Diffusion across a gel–gel interface – molecular-scale mobility of self-assembled ‘solid-like’ gel nanofibres in multi-component supramolecular organogels†

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This paper explores macroscopic-scale diffusion of the molecular-scale building blocks of two-component self-assembled organogel nanofibres using a diffusion cell in which two different gels are in contact with one another. Both components of the ‘solid-like’ nanofibres (lysine peptide dendron acids and amines) can diffuse through these gels and across a gel–gel interface, although diffusion is significantly slower than that of a non-interactive additive in the ‘liquid-like’ phase of the gel. Amine diffusion was probed by bringing similar gels with different amines into contact. Dendron acid diffusion was tested by bringing similar gels with enantiomeric dendrons into contact. Surprisingly, dendron and amine diffusion rates were similar, even though the peptide dendron is more intimately hydrogen bonded in the self-assembled nanofibres. It is proposed that thermal disassembly of the acid–amine complex delivers both components into the liquid-like phase, allowing them to diffuse via a decomplexation/recomplexation mechanism. This is a rare observation in which molecules assembled into solid-like gel nanofibres are mobile – in dynamic equilibrium with the liquid-like phase. Gel nanofibre diffusion and reorganisation are vital in understanding dynamic materials processes such as metastability, self-healing and adaptability.

Introduction

Supramolecular gels are colloidal materials constituted by a ‘liquid-like’ phase with a sample-spanning ‘solid-like’ nanoscale network self-assembled from low-molecular-weight gelators (LMWGs). ¹ They have wide-ranging applications, from current industrial use in greases, personal care products and adhesives, to rapidly developing high-tech uses including tissue engineering and nanoscale electronics. ² One of the most intriguing aspects of such gels is their dynamic nature – they self-assemble in a responsive manner from small molecule building blocks, and typically contain ca. 99% of liquid-like solvent. There has been considerable interest in diffusion within gels – for example, solvent molecule mobility has been studied using NMR methods. ³ Tritt-Goc and co-workers characterised solvent diffusion in supramolecular gels, showing that in the absence of interactions with the gelator network on short timescales solvent diffusion is similar to bulk solvent. ⁴ However, interactions between solvent and gel nanofibres, which increase with gelator concentration, decrease diffusion coefficients by several orders of magnitude, ⁵ although the relationship is not always straightforward. ⁶ In the absence of interactions with gel nanofibres, ionic components in the liquid-like phase can also rapidly diffuse, ⁷ leading to conductivity – important for applications such as solar cells, lithium ion batteries and super-capacitors. ⁷ Molecular additives in the liquid-like solvent phase also have interesting diffusion profiles. Influential work from Adams and co-workers demonstrated that network mesh size could control diffusion, with larger molecules becoming physically trapped within the network. ⁸ This has applications, for example immobilising enzymes for biocatalysis. ⁹ Control over diffusion has also been important in forming unique crystal morphologies in self-assembled gels. ¹⁰ Non-covalent interactions between a nanofibre gel network and molecular additives can also affect diffusion rates, ¹¹ of interest for applications such as drug delivery. ¹² Interestingly, related studies using polymer gels, ¹³ have stimulated considerable theoretical interest in diffusion through gels. ¹⁴

In contrast to polymer gels, supramolecular gels are considerably more dynamic as a result of their ability to disassemble into small molecules. There has been interest in the kinetics/dynamics of gel-assembly, ¹⁵ and increasing focus on the metastability of gel nanostructures. ¹⁶ However, although

† Electronic supplementary information (ESI) available: AFM, SEM and TEM imaging, fitting of diffusion cell data to yield diffusion coefficients and additional spectroscopic and rheological data. See DOI: 10.1039/c8sc01071d
assembly dynamics have been studied, there is less insight into the ability of the molecular-scale components of gel nanofibres to diffuse through gels across macroscopic length scales. In principle, the dynamic nature of supramolecular interactions means supramolecular gels may be able to self-heal when damaged.\textsuperscript{17} However, although self-healing is increasingly recognised, studies of network reorganisation dynamics are rare.\textsuperscript{18} In an influential study, Aida and co-workers reported a gel, which they cut into cubes – when the solvated cube surfaces were brought together, there was healing across the interface yielding a physically robust structure, indicative of nanostructure reorganisation.\textsuperscript{19} More recently, a similar approach was employed using gel blocks either doped or undoped with methyl orange – when healing across the interface occurred, this was accompanied with diffusion of the dye from one block to the next.\textsuperscript{20} Perhaps surprisingly, for supramolecular gels, however, there remains a lack of studies of gel–gel diffusion. This research therefore aimed to explore the diffusion of molecular-scale gel components across gel–gel interfaces, focussing on the ability of the molecules constituting the self-assembled nanofibres to diffuse and exchange between two self-assembled gels.

