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Applications of fast diffusion measurement using Difftrain

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Abstract

Novel applications of fast self-diffusion measurement are presented. Difftrain (Diffusion train), which uses successive stimulated echoes from a single excitation pulse where a portion of the available magnetisation is recovered for each echo, is used to measure self-diffusion by varying the observation time. It is applied to produce the droplet size distribution of an oil-in-water emulsion in less than 4 s. This is verified by comparison with the droplet size distribution produced by a standard pulsed field gradient (PFG) technique. Difftrain is also extended to enable the application of incremental gradients, in addition to varying the observation time. This is used to produce propagators or displacement probabilities of water flowing through a packed bed for a range of 16 observation times in under 10 min. Again verification is provided by acquisition of the same propagators using a conventional PFG technique.

Keywords: Difftrain; PFG; Emulsions; Propagators; Self-diffusion

1. Introduction

Measurement of self-diffusion and displacement propagators or probabilities, using NMR pulsed field gradient (PFG) techniques, is a well-established technique that finds a wide range of applications. Conventionally however, the technique is time consuming, largely due to the need to allow the signal to relax after each excitation. Typically, total acquisition times are of the order of 5–10 min to enable an accurate measurement to be achieved. Whilst this temporal resolution is adequate for 'stable' systems, it does not yield useful information about dynamic, non-equilibrium environments.

Measurement, using NMR, of molecular self-diffusion when it is restricted to various geometric domains, can be exploited to provide the length-scale characterising the restriction [1]. Such an approach is extensively used to size emulsion droplets (e.g. [2,3]), which are dispersions of one liquid phase within another. Emulsions are however thermodynamically unstable systems that will tend to separate over time, and hence conventional PFG is restricted to those emulsions that are stable over time periods of at least tens of minutes. To this end a single shot NMR technique to measure self-diffusion whilst retaining spectral information, Difftrain [4], is used to produce droplet size distributions for emulsions in less than 4 s.

Difftrain is based on varying the observation time, Δ, over which self-diffusion is observed. This technique is extended in this paper to allow the applied gradient strength, g, to also be varied in addition to Δ. This is exploited to produce a set of propagators (displacement probabilities) over a range of Δ, for water flowing in a packed bed of particles. Such measurements are widely applied to characterise the hydrodynamics of various porous media (e.g. [5,6]). This measurement of multiple propagators is acquired in under 10 min, an order of magnitude faster than is the case with conventional PFG techniques.

For both the emulsion droplet sizing and the range of propagators as a function of Δ, results using conventional PFG were produced under appropriately identical conditions and compared directly with those produced using Difftrain.

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2. Background

A number of fast diffusion methods have previously been proposed to study diffusion based on multiple echo acquisition by manipulating both r.f. pulses and magnetic field gradients in a variety of ways. These include using PFG with multiple spin echoes [7], spin echoes with multiple alternating diffusion gradients [8], DOSY with bipolar gradients [9], and the BURST sequence [10].

The Difftrain sequence [4] is an extension of the bipolar pair stimulated echo (BPPSTE) or alternating pulsed gradient stimulated echo (APGSTE) pulse sequence [11]. Difftrain is notable amongst the fast diffusion techniques as it collects and retains all the spectral information from the system under study whilst using a single acquisition. This is essential for the characterisation of emulsion systems, as demonstrated in this work.

3. Experimental

All NMR measurements were performed on a Bruker DMX 300 widebore spectrometer, equipped with a 15 mm diameter birdcage r.f. coil and orthogonal gradients with a maximum gradient strength of 100 G/cm.

The basic Difftrain pulse sequence used is shown in Fig. 1a. It is based on the use of multiple stimulated echoes and bipolar gradients [11] to reduce the effect of background magnetic field gradients. The basic principle is that an echo is acquired after each increase in observation time, Δ_{inc}, and that only a portion of the available signal is used to generate each echo, as determined by the angle, α, where α is the angle of the refocusing pulse.

