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Volume confinement induced microstructural transitions and property enhancements of supramolecular soft materials

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The rheological properties of supramolecular soft functional materials are determined by the networks within the materials. This research reveals for the first time that the volume confinement during the formation of supramolecular soft functional materials will exert a significant impact on the rheological properties of the materials. A class of small molecular organogels formed by the gelation of N-lauroyl-l-glutamic acid di-n-butylamide (GP-1) in ethylene glycol (EG) and propylene glycol (PG) solutions were adopted as model systems for this study. It follows that within a confined space, the elasticity of the gel can be enhanced more than 15 times compared with those under un-restricted conditions. According to our optical microscopy observations and rheological measurements, this drastic enhancement is caused by the structural transition from a multi-domain network system to a single network system once the average size of the fiber network of a given material reaches the lowest dimension of the system. The understanding acquired from this work will provide a novel strategy to manipulate the network structure of soft materials, and exert a direct impact on the micro-engineering of such supramolecular materials in micro and nano scales.

1. Introduction

The intermolecular organization of biomacromolecules, i.e. proteins, polysaccharides etc. is one of the most important structures in living organisms. As the inner and outer cellular structures are found to be composed of a network of proteins and polysaccharides, the correlation between the structures and properties, in particular in a confined space, becomes very crucial in understanding some life-related activities. Moreover, as a class of supramolecular functional materials, organogels have attracted great interest in recent years. They have been found to have a variety of important applications in cosmetics, drug delivery, as scaffolds for tissue engineering and in the synthesis of many nanomaterials due to their porous structure along with other properties, i.e. biocompatibility, elasticity and thermo-reversibility. The micro/nano structure, such as the pore size, and the rheological properties, such as the viscoelasticity, are regarded as the most important characteristics of such a material, which determine the efficiency and even the applicability of the material. Furthermore, the microstructure has been found to be directly related to the rheological properties. In recent years, a large amount of work has been carried out to acquire a better understanding of the formation mechanism in order to engineer the materials with desired structural and rheological performance for some expected applications.

The macroscopic properties of the soft materials depend on the topology and hierarchical structures of the networks, which can be divided into two types. One consists of only one set of fiber network, such as the three dimensional (3D) fibrillar network shown in Fig. 1c and f. A spherulite can be regarded as a fiber network. Once several networks mutually interpenetrate, they will also behave like a “single” fiber network (Fig. 1b and e). As the links between fibers are permanent, this interconnecting network structure comes with strong elasticity (or elastic modulus, G'). The other consists of a multi-domain network, such as the mutually exclusive spherulites (Fig. 1a and d). The elasticity of a material with such a multi-domain network is generally determined by the weakest links, i.e. the physical interactions or contacts between adjacent fiber networks (i.e. spherulites). As the mutually exclusive spherulitic structure commonly exists in polymers, protein crystallites and

![Fig. 1 Micrographs and schemes of different fibre networks: multi-domain network with mutually exclusive spherulites (a, d), single-fibre network with interpenetrated spherulites (b, e) or interconnecting fibrils (c, f). All of the micrographs are taken via optical microscopy of the N-lauroyl-l-glutamic acid di-n-butylamide/ethylene glycol (GP-1/EG) gels obtained under different gelling conditions.](image-url)
supramolecular soft materials, it is important to improve the elasticity and structural homogeneity of these materials for their applications in many fields.

