Experimental report

24/10/2023

Proposal: 9-13-1042 **Council:** 10/2022

Title: Gelator network dynamics in supramolecular gels

Research area: Soft condensed matter

This proposal is a new proposal

Main proposer: Riccardo MORBIDINI

Experimental team: Riccardo MORBIDINI
Katharina EDKINS
Robert EDKINS

Local contacts: Anne MARTEL
Lionel PORCAR
Orsolya CZAKKEL

Samples: bis/Urea gel in D2O/ethanol-d6
Fmoc-FF peptide gel in D2O with NaOD and glucono-¿-lactone (GdL) (~1.3 ¿M) (pH approximately neutral)

Instrument	Requested days	Allocated days	From	To
D22	1	1	13/06/2023	14/06/2023
IN15	4	4	23/06/2023	27/06/2023

Abstract:

Supramolecular gels constitute adjustable materials of great current interest for drug delivery due to their increased viscosity compared to solution and response to triggers such as pH for gel-formation and dissolution. They are characterized by an arrested crystallisation of the low-molecular-weight gelator molecules forming fibrils physically linked by non-covalent interactions such as hydrogen bonds and van der Waals forces.

In this proposal for neutron spin-echo spectroscopy and complementary SANS, we aim to specifically address the slow gelator network dynamics in two types of gels, namely Fmoc-FF peptide gels and bis/Urea gels, made with deuterated solvents and protiated gelator molecules. Even though the scattering signal will be weak, it will be accessible with the ILL instruments IN15 and D22, as it has already been detected by BATS at ILL and previous published SANS.

The gelator dynamics will fundamentally differ from polymer network dynamics and provide new insights on the stability of gels relevant for drug delivery.

This proposal is part of the InnovaXN PhD thesis project of Riccardo Morbidini in collaboration with the industry partner AstraZeneca.

Experimental Report 9-13-1042: "Gelator network dynamics in supramolecular gels"

Riccardo Morbidini, Robert M. Edkins, Tilo Seydel and Katharina Edkins

Scientific case

This experiments is part of the overall endeavour to study drug diffusion in supramolecular gels. Our focus so far has been on diffusion on increasingly bigger guest molecules through the gel network by exploiting ToF and backscattering spectroscopy. QENS data report a differential diffusion on gel with respect to the pure solution state depending on the specific gel surface chemistry. One fundamental assumption of this series of works is that the gelator network dynamics is too slow to be resolved by ToF and backscattering spectrometer resolution thus contributing only to the elastic line. However, due to the increasing size of the guest molecules and their slower dynamics, the crossover between the slower dynamics of the guest and the fluctuation of the gel network might lead to a deviation from a pure Stokes Einstein behaviour. The aim of this work is to probe at what time scale the dynamics of the gelator comes into play, thus exploiting the wide q-range and Fourier time accessible from the neutron spin echo on the IN15 spectrometer. This experiment on IN15 was preceded by SANS measurements on D22, in order to calibrate the q range for the observation of the structural features of the gel network. This work will be part of the PhD thesis "Diffusion in supramolecular gels for drug delivery" in partnership with AstraZeneca.

Experiment details

We measured the following gel systems with their respective backgrounds

- D_2O/EtD_6 7:3 v/v
- Bis urea gel (0.5 wt%) + D_2O/EtD_6 7:3 v/v
- D_2O/NaOD 0.1M in D_2O 9:1 + GdL (4.5 wt%)
- FmocFF gel (0.5 wt%) + D_2O/NaOD 0.1M in D_2O 9:1 + GdL (4.5 wt%)

The FmocFF gel sets by pH change. Specifically the pH has to decrease from a value of 10.4 to 4 via the slow hydrolysis of the glucono-delta-lactone (GdL). Two main challenges have to be tackled: the first one was to dissolve the hydrophobic gelator at 0.5wt% in 0.1M NaOD in D2O. This has been done with an alternation of stirring through vortex and sonication at room temperature until the solution turns into clear. Once the clear solution was reached the GdL was addedd. This step has been done directly on the quartz cuvette, after the solvent sample had been transferred into the sample holder.

