

COLLOIDAL SUSPENSION FLOW AND TRANSPORT BEHAVIOR IN SMALL
CHANNELS BY MAGNETIC RESONANCE MICROSCOPY

by

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ABSTRACT

The research presented addresses colloidal transport issues in small channel systems using Magnetic Resonance Microscopy techniques. In transport phenomena, the interaction between convection or deterministic motions and diffusion or random motions is important in many engineering and natural applications, especially relating to multiphase flows. Magnetic Resonance methods have the ability to separate coherent from incoherent motion, as well as measure spatially resolved velocity, probability distributions of displacement, and microstructure on the pore scale, even within a multiphase colloidal system. A dilute ($\phi < 0.10$) suspension of $\sim 2.5 \mu\text{m}$ Brownian particles under shear flow in a 1 mm diameter glass capillary was investigated using spectrally resolved Pulsed Gradient Spin Echo techniques. The results indicate particle migration inward towards the capillary center. In addition, dispersion coefficients measured via flow-compensated Pulsed Gradient Spin Echo techniques as a function of observation time indicate the onset of irreversible dynamics with increasing total strain. Particle migration and irreversible dynamics are generally not expected to occur in dilute Brownian suspensions and are therefore not considered in the modeling of flow systems. Evidence of these effects, as indicated by the data presented, exhibits the importance of many body hydrodynamics in dilute Brownian suspensions and shows the applicability of chaos theory and non equilibrium statistical mechanics methods to model these systems.

Additionally, blood, a well-studied cellular suspension with controllable aggregation properties, was studied when exposed to shear in a small gap cylindrical Couette rheometer. Shear induced particle migration in inhomogeneous shear flows creates non-uniform particle concentrations and cell depletion near the walls of the flow chambers. Non-uniform particle concentrations affect the overall flow characteristics of the suspension and create spatial variation of effective material properties, such as apparent viscosity. Understanding erythrocyte migration away from vessel walls is useful for identifying physiological transport mechanisms, designing filtration devices and designing microfluidic based sensors for blood. As a non-invasive and non-destructive technique with the ability to probe time and length scale displacements non-invasively, Magnetic Resonance Microscopy provides a unique perspective on the study of complex and opaque colloidal suspension flow.

INTRODUCTION

The thesis research characterized colloidal particle suspension flow and transport behavior in small channels by Magnetic Resonance Microscopy (MRM) techniques. Colloidal particles range from 5 nm to 10 μm and, therefore their motion is influenced by collisions with the suspending fluid molecules[1] causing the particles to undergo Brownian motion, a random diffusion process. In the presence of bulk flow at low Reynolds numbers, the particles experience both random and deterministic motions making colloidal suspensions complex and generally opaque fluids that depend on Peclet number, the ratio of shear to diffusive forces, as well as microstructure, the spatial arrangement and distribution of the particles[2]. The fundamental nature of the analysis of dynamics and structure formation in colloidal suspensions confined to small domains lies in the complexity of the hydrodynamic, physical and chemical interactions present.

The research presented here addresses colloidal transport issues in several small channel systems using Magnetic Resonance Microscopy (MRM) techniques. In transport phenomena, the interaction between convection or deterministic motions and diffusion or random motions is important in many engineering and natural applications, especially relating to multiphase flows. MR methods have the ability to separate coherent from incoherent motion, as well as measure spatially resolved velocity, probability distributions of displacement, and microstructure on the pore scale[3-5], even within a multi-phase colloidal system. A dilute, volume fraction $\phi < 0.10$, suspension of $\sim 2.5 \mu\text{m}$ Brownian particles under shear flow in a 1 mm diameter glass capillary were investigated using pulsed gradient spin echo (PGSE) MR techniques. The results suggest particle

migration and irreversible dynamics are present in the system, effects typically associated with concentrated non-colloidal suspensions[6]. Tracking the motion of the particles themselves is typically quite difficult experimentally, especially simultaneously with the motion of the suspending fluid, and usually requires some sort of optical technique, which limits the types of samples and particle concentrations that can be studied. The use of “core-shell” particles[7], however, allows differentiation between the particulate and fluid phases of this multi-phase flow system due to the spectral resolution between particle core oil and suspending water possible with PGSE techniques. Propagators were obtained showing an increased probability of finding the particle at higher velocities. In addition, velocity imaging shows a parabolic or nearly parabolic bulk velocity profile characteristic of Poiseuille flow where the highest velocity streamlines are located at the centre of the capillary. This evidence indicates that particles are migrating inward. Particle migration of Brownian suspensions under pressure driven flow has been shown previously[8]. However, at dilute concentrations ($\phi \sim 0.05$), evidence of migration was not greater than the measurement uncertainty, unlike the NMR results presented here. Flow models generally only account for particle migration in non-colloidal or concentrated suspensions, but this work implies that theoretical concepts could be applicable to dilute Brownian suspensions. Dispersion coefficients as a function of observation time for the Brownian particles were also measured via flow-compensated PGSE and indicate the onset of irreversible dynamics with increasing total strain. Chaotic dynamics are an indication that many body hydrodynamics impacts the motion of the particles. It appears that concepts governing the time reversibility of shear flows

previously applied to concentrated non colloidal suspensions[9] again could apply to dilute Brownian suspensions.

Additionally, blood, a well-studied cellular suspension with controllable aggregation properties, was studied when exposed to shear in a small gap Couette rheometer. Couette viscometer studies for samples in which erythrocytes (red blood cells) are known to aggregate when exposed to low shear rates have measured an unsteady torque response and red blood cells have been visually observed moving away from the walls of the viscometer. Understanding erythrocyte migration away from vessel walls is useful for identifying physiological transport mechanisms, designing filtration devices[10] and designing microfluidic based sensors for blood[11]. Shear induced particle migration in inhomogeneous shear flows creates non-uniform particle concentrations which impact transport behavior, in particular cell depletion near the walls of the flow chambers, and also depends upon the aggregation tendency of the cells. Non-uniform particle concentrations affect the overall flow characteristics of the suspension and create spatial variation of effective material properties, such as apparent viscosity. In biosensors for environmental or security applications the sampling of small amounts of biological cellular material in microchannels requires understanding of the spatial distribution of the cells induced by the fluid dynamics transporting the material in the sensor.

A Rheo-NMR Couette device with an inner rotating cylinder and fluid gap of 1.05 mm was used to steadily shear three chemically different red blood cell (RBC) suspensions. Velocity profiles as a function of radial position across the fluid gap were

obtained and the derivative of polynomials fitted to these measured velocity profiles gave shear rates at each radial point. In an iterative calculation scheme using the Quemada equation[12], $\eta_r = \frac{\eta_a}{\eta_o} = (1 - 0.5kH)^{-2}$, and assuming a constant torque, $T = 2\pi r^2 \eta_{app} \dot{\gamma}$, across the gap; the radial hematocrit distribution, or volume fraction of RBCs in suspension, was calculated at all radial points. Velocity profiles and corresponding hematocrit distribution profiles were found for three RBC suspensions (which are listed here in order of increasing RBC aggregation): RBCs suspended in isotonic, phosphate-buffered saline containing 0.5% albumin; RBCs in plasma; and RBCs suspended in plasma which had 1.48% by weight Dextran 110 added. The RBC aggregation generates differing RBC concentration distributions resulting in spatially dependent rheological behavior. It was possible, with Magnetic Resonance Microscopy Methods, to use measured velocity data to map the hematocrit distribution as a function of location across the gap for the first time, as well as confirm the presence of a plasma layer at both the rotating and stationary wall of the Couette which becomes larger as the tendency for RBCs to aggregate is increased[13].

In summary, the research probes complex interactions in blood and model colloids within two different experimental apparatus. As a non-invasive and non-destructive technique with the ability to probe time and length scale displacements non-invasively, MRM provides a unique perspective on the study of complex and opaque colloidal suspension flow. This research provides significant advancement to existing theory, verification of existing experimental data and provides complimentary

information to that of traditional techniques such as laser Doppler velocimetry and particle imaging velocimetry[14, 2].

COLLOIDAL PARTICLE SUSPENSIONS

The principle characteristic which determines if a particle is colloidal is its size. The range encompasses particles on the order of nanometers up to the micrometer scale, including paint pigments, red blood cells and fine sand. There are a variety of forces brought to bear by the presence of colloidal particles within a fluid. Hydrodynamic, Brownian, and interparticle forces compete against one another to determine the dynamic and thermodynamic properties of the suspension [1]. Stability and phase behavior are governed by the balance between Brownian motion and interparticle forces such as hydrodynamic interactions, electrostatic repulsion, and attraction due to dispersion forces. These interactions completely determine suspension microstructure. With the application of an external shear field, however, the microstructure is perturbed creating many complex material responses. The response of a colloidal dispersion to an external shear field is highly complicated. Thus, colloidal suspensions are complex fluids that depend on both Peclet number and microstructure, where Peclet number can be thought of as a measure of the suspension's deviation from equilibrium. In order to deconvolve some of the forces present in such a system, a theoretical overview of individual forces and their role in determining the dynamics of the suspension is given. Due to the complexity of most real world dispersions, idealized systems must be analyzed first and built upon. For example, to understand the dynamics of particles interacting with external fields, the motion of an isolated sphere is a good model. For particle interactions, pairs of spheres represent the idealized system.

The short range of interparticle interactions in colloidal suspensions does not generally allow them to recover from high strains, thus precluding visco-elastic behavior as is often seen in polymeric liquids. However, non-Newtonian rheological responses such as shear thinning, shear thickening and the existence of yield stress can still occur. Dilute and moderately concentrated suspensions generally behave as low viscosity fluids, with the possibility of some shear thinning. The bulk of the theoretical overview will assume a monodisperse suspension of hard sphere colloids, which is a simplification, but relevant in many applications and to the experimental data presented.

Interparticle Colloidal Forces

In the hard sphere model, the interparticle interaction is a short range repulsion, which has the effect of not allowing the particles to come in direct contact with each other upon a “collision”. There is no electrostatic contribution, due to a significant charge where ions in the solution may affect the behavior of the particle interactions. Dispersion or van der Waals forces, short range attractive forces caused by local fluctuations in the polarization within one particle inducing a response in another via the propagation of electromagnetic waves, are negated by the short range repulsion of the hard sphere.

Brownian Motion

Due to their size, colloidal particles are impacted by the motion of the suspending fluid molecules, creating a stochastic particle motion called Brownian motion. Stochastic

processes can be modeled by deriving the governing differential equations for a stochastic variable z as it changes with time t . The force exerted on a particle is split into a deterministic and a random part, leading to a Stochastic Differential Equation (SDE), or Langevin equation, where the viscous drag is balanced by a random fluctuating force $\mathbf{R}(t)$ [15].

$$\frac{d^2 z(t)}{dt^2} = -\gamma \frac{dz(t)}{dt} + \mathbf{R}(t) \quad (2.1)$$

where z is the particle position, γ is a damping constant and $R(t)$ has the properties of

$$\langle R(t) \rangle = 0 \quad (2.2)$$

$$\langle R(t)R(t') \rangle = \Gamma \delta(t - t') \quad (2.3)$$

where Γ is the noise intensity. Solution of (2.1) leads eventually to a form for the mean squared displacement of a particle in the z -direction of

$$\langle z^2(t) \rangle = \int_0^t dt' \int_0^{t'} dt'' \langle \mathbf{v}(t') \mathbf{v}(t'') \rangle \quad (2.4).$$

Setting $\tau = t' - t''$ and integrating by parts

$$\langle z^2(t) \rangle = \frac{2\langle v^2 \rangle}{\gamma} \left[t - \frac{1}{\gamma} (1 - \exp(-\gamma t)) \right] \quad (2.5).$$

In the short time limit $t \ll \tau_c$, where τ_c is the correlation time of the velocity fluctuation of a colloidal particle and equal to $1/\gamma$, (2.5) can be expanded via a Taylor Series expansion.

$$\langle z^2(t) \rangle = \frac{2\langle v^2 \rangle}{\gamma} t = \langle v^2 \rangle t^2 \quad (2.6)$$

This is called the ballistic regime.

In the limit as $t \rightarrow \infty$, or even just $t \gg \tau_c$, (2.5) reduces to

$$\langle z^2(t) \rangle = \frac{2\langle v^2 \rangle}{\gamma} t = 2Dt \quad (2.7).$$

This equation is the classic Einstein relation for the diffusion coefficient D .

Alternatively, a conservation of probability could be used to derive the governing differential equation, leading to a Fokker-Planck or Smoluchowski equation for velocity[16].

$$\frac{dP}{dt} = \gamma \frac{d}{d\mathbf{v}} \mathbf{v}P + \frac{\Gamma}{2} \frac{d^2 P}{d\mathbf{v}^2} \quad (2.8)$$

Hydrodynamics

The fluid, though it is essentially a two-phase system consisting of larger colloidal particles suspended in smaller fluid molecules, is generally considered a continuum in the context of spatial averaging over scales larger than individual particles. In the realm of true microfluidics, where the fluid channel dimension is on the order of the colloidal particle size, discrete particle effects become significant and this assumption is no longer valid. However, for the flow systems considered here, it is assumed that the classical conservation laws of mass, momentum, and energy apply. When considering the effect of the sphere on the velocity and pressure fields as propagated through the fluid; *i.e.* the hydrodynamics of the system, it is necessary to solve the equations of motion. The complex role of hydrodynamic interactions in a dilute colloidal suspension, how these

effects are accounted for theoretically and how they are modeled will be the focus of the rest of the chapter, providing context for the discussion of the MR data which is the core of the dissertation.

The Boltzmann Equation and Derivation of the Equations of Motion

The Boltzmann equation is the basic transport equation as derived from kinetic theory of dilute gases. The Boltzmann equation uses probabilistic ideas to try to make the connection between molecular motions and irreversible thermodynamics, in other words it is an attempt to reconcile the idea that a mechanical system reversible on the microscopic scale gives rise to irreversible macroscopic behavior[17]. A phase space is constructed where there is one axis for each canonical coordinate of position and momentum. The ensemble can be described in terms of a distribution function giving the density of all points in phase space. The average properties of the ensemble can then be examined through what is essentially a conservation equation of the one particle distribution function $f_N^{(1)}(\mathbf{R}_1, \mathbf{v}_1, t)$ in phase space, which governs the time evolution of the position $\mathbf{R}_1$ and velocity $\mathbf{v}_1$ of molecule 1 in a dilute gas. In the derivation of this equation, the term dilute gas implies the limitation that only two body, or binary, collisions between molecules occur. Changes in the distribution function can occur in essentially two ways; through streaming, the natural motion of the molecules without any interactions, and through particle collisions where the velocity is changed through a transfer of momentum. By identifying these mechanisms, it is possible to define the flux of mass, momentum and energy, as they relate to the distribution function for hard

spheres[16]. The total change to the distribution function is the sum of the streaming and collision terms. The streaming portion accounts for all changes in position and momentum due to convection and is given by the one particle Louiville equation written here for when no collisions occur.

$$\left(\frac{df_N^{(1)}(\mathbf{R}_1, \mathbf{v}_1, t)}{dt} \right)_{\text{streaming}} = -\mathbf{v}_1 \cdot \nabla_{\mathbf{R}_1} f_N^{(1)}(\mathbf{R}_1, \mathbf{v}_1, t) - \mathbf{F} / m \cdot \nabla_{\mathbf{v}_1} f_N^{(1)}(\mathbf{R}_1, \mathbf{v}_1, t) \quad (2.9)$$

Where $f_N^{(1)}(\mathbf{R}_1, \mathbf{v}_1, t)$ is again the one particle distribution function, $\mathbf{F}$ is any external force acting on the particle, and m is the mass of the particle. To determine the component due to particle collisions, an assumption called the Stosszahlansatz is made[16], where the mean number of particles at a given distance from a given particle is the same as the unrestricted mean and is independent of velocities. Essentially, this assumption of “molecular chaos” states that the probability of a particle collision can be calculated considering only the individual particles, and that this probability does not depend upon any pre-collisional correlation between the particles[16, 17]. Also assuming that $f_N^{(1)}(\mathbf{R}_1, \mathbf{v}_1, t)$ does not change appreciably over the spatial range of intermolecular forces, the change in the distribution function with regard to collisions can be written in terms of momentum only.

$$\left(\frac{df_N^{(1)}(\mathbf{v}_1, t)}{dt} \right)_{\text{collisional}} = \int \left\{ f_1'(\mathbf{v}_1, t) f_2'(\mathbf{v}_2, t) - f_1(\mathbf{v}_1, t) f_2(\mathbf{v}_2, t) \right\} \mathbf{v} \sigma(\theta) d\Omega d\mathbf{v}_2 \quad (2.10)$$

Where the primes denote post-collisional states and the integration is over the geometry of the collision where $\sigma(\theta)$ is the differential cross section for scattering with angular

deflection between θ and $\theta + d\theta$ and $d\Omega$ is the element of solid angle $\sin\theta d\theta d\varepsilon$. The polar angle ε is measured from the same line as the impact parameter b .

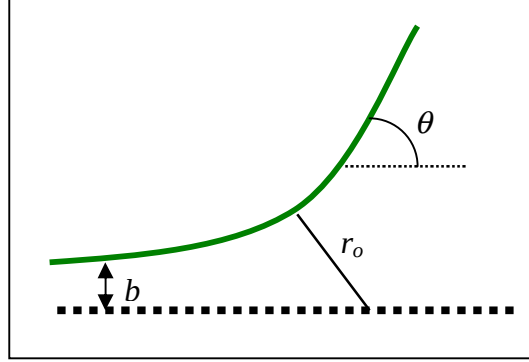


Figure 2.1. Geometry of a binary collision in relative polar coordinates (redrawn from [16]). The distance of closest approach is r_o , b is the impact factor, and θ is the angle of deflection.

The summation of these two terms yields the Boltzmann equation[17, 16].

$$\begin{aligned} \frac{df_N^{(1)}(\mathbf{R}_1, \mathbf{v}_1, t)}{dt} + \mathbf{v}_1 \cdot \nabla_{\mathbf{R}_1} f_N^{(1)}(\mathbf{R}_1, \mathbf{v}_1, t) + \mathbf{F} / m \cdot \nabla_{\mathbf{v}_1} f_N^{(1)}(\mathbf{R}_1, \mathbf{v}_1, t) \\ = \int \left\{ f_1'(\mathbf{v}_1, t) f_2'(\mathbf{v}_2, t) - f_1(\mathbf{v}_1, t) f_2(\mathbf{v}_2, t) \right\} \mathbf{v} \sigma(\theta) d\Omega d\mathbf{v}_2 \end{aligned} \quad (2.11)$$

One of the most important consequences of this equation is the implication that the entropy of an isolated system will increase due to irreversible processes, the second law of thermodynamics, which is related to Boltzmann's H-theorem. Defining a time dependent function H where $f = f_N^{(1)}(\mathbf{R}_1, \mathbf{v}_1, t)$, the one particle distribution function, as

$$H = \int f \ln f d\mathbf{R} d\mathbf{v} \quad (2.12)$$

And taking the derivative of Equation (2.12) with respect to time,

$$\frac{dH}{dt} = \int \frac{df}{dt} (\ln f + 1) d\mathbf{R} d\mathbf{v} \quad (2.13).$$

The streaming terms of the distribution function vanish upon integration and this equation may be written,

$$\frac{dH}{dt} = \frac{1}{4} \int \ln \left(\frac{f_1 f_2}{f'_1 f'_2} \right) \{ f'_1 f'_2 - f_1 f_2 \} \mathbf{v} b d\mathbf{b} d\boldsymbol{\varepsilon} d\mathbf{v}_2 d\mathbf{v}_1 d\mathbf{R}_1 \quad (2.14).$$

The two terms in the integral must have opposite signs and therefore the time dependent function H does not increase, analogous to entropy.

$$\frac{dH}{dt} \leq 0 \quad (2.15)$$

An additional property is that for H to be constant in time,

$$f'_1 f'_2 = f_1 f_2 \quad (2.16).$$

By taking the natural logarithm, (2.16) becomes

$$\ln f'_1 + \ln f'_2 = \ln f_1 + \ln f_2 \quad (2.17).$$

This equation states that $\ln f$ must be conserved in the case of the equilibrium solution.

Since the quantities conserved in a binary collision are known and include the number of particles, the linear momentum and the kinetic energy, $\ln f$ can be represented, following [16], as a linear combination of these quantities.

$$f = A'' \exp \left[\frac{-Dm}{2} (\mathbf{v} - \mathbf{B} / D^{1/2})^2 \right] \quad (2.18)$$

The variables A, B and D can be evaluated when the basic molecular properties that are conserved, mainly the number density $\langle n \rangle$, average velocity $\langle \mathbf{v} \rangle$ and temperature $\langle T \rangle$ are defined by averaging $f_N^{(1)}(\mathbf{R}_1, \mathbf{v}_1, t)$ over the velocity space.

$$\langle n \rangle = \int f_N^{(1)}(\mathbf{R}_1, \mathbf{v}_1, t) d\mathbf{v} \quad (2.19)$$

$$n \langle \mathbf{v} \rangle = \int \mathbf{v} f_N^{(1)}(\mathbf{R}_1, \mathbf{v}_1, t) d\mathbf{v} \quad (2.20)$$

Here is it convenient to define a fluctuation velocity,

$$\mathbf{u} = \mathbf{v} - \langle \mathbf{v} \rangle \quad (2.21).$$

The temperature representation of the energy is

$$\langle T \rangle = \int \mathbf{u}^2 f_N^{(1)}(\mathbf{R}_1, \mathbf{v}_1, t) d\mathbf{v} \quad (2.22).$$

And (2.18) then becomes the Maxwell distribution for the velocities C of molecules at thermal equilibrium.

$$f = n \left(\frac{m}{2\pi kT} \right)^{3/2} \exp(-mC^2 / 2kT) \quad (2.23)$$

The probabilistic nature of the Boltzmann equation leads to a general “law” of conservation through the idea of ergodicity, where for systems of larger degrees of freedom, most of the phase space is taken up by regions where the macroscopic properties of systems have values very close to thermodynamic equilibrium. In turn, this leads to the idea that the time average (at long enough times) is equal to the ensemble average[17]. Since the ensemble average is the equilibrium thermodynamic value for the

system, continuum equations for the conservation of mass, momentum and energy can be derived through averaging of the Boltzmann equation[16]. The quantities defined in (2.19), (2.20) and (2.22) are, from their definition, velocity moments of the distribution function f . Therefore, the Boltzmann equation can be redefined to monitor the behavior of these quantities as functions of time and space. The conservation of mass equation is obtained by multiplying the Boltzmann equation by one and integrating with respect to velocity. To get a conservation of momentum equation, Boltzmann's equation is multiplied by velocity and again integrated with respect to velocity. The same procedure is applied to get a conservation of energy equation by multiplying by the square of the velocity fluctuation. The solution procedure leading to the following forms of the continuum equations is not trivial, and many extensive methods exist[18], including the Chapman-Enskog method[17]. The resulting continuum equations of motion are

$$\frac{\partial \rho}{\partial t} + \nabla \cdot (\rho \mathbf{v}) = 0 \quad (2.24)$$

$$\rho \frac{d\mathbf{v}}{dt} + [\nabla \cdot \rho \mathbf{v} \mathbf{v}] = \rho \mathbf{g} + [\nabla \cdot \boldsymbol{\sigma}] \quad (2.25)$$

$$\frac{3}{2} nk \frac{dT}{dt} = -\boldsymbol{\sigma} : \nabla \mathbf{v} + \nabla \cdot \mathbf{q} \quad (2.26)$$

where ρ is the density of the fluid, $\mathbf{g}$ is the gravitational force, $\boldsymbol{\sigma}$ is the molecular stress tensor and $\mathbf{q}$ is the heat flux. These equations are considered continuum equations, applicable to real fluids instead of merely the dilute gas assumption that was used to derive them. These equations can also be derived from the more traditional engineering viewpoint of transport phenomena, where mass, momentum and energy are considered to

be conserved at a continuum differential volume element scale and balances may be written[19]. This derivation from the statistical mechanics approach of the Boltzmann equation to the continuum equations of hydrodynamics is central to statistical mechanics modeling of macroscale behavior in complex systems.

The equations of motion can be simplified further for specific conditions. In the case of a constant density fluid, (2.24) becomes

$$\nabla \cdot \mathbf{v} = 0 \quad (2.27).$$

The stress tensor for a Newtonian fluid can be written as

$$\boldsymbol{\sigma} = -P\boldsymbol{\delta} - \mu(\nabla\mathbf{v} + (\nabla\mathbf{v})^T) \quad (2.28)$$

where $P\boldsymbol{\delta}$ is an isotropic pressure and μ is the viscosity of the fluid. When the isotropic pressure and the effect of gravity are combined into a dynamic pressure p , the conservation of momentum equation (2.25) can be combined with (2.27) and (2.28) and reduces to the Navier-Stokes equation[19].

$$\rho \frac{\partial \mathbf{v}}{\partial t} + \rho(\mathbf{v} \cdot \nabla \mathbf{v}) = -\nabla p + \mu \nabla^2 \mathbf{v} \quad (2.29)$$

The Navier-Stokes equation is the classic form for the conservation of momentum and is an adequate description for many applications. Non-Newtonian behavior requires the derivation of constitutive equations to provide a form for $\boldsymbol{\sigma}$. For example, the derivation of macroscale averaged stresses $\langle \boldsymbol{\sigma} \rangle$ for solid-liquid suspensions in averaged transport theory[20] involves fluctuations about the average of the continuum equation, as discussed in the Averaged Transport Theory section of this Chapter.

Non-dimensionalization of the Navier-Stokes equation gives rise to a dimensionless group, the Reynolds number Re , which is a measure of inertial to viscous forces.

$$Re = \frac{\rho a^2 \langle \dot{\gamma} \rangle}{\mu} \quad (2.30)$$

where ρ and μ are the fluid density and viscosity respectively, a is the characteristic length, and $\langle \dot{\gamma} \rangle$ is the average shear rate. In the context of colloidal suspensions, the proper characteristic length is based upon the particle radius a . It can then be noted that the inertial forces will generally be smaller in comparison to the viscous forces. At these low Re , inertial terms may be neglected and the mass and momentum equations simplify to what are called the Stokes equations[19, 1].

$$\nabla \cdot \mathbf{v} = 0 \quad (2.31)$$

$$\nabla p = \mu \nabla^2 \mathbf{v} \quad (2.32)$$

Where $\mathbf{v}$ is the velocity field, p is the pressure field. The most useful properties of these equations are that they are linear and reversible in time. Therefore, simple solutions may be superimposed to model more complex conditions.

Colloidal Suspension Transport Theory

When considering the conservation equations in the context of multi-phase colloidal particle suspension flow, the question arises about the effect that the presence of the particles has on the flow field and what impact this has on the effective bulk

properties of the suspension such as viscosity. Again the microscopic scale structure of the particles and how they respond to the imposition of an external field is related to macroscopically measurable quantities, in direct analogy to development of the macroscale continuum equation from microscale molecular statistical mechanics. The suspension is essentially a two-phase system consisting of larger colloidal particles suspended in a fluid continuum of small molecules. In the realm of true microfluidics, where the fluid channel dimension is on the order of the colloidal particle size, discrete particle effects become significant and the treatment of the suspension as an effective fluid medium is no longer valid. However, for the flow systems considered here, it is assumed that the classical laws of mass, momentum, and energy apply to the suspension considered as an effective medium. When considering the effect of the sphere on the velocity and pressure fields as propagated through the fluid; *i.e.* the hydrodynamics of the system, it is necessary to solve the equations of motion. In opposition to the assumption of hard sphere “billiard balls” in the derivation of the Boltzmann equation, particles in a fluid affect each other through long range hydrodynamic interactions, where the influence of one particle on another is propagated through the suspending fluid[21]. The solution for the velocity field must account for these interactions.

