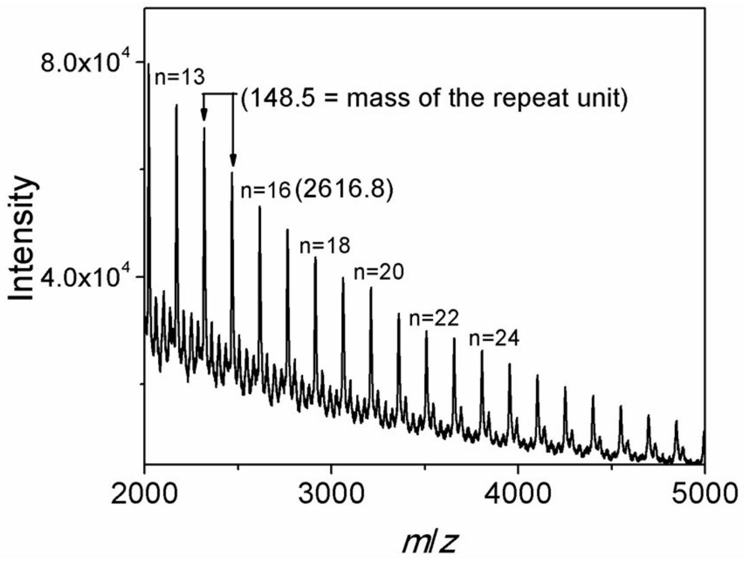

Fig. S4 MALDI-ToF spectrum of **P1b**. *m*/*z* = 2616.8 matches with (16x148.5(mass of repeat unit) + 2x110.01(mass of pyridyl sulfide)+22.99 (mass of sodium)

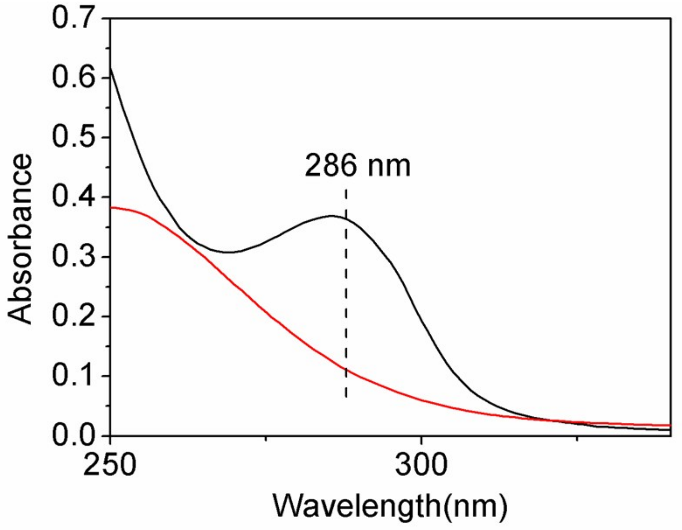

Fig. S5 UV-vis spectra of **P1b** (black) and **P2b** (red) in $CHCl_3$ (c = 1.0 mg/10 mL, 1.0 cm pathlength) showing absence of pyridyl group in **P2b**

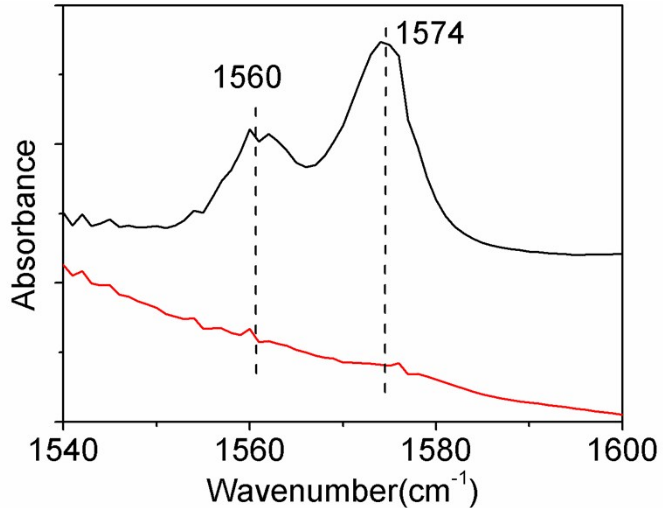

Fig. S6 Comparative FT-IR spectra of **P1b** (black) and **P2b** (red) show absence of the peaks corresponding to C=N stretching (at 1574 and 1560 cm^{-1}) in **P2b** (KBr window)

