Experimental report

14/02/2018

Proposal: 9-13-634 **Council:** 4/2016

Title: Diffusion of active pharmaceuticalingredients in supra-molecular gels

Research area: Other...

This proposal is a continuation of 9-13-574

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Samples: Paracetamol in 7:3 water/ethanol
Paracetamol in 7:3 water/ethanol gel
Erythromycin in 7:3 water/ethanol
Erythromycin in 7:3 water/ethanol gel

Instrument	Requested days	Allocated days	From	To
IN16B	4	4	17/11/2016	21/11/2016

Abstract:

Preliminary time-of-flight experiments reveal an interesting difference in diffusion between the free bulk solvent and the solvent in supramolecular gels. This observation is remarable, because it is seen at a gelator contents of only 0.3wt%. In the previous experiment we investigated the diffusion of ibuprofen sodium as pharmaceutical drug load in gels and see the same trend of faster diffusion in gels compared to bulk solvent. We now propose to measure two more pharmaceutical drugs, paracetamol and erythromycin, in order to systematically investigate this effect. This data will enable us to draw conclusions towards supramolecular gels as drug delivery vehicle as well as fundamental insight into the diffusion in soft confinements.

Report on experiment 9-13-634, November 17-21, 2016
Guest molecule diffusion in supramolecular gels

IN16B was used in the standard unpolished Si(111) analyzer configuration; the reactor power was 55.8MW; the PST chopper operated at 7100rpm; the sample environment was the 70mm bore cryostat. The samples were held in double-walled cylindrical Al sample holders with 22mm outer diameter and 0.25mm gap sealed with indium wire.

The samples consisted of a D2O/d-ethanol 7:3 solvent and optionally
- a supramolecular gelator (0.3% weight percent)
- a protonated drug guest molecule (5 and 10% paracetamol, 5 and 8% tetracycline, 5% ibuprofen)
All measurements were performed at both T=265K and 270K.

The goal of the experiment was to compare the guest molecule diffusion in the gel and corresponding pure solvent. The spectra for the entire scattering vector range were fitted at once in a global fit approach. To this effect, in the first step, the pure solvent and pure gel spectra, respectively, were fitted. Subsequently, the spectra from the guest molecule samples were fitted by keeping the solvent contribution fixed in the model. Example spectra are depicted below:

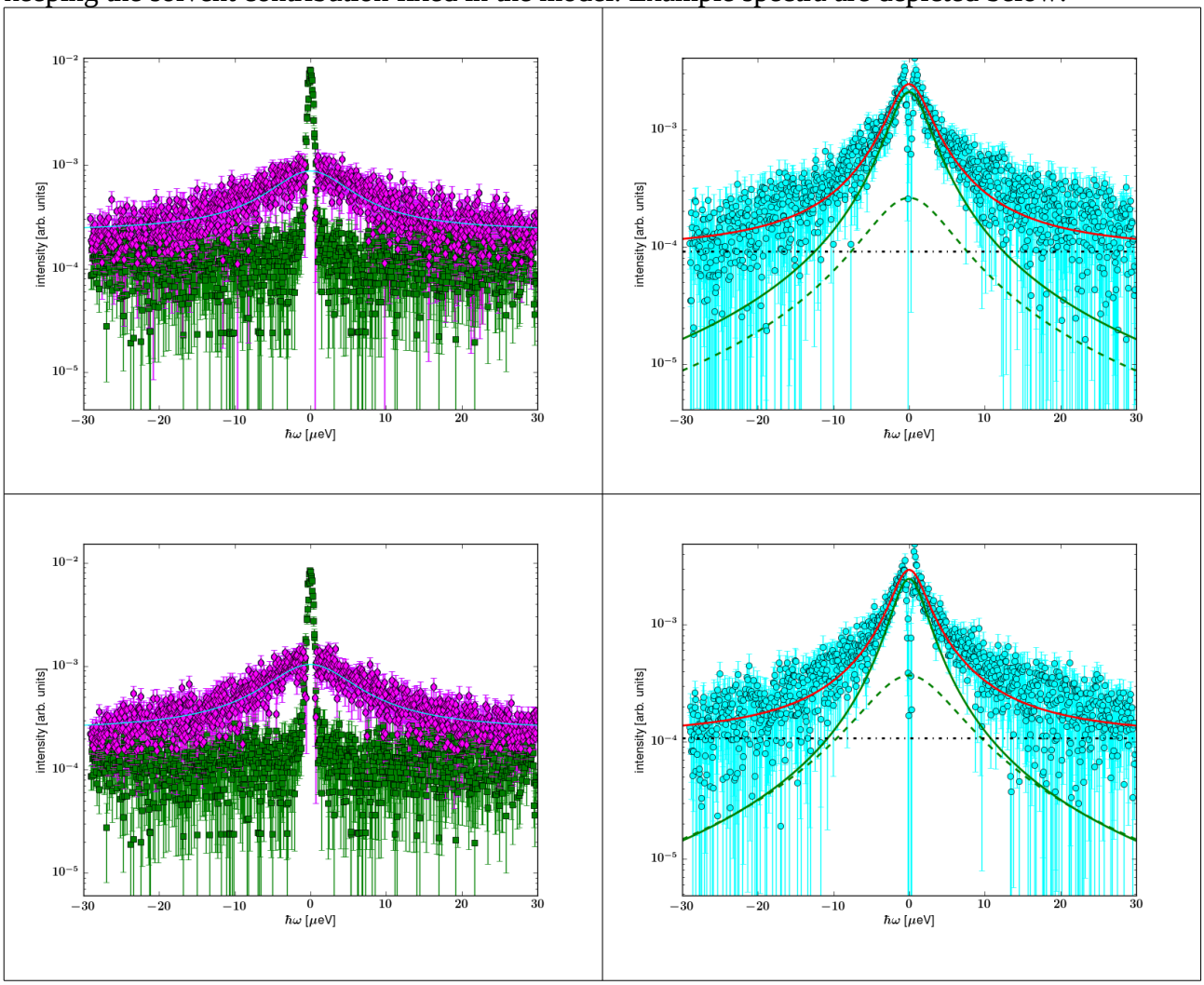

Figure: Left column: Pure gel (top) and pure solvent (bottom) (diamond symbols) and empty can signal (square symbols). Right column: 8%TTC in a gel (top) and pure solvent (bottom) (circle symbols). All example spectra are shown for q=0.82/Å. The lines denote fits. The fit components in the right column denote the Lorentzians describing the guest molecule diffusion (green solid) and two solvent components (dashed and dash-dotted). The spectra were measured at T=265.

The global fit approach assumes a Brownian tracer diffusion of the guest molecules. The solvent is modeled by two Lorentzian contributions. Further modeling and fitting is currently in progress. The present fit results indicate that the guest molecule diffusion is faster in the gels than in the corresponding pure solvent. For the depicted example, we find for the guest molecule diffusion:

D = (5.09195+/-0.10718) A^2/ns for the guest (8%TTC) in the pure solvent (T=265K)
D = (5.90657+/-0.09909) A^2/ns for the guest (8%TTC) in the 0.3% gel (T=265K)

We note, however, that the fits are still subject to further testing.