Electronic Supplementary Information:

Shape-Selective, Stoichiometric Sensing of Fatty Acids with a Mixed Polydiacetylene Liposome

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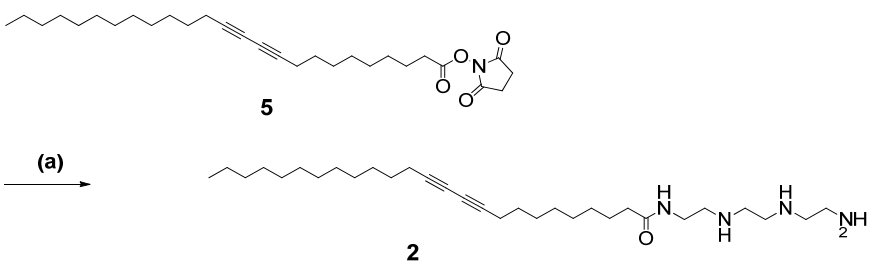
General Information

All chemicals were purchased from Sigma-Aldrich and used directly without further purification. All moisture or air sensitive experiments were performed under a positive pressure of argon in flame dried glassware equipped with a rubber septum inlet. Solvents and liquid reagents were transferred by an argon flushed syringe or cannula. Reaction mixtures were stirred with Teflon coated magnetic stirring bars. Analytical thin layer chromatography was performed using Merk 60 F254 precoated silica gel plates. Subsequent to elution, ultraviolet illusion at 254 nm allowed for visualization of UV active materials. Column chromatography was carried out Merck silica gel 60 (230-400 mesh). The nuclear magnetic resonance spectra were determined on an AM-300 Bruker [^{1}H NMR (300 MHz), ^{13}C NMR (75 MHz)] instrument unless otherwise noted. Mass spectral analysis was recorded on JEOL JMS-AX505WA and is reported in units of mass to charge (m/z). HRMS were performed by Korea Basic Science Center, Kyung-Pook National University. UV/Vis absorption spectra were taken on a Hewlett Packard Agilent 8453. Either a 1 mL disposable cuvette was used for experiments.

Synthesis

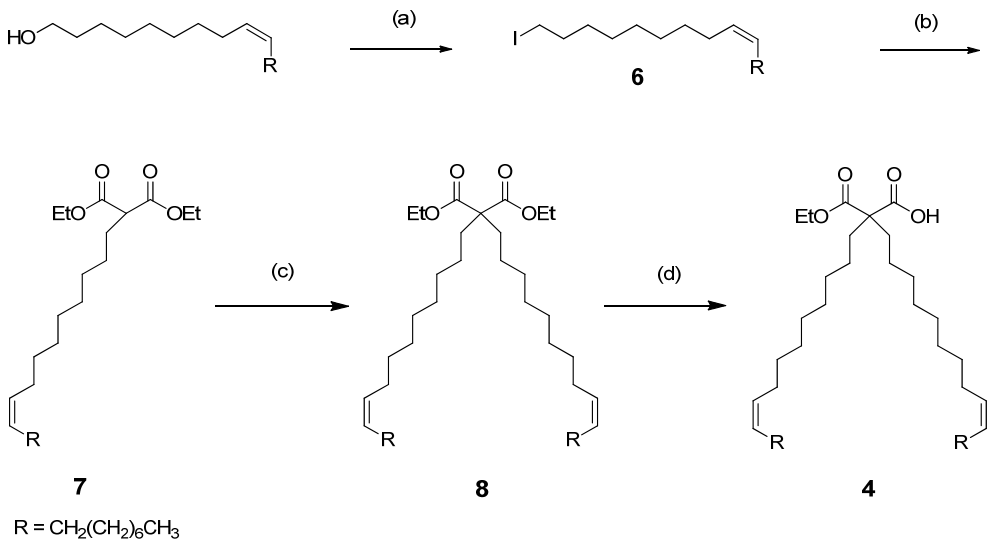
The synthesis of liposome components **1** and **5** were carried out according to the reported procedure.[13] The synthesis of other compounds are described below.