Converting the domain network structure of a soft material into a 3D interconnecting fiber network has been proved to be an effective method to alter substantially the rheological properties of the material.\(^7\) In such a conversion, the set of a weak networks is replaced with a strong one. To engineer a soft material, i.e. an organogel, different approaches have been reported in terms of chemical, thermal, sound stimuli, etc.\(^9\) Additives, such as polymers and surfactants,\(^10\) have been demonstrated to be able to regulate effectively the initial nucleation and the subsequent network formation of the fibers. Therefore the additive-mediated approach can be considered as an effective means to manipulate the microstructure and the corresponding rheological properties of such soft materials. Nevertheless, the methods mentioned above will bring about external disturbance to the material. Adjusting the thermodynamic driving force during the materials formation is another effective technique to control the gelation process.\(^11\) Supersaturation \(\xi\), defined as \((T - T_c)T_c\), where \(T\) is the equilibrium temperature of a gel at a certain gelator concentration and \(T_c\) is the temperature at which the soft material is formed, describes how far the system deviates from the equilibrium state and is the thermodynamic driving force for network formation.\(^8\) The quantitative correlation between supersaturation and the microstructure, i.e. pore size, for some organogel systems has been established.\(^12\) Other methods, such as ultrasound stimulus\(^13\) as well as controlling the initial gelator nucleation,\(^14\) have also been reported. The elasticity of the soft materials can be improved many times by the engineering of the fiber network.

Despite the significant advances mentioned above, the focus has concentrated only on materials where the influence from the system size was not crucial. The size of the material is either equal to the size of a single fiber network (fiber network dominated, Fig. 1f), or is many times larger than a single fiber network (domain network dominated, Fig. 1d). The transition from domain network dominated to fiber network dominated via the change of the size of the system and the resulting impact on the corresponding rheological properties has never been considered before. In reality, soft materials at a significantly reduced length scale such as micro/nano gels have important applications in many fields such as tissue engineering and nanoreactors.\(^15\) Due to the volume confinement effect, a soft material formed in a limited space may behave very differently from one formed in a free space.\(^16\) Therefore, it is important to acquire a good understanding of the structural and rheological properties of a soft material formed within a confined volume.

In this work, we take N-lauroyl-L-glutamic acid din-butylamide/ethylene glycol (GP-1/EG) system as an example, to examine the influence of volume confinement on the gelation of an organogel, in particular on the network structure and the subsequent macroscopic rheological properties of such a material. We will show that within a one dimensional (1D) finite space, the storage modulus of the gel can be greatly enhanced more than 15 times after a structural transition from a multi-domain dominated to a single-fibre network dominated system. This gives rise to a wide range of applications and implications in the fields such as drug delivery, the templated synthesis of nanomaterials, and the supramolecular self-assembly of biomolecules in living organisms.

2. Strategy of structural analysis and control

A soft material consisting of a 3D fibrous network structure can entrap a liquid within it. The spherulitic network structure, as shown in Fig. 1a, commonly exists in polymers, proteins, and other supramolecular materials. Systems with such a network often have weak elasticity because of the boundary effect between adjacent domains. As the formation of many supramolecular materials, i.e. physical gels, is to a large extent determined by the nucleation and growth of fiber networks,\(^17\) the thermodynamic driving force, i.e. supersaturation,\(^18\) has been proved to be one of the key factors affecting the network formation and subsequent rheological properties of such a material. Controlling the supersaturation will therefore give rise to the transition from a multi-domain dominated to a single network dominated system, or vice versa.\(^8\)

\[(1) \text{ Structural analysis and corresponding rheological properties} \]

A network structure can be topologically regarded as fibers and their connections, including the permanent joints (branchings) and transient joints (entanglements).\(^8\) A single-fibre network might consist of only one network while, more frequently, it is formed by the interpenetrating or interconnecting of adjacent networks. The structure of a single-fibre network is normally described with two constant parameters: the branching rate \(z\) (the number of branches from each branching point) and correlation distance \(\xi\), which can be approximated by the average distance between two adjacent branching points in the network.\(^8\) These two parameters together characterize the branching density of the fiber network, and eventually determine the rheological properties of a supramolecular soft material. A Cayley tree-like structure is a typical example of the single-fibre networks with strong and permanent branching junctions. In our previous work, we have shown that for a given type of networks there is a power law relationship between the correlation length \(\xi\) and the storage modulus \(G'\) as \(G'_{\text{fiber}} \sim \xi^{-\rho}\) \((\rho = 0.5 - 1.7 \text{ depending on the gelling systems})\).\(^12\)