The initial three pulses flip the signal into z storage, from where only ($\sin\alpha$) is retrieved and manipulated via a stimulated echo. ($\mathrm{Cos}\,\alpha$) of the signal remains to be manipulated to form subsequent echoes at successively longer observation times. The train of echoes are thus encoded with successively increasing observation times, data from which the diffusion co-efficient or propagator can be extracted. This train of echoes, as shown in Fig. 2a, however also suffers from T_1 relaxation. To compensate for this T_1 relaxation as well as the diminishing magnetisation available due to partial excitation, a second train of echoes is acquired in which the bipolar magnetic field gradients are switched off (such a train is shown in Fig. 2b); by dividing the original echo train by this second train, it is possible to account for the effects of T_1 relaxation and partial excitation on the acquired echo train. When using the Difftrain sequence, note must be taken of the T_1 of the system as this will limit the number of usable echoes. In our experience, T_1 must be greater than 0.25 s in order for sufficient echoes to be acquired such that meaningful data are produced. The

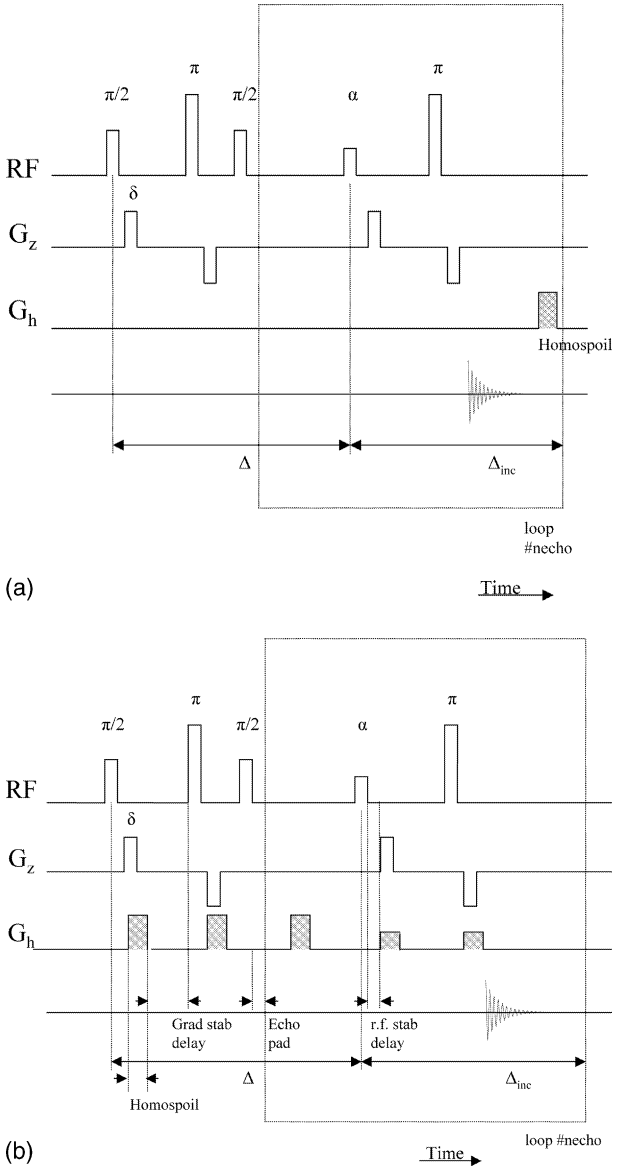


Fig. 1. (a) The basic Difftrain pulse sequence, the dashed box indicates the multiple echo acquisition loop. (b) Modified Difftrain pulse sequence to include homospoil gradients around the π r.f. pulses. The echo pad delay can be altered to make Δ and Δ_{inc} equal; gradient and r.f. stabilisation delays are present to minimise switching instabilities.

use of stimulated echoes means that the Difftrain technique is robust with respect to systems with short T_2s.

The implemented Difftrain sequence used in our work is shown in Fig. 1b. Homospoil gradients were added to either side of the refocusing r.f. pulses and at the beginning of the looping portion of the decode sequence in order to destroy secondary echoes, improving the robustness of the technique. This had an additional effect of shortening the overall scan time as a complex phase cycle was not necessary. The two-step phase cycling procedure used stores coherences alternately along the + and − z-axis to cancel magnetisation arising from longitudinal relaxation [12].