Averaged Transport Theory

Two-phase flows can be studied in the context of averaged transport theory. The hydrodynamic conservation equations, which as we have seen are averaged quantities already, are averaged again at a scale large relative to the fluid molecules and individual colloidal particles but small relative to the overall system size. This averaging process

introduces additional stress terms that take the form of Reynolds stresses as in turbulent flow[19]. These extra stress terms take into account the additional impact of the presence of the particles. Individual conservation equations for both the solid particle phase and the suspending fluid phase can be developed and assuming no phase changes, the averaged equations for mass, momentum and energy respectively become[22-24]

$$\frac{\partial \alpha_k \bar{\rho}_k^x}{\partial t} + \nabla \cdot \alpha_k \bar{\rho}_k^x \bar{v}_k^{xp} = 0 \quad (2.33)$$

$$\frac{\partial \alpha_k \bar{\rho}_k^x \bar{v}_k^{xp}}{\partial t} + \nabla \cdot \alpha_k \bar{\rho}_k^x \bar{v}_k^{xp} \bar{v}_k^{xp} = \nabla \cdot \alpha_k (\bar{T}_k^x + T_k^{\text{Re}}) + \alpha_k \bar{\rho}_k g + M_k \quad (2.34)$$

$$\begin{aligned} & \frac{\partial}{\partial t} \alpha_k \bar{\rho}_k^x [\bar{u}_k^{xp} + \frac{1}{2} (\bar{v}_k^{xp})^2 + u_k^{\text{Re}}] + \nabla \cdot \alpha_k \bar{\rho}_k^x \bar{v}_k^{xp} [\bar{u}_k^{xp} + \frac{1}{2} (\bar{v}_k^{xp})^2 + u_k^{\text{Re}}] \\ & = \nabla \cdot \alpha_k [(\bar{T}_k^x + T_k^{\text{Re}}) \cdot \bar{v}_k^{xp} - \bar{q}_k^x - q_k^{\text{Re}}] + \alpha_k \bar{\rho}_k (r_k + g \bar{v}_k^{xp}) + E_k + W_k \end{aligned} \quad (2.35)$$

For (2.33)-(2.35) in terms of phase k (solid particle or suspending liquid), α_k is the volume fraction, $\bar{\rho}_k^x$ and $\bar{v}_k^{xp}$ are the averaged density and velocity, $\bar{T}_k^x$ and T_k^{Re} are the average stress and Reynolds stress, M_k is the interfacial force density, v_{ki}^m and v_{ki}^e are the interfacial velocities, $\bar{u}_k^{xp}$ and u_k^{Re} are the internal energy density and fluctuation kinetic energy, $\bar{q}_k^x$ and q_k^{Re} are the average heat flux and Reynolds energy flux, E_k is the interfacial energy flux, W_k is the interfacial work, and u_{ki} is the interfacial internal energy. The additional stress and interfacial terms are due to the random component of the particle velocity, the velocity fluctuations. At this point, a parallel can be drawn with the derivation of the Boltzmann equation via statistical mechanics arguments in that gas molecules have a pressure due to velocity fluctuations from collisions that change their

trajectories, while in a colloidal suspension the pressure arises due to collisions and hydrodynamic interactions causing fluctuations to the colloidal particle velocity. The form of the additional stresses and the interfacial force must be represented by constitutive equations that account for the effects of the particle velocity fluctuations. A familiar and often used method to get forms for these constitutive equations is by returning again to a simple solution, which can then be built up to apply to more complex systems. In one approach, Drew has used the specific method of solving the equations of motion for flow around a single sphere and then averaging the solutions to obtain constitutive equations for the force on the dispersed phase, the average stress, the Reynolds stress, and the interfacial pressure[24]. In addition, a conservation of kinetic energy, or temperature, equation was derived, using a similar procedure to what Boltzmann used in deriving the conservation of energy, where the velocity fluctuation is multiplied by the conservation of energy equation.

$$\alpha_d \rho_d \left(\frac{\partial u_d^{\text{Re}}}{\partial t} + v_d^{\text{xp}} \cdot \nabla u_d^{\text{Re}} \right) - \alpha_d T_d^{\text{Re}} : \nabla \bar{v}_d^{\text{xp}} = -\nabla \cdot \alpha_d (q_d^K + q_d^T) + W_d \quad (2.36)$$

The parameter definitions here are the same, but d refers for the dispersed or particle phase. Temperature is the quantity of choice for characterizing velocity fluctuations and the concept is used not only in colloidal systems, but also granular systems.

There are many approaches, particularly for modeling concentrated colloidal suspensions[25] and for calculations from numerical simulations[21] and this is an open area of research. Any connections to these models will be indicated in the following discussion.

Accounting for the particle velocity fluctuations due to hydrodynamic interactions by including additional stress terms in the equations of motion is one way of analyzing colloidal particle suspensions. An alternative method utilizes the convenient linear form of the Stokes equations and the applicability of the creeping flow assumption to many colloidal systems.

Stokeslets Model

The impact of the presence of particles on the velocity field can be modeled via the Stokeslet model, based on a Green's function for the Stokes equation, where the particle is considered a point force using the Dirac delta function δ . At distances far from the particle, the impact of a point force on the velocity field is the same as the force for a discrete sized particle. This is a “far field” approximation. The Stokes equation with the inclusion of the point force in the x-direction is

$$\nabla p = \mu \nabla^2 \mathbf{v} + \delta(\mathbf{x}) \mathbf{f} \quad (2.37).$$

The Dirac delta function has some special relationships to the Fourier Transform, which may be utilized to solve this equation. As a reminder, the Fourier relationships between a function $f(\mathbf{x})$ and its reciprocal function $\hat{f}(\mathbf{k})$ are

$$f(\mathbf{x}) = \frac{1}{2\pi} \iiint \hat{f}(\mathbf{k}) e^{i\mathbf{k} \cdot \mathbf{x}} d\mathbf{k} \quad (2.38)$$

$$\hat{f}(\mathbf{k}) = \iiint f(\mathbf{x}) e^{-i\mathbf{k} \cdot \mathbf{x}} d\mathbf{x} \quad (2.39).$$

The Stokes equations, both the conservation of mass for an incompressible fluid (2.31) and (2.37), can be transformed into the reciprocal Fourier domain and become,

$$\mathbf{k} \cdot \mathbf{v}_k = 0 \quad (2.40)$$

$$-\mu k^2 \mathbf{v}_k + i \mathbf{k} p_k = -\mathbf{f} \quad (2.41)$$

where $k^2 = \mathbf{k} \cdot \mathbf{k}$. Taking the dot product of (2.41) with $\mathbf{k}$, (2.41) becomes

$$-\mu k^2 \mathbf{k} \cdot \mathbf{v}_k = -i \mathbf{k} \cdot \mathbf{k} p_k - \mathbf{k} \cdot \mathbf{f} \quad (2.42).$$

From (2.40) the left hand side of (2.42) is zero and it is then possible to solve (2.42) for the reciprocal pressure field p_k algebraically.

$$p_k = \frac{\mathbf{k} \cdot \mathbf{f}}{i k^2} \quad (2.43)$$

Substitution of (2.43) into (2.42) yields

$$\mathbf{v}_k = \frac{1}{\mu k^2} \left(\mathbf{f} - \frac{(\mathbf{k} \cdot \mathbf{f}) \mathbf{k}}{k^2} \right) \quad (2.44).$$

Fourier transforming (2.44) back into the real domain gives a velocity distribution of

$$\mathbf{v}(\mathbf{x}) = \mathbf{I} \cdot \mathbf{f} \quad (2.45)$$

where $\mathbf{I}$ is the Oseen tensor.

$$\mathbf{I} = \frac{1}{8\pi\mu x} \left(\boldsymbol{\delta} - \frac{\mathbf{x} \cdot \mathbf{x}}{x^2} \right) \quad (2.46)$$

In reality, there is never a single isolated sphere, but the linearity of the Stokes equations can be used to generalize the velocity distribution due to n particles as a summation. For example, in the case of spherical particles of radius a moving through

an unbounded fluid, the velocity of particle i is the sum of the steady state velocity

$\mathbf{v}_0 = F\rho / 6\pi\mu a$ for a single particle and the velocity due to the presence of n particles[26].

$$\mathbf{v}_i = \mathbf{v}_0 + a\mathbf{v}_0 \cdot \sum_{j \neq i}^n \mathbf{I}(\mathbf{x}_i - \mathbf{x}_j) \quad (2.47)$$

The summation of $\mathbf{I}(\mathbf{x}_i - \mathbf{x}_j)$ models the impact that particle j has on the velocity of particle i .

The two body problem, considered dominant in dilute suspensions, can be analyzed using the tools of the Stokeslet model and since the analytical solution does not indicate irreversibility due to these interactions[27, 26], particles should not cross a streamline after collision with only one other particle.

Another useful and interesting application of the point force model is in the derivation of Faxen's Laws. Using (2.45) again as the solution for the Stokes equations for the velocity field accounting for the particle as a point force, equating the velocity $\mathbf{v}(\mathbf{x})$ to the velocity at the surface of the sphere $\mathbf{V}$, which is a combination of the translational and rotational velocity of the sphere $\mathbf{V} = \mathbf{V}_0 + \boldsymbol{\Omega} \times (\mathbf{x} - \mathbf{x}_0)$, integrating over the surface of the sphere, and finally expanding about the sphere center gives

$$\mathbf{F} = 6\pi\mu a[(\mathbf{v}_\infty + \frac{1}{6}a^2\nabla^2\mathbf{v}_\infty)_0 - \mathbf{V}_0] \quad (2.48).$$

This equation applies again only in the creeping flow regime. Faxen's first law then allows derivation of the Stokes drag on a particle. Stokes drag is traditionally derived by solving the Stokes equations, calculating the stress tensor and integrating over the sphere

surface, a complicated endeavor. However, using Faxen's first law, it can be obtained by merely setting $\mathbf{V}_0$ or $\mathbf{v}_\infty = 0$ [1].

$$\mathbf{F} = 6\pi\mu a \mathbf{V}_0 \quad (2.49)$$

Faxen's second law is again derived from the solution to the Stokes equation for an isolated sphere represented as a point force. The form for the torque $\mathbf{L}$ on the sphere is

$$\mathbf{L} = 8\pi\mu a^3 \left[\frac{1}{2} (\nabla \times \mathbf{v}_\infty)_0 - \boldsymbol{\Omega} \right] \quad (2.50).$$

The stresslet $\mathbf{S}$ on the sphere is

$$\mathbf{S} = \frac{10}{3} \pi\mu a^3 \left(1 + \frac{1}{10} a^2 \nabla^2 \right) (\nabla \mathbf{v}_\infty + (\nabla \mathbf{v}_\infty)^T) \quad (2.51).$$

When (2.51) is examined in the case of a suspension of freely suspended spheres undergoing simple shear, it can be used to derive the bulk stress and ultimately leads to the Einstein relation for the effective viscosity of a dilute colloidal suspension[1].

$$\eta = \mu \left(1 + \frac{5}{2} \phi \right) \quad (2.52)$$

Computer simulations often lend insight into dynamics of colloidal suspensions. Stokesian Dynamics Simulations[21, 2, 14, 28-30] use an evolution equation for the suspension microstructure by calculating each particle's motion due to interactions with all other particles at discrete timesteps. Simulations utilize the methods of theory, in this case the Langevin equation, the Stokeslets model, the conservation of probability distributions and the definition of transport coefficients as averaged quantities, to model colloidal suspension dynamics.

The suspension dynamics and microstructure are constructed in the form of a N-body Langevin equation, as discussed with respect to Brownian motion theory.

$$m \cdot \frac{d\mathbf{V}}{dt} = \mathbf{F}^H + \mathbf{F}^P + \mathbf{F}^B \quad (2.53)$$

The linearity of the Langevin equation allows forces to be separated with respect to their sources, which is the most amenable approach for computer simulation calculations. $\mathbf{F}^H$ is the hydrodynamic force and is defined as

$$\mathbf{F}^H = -\mathbf{R}_{FU} \cdot (\mathbf{V} - \mathbf{V}_\infty) + \mathbf{R}_{FE} : \mathbf{E}_\infty \quad (2.54)$$

where $\mathbf{V}$ is the particle velocity, $\mathbf{V}_\infty$ is the velocity of the bulk shear flow, and $\mathbf{E}_\infty = (\nabla \mathbf{v} + (\nabla \mathbf{v})^T)$ is the symmetric part of the velocity gradient tensor and $\mathbf{R}_{FU}$ is the resistance matrix, which represents the torque or the hydrodynamic force, on the particle relative to the fluid. In the single particle case, the resistance $\mathbf{R}_{FU}$ is the Stokes drag, (2.49). $\mathbf{R}_{FE}$ is the resistance matrix relative to the external shear field. $\mathbf{F}^P$ can represent any type of interparticle or external force and its form is arbitrary. $\mathbf{F}^B$ is a Brownian force, and is exactly the form of (2.2) and (2.3) with the noise intensity going as $2kT\mathbf{R}_{FU}$.

$$\langle \mathbf{F}^B \rangle = 0 \quad (2.55)$$

$$\langle \mathbf{F}^B(0) \mathbf{F}^B(t) \rangle = 2kT\mathbf{R}_{FU} \delta(t) \quad (2.56)$$

The resistance matrices and their inverse, the mobility matrices, are instrumental in describing the impact on the particles of hydrodynamic interactions. Alternatively, the

evolution equation can be represented in a continuum form through the conservation of a probability distribution function.

$$\frac{dP}{dt} + \nabla \cdot \mathbf{v}P = 0 \quad (2.57)$$

Integrating (2.53) with respect to time twice, or (2.57) with respect to time once both result in an equation which maps the change in particle position. The velocity is

$$\mathbf{v} = \mathbf{V}_\infty + \mathbf{R}_{FU}^{-1} \cdot (\mathbf{R}_{FE} : \mathbf{E}_\infty + \mathbf{F}^P - kT\nabla \ln P) \quad (2.58).$$

The right hand side of the equation is again a combination of the various forces. In order to relate the simulations to macroscopic transport properties such as a sedimentation velocity, diffusion, or a bulk stress, averaged expressions are obtained from many individual runs of the simulation. For example, the long time self-diffusivity D_∞^S , where the particle has wandered far from its starting point, is given by

$$D_\infty^S = \lim_{t \rightarrow \infty} \frac{1}{2} \frac{d}{dt} \langle (x_i - \langle x_i \rangle)^2 \rangle \quad (2.59).$$

With the form of an evolution equation in place, and macroscopic properties defined, the remaining problem is to calculate the resistance matrices. Using the integral solution to the Stokes equations which is valid in the low Re regime and Faxen's laws for particle velocities, a grand mobility matrix is constructed. The force density on the surface of each particle is expanded in series of moments, where the zeroth moment is the total force and the first moment is split into an antisymmetric and symmetric part corresponding to the torque and stresslet respectively. Upon inversion of the grand

mobility matrix into the grand resistance matrix, we have a far field approximation as was used in the Stokeslet model discussed above[21].

Transport Coefficients in terms of Time Correlation Functions

The discussion of computer simulations, as well as the discussion of Brownian motion, has led to an interesting form for the diffusion coefficient based upon particle velocity fluctuations, which are quickly becoming a central theme in the analysis for colloidal suspension dynamics. The origin of transport coefficients represented as dependent on velocity fluctuations has its basis in fluctuation-dissipation theorems, as did derivation of the Einstein relation for diffusion from Brownian Motion theory[15]. At the continuum level, the hydrodynamic equations govern transport phenomena, or the space-time behavior of the set of conserved variables: mass, momentum and energy. The basic assumption is that changes occur slowly enough in the fluid that the system can be considered to be in a local state of thermodynamic equilibrium. Transport coefficients are experimentally accessible quantities that can describe the transport properties of a fluid due to thermal fluctuations within the system, or in response to an external perturbation. In other words, the processes of diffusion, viscous flows and thermal conduction are dissipation phenomena related to the relaxation process of a system after a perturbation from equilibrium, the well-known fluctuation-dissipation theorem. Since the assumption that the fluid is in a local thermodynamic equilibrium is only an approximation, we would expect there to be some deviation from the predictions of the hydrodynamic equations. One method to predict the magnitude of this deviation would be to relate microscale fluid structure and molecular relaxation processes to the

continuum hydrodynamic equations via time and space dependent transport coefficients[16]. Therefore, in the case of shear flow of colloidal suspensions, the particle diffusion would be actually related to the source of the dissipation, which physically are random velocity fluctuations arising from long range hydrodynamic interactions and collisions between particles. Velocity fluctuations are quantified by the velocity correlation functions, which are a measure of how quickly a particle loses memory of its previous position and velocity, or how long particle velocities remain correlated. The relationship between transport coefficients and time-correlation functions can be derived, via a procedure similar to the Chapman-Enskog solution to the Boltzmann equation, to get the Green-Kubo formula[17]. Again using the example of a diffusion coefficient, we have the diffusivity in the long wavelength $q \rightarrow 0$ limit,

$$D_{ii}^*(t) = \int_0^t \langle \mathbf{v}_i(\tau) \mathbf{v}_i(0) \rangle d\tau \quad (2.60).$$

This time-dependent property is most relevant to the MR measurements since it is directly measured.

An overview of the equations of motion and how they may be used to model the impact of colloidal particles on the velocity field has been given, as well as the link between experimentally accessible transport coefficients and microscopic colloidal behavior. However, what are the possible physical particle interactions that occur in these systems? Turning again to simple models, the interaction of a pair of spheres will be analyzed. In fact, for dilute suspensions the assumption is often that two body interactions dominate the fluid response.

Particle Interactions in Dilute Colloidal Suspensions

For dilute suspensions, defined here as the volume fraction regime $\phi < 0.1$, in the limit as Re goes to zero, it is generally assumed that particle interactions occur predominantly between two particles. A two particle interaction can result in the formation of a permanent doublet due to a collision where the spheres touch, a temporary doublet where the spheres orbit around each other or a transitory interaction where the spheres separate[31]. The type and strength of the interparticle forces present dictate which response occurs. The particle trajectories of two equally sized spheres of radius b in a simple shear flow based on Jeffrey orbits extended to apply to doublets where interaction forces are present are given by[31].

$$\frac{dr^*}{dt^*} = A(r^*) \sin^2 \theta \sin 2\phi + \Gamma(r^*) \quad (2.61)$$

$$\frac{d\theta}{dt^*} = \frac{B(r^*)}{4} \sin 2\theta \sin 2\phi \quad (2.62)$$

$$\frac{d\phi}{dt^*} = \frac{1}{2} \{1 + B(r^*) \cos 2\phi\} \quad (2.63)$$

The coordinate system of these equations has its origin at the midpoint between the centers of the spheres, which are the distance r apart. θ and ϕ are the polar coordinates which determine the direction of the line of centers with respect to the polar axis X_1 , the vorticity axis of flow.

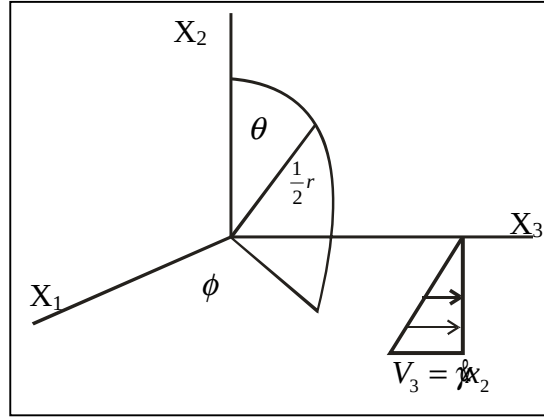


Figure 2.2. Coordinate system for the particle trajectory equations, redrawn from Mazo[16].

The dimensionless distance is $r^* = r/b$, the dimensionless time is $t^* = t\dot{\gamma}$, and $\dot{\gamma}$ is the shear rate. The definition for $A(r^*)$ is

$$A(r^*) = g_1(r^*) / g_2(r^*) \quad (2.64)$$

where

$$g_1(r^*) = \frac{4}{3} \sinh^4 \xi \sum_{n=1}^{\infty} \frac{n(n+1)(2n+1)}{\Delta_n} \quad (2.65)$$

$$g_2(r^*) = \frac{4}{3} \sinh \xi \sum_{n=1}^{\infty} \frac{n(n+1)}{2\Delta_n} \left[\frac{2n+1}{2(2n-1)} e^{2\xi} + \frac{2n+1}{2(2n+3)} e^{-2\xi} + \frac{4e^{-(2n+1)\xi}}{(2n-1)(2n+3)} - 1 \right] \quad (2.66)$$

and

$$\Delta_n = 2 \sinh(2n+1)\xi - (2n+1) \sinh 2\xi \quad (2.67)$$

$$\xi = \cosh^{-1}(r^*/2) \quad (2.68).$$

$B(r^*)$ is defined as

$$B(r^*) = \frac{r_e(r^*)^2 - 1}{r_e(r^*)^2 + 1} \quad (2.69).$$

Forms for $r_e(r^*)$ can be found in [32]. The interaction term $\Gamma(r^*)$ is

$$\Gamma(r^*) = C(r^*) \left[F_{\text{int}}(r) / 3\pi\eta b^2 \right] \quad (2.70)$$

where

$$C(r^*) = 1 / g_2(r^*) \quad (2.71).$$

The viscosity of the suspending fluid is η . When $F_{\text{int}} > 0$, the force is repulsive and $F_{\text{int}} < 0$ means that the force is attractive. Several possibilities exist for the form of the interaction forces. In the case where the force is always attractive, due to opposite charges or van der Waals forces, the spheres when they approach each other will touch and form a primary doublet, the first step in aggregation, or rotate around each other until settling into a stable orbit. If the interaction force is repulsive at all distances, due to an electrostatic or dispersion force, then the spheres will either separate immediately after collision or rotate around each other in increasing orbits, separating slowly. Cases where the force varies with respect to distance leads to a number of possibilities; including touching doublet formation which causes the spheres to rotate as a single rigid body, non-touching doublets where the spheres orbit around each other and simple sphere separation[31].

In the absence of interparticle forces, a two body collision will not result in a net displacement of the particle from its precollisional streamline[31]. These interactions are

therefore considered to be reversible in the limit as $Re \rightarrow 0$, the creeping flow regime where the Stokes equations apply[27], as shown in Figure 2.3.

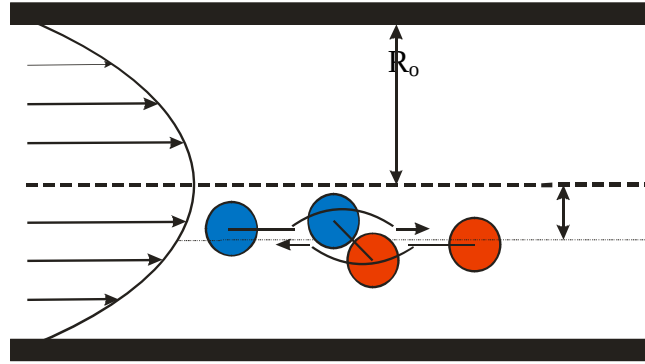


Figure 2.3. A reversible two body particle interaction, redrawn from [33].

Reconciling the reversibility of these particle interactions in dilute suspensions and the inherently irreversible and inevitable diffusion that occurs can be addressed by considering the unavoidable small microscopic forces present in any experimental system or simulation.

Irreversibility in Two Body Interactions

Factors which may cause particles to cross streamlines after a two body collision, which would therefore make the collision irreversible, include surface roughness of the hard sphere[34, 35], the strength of the interparticle interaction force or Brownian forces[36, 37, 14, 29, 30] and their impact on the particle distribution function, a measure of the microstructure of the suspension.

During the process of an interaction between two particles, the separation between them can be less than 10^{-4} of the radius and therefore a very small amount of roughness on the surface of a smooth particle can cause particles to move off their streamlines[34].

The presence of an imperfection on the surface of the particle creates a normal force as the spheres approach each other, but there is no resistance to separation. The spheres are not allowed to come into direct contact and so closed trajectory streamlines, which result in permanent primary doublets of particles, are not accessed in a collision[35]. It would require the presence of either a three particle interaction or Brownian forces to force a particle into the closed trajectory of another particle. Depletion of pairs of particles causes an asymmetry in the pair distribution function. The pair distribution function is a pair-particle conditional probability distribution function normalized by the average particle density. The pair distribution function for purely hydrodynamic interactions as originally calculated by Batchelor and Green[32] was found to be symmetric and independent of type of linear shear flow.

A hard sphere repulsive force has as much of an effect on particle interactions as surface roughness. The hard sphere repulsive force causes fore-aft symmetry of the particle distribution function at large concentrations, indicating that particles do not enter the closed trajectories of other particles to form permanent doublets without a three body interaction. There is a hard sphere “envelope” where an interaction between two spheres would result is a normal stress and therefore particle migration and irreversibility[38].

In addition, particles may move off their streamlines due to Brownian forces. With the application of a shear field, Brownian forces lead to a phenomena called Taylor Dispersion[39-41]. In the case of laminar cylindrical capillary flow, this random component to the motion eventually causes the colloidal particle to sample different velocity streamlines, resulting in an increase in effective diffusion in the flow

direction[39]. In the short time scale $t \ll R^2 / D_{SE}$ where R is the tube radius and D_{SE} is the Stokes-Einstein diffusivity of the colloidal particle $D_{SE} = kT / 6\pi\mu a$, the dispersion is time dependent and can be represented as a power series expansion based on the eigenfunction solution of the Fokker-Plank equation for the Taylor Dispersion problem.

$$D(t)^* = D_{SE} + \frac{1}{6}v^2t + \frac{4}{3}D_{SE}v^2 / R^2t^2 + \dots \quad (2.72)$$

In the long time limit, or Taylor-Aris limit $t \gg R^2 / D_{SE}$, the effective dispersion coefficient asymptotes to the Taylor dispersion coefficient.

$$D^* = D_{SE} + v^2R^2 / 48D_{SE} \quad (2.73)$$

This effect occurs on a timescale corresponding to the longer length scale of the tube radius, instead of the particle radius.

Irreversibility and Chaos

Neglecting the inertial term in the Navier-Stokes equation at low Reynolds numbers to get the Stokes equations eliminates nonlinearity in the governing conservation of momentum equation, resulting in a reversible dynamical system. To consider the concept of reversibility, it is helpful to consider the classic case demonstrated by Taylor in [41] where a drop of dye is inserted into a fluid undergoing low Reynolds number flow in a capillary. Essentially, the drop of dye would spread out due to velocity gradients associated with shear. If the flow were reversed after a certain amount of time, the dye molecules would return to their original position in the given time, with a slight blurring due to Brownian diffusion. However, in the case of colloidal

particles in suspension, the colloidal particles are not on the order of the size of the fluid particles, but are larger, introducing inter-phase interactions. These long range hydrodynamic interactions strongly influence the fluid dynamics and the effects are nonlinear for more than two particle interactions[26], leading to the possibility of irreversibility in even slowly sheared dispersions. The question is then how do reversible equations give rise to irreversible behavior? To answer this question, transport phenomena can be considered in light of the chaotic properties of reversible dynamical systems.

The definition of chaos is an extreme sensitivity to initial conditions[17]. In dynamical systems theory, the measure of chaos is a positive Lyapunov exponent λ . The Lyapunov exponent is calculated by considering an initial state in phase space, tracking the particle trajectories evolution in time and then perturbing the system by adding a random displacement. The particle trajectories are tracked again in the same manner and the differences in the particle positions after the perturbation are a measure whether or not chaotic behavior is present in the system.

Since chaotic behavior is defined by sensitivity to initial conditions, a Lyapunov exponent exists for each particle configuration. To obtain a single value, λ is ensemble averaged over many initial conditions, or equivalently, by a time average. The positive λ is therefore representative of an exponential separation of particle trajectories, indicating chaos. A distinct parallel can be drawn to the Green-Kubo representation of the diffusion coefficient[17]. Velocity correlation functions describe velocity fluctuations, which compose the stochastic components of motion and the correlation between particles,

while Lyapunov exponents are a different measure of correlation between particle velocities and memory loss, just measured by noting changes in particle trajectories.

Chaotic behavior, or a sensitivity of the final particle trajectory to initial conditions, has been noted in the modeling of the three body interaction problem via the Stokeslets model[26] and Stokesian Dynamics simulations[9]. It has been shown that typically two particles form a loose couple, while the third, since a doublet moves faster than a single particle, lags behind[26]. Which particle is left out and how long it takes for the structure to settle in is not determined and depends upon initial particle positions and velocities. In concentrated suspensions, time reversibility fails beyond a certain deformation threshold and chaotic dynamics become significant[9].

Shear-Induced Particle Migration

Irreversibility of a particle interaction is a symptom of particles crossing streamlines. Shear-induced migration to a certain spatial location in capillary flow is a specific result of irreversibility. In this particular geometry, where the shear rate varies, a normal stress is generated during a particle interaction, which then causes a deterministic migration of particles and irreversibility.

In flows where a varying shear rate is present, such as capillary flow, particles in suspension will preferentially migrate to a specific location in the shear field, even in the low Reynolds number regime where inertial forces are negligible. This phenomena was initially postulated to be a balance between particles moving from regions of high to low shear due to more collisions occurring from the high shear side and particles moving down a concentration gradient, a “diffusive flux” model[42]. In this case, a diffusion

equation is solved in conjunction with the continuity and momentum equations for the whole suspension. The difficulty with this model is that at zero shear rate, *i.e.* the center of a cylindrical capillary, the diffusive flux is zero and no migration should occur.

Alternatively, a “suspension balance” model was developed[29]. In this model, the microstructure established by particle migration was thought to maintain a constant particle pressure. Therefore, in regions of low shear, a higher particle concentration is needed in order to balance the flux of particles. It is the random fluctuations in particle velocity, caused by hydrodynamic interactions, which induce a particle pressure. The “suspension temperature” is a measure of these fluctuations and so the governing conservation equation is developed in terms of temperature. This model is more suitable in concentrated suspensions where the non-hydrodynamic forces are dominant, but breaks down at dilute concentrations due to the averaging process used to derive it[38]. It is when the symmetry of a particle interaction is broken, whether by surface roughness or interparticle forces, that normal forces are generated[35]. These effects are present in concentrated suspensions[38, 43, 2] and should still lead to positive normal stress differences in dilute suspensions.