A two-component organogel based on a lysine peptide dendron acid combined with an amine (e.g., Fig. 1) was selected for study. This acid–amine gelation system is well-established in our research group and well understood.\textsuperscript{21} It assembles primarily via intermolecular hydrogen bond interactions between peptides, with the amine complexing the acid, modifying solubility, and promoting assembly and gelation. Advantageously, such gels can form \textit{in situ} with rapid kinetics on simple mixing of the two components in toluene.\textsuperscript{22} NMR has demonstrated that adding a different amine, in solution, to these gels leads to amine exchange on the self-assembled nanofibres, to give the thermodynamically most stable system.\textsuperscript{23} This led us to believe a degree of diffusion of the ‘solid-like’ components may be possible in this system. Furthermore, having two components, this organogel provides the opportunity to probe the diffusion of each constituent part of the solid-like nanofibres.

**Results and discussion**

We proposed to use different amines and/or acids and monitor diffusion across a gel–gel interface (Fig. 1). Initially, gels were based on a lysine peptide dendron acid (L-Lys-G2-COOH) combined with either (i) hexylamine (non-fluorescent) or (ii) 1-naphthylmethylamine (fluorescent) (referred to as L-Lys-HexGel and L-Lys-NaphGel respectively, Fig. 1 (top)). All gels were formed with 1 : 1 acid : amine ratios. We reasoned that if such gels were brought into contact, amine diffusion across the interface, could be visualised with a simple fluorescent output.

**Characterisation of gels**

Prior to studying diffusion, we characterised these two organogels. At a concentration of 10 mM, L-Lys-HexGel and L-Lys-NaphGel had similar thermal stabilities ($T_{gel}$) of ca. 70 °C, determined using simple reproducible tube inversion methodology – suggesting the two gels have similar thermodynamic stability. Rheology was used to follow the gelation process \textit{in situ}, and it was observed that on mixing the two components in solution under ambient conditions a rapid gelation event took place, with an increase in elastic modulus, followed by a further slower increase in modulus as the network aged and optimised the formation of a sample-spanning network (Fig. S1 and S2, ESI†). This suggests significant dynamic character to these gels. Similar changes were observed for both L-Lys-HexGel and L-Lys-NaphGel suggesting the mechanism of gelation is similar in each case. Atomic Force Microscopy (AFM), scanning electron microscopy (SEM) and transmission electron microscopy (TEM) were used to probe morphology (Fig. S3–S7, ESI†). Both systems assembled into nanoscale fibrillar morphologies. In general, L-Lys-HexGel nanofibres were wider than L-Lys-NaphGel, especially for the gel formed by simple mixing at ambient temperature. It is likely there is greater bundling of L-Lys-HexGel fibrils than for L-Lys-NaphGel, with the latter being more compatible with the toluene solvent as a result of π–π stacking. The difference in diameter was less marked for samples produced using a heat-cool cycle, during which the L-Lys-HexGel nanofibres can rearrange into a more thermodynamically favoured form. In summary, L-Lys-HexGel and L-Lys-NaphGel formed gels with equivalent thermal stabilities underpinned by fibrillar solid-like self-assembled morphologies. There were some differences in fibre diameter dependent on the amine, but the gels were similar – suitable for study in diffusion experiments.

**Qualitative diffusion experiment**

In a qualitative initial experiment to test the hypothesis that components of the solid-like gel nanofibres may diffuse, simple vials were used and two gels formed on top of one another by stepwise room-temperature mixing of components to form each gel layer in turn. The bottom layer was formed by mixing L-Lys-G2-COOH and 1-naphthylmethylamine in toluene, then once it had formed, the upper layer was formed on top of it by mixing L-Lys-G2-COOH and hexylamine in toluene. Diffusion of the fluorescent amine was tracked visually under UV irradiation (Fig. 2). At the start of the experiment, the lower layer of the gel

![Fig. 1 Structures of components used to assemble two-component organogels in toluene for diffusion studies and schematic of key diffusion experiments to probe mobility of acid and amine components in two-component organogels.](image-url)
was fluorescent (L-Lys-NaphGel), while the upper layer was not (L-Lys-HexGel). After 5 hours, the fluorescent amine (Naph) had diffused somewhat into the upper gel layer. After 48 hours, diffusion of the fluorescent amine appeared (visually) to be reasonably complete.