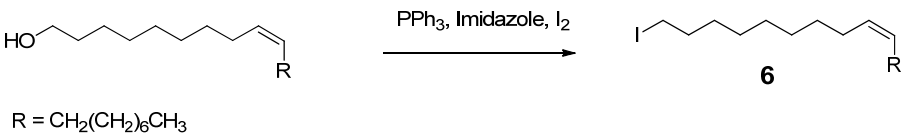
Scheme S1 Synthesis of liposome component **2**. (a) triethylenetetraamine, 25 °C, 8 h

N-(2-(2-(2-aminoethylamino)ethylamino)ethyl)pentacosa-10,12-diynamide (2).

To a solution of triethylenetetraamine (1.5 g, 10 mmol) in 30 mL of dichloromethane was slowly added (2,5-dioxopyrrolidin-1-yl)pentacosa-10,12-diynoate **5** (472 mg, 1.0 mmol). The mixture solution was stirred for 8 h at room temperature. The solvent was evaporated and mixture was washed with water repeated 3 times. The residue was purified by simple filtration to afford *N*-(2-(2-(2-aminoethylamino)ethylamino)ethyl)pentacosa-10,12-diynamide **2** as a white solid (502 mg, 99 %). mp 83 °C: ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.20. (s, 1H), 3.31 (q, J = 6.0 Hz, 2H), 2.65 -2.83 (m, 10H), 2.26–2.16 (m, 6H), 1.72–1.61 (m, 10H), 1.48 (m, 4H) 1.39–1.06 (m, 26H), 0.88 (t, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.90, 76.96, 76.74, 64.81, 64.75, 51.66, 48.58, 48.44, 48.20, 41.12, 38.22, 36.24, 31.42, 29.14, 29.13, 29.11, 28.98, 28.84, 28.69, 28.60, 28.44, 28.37, 28.29, 28.87, 28.82, 22.18, 18.71, 13.61; HRMS (FAB) calcd. for $C_{31}H_{58}N_4O$ (M + H^+) 502.4611. found 503.4685.



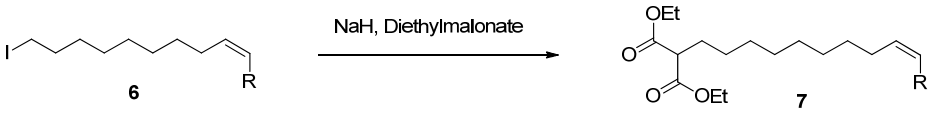
Scheme S2 Synthesis of compound **4**. (a) triphenylphosphine, imidazole, iodine, diethyl ether/acetonitrile, 0 °C to 25 °C, 2 h. (b) Sodium hydride, dimethylmalonate, DMF, 25 °C to 80 °C, 12 h. (c) Sodium hydride, Oley iodide, DMF, 25 °C to 80 °C, 12 h. (d) 50% aqueous KOH, EtOH, 80 °C, overnight.



(Z)-1-iodooctadec-9-ene (6).

Triphenylphosphine (1245 mg, 4.8 mmol) and imidazole (430 mg, 6.3 mmol) were dissolved in 200 mL of 3:1 Et_2O/CH_3CN at room temperature. To this solution was added 1204 mg (4.7 mmol) of iodine at 0-5 °C.

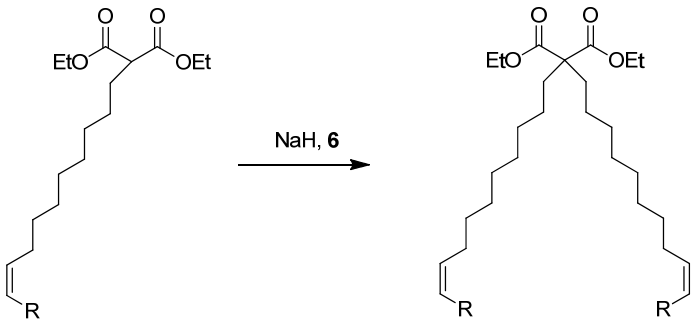
After the addition was complete, the mixture was stirred at the same temperature for an additional 20 min. To this mixture was added dropwise 548 mg (3.1 mmol) of (Z)-octadec-9-en-1-ol over 15 min. The reaction mixture was warmed to room temperature and left for 1h. After work-up, the product was purified on a silica gel column to give **6** in 98% yield: ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.33 (qn, J = 3.6, 1.98 Hz, 2H), 3.16 (t, J = 7.08 Hz, 2H), 2.01 (d, J = 5.76 Hz, 4H), 1.81 (qn, J = 7.08 Hz, 2H), 1.27 (m, 24H), 0.88 (t, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 129.98, 129.73, 33.68, 32.72, 32.02, 30.62, 29.88, 29.80, 29.65, 29.43, 29.27, 29.13, 28.64, 27.31, 27.26, 22.80, 14.24, 6.93.