On the other hand, a multi-domain network is composed of a number of weakly interacting single networks. For a supramolecular material with a multi-domain network, i.e. the mutually exclusive spherulites (Fig. 1d), as the strength of the network is determined mainly by the weak links (the physical contacts between adjacent domains) these greatly influence the macroscopic properties, such as the elasticity of the material. Consequently, the boundary effect becomes one of the key factors in determining the rheological properties of the material. The storage modulus \(G'_{\text{domain}}\) is usually much lower than in a material with a single network even for the same gelling system. In this context, another parameter, \(\zeta\), the average distance between two adjacent spherulites, is expected to be employed to characterize the rheological properties of such a material.
(2) Supersaturation dependence of the multi-domain and single-fibre networks

It was found that the formation of a domain network in a physical gel experiences the primary nucleation of the fiber networks, the growth of fibers and subsequently the formation of fiber networks once the thermodynamic driving force is applied (Fig. 2). In this regard, each primarily formed nucleus will develop into an individual fiber network. In a multi-domain network, the number of active nucleating centres in a unit volume will determine the number and eventually the size of the spherulites per unit volume in the system. The initial primary nucleation rate \(J\), defined as the number of nuclei successfully generated per unit time/unit volume, is governed by the supersaturation \(\sigma\) as follows:  

\[
J \sim N_f f \exp(-\Delta G/kT)
\]

where  

\[
\Delta G = \frac{16\pi\gamma_C \Omega^2}{3(kT)^2} f
\]

and  

\[
\Delta \mu / kT = \ln(1 + \sigma) \approx \frac{\Delta H_{\text{diss}}}{kT} (T^* - T)
\]

where \(N\) denotes the number of active nucleating centres, \(f'\) and \(f\) are factors describing the correlation between the substrate, i.e. nucleating centers, and the nucleation phase, \(B\) is the kink kinetics coefficient, \(k\) is the Boltzman constant, \(\Delta G^*\) denotes the nucleation energy barrier, \(\gamma_{Cf}\) denotes the interfacial free energy between the two phase, \(\Omega\) denotes the volume of the growth units, and \(\Delta H_{\text{diss}}\) denotes the molar dissolution enthalpy of the nucleating phase, \(T^*\) and \(T\) denote the equilibrium and gelling temperature of the solution, respectively. \(T^* - T\) can be described as supercooling \(\Delta T\). Here, \(\Delta \mu\) corresponds to the chemical potential difference between solute molecules in the fiber state and in the liquid, and \(\Delta \mu / kT\) denotes the thermodynamic driving force for the gelation (the degree of supercooling).

Eqn (1)-(3) indicate that for a gelling system with a given solute concentration, the nucleation rate \(J\) can be controlled by the gelling temperature \(T\). An elevated temperature corresponds to a lower thermodynamic driving force \(\Delta \mu / kT\) (eqn (3)). As a result, a lower nucleation rate \(J\) can be obtained. This implies the formation of fewer but larger spherulites. We notice that if the supersaturation or thermodynamic driving force is relatively low, the branching density \(1/\xi\) can be very low. Then the fibers from the adjacent spherulites can mutually penetrate. Therefore, the boundary between the adjacent fiber networks will become less sharp. Physically, the two fiber networks are merging. The decreased boundary effect would eventually result in the increase of the elasticity or \(G\). In the merging fiber networks, the number of the primary nucleation sites is no longer a key factor affecting the final properties of the soft material. Instead, the influence of supersaturation on the subsequent branching of the fibers becomes predominant. A power law \(\xi \sim \sigma^{b}\) was found to operate in this case (\(b\) is a constant factor for certain materials, such as \(b = -1.25\) for \(N\)-lauroyl-L-glutamic acid di-2-butylamide/isostearyl alcohol (GP-1/ISA) gel). Based upon \(G_{\text{fiber}} \sim \xi^{2}\), we can conclude that an elevated \(T_g\) (decreased \(\sigma\)) would result in the decrease of \(G\), indicating a drop in the elasticity of the material, which is opposite to what is observe in the multi-domain network.