MAGNETIC RESONANCE MICROSCOPY

Magnetic Resonance (MR) Microscopy is a non-invasive technique with which magnetic properties, spectral information, spatial information, displacement and diffusion may be encoded. Several nuclei properties make MR techniques possible, including their spin angular momentum and therefore the magnetic moment arising from this spin. The physics behind this technique is fundamentally rooted in quantum mechanics, but due to the large number of nuclei involved when performing MR microscopy experiments, the particles' behavior becomes continuous. This is called ensemble behavior, which allows most MR phenomena to be explained with a semi-classical approach. The basic topics covered below, as well as extensive expansions on these topics, can be found in references [44],[3],[45, 46], and [47], to name only a few.

Basic Concepts of MR Microscopy

According to quantum mechanics, nuclei possess an electric charge and an intrinsic spin angular momentum. Due to this spin, a magnetic dipole moment is present in the nuclei. This means that nuclei, in the presence of a magnetic field, will act like tiny magnets and align with the field. The unit I , the angular momentum quantum number or spin quantum number, characterizes the nucleus in its ground state and quantifies spin into integer and half integer values. Nuclei possess $2I+1$ energy levels in which the spins can reside. For example, protons and C^{13} atoms have a spin $\frac{1}{2}$, and therefore 2 possible energy levels where spins can be found. Deuteron has an I of 1 and 3 energy levels. Protons are what we will be concerned with here. At thermal equilibrium,

which energy level the spins fall into can be represented by a mathematical probability called the Boltzmann Distribution[45].

$$\frac{N_-}{N_+} = \exp(-\Delta E / kT) = \exp(-\gamma \hbar B_o / kT) \quad (3.1)$$

where N_- and N_+ are the populations of spins in the lower and higher energy states, ΔE is the change in energy between these states, k is the Boltzmann constant, T is temperature, $\hbar$ is Planck's constant, B_o is the static magnetic field and γ is the gyromagnetic ratio (the constant of proportionality between the magnetic moment and angular momentum of a nuclei).

Behavior of Nuclei in a Static Magnetic Field

From a quantum mechanical point of view, the interaction between the nucleus' magnetic moment and a static magnetic field B_o creates an important effect called the Zeeman Interaction. The Hamiltonian, or energy, operator for B_o oriented with the z-axis is

$$H = -\gamma \hbar I_z B_o \quad (3.2).$$

Values of I_z are the eigenvalues of I going from $-I$ to I , and for a spin $\frac{1}{2}$ proton give rise to a constant energy separation between levels of $\gamma \hbar I_z B_o$. Due to the Zeeman interaction, the difference in energy between levels is always the same. Another important effect can be described with the Schrodinger equation. When the above Hamiltonian operator is constant with time, this equation is solved and gives rise to an evolution operator.

$$U(t) = \exp(-i\mathcal{H}_z B_o t) \quad (3.3)$$

When considering a free spin state of Ψ , this equation is showing a clockwise rotation of the state about the z-axis and at an angle of $\gamma B_0 t$. Basically, the presence of the magnetic field causes all states to precess about the field at a specific frequency called the Larmor frequency.

$$\omega_0 = \gamma B_0 \quad (3.4)$$

This precession behavior can also be easily described using a classical approach. The nuclei in a magnetic field experience a torque, the force over a lever arm.

$$\mathbf{T} = \boldsymbol{\mu} \times \mathbf{B}_0 \quad (3.5)$$

where $\boldsymbol{\mu}$ is the magnetic moment

$$\boldsymbol{\mu} = \gamma \hbar \mathbf{I} \quad (3.6)$$

and $\mathbf{B}_0$ the imposed field. Also,

$$\mathbf{T} = d\mathbf{J} / dt \quad (3.7)$$

where $\mathbf{J}$ is angular momentum. This indicates that angular momentum changes with time. With this motion only the direction changes, not the magnitude. Therefore, it is shown that spins placed in a magnetic field precess about $\mathbf{B}_0$ at the Larmor frequency ω_0 .

Net Magnetization and the Rotating Frame of Reference

Generally, the nuclei's magnetic moments are oriented randomly in space. In the presence of a magnetic field B_0 , however, they want to align with the field. For the example of spin $\frac{1}{2}$ protons, there are two allowable energy levels. One level corresponds

to being parallel to B_o and one is anti-parallel. According to the Boltzmann Distribution, slightly more spins will occupy the lower, or parallel, energy level. This alignment creates a slight net magnetization in the direction of B_o , say the z-direction, called M_z . There is no magnetization in the transverse plane, perpendicular to B_o , because there is no phase coherence between spins. The magnetization is also precessing about the z-axis and this makes the concept very difficult to conceptualize and work with on a daily basis and so the concept of the rotating frame is put into use. The frame is said to be rotating at the Larmor frequency, or the frequency at which the spins are precessing, and therefore within the rotating frame, the net magnetization will look stationary. It is comparable to a person throwing a ball into the air. The earth is actually turning at a certain speed, but when viewed by a person also traveling at that speed, the ball appears to be moving straight into the air. The rotating frame of reference allows the use of a vector model when analyzing the evolution of the magnetization.

Excitation

In MR techniques, spins are excited from their equilibrium state by adding energy in the form of a radio frequency (rf) pulse which induces a magnetic field B_1 perpendicular to the main field. Rf pulses are used because their frequency is of the order of the spins natural Larmor frequency. To show how spins are excited, it is useful to describe the ensemble of spin in terms of the spin magnetization vector $\mathbf{M}$. When the torque is related to the time rate of change of the angular momentum

$$d\mathbf{J} / dt = \mathbf{M} \times \mathbf{B} \quad (3.8)$$

and $\mathbf{J}$ is $\hbar\mathbf{I}$, then

$$d\mathbf{M} / dt = \gamma\mathbf{M} \times \mathbf{B} \quad (3.9).$$

If a magnetic field B_o is applied along the z -axis, the solution to this equation is

$$M_x(t) = M_x(0) \cos(\gamma B_o t) + M_y(0) \sin(\gamma B_o t) \quad (3.10)$$

$$M_y(t) = M_y(0) \cos(\gamma B_o t) + M_x(0) \sin(\gamma B_o t) \quad (3.11)$$

$$M_z(t) = M_z(0) \quad (3.12).$$

This shows that M_z is not varying with time, but is precessing about B_o at the Larmor frequency. If a second field oscillating at ω_o is applied in the $z = 0$ plane, the magnetization can be rotated about the second field. B_1 can be represented by the equation below.

$$\mathbf{B}_1(t) = B_1 \cos(\omega_o t) \mathbf{i} - B_1 \sin(\omega_o t) \mathbf{j} \quad (3.13)$$

Where $\mathbf{i}$, $\mathbf{k}$, and $\mathbf{j}$ are unit vectors along the x , y and z axes. With respect to B_o and B_1 , equation (3.7) yields

$$dM_x / dt = \gamma[M_y B_o + M_z B_1 \sin(\omega_o t)] \quad (3.14)$$

$$dM_y / dt = \gamma[M_z B_1 \cos(\omega_o t) + M_x B_o] \quad (3.15)$$

$$dM_z / dt = \gamma[-M_x B_1 \sin(\omega_o t) + M_y B_1 \cos(\omega_o t)] \quad (3.16).$$

Under the initial condition $\mathbf{M}(t) = M_o \mathbf{k}$,

$$M_x = M_o \sin(\omega_1 t) \sin(\omega_o t) \quad (3.17)$$

$$M_y = M_o \sin(\omega_1 t) \cos(\omega_o t) \quad (3.18)$$

$$M_z = M_o \sin(\omega_1 t) \quad (3.19)$$

Where

$$\omega_1 = \gamma B_1 \quad (3.20)$$

indicating that $\mathbf{M}$ precesses about B_o at ω_o and about B_1 at ω_1 . In the rotating frame, it appears to precess only about B_1 . The application of a radiofrequency, or rf, pulse of duration t will rotate the angle of the magnetization by $\omega_1 t$ about the direction of B_1 . In effect, the spins are flipped into the transverse plane. In this manner, a net magnetization in the rotating frame is created.

Relaxation

When an rf pulse with a strength chosen to flip the spins 90° is applied, the spins are equally divided between the two energy levels and the magnetization in the z -direction is zero. Due to the natural energy exchange between the spins and the surrounding thermal reservoir, the spins gradually return to their equilibrium state and recover M_z , a process called spin-lattice, or longitudinal, relaxation. A simple first order rate law description of this process is given mathematically by

$$dM_z / dt = -(M_z - M_o) / T_1 \quad (3.21)$$

where M_o is the magnetization directed along B_o at equilibrium. The solution of this equation is

$$M_z(t) = M_z(0) \exp(-t/T_1) + M_o(1 - \exp(t/T_1)) \quad (3.22)$$

where T_1 is the spin-lattice relaxation time.

Another form of relaxation occurs in the transverse plane. The energy exchange between spins makes the initial coherent magnetization in the y -direction disperse due to dephasing. This process is spin-spin, or transverse, relaxation and is characterized by the first order rate law equation

$$dM_{x,y}/dt = -M_{x,y}/T_2 \quad (3.23).$$

The solution is

$$M_{x,y}(t) = M_{x,y}(0) \exp(-t/T_2) \quad (3.24)$$

where T_2 is the spin-spin relaxation time. Some indirect energy exchange with the lattice contributes to this time, but other direct interactions are largely responsible. Since transverse magnetization corresponds to a state of phase coherence between the nuclear spin states, transverse relaxation is sensitive to interactions that cause the spins to dephase. In other words, as can be seen from equations (3.13)-(3.15), M_z is effected only by components of the magnetization in the x - y plane, while M_x and M_y are additionally influenced by the z component. Due to these effects, $T_2 \leq T_1$.

A description of $\mathbf{M}$ may now be written with relaxation taken into account.

$$dM_x/dt = \gamma M_y(B_o - \omega/\gamma) - M_x/T_2 \quad (3.25)$$

$$dM_y/dt = \gamma M_z B_1 - \gamma M_x(B_o - \omega/\gamma) - M_y/T_2 \quad (3.26)$$

$$dM_z / dt = \gamma M_y B_1 - (M_x - M_o) / T_1 \quad (3.27)$$

where ω is the frequency of the rotating frame. These are the Bloch equations[44].

Signal Detection and Transformation

The semi-classical model is best for explaining this phenomenon. When the magnetization is present in the longitudinal direction, no signal is detected due to the dominance of $\mathbf{B}_0$. Once it moves into the transverse plane, however, the magnetization due to the spins precession can induce a signal in the tuned coil. A changing magnetic field induces a current in a wire and therefore an electromagnetic field (emf) that reflects the behavior of the transverse magnetization is induced in the tuned coil. The receiver mixes the signal emf with a reference rf oscillator[45]. The method is intrinsically phase sensitive and when the two signals are 90° out of phase with each other the output signals become effectively M_x and M_y . The signals are best represented by complex numbers where M_x and M_y are real and imaginary components respectively. When added, they produce a magnitude signal that decays due to spin-spin relaxation. The Free Induction Decay, or FID, has an amplitude proportional to the magnetization and therefore the number of spins.

The FID is a combination of all the different frequencies that are present in the sample. Often it is convenient to break down the FID into its individual frequencies. In other words, the time domain information must be transformed into the frequency domain through the Fourier Transform (FT). When a single frequency is present due to a single type of spin and there is no relaxation occurring, the FT of the signal would be a delta

function of frequency ω_0 . Both real and imaginary parts of the signal must be collected in order for the FT to differentiate between positive and negative frequencies. When relaxation is taken into account, the lineshape is essentially the convolution of the delta function and a Lorentzian, or the FT of an exponential, which results in a Lorentzian. The lineshape then has a full width half maximum $1/\pi T_2$.

Magnetic Field Inhomogeneity

It is inevitable that some variation in the applied magnetic field B_0 will occur and this can lead to a broadening of the spectral line. In other words, inhomogeneities of any sort; whether from a varying B_0 or due to susceptibilities, chemical environments or electric shielding; can cause the FID to decay at a faster rate than with only T_2 effects. The apparent relaxation time is then called T_2^* . It is important to note, however, that the coherence loss due to magnetic field inhomogeneities can be refocused with the correct pulse sequences. In addition, spectrometers come equipped with several small adjustable capacitance “shim” coils oriented in various directions within them. With each new sample, the capacitance and therefore the coils’ contribution to the net magnetic field can be adjusted to achieve a more homogeneous field across the sample.

Dipolar Interactions

Nuclei’s magnetic dipoles also exert influences on each other. The magnetic field associated with a dipole moment will act on the dipole moments of remote spins. The Hamiltonian associated with the interaction of two dipoles is[3]

$$H_D = [(\mu_i \mu_k) / r_{jk}^3 - 3(\mu_i r_{jk})(\mu_k r_{jk}) / r_{jk}^5] \quad (3.28)$$

where μ is again the magnetic moment.

For non-viscous liquids, where the molecular tumbling motion is faster than the dipolar interaction strength, the dipolar Hamiltonian is negligible. It has been noted however [48],[49], [50] that in samples with a high concentration of MR active nuclei, a combination of effects from a distant dipolar field (DDF) and an effect called radiation damping (RD) can generate chaotic evolution of magnetization which may effect even the most simple of MR imaging applications. Radiation damping essentially is a feedback mechanism where the FID in the receiver coil induces a small deviation in magnetization in the sample, which in turn is reflected back in to the receiver coil, affecting the data collected. “Crusher” gradients are often used to dephase any lingering magnetization from this effect, but when additional perturbations to the magnetic field are present due to residual dipolar couplings in solution, or the distant dipolar field, longitudinal magnetization recurrence can be triggered and amplified. With the push towards high resolution and therefore higher imaging gradients, this reappearance of residual magnetization has become more prominent.

Chemical Shift

The electron clouds surrounding nuclei in condensed matter interact with the nuclei’s spin angular momentum, causing a magnetic shielding. Magnetic shielding arises when the electron orbitals are slightly altered by the applied magnetic field and is dependent upon the local electronic environment of the nuclei, essentially giving each nuclei a “chemical fingerprint”[3]. The nuclei precess at different frequencies depending

upon their chemical environment, an effect known as chemical shift. This is the basis for NMR spectroscopy and is an invaluable and common tool for organic chemists. While chemical shift can be exploited for positive use in microscopy and imaging applications, it can also lead to severe distortions or artifacts, if its effects are not taken into account. In the process of reconstructing an image, it is assumed that the Larmor frequency of the spin is directly related to the imposed linear gradient and therefore the spin's position within the sample. Should there be two significantly different Larmor frequencies due to chemical environment contributing to the image, the chemical shift would result in two superimposed images, one for each Larmor frequency present in the sample. Due to T_2 relaxation the infinitely narrow spectral line, which should theoretically exist in the absence of an applied gradient when the Larmor frequency directly corresponds to position, has a finite linewidth. In order to keep a narrow enough linewidth that the impact on the spatial image is less than a pixel, there is a minimum value for the bandwidth and imaging gradient. When chemical shift occurs and there are more than one Larmor frequency contributing to the signal, the imaging gradients or bandwidth must be made larger in order to shrink the linewidth to less than one pixel and therefore avoid artifacts.

Signal Averaging

NMR has a fairly low sensitivity when compared to optical methods. In order to correct this, a number of FIDs are collected and averaged, which in turn enhances the signal-to-noise ratio (SNR). With each successive addition, the signals add coherently and the noise adds randomly thereby improving the SNR by $N_A^{1/2}$, where N_A is the

number of averages. The T_1 relaxation time is a limiting factor, however. In order to retain the entire signal strength, a time delay of several relaxation times must be imposed between averages. The system must be allowed to recover the z-axis magnetization. Should the repetition time exceed these limitations, the image will be T_1 -weighted.

Phase Cycling

With the application of a series of rf pulses that excite the sample, termed the pulse sequence, the evolution of the magnetization becomes very complicated. A useful way of visualizing the effects of the rf pulses is to return to the underlying quantum mechanics and use the concept of coherence transfer pathways. Often there are many possible magnetization trajectories, or coherence pathways, that can occur, but only one returns the desired information. One way to select the desired pathway is to use phase cycling. Phase cycling is the process of systematically varying the relative phases of the rf pulses within the sequence and repeating the pulse sequence until the desired pathway for the signal is selected. For example, background gradient interference can be eliminated from the FID signal by transmitting and collecting signal on the same axis, then shifting both the transmitter and receiver phases by 180° . The desired signal will add together, while the signal from background noise will cancel out. This process of coherent noise cancellation can be written as a phase cycle in the form $(0^\circ, 0^\circ) - (180^\circ, 180^\circ)$. For the first pass of the pulse sequence $(0^\circ, 0^\circ)$ represents the phases of the rf transmitter and rf receiver respectively. For the second pass, the phases are shifted to $(180^\circ, 180^\circ)$. This is the most simplistic example of a phase cycle. Other schemes can be used to correct for phase and amplitude anomalies in quadrature detection, echo artifacts

from pulse amplitude errors and transverse magnetization interference due to rapid pulse repetition. An example of a commonly used sequence is the CYCLOPS sequence[3].

With this, phase and amplitude errors in quadrature detection, primary sources of artifacts in NMR imaging, can be corrected. The four-phase cycle, $(0^\circ, 0^\circ) - (90^\circ, 90^\circ) - (180^\circ, 180^\circ) - (270^\circ, 270^\circ)$, successively switches the channels used to acquire the real and imaginary signals. This is essentially the same thing as shifting the transmitter and receiver by 90° with each pass through the pulse sequence. Also contained within this four-cycle is coherent noise cancellation as described previously.

Spin Echo

An amount of inhomogeneity in the applied magnetic field $\mathbf{B}_0$ is impossible to avoid. This effect will cause spins to precess at slightly different frequencies due to their location within the sample. Following the application of a 90° rf pulse, or a $\pi/2$ pulse, the field differences across the sample ΔB_0 will cause the transverse magnetization to dephase, severely limiting the amount of time signal can be detected and manipulated. Fortunately, this coherence loss can be refocused. At a time τ after the initial $\pi/2$ pulse, a second π pulse is applied which rotates the transverse magnetization about the x-axis and reverses the spin motion. The spins which were dephasing and degrading the transverse magnetization will rephase to recover the magnetization at a time 2τ . The signal detected from this refocusing of the magnetization is called a spin echo, or Hahn echo.

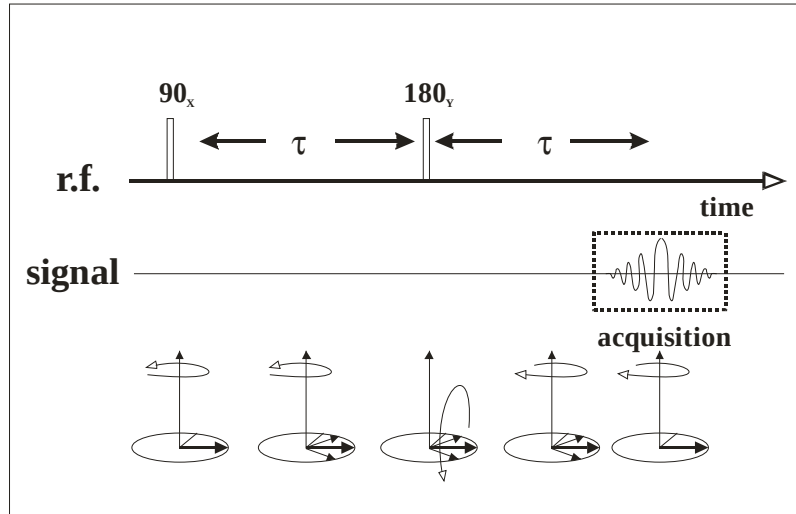


Figure 3.1 A spin echo pulse sequence. The first line outlines the radiofrequency pulses applied and the second line is the echo signal acquired. At the bottom, the evolution of the magnetization is diagramed. With the first 90° rf excitation, the magnetization is flipped into the transverse plane, where it precesses with a certain frequency. Due to unavoidable inhomogeneities in the applied magnetic field, spins in varying spatial locations precess at slightly different frequencies. This, in addition to T_2 relaxation, causes a spreading of the frequencies in the transverse plane over the time τ and a subsequent dephasing of the magnetization. With the application of the 180° rf pulse, the sense of spin precession is reversed, so spins are precessing in the opposite direction. Over the time τ again, the magnetization is refocused as the spins return to their original phase. This is the echo and its decay is a function of T_2 relaxation only.

An echo, therefore, allows more time to sample the signal and has signal decay due only to T_2 relaxation. E. Hahn was the first to recognize the reversibility of spin coherence loss due to inhomogeneous broadening[51]. The use of a Carr-Purcell-Meiboom-Gill echo train, where a series of π pulses are applied which generate a series

of echoes whose envelopes are determined by T_2 decay alone, can supply a T_2 relaxation measurement in a single experiment.

Gradient Echo

Magnetization is dephased in the presence of applied field gradients. By applying another gradient of opposite phase, the signal is refocused into a gradient echo.

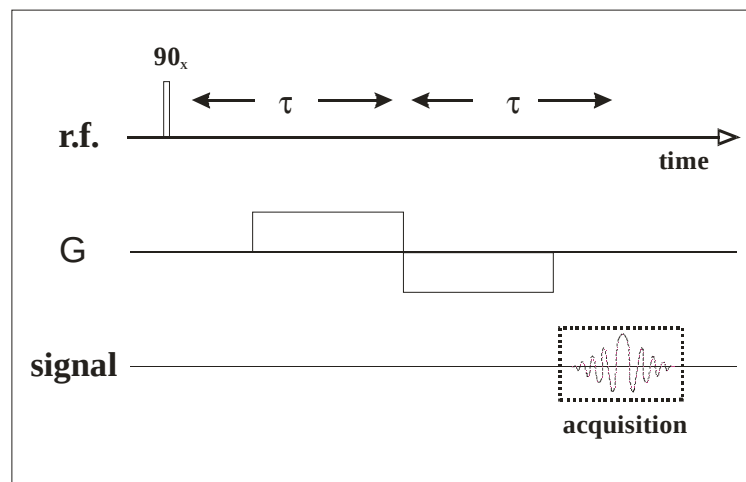


Figure 3.2 A gradient echo pulse sequence. The magnetization is refocused forming an echo which decays as a function of T_2^* .

The application of the magnetic field gradient G causes accelerated dephasing by imposing a range of frequencies across the sample. When another gradient of opposite sign and exact area is applied, the spins are still precessing in the same sense, but the fastest spin is now the slowest. Since the gradients don't actually refocus spins that dephase from inhomogeneities, the signal decay is due to T_2^* , as opposed to just T_2 for the spin echo.

Stimulated Echo

Due to the fact that T_1 is often much longer than T_2 , experiments can be limited by T_2 . Since T_2 relaxation only occurs in the transverse plane, it is sometimes desirable to “store” the transverse magnetization in the longitudinal direction for a time. To store the magnetization, it is flipped another 90° from the transverse plane onto the z-axis at a negative value. During this time, only T_1 relaxation occurs. There is no decay of the transverse magnetization and it can be recalled, or flipped back into the x-y plane at a later time and refocused. This is called a stimulated echo.

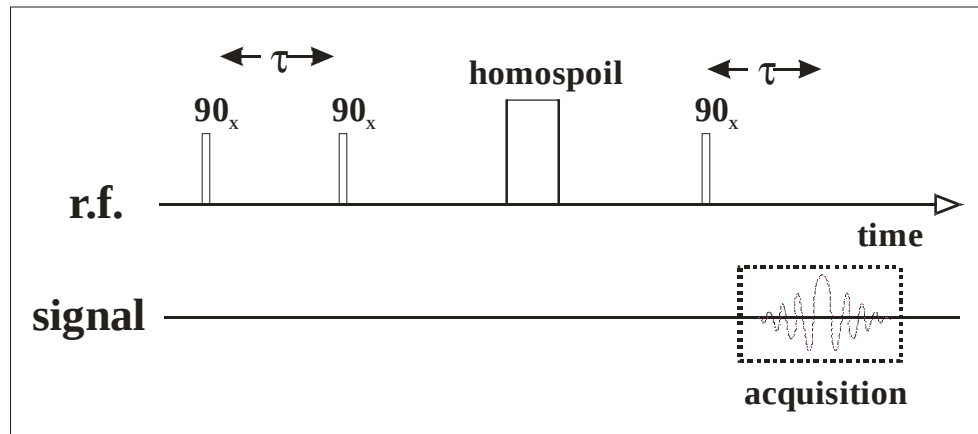


Figure 3.3. Pulse sequence for a stimulated echo. The first line is again the rf pulses. After 90° r.f. excitation pulse, the transverse magnetization is stored on the negative z-axis where T_2 relaxation does not occur by an additional 90° pulse. A third 90° rf pulse returns the magnetization to the transverse plane and an echo is formed. A homospoil gradient is one method of dephasing the undesired magnetization present in the transverse plane from presence of two extra FIDs, one from the second 90° and one from the third, without effecting the magnetization stored along z.

Imaging

Effect of Linear Gradients in a Magnetic Field

The effect that a varying magnetic field has on Larmor frequencies can be deliberately exploited with the use of linear gradients in order to gain spatial information. When a laboratory magnet has been constructed to achieve as homogeneous a static field as possible, a gradient can be applied linearly across the sample to vary the spread of frequencies due to the gradient by a known amount. In this manner, the difference in spin frequencies will be related directly to the spatial location of the spins, a fundamental precept in MR imaging[52]. The local Larmor frequency is then defined as

$$\omega(\mathbf{r}) = \gamma B_0 \mathbf{e}_z + \gamma \mathbf{G} \cdot \mathbf{r} \quad (3.28)$$

where $\mathbf{G}$ may be applied in any direction that spatial encoding is required.

k-Space, Frequency Encoding and Phase Encoding

When looking at the MR signal from the nuclear spins occupying an element of volume dV and at a position $\mathbf{r}$ in the sample, there are $\rho(\mathbf{r})dV$ spins present in the volume element where $\rho(\mathbf{r})$ is the spin density. The signal may then be written as

$$dS(\mathbf{G}, t) = \rho(\mathbf{r})dV \exp[i(\gamma B_0 + \gamma \mathbf{G} \cdot \mathbf{r})t] \quad (3.29).$$

For phase-sensitive detection, a process called heterodyne mixing is utilized. The rf signal is mixed with a reference oscillation that has a frequency of γB_0 , essentially canceling out the contribution of γB_0 in (3.29). This on-resonance condition means that the signal will oscillate at $\gamma \mathbf{G} \cdot \mathbf{r}$ and the integrated amplitude of (3.29) becomes

$$S(t) = \iiint \rho(\mathbf{r}) \exp[i\gamma \mathbf{G} \cdot \mathbf{r}t] d\mathbf{r} \quad (3.30)$$

where the symbol $d\mathbf{r}$ is used to represent volume integration. Introducing the variable $\mathbf{k}$ as follows

$$\mathbf{k} = (2\pi)^{-1} \gamma \mathbf{G}t \quad (3.31)$$

it can be seen that there is a Fourier transformation relationship between the signal and the spin density with $\mathbf{k}$ being interpreted as a reciprocal space vector or the Fourier reciprocal wavenumber. With the advent of Fast Fourier Transforms (FFTs) and computer hardware and software advances, this relationship turns out to be very convenient for data collection and analysis. (3.31) implies that sampling $\mathbf{k}$ is done by varying either the gradient or time, but the direction of the movement is determined by the vector direction of $\mathbf{G}$. We are essentially sampling a dimensional space, k -space, in order to Fourier transform the signal acquired and get the spin density. With this concept of k -space in effect, the signal and the spin density are

$$S(\mathbf{k}) = \iiint \rho(\mathbf{r}) \exp[i2\pi \mathbf{k} \cdot \mathbf{r}] d\mathbf{r} \quad (3.32)$$

and

$$\rho(\mathbf{r}) = \iiint S(\mathbf{k}) \exp[-i2\pi \mathbf{k} \cdot \mathbf{r}] d\mathbf{k} \quad (3.33).$$

Experimentally, for a one dimensional image, k -space is traditionally sampled by collecting N points of MR signal over a time τ_s in the presence of a constant gradient called the read gradient G_{rd} . The distance between points in the frequency domain is then $1/N_s\tau_s$ and the bandwidth of the image is $1/\tau_s$. This is called frequency encoding and

along with the Fourier relationships leads to the fact that $S(\mathbf{k})$ is measured in the time domain and $\rho(\mathbf{r})$ is actually a variable in the frequency domain. Therefore, it can be said that there is a correspondence between real space and frequency, and between the reciprocal space and time.

