Creation of polynucleotide-assisted molecular assemblies in organic solvents: general strategy toward the creation of artificial DNA-like nanoarchitectures

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The influence of added polynucleotide on the gelation ability of nucleobase-appended organogelators was investigated. Uracil-appended cholesterol gelator formed a stable organogel in polar organic solvents such as *n*-butanol. It was found that the addition of the complementary polyadenylic acid (poly(A)) not only stabilizes the gel but also creates the helical structure in the original gel phase. Thymidine and thymine-appended gelators can form stable gel in apolar solvents, such as benzene, where poly(A)–lipid complex can act as a complementary template for the gelator molecules to create the fibrous composites. Based on these findings, we can conclude that self-assembling modes and gelation properties of nucleobase-appended organogelators are controllable by the addition of their complementary polynucleotide in organic solvents. We believe, therefore, that the present system can open the new paths to accelerate development of well-controlled one-dimensional molecular assembly systems, which would be indispensable for the creation of novel nanomaterials based on organic compounds.

Introduction

The recent focus of interest in supramolecular chemistry has been directed toward the creation of one-dimensional supramolecular nanoarchitectures.[1] In particular, control of molecular arrangement in the resultant one-dimensional structures is a challenging research subject, due to their potential applications as nanowires, memories and switches. To control the molecular arrangement in a supramolecular nanofiber structure, low molecular-weight gelators are fascinating candidates, due to their variety of self-assembling capabilities, as well as functionalities.[2] Advantageously, when some additive which can interact with gelator molecules through exact molecular recognition is added, the morphology, as well as functionality, of the created one-dimensional architectures is easily affected by this additive.[3–7] One may expect, therefore, that if a polymer with a molecular recognition site is added as a template for gelator molecules, one-dimensional arrangement of gelator molecules would be controllable through exact interactions between the polymer and gelator molecules.

Biomolecules exhibit various unique higher-order structures, so that they should act as fascinating templates to create well-regulated one-dimensional molecular assemblies. In fact, it has been demonstrated by several research groups that biopolymers could be utilized as templates in the creation of desired molecular arrangements.[8] Among these biological molecules, DNA is one of the most attractive templates because of its well-regulated sequence, in addition to micrometre length and uniform 2 nm diameter in its double-stranded structure, which cannot be prepared by artificial polymers. It thus occurred to us that when polynucleotide acts as a template for gelator molecules bearing complementary nucleobase, they would be arranged along the template polynucleotide through the exact hydrogen-bonding interaction, leading to the creation of well-regulated one-dimensional molecular architectures.[9] We herein report our novel findings that polyadenylic acid (poly(A)) can act as an excellent template for thymine- or uracil-appended organogelators through hydrogen-bonding interactions to form artificial double-stranded DNA-like structures in an organic solvent.

Here, to use polynucleotide as a template for organogelators in an organic solvent, one has to overcome an essential problem arising from the mismatching properties between polynucleotide and organic molecules; that is, organogelators can exhibit their self-assembling capabilities only in an organic solvent, whereas polynucleotide by itself is virtually soluble only in water, so that some appropriate solvent system which can dissolve both components must be found out. We here propose the potential solutions to overcome these difficulties: one is to design an organic molecule which can gelate a polar organic solvent being miscible with water and another strategy is to dissolve polynucleotide into an organic solvent by exchanging potassium counter cation for a cationic surfactant.[12] Fig. 1 summarizes the nucleobase-appended organogelators we used in the present study.

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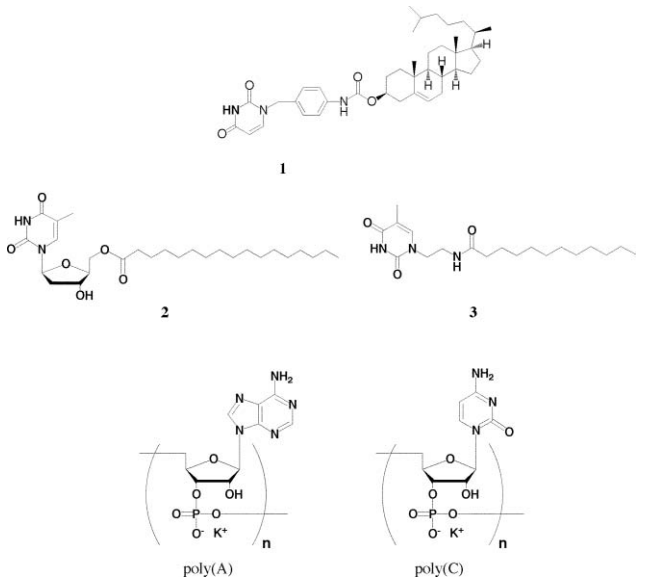


Fig. 1 (a) Structure of nucleobase-appended organogelators, (b) complementary or non-complementary polynucleotides, *i.e.*, poly(A) and poly(C), respectively.