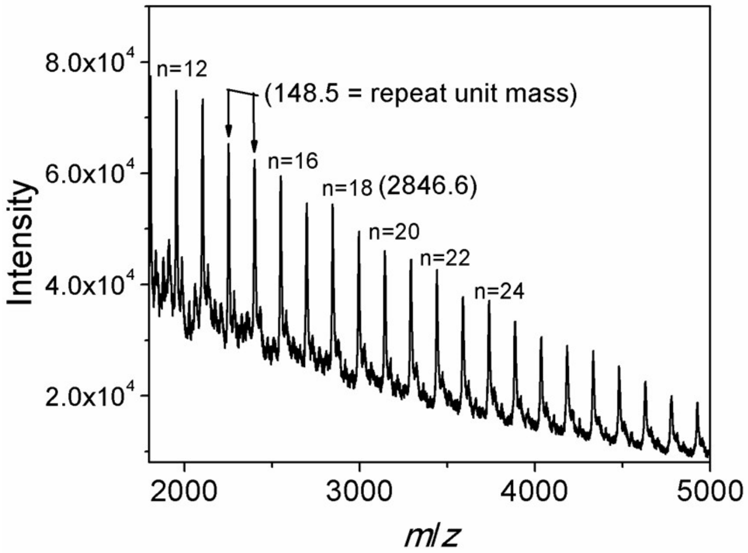

Fig. S7 MALDI-ToF spectrum of **P2b**. *m/z* = 2846.6 matches with (18x148.5(mass of repeat unit) + 2x77.13(mass of 2-mercaptoethanol)+22.99 (mass of sodium)

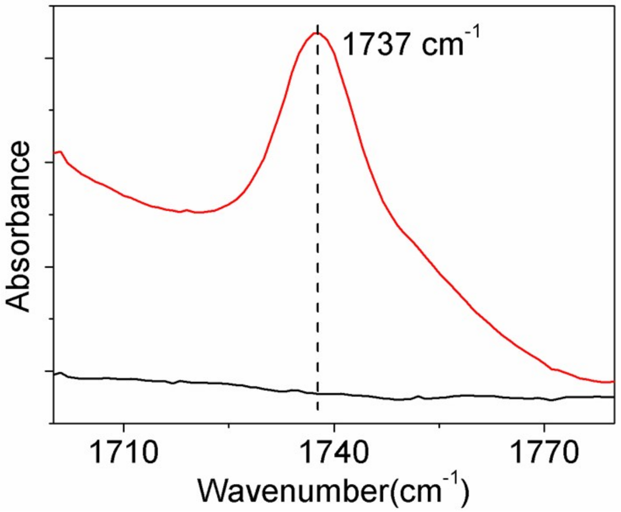

Fig. S8 Selective region of comparative FT-IR spectra of **P3b** (red) and **P2b** (black) (KBr window)