The process of frequency encoding essentially samples an entire line of k -space in one transverse direction according to

$$\Delta k_{rd} = -\gamma G_{rd} \tau_s \quad (3.34)$$

where the time is the variable changed, yielding a 1-D image. If a 2-D image is desired, a second gradient applied 90° out of phase with the read gradient, called the phase gradient G_{pe} , is applied during the sequence in Fig (3.2). This causes a slight phase shift of the spins in real space, which corresponds to a shift in k -space in the direction of G_{pe} where

$$\Delta k_{pe} = -\gamma(\Delta G_{pe})t_{pe} \quad (3.35).$$

While k -space can be traversed in the phase encoding direction by changing the time increment, to avoid artifacts it is generally the magnitude of the gradient that is varied, a process termed ‘spin warp imaging’. By varying the gradient strengths to get echoes of varying phase shifts, the data can effectively be mapped onto a k -space grid. This is known as phase encoding. Assuming that the read gradient is applied in the x -direction and the phase gradient is applied in the y -direction, this sampling process is shown in Figure 3.4.

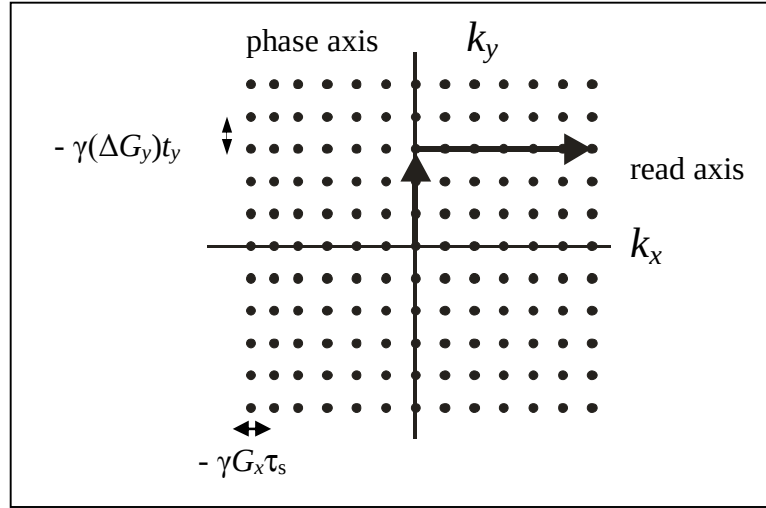


Figure 3.4. Two dimensional data acquisition scheme showing the sampling of k -space using frequency and phase encoding.

The signal is then

$$S(t) \propto \int \int \int \rho(x, y, z) \exp[i(k_x x + k_y y)] dx dy dz \quad (3.36).$$

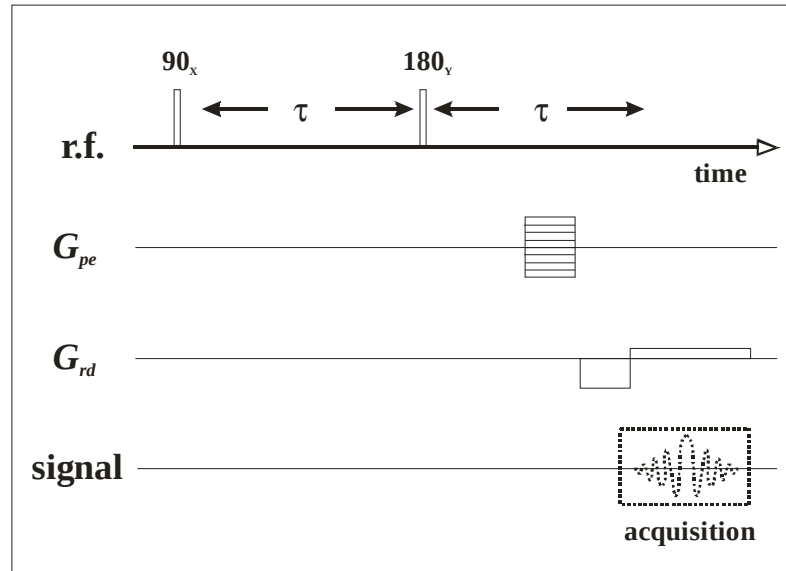


Figure 3.5. Frequency and phase encoding through the application of G_{rd} and G_{pe} are shown in the second and third lines, respectively. The strength of G_{pe} is incremented in order to traverse k -space in the phase direction, while G_{rd} is applied at a constant amplitude and incrementing time.

The pulse sequence has the form shown in Figure 3.5. The collected data must then be Fourier transformed. To produce an image without artifacts, the k -space matrix must be fully sampled, as a single point in k -space affects every point in the reciprocal space of the image. The center of k -space corresponds to the low spatial frequency data, which are the general outlines and overall shape of the image. The high frequency data farther out in k -space sharpens the image by adding fine detail. A missing point of k -space would result in a frequency missing from the image, which affects the quality of the entire image.

There are many other innovative methods of sampling k -space besides frequency encoding, such as the use of two phase gradients instead of one phase and one read gradient. This has the effect of sampling single points in k -space versus whole lines. While much more time consuming, phase encoding has its advantages for certain samples, such as in short T_2 samples or when spectral data at each point in the image is desired. This allows chemical different species within the same sample to be imaged and is called Chemical Shift Imaging (CSI).

Slice Selection

In order to excite only a small section of the sample, which adds a third dimension to our image without needing to phase encode another dimension, an rf pulse whose duration and shape are specified must be applied. In the presence of a linear gradient, where the Larmor frequencies are spread spatially throughout the sample, a selective rf pulse can excite a certain layer of the sample corresponding to a certain frequency. Usually, the rf pulse will excite all spins whose Larmor frequency is near that of the

pulse. A pulse of duration T will excite spins within a frequency deviation from that of the pulse up to $1/T$. The bandwidth resulting from this arises from the width of the pulse. Should a $\pi/2$ pulse be applied, all on-resonance spins will flip 90° into the transverse plane. The spins slightly off-resonance will not experience as sharp of an angle. They are part of an effective field that is tilted in the rotating frame at an angle less than 90° . A selective rf pulse uses rf pulse shape to determine which Larmor frequencies will be excited and the Fourier Transform of this shape establishes the degree of rotation each frequency of spins will experience. A “hard” pulse entails intense broadband, or nonselective, excitation. A “soft” pulse is a weaker, narrowband pulse. A sinc-shaped soft pulse will excite a range of frequencies through 90° and leave the remainder of the sample unexcited. This is due to the fact that the Fourier Transform of the sinc function is a rectangular or Hat function. When applied in concert with a linearly varying magnetic field gradient, which gives a frequency label corresponding to position in the sample, a spatial slice is selected. The response of the spin frequencies should have a rectangular profile and therefore the time domain form of the rf pulse is a sinc function. The range of frequencies excited is determined by the bandwidth of the sinc pulse as

$$\Delta\omega = 4\pi / T \quad (3.38)$$

where T is the duration of the main lobe of the sinc function. The slice location in the sample is determined by the rf carrier frequency, while the gradient direction and strength is what controls the width and orientation of the slice. Due to the application of the gradient, dephasing of the spins occurs. A refocusing gradient must then be applied after the pulse to refocus the spins. When a soft slice selective π pulse is applied, an

additional reverse gradient is not necessary. A π rf pulse is essentially changing the direction of precession and so for half the pulse, the spins are spreading out in frequency in one direction, for the other half of the pulse, they're coming back to their original phase. The π pulse is therefore self refocusing. A typical imaging pulse sequence using frequency and phase encoding and demonstrating slice selection is shown in Figure 3.6.

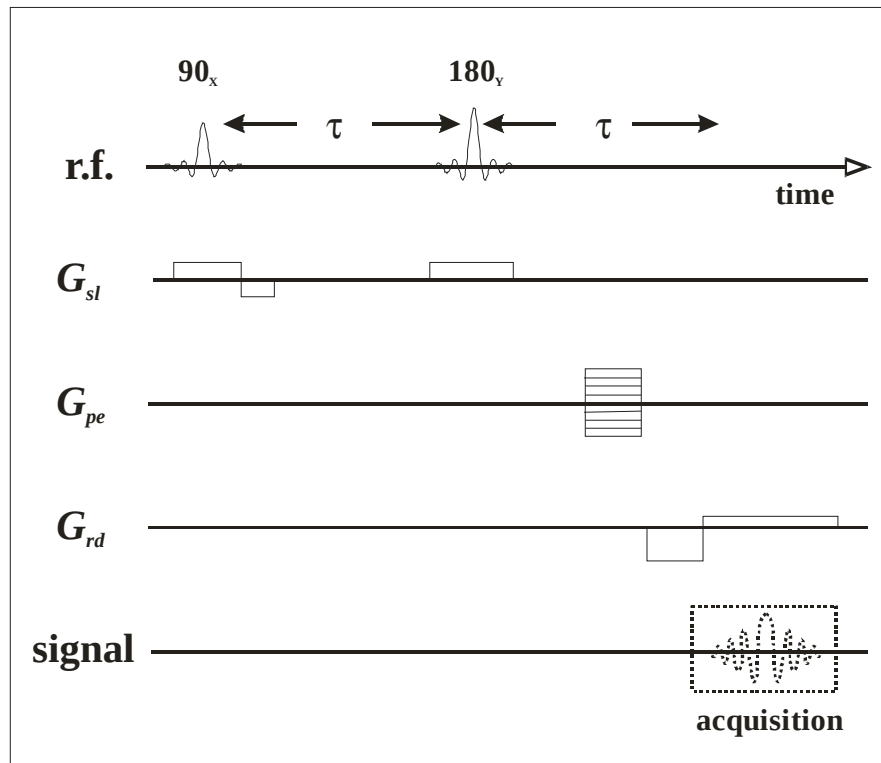


Figure 3.6. A typical imaging pulse sequence. The first line is again the application of radiofrequency pulses with an initial 90° excitation and a refocusing 180° pulse. The sinc shape of the pulses, along with the application of the gradient G_{sl} shown in the second line performs slice selection. The additional gradients G_{pe} and G_{rd} are phase and frequency encoding, respectively.

Translational Motion Effects

Self-Diffusion

In imaging, spins are mapped spatially under the assumption that their Larmor frequency does not change. Essentially, this means that the spins cannot move during imaging. However, in reality, we are generally dealing with liquid molecules and some translation motion is inevitably going to occur due to molecular self-diffusion. As the spins diffuse, their Larmor frequency changes with position, it fluctuates as they move and the effect on the echo is a distribution of residual phase shifts. Self-diffusion causes an intrinsic limit to spatial resolution because of this effect. On the bright side, the fact that the MR signal is modulated due to motion allows the measurement of molecular displacement in the sample.

The Pulsed Gradient Spin Echo Sequence

The pulsed gradient spin echo (PGSE) sequence is a generalized and time efficient method of obtaining translational motion measurements, whether the motion is due to molecular self-diffusion, coherent velocity, or dispersion[53, 3, 39, 4]. PGSE sequences entail the application of rectangular narrow gradient pulses (which according to the narrow pulse approximation are assumed to be short enough that spin translational motion does not occur during the application of the pulses) of amplitude g , duration δ and separation Δ during the dephasing and rephasing portions of the spin echo or stimulated echo sequence. The application of a gradient during the evolution of the magnetization

affects the phase of the signal and so the measured echo signal is the ensemble average of the phase of all the nuclei.

$$E(t) = \langle \exp\{i\phi(t)\} \rangle \quad (3.39)$$

Applying the cumulant expansion where the cumulants are defined as

$$\langle x \rangle_c = \langle x \rangle \quad (3.40)$$

$$\langle x^2 \rangle_c = \langle x^2 \rangle - \langle x \rangle^2 \quad (3.41)$$

$$\langle x^3 \rangle_c = \langle x^3 \rangle - 3\langle x^2 \rangle \langle x \rangle + 2\langle x \rangle^3 \quad (3.42)$$

to determine the average results in,

$$E(t) = \exp\{i\langle \phi(t) \rangle\} \exp\{-\alpha(t)\} \quad (3.43)$$

where for a Gaussian process the higher order cumulants can be expressed in terms of the second order cumulant.

$$\alpha(t) = \frac{1}{2} \langle \phi^2(t) \rangle \quad (3.44)$$

The first exponential in (3.43) is the average and the second exponential refers to the attenuation due to random motions and for a Gaussian is the variance. All higher order terms are neglected since the expansion is truncated at second order for a Gaussian. The signal is therefore phase modulated in the first term by coherent velocity and damped in the second term due to random motion. To understand what effect the phase modulation has on the signal, we note that if a spin has moved in the time period Δ , then

there is a residual phase shift associated with this motion. The phase shift at a time t experienced by spins in the presence of a gradient $\mathbf{g}(t')$ and following a path $\mathbf{r}(t')$ is

$$\phi = \gamma \int_0^t \mathbf{r}(t') \cdot \mathbf{g}(t') dt' \quad (3.45).$$

Taking a Taylor series expansion of $\mathbf{r}(t')$ about $t = 0$

$$\mathbf{r}(t') = \mathbf{r}_0 + \frac{t'}{1!} \frac{d\mathbf{r}}{dt'} \Big|_{t=0} + \frac{t'^2}{2!} \frac{d^2\mathbf{r}}{dt'^2} \Big|_{t=0} + \dots + \frac{t'^n}{n!} \frac{d^n\mathbf{r}}{dt'^n} \Big|_{t=0} \quad (3.46)$$

$$\mathbf{r}(t) = \mathbf{r}_0 + \mathbf{v}t + \frac{1}{2}\mathbf{a}t^2 + H.O.T. \quad (3.47)$$

generates the magnetization phase dependence on position and motion through the temporal moments of the effective gradient in the direction of $\mathbf{g}$.

$$\phi = \gamma_0 \int_0^t g(t') dt' + \gamma_1 \int_0^t g(t') t' dt' + \gamma_2 \int_0^t g(t') t'^2 dt' \quad (3.48)$$

The zeroth moment generates the phase shift due to nuclei position while the first moment generates a phase shift due to velocity.

$$m_0 = \int_0^t g(t') dt' \quad (3.49)$$

$$m_1 = \int_0^t g(t') t' dt' \quad (3.50)$$

It is assumed that the velocity and position are not functions of time, but are stationary components. The moments continue on to higher order n with the second moment generating an acceleration phase shift[3, 5].

$$m_n = \int_0^t g(t') t'^n dt' \quad (3.51)$$

It is therefore possible to design effective gradient patterns which return information about the desired translational motion via selection or nulling of the corresponding temporal moments. The typical PGSE sequence using a single bipolar gradient pair as shown in Figure 3.7 effectively nulls the zeroth moment.

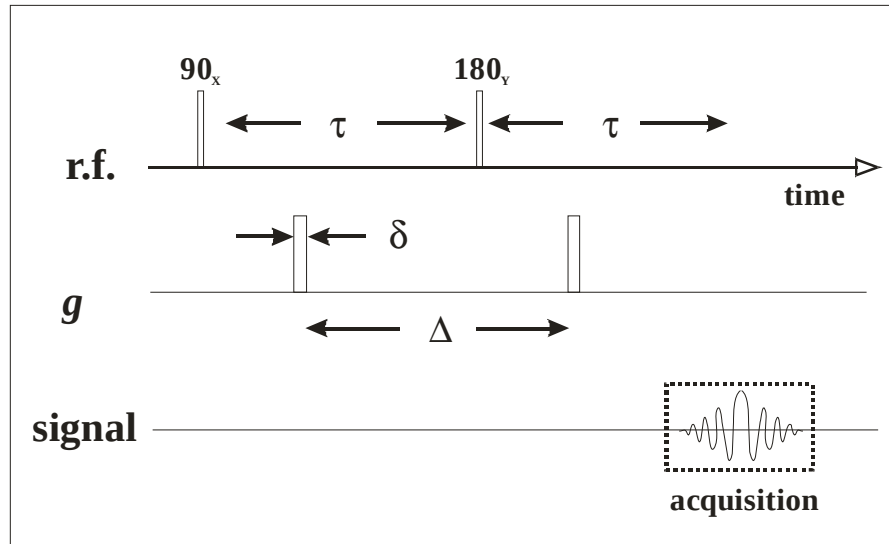


Figure 3.7. A spin echo pulse sequence combined with a pulsed gradient spin echo (PGSE) gradient g pair. The $\pi/2$, or 90° radio frequency (rf) pulse, followed by the π , or 180° rf pulse, with the addition of the PGSE gradient pulse pair, gives a residual phase shift in the echo that provides a record of the displacement of the spins.

The phase shift is then dependent only upon spin movement instead of position. Solving (3.48) for the gradients applied in the pulse sequence shown in Figure 3.7 gives

$$\phi = \gamma g \delta(\mathbf{r} - \mathbf{r}') \quad (3.52)$$

where $\mathbf{r} - \mathbf{r}'$ is the displacement of the spin. Velocity in this case is merely the displacement divided by the observation time Δ .

The Propagator Formalism and q-space

By using the narrow gradient pulse approximation, PGSE data can be analyzed using the propagator formalism. The propagator $P_s(\mathbf{r}|\mathbf{r}', \Delta)$ is actually the conditional probability that a molecule starting at a position $\mathbf{r}$ will move to the position $\mathbf{r}'$ over a time period designated by Δ . The propagator can describe any conditional probability distribution such as for a stationary Markov process like random Brownian motion, where the future state of the system depends only on the present, not the past. For such a case, the propagator is Gaussian[54]. Keeping in mind that the echo signal is an ensemble average of the phase of the nuclei and that the phase under the influence of a PGSE bipolar pair was as in (3.52), the normalized echo attenuation (normalized by the signal amplitude at zero gradient in order to cancel any effects on the signal due to relaxation) for the PGSE experiment can then be written as the phase weighted by the probability of a spin to have moved from point $\mathbf{r}$ to $\mathbf{r}'$,

$$E(\mathbf{q}, \Delta) = \iint \rho(\mathbf{r}) P_s(\mathbf{r}|\mathbf{r}', \Delta) \exp[i2\pi\mathbf{q} \cdot (\mathbf{r} - \mathbf{r}')] d\mathbf{r} d\mathbf{r}' \quad (3.53)$$

where $\rho(\mathbf{r})$ is the usual spin density and $\mathbf{q}$ is a reciprocal space vector represented by $(2\pi)^{-1}\gamma\mathbf{g}\delta$. Defining the average propagator as the time for any molecule to be displaced by $\mathbf{R} = \mathbf{r} - \mathbf{r}'$ over a time Δ as

$$\bar{P}_s(\mathbf{R}, \Delta) = \int \rho(\mathbf{r}) P_s(\mathbf{r}|\mathbf{r}', \Delta) d\mathbf{r} \quad (3.54)$$

the normalized signal is then

$$E(\mathbf{q}, \Delta) = \iint \bar{P}_s(\mathbf{R}, \Delta) \exp[i2\pi\mathbf{q} \cdot \mathbf{R}] d\mathbf{R} \quad (3.55)$$

Equation (3.55) shows a clear Fourier relationship between the PGSE experiment signal and the average propagator, much like that in k -space imaging. However, $\mathbf{q}$ is conjugate to a dynamic displacement $\mathbf{R}$, while $\mathbf{k}$ is conjugate to a position $\mathbf{r}$. They are very similar in that signal is measured in the Fourier reciprocal space of k or q and then transformed. The resolution of a PGSE experiment, unlike traditional k -space imaging which intrinsically is limited to around 10 μm , is limited only by the strength of the gradients. From the average propagator, a distribution of displacements is obtained, which can be converted to a probability of velocity by transformation of variables from (z, Δ) to $(z/\Delta = v)$. The propagator also provides characterization of diffusion and dispersion hydrodynamic dynamics.

The Stejskal-Tanner Relation

The PGSE approach was originally and most commonly used as a means of measuring molecular self-diffusion coefficients in liquids. In the case of free diffusion,

the average propagator has the form of a Gaussian. If only a single q direction, say the z -direction, is considered, the one dimensional form of the Gaussian propagator is

$$\bar{P}_s(Z, \Delta) = (4\pi D\Delta)^{-1/2} \exp(-Z^2 / 4D\Delta) \quad (3.56)$$

and the normalized signal then becomes the classic Stejskal-Tanner relation[55].

$$E(g, \Delta) = \exp[-4\pi^2 q^2 D(\Delta - \delta/3)] \quad (3.57)$$

The narrow pulse approximation assumes δ is small enough with respect to Δ that the $\delta/3$ term in (3.57) can be neglected. However, in practice it is wise to consider retaining this term at longer δ times because the purpose of applying the g gradient pulse is to effectively label the spin position. The longer this pulse is applied, the higher the chance that a spin will have moved while the gradient is on, effectively smearing out the initial position label. The $(\Delta - \delta/3)$ term is therefore an effective displacement observation time that accounts for a finite gradient pulse length. The slope of a semi logarithmic plot of E versus $q^2 \Delta$ then returns the self-diffusion coefficient D .

Regardless of the form of the propagator however, the initial 30% of the echo signal attenuation yields information about the mean squared displacement of the spins[56]. From (3.55) remember that the exponential term, $\exp[i2\pi qZ]$, is simply the average phase shift. Taking a Taylor series expansion and truncating at the second term as in the Gaussian case, the signal attenuation is

$$E \approx 1 - \frac{1}{2} q^2 \langle Z^2 \rangle \quad (3.58)$$

where

$$D^* = \langle Z^2 \rangle / 2\Delta \quad (3.59).$$

Therefore, the diffusion coefficient is returned from the initial attenuation of the echo.

Velocity Imaging

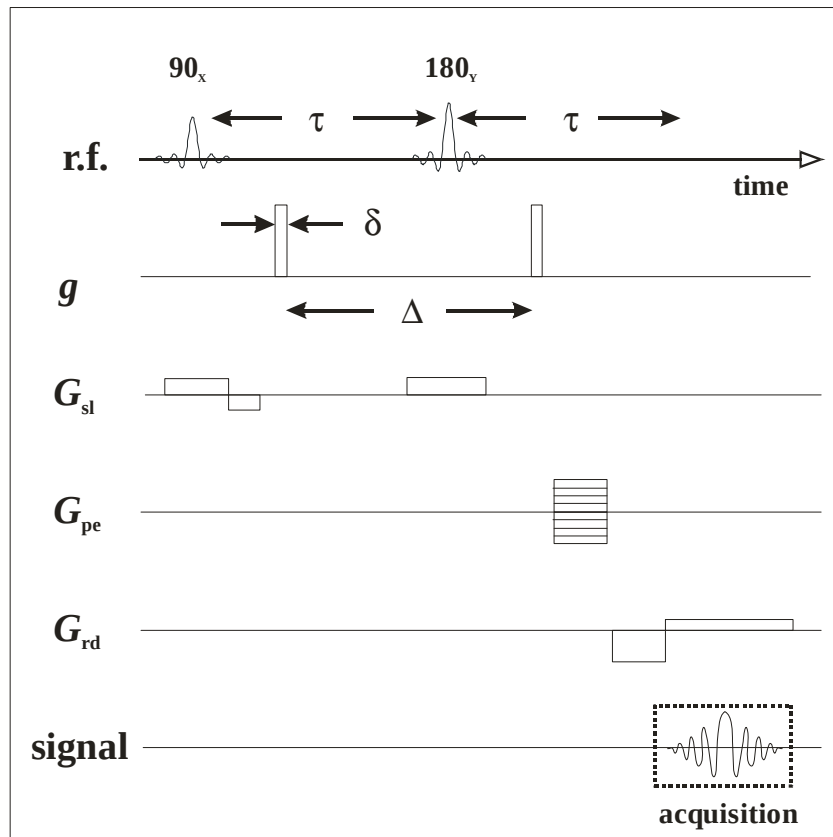


Figure 3.8. A spin echo pulse sequence combined with a pulsed gradient spin echo (PGSE) gradient g pair to give a velocity imaging sequence. The $\pi/2$ rf pulse, followed by the π rf pulse and including three spatial encoding gradients, G_{sl} , G_{pe} , and G_{rd} , applied in orthogonal directions creates a two dimensional image averaged over a slice in the sample. With the addition of the PGSE gradient pulse pair, a residual phase shift provides a record of the displacement of the spins.

In order to measure velocity the phase shift must not depend on position, but on displacement. Nulling the zeroth moment by the application of the bipolar PGSE gradient pair, and overlaying the necessary gradients for imaging, gives a pulse sequence for velocity imaging. Solving for the first moment (3.50) in terms of the motion sensitizing gradient pair of amplitude g , duration δ and separation Δ , the phase shift due to velocity is

$$\phi_v = \gamma g \delta \Delta v \quad (3.60).$$

Equation (3.60) assumes that Δ is small enough that velocity is constant over this time. The phase shift can be calculated from the real and imaginary parts of the quadrature detected signal.

$$\phi_{signal} = \tan^{-1}\left(\frac{\text{Im}}{\text{Re}}\right) \quad (3.61)$$

The rest of the variables are experimentally controlled, so velocity can be calculated. In practice, two experiments are performed using two different gradient values and identical duration times, δ and Δ . The phase shifts at each pixel in the image associated with each of these gradient values are then subtracted from each other providing the velocity in each pixel in the image[5]. Another method to create a velocity map would be to collect a number of q points (ie: 4-8 different gradient strengths) and plot phase ϕ_v versus $\gamma g \delta \Delta$ for each pixel[3]. The slope of this line is therefore the average velocity within the pixel. In order to obtain both diffusion and flow maps from one experiment, dynamic microscopy can be employed[57]. The exact same pulse sequence or imaging sequence would be used, but the entirety of q -space is sampled. Applying imaging gradients $\mathbf{G}$ as

well as the displacement encoding bipolar pair $\mathbf{g}$ causes the normalized signal to be modulated in both k - and q -space.

$$S(\mathbf{k}, \mathbf{q}) = \int \rho(\mathbf{r}) \left[\int \bar{P}_s(\mathbf{R}, \Delta) \exp(i2\pi \mathbf{q} \cdot \mathbf{R}) d\mathbf{R} \right] \times \exp\{i2\pi \mathbf{k} \cdot \mathbf{r}\} d\mathbf{r} \quad (3.62)$$

where $\bar{P}_s(\mathbf{R}, \Delta)$ is the averaged propagator at each pixel of the image. In this case, a map of velocity is obtained by performing a double inverse Fourier Transform. This method is contains more information, including diffusion/dispersion since it essentially measures a full propagator at each pixel in the image, but is also more time consuming.

Flow compensated PGSE

At times, it can be advantageous to cancel out the effects of flow and measure only diffusion, for example, when estimating the effects of Taylor dispersion. A flow compensated PGSE pulse sequence can be utilized to separate coherent motion due to velocity shear from spin displacements due to stochastic dispersion. A flow compensated PGSE sequence encodes for fluctuations in the motion, since phase shifts due to coherent motion are effectively cancelled. Essentially, it's as if the flow were reversed after an observation time Δ and all spins that have moved due to the velocity gradients associated with shear return to their original position in the given time. At this point, only phase shifts corresponding to displacements due to stochastic motion are recorded. This is achieved by the application of one velocity sensitizing bipolar gradient pair followed by another bipolar pair of opposite sign which effectively nulls the zeroth moment corresponding to position as well as the first moment corresponding to velocity.

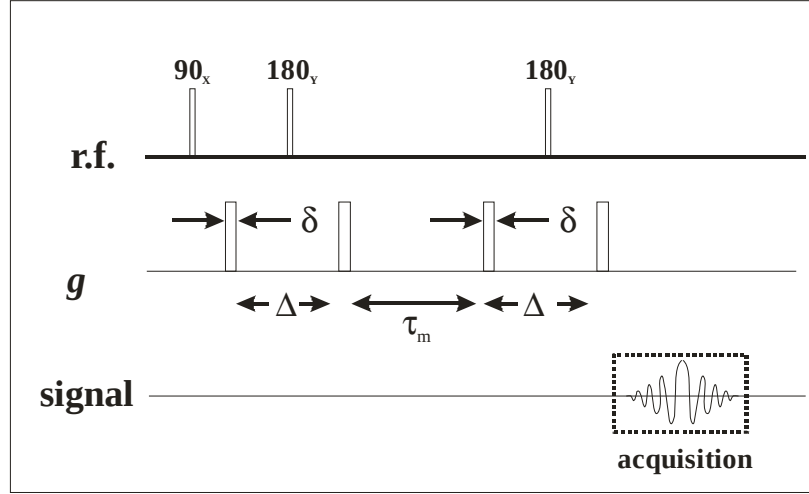


Figure 3.9. The flow compensated pulsed gradient spin echo (PGSE) pulse sequence which cancels coherent motion.