The bis urea gel sets by temperature change. After dissolving 0.3 wt% and 0.5 wt% bis urea gelator in 7:3 v/v D_2O:Ethanol-D_6 the clear solution was heated above 80°C and cooled down at room temperature. The gel state was reached within 5 minute during the cooling phase. We followed the same procedure even for the bulk solvent samples in order to make the batches as much comparable as possible.

Preliminary analysis: From SANS data no feature has been observed in the q range explored (Fig.1). At low q we can distinguish a sharp power law of $q^{-\alpha}$, $\alpha = 4$, compatible with an high polydispersity of nanometric fibers in supramolcular gels. This calibration outcome forced us to focus on the lowest q on IN15. The intermediate scattering function show deviations from linearity only in the case of FmocFF gel at high Fourier time (> 100 ns) (Fig.2). On the other hand bis urea gel data are noisier and show no decorrelation within the accessible Fourier times. This might be due to the evaporation of the volatile solvent from the quartz cuvette since the sample was prepared one day before the experiment Fig.3. The crystallinity of the sample after the measurement seems to confirm this hypothesis.

From these preliminary results, we can already say that, at least for FmocFF, the gel network fluctuates on a longer timescale than the one probed through ToF spectroscopy. Further fit based on a single exponential decay (eq.1) will quantitatively give the characteristic diffusion coefficient $D_c(t)$ for the gel network.

$$\frac{I(q,t)}{I(q,t=0)} = \mathrm{DWF} \cdot \exp\left[-\left(\frac{t}{\tau}\right)\right] \tag{1}$$

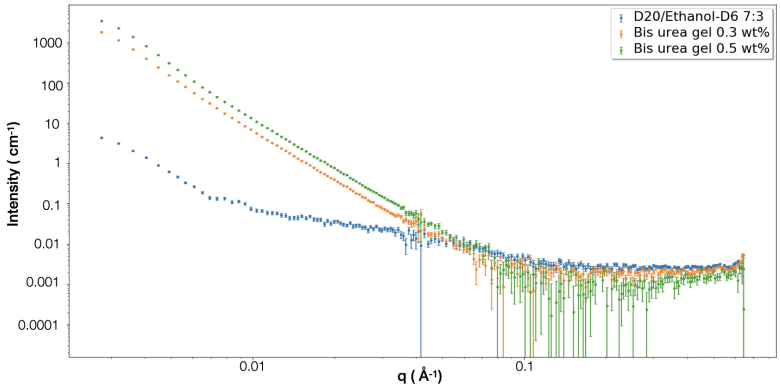

Fig. 1. SANS data for Bis urea gel at two different concentrations 0.3 wt% and 0.5wt%

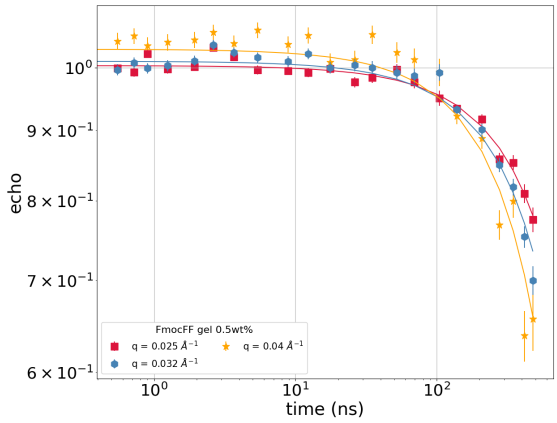

Fig. 2. Intermediate scattering function for FmocFF gel (0.5 wt%).

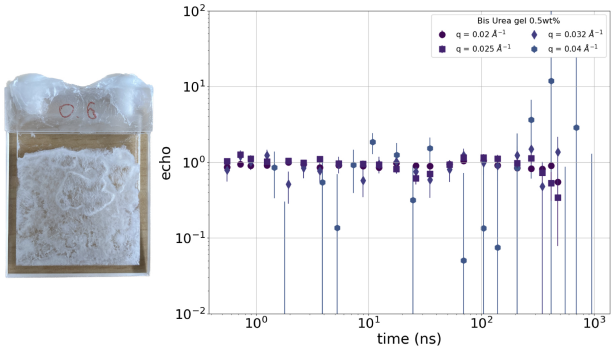

Fig. 3. Intermediate scattering function for Bis urea gel (0.5 wt%)