Bio-inspired supramolecular materials by orthogonal self-assembly of hydrogelators and phospholipids

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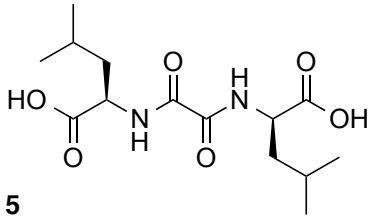
Materials

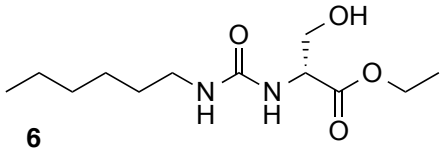
Bis(leucine) oxalyl amide (5)



5

The bis(leucine) oxalyl amide (**5**, $Ox(Leu)_2$) was prepared according to reference 1, yielding **5** as a white powder. ^{1}H-NMR (400 MHz, d6-DMSO , 25°C) δ ppm: 8.60 (d, 2H), 4.22 (dt, 2H),1.75 ± 1.54 (m, 6H), 0.87 (2d, 12H); ^{13}C-NMR (100 MHz): 174.5, 160.1, 51.8, 40.2, 24.6, 23.1, 21.6; [M/z] (calc): 316.16 [M/z]; (found -H) = 315.1.

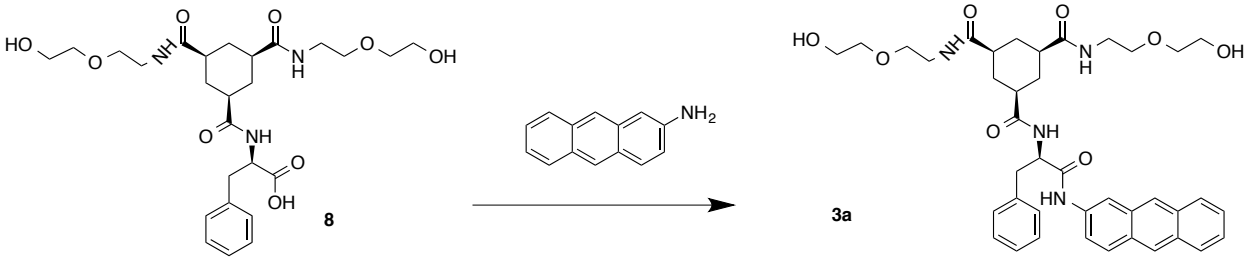
Urea Gelator 6



6

Triethylamine (0.51 mL, 1.5 eq) and hexylisocyanate (312 mg, 1 eq.) were added to ethylserine (500 mg, 1.2 eq) in 20 mL dichloromethane at 0 °C. The reaction was stirred in an ice bath under nitrogen for 24 h. Then the mixture was concentrated, and the residue was taken up in dichloromethane and washed with water three times. The organic layer was dried over sodium sulfate, and the solvent was removed to give the crude product. To remove the di-adduct resulting from the additional coupling between the alcohol and the isocyanate, filtration on a paper filter was carried out from hot water (T~80°C). After freeze-drying of the aqueous solution, the compound was recrystallized twice from acetonitrile, to give a white crystalline material. ^{1}H NMR δ (400 MHz, $CDCl_3$, 25°C) δ ppm: 4.43 (dd, J= 3.84 Hz, 3.92 Hz, 1H), 4.18 (m, 2H), 3.84 (m, 2H), 3.12 (t, J=7.18Hz, 2H), 1.46 (m, 2H), 1.29-1.22 (m, 9H), 0.85 (t, J=6.84Hz, 3H); ^{13}C d NMR (100 MHz) 170.6, 157.2, 61.9, 61.2, 56.3, 40.6, 31.5, 29.6, 29.5, 26.5, 22.6, 14.1, 14.0; [M/z] (calc.) = 260.17; [M/z] (found+Na)= 283.1.