Organogelator–polynucleotide complex formation in alcohol–water mixed solvent

Firstly, we designed a cholesterol-based gelator **1** which is functionalized by an uracil group as a recognition site (Fig. 1). We estimated the gel-forming ability of gelator **1** in various organic solvents and found that gelator **1** can gelate *n*-butanol being miscible with water. The result suggests that in a *n*-butanol–water mixed solvent, gelator **1** would interact with polynucleotide to form a one-dimensional architecture through the complementary hydrogen-bonding interactions, in addition to the cholesterol packing interactions. Accordingly, to create the gelator **1**–polynucleotide fibrous composite, we mixed an *n*-butanol solution containing gelator **1** with an aqueous solution containing a complementary polynucleotide. Here, we used poly(A) (10 mg ml^{-1}) as a complementary polynucleotide. The general procedure for the gelation test is as follows. Gelator **1** (5.0 mg, 7.9×10^{-3} M) was dispersed in *n*-butanol (0.10 ml) and the mixture was warmed in a septum-capped test tube. This solution was immediately poured into the aqueous poly(A) solution (5.0 μl).[10] Although this treatment afforded a clear solution suitable for spectroscopic analyses, precipitate was formed after leaving for several days due to the hydrophobic properties of cholesterol groups. Therefore, to remove water from the sample, the water–*n*-butanol mixed solvent (*n*-butanol : water = 20 : 1 (v/v)) was concentrated to dryness under reduced pressure for 1 h, and then *n*-butanol (0.10 ml) was added to the mixture (final concentration was adjusted to [**1**] = 5.0% (w/v), 7.9×10^{-2} mol ml^{-1}). The solution was warmed until it became clear. After cooling to room temperature, we could obtain a stable gel. As a reference experiment, we estimated the gel-forming ability of gelator **1** by itself under the same conditions. However, gelator **1** by itself could not form a stable gel, supporting the view that poly(A) would assist the one-dimensional arrangement of gelator **1** through the complementary hydrogen-bonding interaction.

The stabilities of organogels are usually evaluated with sol-gel phase transition temperature (T_{gel}). Therefore, the T_{gel} values of gelator **1** were determined as a function of added poly(A). It was found that the stability of the obtained gel tends to increase even in the presence of a small amount of poly(A) ([adenine base] : [**1**] = 0.05 molar ratio) and the T_{gel} values reach a maximum (76 °C) at [adenine base] : [**1**] = 0.3 molar ratio. At [**1**] = 7% (w/v) and 10% (w/v), the T_{gel} values were further enhanced up to 82 °C and 91 °C, respectively. The findings indicate that gelator **1** aggregates into a one-dimensional columnar stack with the aid of the complementary hydrogen-bonding interactions between poly(A) and the uracil moieties in **1**.

To further confirm whether poly(A) is really incorporated into the created organogel fibers, we observed CLSM (confocal laser scanning microscope) images of the obtained organogel, where tetramethyl-rhodamine (TAMRA)-labeled oligo(dA)$_{45}$ was used as a complementary nucleotide. As one can recognize from the CLSM image shown in Fig. 2, the fluorescence image arising from TAMRA well overlaps the fibrous image of the organogel fiber structure. The result strongly supports the view that the added oligo(dA)$_{45}$ is incorporated into the gel fiber and acts as the template for the gelator molecules.

We prepared organogel also using poly(C) (polycytidylic acid), the nucleobase of which is not complementary to **1**, expecting that the stability of the obtained gel is not affected by the addition of poly(C). In contrast to our expectation, however, we found that poly(C) is also effective to the gel formation; that is, the gel formation was recognized at [cytosine base] : [**1**] = 0.1 molar ratio and the T_{gel} values were almost comparable to those of the **1**–poly(A) system. The finding implies that to stabilize the gel, formation of the hydrogen bonds between gelator and polynucleotide is crucial but they are not necessarily complementary.

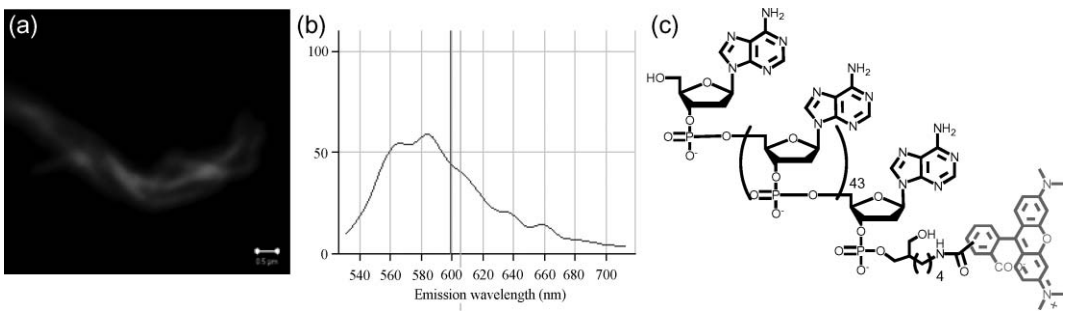


Fig. 2 (a) Fluorescence image of organogel fibers containing TAMRA-labeled oligo (dA)$_{45}$, (b) fluorescence spectrum obtained from the gel fiber and (c) structure of TAMRA-labeld oligo(dA)$_{45}$. Excitation at 514 nm, **1** (5% (w/v), 7.9×10^{-2} M) + (dA)$_{45}$-3′Rh (4.5×10^{-10} M per base).