(3) Structural transition between multi-domain and single-fibre network within a confined volume

In contrast to the fiber network dominated system, in a multi-domain network dominated system, an elevated \(T_g\) would result in a lower nucleation rate \(J\) (cf. eqn (1)), and the formation of fewer but larger spherulites. Consequently, within a confined space, a critical condition would occur between the two types of network through controlling the gelling temperature (Fig. 3). As \(T_g\) increases, the number of the domains \((L)\) decreases (\(L\): dimension of the system) within a given system (with a length of \(L\)) decreases. When the total number decreases from much larger than 1 (as in a multi-domain network) to 1 (at which only one spherulite exists), a transition from a multi-domain to a single-fibre network takes place. It follows that \(G\) will change from \(G_{\text{domain}}\) to \(G_{\text{fiber}}\), which is manifest as an abrupt increase of the storage modulus. This might be an effective method to promote the elasticity of the material. One of the advantages of this approach is that it is simple, since the conversion can be induced solely by changing the temperature for gel formation.

3. Materials and experiments

Materials

Gelator \(N\)-lauroyl-L-glutamic acid di-2-butylamide (GP-1, as shown in Scheme 1, >98%) was obtained from Ajinomoto, solvent ethylene glycol (EG, >99%) and propylene glycol (PG, >99%) were bought from Sigma-Aldrich. All of them were used as received.

![Fig. 2](image-url)  
Fig. 2 A real-time observation showing the nucleation and subsequent growth of a spherulitic structure, for 5 wt% \(N\)-lauroyl-L-glutamic acid di-2-butylamide/proplyene glycol (GP-1/PG) system gelled at 50 °C. (b) and (c) were taken 1 and 10 min after (a), respectively.

![Fig. 3](image-url)  
Fig. 3 Schematic of the relationship between the storage modulus \(G\) and the gelling temperature \(T_g\) for gels with a mutually exclusive spherulitic structure within a confined volume. \(L\): the macroscopic size of the gel; \(n\): the dimension of the system.
Rheological measurements

The rheological measurements were performed on an Advanced Rheological Expansion System (ARES, Research Instruments), using a parallel plate geometry with a diameter of 25 mm. The sol-to-gel transition process occurred between the plates with a fixed gap of 0.85 mm or other values specified in the text. A high cooling rate of 30 °C per minute was employed, to bring the system “immediately” to the preset condition before the notable gelation takes place in the gelling system. A dynamic temperature ramp test was carried out in situ to monitor the change of storage modulus \( G' \) and loss modulus \( G'' \) during the gelling process, with a constant frequency of 0.1 Hz and a strain of 0.05%. A frequency sweep test (from 0.1 to 10 rad s\(^{-1}\)) and a transient stress relaxation test were then carried out to learn about the characters of the gel, followed by a dynamic strain sweep test (from 0.05 to 200%). A cover was used to avoid solvent evaporation or water absorption during the whole measurements.

Real-time optical microscopic observations

To prepare a gel, a certain amount of GP-1 was mixed with the solvent in a glass tube and kept at 120 °C until the solid was dissolved completely. The gelator concentration used in this study was 1 wt% unless otherwise specified. For the optical observations, aliquots of the hot solution were sealed in self-made glass cells with certain size gaps, from 0.1 to 1.5 mm. The hot solution was first dropped between two cover slides with a spacer of a certain thickness. It was then impacted and sealed to make glass cells with certain size gaps, from 0.1 to 1.5 mm. The sol-to-gel transition process and the microstructure of the obtained gel were observed by a microscope video system.