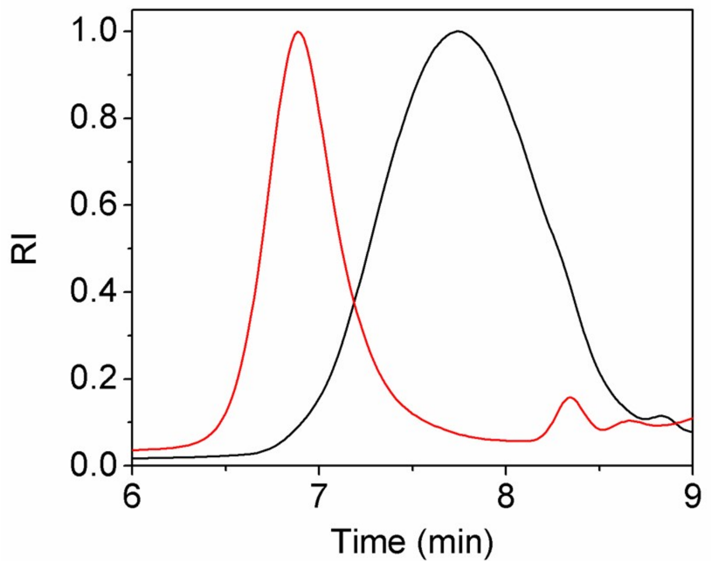

Fig. S9 GPC traces of **P4b** (red) and **P3b** (black) in THF

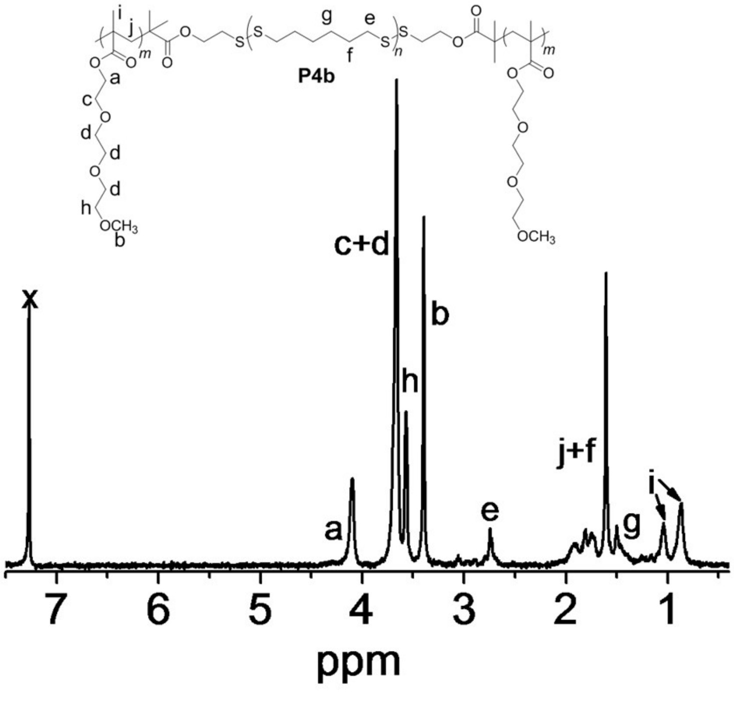

Fig. S10 ^{1}H NMR of **P4b** in $CDCl_3$, X indicates peak corresponding to the residual $CHCl_3$ in $CDCl_3$

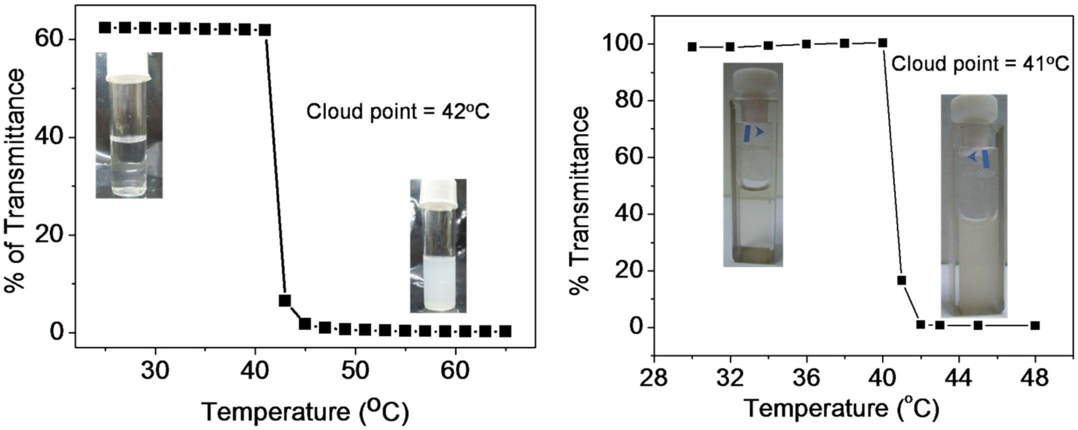

Fig. S11 Influence of temperature on transmittance of (left) **P4a** and (right) **P4b** (c = 5×10^{-5} M, 1.0 cm pathlength)