Gelator 3a



In a round bottom flask, 500 mg (0,93 mmol) precursor **8** and 198 mg (1,02 mmol) 1-amino anthracene were dissolved in DCM and MeOH (5:1) and stirred for 30 minutes. Then, 281,5 mg (1,02 mmol) 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride (DMTMM) and 101 mg (1,02 mmol) triethylamine was added. This mixture was stirred for 24 h at RT. The crude mixture was purified by column chromatography (solid Si - 100% DCM-20% MeOH 80% DCM). This yielded a brown crystalline solid (120 mg, 0,168 mmol, 18%). ^{1}H-NMR (DMSO, MeOD, 400 MHz) δ ppm: 1.25-1.45 (m, 3H), 1.55 (d, J_2, 13.0 Hz, 1H), 1.69 (tr, J_2, 13.6 Hz, 1H), 2.18 (tr, J_2, 13.6 Hz, 2H), 2.30 (t, J_2, 12.50 Hz , 2H), 2.91 (t, J_2, 12.1 Hz, 1H), 3.12 (s, 4H), 3.18 (m, 4H), 3.38 (m, 8H), 3.58 (m, 4H), 7.10-7.35 (m, 5H), 7.45 (tr, J_2, 6.6 Hz, 1H), 7.54 (d, J_2, 9.7 Hz, 1H), 8.02 (d, J_2, 9.7 Hz, 3H), 8.42 (s, 1H), 8.46 (s, 2H); [M/z] (calc.): 712.35, [M/z] (found): 713.4 [M + H].

Supporting Figures

Cryo-TEM

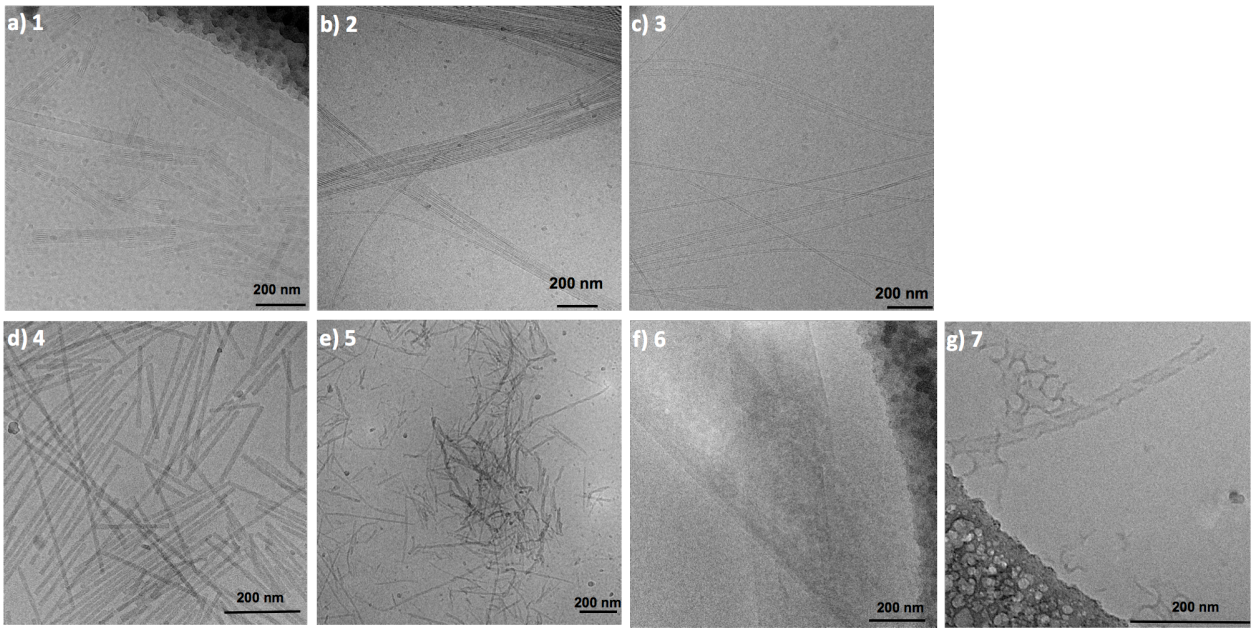


Figure S1. Cryo-TEM micrographs of 1,3,5-triamide cis,cis-cyclohexane derivatives **1** (**a**)**, 2** (**b**) and **3** (**c**). Micrographs of dibenzoyl cystine **4** bis(leucine) (**d),** oxalyl-amide **5 (e**), monourea ethyl serine gelator **6** (**f)** and gemini tartrate **7** (**g**)**.**