R = $CH_2(CH_2)_6CH_3$

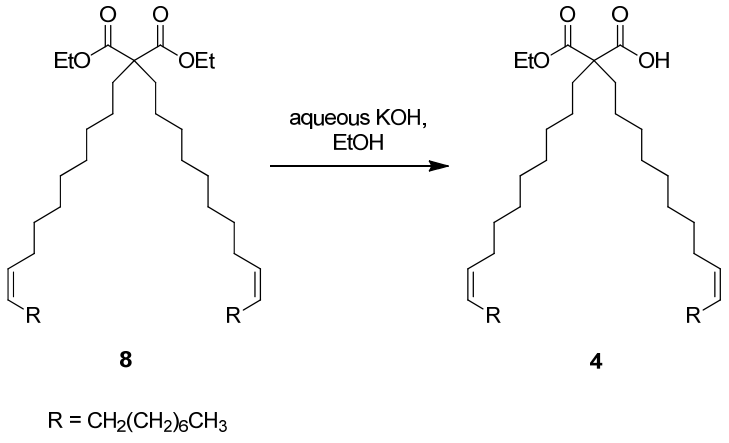
Diethyl 2-((Z)-octadec-9-enyl)malonate (7).

To stirred suspension of NaH (60% suspension in oil; 120 mg, 3 mmol; washed with petroleum ether before use) in anhydrous DMF (10 mL) under argon atmosphere was added a solution of diethyl malonate (160 mg, 1 mmol) in anhydrous DMF (7 mL). After being stirred for 1 h at room temperature, (Z)-1-iodooctadec-9-ene **6** (1170 mg, 3.1 mmol) in anhydrous DMF (7 mL) was added to the mixture dropwise, and the resulting mixture was heated to 80 °C and stirred for 12 h. After being cooled to room temperature, the reaction mixture was treated with water (100 mL), and then subjected to extractive workup with diethyl ether (3×100 mL). The organic fraction was washed with brine (3×100 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was obtained as brown oil (400 mg, 97%) and used for the next step without further purification: ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.33 (qn, J = 3.6, 1.98 Hz, 2H), 4.17 (q, J = 7.1 Hz, 4H), 3.29 (t, J = 7.53 Hz, 1H), 1.98 (d, J = 5.43 Hz, 4H), 1.86 (d, J = 6.57 Hz, 2H), 1.27 (m, 30H), 0.86 (t, J = 6.84 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.67, 130.02, 129.90, 61.30, 52.16, 32.71, 32.01, 29.87, 29.84, 29.76, 29.71, 29.62, 29.51, 29.42, 29.34, 29.32, 28.84, 27.42, 27.30, 22.78, 14.18, 13.89.



Diethyl 2,2-di((Z)-octadec-9-enyl)malonate (8).

To stirred suspension of NaH (60% suspension in oil; 30 mg, 0.75 mmol; washed with petroleum ether before use) in anhydrous DMF (3 mL) under argon atmosphere was added a solution of diethyl 2-((Z)-octadec-9-enyl)malonate **7** (150 mg, 0.36 mmol) in anhydrous DMF (2 mL). After being stirred for 1 h at room temperature, (Z)-1-iodooctadec-9-ene **6** (150 mg, 0.25 mmol) in anhydrous DMF (2 mL) was added dropwise to the reaction mixture and it was heated to 80 °C for 12 h. After being cooled to room temperature, water (50 mL) was added and the mixture was extracted with diethyl ether (3×50 mL). The organic fraction was washed with brine (3×50 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was obtained as brown oil (230 mg, 97%) and used for the next step without further purification: ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.34 (qn, J = 3.6, 1.9 Hz, 4H), 4.17 (q, J = 6.54 Hz, 4H), 2.00 (d, J = 5.58 Hz, 8H), 1.65 (t, J = 6.99 Hz, 4H), 1.26 (m, 54H), 0.88 (t, J = 6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.33, 130.14, 129.90, 64.24, 57.69, 32.75, 32.05, 29.91, 29.85, 29.80, 29.67, 29.63, 29.53, 29.47, 29.32, 28.65, 27.36, 27.31, 25.96, 22.83, 14.26, 13.97.