Higher order terms, such as acceleration, are small enough that they can usually be neglected. Therefore, from the PGSE signal as shown in (3.43), the first exponential term goes to 1 and the remaining phase dependence of the signal is purely from incoherent motion.

$$E(t) = \exp(-\alpha(t)) = \exp\left(-\frac{1}{2}\langle\phi^2(t)\rangle\right) \quad (3.63)$$

From the definition of the phase again assuming the pulsed gradients g are applied in the z -direction, the mean squared phase is

$$\langle\phi^2(t)\rangle = \gamma^2 \int_0^t g(t') \int_0^{t'} g(t'') \langle z(t') z(t'') \rangle dt'' dt' - \gamma^2 \left[\int_0^t g(t') \langle z(t') \rangle^2 dt' \right]^2 \quad (3.64).$$

In the case of pure molecular diffusion, $\langle z(t') \rangle$ goes to zero and the second term vanishes, leaving

$$\alpha(t) = -\frac{1}{2} \gamma^2 \int_0^t g(t') \int_0^{t'} g(t'') \langle z(t') z(t'') \rangle dt'' dt' \quad (3.65).$$

From the non-equilibrium Einstein relation, the form in one dimension for the diffusion coefficient can be shown to be[15]

$$D(t) = \frac{\langle z(t)^2 \rangle}{2t} \quad (3.66).$$

Substituting this into (3.65),

$$\alpha(t) = -D \gamma^2 \int_0^t \left(\int_0^{t'} g(t'') dt'' \right)^2 dt' \quad (3.67).$$

Then integrate to get again the classic Stejskal-Tanner result for the echo attenuation, even in the presence of flow.

$$E(g, \Delta) = \exp[-8\pi^2 q^2 D(\Delta - \delta/3)] \quad (3.68)$$

This is exactly the same result given by the single PGSE sequence in the absence of coherent motion, with the exception of a factor of 2 since the magnetization evolves over 2Δ for a double PGSE sequence. For the single PGSE experiment in the absence of flow, the coherent velocity itself is zero, while the double PGSE allows the dynamics on different scales to be separated by nulling the first moment of the gradient.

ADVANCED TOPICS IN MRM

Spectral ResolutionMotivation

A large part of the thesis work was conducted using model “MR-active” latex core-shell colloidal particles. Core-shell particles are micron scale particles which consist of a liquid hexadecane core and a hard outer poly(methylmethacrylate) (PMMA) shell[58]. The use of such particles is advantageous in MR studies since the current system at the Magnetic Resonance Microscopy laboratory at MSU detects signal from only protons, H^1 , in the liquid state. Solids have an extremely short spin-spin relaxation time and so solid state MR has different hardware requirements than for liquids. Most micron-sized model particles are solid and therefore not detectable with the MR equipment and techniques available, especially when it is desired to obtain solid particle phase dynamics in conjunction with the suspending fluid phase. Therefore, conclusions about the transport of the colloidal particles and their complex behavior can often only be drawn from the changes to the suspending medium as measured by MR[59, 60]. By having particles which have a liquid core with a separate chemical signature from the suspending medium (water), the particles themselves can be tracked and differentiated from the fluid flow behavior of the suspending medium[7, 61]. However, a very small fraction of the MRM signal actually arises from the hexadecane core oil due to the small volume fraction of particles in suspension at the dilute concentrations studied here. The overwhelming amount of the MRM signal due to the suspending water creates a broad

peak which, due to the small resonant frequency difference between the two substances, overlaps with the oil peak and causes information about the oil to be lost. Therefore, the excess water signal must be reduced in some way. To achieve the nullification of water signal and therefore achieve spectral resolution, several methods were considered including chemical shift imaging, T_1 Inversion Recovery, and use of a paramagnetic doping agent to decrease the T_1 relaxation time of the water.

Chemical Shift Contrasting

Chemical shift, while often a cause of artifacts in traditional imaging techniques, can be useful when spectral resolution is exploited correctly. There are forms of imaging which deliberately separate the spectral and spatial dimensions in order to select for certain substances within a sample. In traditional imaging, the acquiring of signal in the presence of a read gradient, frequency encoding, samples an entire line of k -space in one acquisition which saves time but also has the effect of eliminating any information about the spectra. Chemical Shift Imaging (CSI), on the other hand, samples the echo signal in the absence of a gradient, termed phase encoding, and essentially creates a fourth dimension of frequency. In this imaging scheme, k -space is sampled one point at a time, which has the negative effect of increasing the experiment time of an $N \times N$ pixel image by a factor of N . Another option would be to use a chemically selective, narrow-band radiofrequency pulse to excite only a specific molecule type to image. Since the major inhibiting factor to obtaining spectral resolution with the colloidal suspension is an overabundance of water signal flooding into the oil peak, neither of these techniques is particularly helpful. In fact, imaging itself was not necessary for attaining useful

information about the dynamics of the suspension. It was decided that PGSE techniques, with the ability to measure motion without compromising spectral resolution or adding to the experiment time, were more suited to this application. The overabundance of water signal was still a problem to be overcome. One possible option to solve this dilemma was to add a large amount of a doping agent, causing the majority of the water to relax during the observation time Δ of the PGSE experiment. This approach, however, severely limited the range of times where motion for both oil and water signal could simultaneously be probed. Therefore, the next simplest appearing technique was Inversion Recovery nulling. In this case, the inherent difference between T_1 recovery times of hexadecane and water was utilized to provide the necessary contrast, theoretically allowing propagators and diffusion coefficients to be measured for each component in the multi-phase system.

Relaxation

In order to properly explain both the Inversion Recovery method and the use of a paramagnetic doping agent in spectral selection of a desired component, it is appropriate to review the process of relaxation itself. Atomic nuclei have a property associated with them known as spin and the spin quantum number I characterizes the nature of the spin. A spin of $I = \frac{1}{2}$ has two energy states and at thermal equilibrium the spins are distributed according to the Boltzmann relation.

$$\frac{N_+}{N_-} = \exp(-\Delta E / kT) \quad (4.1)$$

A slight preference for the lower energy state gives rise to a net magnetization in the direction of the applied field, B_0 . The magnitude of this magnetization is, according to Curie's Law,

$$M_0 = \frac{N\gamma^2\hbar^2 I(I+1)}{3kT} B_0 \quad (4.2).$$

The growth of this magnetization to equilibrium does not happen instantaneously upon application of the applied field B_0 but is a function of time due to the nature of the spins' distribution within energy states and the transitions needed to establish the new distribution. The time required is referred to as spin-lattice relaxation or T_1 and is the time required for the spin system to return to thermal equilibrium after a disturbance[46, 44, 45, 3, 47]. In order for transitions between energy states to occur, there must be a place and a mechanism for the energy to be exchanged. The place is generally called the lattice and is essentially a thermal reservoir made up from the rotations, vibrations and translations of the molecules composing the system. The heat capacity of the spin system is assumed to be small enough that the spin energy does not change the lattice temperature. The mechanism to stimulate these transitions and the resulting energy exchange between the spin and the lattice is the presence of a field which fluctuates in the vicinity of the spin and at its Larmor frequency. In the case of ^1H protons, which have spin $\frac{1}{2}$, the fluctuating field is a magnetic field which interacts with the magnetic dipole moment of the spin. There are several sources of these fields. When the field is only due to the presence of another nuclear dipole moment, it is generally thermal motion which causes the magnetic moments of the protons to appear as fluctuating magnetic fields.

There is a wide range of motional frequencies present in liquids, but the magnitude of the components at the Larmor frequency, two times the Larmor frequency and at zero frequency are important in relaxation mechanisms. When two protons within the same vicinity experience fluctuations of the same frequency energy, transitions are stimulated and relaxation occurs. Relaxation is commonly modeled as an exponential function, $\exp(-t/\tau_c)$, and although this is an often incorrect assumption, the relaxation rate is usually well characterized by the reciprocal of the first order rate constant, or the relaxation time $1/T_1$. The real relaxation process is actually not first order, but much more complicated, and this can lead to non-exponential relaxation processes. Several mechanisms contribute to spin-lattice relaxation due to transitions induced by the interaction of magnetic dipoles, including dipole-dipole interactions, scalar relaxation of the first and second kind, spin rotation, and chemical shift anisotropy[45]. T_1 relaxation therefore gives very useful insight into the nature of the molecular motion present. In the special case that the fluctuating magnetic fields are caused by the presence of an unpaired electron with a large magnetic moment (in comparison to the proton), the larger fields trigger a greater number of transitions and relaxation is enhanced. The addition of such paramagnetic molecules is often used in practice as a means to control relaxation times in order to decrease experiment time or enhance relaxation contrast[3]. An additional type of relaxation is spin-spin relaxation or T_2 . The T_2 relaxation time is the rate of decay of the x-y component of the magnetization, transverse to the applied magnetic field B_0 , that is present after the spin system has been disturbed from equilibrium, or in other words, how long it takes for the spins to come into equilibrium with each other. Relaxation is

both a limitation to the temporal ranges achievable using MRM techniques and a tool for investigating fundamental molecular properties and dynamics.

Mechanisms For Relaxation

The frequency dependence of the power (of the interaction between two spins) is called the spectral density, $J(\omega)$. This is essentially the amount of energy available for energy level transitions at each frequency ω . Random molecular motion of the molecules causes the interaction energy to be distributed in frequency and time[45], since the local magnetic fields change as molecules move in relationship to each other. The local field fluctuations due to this random molecular motion can be represented by a correlation function $G(t)$, where $G(t)$ is a measure of how quickly the local field changes in magnitude and direction. In a truly random process, the correlation function can be represented as an exponential function $\exp(-t/\tau_c)$ where τ_c is the characteristic time between molecular collisions and is called the correlation time. The correlation time is a measure of how long the molecule “remembers” its previous motion. There is a Fourier relationship between spectral density and the correlation function.

$$J(\omega) = \int_{-\infty}^{\infty} G(\tau) \exp^{i\omega\tau} d\tau \quad (4.3)$$

When a parameter is changed, such as temperature, the correlation time varies which in turn changes the distribution of frequencies available for energy exchange. When the $\ln T_1$ is plotted against $1/T$, it can be seen that the T_1 relaxation time goes through a minimum at the point where the spectral density contribution at the Larmor frequency is a maximum, in other words when the most energy is available for exchange[47].

The main mechanism for spin-lattice relaxation in liquid systems of spin $\frac{1}{2}$ is a dipole-dipole interaction, where the presence of another magnetic moment undergoing random motions causes fluctuating local magnetic fields, which induces energy transitions. This effect depends on the strength of the magnetic moments and the inter-molecular separation of two spins on the same molecule due to the rotational motion of the molecule, as well as the intra-molecular separation from translational motion[62]. For the case of an inter-molecular dipole interaction where two nuclear dipoles on the same randomly rotating molecule are at a distance R apart, there are essentially four energy states in which the two spins may reside corresponding to two spins down, two spins up and two mixed states. The spectral densities from the motion of the molecule are:

$$J^{(0)}(\omega) = (24/15R^6)[\tau_c / (1 + \omega^2 \tau_c^2)] \quad (4.4)$$

$$J^{(1)}(\omega) = (1/6)J^{(0)}(\omega) \quad (4.5)$$

$$J^{(2)}(\omega) = (2/3)J^{(0)}(\omega) \quad (4.6)$$

where $J^{(0)}$ corresponds to no net spin flip or transition between energy levels, which can include transitions between the two mixed states since they are essentially of the same energy. $J^{(1)}$ corresponds to a transition where one of the two spins flip and $J^{(2)}$ to when both spins flip.

The relationship between T_1 and T_2 and the spectral densities is derived through time dependent perturbation theory of Bloembergen, Purcell and Pound or by the density matrix[46, 44]. These 2 methods give equivalent results.

$$1/T_1 = (3/2)\gamma^4\hbar^2 I(I+1)[J^{(1)}(\omega) + J^{(2)}(2\omega)] \quad (4.7)$$

$$1/T_2 = \gamma^4\hbar^2 I(I+1)[(3/8)J^{(0)}(0) + (15/4)J^{(1)}(\omega) + (3/8)J^{(2)}(2\omega)] \quad (4.8)$$

Notice that the equation for T_2 or spin-spin relaxation contains an extra term. $J^{(0)}$ represents slower motions, *i.e.* longer correlation times, where the spectral density function is more concentrated at lower frequencies. Therefore, within the range of interest, the Larmor frequency of the spins, it becomes frequency independent. $J^{(1)}$ contributes to relaxation due to fluctuations at the Larmor frequency and $J^{(2)}$ contributes due to fluctuations at twice the Larmor frequency, which correspond to faster correlation times. Therefore, T_2 is dependent upon slow and fast motions, while T_1 is only dependent upon fast motions. The presence of the $J^{(0)}$ term is what causes $T_2 < T_1$, although in liquid systems, the contribution from $J^{(0)}$ is mostly averaged out due to molecular tumbling, causing $T_2 \sim T_1$. The frequency independence of $J^{(0)}$ is also why T_2 does not go through a minimum with increasing temperature as T_1 does. The equations for the spectral densities and their relationship to T_1 and T_2 are slightly different for inter-molecular dipole-dipole interactions, which correspond to translational molecular motion, but contain the same frequency dependencies of the spectral densities.

Several other mechanisms can contribute in certain situations[45, 44, 46, 47].

Scalar relaxation of the first kind occurs when there is scalar coupling between two magnetically different nuclei. As chemical exchange occurs, with a nucleus I jumping in and out of a site that is coupled with nucleus S, the resulting fluctuation in their local magnetic fields can cause relaxation. Nucleus S becomes a mechanism for relaxation of nucleus I when the characteristic time of chemical exchange is shorter than the T_1 of

either molecule. Scalar relaxation of the second kind is different in that relaxation mechanisms not related to the coupling for S end up enhancing the relaxation of I. If S has a short relaxation time, it can be considered at thermal equilibrium with the lattice. Therefore, its perturbations can be thought of as part of the lattice and enhances the relaxation rate of I. Relaxation due to spin rotation arises when small spherical molecules are free to rotate in the absence of other relaxation mechanisms, for example, in gases. This is generally a weak relaxation mechanism that occurs due to the interaction between the spin and molecular magnetic moment which arises from the angular momentum of the rotating molecule. Additionally, the quadrupolar interaction due to an electric quadrupole moment creating a fluctuating electric field induces relaxation. This mechanism is only applicable for spins with $I > 1/2$. Finally, chemical shift anisotropy is another mechanism, but is more important for nuclei with larger chemical shifts, such as fluorine or carbon, not protons.

Inversion Recovery

Inversion Recovery is a method used to directly measure spin-lattice, or T_1 , relaxation times and also to suppress signal from undesired components[3, 62, 63]. In this process, a 180° rf pulse, or π pulse, is applied, thereby disturbing the spins farthest from equilibrium. After a set inversion recovery delay time t_d the spins are flipped into the transverse plane via a 90° rf or $\pi/2$ pulse and the resulting FID signal is collected.

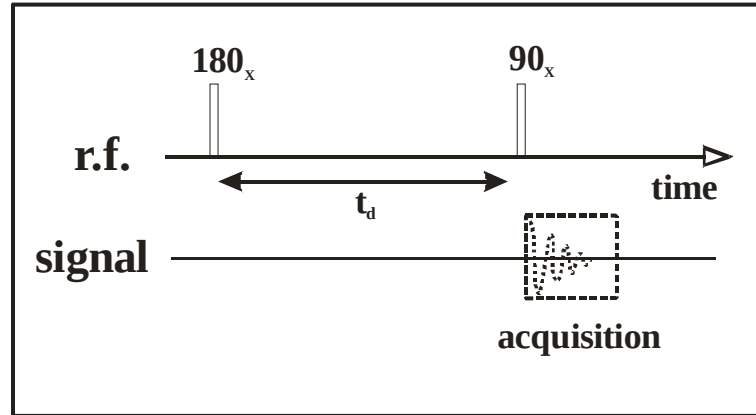


Figure 4.1. Pulse sequence where the first line shows the radiofrequency pulses and the second line is the resulting signal. The 180° rf pulse inverts the spins from their equilibrium position and then the 90° rf pulse returns the magnetization to the transverse plane where signal is collected.

This allows inspection of the evolution of the magnetization back toward equilibrium. If the large applied field B_0 is said to be in the z-direction, the net magnetization amplitude M_0 upon excitation from thermal equilibrium via the 180° rf pulse as a function of time is the solution to Equation (3.22).

$$M_z(t) = M_0[1 - 2\exp(-t/T_1)] \quad (4.28)$$

Over time, relaxation causes the longitudinal magnetization to recover, or return to equilibrium, over a time T_1 which is specific to the material[3, 44, 46]. The amplitude of M_z will cross from the negative z-axis to the positive through zero as shown mathematically in (4.28) and graphically in Figure 4.2. At the point of zero magnetization amplitude, the following relationship exists

$$t_1 = 0.6931T_1 \quad (4.29).$$

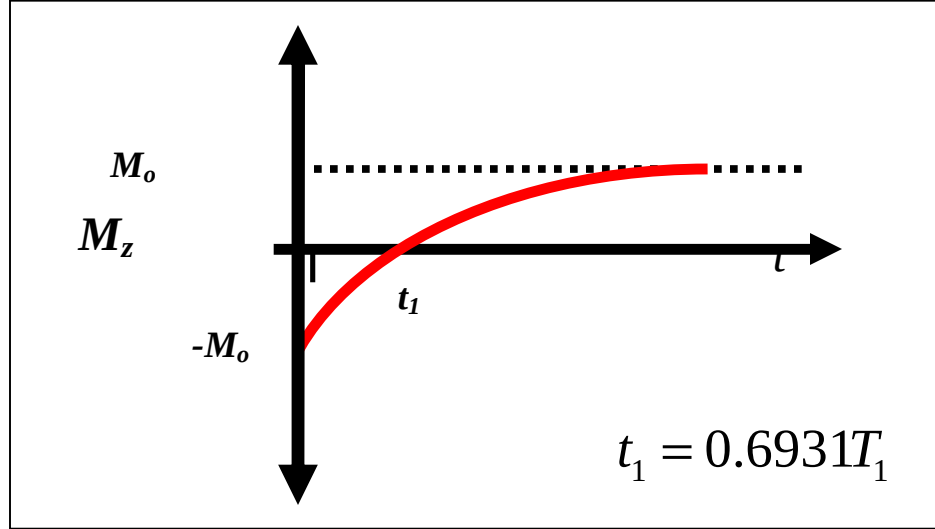


Figure 4.2. Evolution of the magnetization M_z , which is in the direction of the bulk magnetic field B_0 , after a 180° rf pulse

Therefore, by tracking the amplitude of the magnetization as a function of delay time between the 180° rf pulse and the 90° rf pulse and identifying the minimum, a number for the T_1 relaxation time can be calculated. In addition, the difference in relaxation properties between different materials can be exploited to achieve signal suppression. Applying a π pulse and then waiting a time equal to $0.6931T_1$ minimizes the undesired signal component. In order to exploit this property, the spectral resolution of the experiment must be smaller than the frequency difference between the components. Sweep width is the range of frequencies detected during the experiment and is directly proportional to the acquisition time and sampling rates through the Fourier relationship between the time and frequency domains. For example, hexadecane, the oil in the core of the model colloids, is shifted approximately 750 Hz or 3 ppm from the water frequency. Spectral resolution was achieved for these two components by selecting a sweep width, which is the maximum frequency range detectable, of 4960 Hz and sampling 128 points to get 3960 Hz/128 pts $\sim$ 39 Hz/point, well below the 750 Hz resolution required to

differentiate between them. There are other more complicated and effective methods to suppress signal[3, 64], but Inversion Recovery is the simplest. Figure 4.3 is a standard PGSE pulse sequence as discussed in Chapter 3 section 5 with the addition of a 180° inversion recovery rf pulse at the front, where the inversion delay time t_d can be manipulated to select for specific components of signal.

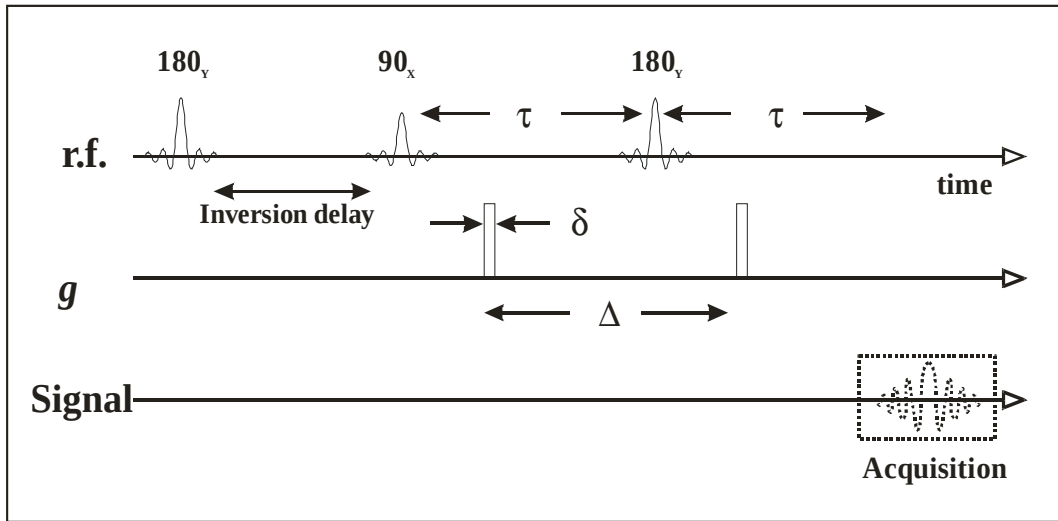


Figure 4.3. PGSE pulse sequence with the addition of a 180° inversion recovery pulse prior to the start of the sequence.

Determination of Suspension T_1 Relaxation Times

A key component in the success of implementing a T_1 Inversion Recovery experiment is proper identification of the relaxation times present in the sample. In the case of dilute ($\phi = 0.04$ and $\phi = 0.08$) colloidal suspensions consisting of core-shell particles of $2.44 \pm 0.32 \mu\text{m}$ diameter suspended in water, the T_1 relaxation time of water is easily characterized and can be altered via the addition of a paramagnetic relaxation enhancing agent. The inversion delay time t_d was selected based upon the recovery time

of the oil. T_1 relaxation is a complicated mechanism, dependent upon energy exchange between the particular molecule and the lattice as discussed in the relaxation section in Chapter 4, section 1 and in [46, 44, 45]. This energy exchange can be affected by things such as magnetic susceptibility gradients or restricted diffusion as is present due to the oil restriction within the hard PMMA shell of the particle[3]. These effects in combination with the low volume fraction of particles in suspension made it impossible to obtain a pure T_1 measurement for the particles. A suspension sample was dried in an attempt to isolate the oil signal, but the lingering presence of trapped water and low signal to noise prohibited quantifying an accurate value for T_1 . An alternate method for obtaining a general value for T_1 , and therefore an optimum inversion delay time, involved merely inverting all spins in the sample via a 180° rf pulse, waiting an increasing range of times, applying the 90° and 180° rf excitation pulses of a standard PGSE sequence and collecting the resulting echo signal as shown in Figure 4.3. While testing, the pulse sequence should be kept as similar as possible to the actual sequence needed to make the desired propagator and diffusion measurements. Therefore, the standard PGSE sequence with the addition of a 180° inversion pulse as in Figure 4.3 is used, but modified so that data is collected at just one value of q and it is the delay time which is incremented between scan acquisitions. By plotting the absolute value of the signal amplitude from both peaks as a function of delay time, a minimum in both the water and the oil signal could be observed, revealing in Figure 4.4 that the oil relaxation time was approximately $450\text{ms}/0.6931 \sim 650\text{ ms}$. For the purpose of the experiments at hand, this method is not only sufficient for determining the optimum delay time necessary to minimize the water

signal, but in some ways preferred as the actual pulse sequence being implemented in the dynamics study is used to determine the minimum.

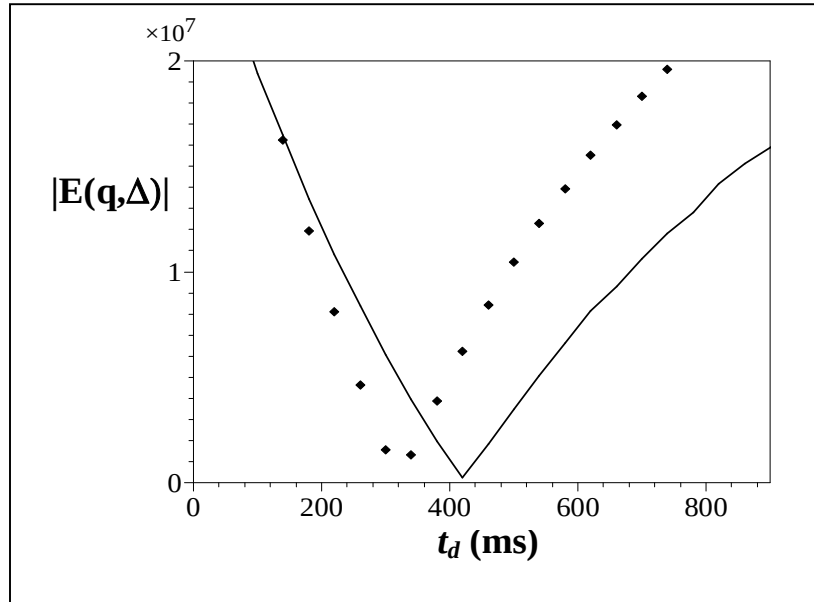


Figure 4.4. The absolute value of the echo signal amplitude as a function of inversion delay time t_d for oil (diamonds) and water (line)

There are several factors beyond experimental spectral resolution influencing how well the oil and water peaks may be resolved. T_1 , and also T_2 spin-spin relaxation, are highly frequency dependent parameters due to the complex mechanisms responsible for relaxation[44, 46]. Due to oil restriction within the hard shell of the particles, some spins recover more slowly or more quickly than average and the resulting range of frequencies present in the sample make it impossible to null all signal at a single inversion delay time. T_1 is not a single value, but due to any small frequency variations across and within the sample is a range, and this must be taken into account when applying the Inversion Recovery sequence. To achieve the most efficient signal

nullification, the spectral linewidth should be as narrow as possible which corresponds to a narrow distribution in T_2 and a long T_2 relaxation time. The homogeneity of the bulk magnetic field B_0 is therefore highly important and care must be taken during the shimming process, where the magnetic field is made as homogeneous as possible. The effect of the range of relaxation times and therefore frequencies can be seen in shape of the spectra after application of an inversion recovery pulse. The spectra for a 4% by volume suspension of core-shell particles with and without T_1 inversion is shown in Figure 4.5.

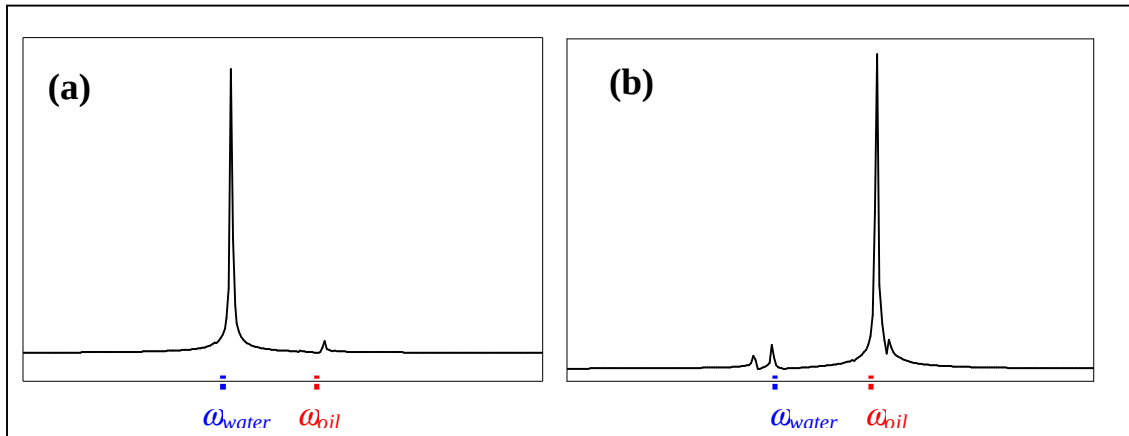


Figure 4.5. (a) Spectra for a 4% by volume core-shell particle suspension showing the frequency difference between the oil and water peaks. (b) Spectra for the same suspension collected when a 180° inversion recovery rf pulse has been applied. Note the absence of the majority of the water signal, but residual signal reflects spins with T_1 and T_2 relaxation times not influenced by the target inversion delay time. The oil signal is unchanged and so the overall signal has been reduced. The y-axis is therefore scaled to allow visibility of the details of the spectra.

From Figure 4.5, it is clear that there is some residual water signal from the frequencies not targeted by the chosen delay time even though the majority of the signal has been nullified.