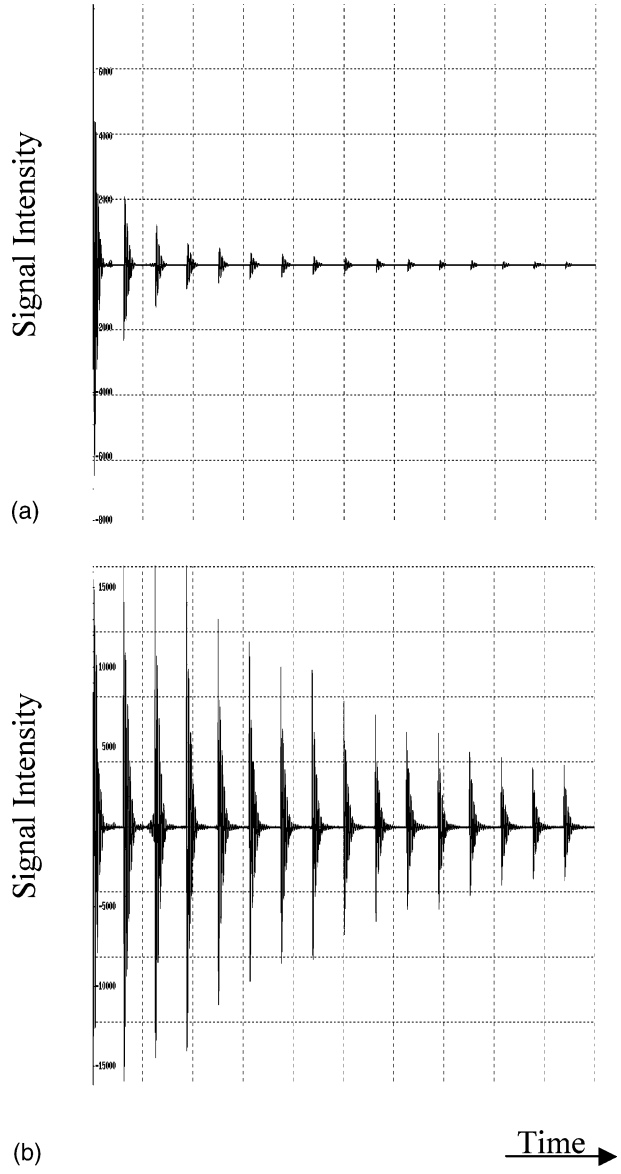


Fig. 2. (a) Difftrain ($\delta = 1$ ms, $g = 45$ gauss/cm) echo train with signal attenuation due to T_1 relaxation and self-diffusion. (b) Difftrain ($g = 0$ gauss/cm) echo train with signal attenuation due to T_1 relaxation only.

Details regarding the implementation specific to the determination of emulsion droplet size distributions and propagators characterising liquid transport through a packed bed are now addressed separately.

3.1. Emulsion droplet size distributions

For our implementation, an optimum value of 15° was selected for α. The gradient strength used was 24.4 G/cm and δ was 5 ms. This allowed a total of 16 echoes to be acquired within a total scan time of 1.4 s. Thus with the reference scan to eliminate T_1 effects, the total time required to produce a droplet size distribution for the emulsions was less than 4 s. For the emulsions, the attenuation, R, of the oil peak, as extracted from the train of echoes following Fourier Transform, can be modelled [13]; the attenuation due to a droplet of radius a is given by:

$$\ln R(\Delta, g, \delta, a) = -2\gamma^2 g^2 \sum_{m=1}^{\infty} \frac{1}{\kappa_m^2(\kappa_m^2 a^2 - 2)} \times \left\{ \frac{2\delta}{\kappa_m^2 D} - \frac{2 + e^{-\kappa_m^2 D(\Delta-\delta)} - 2e^{-\kappa_m^2 D\Delta} - 2e^{-\kappa_m^2 D\delta} + e^{-\kappa_m^2 D(\Delta+\delta)}}{(\kappa_m^2 D)^2} \right\}, \quad (1a)$$

where δ is the total duration of the pulsed field gradient, Δ is the observation time, g is the magnitude of the pulsed field gradient, D is the bulk self-diffusion coefficient of the material in the droplet phase, γ is the gyromagnetic ratio for the proton ($2.675 \times 10^8\ T^{-1}\ s^{-1}$), and the κ_m are given by the positive roots of the equation,

$$J_{3/2}(\kappa a) = \kappa a J_{5/2}(\kappa a), \quad (1b)$$

where J is a Bessel function of the first kind. However, an emulsion consists of droplets with a distribution of radii. The NMR attenuation observed is a volume weighted average of the attenuations due to the range of droplet sizes. The observed attenuation can be expressed as

$$R(g) = \frac{\int_0^\infty a^3 P(a) R(g,a)\, da}{\int_0^\infty a^3 P(a)\, da}, \quad (2)$$

where $P(a)$ is the droplet size distribution of the emulsion.

