

An incoherent QENS study on the dynamic processes occurring in chemical hydrogels based on poly(vinyl alcohol)

Dynamic behaviour of water in hydrogels is a major issue for understanding how a polymeric matrix can function as drug delivery system (DDS).

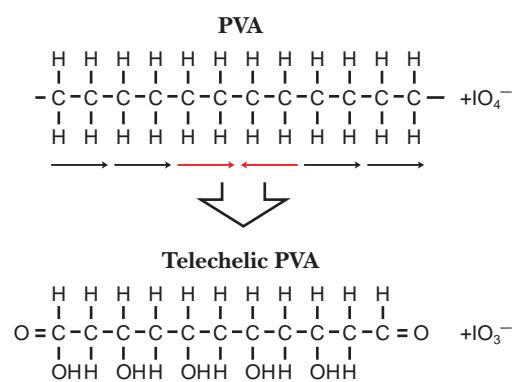
It is known that hydrogen bonded liquids confined in mesoscopic domains display significant modifications of their structural and dynamic bulk properties. Surely water embedding a polymeric matrix, i.e any hydrogel used as drug delivery device, has to be regarded under this aspect as the release properties of the system will strictly depend on diffusive behaviour of the caged water.

In recent years pharmacological research has considered that the problem of the bioavailability, and therefore of the release of drugs by the carrier, is as important as the synthesis of pharmacologically-active new molecules. Moreover, some innovative therapeutic approaches, for instance gene therapy, are now abandoning the use of 'small molecular weight molecule' drugs, pursuing treatments with 'high molecular weight molecule' drugs, i.e. macromolecular species as nucleotide chains or active peptides. This poses some basic problems as the state of the medium (basically water) confined in heterogeneous (bio)systems, often hydrogels, used as drug carriers.

A versatile biocompatible material eligible for DDS is poly(vinyl alcohol), PVA, one of the few biocompatible synthetic polymers. PVA is known to form thermoreversible (physical) hydrogels upon freeze-thaw cycles. Also, chemical hydrogels based on PVA can be obtained by adding suitable bifunctional short molecules able to cross-link PVA chains and consequently to form a network. For the last few years we have focused on obtaining a family of chemical hydrogels with enhanced physical and chemical stability, without introducing cross-linkers chemically different from PVA. This is an important aspect of the final product as a biocompatibility comparable to that of the starting PVA is required.

Our method for obtaining PVA chemical hydrogels is based on the presence in a PVA chain of a small but measurable amount of sequence defects. Generally, repeating units

are regularly spaced in ‘head-to-tail’ sequences along the chain, and a ‘head-to-head’ kink seldom occurs. The amount of such defects can vary depending on the polymerization conditions of PVA. We developed a convenient way of determining the number of the ‘head-to-head’ sequences contained in the starting



The number of $\longrightarrow \longleftarrow$ sequences is determined with a microcalorimetric experiment:

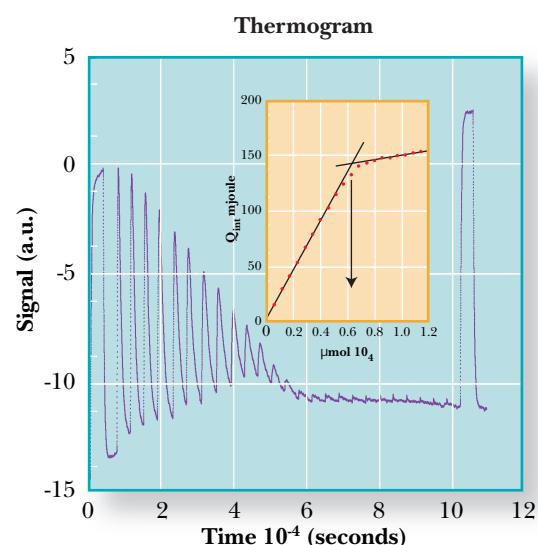


Fig. H21.1. Obtainment of telechelic PVA is based on the specific splitting of the 'head-to-head' sequences (red arrows) from the 'head-to-tail' sequences (black arrows). The amount of the 'head-to-head' sequences is determined by a microcalorimetric titration and corresponds to the end point of the titration (shown by the vertical arrow in the inset).

PVA chains by a microcalorimetric titration, as shown in Fig. H21.1.