Mobility of the fluorescent amine component of the nano-scale network clearly appears to be allowed. This was a remarkable result, as such networks are usually considered ‘solid-like’. We anticipated that the non-fluorescent amine may also diffuse in the opposite direction, but it obviously cannot be detected using this simple approach.

**Experimental design of gel–gel diffusion cell**

To understand the intriguing diffusion event described above in a more quantitative way, we designed an experiment to probe diffusion across a gel–gel interface. This presented considerable difficulties as a result of the volatility of toluene and its ability to dissolve or leach into plastics. Glass and metal were used for the construction of the diffusion cell. The cell design (Fig. 3 and S10–S12†) had length (4 cm), width (3.5 cm) and height (2.5 cm), was made of soda glass, and has the capacity to load two gels, one on each side. The volume of each gel introduced into the cell was 5.44 mL creating an interfacial area of 1.6 cm² between the two gels. Separation between the two sides of the cell during loading was achieved using a home-made ultra-thin aluminium ‘separator’, which was sufficiently thin that, when removed, the two gels come into direct contact. Given the gels are formed in situ within the cell (see below), it was essential to eliminate any leakage. A silicone seal was used to join the two sides of the diffusion cell, swollen in toluene, and trimmed – the aluminium separator intimately contacted this seal (see ESI†).

Loading the gels (5 mM) in the cell was initially attempted by simple room temperature mixing of acid and amine leading to rapid in situ gelation. However, gelation kinetics were faster than mixing kinetics and to obtain homogeneous gels, hot solutions (>Tgel) of the chosen acid–amine complexes were instead poured into either side of the cell, with gels forming on cooling. Gel homogeneity must be high to form an effective gel–gel interface. To avoid toluene evaporation, the diffusion cell was placed in a chamber containing solvent.

Fig. 3 illustrates fluorescent L-Lys-NaphGel loaded into the left-hand-side of the cell and non-fluorescent L-Lys-HexGel loaded into right-hand-side at the start of an experiment. The choice of a fluorescent amine once again allowed us to visually monitor progress. After some time had elapsed, it was clear the fluorescent amine had diffused into the right-hand-side of the cell. No disruption of the gels on either side of the gel–gel interface was observed.

It was necessary to sample from the gel to quantify the diffusion of both fluorescent 1-naphthylmethylamine and non-fluorescent hexylamine. The fluorescent amine could have been quantified by non-invasive fluorescence imaging, but this was not possible for hexylamine – sampling was therefore combined with NMR for quantification. The cuvette was artificially divided into six regions of equivalent size (Fig. 4). Regions 3 and 4 are closest to the gel–gel interface, and regions 1 and 6 are most distant. Gel was sampled from each of the regions, transferred to a numbered vial, evaporated to dryness, and fully dissolved in d₄-methanol. The concentration of amine in each region was quantified with reference to the dendron acid (L-Lys-G₂-COOH), which has a constant known concentration (5 mM) across the cell and hence acts as an internal standard. The amines had NMR spectra that could be differentiated from one another and L-Lys-G₂-COOH, allowing quantification of all components. Specifically, we used the ¹H NMR resonances for the four aromatic protons on the unsubstituted naphthalene ring for 1-naphthylmethylamine, the CH₂–NH₂ protons for hexylamine.
and the proton at the chiral centre closest to the carboxylic acid for L-Lys-G2-COOH. Sampling from the cell disrupts the diffusion experiment, and to investigate multiple timepoints, a number of cells were used in parallel.