In our case Δ is varied, using conventional PFG either δ or g are usually varied. Eq. (1a) is appropriate only for a single size of droplet; therefore the emulsion droplet size distributions, $P(a)$ were extracted using regularisation methods based on Eq. (2) [14]. This method of extracting $P(a)$, makes no assumption regards the shape or form of $P(a)$. It minimises the sum of errors squared between the predicted and experimental values of $R(g)$, with the addition of a penalty function to prevent an oscillatory and hence physically unrealistic solution for $P(a)$.

The specific emulsion system investigated consisted of 5 cSt DMPS (dimethyl polysiloxane; mono-disperse in size with an average molecular weight of approximately 770, supplied by Sigma–Aldrich, UK. It has a D value of $1.2 \times 10^{-10}\ m^2\ s^{-1}$, as required by Eq. (1a), which was measured using the conventional PFG technique) emulsified in water at a volumetric oil:water ratio of 30:70 with Tween 80 (polyoxyethylene sorbitan monooleate, supplied by Sigma–Aldrich) as the surfactant dissolved in water at a concentration of 1 part in 100. Emulsification was achieved using an Art Micra D8 homogenizer at room temperature operating at 10,800 rpm for 5 min. Adequate spectral information was contained in the Difftrain spectra to enable the DMPS signal to be selectively detected and manipulated.

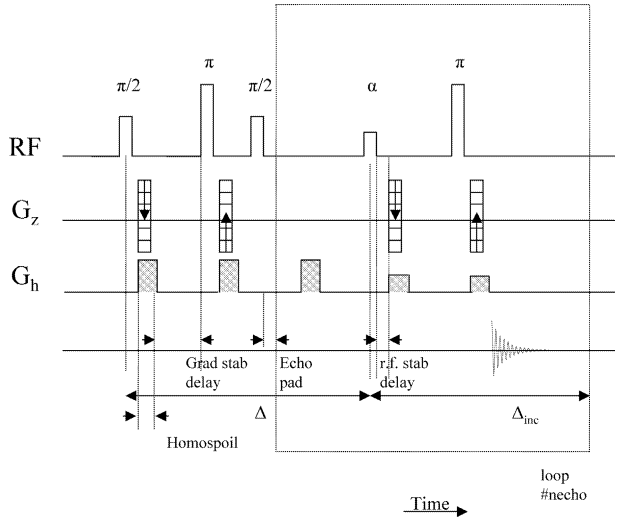


Fig. 3. The Difftrain pulse sequence with the addition of ramped magnetic field gradients to provide data from changes in both Δ and g.

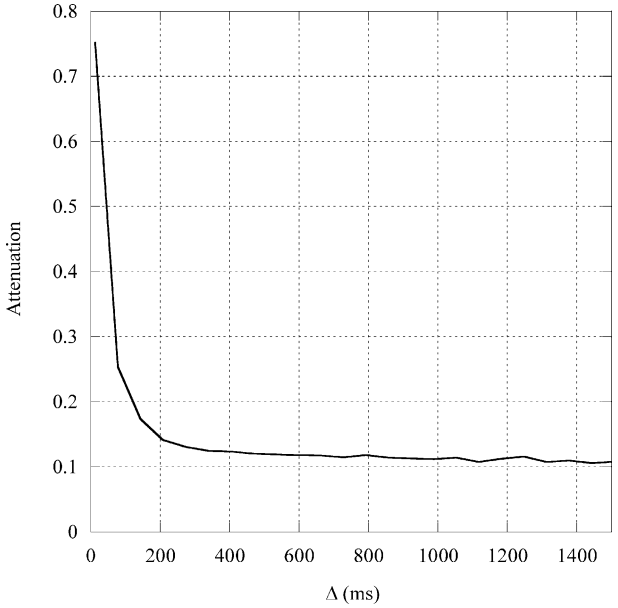


Fig. 4. Difftrain signal attenuation curve with increasing Δ, due to restricted diffusion of DMPS within emulsion droplets.