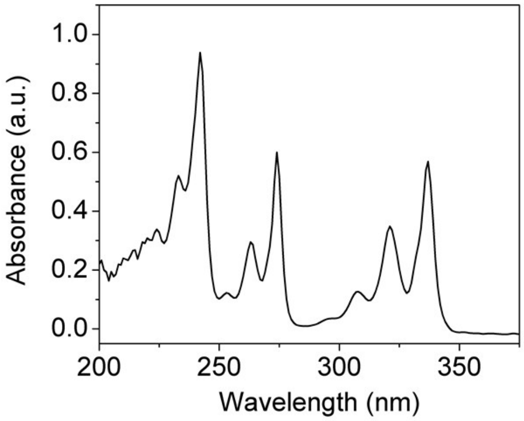

Fig. S12 Absorption spectra of pyrene in dichloromethane (pyrene concentration: 1×10^{-5} M), pathlength of cuvette = 1 cm, temperature = 25 °C

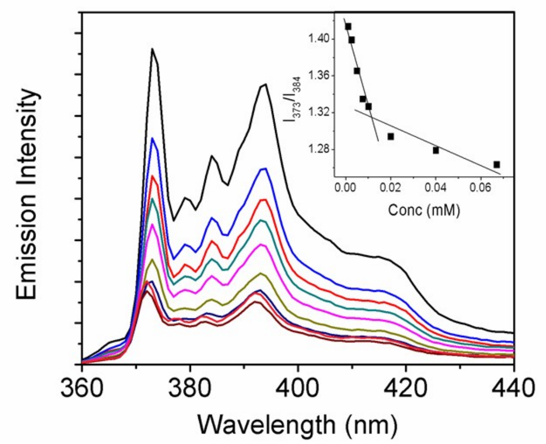

Fig. S13 Emission spectra of pyrene encapsulated in aqueous solution of **P4b** at varying concentrations; (inset) Variation of I_{373}/I_{384} in pyrene emission spectra as a function of **P4b** concentration, pyrene concentration was kept constant (c = 1×10^{-5} M) in all cases

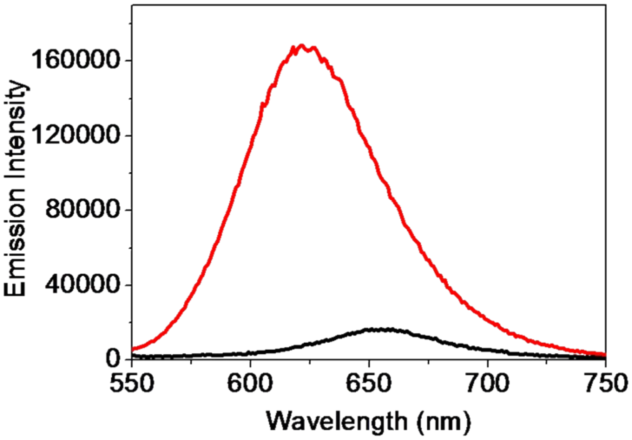

Fig. S14 Comparison of Nile red (NR) emission in water (black) and NR-encapsulated **P4a** polymer (red), λ_{ex} = 530 nm

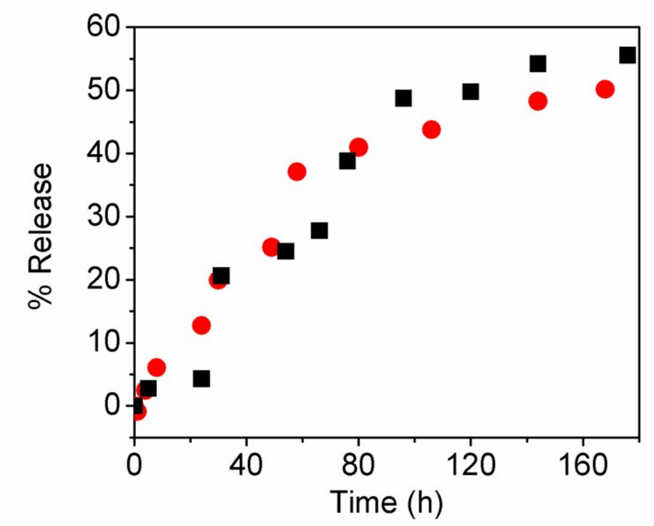

Fig. S15 Comparative NR release profile of **P4b** upon treatment with different GSH concentrations: 20.0 mM (red circle), 60.0 mM (black box)

References:

1. D. Basak, R. Kumar and S. Ghosh, *Macromol. Rapid Commun*., 2014*,* ***35,*** 1340−1344.