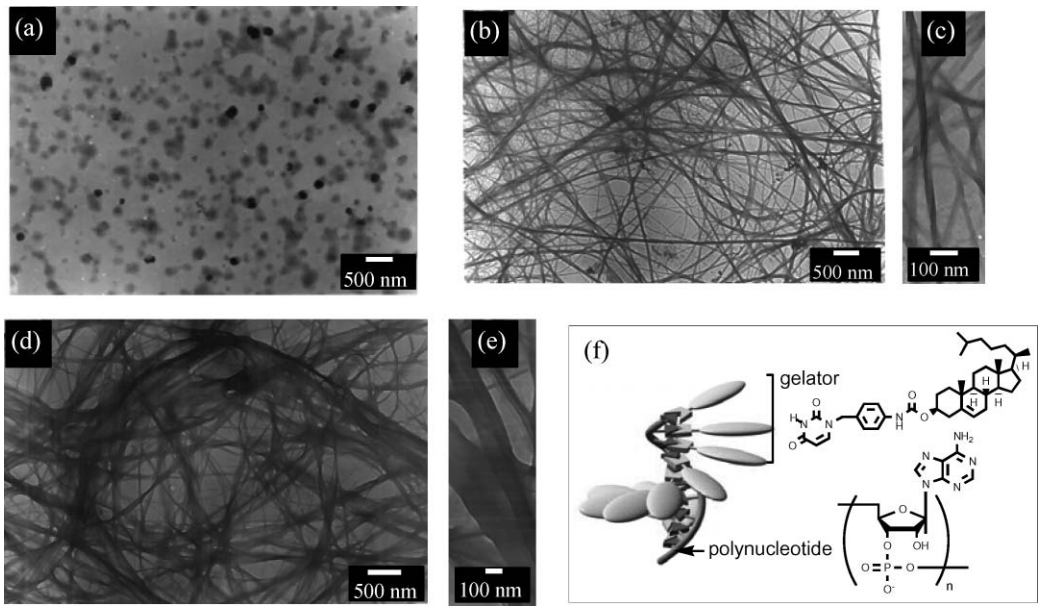


Fig. 3 (a) TEM image of spherical aggregate of gelator **1**, (b) TEM image obtained from **1**–poly(A) gel (5.0% (w/v), [adenine base] : [**1**] = 0.3) and (c) its magnified image. (d) TEM image obtained from **1** (5.0% (w/v)) + poly(C) and (e) its magnified image. (f) Schematic illustration of **1**–poly(A) gel fiber structure.

We could recognize, however, that the complementary hydrogen-bonding interactions would force the gelator molecules to organize along the template poly(A), leading to the creation of fibrous architectures reflecting the inherent morphology of poly(A). In the transmission electron microscope (TEM) observation, **1** in *n*-butanol solution (5.0% (w/v)), which gave the sol phase, resulted in spherical aggregates (Fig. 3a). When poly(A) (10 mg ml^{-1}) was added ([adenine base] : [**1**] = 0.3 molar ratio), the aggregate structure was changed to a well-developed fibrous network structure with 50–100 nm diameters and the solution was gelated (Fig. 3b). The close-up picture reveals that most tape-like fibers are twisted in a helical fashion with 600–700 nm pitches (Fig. 3c). Interestingly, we noticed that both the pitch length and the tape width become shorter with the increase in the [adenine base] : [**1**] molar ratio, reflecting the original morphology of poly(A): *e.g.*, they are 20 nm diameter and 30 nm pitch at [adenine base] : [**1**] = 0.7 molar ratio (Fig. 4a and 4b). The similar phenomenon was previously observed by Huc *et al.*, for cationic gemini surfactants having chiral tartrate counterions; the helical pitch becomes shorter with the increase in the *e.e.* of tartrate counterions.[11] One may consider, therefore, that added poly(A) enforces the gelator molecules to be closely packed and to grow up as a helical structure. In contrast, the **1** + poly(C) mixture gives a fibrous network but the helical structure is not found even in the close-up picture (Fig. 3d and 3e). The finding implies that although the nonspecific **1** + poly(C) interaction is effective in the enhancement of T_{gel}, it is not powerful as to induce the helical motif in the complexed supramolecular assembly. Only when the nucleobase in the gelator molecule is complementary to that in polynucleotide, does the well-ordered periodical superstructure appear along the created fibrous assembly. These findings show that only poly(A) can act as a complementary polynucleotide, along which gelator molecules are arranged through the hydrogen-bonding interaction to create artificial DNA-like double-stranded architectures.