**Diffusion of amines across the gel–gel interface**

Diffusion cells were prepared, filled with L-Lys-HexGel and L-Lys-NaphGel (5 mM) and diffusion monitored at a controlled temperature of 25 °C. NMR analysis generated profiles representing amine concentration and diffusion distance for given times (Fig. 5). Pleasingly, the concentration graphs are broadly symmetric about the gel–gel interface and show reliable, reproducible trends. As time progresses, the concentration of hexylamine in cell region 3 increases, while that in cell region 4 decreases, suggesting the diffusion of hexylamine from right to left in the diffusion cell. The same trends are seen, but with smaller concentration changes in cell regions 2 and 5, as expected given they are further away from the gel–gel interface. Concentration changes in cell regions 1 and 6, most distant from the gel–gel interface, are small. The concentration plots for 1-naphthylmethylamine indicate it diffuses in the opposite direction (i.e., left to right) – concentration increases in cell region 4 (and to a lesser extent 5) and decreases in cell region 3 (and to a lesser extent 2). This experiment indicates both amines diffuse through these gels, across the gel–gel interface and exchange with one another, even though they are an integral part of the self-assembled fibre network. However, even after 300 hours (12.5 days) diffusion is incomplete and the system has not fully equilibrated.

TEM imaging was performed on each region of the gel after 48 h of diffusion (Fig. S13–S18, ESIF). Regions 1–3 showed narrow nanofibre morphologies typical of L-Lys-NaphGel, and regions 4-6 showed wider nanofibres typical of L-Lys-HexGel. However, in region 4, the nanofibres associated with L-Lys-HexGel had a clear helical bias. We suggest this may result from 1-naphthylmethylamine interacting with fibres that predominantly include hexylamine, leading to a subtle change in morphology. Furthermore, TEM imaging of region 3 suggested the narrow L-Lys-NaphGel fibres were better defined than in regions 1 and 2 – i.e., they could be more clearly imaged. This may suggest an increasing influence of hexylamine diffusing into this side of the cell.

**Diffusion of a non-interactive small molecule**

The results for amine diffusion were compared with a system in which a non-interactive additive was added to the gel and allowed to diffuse from one side of the cell to the other. In this case, L-Lys-HexGel was loaded into each side of the cell, but on one side (regions 4–6) diphenylmethane (5 mM), a small molecule which does not interact with the gel network, was also added. In this case, we sampled from the gel at time points of hours rather than days (Fig. 6). The concentration of diphenylmethane on the right-hand side of the cell rapidly decreased, while that on the left-hand side of the cell increased. After 48 hours, an equal concentration of diphenylmethane was observed across the cell. This is different to amine diffusion, which was only partial, even after 300 hours. This clearly indicates that although the amine gel components can diffuse through the gel, they do so much more slowly than an unrestrained small molecule. This leads us to propose a mechanism in which the amine de-complexes from

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**Fig. 5** Concentration profiles of (top) hexylamine and (bottom) 1-naphthylmethylamine between regions 1 and 6 of the diffusion cell. At the start of the experiment, hexylamine is loaded in regions 4–6 of the diffusion cell and 1-naphthylmethylamine is loaded in regions 1–3. As time progresses, the concentrations of the amines change as diffusion leads to exchange across the gel–gel interface. The points in these graphs are joined together solely as a guide to the eye.

**Fig. 6** Concentration profiles of diphenylmethane between regions 1 and 6 of the diffusion cell. At the start of the experiment, diphenylmethane is loaded in regions 4–6 of the cell. The points in these graphs are joined together solely as a guide to the eye.
the nanofibres, and diffuses through the gel between acidic sites of 1-Lys-G2-COOH (see below for further evidence). As such, amine diffusion is restrained by its non-covalent interactions. This is in analogy with reports of drug delivery using LMWGs, in which drug release can be controlled by non-covalent interactions with a self-assembled gel network.11

Temperature dependence of amine diffusion

The effect of temperature on amine diffusion was then investigated, with experiments performed at 5 °C and 45 °C. As previously, diffusion from one side of the gel to the other was observed, but progress was significantly less at 5 °C (Fig. 7) than 25 °C (Fig. 5). Indeed, at 5 °C, diffusion had barely progressed at all into sections 2 and 5 of the cell. At 45 °C (importantly still <Tgel), it was more difficult to obtain reliable results as on extended standing, the gels began to dry. Nonetheless, the first four days of diffusion were monitored (Fig. 7) – the rate of concentration change was much greater. After only 96 h, the concentration of hexylamine in cell region 3 had risen to ca. 2 mM and in cell region 1, distant from the gel-gel interface, to 1 mM. After 140 h, amine concentrations were close to the equilibrium value of 2.5 mM across the diffusion cell.