Due to the intimate relationship between T_1 and T_2 relaxation[44, 46, 45] as discussed in the relaxation section in Chapter 4 section 1, an additional factor impacts the efficiency of signal nullification using the pulse sequence in Figure 4.3. The restriction of the hexadecane within the hard shell of the particle causes not only a distribution of T_1 relaxation times, but of T_2^* as well, including some extremely short times[65]. T_2^* accounts for not only the mechanisms of spin-spin relaxation, but also additional external contributions to relaxation from magnetic field inhomogeneities and susceptibility. At a smaller displacement time Δ of the PGSE experiment and subsequent shorter echo time, there is less dephasing of the transverse magnetization due to T_2^* . This not only gives more signal, but increases the range of frequencies contributing to the signal. The spectral peak therefore is broader, which has the dual effect of giving more leniencies to the choice of delay time, but being less effective in signal cancellation. At longer echo times and Δ , the shorter T_2^* signal dies out, leaving signal with a smaller range of T_1 that may be more cleanly inverted by the 180° rf pulse. Since it is the particles that have the short T_2^* and the particle concentrations studied here are low, the water signal is generally not impacted by many of these factors and nullification is fairly straight forward. In the case of a higher particle concentration, susceptibility effects may shorten the T_2^* of the suspending liquid phase.

An additional experimental complication is the temperature dependence of T_1 . Due to ambient conditions on different days and the transfer of heat through the application of magnetic field gradients, temperatures may vary between experiments or even during experiments. This could cause the optimal delay time to change, impacting the experimental results. The use of a controlled cooling system within the gradient coil mitigates these difficulties by maintaining a set temperature for the gradient coil, which in turn preserves the desired temperature in the radiofrequency coil and sample.

Influence of Flow on the Signal

With the application of a flow field, additional factors become important in making the proper choice of inversion delay time, in addition to the previously discussed need for a minimum amount of water signal. As it turns out, the evolution of the magnetization becomes much more complex with the application of flow to the system. In order to test the sequence, the basic system of water flowing at low Reynolds numbers; *ie*, the laminar flow regime in a 1 mm diameter glass capillary; was used. Water had a much longer relaxation time than the oil, which was advantageous in separating them, but also caused overly long experiment times due to the need for long repetition times. By controlling the relaxation time through the addition of the paramagnetic relaxation enhancing agent Magnevist, the relaxation minimum for water was selected to occur at ~500 ms, a different time than the oil minimum, but also within a reasonable delay time. Magnevist contains gadopentetate dimeglumine and the dipolar interaction between the

electron moment of the metal ion Gd^{3+} and the nuclear magnetic moment of adjacent water molecules causes enhanced relaxation, primarily T_1 relaxation.

Initial testing of the inversion recovery sequence revealed a distinct artifact. The propagator was not the expected hat function[56] due to the equal probability of velocities present in laminar flow in a cylindrical capillary, but was skewed towards either slower or faster velocities. Typical sources for this sort of behavior were systematically eliminated. The phase cycle was selected, as for a typical PGSE sequence, to record only signal from the desired coherence pathway[66] and was found to work properly without the use of the inversion recovery pulse in the sequence. Truncation of the signal during acquisition would lead to a roll across the entire data set in the reciprocal q domain which can have the appearance of a skewed hat function should the frequency of oscillation match up with the displacement range of the propagator and so care was taken to sample to high enough gradient values that the signal was fully into the noise. Finally, inflow/outflow effects were compensated for by making sure the active region was either fully refreshed with new spins flowing in between experimental scans, eliminating any artifacts due to residual effects on the magnetization that the previous scan would have on the spins before they fully recovered or that the spins had fully recovered by relaxation. A long repetition time accomplished both of these measures. None of these measures eliminated the artifact because with the inversion sequence, an additional complication is the delay time between the inversion 180° rf pulse and the excitation 90° pulse. In this time t_d , non-inverted spins can flow into the region that is to be excited and their full signal will dominate the acquired signal from the subsequent

PGSE sequence. In this case, a long TR does not eliminate t_d related inflow artifacts as the intervals are independent.

Propagators were measured at four different delay times using the sequence in Figure 4.3; note that the negative values of velocity only indicate an arbitrary direction of flow along the axis of the large magnetic field B_0 . Notice that the propagators collected after inversion delay times t_1 and t_4 are the expected hat function. However, at t_2 the propagator is skewed towards higher velocities and at t_3 the propagator is skewed towards slower velocities. This is because spins which have been inverted have an 180° phase difference from the spins which have recovered.

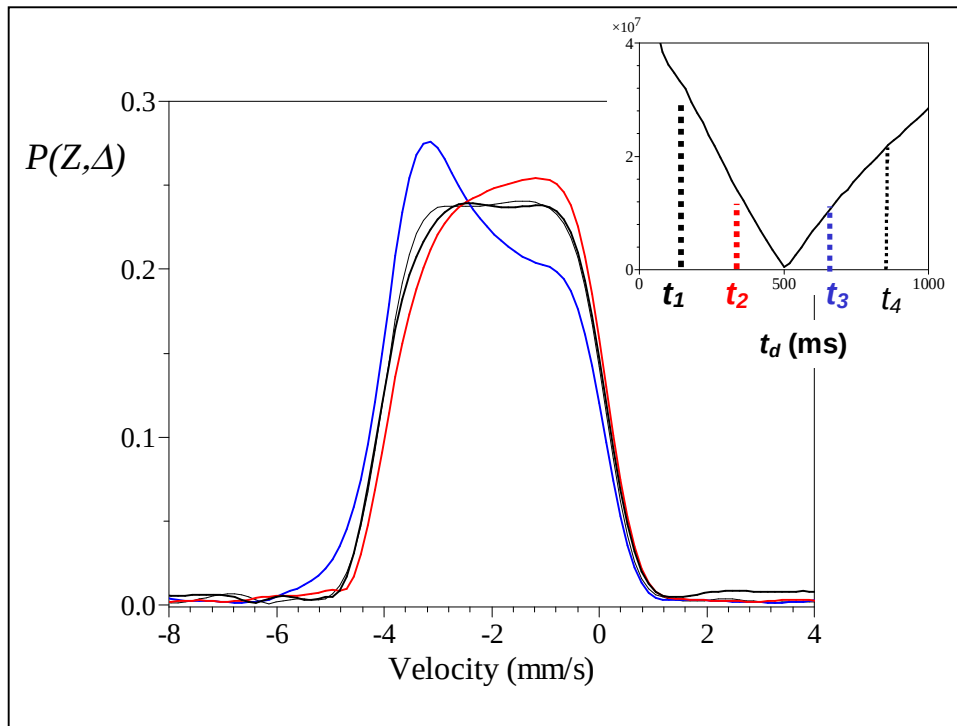


Figure 4.6. Propagators for water flowing in a 1 mm capillary with an average velocity $V_{ave} \sim 2$ mm/s, $\Delta=30$ ms, $TR=4$ sec, $\delta = 2$ ms and $g_{max}=1.738$ T/m, corresponding to the different inversion delay times shown in the insert: $t_1=100$ ms (thick black line) $t_2 = 400$ ms (red line) $t_3 = 575$ ms (blue line) and $t_4 = 2000$ ms (thin black line). The propagators demonstrate the impact of the inflow artifact as related to delay time.

In other words, the magnetization resides in the negative z -axis when it is excited from equilibrium by the 90° rf pulse as opposed to the positive z -axis and therefore the spin's response to subsequent rf pulses is different. At short enough time $t_1 = 100$ ms, the spins have not significantly recovered and not enough time has passed between 180° inversion recovery pulse and the 90° rf excitation pulse for fresh spins to enter the coil. Over the 100 ms t_d , on average the spins have only moved a length $L_{ave} \sim t_d \langle v \rangle \sim 0.088$ mm, making the percentage of inflow spins only 0.5% of the total signal. Even if this contribution were to be calculated using the maximum velocity in the system $L_{max} \sim t_d v_{max}$, the percentage of signal composed of inflow spins is only 1.2%. Therefore the spins are all in phase with each other as they undergo manipulation by the pulse sequence and the propagator is a hat function. In the long time limit, nearly all of the spins have undergone T_1 relaxation and recovered during the delay time $t_4 = 2000$ ms, and so again they are in-phase. In this case, fresh spins flowing into the coil during the delay time t_d contribute nearly 12% of the total signal, as based on the average velocity, and they are also in-phase with recovered spins. Both effects contribute to the propagator as a hat function since all spins confer the same phase. For intermediate delay times however, the phase of the signal is a combination of inverted spins, recovered spins, and inflow spins. Before the minimum $t_2 = 400$ ms, relaxation is occurring, but the majority of the signal is inverted in negative z . There is also some refreshing. Spins which flow into the active region of the coil, weighted mostly by the faster spins at higher velocities that were not in the coil and have not been inverted, are in the positive z -axis at the time of the 90° pulse. The combination of the 2.5% (based on average velocity)- 4.7% (based on maximum

velocity) of the signal that arises from inflow spins and the spins which have recovered during the 400 ms delay time results in a propagator where the phase difference between the inverted and un-inverted spins creates a cancellation of signal at high velocities. At $t_3 = 575$ ms, immediately following the relaxation minimum, more of the inverted spins have recovered than remain in the negative z-axis. In addition, more time has passed allowing the influx of refreshed spins to be greater, approximately 3.4%- 6.7% of the total signal. The combined effect on the propagator is a weighting towards higher velocities which is greater than the weighting towards lower velocities that occurs at t_3 . When using an inversion recovery pulse sequence, it must be noted that phase cycling cannot differentiate between positive and negative axis of the z magnetization[67] and so this effect may not be eliminated by additional phase cycling. Phase cycling differentiates between coherence pathways as they evolve from the application of radiofrequency pulses. In the inversion recovery sequence, whether the magnetization is in the positive or negative z-axis, the z-axis itself has a single quantum coherence state and therefore the pathway for positive z magnetization is the same as for negative z magnetization. Further verification of the flow artifact was observed when hexadecane was pumped through the 1 mm diameter capillary. Figure 4.7 shows the same skewing of the propagator shape was a function of delay time.

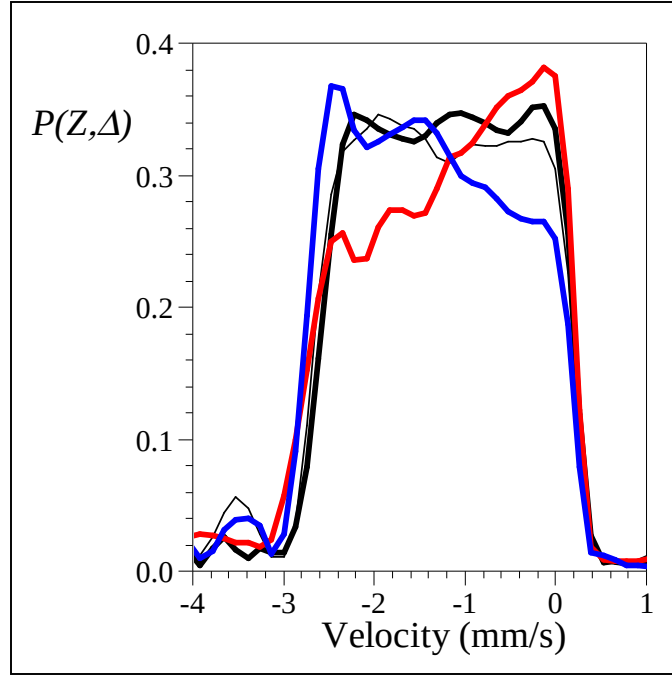


Figure 4.7. Propagators for hexadecane flowing in a 1 mm capillary with an average velocity $V_{ave} \sim 1.5$ mm/s, $\Delta=30$ ms, $TR=4$ sec, $\delta = 2$ ms and $g_{max}=1.738$ T/m, corresponding to the different inversion delay times $t_1 = 100$ ms (thick black line) $t_2 = 350$ ms (red line) $t_3 = 540$ ms (blue line) and $t_4 = 2500$ ms (thin black line). The propagators demonstrate the impact of the inflow artifact as related to delay time.

This sequence must be used very carefully for the study of flow systems. Only delay times much longer or much shorter than the $0.6931T_1$ of the desired signal component should be used. Since the purpose in this particular application was to minimize dominating water signal, the shortest delay time possible should be used in order to minimize water inflow artifacts.

To test the quality of signal separation during the inversion recovery sequence, a phantom was constructed consisting of a 1 mm diameter capillary encased in a larger 5

mm diameter capillary. The smaller capillary was plumbed to allow flow-through, while the larger was filled with water and sealed so as to remain stationary. This system effectively separates the signal into two flow regimes, which creates an additional mode of signal separation. Water signal will only appear centered around zero velocity and its influence on the oil signal due to the broadness of the peak would be easily discerned from the flowing portion of the oil.

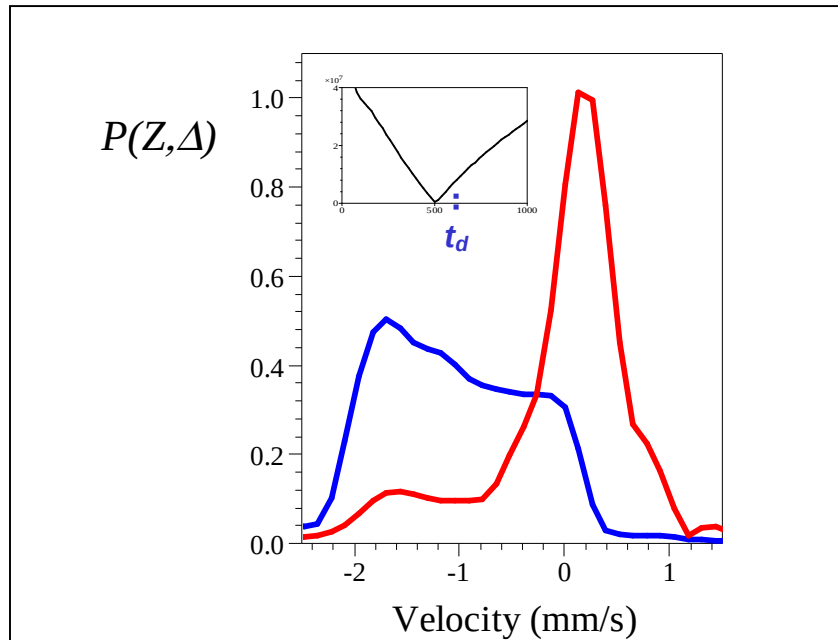


Figure 4.8. Propagators for hexadecane flowing in a 1 mm capillary with an average velocity $V_{ave} \sim 1$ mm/s surrounded by stationary water. The experimental parameters are $\Delta=80$ ms, $TR=4$ sec, $\delta = 2$ ms and $g_{max}= 1.738$ T/m. The blue line is a propagator representing the motion of the flowing oil obtained by spectrally resolved PGSE using the inversion recovery sequence of Figure 4.3. The red line is the same experiment with signal summed over the same frequency range where no inversion recovery pulse is applied. Stationary water signal centered at zero velocity clearly dominates.

In Figure 4.7, the oil propagator reflects the now expected skewing towards faster velocities for the chosen delay time t_d immediately following the inversion minimum. The exact same PGSE experiment run without an 180° inversion pulse applied and where the signal is summed over the same frequency range demonstrates how the stationary water signal contributes to the propagator shape. The absence of a zero velocity peak when the inversion recovery pulse sequence is utilized shows its efficiency in eliminating unwanted signal components.

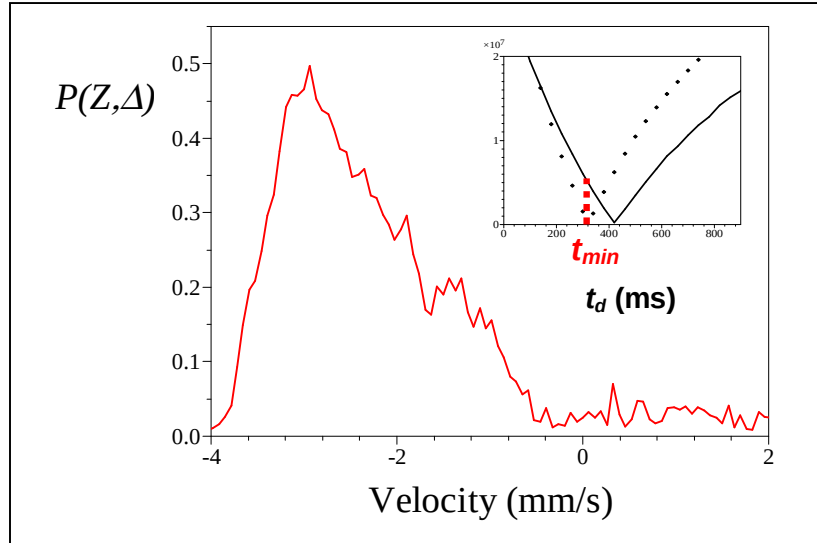


Figure 4.9. Propagator obtained from the oil signal of a 4% by volume core-shell particle suspension flowing in a 1 mm capillary with an average velocity $V_{ave} \sim 2$ mm/s with $\Delta=30$ ms, $TR=4$ sec, $\delta = 2$ ms and $g_{max}= 1.738$ T/m at $t_d = 350$ ms. The propagator is skewed towards higher velocities, in conflict with the expected artifact.

Initial results using the inversion recovery pulse sequence to measure particle dynamics in a dilute ($\phi = 0.04$) model core-shell colloidal suspension revealed a distinct weighting of the particle velocities towards higher velocities, as shown in Figure 4.9.

The inversion delay time for this experiment was selected at the exact minimum for water which was also doped to be just shorter than the minimum for oil. According to Figures 4.6 and 4.7, a propagator measured at this delay time should demonstrate an artifact which skews the propagator towards slower velocities. The exact opposite is seen. This result indicate that there is a higher probability of finding an oil molecules moving at a faster velocity, which could be a result of either shear induced particle migration towards the center of the capillary and faster velocity streamlines, or power law behavior of the suspension[68]. In addition, entrained air present in the sample used to obtain the data in Figure 4.9 could have introduced error in the measurement due to disruption of the suspension microstructure. To further clarify the actual particle dynamics and separate possible transport mechanisms responsible for the propagator shape in Figure 4.9, any experimentally induced artifacts needed to be eliminated. Therefore, the sample preparation procedure was refined to include rigorous degassing of the suspension and additional MRM techniques such as bulk velocity imaging were applied. Most importantly, the inability to avoid flow artifacts using this approach caused it to be abandoned for further study of dilute core-shell colloidal suspensions under flow. The technique is however robust and highly effective in determining the diffusion behavior in multi-component systems where flow is not present, such as for diffusion studies of biofilms[69].

Enhanced T_1 Relaxation

Due to unavoidable flow artifacts present in the application of the Inversion Recovery sequence to this system, the water signal was removed by adding a high

concentration (2.349 ml/ 200 ml 8% by volume core-shell suspension) of the paramagnetic relaxation enhancing agent Magnevist. Due to the hard polymer shell of the core-shell particles, the relaxation time of the oil core is unaffected. This was tested by measuring the signal response immediately following addition of Magnevist, then periodically checking the signal over a several week period. No changes were observed in the core oil signal over this time, indicating that the gadolinium compound was not penetrating the hard polymer shell of the particles. The suspending water T_1 relaxation time was therefore short enough that during the observation time of the experiment Δ , the water signal nearly completely recovered and was no longer visible in the transverse plane where signal is collected. Figure 4.10 shows the difference in the spectra between a non-doped suspension and a highly doped suspension as a function of q . For the undoped suspension, the larger amount of water signal deems the oil signal nearly undetectable, while for the doped suspension the spectra are clearly resolved.

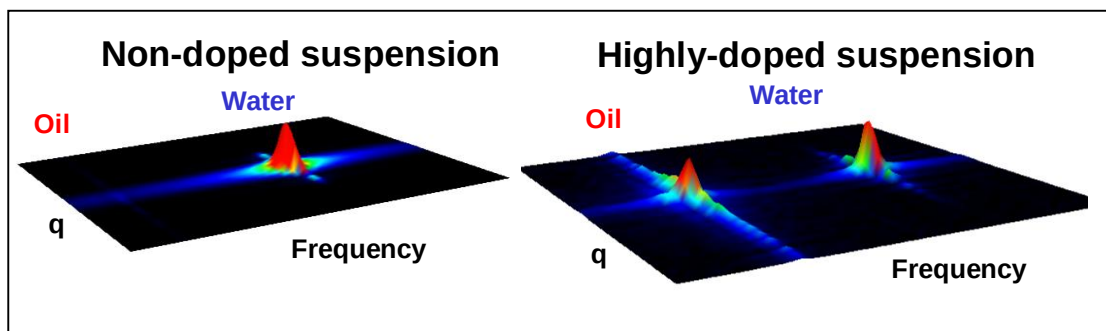


Figure 4.10. Chemical Spectra showing the frequency difference between oil and water, as well as the effect that doping has on the water signal.

Some difficulties do arise from using this method to obtain spectral resolution between the oil and water. It is not possible to measure water dynamics at long observation times due to signal relaxation. In addition, the relaxation time is so fast that the signal recovers significantly during a single scan. When using a flow-compensated PGSE sequence such as that in Figure 3.9, the recovered signal makes up a significant percentage of the signal. It is possible, however, to phase cycle out the contribution from recovered spins. Therefore, the results in Chapter 6 were ultimately obtained by the addition of a paramagnetic relaxation enhancing agent.

Magnetic Resonance Microscopy of Complex Fluid Flows

Velocity Imaging

Velocity imaging is a powerful tool in the visualization of complex fluid flows. Complex fluids, those that exhibit timescale-dependent liquid- and solid-like behaviours, include polymer solutions, liquid crystals, micellar surfactant phases, suspensions and emulsions. Rheology studies of such complex, or non-Newtonian, fluids provide insight into the macroscopic material response to a mechanical deformation[70] and are of interest since there are many complex fluids in biology, food and material processing, oil recovery and biotechnology applications[71-73]. The use of Rheo-NMR Microscopy offers a unique perspective in the investigation of such systems, since a shear cell is contained within the spectrometer and the sample may be studied non-invasively and non-destructively while in motion. A variety of traditional shear cell geometries have been developed for use within the NMR spectrometer, including the cylindrical Couette,

cone-and-plate, four roll mill, and the bi-axial extension cell[74, 72]. Velocity imaging not only provides visualization of heterogeneous shearing common to complex fluids, but the velocity profiles can be used to elucidate additional information, such as a spatially resolved shear rate[13]. Flow patterns in the Rheo-NMR shear cell can be measured and displayed directly with MRM techniques. Other measurements usually infer the presence of non-viscometric secondary flow, such as vortices or other complex flow structures from indirect torque data.

One use of velocity imaging of complex flows is to probe and characterize hydrodynamic instability in a flow system. Stability in a hydrodynamic system depends upon the system response to a small perturbation. If the perturbation gradually dies down and the system returns to its stationary state, then the system is stable. However, if the perturbation does not die down, and becomes magnified until the state of the flow system is changed, then the system is said to be unstable. One example of hydrodynamic instability is the presence of Taylor vortices in flow between two rotating coaxial cylinders. The stability of this type of flow depends upon the radii R_1 and R_2 of the two cylinders, the angular velocities of their rotations Ω_1 and Ω_2 and the fluid kinematic viscosity ν . A non-dimensional number accounting for the ratio of inertial to viscous forces based on these parameters is defined as the Taylor number.

$$T = \frac{4\Omega_1^2 R_1^4}{\nu^2} \frac{(1-\mu)(1-\mu/\eta^2)}{(1-\eta^2)^2} \quad (4.30)$$

where

$$\eta = R_1 / R_2 \quad (4.31)$$

and

$$\mu = \Omega_1 / \Omega_2 \quad (4.32)$$

At a critical Taylor number for a given system, instability sets in[75]. In the case of cylindrical Couette flow, instability begins with the emergence of secondary flows which are superimposed upon the main tangential flow and are periodic in the axial direction. These are called Taylor vortices and still constitute laminar motion since they have a coherent structure and are stable themselves. Such coherent flow structures often make quantification of transport in convection systems through the mass transfer coefficient not viable. It is difficult to incorporate the fine microscale detail present in the advection field into a macroscopic mass transfer coefficient model. However, Taylor vortices are important flow patterns in biological mixers and reactors which generate vortex flows and are common in planktonic cell and biofilm reactor applications. With an increase in angular velocity, the centers of the vortices become traveling waves and therefore have periodicity not only in the axial direction, but in the tangential, or primary, flow direction. Turbulence quickly appears as angular velocity is further increased. MRM imaging presents a way to characterize the dynamics of hydrodynamic instabilities by generating Taylor vortices in a Rheo-NMR cylindrical Couette shear cell. Figure 4.10 shows a simple Newtonian fluid, water, and the appearance of Taylor vortices as angular velocity was increased in a cylindrical Couette with an inner rotating cylinder and outer stationary cylinder.

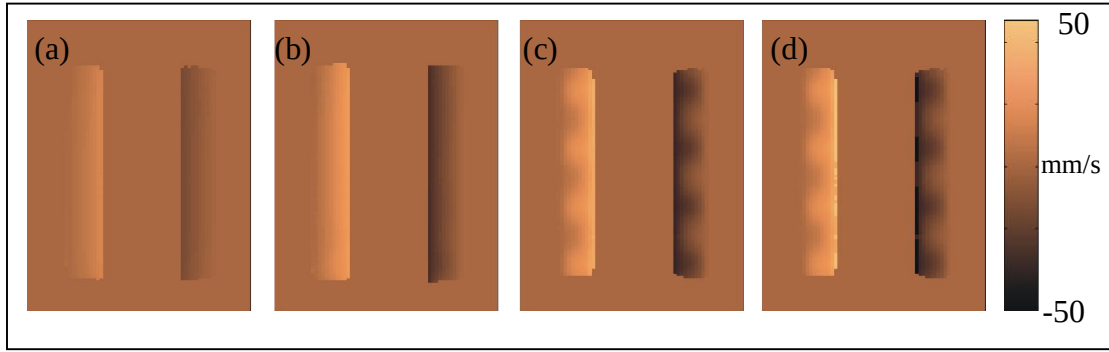


Figure 4.10. Images of the y velocity component velocity corresponding to the tangential direction for water in a Couette with a 2 mm fluid gap with $\sim 16 \times 23 \mu\text{m}$ spatial resolution. From left to right, the images monitor the transition to Taylor vortices with increasing angular velocity. Experimental parameters were: $T_R = 1000 \text{ ms}$, $t_e = 20 \text{ ms}$, $\delta = 1 \text{ ms}$, $\Delta = 10 \text{ ms}$, acquisition time = 17 min, slice thickness = 1 mm (a) The maximum velocity $v_{y,max}$ is $\sim 15 \text{ mm/s}$ for an angular velocity $\Omega \sim 6 \text{ s}^{-1}$ and $T \sim 1,010$ (b) $v_{y,max}$ is $\sim 31 \text{ mm/s}$, $\Omega \sim 13 \text{ s}^{-1}$ and $T \sim 4,700$ (c) $v_{y,max}$ is $\sim 39 \text{ mm/s}$, $\Omega \sim 16 \text{ s}^{-1}$ and $T \sim 7,170$ (d) $v_{y,max}$ is $\sim 47 \text{ mm/s}$, $\Omega \sim 19 \text{ s}^{-1}$ and $T \sim 10,100$

From Figure 4.10, it appears that the critical Taylor number, the value at which vortices appear, lies between 4,700 and 7,100. The cylinder length in the axial direction was assumed to be infinite in the derivation of the Taylor number and this is not true for this system. The Taylor numbers reported here are an approximation as end effects may cause the onset of vortices at a slower angular velocity than expected[75]. Velocity images were obtained with the pulse sequence in Figure 3.8.

The presence of colloidal sized particles, which include most biological cells, changes the material response to a mechanical deformation often through an alteration of flow patterns. A biological colloidal system comprised of cylindrical bacterial cells ($\sim 2 \times 20 \mu\text{m}$), *Fusobacterium nucleatum*, suspended in water at a concentration of $\sim 10^{11}$ cells/ml were also imaged in the cylindrical Rheo-NMR Couette shear cell with a 2 mm fluid gap and are shown in Figure 4.11.