Dynamic Light Scattering

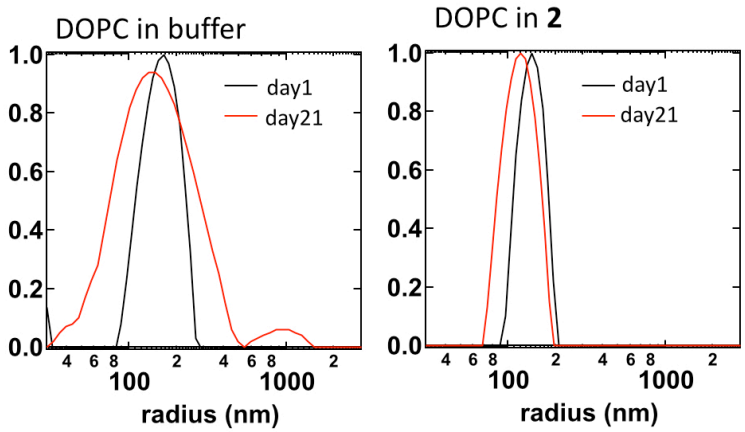


Figure S2. DLS profiles of DOPC in buffer and DOPC in a gel of **3** on day 1 and day 21.

Fluorescence Lifetime Imaging Microscopy

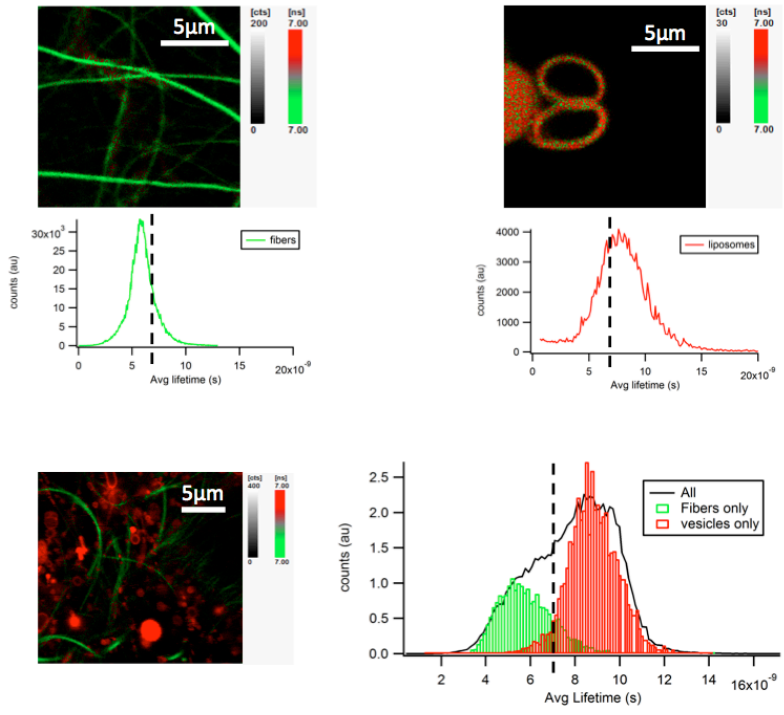


Figure S3. FLIM micrographs and corresponding intensity-weighted histograms of the average lifetimes of the image pixels. In the histograms, the vertical dashed cursor defines the upper and lower limits of the lifetime green/red color code in the corresponding image. For fibers of **3** with **3a** (top left) and for the liposomes with NBD-PE (top right), the histograms show a Gaussian-like distribution around 5-6 ns and 8-9 ns, respectively. This denotes a homogeneous lifetime distribution within the studied area. The lifetime histogram of the mixture of liposomes and fibers displays two populations, corresponding each one to either fibers or liposomes (see Figure S4 for more details). Setting the cursor of the color scale at 7 ns reveals the fibers and the liposomes separately in the FLIM image.