(11Z)-2-(ethoxycarbonyl)-2-((Z)-octadec-9-enyl)icos-11-enoic acid (4).

The diester **8** (330 mg, 0.5 mmol) was dissolved in 96% ethanol (10 mL), which was treated with KOH (50% aqueous solution, 10 mL). The reaction mixture was heated at 80 °C overnight. After cooling, the reaction mixture was acidified with 36% aqueous solution HCl (pH ~ 2). A brown precipitate was filtered and washed with water (100 mL), and then dissolved in ethyl acetate, the resulting solution was dried over Na_2SO_4. Ethyl acetate was removed under reduced pressure and crude acid **4** was obtained (300 mg) as a brown solid. Crude product was recrystallized from hot toluene to give **8** (200 mg, 69%) as a pale yellow powder. The next crop of **4** (50 mg, 20%) was obtained by concentration of the mother liquor: ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.34 (qn, J = 3.54, 2.07 Hz, 4H), 3.79 (s, 2H), 1.99 (d, J = 5.97 Hz, 8H), 1.86 (d, J = 6.57 Hz, 4H), 1.26 (m, 51H), 0.88 (t, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.33, 130.11, 129.94, 57.95, 53.13, 35.82, 32.76, 29.91, 29.89, 29.85, 29.80, 29.74, 29.67, 29.56, 29.51, 29.47, 29.39, 27.36, 25.00, 22.83, 14.26.

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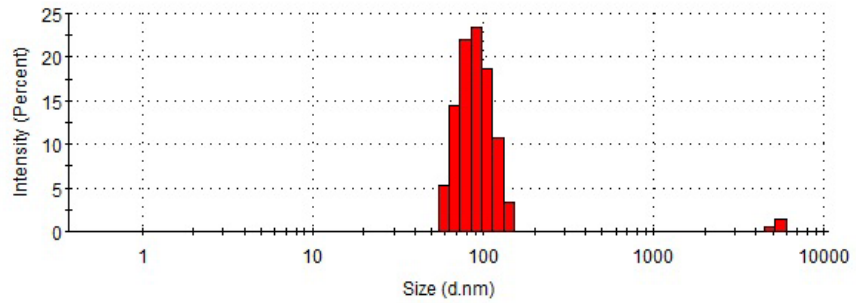

Fig. S1 The mean size distribution of liposome **3**.

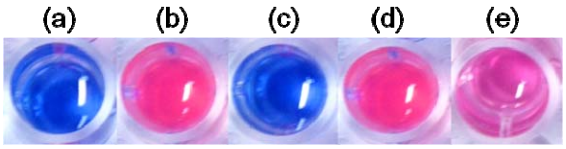

Fig. S2 Competitive colourimetric response of liposome **3** to oleic (bent) and/or stearic (linear) acids in HEPES buffer (10 mM, pH 7.4): (a) liposome **3** only (200 μM), (b) a mixture of stearic acid (400 μM) and oleic acid (400 μM), (c) stearic acid (800 μM), (d) addition of stearic acid (400 μM) for 10 min, followed by oleic acid (400 μM), (e) addition of oleic acid (400 μM) for 10 min, followed by stearic acid (400 μM).