There are two possible reason for the increased diffusional mobility of amines at elevated temperatures:

(1) Increase of internal mobility of all liquid-like substances within the gel because of an increase of translational kinetic energy.

(2) Disruption of the acid/amine complex on increasing temperature increases [amine] in the liquid-like phase (and the on–off rate) and may thus have very significant impact on the observed diffusion rate.

To approximate an effective diffusion coefficient to reflect the rate of mass transfer, Fick’s second law (eqn (1)), which relates the rate of change of concentration at position x and time t to the rate of change of the gradient of concentration at the same position, was used.14

\[
\frac{\partial C(x,t)}{\partial t} = D \frac{\partial^2 C(x,t)}{\partial x^2}
\]  

(1)

Assuming the solute is initially present in half of the container, the concentration profile at any time can then be calculated using eqn (2).15

\[
C(x,t) = \frac{1}{2} \text{erf} \left( \frac{x}{2\sqrt{Dt}} \right) + \frac{1}{2}
\]

(2)

This model was compared with the data obtained at each timepoint, and fitting of all data for each diffusion event was performed using least squares error analysis (Fig. S19–S24, ESI†). This allowed us to estimate average diffusion coefficients for each amine at each temperature (Table 1). The resulting D values of ca. 5 × 10⁻⁷ cm² s⁻¹ are below typical diffusion coefficients of liquids (ca. 1 × 10⁻⁵ cm² s⁻¹), but significantly higher.

Fig. 7 Concentration profiles of (left) hexylamine and (right) 1-naphthylmethylamine between regions 1 and 6 of the diffusion cell at temperatures of (top) 5 °C and (bottom) 45 °C demonstrating the very significant impact of temperature on diffusion kinetics. At the start of the experiment, hexylamine is loaded in regions 4–6 of the diffusion cell and 1-naphthylmethylamine is loaded in regions 1–3. The points in these graphs are joined together solely as a guide to the eye.
bound to gel nano-
a result of Le Chatelier’s principle, and in this way, the system
from the acid mobile amine is coupled with decomplexation of the amine
complex responsible for gelation, and promoting mobility of
ature acts through mechanism (ii), disrupting the acid
internal mobility of the liquid-like substances within the gel
ca. >10-fold on increasing temperature from 278 K to 318 K,
which state a material is in. For a liquid this is expressed by the
D in agreement with the derived
equation. Assuming viscosity is constant with
temperature (as is essentially the case in gels), diffusion coeffi-
cients should be proportional to absolute temperature. This is
not the case here, as the amine di-
cision than the amines, and in-line with
expectations for the diffusion of a liquid/solute.
Increasing temperature increased the apparent average
diffusion coefficients of the amines (Table 1). It should be noted
that the fitting of the data at 45 °C was less robust, for reasons
described above, but it was clear from visual inspection that
diffusion was significantly faster (ca. one order of magnitude),
in agreement with the derived D values. The relationship
between diffusion coefficient and temperature depends on
which state a material is in. For a liquid this is expressed by the
Stokes Einstein equation.23 Assuming viscosity is constant with
temperature as is essentially the case in gels, diffusion coeffi-
cients should be proportional to absolute temperature. This is
not the case here, as the amine diffusion coefficient increases
cat. >10-fold on increasing temperature from 278 K to 318 K,
when a 1.14-fold increase would be predicted. Clearly, enhanced
diffusion is not just due to mechanism (i) in which greater
internal mobility of the liquid-like substances within the gel
courages enhanced mobility. We therefore suggest temperature
acts through mechanism (ii), disrupting the acid–amine
complex responsible for gelation, and promoting mobility of the amine within the gel.