Scanning electron microscopy (SEM) analysis

The SEM images of the gels were taken using a field emission scanning electron microscope (FESEM, JEOL JSM-5600LV) at 5.0 kV. The gels formed at different gelation temperatures with rheological dynamic temperature ramp tests. Typical curves are shown in Fig. 5. At \( T_g \) below 70 °C, the solution gels quickly, \( G' \) increases and reaches a plateau within 1000 s. For \( T_g \) above 85 °C, the gelation slows down because of the decrease in supersaturation. At higher gelling temperatures, especially above 95 °C, the \( G' \) of the samples is low, indicating that a self-supporting material cannot form any more due to the inability of the low fiber mass to trap the liquid. An exception was observed between 72.5 and 80 °C. Within this temperature range, \( G' \) keeps growing and has not arrived a constant value even after a long time (9000 s), indicating the formation of a different microstructure. The measurement was terminated after 9000 s due to the consideration that the gelation condition might be disturbed after a long time.

In order to explain the cause of the changing \( G' \), a parallel optical observation was carried out to monitor the gelling process of the gels formed at different \( T_g \) and to obtain the

4. Results and discussion

(1) The \( T_g \) dependence of \( G' \) for gels formed within confined volume

The GP-1/EG system was gelled within a confined volume to obtain the \( T_g \) dependent rule of the storage modulus. The gel was formed within a constant space of 0.85 mm thickness at different gelling temperatures. The storage modulus \( G' \) and the loss modulus \( G'' \) were measured in situ. \( G' \) was much higher than \( G'' \), which is a characteristic property of elastic gels. The correlation between \( T_g \) and the corresponding \( G' \) is shown in Fig. 4. By elevating \( T_g \), \( G' \) increases slightly from about 1.0 × 10\(^4\) Pa (15 °C) to 4.2 × 10\(^4\) Pa (70 °C), which can be described in terms of supercooling by a power law \( G' = 1.29T^{–0.5} \) as a result of the decreased boundary effect as described in the second part of Section 2. At \( T_g = T_{c1} \), a drastic change in \( G' \) for the case of gap = 0.85 mm occurred, a sharp jump in \( G' \) (more than 15 fold) was observed at \( T_g > T_{c1} = 70 °C \), followed by a steep drop when \( T_g > T_{c2} \) once \( T_g \) increases further. A similar phenomena of a sharp increase in the \( G' - T_g \) plot at around 70 °C was observed in the system within a smaller gap of 0.7 or 0.5 mm. On the other hand, no such jump was observed for the same system at the gap = 1.50 mm setting. This sharp jump of \( G' \) has never been observed before.

A similar phenomenon was also observed in other gelling systems, i.e. GP-1/PG (2 wt%) and GP-1/Tween 20 (1 wt%), except the different turning point of \( T_g \) (≈50 and ≈58 °C, respectively).

To acquire a good understanding on the enhancement of \( G' \), the sol-to-gel transition processes were monitored at different gelling temperatures with rheological dynamic temperature ramp tests. Typical curves are shown in Fig. 5. At \( T_g \) below 70 °C, the solution gels quickly, \( G' \) increases and reaches a plateau within 1000 s. For \( T_g \) above 85 °C, the gelation slows down because of the decrease in supersaturation. At higher gelling temperatures, especially above 95 °C, the \( G' \) of the samples is low, indicating that a self-supporting material cannot form any more due to the inability of the low fiber mass to trap the liquid. An exception was observed between 72.5 and 80 °C. Within this temperature range, \( G' \) keeps growing and has not arrived a constant value even after a long time (9000 s), indicating the formation of a different microstructure. The measurement was terminated after 9000 s due to the consideration that the gelation condition might be disturbed after a long time.

In order to explain the cause of the changing \( G' \), a parallel optical observation was carried out to monitor the gelling process of the gels formed at different \( T_g \) and to obtain the

Fig. 4 The storage modulus (\( G' \)) of the gels formed at different gelling temperatures (\( T_g \)), obtained from dynamic rheological measurements. Hollow round points: \( G' \) of the gels formed within a 1.50 mm gap.