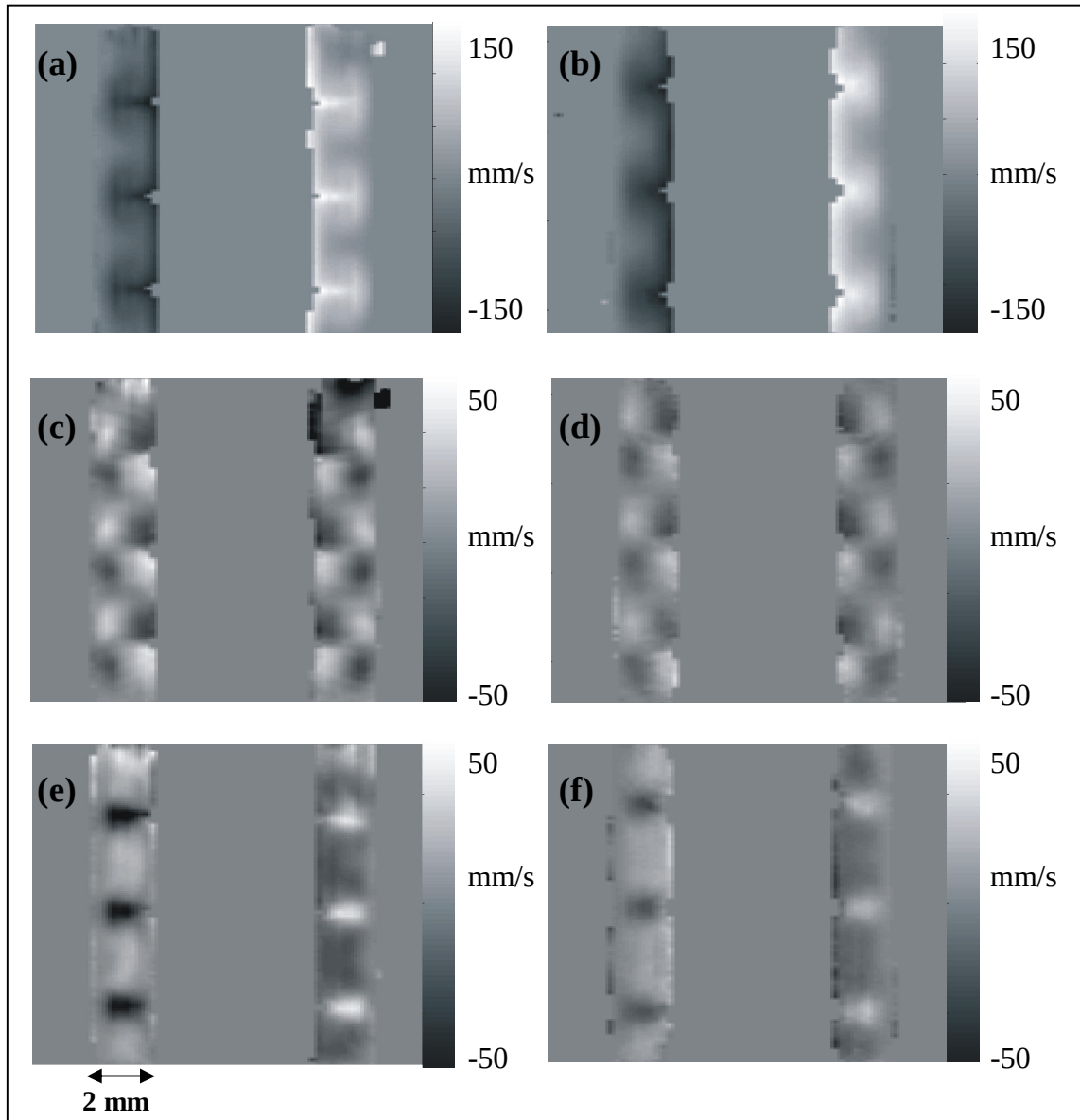


Figure 4.11. MR velocity maps of a cross section through the center of the Couette cell with a 2 mm fluid gap with $15 \times 23 \mu\text{m}$ resolution. The inner cylinder is rotating at 6 rps with $v_{y,\text{max}} = 94 \text{ mm/s}$, $\Omega = 38 \text{ s}^{-1}$. Experimental parameters were: $T_R = 1000 \text{ ms}$, $t_e = 20 \text{ ms}$, $\delta = 0.5 \text{ ms}$, $\Delta = 10 \text{ ms}$, acquisition time ~ 17 minutes, slice thickness = 1 mm. (a), (c) and (e) are for pure water, while (b), (d) and (f) are the same x , y and z components of velocity, respectively, for cylindrical bacterial cells, *Fusobacterium nucleatum* ($\sim 2 \times 20 \mu\text{m}$), suspended in water at a concentration of $\sim 10^{11}$ cells/ml. (a) y component of velocity v_y corresponding to the tangential direction with flow out of the plane (black) and flow into the plane (white). (c) z component of velocity v_z corresponding to the axial direction with flow up (black) and down (white). (e) x component of velocity v_x corresponding to the radial direction with flow left (black) and flow right (white).

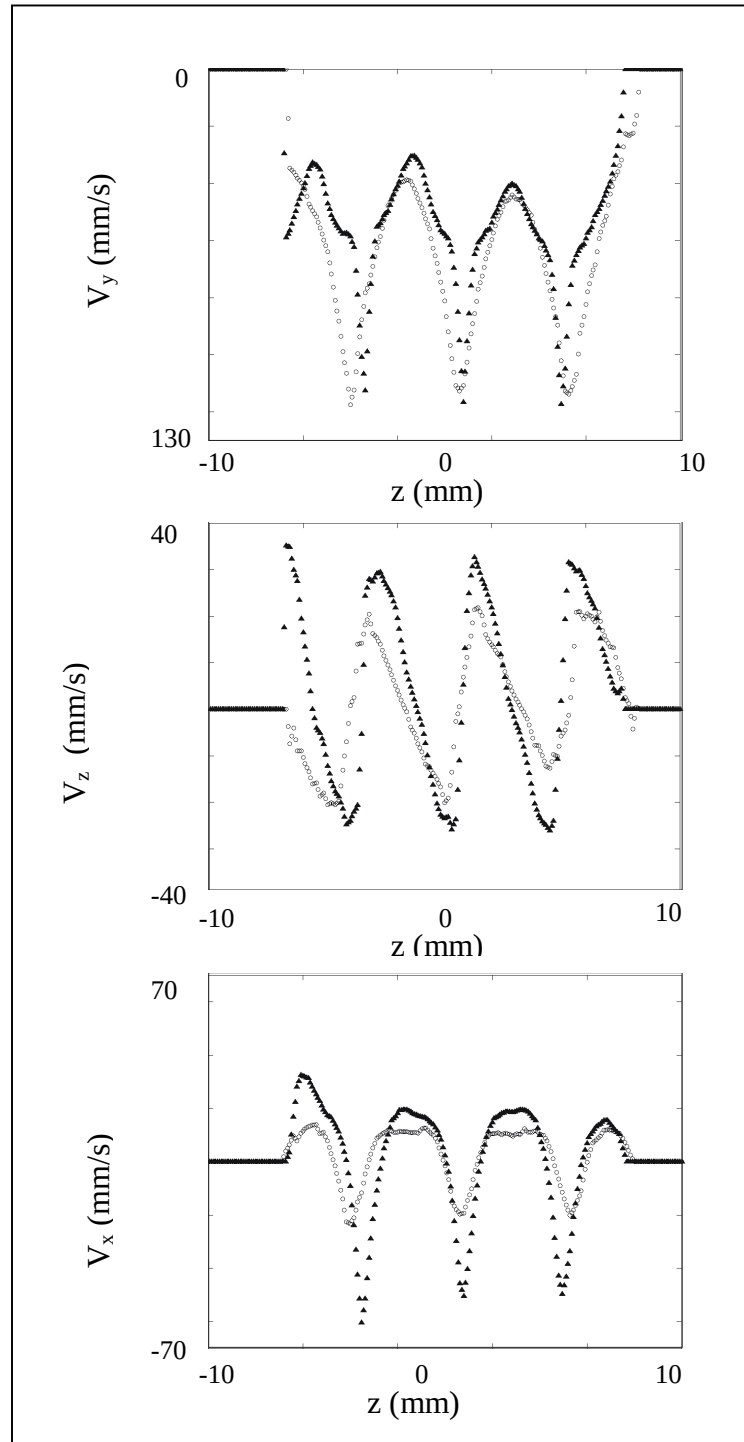


Figure 4.12. Quantitative velocities for water (closed triangles) versus the cylindrical cell suspension (open circles) at the same radial position, $r = 3.45$ mm, close to the center of the Couette gap, for the tangential, axial and radial directions respectively.

Since the nature of Taylor vortices is dependent upon the viscosity of the fluid and the presence of cells has an effect on viscosity, the vortical structure is changed by the presence of cells. Variations in the secondary flow features are evident in Fig 4.11. The velocity amplitude of the vortical structure appears dampened in the cylindrical cell suspension relative to the pure water. Fig 4.12 takes a quantitative look at the velocity differences between the two samples by selecting a profile through each of the images at a specific radial position $r = 3.45$ mm. A shift in the velocity maxima is seen for the cell suspension with respect to the pure fluid in all three directions, as well as a decrease in the maximum velocity value. The greater difference in the axial and radial directions corresponding to secondary flows demonstrates the significance that secondary flows have on mass transport and reiterates the deficiency in mass transport coefficient models that rely on tangential or axial based Reynolds numbers.

Spatial Coherence Phenomena: “Diffraction” effects

Position Diffraction

The concept of diffraction patterns is traditionally familiar to scientists and engineers due to the broad use of optical methods, X-ray scattering or neutron elastic scattering where the detectable signal is the conjugate Fourier space to structural density of the scattering medium. Therefore features, or diffraction patterns, present in the signal relate to the sample’s structure[3]. Diffraction patterns in the NMR signal as a function of applied gradient strength can arise from spatial phase regularity between spins due to sample structure. This phase regularity therefore relates to the spin density, which leads

to the familiar concept of sampling k-space through phase encoding and fourier transforming to obtain a one dimensional image. The diffraction pattern is actually the power spectrum of the signal $|S(\kappa)|^2$ [3]. Phase encoding in imaging, the application of a single pulsed magnetic field gradient which generates a helix of magnetization in space, can therefore also be called “position diffraction”. While it is rarely thought of in this manner in clinical MRI applications today, the foundation for modern NMR imaging originated from the paper of Mansfield and Grannell entitled “NMR diffraction in solids”[52]. In this paper the connection between spatial structure and the modulation of the signal amplitude was first made. The unique aspect of NMR as related to the methods mentioned above is that due to sampling both real and imaginary signal components, full phase information is retained, allowing the use of the Fourier Transform to construct an image in the reciprocal space. In X-ray scattering for example, phase information is lost and therefore the Fourier Transformation is not an image of the spatial structure, but an image of the density autocorrelation, or Patterson function[76]. In this case, transformation of the raw data actually obscures structural information and working in the raw data space is preferable. The technique is therefore indirect and somewhat limiting.

Displacement Diffraction

With the use of a pair pulsed magnetic field gradients, PGSE NMR, spatial phase coherence and the resulting coherence features in the echo signal are present for different

reasons. Consider, for example, Poiseuille flow in a pipe where there is a velocity distribution for a Newtonian fluid of

$$v(r) = \frac{v_{\max}}{2} \left(1 - \frac{r^2}{R^2}\right) \quad (4.33).$$

The probability of spin displacement, or the average propagator, for such a system is equal to

$$\bar{P}(Z, \Delta) = H(Z - v_{\max} \Delta) \quad (4.34)$$

where $v_{\max}$ is the maximum axial velocity. The propagator is the Heaviside hat function[77], the Fourier transform of which is a sinc function. The form for the echo attenuation then becomes

$$E(q, \Delta) = \exp(i\pi q v_{\max} \Delta) \text{sinc}(\pi q v_{\max} \Delta) \quad (4.35).$$

The first diffraction minimum corresponds to the mean velocity. The shape of the signal can then be thought of as “displacement diffraction”, since the phase coherence comes from an intrinsic property of the flow field, the distribution of velocities[3, 56, 78].

Traditionally, the echo signal would be Fourier Transformed to obtain a propagator, but there is often much to be learned without this step. Analysis in the q domain allows relaxation of the signal sampling and gradient strength constraints necessary to obtain a full artifact free propagator and experiment time can be greatly reduced[56].

Diffusive Diffraction

When the dynamic mechanism for generating a diffraction pattern is due to some physical restriction to spin motion such as a solid-fluid interface, there are two effects possible: “diffusive diffraction” and “flow diffraction”[56, 79, 80]. Anytime there is restriction of the spins, there is a correlation between the initial and final position of the spins due to such things as wall collisions. Therefore, if the observation time is sufficiently long enough that the spins have sampled the entire pore space via Brownian motion, the propagator is related to the pore structure. For the case of restricted diffusion in a pore the echo attenuation has a “diffusive diffraction” pattern which strongly depends on the shape and characteristic of the pore[79, 3, 80, 81]. Figure 4.13 shows a particle path as it diffuses throughout a parallel plane pore of width a , while Figure 4.14 demonstrates the shape of the probability of spin displacement for such a restricted particle and the corresponding features in the echo attenuation.

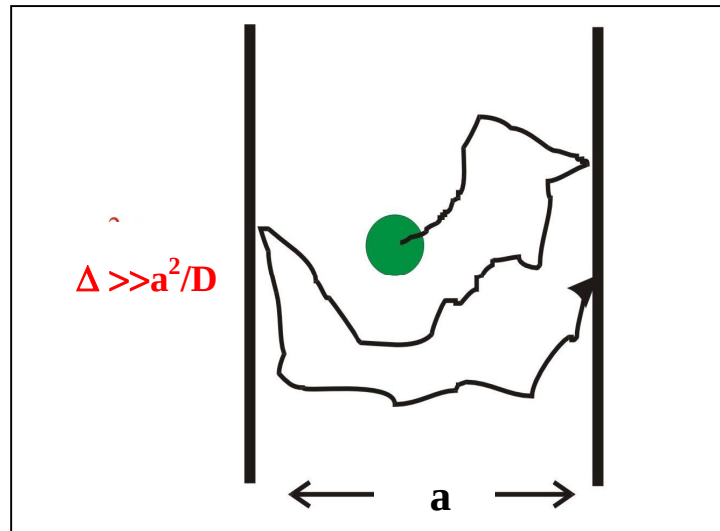


Figure 4.13. Restricted diffusion of a particle between two planes.

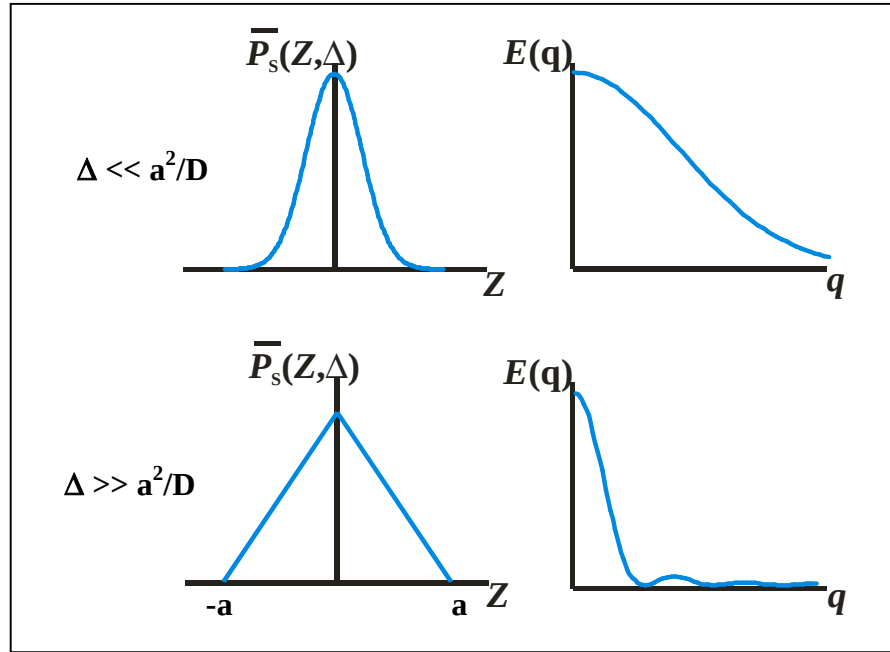


Figure 4.14. Top: Propagator profile for unrestricted diffusion and the corresponding signal. Bottom: Propagator for restricted diffusion and signal observed where a is the radius of the pore.

For a short time $\Delta \ll a^2 / D$, where a is the median pore size and D is the molecular self-diffusion coefficient, the particle has not had time to fully sample the pore dimension and the form of the propagator remains Gaussian as for free diffusion. At longer times $\Delta \gg a^2 / D$, the particle “feels” the presence of the walls and the probability of displacement becomes influenced by the inability of the particle to move farther than the pore dimension. By the Fourier relationship, the echo signal attenuation then takes on a sinc^2 form which reflects the pore boundaries. Analysis of the echo attenuation for spins completely confined to a perfectly reflecting pore can be conducted by realizing that in the long time limit $\Delta \gg a^2/D$ the probability of spin displacement for a single spin reduces to the pore molecular density function $\rho(\mathbf{r}')$.

$$P_s(\mathbf{r}|\mathbf{r}', \Delta) = \rho(r') \quad (4.36)$$

The spin may diffuse only as far as the dimensions of the pore. The normalized form of the echo attenuation assuming the narrow pulse approximation where $\delta \ll \Delta$, when combined with the definition of the average propagator and (4.36) reduces to

$$E(\mathbf{q}, \Delta) = \iint \rho(\mathbf{r})\rho(\mathbf{r} + \mathbf{R}) \exp[i2\pi\mathbf{q} \cdot \mathbf{R}] d\mathbf{r} d\mathbf{R} \quad (4.37)$$

where $(\mathbf{r} - \mathbf{r}') = \mathbf{R}$. It can be seen from (4.37) that the average propagator in this case becomes an autocorrelation function of the spin density $\rho(\mathbf{r})$. [3, 62]

$$\bar{P}_s(\mathbf{R}, \infty) = \int \rho(\mathbf{r})\rho(\mathbf{r} + \mathbf{R}) d\mathbf{R} \quad (4.38)$$

The Weiner-Khintchine theorem, from the theory of light scattering, states that the Fourier transform of a time autocorrelation function is the frequency power spectrum[56]. Therefore, the Fourier relationship between $\rho(\mathbf{r})$ and $S(\mathbf{q})$ can be utilized to express the echo signal in terms of the power spectrum of $\rho(\mathbf{r})$.

$$E(\mathbf{q}, \infty) = |S(\mathbf{q})|^2 \quad (4.39)$$

This form of the signal is mathematically analogous to optical diffraction by a single slit[82] and reflects the diffraction pattern of the pore. For a rectangular pore as shown in Figure 4.13, the power spectrum can be written as

$$E(\mathbf{q}, \infty) = |S(\mathbf{q})|^2 = |\sin c(\pi\mathbf{q}a)|^2 \quad (4.40).$$

This form of the echo attenuation nicely reiterates the sinc^2 pattern where minima correspond to the pore dimension a .

In real systems, such as porous sandstones, the effect of wall relaxation on the modulation of the echo signal can be profound[83, 84]. The coherence features can become damped or the diffraction minimum can be shifted to higher values of q , which reduces the apparent radius. In addition, the finite duration of the pulsed magnetic field gradient δ , sometimes necessary due to gradient amplitude hardware constraints, generates a distribution in the starting spin phases which then impacts the pores size effects on the propagator[85]. Therefore, when the propagator does not reduce exactly to the pore molecular density function, as in the case of a finite δ and wall relaxation effects, a different method must be used to obtain the correct form of the propagator. Incorporation of wall relaxation or finite gradient durations using corrections to the propagator is required to obtain accurate structural parameters from fitting the NMR data.

The governing differential equation for the probability of displacement, Fick's 2nd Law[19],

$$D\nabla'^2 P_s = \partial P_s / \partial t \quad (4.41)$$

can be solved via an eigenfunction expansion where the form of the propagator is

$$P_s(\mathbf{r}|\mathbf{r}', t) = \sum_{n=0}^{\infty} \exp(-\lambda_n t) u_n(\mathbf{r}) u_n^*(\mathbf{r}') \quad (4.42)$$

where $u_n(\mathbf{r}')$ are a set of orthonormal solutions to the Helmholtz equation $\nabla^2 \Psi = \lambda_n$ with eigenvalue λ_n [77].

Due to the identity

$$\delta(\mathbf{r} - \mathbf{r}') = \sum_{n=0}^{\infty} u_n(\mathbf{r}) u_n^*(\mathbf{r}') \quad (4.43)$$

the form of the propagator satisfies the initial condition

$$P_x(\mathbf{r}|\mathbf{r}', 0) = \delta(\mathbf{r} - \mathbf{r}') \quad (4.44).$$

To account for wall relaxation, the eigenvalues λ_n depend upon the boundary condition

$$D\hat{\mathbf{n}} \cdot \nabla P_s + MP_s = 0 \quad (4.45)$$

where $\hat{\mathbf{n}}$ is the outward surface normal. Once the form of the propagator is obtained, it is possible to get the proper form for the echo attenuation. This solution has been obtained for several different pore geometries[83, 86, 87], including parallel-plane pores, spherical pores and cylindrical pores. As an example, the eigenfunction expansion of the propagator for a cylindrical pore yields

$$P_x(\mathbf{r}|\mathbf{r}', t) = \sum_{nk}^{\infty} \exp[-\beta_{nk}^2 D \Delta / a^2] J_n(\beta_{nk} \mathbf{r} / a) \times J_n(\beta_{nk} \mathbf{r}' / a) A_{nk}^2 \cos(n\theta) \cos(n\theta') \quad (4.46)$$

where for $n \neq 0$

$$A_{nk}^2 = (2 / \pi a^2) (\beta_{nk}^2 / J_n^2(\beta_{nk})) / [(Ma / D)^2 + \beta_{nk}^2 - n^2] \quad (4.47)$$

and

$$A_{0k}^2 = (1 / \pi a^2) (\beta_{0k}^2 / J_0^2(\beta_{0k})) / [(Ma / D)^2 + \beta_{0k}^2] \quad (4.48).$$

J_n are cylindrical Bessel functions and the eigenvalues β_{nk} come from the equation

$$\beta_{nk} J_n'(\beta_{nk}) / J_n(\beta_{nk}) = -Ma / D \quad (4.49)$$

where M controls the degree of wall relaxation accounted for in the equation. For example, $M = 0$ represents perfectly reflecting walls. The expression for the echo attenuation in a chosen q -direction then becomes

$$\begin{aligned}
 E(q, \Delta) = & \sum_k 4 \exp[-\beta_{0k}^2 D \Delta / a^2] \frac{\beta_{0k}^2}{[(Ma/D)^2 + \beta_{0k}^2]} \\
 & \times \frac{\{(2\pi qa)J_0'(2\pi qa) + (Ma/D)J_0(2\pi qa)\}^2}{[(2\pi qa)^2 - \beta_{0k}^2]} \quad (4.50). \\
 & + \sum_{nk} 8 \exp[-\beta_{nk}^2 D \Delta / a^2] \times \frac{\beta_{nk}^2}{[(Ma/D)^2 + \beta_{nk}^2 - n^2]} \\
 & \times \frac{\{(2\pi qa)J_n'(2\pi qa) + (Ma/D)J_n(2\pi qa)\}^2}{[(2\pi qa)^2 - \beta_{nk}^2]}
 \end{aligned}$$

The minima corresponds to $1/a$, where a is the average pore radius. From this diffraction pattern of the echo attenuation, the pore structure can be characterized. The solution for a parallel plane using the eigenmode expansion leads again to a modified sinc² behavior as expected[83].

Figure 4.14 demonstrates the appearance of these coherence features experimentally in an idealized system consisting of a bundle of 34 μm inside diameter glass capillaries that were filled with water and then sealed at the ends. The echo signal was normalized by the signal at zero gradient strength $q=0$, the standard procedure to account for relaxation effects in the echo attenuation. The signal E , measured in the direction of the restriction, clearly dips dramatically at a q point corresponding to the inverse of the length scale $a \sim 33 \mu\text{m}$, which is the diameter of the capillary. If the

gradients were oriented differently, say in the axial direction along the length of the capillary, then the spins would essentially experience no restriction over the timescale of the experiment and the echo attenuation would be featureless, as for free diffusion shown by the dotted line of the echo attenuation in the z-direction at $\Delta=200$ ms, in Figure 4.14 and schematically in Figure 4.13a. Figure 4.14 also shows the evolution of the diffraction pattern as a function of the observation time Δ . At 50 ms, the coherence features are not fully formed, since all of the spins have not had the time to fully sample the entire diameter of the capillary. With increasing time, the coherence peak becomes more and more pronounced.

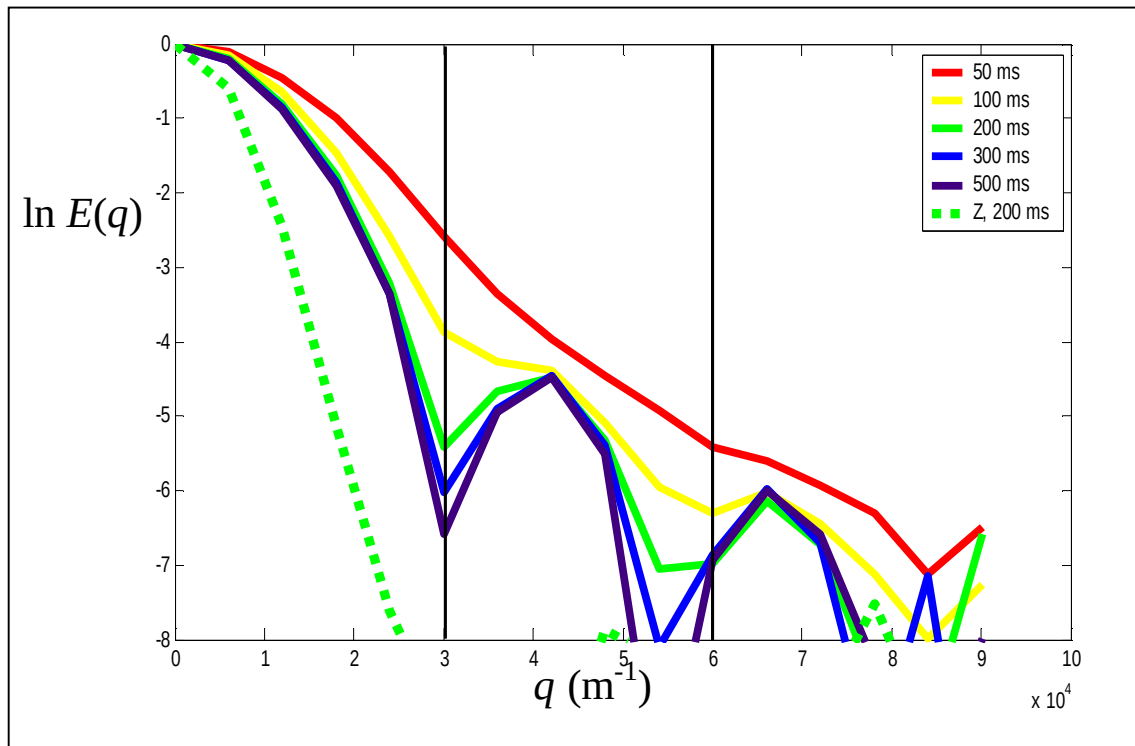


Figure 4.14. q -space plot of water in $34\mu\text{m}$ capillaries as Δ varies showing coherence features at ~ 33 microns and ~ 18 microns.

Heterogeneity in the sample can obscure diffraction patterns in the echo signal. Due to the variety of length scales present in differently sized pores, the form of the propagator is not uniquely defined by a single length scale and there is no direct connection to coherence features in the echo attenuation. This effect is demonstrated in Figure 4.15 where the sample is blood in the same capillaries as in Figure 4.14. Water therefore is confined not only by the walls of the capillaries, but the red blood cell walls[88-91] also restrict diffusion and therefore the coherence features are dampened.

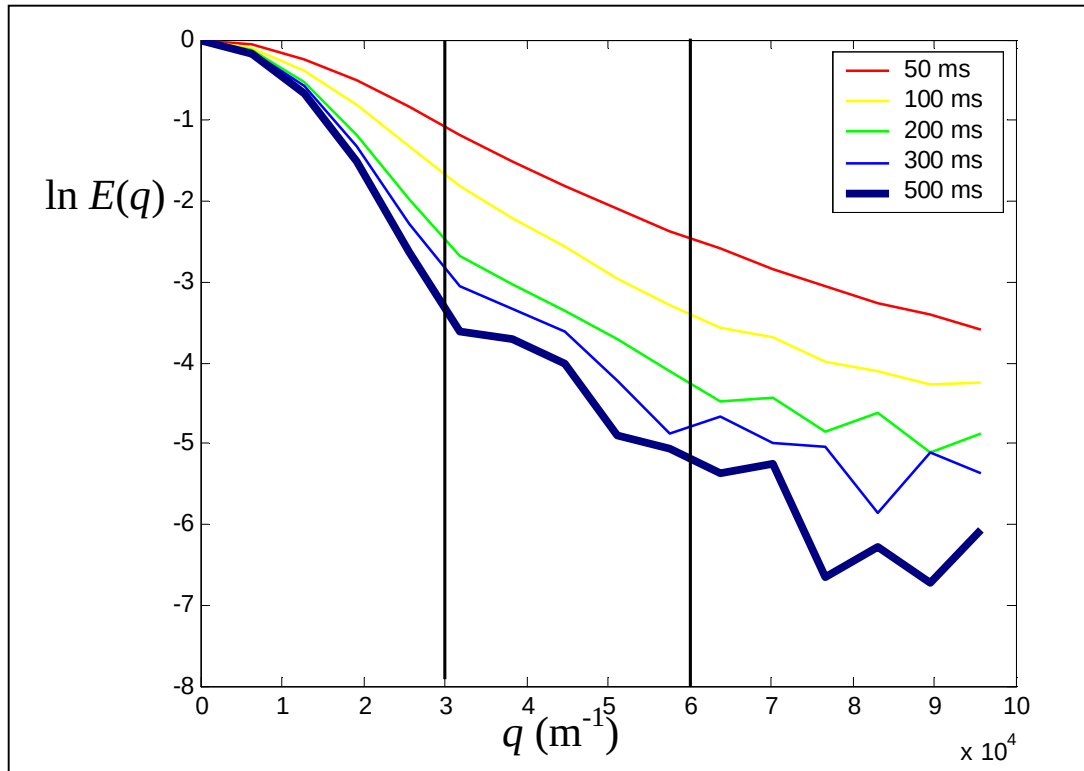


Figure 4.15. q -space plot of blood in 34 μm capillaries as Δ varies showing coherence features that are restricted and damped by the presence of red blood cells.