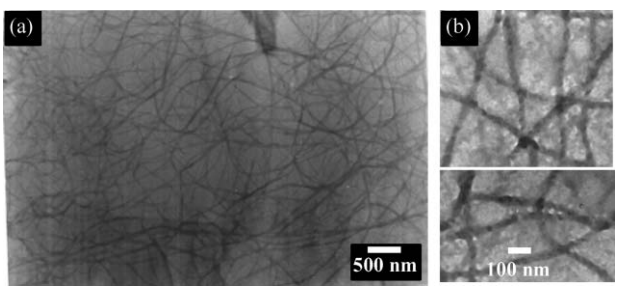


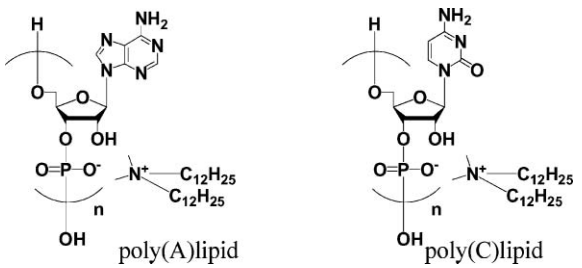
Fig. 4 (a) TEM image obtained from **1**–poly(A) gel (5.0% (w/v), [adenine base] : [**1**] = 0.7) gel and (b) its magnified image.

Organogelator–(polynucleotide–lipid) complex formation in benzene

Recently, we have reported a family of thymidine-based organogelators and found that some of them show good gelation abilities with nonpolar organic solvents.[9f] For example, 5′-esterificated thymidine derivative **2** aggregates through the hydrogen bonding interaction, van der Waals interaction and π–π stacking, and forms organogels with benzene, toluene, CCl_4, tetrahydronaphthalene (THN), hexane and cyclohexane. Gelator **3** is also functionalized as a thymine nucleobase and has a similar gelation ability with nonpolar organic solvents as observed in the gelator **2** system. However, unlike gelator **1**, both gelator **2** and gelator **3** could not form a stable gel in tested organic polar solvents. This is in contrast to the gelator **1** system; that is, the polynucleotide cannot act as a template for these gelator molecules due to the mismatching properties between the polynucleotide and the organic molecule. Therefore, to form a polynucleotide-templated organogel, the polynucleotide should be solubilized into an organic solvent in which gelator **2** and gelator **3** can

form a stable gel. So far, Okahata *et al.*, have demonstrated that polynucleotide can easily be solubilized in an organic solvent by exchanging cationic counterions with cationic surfactant.[12] According to this paper, we prepared polynucleotide–lipid complexes using didodecyldimethylammonium bromide (DDAB) as a cationic surfactant and mixed them with gelator **2** or gelator **3** in an organic solvent, expecting that these gelator molecules would adopt a highly-ordered one-dimensional architecture to form artificial double-stranded DNA-like structures in an organic solvent.

When a stoichiometric amount of poly(A)–lipid was mixed with **2** in benzene (2.0% (w/v)) and the mixture was heated until it became clear, a transparent gel was formed after cooling the solution to room temperature. In contrast, gelator **2** by itself gave an opaque gel at the same concentration in benzene. The result suggests that poly(A) would be incorporated into the original gel fiber formed by **2** through the complementary hydrogen-bonding interactions. As a reference experiment, when we used non-complementary poly(C)–lipid instead of poly(A)–lipid, the original opaque gel was obtained. The result also supports the view that there is no effective interaction between gelator **2** and poly(C)–lipid.



To evaluate the bulk gelation property of gelator **2**, we measured T_{gel} values ([**2**] = 2.0% (w/v), [adenine or cytosine base] : [thymine base] = 1.0). The vial containing the gel was immersed inversely in a thermo-controlled oil bath, and the temperature was increased at the rate of 1.0 °C min^{-1}. In the case of **2** gel by itself and **2** gel + (poly(C)–lipid), the samples were heavily turbid and gradually spilled the solvent out between 40 to 70 °C. These phenomena are often seen for the crystalline gel. In contrast, **2**–(poly(A)–lipid) gel was transparent and a sharp sol-to-gel phase transition temperature appeared at 60 °C. These results indicate that the bulk property and stability of the present gel system would be controlled by the complementary hydrogen bond.