Scheme 1 Molecular structure of GP-1
correlation between the elasticity and spherulitic size. Fig. 6 shows the optical microscopic images for the microstructures of the network, from which we can clearly identify the mutually exclusive spherulites within the gel. With rising $T_g$, the size of the spherulites increases from tens of micrometres to more than 1 millimetre at around 80 °C. A gap of 0.1 mm was adopted for sample preparation for optical observations, due to the fact that the size of the spherulites formed within a variety of gaps (from 0.1 to 1.0 mm) shows no obvious difference in our experiments. The SEM image in the bottom right is a local magnified graph of the structure of the spherulites. It shows the typical topological network structure of the gel after freeze-drying. At such a small length scale, the spherulites look like fibrillar-like aggregates formed by crossing strands or side branching fibers, which is consistent with previously reported results.

As described in Section 2, for a gelling system with a given solute concentration, the spherulitic size depends on $T_g$ for a multi-domain network. An elevated $T_g$ (decreased supersaturation $\sigma$) would reduce the nucleation rate $J$ and lead to the formation of larger spherulites. This eventually enhances the elasticity of the gel. Here, a power law relationship between the elasticity and the spherulites distance (spherulitic size) $\zeta$ can be obtained from the optical images and rheological measurements as $G' = 2.0 \times 10^4 \zeta^{-0.12}$. A similar correlation was obtained from other gelling systems such as GP-1/PG and GP-1/Tween 20.

Notice that at the gelling temperatures above 70 °C, the size of the spherulites grows to be more than 1 mm which is even larger than the gap value in the rheological measurements (0.85 mm). We can expect that within the confined space, the narrow gap can only accommodate one spherulite in the respective direction of the system ($Lz = 1$), indicating a structural transition from a multi-domain to a 1D dominated single network system (Fig. 7). As the spherulites are densely branched, they are much stronger than non-spherulitic structures. This leads to the sharp jump of $G'$ as shown in Fig. 4.

In the structural transition, one of the key factors is the confined volume. The space thickness $L$ between the rheological test tools was then changed from 0.85 mm to 1.50 mm, greater than the size of the spherulites. The obtained values of $G'$ at different $T_g$ is plotted (hollow round points) in Fig. 4. No sharp jump can be observed any more. Within the space larger than the size of individual spherulites, more than one domain coexists ($Lz > 1$) and the boundaries around the spherulites return. The network turns into the multi-domain type again.

(2) Structural dependence of the macroscopic rheological properties

The strain dependence of $G'$ is also an important rheological property of a gel, as it is a measure of the brittleness and rigidity of the junctions within the structure.^{8,12} The critical strain $\gamma'$, referring to the critical point at which a sharp decrease in $G'$ begins to occur, is attributable to the breakdown of the network structure under the applied strain. The occurrence of this is normally regarded as a characteristic property of permanent junctions.^{12} Fig. 8 shows the strain dependence of $G'$ of gels formed at different $T_g$ within the same space. From the $\gamma'$-$T_g$ plots shown in Fig. 8b different rules can be obtained for gels with different network structures. For the multi-domain network (below 70 °C), $\gamma'$ decreases with elevated $T_g$ (decreased supercooling) in a power law as $\gamma' = 6.66 \times 10^{-2} \Delta T^{0.56}$. This implies that the presence of larger spherulites would make the network more resistant to an external strain. This is in contrast to the relationship for the interconnecting fibrillar network obtained from the GP-1/ISA gel.^{12} For the gels above 70 °C, at which a single spherulitic network formed within the material, no obvious $T_g$ dependence for $\gamma'$ can be observed. At the same time, another turning point emerges gradually at a much higher strain value of about 10% especially for gels formed above 80 °C, which might come from the sliding between the whole gel and the plates of the testing tool.

Fig. 9a shows the frequency dependence of $G'$, from which we can learn about the nature of the bonds forming the network. It is known that if the bonds are permanent, only a small frequency dependence is expected, and $G'$ is larger than $G''$ at all frequencies.^{17} On the other hand, if the junctions are transient and...
understanding the supramolecular self-assembly of bio molecules such as proteins in cells, and shows attractive foreground for the micro-engineering especially on micro and nano scales.

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Notes and references