3.2. Propagators characterising flow through a packed bed

A further development of the Difftrain sequence was to collect trains of echoes at increasing Δ values, whilst ramping up the strength of the diffusion gradients, g. The pulse sequence used to accomplish this is shown in Fig. 3. An echo train is acquired for each value of g. The resultant 3D data set can be manipulated to produce propagators at a range of observation times, Δ, by Fourier transforming along the direction corresponding to increasing g [15]. Compared to conventional PFG techniques, the total time required is reduced by a factor equal to the number of observation times used. In our implementation, propagators were produced at 16 observation times; consequently the total acquisition time was reduced by a factor of 16.

The 3D Difftrain pulse sequence was used to produce propagators for water flowing through a 1.5 ml volume HiTrap desalting column packed with Sephadex G-25 superfine with a bead size of 15–75 μm (supplied by Amersham Pharmacia Biotech). This was done over a range of Δ extending from 45 to 720 ms with g ranging from −73.1 to 73.1 G/cm and δ equal to 2 ms. The flow rate of water through the packing was set to 7.3 ml/min and was fed by a P500 syringe pump (Amersham Pharmacia Biotech).

4. Results and discussion

4.1. Emulsion droplet size distributions

The raw attenuation data for the DMPS content of the emulsion, as produced by Difftrain, is shown in Fig. 4. Three regions are clearly evident; at short observation times there is rapid signal attenuation as the molecules experience little restriction to their self-diffusion. This is followed by a concave transition stage as more molecules experience restricted self-diffusion and finally a plateau where further increases in observation time produce no further signal attenuation, i.e., all memory of initial position is lost.

The emulsion droplet size distribution extracted from the data in Fig. 4 is shown in Fig. 5. Also shown is the droplet size distribution produced using a conventional PFG technique in which the value of g is varied and Δ is kept constant. The agreement in shape is excellent and the modes of the two distributions differ by only 1 μm.

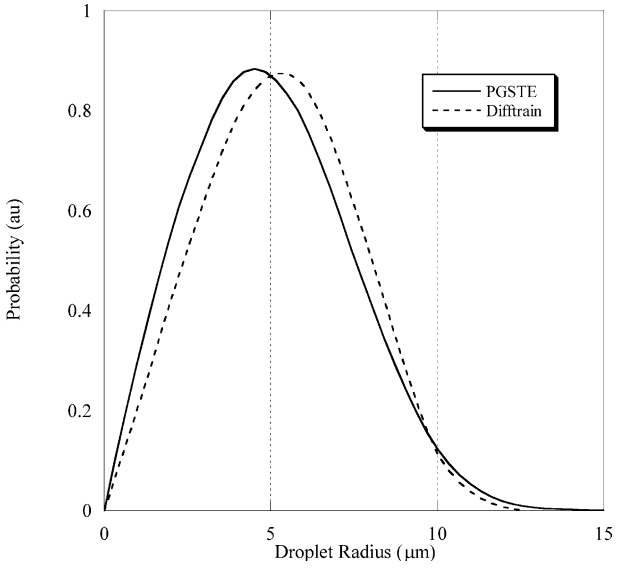
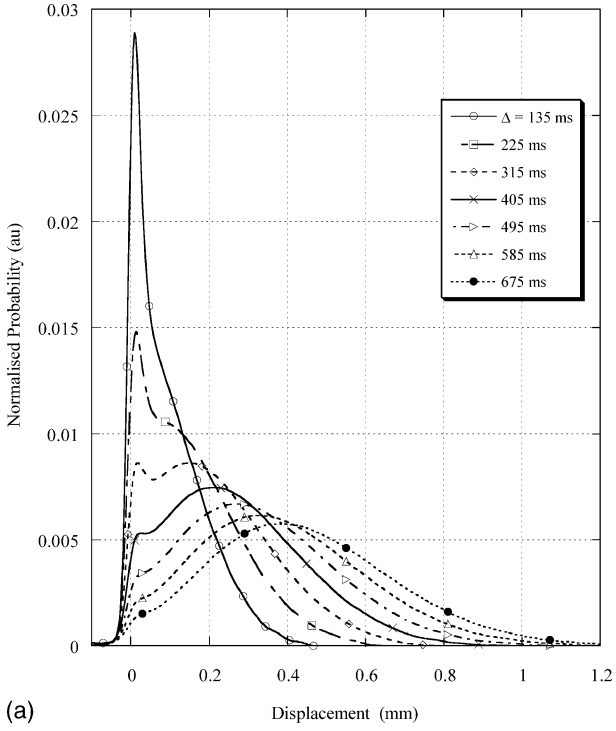


Fig. 5. The emulsion droplet size distribution curve extracted from the data shown in Fig. 4. Agreement with the distribution produced using conventional PFG (PGSTE) is excellent.