The complementary hydrogen-bonding interaction also plays a crucial role for the gelator **3** system. Gelator **3** by itself did not form any stable gel in benzene at 1.0% (w/v) concentration. On the other hand, upon mixing with a stoichiometric amount of poly(A)–lipid, the gelator **3** molecule afforded a stable transparent gel as seen in the **2**–(poly(A)–lipid) gel system. The result indicates that the complementary hydrogen-bonding interaction between thymine base and poly(A)–lipid would promote the one-dimensional assembly of gelator **3** molecules. In fact, as a reference experiment, when gelator **3** was mixed with non-complementary poly(C)–lipid, we could not confirm any gel formation, indicating that there is no effective interaction between the gelator **3** molecule and poly(C)–lipid. These findings observed for the gelator **3** system are consistent with that observed for the gelator **2** system.

The stoichiometry between gelator molecules and adenine bases was evaluated by using gelator **3**; that is, critical gelation concentration (CGC) values were evaluated by gradually changing the [adenine base] : [**3**] molar ratios from 0.25 to 2.0. One can see from Fig. 5 that when [adenine base] : [**3**] molar ratios increase from 0.25 to 2.0, CGC values continuously decrease and reach the constant at [adenine base] : [**3**] = 1.0. The result indicates that the stoichiometry between gelator **3** molecule and adenine base can be estimated to be 1.0, suggesting the formation of the complementary Watson–Crick type hydrogen bond.

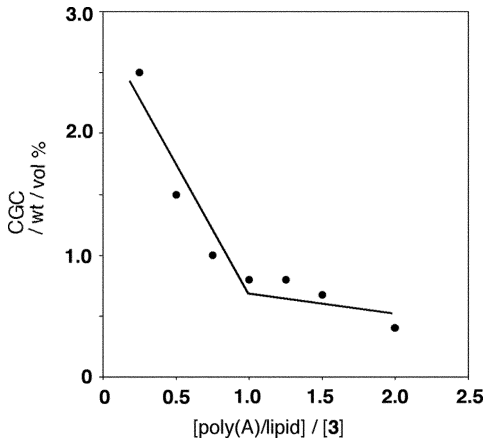


Fig. 5 Plots of CGC values as a function of the [adenine base] : [**3**] ratio.

The existence of the complementary Watson–Crick type hydrogen bond was also evidenced by ATR-FTIR spectra. For example, as shown in Fig. 6, gelator **2** by itself gave a characteristic peak at 3431 cm^{-1}, which is attributed to the hydrogen-bonding interaction among 3′-OH groups in **2**. Upon addition of poly(A)–lipid, however, this peak disappeared at [adenine base] : [**2**] = 1.0 molar ratio, indicating that poly(A)–lipid causes a change in the packing mode among **2** molecules. The contribution of complementary A–T base paring can be easily discussed by the C=O stretching band in thymidine appearing around 1650–1700 cm^{-1}. The original **2** gel shows a strong peak at 1659 cm^{-1}, which is attributed to the C=O stretching band arising from non-complementary T–T hydrogen-bonding pairs or 3′-OH–T hydrogen-bonding among **2** molecules.

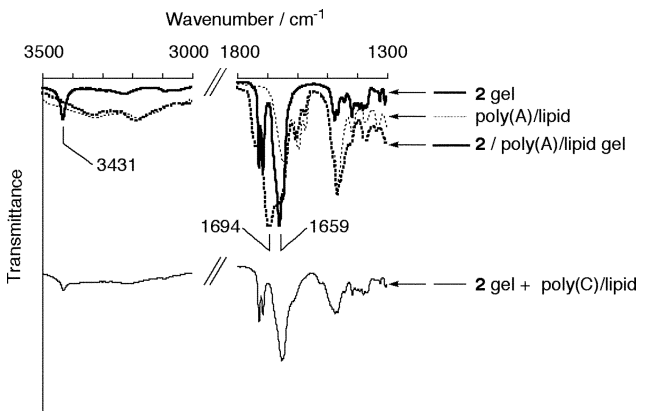


Fig. 6 ATR-FTIR spectra of xerogel obtained from **2** gel (bold line), **2**–(poly(A)–lipid) gel (bold dotted line), poly(A)–lipid (dotted line) and **2** gel + poly(C)–lipid (thin line). The molar ratio ([adenine or cytosine base] : [**2**]) was fixed to be 1.0.