The PVA network is obtained by splitting the 'head-to-head' sequences by a selective oxidizing agent (periodate) and producing the macromer cross-linking agent, i.e. the *telechelic* PVA. In a second step the cross-linking reaction between the terminal functional group and the 'head-to-tail' glycolic sequences is allowed, yielding a network that can be schematically represented in Fig. H21.2. Water acting as reaction medium is confined inside the gel as a consequence of the network formation. Its dynamic behaviour is modified by the confinement according to QENS experiments carried out at the IRIS beamline.

We carried out incoherent QENS experiments on telechelic PVA hydrogels in water and in D_2O at different temperatures and cross-linking degrees. The change of solvent was necessary in order to separate as much as possible water and polymer proton contributions to the observed incoherent scattering functions, therefore gaining insight into the dynamic behaviour of both components. Owing to the difference in the incoherent cross-section between protons and deuterons, PVA hydrogels containing water were mainly dominated from the diffusive motions of water protons, whereas incoherent QENS measurements carried out in D_2O were dominated by the incoherent scattering of the non-exchangeable protons contained in the polymer moiety. In Fig. H21.3 the observed dynamic structural factor, $S(q, \tau)$, obtained for the same hydrogel embedded in H_2O and in D_2O at a scattering vector q of 1.222 \AA^{-1} and at 303 K is shown. The spectra were analyzed as a convolution of the instrument resolution with a linear combination of lorentzians with different line broadening factors.

Parameters of the diffusive processes taking place in the hydrogels can be extracted from these measurements with the aid of

appropriate models, i.e random jump diffusion, allowing for a diffusion coefficient and a residence time between consecutive jumps. The results show that water behaves as a supercooled liquid when it is confined within these matrices. These features are common to other bi- and tridimensional matrices containing hydrogen bonded liquids.

The experiments carried out in D_2O allowed an evaluation of the dynamics of the PVA polymer chains between two cross-linking points. One dynamic feature was an average characteristic displacement of the chains of about 10 \AA . Comparable values are usually detected in polymer melts above the glass transition temperature.

In conclusion, QENS has proved to be a valuable approach for the study of water and polymer moieties in confined systems. In PVA matrices dynamics of water are characterized by an enhanced supercooled behaviour. On the other hand PVA polymer networks feature a confined chain diffusion due to the presence of chemical cross-links. Dynamics of the two components are strongly influenced by the confinement. These findings compare with the results obtained with other very different mesoscopic systems, which suggests a common behaviour of water considered as a confined hydrogen-bonded liquid.

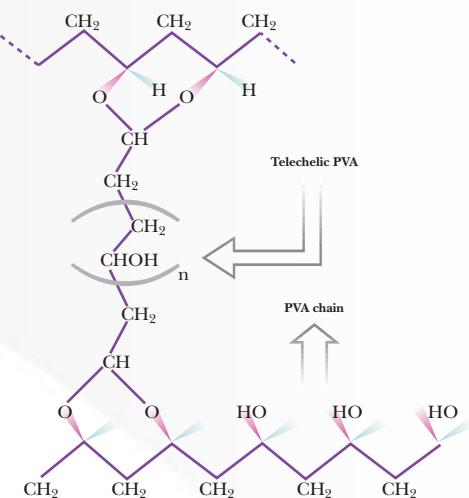


Fig. H21.2. Schematic representation of the chemical hydrogel based on telechelic PVA.

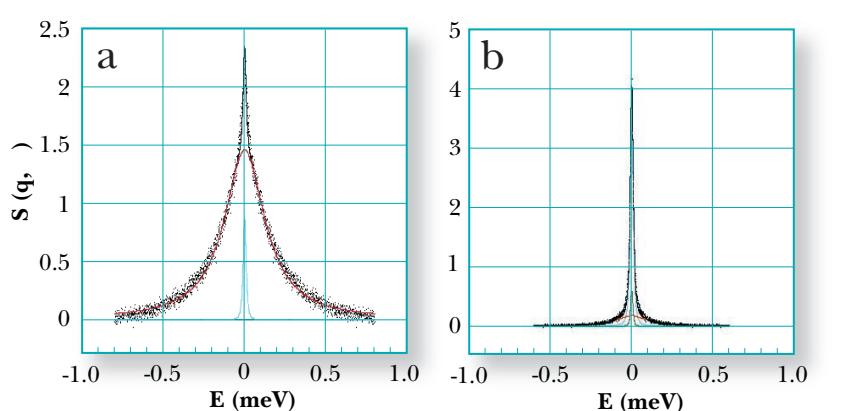


Fig. H21.3. Change in the lineshape of the scattering function of the telechelic PVA hydrogels in water (a) and in D_2O (b).