We have previously studied gels formed by L-Lys-G2-COOH
and hexylamine, 1-naphthylmethylamine and mixtures of the
two in some detail.32 We used VT 1H NMR spectroscopy to
demonstrate that for these gels, increasing amounts of amine
become mobile, and hence visible in the NMR spectrum, on
raising temperature. At 25 °C, ca. 10% of the amine (or the
dendron, Fig. S8 and S9†) in L-Lys-HexGel was mobile on the
NMR timescale.22e This clearly suggests that there is indeed
some molecular-scale mobility of the amine component
possible in L-Lys-HexGel and that the ‘on–off’ rates of the complexes are relatively fast. Similar amounts of 1-naph-
thylmethylamine were mobile in L-Lys-NaphGel. Interestingly,
however, in our diffusion experiment here (Fig. 5), by the end of the experiment >20% of the total amine has diffused across the
gel–gel interface. It is therefore clearly not only the initial
‘mobile amine’ (ca. 10%) that diffuses, while the rest remains
bound to gel nanofibres. We propose that diffusion of the mobile amine is coupled with decomplexation of the amine
from the acid–amine complex (and from the nanofibres) as
a result of Le Chatelier’s principle, and in this way, the system
equilibrates, with diffusion acting to exchange components. These observations are compatible with a mechanism in which
amine diffusion is partially liquid-like, but with reversible
interactions being possible with the acid groups on the nano-
fibre network. We also previously reported22e that hexylamine has a higher pKₐ than 1-naphthylmethylamine and for this
reason the acid–amine complex formed by hexylamine is
stronger. This meant that when gels were formed from a mixture of the two amines, hexylamine was preferentially
incorporated over 1-naphthylmethylamine (Fig. S9†). This
previous work therefore demonstrated that the acid–amine
complexation event played a key role in determining the
incorporation of amines into the gel-phase nanofibres. Furthermore, we also previously reported22e that if a sample of
NaphGel was challenged with the addition of hexylamine, the amine immobilised on the gel fibres changed – clearly
demonstrating a reversible exchange mechanism. We thus
propose that acid–amine decomplexation is the likely mecha-
nism by which mobility of these components through the gel
becomes possible. Ultimately, when coupled with diffusion of the amines, this mechanism gives rise to compositional change
of these gels, which impacts on physical properties (e.g. fluo-
rescence and nanofibre morphology).

### Table 1 Average diffusion coefficients (D, cm² s⁻¹) for amines at different temperatures in our experimental set-up

<table>
<thead>
<tr>
<th>Temperature</th>
<th>5 °C</th>
<th>25 °C</th>
<th>45 °C</th>
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<tbody>
<tr>
<td>Hexylamine</td>
<td>1 × 10⁻⁷</td>
<td>7 × 10⁻⁷</td>
<td>6 × 10⁻⁶</td>
</tr>
<tr>
<td>1-Naphthylmethylamine</td>
<td>3 × 10⁻⁷</td>
<td>5 × 10⁻⁷</td>
<td>6 × 10⁻⁶</td>
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**Diffusion of dendron acids**

We then turned our attention to the diffusion of the other
component of the solid-like nanofibres. The self-assembly
model for these two-component gels relies on intermolecular
amide–amide hydrogen bond interactions between peptide
dendron acids, and it might thus be anticipated that this
component is less able to diffuse through the gel. NMR could
not be used to quantify diffusion, as changing the structure of
the dendron acid can quite radically affect self-assembly.24 An
experiment was therefore proposed taking advantage of dend-
ron chirality. There are various possible stereoisomers for the
dendron acid, and we used the L,L,L form as above (L-Lys-G2-
COOH) and the D,D,D enantiomer (D-Lys-G2-COOH). Gels
formed from these enantiomers are identical in every way,
except for properties associated with chirality. When combined
with hexylamine the enantiomeric dendrons form mirror image
gels with equivalent thermal stabilities and nanoscale
morphologies but equal and opposite circular dichroism (CD)
spectroscopy signals.27 Diffusion experiments were planned
using our diffusion cell, with one side of the cell loaded with L-
Lys-HexGel (5 mM) and the other side loaded with D-Lys-HexGel
(5 mM) (Fig. 1 (bottom)). Samples would be taken from the six
regions of the gel and analysed using CD spectroscopy to
determine the enantiomeric excess in each case, to uncover the
extent to which the L,L,L dendron acid diffused into the gel
based on the D,D,D acid and vice versa.

In many cases, mixing enantiomers disrupts gelation28 – this
would be highly undesirable in this diffusion experiment as it
would potentially lead to destruction of the gels as diffusion
progressed. The thermal stability of gels formed from mixtures
of enantiomeric dendrons was therefore probed using simple
reproducible tube inversion methodology (Fig. 8). Importantly,
mixing enantiomers had limited impact on thermal stability (ca. 70 °C), allowing enantiomeric dendrons to be used to test diffusion.