Upon addition of poly(A)–lipid, the strength of the peak decreased and a new peak appeared at 1694 cm^{-1}, which is assignable to the formation of A–T hydrogen-bonding. The result suggests that non-complementary T–T hydrogen-bonding pairs or 3′-OH–T hydrogen-bonding among gelator **2** molecules are re-assembled to the complementary A–T hydrogen-bonding pairs by the addition of poly(A)–lipid. It should be noted that the IR spectral change by the addition of poly(A)–lipid was saturated at [adenine base] : [**2**] = 1.0 molar ratio, suggesting that gelator **2** would be continuously aligned on a poly(A) template with the aid of the Watson–Crick type hydrogen-bonding interaction. The similar tendency in ATR-FTIR spectra was also observed for the gelator **3** system. As shown in Fig. 7, a characteristic peak of gelator **3** by itself appears at 1681 cm^{-1}, which is attributed to the C=O stretching band of thymine. Upon addition of poly(A)–lipid ([adenine] : [**3**] = 1.0), however, the original peak at 1681 cm^{-1} disappeared, whereas a new peak appeared at 1670 cm^{-1}. The significant peak shift is due to the complementary hydrogen-bonding interaction between thymine base and adenine base. When gelator **3** was mixed with poly(C)–lipid under the same conditions, we could not confirm any spectral change of **3** in IR spectra, supporting the view that the complementary hydrogen-bonding interactions actually exist in the created **3**–(poly(A)–lipid) gel fibers.

To observe the morphological change caused by the addition of polynucleotide, we carried out SEM observations. As can be recognized in Fig. 8b, gelator **2** by itself gave the plate-like crystalline structure. On the other hand, it was revealed that the plate-like structure turned into shreds upon mixing with poly(A)–lipid, leading to the creation of the 3-D entangled fiber structure (Fig. 8c). The morphological changes of **2** gel thus observed were also saturated at around 1.0 equivalent of poly(A)–lipid, supporting the view that Watson–Crick base-paring would be created in the obtained gel fiber structure. As expected from foregoing gel turbidity and IR spectral similarity, the plate-like structure was also recognized for **2** gel + poly(C)–lipid (Fig. 8d). The result also supports the view that no effective interaction

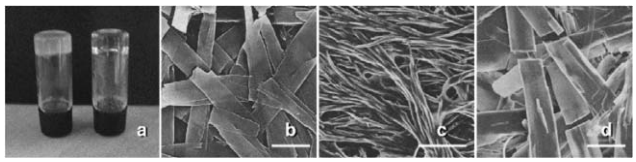


Fig. 8 (a) Photo image of gel sample created by **2** gel (left) and **2**–(poly(A)–lipid) gel (right). SEM images of (b) **2** gel, (c) **2**–(poly(A)–lipid) gel and (d) **2** gel + (poly(C)–lipid); [adenine base or cytosine base] : [thymidine] = 1.0. All scale bars indicate 5 μm.

between gelator **2** and poly(C)–lipid occurs. One can also recognize in Fig. 8c that the surface is rough and the fiber structure entangled windingly. This result shows that crystallinity of the obtained composite is somewhat lower than that of the original **2** gel. The crystallinity of the aggregate was confirmed more directly by X-ray diffraction (XRD); that is the peak intensities of **2** gel are decreased by adding poly(A)–lipid (Fig. 9). This result indicates

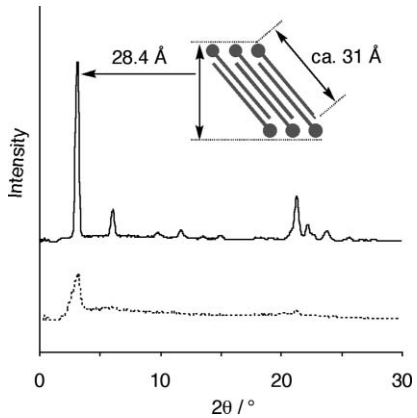


Fig. 9 X-ray powder diffraction diagrams of xerogel obtained from **2** (solid line) and **2**–(poly(A)–lipid) gel (dotted line) : [**2**] = 2.0% (w/v), [adenine base] : [**2**] = 1.0. Inset figure shows a possible molecular packing of **2** in the created fibrous structure.