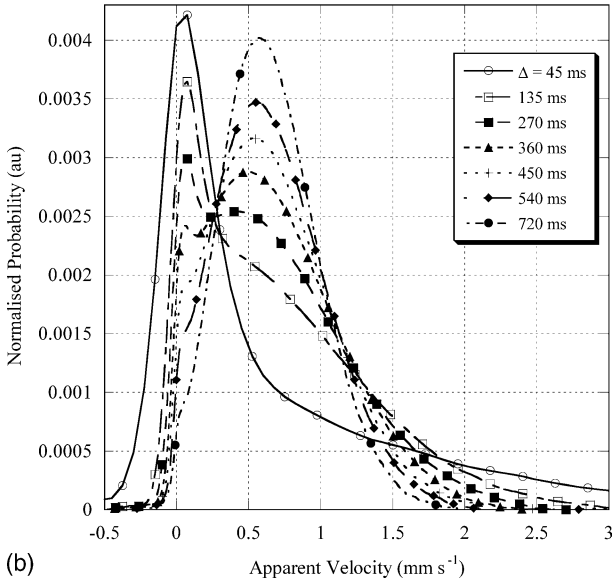


Fig. 6. (a) Displacement probabilities or propagators for water flowing through a Sephadex packing with increasing Δ. (b) Apparent velocity distributions extracted from the displacement data (Fig. 6a) for water flowing through Sephadex packing with increasing Δ.

The sensitivity of the droplet size distribution extracted to the range of observation times used in Difftrain is the subject of ongoing work.

4.2. Propagators characterising flow through a packed bed

The propagators produced for the water flowing through the Sephadex packing, are shown in Fig. 6a. The transition in the shape of the propagators from an exponential to a Gaussian is clearly evident and has been widely reported elsewhere (e.g., [6]). By dividing each displacement axis by the relevant observation time, the data can be presented as a distribution of velocities (distorted by self-diffusion). This was performed to produce Fig. 6b. In Fig. 6b, two distinct peaks are evident, the first peak corresponds to intra-particle water whilst the second peak corresponds to water which is predominately inter-particle. The diffusion of water out of the particles and into the flowing pore space as observation time is increased, is clearly evident. Comparison of these propagators with propagators produced using conventional PFG techniques are presented in Fig. 7, the agreement is excellent for all values of Δ considered.

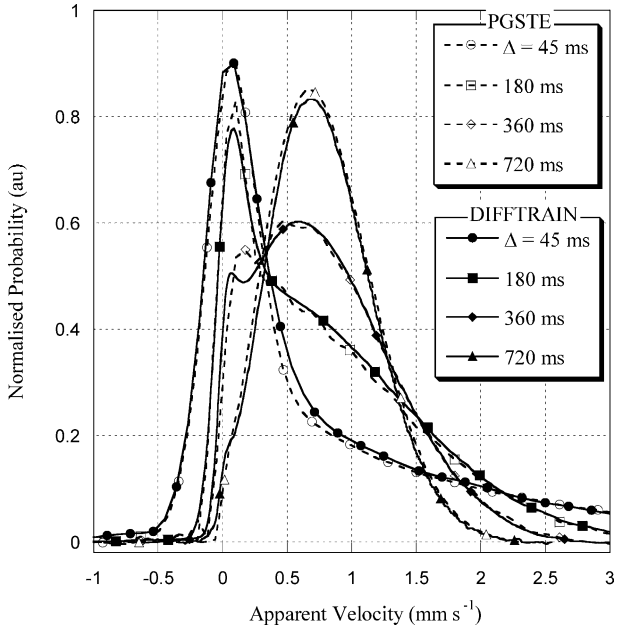


Fig. 7. Comparison of the apparent velocity distributions as produced using Difftrain and conventional PFG, for water flowing through a Sephadex packing at observation times of 45, 180, 360, and 720 ms.

5. Conclusions

Novel applications of the fast self-diffusion measurement technique, Difftrain, are presented. These include the sizing of emulsion droplets in 4 s and the acquisition of multiple propagators as a function of observation time, Δ, for which an order of magnitude decrease in total acquisition time was achieved. Both applications compare very favourably with the results of conventional PFG measurements.

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