To quantify the extent of diffusion, CD spectroscopy was used. It was essential to check this approach could be used in a quantitative way. CD spectra were measured in methylcyclohexane : dioxane (95 : 5) as, unlike toluene, this solvent is optically transparent in the relevant part of the spectrum and also supports assembly.23 We prepared samples with mixed enantiomers (total concentration 5 mM) and plotted the ellipticity of the CD signal at 222 nm, associated with the peptide chromophore, against % enantiomer content. A linear relationship was observed at this concentration (Fig. 9), making analysis very simple as CD signal can be directly related to composition.

In our experimental method, after specific diffusion times, the cells were sampled from their six different regions into six different vials, which were evaporated and weighed on an accurate balance. Solvent (methylcyclohexane/dioxane 95/5) was then added to the weighed samples in order to obtain concentrations of 5 mM in each vial, ensuring that the extent of self-assembly is the same in each case, and the samples were then analysed by CD. All samples were left to stand for 15 min in the quartz cell prior to analysis.

Fig. 10 presents data from a diffusion cell sampled after 240 h (other timepoints can be found in Fig. S28–S30, ESI†). The most intense CD signals (negative and positive) correspond to regions 1 and 6 of the cell. They have the highest absolute values because they are most distant from the gel–gel interface and have not experienced any mixing of chirality from the diffusing enantiomeric dendrons. However, in regions 3 and 4 closest to the gel–gel interface, there is a significant decrease of the expected CD signal. This suggests diffusion of dendrons is occurring, decreasing the enantio-purity of the gels either side of the interface. These results therefore suggest that, like the amines, the dendron acids are also able to diffuse across and away from the gel–gel interface.

Comparing the results in a simple qualitative way against the diffusion of the amines described above, at ca. 140 hours, the dendron has achieved ca. 30% diffusion into Section 3, and 10% diffusion into Section 2. At the same time, hexylamine had diffused ca. 40% into Section 3 and ca. 10% into Section 2, while 1-naphthylmethylamine had diffused ca. 30% into Section 4 and <10% into Section 5. It would therefore appear that the
gels. We note that these two-component organogels have very
recomplexation mechanism. This is supported by the e
comes into contact with a complementary binding partner in
decomplexes from the gel nano
starts di
each component therefore di
bonding interactions. This suggests that the acid and amine can
able to move within the gel,
surprising to us, and suggests that both components are equally
iotionally immobilised as a result of peptide
is very similar.

Concentration pro
the dendron acids in this experiment, using the same methods
for both L-Lys-COOH and D-Lys-COOH at 25
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Conclusions

In summary, this paper reports an experimental approach to
study diffusion across a gel–gel interface. Diffusion in self-
assembled gels is crucial in a variety of settings, such as
energy technology and controlled drug release. A non-
interactive additive (diphenylmethane) diffused rapidly
(hours) across the gel–gel interface consistent with its behav-
our as a solution-phase ‘liquid-like’ species. It was then
demonstrated that both components of a two-component acid–
amine organogel could slowly diffuse (days) across the gel–gel
interface in spite of being integrated within the ‘solid-like’ self-
assembled nanofibres of the material. The diffusion of amines
was probed by bringing similar gels with different amines into
contact with one another. Diffusion was highly temperature
dependent, which was ascribed to thermally induced disrup-
tion, delivering more of the amine into the liquid-like state and
hence diffusing through the cell. The diffusion of dendron acids
was probed by bringing enantiomeric gels into contact, and
using CD spectroscopy to determine the extent of mixing.
Surprisingly, the diffusion rate of the dendron acids was similar
to that of the amines, even though the lysine dendrons are more
directly engaged in the self-assembled nanofibres via intermo-
olecular amide–amide hydrogen bonds. We propose that disas-
sembly delivers both components into the liquid-like state and
using through the cell. The di
fusion across a gel
–
gel interface. Di
bres and the solution-phase in order for this
diffusional mechanism to be possible. This is more likely to be
the case in multi-component gels in which a reversible inter-
action between two units is required to form the active gelator.
Furthermore, we suggest that simple NMR observations may
offer a good predictive approach for finding gels in which
components of the solid-like nanofibres are able to diffuse and
reorganise on experimentally useful timescales, as in such gels,
NMR resonances will be observed even in a standard
H NMR
experiment, whereas in less dynamic gels, all of the NMR
resonances will be fully broadened. As such, we suggest NMR as
a useful screening tool for gels that are capable of diffusional
reorganisation of their nanofibres.

dendron acid and the amines have similar mobilities. More
quantitatively, we estimated average diffusion coefficients
for the dendron acids in this experiment, using the same methods
outlined above (Fig. S26 and S27, ESI†), and found $D$ values of 3
$\times 10^{-7}$ cm$^2$s$^{-1}$ for both l-Lys-COOH and d-Lys-COOH at 25 °C.
This is a little lower than the diffusion coefficients reported for
the amines, which may suggest slightly slower diffusion rates
for peptide acids, but given the limitations of the methodology,
is very similar.