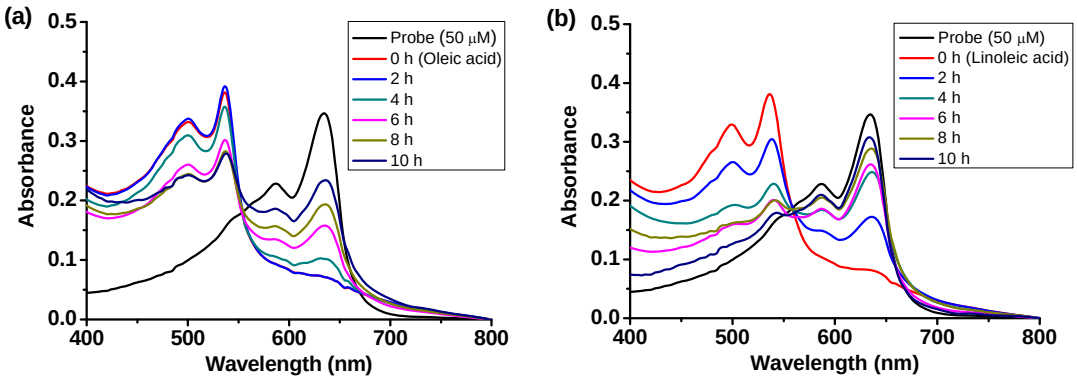

Fig. S3 UV/Vis spectral changes of (a) oleic acid and (b) linoleic acid with liposome **3** after heating at 200 °C for given times (0–10 h). Each fatty acid sample (50 μM) was treated with liposome **3** (50 μM) in HEPES buffer (10 mM, pH 7.4).

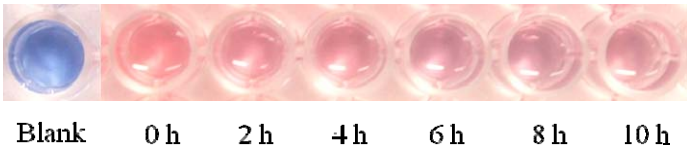

Fig. S4 Colourimetric sensing of soybean oil with liposome **3** after heating at 200 °C for given times (0–10 h). Each soybean oil sample (50 μM) was treated with liposome **3** (50 μM) in HEPES buffer (10 mM, pH 7.4).

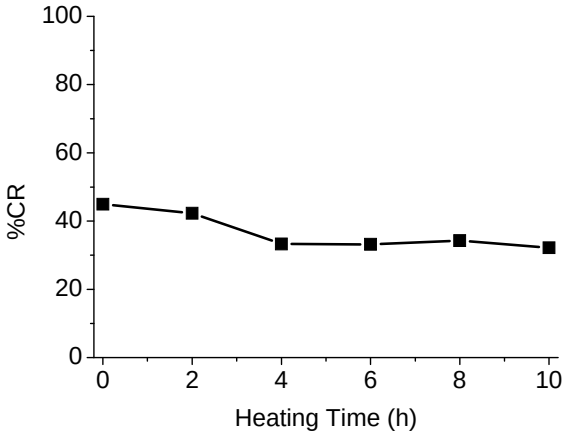

Fig. S5 Plots of the %CR value of *cis*-fatty acids in soybean oil (50 μM) with respect to the heating time. Each fatty acid sample was treated with liposome **3** (50 μM) in HEPES buffer (10 mM, pH 7.4).

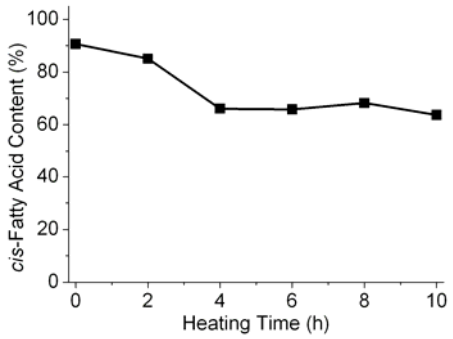

Fig. S6 The content of *cis*-fatty acids in a commercial soybean oil sample after heating at 200 °C for the given time (0–10 h), estimated from UV-Vis titrations with liposome **3.** Each fatty acid sample (50 μM) was treated with liposome **3** (50 μM) in HEPES buffer (10 mM, pH 7.4).

Sample		Time (h)					
		0 h	2 h	4 h	6 h	8 h	10 h
Oleic acid	CR (%)	49.6	50.1	42.6	29.7	23.3	18.3
	Conc. (μM)	50.2	50.7	42.8	29.2	22.5	17.2
Linoleic acid	CR (%)	47.7	28.4	11.6	6.8	4.1	2.2
	Conc. (μM)	48.2	27.8	10.1	5.1	2.2	0.2
Soybean oil	CR (%)	44.9	42.3	33.3	33.2	34.3	32.2
	Conc. (μM)	45.2	42.5	33.0	32.9	34.1	31.8

Table S1 Monitoring of *cis*-fatty acid concentration in oleic acid, linoleic acid and soybean oil (50 μM) with respect to the heating time. Each fatty acid sample was treated with liposome **3** (50 μM) in HEPES buffer (10 mM, pH 7.4).