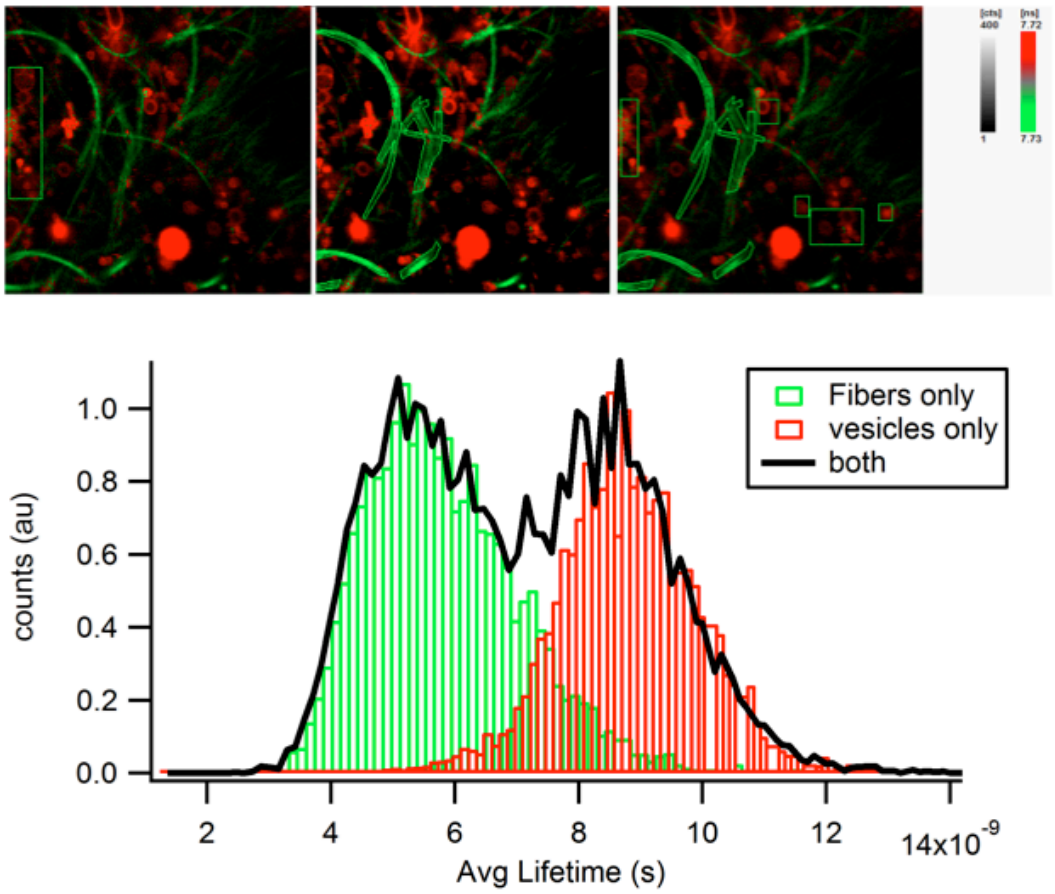


Figure S4. FLIM micrographs of the mixture of liposomes and fibers (see Figure S3). Intensity-weighted histograms of the average lifetimes of the image pixels of different ROI's (regions of interest delimited by green-bordered areas). For liposomes selected in the image on the left, the histogram is centered around 8-9 ns, whereas for fibers selected in the center image, the histogram is centered around 5-6 ns. When both liposomes and fibers are selected in the image on the right, a double population of lifetimes can clearly be distinguished.

References

1 J. Makarević, M. Jokić, B. Perić, V. Tomisić, B. Kojić-Prodić, M. Zinić, *Chem. Eur. J.* **2001**, *7*, 3328-3341.