The similarity between amine and acid diffusion was
surprising to us, and suggests that both components are equally
able to move within the gel, i.e., the dendron acid is not addi-
tionally immobilised as a result of peptide–peptide hydrogen
bonding interactions. This suggests that the acid and amine can
each dissociate from the gel nanofibres, probably associated
with breakage of the acid–amine complex, and either com-
ponent can then be delivered into the ‘liquid-like’ phase, where it
starts diffusing down the concentration gradient. We propose
each component therefore diffuses via a mechanism in which it
decomplexes from the gel nanofibres and then recomplexes if it
comes into contact with a complementary binding partner in
the gel network. We refer to this as a decomplexation/rec-
complexation mechanism. This is supported by the effect of
diffusion on the nanoscale morphology of the gel.

It is interesting, and important, to speculate how general this
unexpected phenomenon might be amongst self-assembled
gels. We note that these two-component organogels have very
rapid gelation kinetics – indeed they form gels simply on mixing
the two-components. This suggests a low kinetic barrier to gel
assembly. Furthermore, NMR experiments previously indicated
that some of the acid and amine are both observed by NMR
indicating a degree of liquid-like behaviour, suggesting the
molecular components of these self-assembled nanofibres have
relatively fast ‘on-off’ kinetics (see NMR spectra in ESI†). It
therefore seems likely that the highly dynamic nature of this
gelation system is one of the reasons that the components of the
nanofibres themselves show significant diffusional mobility.
Many gels are based on one-component systems, that become
fully immobilised on the NMR timescale, and we would suggest
that such systems show limited diffusional mobility – as evi-
denced by the many studies in which a drug is shown to be
released from a self-assembled gel, while the components of the
nanofibres themselves are not. We would therefore suggest
that it is important to have dynamic equilibrium between gel-
phase nanofibres and the solution-phase in order for this
diffusional mechanism to be possible. This is more likely to be
the case in multi-component gels in which a reversible inter-
action between two units is required to form the active gelator.
Furthermore, we suggest that simple NMR observations may
offer a good predictive approach for finding gels in which
components of the solid-like nanofibres are able to diffuse and
reorganise on experimentally useful timescales, as in such gels,
NMR resonances will be observed even in a standard
H NMR
experiment, whereas in less dynamic gels, all of the NMR
resonances will be fully broadened. As such, we suggest NMR as
a useful screening tool for gels that are capable of diffusional
reorganisation of their nanofibres.
molecular-scale components assembled into solid-like nanofibres are shown to be mobile within a gel, and capable of diffusing across a gel–gel interface.

We anticipate that gel nanofibres such as those reported here in which the molecular-scale components are dynamic and have the capacity to diffuse will be particularly suitable for use in adaptive and self-healing materials. Given the importance of this in a wide range of applications, we suggest that this approach to understanding the diffusion potential of solid-like nanofibres in self-assembled gels has considerable general significance and should, in the future, be explored for a wide range of different gelation scaffolds. Simple NMR experiments may provide a useful screening tool to identify gels capable of this type of intriguing and potentially useful type of behaviour.

Conflicts of interest
There are no conflicts to declare.

Acknowledgements
This research was supported by European Commission Marie Curie ITN 316656 SMARTNET [JRO]. We thank William Edwards for providing thermal stability analysis of the enantiomeric mixtures of Lys-HexGel.

Notes and references


24 It should be noted that gels are often considered as porous materials, although the solid-like network constitutes <1% of the material in this case. It is difficult to experimentally determine the porosity of solvated gels, and for this reason we decided to use a simple Fickian approach to approximate diffusion coefficients, which are very useful for comparative purposes: A. Fick, Ann. Phys., 1855, 170, 59–86.