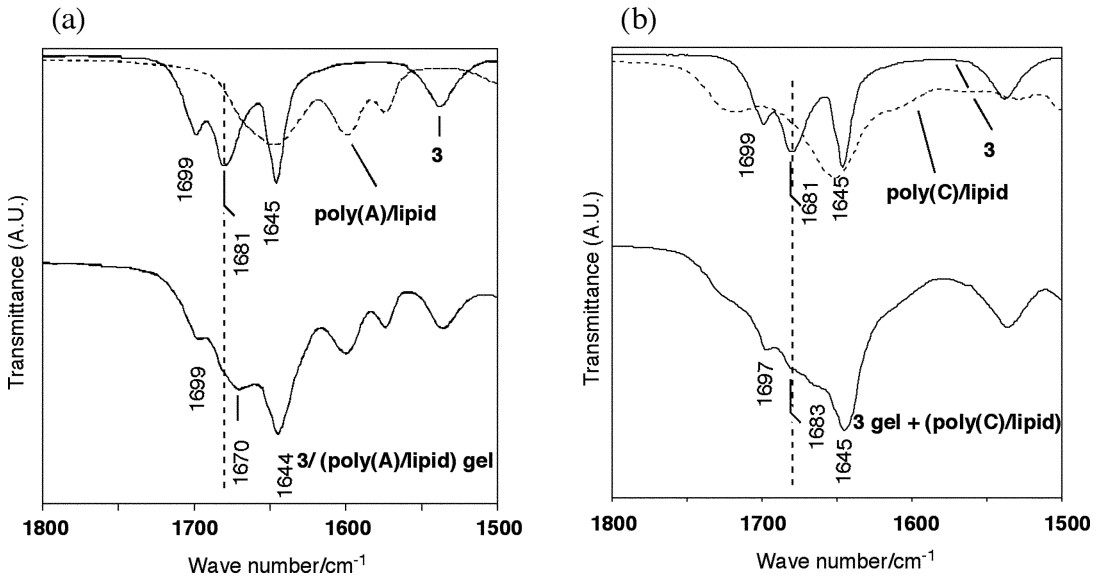


Fig. 7 (a) ATR-FTIR spectra of xerogel obtained from **3** gel (solid line), poly(A)–lipid (dotted line) and **3**–(poly(A)–lipid) gel (lower part). (b) ATR-FTIR spectra of xerogel obtained from **3** gel (solid line), poly(C)–lipid (dotted line) and **3** gel + (poly(C)–lipid) (lower part).

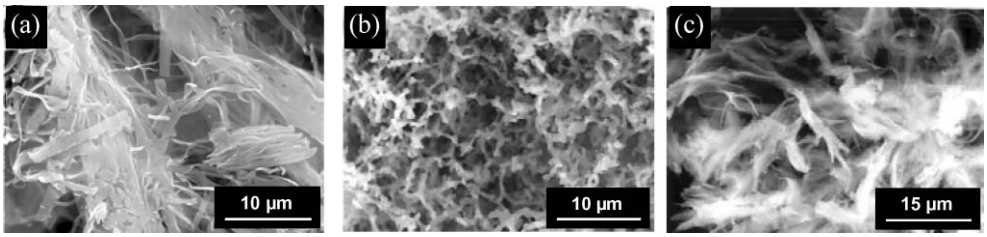


Fig. 10 SEM images of xerogel obtained from (a) only **3**, (b) **3**–(poly(A)–lipid) ([adenine base] : [**3**] = 1.0) and (c) **3** gel + (poly(C)–lipid) ([cytosine base] : [**3**] = 1.0).

that poly(A)–lipid prevents the bilayer assembly structure of **2** (inset in Fig. 9) from growing up to multi-layers.

The similar morphological changes can be observed for gelator **3** system. SEM images shown in Fig. 10 revealed that the complementary hydrogen-bonding interaction between gelator **3** and poly(A)–lipid also causes the drastic changes of the molecular packing among gelator **3** molecules. As shown in Fig. 10b, one can recognize that **3**–(poly(A)–lipid) gel gives a well-developed fibrous network structure. In contrast, gelator **3** by itself gives the plate-like structure as seen in Fig. 8b. Even when gelator **3** was mixed with the non-complemenatry poly(C)–lipid, any morphological change did not occur (Fig. 10c). These phenomena are similar to those observed for the gelator **2** system.

We have shown through the second part that poly(A)–lipid exhibits the precise molecular recognition abilities toward both gelator **2** and gelator **3**. These gelator molecules have basically the same gel-forming abilities in the presence of poly(A), implying that only thymine base plays a crucial role for the stable gel formation. We believe, therefore, that the present system can be extended to other organic molecules. Considering the difficulty in creating DNA-templated organic nanofibers, the present approach would accelerate the wide-use of polynucleotide in an organic media to create a functional nanofiber based on organic molecules.

Conclusions

We have demonstrated that single-stranded poly(A) and poly(A)–lipid can act as the templates for the organogelators bearing the complementary nucleobases, *i.e.*, gelator **1**, gelator **2** and gelator **3**. Gelator **1** can gelate polar organic solvent, such as *n*-butanol, in the presence of poly(A), whereas gelator **2** and gelator **3** can commonly form stable gel with organic solvents in the presence of poly(A)–lipid complex. From the various spectroscopic and the microscopic investigations, in the created gel fiber structures, the incorporated polynucleotide template forces the gelator molecules to adopt the highly-ordered one-dimensional architectures, through the complementary hydrogen-bonding interactions. These results imply that nucleobase-appended organogelators bearing adenine, cytosine or guanine in addition to thymine (uracil) would also be arranged on polynucleotide templates with a programmed-sequence to create more sophisticated nanofiber structures. We believe, therefore, that the present system can open the new paths to accelerate development of one-dimensional molecular assembly systems taking advantage of DNA-based functions, leading to the creation of novel one-dimensional functional nanomaterials.

Experimental

General

UV/Vis absorption and fluorescence spectra were measured on a Shimadzu UV-2500PC spectrometer and a Hitachi F-4500 spectrometer, respectively. ^{1}H-NMR spectra were recorded on a Bruker DRX600 spectrometer at 25 °C. Matrix assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectra were recorded on a PerSeptive Biosystems Voyager-DERP biospectrometry workstation. A confocal laser scanning microscope (CLSM) was used for taking the fluorescence image of TAMRA-laveled oligo(dA)$_{45}$. CLSM images were taken using a Carl Zeiss LSM 510, where the excitation wavelength was 488 nm. TEM images were acquired using a JEOL TEM-2010 (accelerate voltage 120 kV). The TEM grid was dried under reduced pressure for 6 h before TEM observation. Scanning electron microscopy (SEM) studies were carried out on a Hitachi S-5000. Xerogel was shielded with platin before SEM measurements. The accelerating voltage was 25.0 V and the emission current was 10 μA. Poly(A) and poly(C) were purchased from Amersham Pharmacia Co. TAMRA-labeled oligo(dA)$_{45}$ were purchased from Hokkaido System Science. Gelator **1** and **2** were synthesized according to the preceding paper reported by us.[9e,f] Gelator **3** was newly synthesized according to the following procedure, where the precursors **4** and **5** were synthesized according to the reported procedure.[13]

Synthesis of gelator 3

1-(2-Phthalimidethyl)thymine (4). Thymine (4.2 g, 33 mmol) was dissolved in 100 ml of DMSO. To the DMSO solution, K_2CO_3(4.6 g, 33 mmol) and *N*-(2-bromoethyl)phthalimide (4.4 g, 17 mmol) were added and the mixture was stirred for 24 h at 40 °C. The reaction mixture was evaporated *in vacuo* to remove solvent. The residue was dissolved in chloroform and washed with distilled water several times. Compound **4** was obtained as a white powder (2.8 g, 66%). ^{1}H NMR (600 MHz, DMSO-d_6, 25 °C) δ 1.65 (s, 3H, thymine 5-CH_3), 3.85 (m, 4H, NCH_2CH_2N), 7.51 (s, 1H, thymine 6-H), 7.84 (m, 4H, Ar*H*); MALDI-TOF-MS: (dithranol) $[M + H]^+ = 300.00$ (calc. 300.10).

1-(2-Aminoethyl)thymine (5). Compound **4** (1.1 g, 3.5 mmol) was dissolved in a mixed solvent (*n*-butylamine : methanol (1 : 4 (v/v)). After reflux for 2 days, the reaction mixture was concentrated to dryness. The residue was re-dissolved in 0.5 M HCl (50 ml) and washed with diethyl ether (50 ml). The aqueous portion was evaporated under reduced pressure to give the crude product. Recrystallization from MeOH–diethylether–chloroform

afforded compound **5** as a white powder (609 mg, 99%). ^{1}H NMR (600 MHz, DMSO-d_6, 25 °C) δ 1.76 (s, 3H, 5-CH_3), 3.06 (t, 2H, J 5.7, NCH_2CH$_2$N), 3.88 (t, 2H, J 5.7, NCH_2CH$_2$N), 7.48 (s, 1H, thymine 6-H), 7.93 (s, 2H,–NH_2), 11.3 (s, 1H,–NH–); MALDI-TOF-MS: (dithranol) $[M + H]^+ = 170.10$ (calc. 170.09).

Gelator 3

To compound **5** (500 mg, 2.96 mmol), triethylamine (0.50 ml), *n*-dodecanoyl chloride (0.77 ml, 3.55 mmol) and dry-DMF (30 ml) were added and the resultant solution was stirred for 30 min at room temperature The mixture was diluted with chloroform and washed with distilled water. The organic layer was dried over anhydrous magnesium sulfate. After removing the solvent, gelator **3** was obtained as a white powder (977 mg, 94%). ^{1}H NMR (300 MHz, DMSO-d_6, 25 °C) δ 0.85 (t, 3H, J 6.3,–CH_3), 1.23 (m, 16H,–(CH_2)$_8$–) 1.44 (m, 2H, NHCOCH$_2$CH_2–), 1.72 (s, 3H, thymine 5-CH_3), 2.00 (t, 2H, NHCOCH_2CH$_2$-), 3.33 (m, 2H, NCH$_2$CH_2N), 3.64 (t, 2H, J 5.7, NCH_2CH$_2$N), 7.31 (s, 1H, thymine 6-H), 7.86 (s, 1H,–NHCO–), 11.2 (s, 1H, –NH–). IR (KBr, cm^{-1}): 3389, 3161, 3039, 2914, 2849, 1678, 1645, 1536, 1469. MALDI-TOF-MS: (dithranol) $[M + H]^+ = 352.30$ (calc. 352.25). Anal. Calcd. for $C_{19}H_{33}N_3O_3 \cdot 0.07CHCl_3$:C, 63.65; H, 9.26; N, 11.68. Found: C, 64.01; H, 9.26; N, 11.65 (The final compound includes a small amount of chloroform).

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