When a pore is not isolated, but has a structure and connectivity to other pores, what the signal means as a representation of the propagator becomes again more difficult

to interpret[80, 79, 81, 4]. Several theories estimate a form for the conditional probability, including the Gaussian Envelope approximation, pore-hopping models, and exact eigenmode expansions[79], as well as accommodation for relaxation effects. The simplest representation of the echo attenuation for interconnected pores is obtained through the pore hopping formalism[80, 81].

$$E(q, \Delta) = |S_o(q)|^2 F(q, \Delta) \quad (4.51)$$

Where $|S_o(q)|^2$ is a form factor related to the pore structure, while $F(q, \Delta)$ is related to the motion between pores. This equation is dependent upon the pore equilibrium assumption, where shortly[81] after a molecule jumps to another pore, it has an equal probability of being anywhere within the pore, *i.e.* $a^2/D_0 \ll b^2/D_{eff}$ where a is the pore size and b is the characteristic distance between pores. In the case of an orientationally disordered pore glass, an experimental model of which would be a monodisperse random packing of spheres, the echo attenuation in (4.50) becomes

$$E(q, \Delta) = |S_o(q)|^2 \exp\left\{-\frac{6D_{eff}\Delta}{b^2 + \xi^2} \times [1 - \exp(-2\pi^2 q^2 \xi^2) \frac{\sin(2\pi qb)}{2\pi qb}]\right\} \quad (4.52)$$

where ξ is the pore-spacing standard deviation and D_{eff} is the diffusion coefficient for migration between pores[81]. A coherence peak, or signal maxima, occurs at $q = b^{-1}$.

Flow Diffraction

Flow diffraction refers to the case where flow is present in a restricted environment such as a porous media. The appropriate propagator is then a function of

both the pore space and the flow field, since displacements will depend on the pore size as well as hydrodynamic transport[92-94]. One useful thing about flow diffraction is that larger pore size porous media which cannot be characterized via Brownian motion alone due to the diffusion time scale being much longer than is available to PGSE NMR because of relaxation effects can be characterized. By imposing flow, the mechanism for sampling of the pore is convective, or advective, not purely diffusive. In other words, the timescale for the spins to sample the pore space is the advective time scale $\Delta \gg \frac{b}{\langle v \rangle}$ allowing the observance of the coherence peak at $q = b^{-1}$ due to pore structure at observation times accessible with NMR. An increase in the flowrate is essentially as if the observation time were increased in the absence of flow[56, 92]. Another interesting aspect of flow diffraction is the directional asymmetry imposed by flow through the porous media. There is a preferred direction of motion and so the diffraction pattern will be different depending upon whether the q -direction sampled is aligned with flow.

The one commonality of these types of diffraction patterns is that the microstructure of a system can be characterized at much smaller length scales than for imaging. Since the signal is not acquired in the presence of a gradient, the resolution is not intrinsically limited by self-diffusion[3].

Spatially Resolved Diffusive Diffraction

Heterogeneity in a sample is a limiting factor to obtaining reliable pore structure and many practical applications possess a distribution of pore sizes. The presence of heterogeneous structure in the media dilutes and distorts the diffraction peaks. By also

spatially resolving the sample during the diffusive diffraction experiment, the pore structure in areas of homogeneity within the heterogeneous sample can be characterized, even down to pore sizes below the pixel resolution of the experiment. The combination of imaging, which labels the spatial positions of pore dimensions, and PGSE allows the measurement of diffraction patterns within each pixel. This is essentially the same practice as for velocity imaging or dynamic imaging (as discussed in the PGSE section of Chapter 3)[95], but with a few parameter changes. Only positive q needs to be sampled, gradient strengths need to be optimized for the appropriate length scales to be accessed and enough resolution in q , *i.e.* gradient amplitude g , is needed to properly measure the coherence structure.

Figure 4.16 shows images of a phantom constructed from four bundles of capillaries, each bundle being composed of a different diameter of capillary. The spatial sampling matrix size was 64x64 with a Field of View (FOV) of 50x50 mm, resulting in a spatial resolution of $\sim 78 \times 78 \mu\text{m}$. The parameters for this experiment were: $TR = 4 \text{ s}$, $\Delta = 100\text{ms}$, $\delta = 1.5 \text{ ms}$, 16 q points ranging $g = 0$ to 1.5 T/m , $ST = 10\text{mm}$, and 44 averages. The images for 5a, b and c were selected for increasing values of q from left to right so that all four areas could be seen. Water in the larger diameter capillaries at small gradient values, as shown in 4.16a, is much more visible due purely to the larger volume of spins within a voxel for these capillaries. As the gradient strength is increased, 4.16b and 4.16c, diffusive attenuation decreases the signal present in these larger capillaries and the signal from the smaller capillaries becomes more visible. This is the familiar diffusive edge enhancement effects as shown in [96].

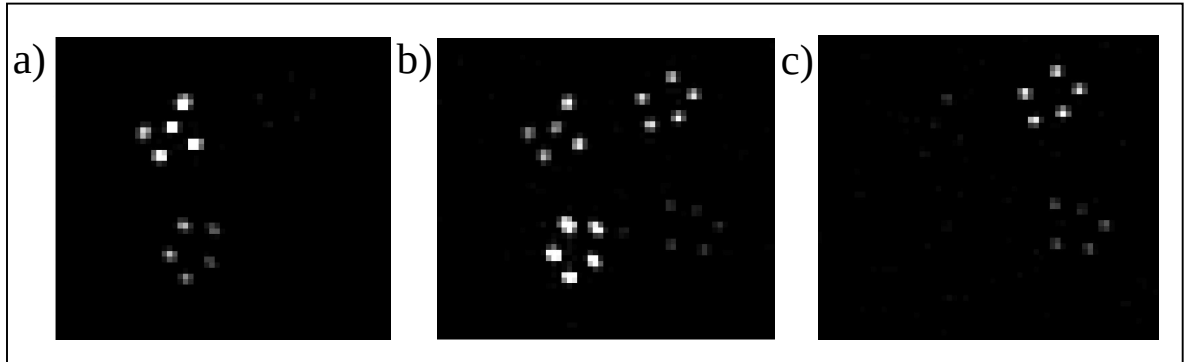


Figure 4.16. Images of four bundles of different sized capillaries filled with water. $5\text{ }\mu\text{m}$ diameter capillaries are at lower right, $9\text{ }\mu\text{m}$ at upper right, $25\text{ }\mu\text{m}$ at lower left, and $49\text{ }\mu\text{m}$ at upper left. a) to c) are increasing values of q .

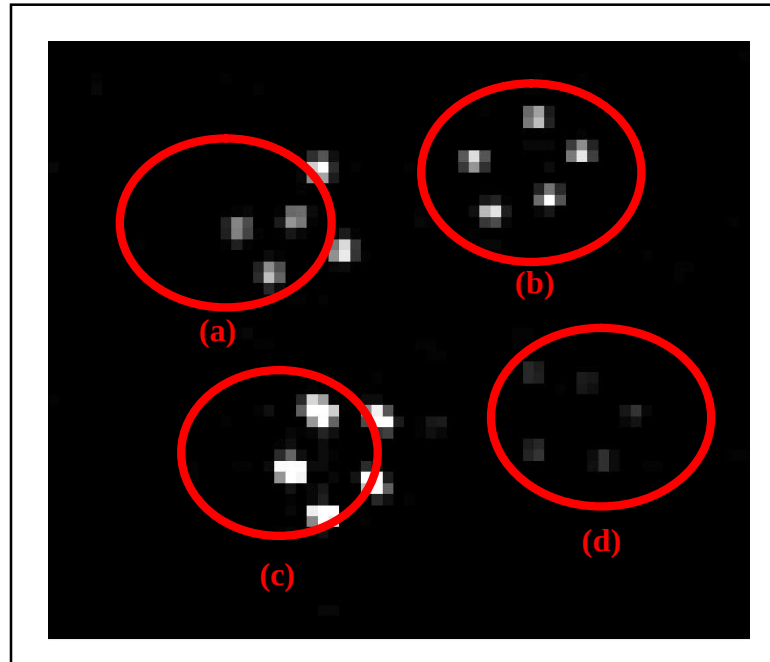


Figure 4.17. Image. The four regions of interest are circled in red. a) $49\text{ }\mu\text{m}$ diameter capillaries. b) $9\text{ }\mu\text{m}$ diameter. c) $25\text{ }\mu\text{m}$. d) $5\text{ }\mu\text{m}$

The images were divided into four regions of interest corresponding to bundles of capillaries consisting of five capillaries of each inner diameter dimension; 49 μm , 25 μm , 9 μm , and 5 μm ; as shown by the red circles in Figure 4.17. The total signal within these regions was then summed and plotted in Figure 4.18 versus q in the typical manner for viewing coherence features.

The data was then fitted with the appropriate theoretical form of the echo attenuation for a cylindrical pore, from Equation (4.50). M was assumed to be zero for perfectly reflecting walls, a reasonable assumption for uniform glass capillaries. Equation (4.50) then simplifies to

$$E(q, \Delta) = \sum_k 4 \exp[-\beta_{0k}^2 D \Delta / a^2] \times \frac{\{(2\pi q a) J_0'(2\pi q a)\}}{[(2\pi q a)^2 - \beta_{0k}^2]} \quad (4.53)$$

$$+ \sum_{nk} 8 \exp[-\beta_{nk}^2 D \Delta / a^2] \times \frac{\beta_{nk}^2}{[\beta_{nk}^2 - n^2]} \times \frac{\{(2\pi q a) J_n'(2\pi q a)\}}{[(2\pi q a)^2 - \beta_{nk}^2]}$$

where again J_n are cylindrical Bessel functions and the eigenvalues β_{nk} come from Equation (4.49) with $M = 0$. The values of n and k used for calculation were obtained as in [83], assuming a maximum β_{nk} value of around 20.

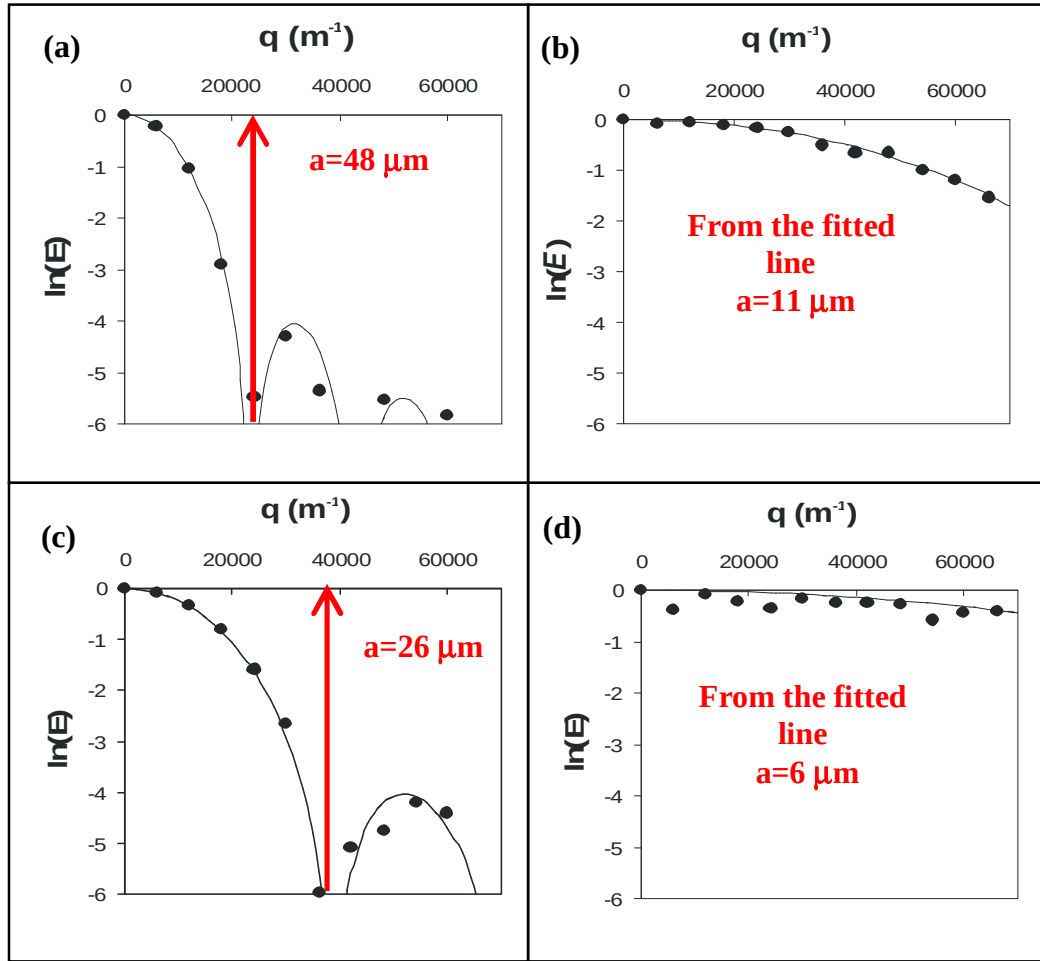


Figure 4.18. q -space plots where (a), (b), (c) and (d) correspond to the four spatially resolved regions shown in Figure 4.17. The fitted lines are from the theory for echo attenuation within cylindrical pores, Equation (4.53). In (a) and (c), the red lines show where the coherence peaks correspond to $1/a$, where a is the average pore size. In (b) and (d), average pore size is determined from the fitted lines.

Due to the resolution needed in the q dimension, the requirements and resolution needed for imaging, and the low signal to noise demanding a high number of signal averages, the experiment time was ~ 50 hrs. This is prohibitively long, and therefore not practical for routine investigation, but the experiment does offer a nice demonstration of

the synergistic capabilities between NMR techniques to characterize heterogeneous porous media.

An attempt to quantify the impact of the capillary size distribution on the bulk effective diffusion coefficient measurement was made by calculating an expected diffusion coefficient D_n as a function of observation time Δ and weighting it by the volume fraction of signal ϕ contributed to the bulk sample signal by each size capillary. At long enough times that the spins have sampled the entire pore, the displacement is simply the diameter of the respective capillary and the diffusion coefficient can be calculated from this displacement using the Einstein relation.

$$\langle z^2 \rangle = 2D(\Delta - \delta/3) \quad (4.54)$$

where the observation time of the experiment Δ has been modified to account for the finite gradient length δ . At shorter observation times where the walls have not been encountered, D is assumed to be the self-diffusion coefficient for the fluid $D_0 = 2 \times 10^{-9} \text{ m}^2/\text{s}$ for water. The Δ at which we would expect restriction to occur can be estimated by again using Equation (4.54) and the inserting the diameter of the capillary d_c for z .

Table I.

d_c (μm)	$\Delta_{restricted}$ (ms)	ϕ
5	6	0.01
9	17	0.03
25	131	0.2
49	501	0.77

For each capillary diameter and each Δ , the calculated $D_n = \frac{d_c^2}{2(\Delta - \delta/3)}$ was multiplied by the volume fraction for that capillary size. The weighted D_n were then summed together to produce a “bulk” diffusion coefficient for each Δ . Since the largest capillaries, $d_c = 49\mu\text{m}$, composed 77% of the liquid signal volume, and at the experimental observation times used free diffusion dominated, the composite diffusion coefficients ranged from 1.7×10^{-9} to 2.1×10^{-9} . The actual diffusion coefficients D_{eff} obtained from bulk PGSE measurements, where the diffusion coefficient is merely the slope of the line in a standard Stejskal-Tanner plot, were much slower, from 1.26×10^{-10} to 6.12×10^{-10} .

Table II.

Δ (ms)	$D_{eff,bulk}$ (m ² s ⁻¹)	$D_{n,calc}\phi$ (m ² s ⁻¹)				sum($D_{n,calc}\phi$) (m ² s ⁻¹)	$D_{total\ signal}$ (m ² s ⁻¹)
		d_c (μm)					
		5	9	25	49		
50	6.12E-10	2.0E-12	2.1E-11	4.0E-10	1.5E-09	2.0E-09	
100	4.39E-10	1.0E-12	1.0E-11	4.0E-10	1.5E-09	1.9E-09	3.1E-10
200	2.92E-10	5.0E-13	5.2E-12	3.1E-10	1.5E-09	1.9E-09	
300	2.05E-10	3.3E-13	3.5E-12	2.1E-10	1.5E-09	1.7E-09	
500	1.26E-10	2.0E-13	2.1E-12	1.2E-10	1.5E-09	1.7E-09	

The most likely reason for a slower observed diffusion coefficient is that restriction is actually felt much sooner than at the limit of z equaling the capillary diameter. There are a percentage of spins which interact with the walls long before all the spins can sample the entire pore and whose displacement is retarded by the presence of the walls, resulting in a slower diffusion coefficient. For a similar reason, coherence features are present in

the data even when the observation time $\Delta \sim a^2/D_o$, as opposed to $\Delta \gg a^2/D_o$, making it possible for the imaging experiment to be conducted at $\Delta=100$ ms. When signal from the entire spatially resolved q-space image is summed, thereby obtaining the signal contribution from all the capillaries, and a D_{eff} value that is very close to the bulk measurement at $\Delta=100$ ms, shown in the last column of Table II. Therefore, signal extraction from a spatially resolved image yields diffusion coefficients which accurately portray the pore structure in the specified region and summation of this signal corresponds to bulk measurements. However, using a mean squared displacement limited by the pore dimension to calculate a diffusion coefficient which is then weighted by the volume fraction of signal in the sample is proven to be too simplistic a representation and does not represent the bulk signal.

MAGNETIC RESONANCE MICROSCOPY DETERMINED VELOCITY AND HEMATOCRIT DISTRIBUTIONS IN A COUETTE VISCOMETER

Introduction

The introduction of the air-bearing supported electromagnetic concentric cylinder viscometer allowed the rheological properties of blood to be determined at these very low shear rates[97]. In systems where aggregation was known to occur, an unsteady torque response as a function of time was measured in this device despite a continuously steady rotation of the Couette's inner cylinder [98]. In addition, visual evidence has shown a depletion of red blood cells at the walls of the Couette viscometer[98, 99]. This evidence suggests that red blood cells (RBCs) migrate from walls in shear flow. Characterizing erythrocyte migration away from vessel walls is important for identifying physiological transport mechanisms, but the exact nature of the inhomogeneous cell distribution has never been measured across the fluid gap. In this study, magnetic resonance microscopy (MRM)[3] was used to determine the velocity as a function of radial position for three types of red blood cell (RBC) suspensions: RBCs suspended in isotonic, phosphate-buffered saline containing 0.5% albumin, RBCs in plasma (normal blood), and RBCs suspended in plasma which had 1.48% Dextran 110 added to it. The above samples are listed in order of increasing tendency to aggregate. A Rheo-NMR Couette device[100] with a fluid gap of 1 mm was modified specifically for the superconducting magnet at MSU and was used to study the effect of shear on particle distribution in the blood samples[13]. The modification and construction of the MR

compatible small gap Couette insert represented a significant experimental challenge. While a 1 mm gap does not necessarily constitute the range of microfluidics, it is smaller than previously developed for these types of instruments and the construction of even smaller gaps is not trivial.

Since MR velocity imaging allows for spatial resolution of velocity even within opaque fluids, properties of the velocity profile were analyzed to give clues as to the fluid behavior. For example, the shape of the spatial velocity distribution indicates Newtonian or non-Newtonian fluid behavior. Taking this idea even further, the definition of shear rate was utilized to calculate the spatial shear rate distribution, and related to apparent viscosity. The constitutive equation modeling the RBC rheological dependence on cell concentration in fluid, the Quemada equation, was then used to quantitatively determine the particle distribution across the fluid gap and discern the effect of aggregation on the particle distribution. While Magnetic Resonance methods have been used to study the shear induced migration of noncolloidal particles[101], the rheology of colloidal micelles[102, 103] and the flow induced microstructure of oil-water colloidal dispersions[104] among other rheological applications[100], MR studies of human blood have focused on the structure and orientation of cells[88, 91]. Rheological studies have been conducted for pig blood during pipe flow[105], but the data presented here provide the first non-invasive quantitative measurement of the aggregation dependent depletion of erythrocytes (RBCs) at both the rotating and stationary walls of a Couette flow cell.

Materials and Methods

Blood Sample Preparation

Human blood is a complex colloidal suspension consisting of erythrocytes (red blood cells) which compose 97% of the cell volume, and white blood cells and platelets suspended in plasma. Plasma is a Newtonian fluid containing molecules ranging from small ionic species to large macromolecules called proteins which make up approximately 7% by weight of the blood, half of this being albumin MW=69,000)[106]. The red blood cells have a biconcave discoid shape with a major diameter of 8.1 μm and a maximum thickness of 2 μm . The cell membrane is thin and flexible, allowing deformation of the particle. The interior of the cell consists of a nearly saturated hemoglobin solution. When aggregation occurs, the cells stack face-to-face into a rouleaux. The rouleaux can also form secondary aggregates.

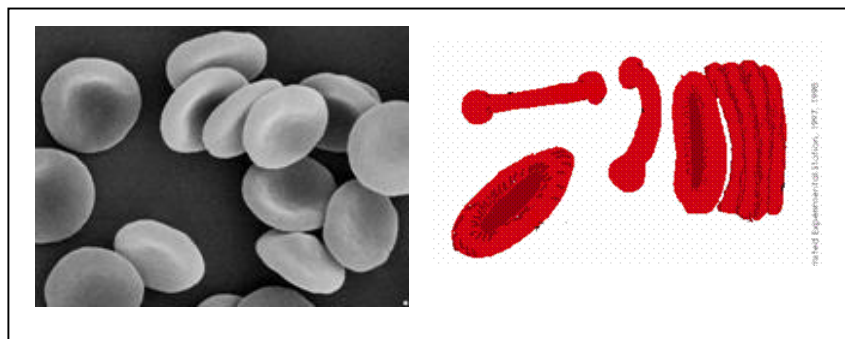


Figure 5.1. Shape and aggregation of erythrocytes.

For the experiments in this thesis, human blood was drawn by venipuncture from a healthy volunteer. The blood was collected into standard Vacutainers where the anticoagulant was ethylene diamine tetraacetic acid (EDTA) and then centrifuged in a

Sorvall refrigerated centrifuge, model RC5C with a 5 inch rotor, at 5000 rpm for 5 minutes at 4C minutes at 4C[13]. The RBC pack and plasma were separated, and the buffy coat region, containing white blood cells and platelets was discarded. The absence of the white blood cells and platelets does not affect the experimental results since they constitute less than 1% of the blood volume. Half of the plasma had Dextran 110 (Pharmacia, MW=110,000) added to it to a concentration of 1.48% by weight, while the other half was left unchanged. The Dextran was added to increase the RBC aggregation [107]. Additionally, a phosphate buffered, isotonic saline containing 0.5% (by weight) albumin (Research Organics) was prepared (pH=7.2, osmotic pressure = 297 mOsm). RBCs were added to these three suspending media to make suspensions with the desired average hematocrits (H). The first suspension was RBCs in isotonic saline with 0.5% albumin with an average hematocrit H of 0.400 and a suspending medium viscosity of $\eta_0 = 1.20 \text{ mPa s}$ at 23C. The second was RBCs in plasma with an average H of 0.402, and η_0 of 1.71 mPa s at 23C. The third was RBCs in plasma with 1.48% Dextran 110, an H of 0.402, and $\eta_0 = 2.83 \text{ mPa s}$ at 23C. The apparent viscosities of the three blood samples and also that of the suspending media were determined with a Brookfield digital cone-and-plate viscometer, model $\frac{1}{2}$ RVTDV-I200CP, at 23C. This viscometer has a nominal lowest shear rate of 7.5 s^{-1} when using a 0.5 degree cone. It was calibrated with glycerol-water solutions[13].

MR Imaging System

The MRM experiments were performed on a Bruker Avance DRX spectrometer attached to 250 MHz superconducting magnet. Gradient amplifiers and a Bruker Micro5 gradient probe, producing magnetic field gradients with a maximum strength of 1.7 T/m, were used to image the velocity distribution. A 10 mm internal diameter radio frequency (rf) coil was used in all couette flow and ice core experiments. A 5 mm internal diameter rf coil was used for all capillary flow experiments. The Bruker software package Paravision was used in the acquisition of all the MR data. Data analysis was conducted using Matlab (The MathWorks Inc.) and Prospa (Magritek Ltd.) software.

Experimental Flow Cell

A Bruker Rheo-NMR Couette device consisting of a 5 mm OD glass MR tube sitting inside a 10 mm OD (7.1 mm ID) glass MR tube was used in the shearing of the blood samples, see Figure 5.2. The inner tube is centered using two Teflon spacers placed in the bottom and top of the outer tube. The width of the gap between the tubes where the sample fluid resides is 1.05 mm. The inner tube is filled with a marker fluid, glycerol. The Couette cell sits within the 10 mm rf coil. A drive shaft assembly connects the inner Couette cylinder with a stepper motor drive system that sits on top of the magnet and rotates the inner tube at a fixed frequency.

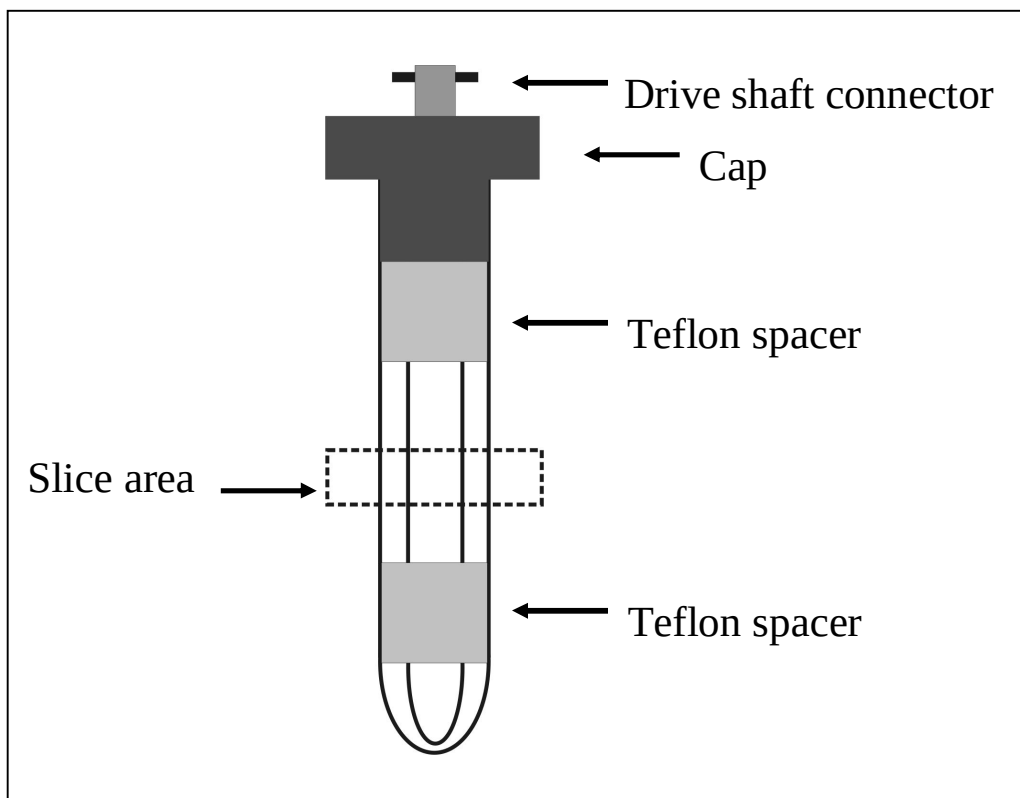


Figure 5.2. The Rheo-NMR Couette flow cell. The inner cylinder has an outer radius of 5 mm and the outer cylinder has an inner radius of 7.1 mm, resulting in a fluid gap of approximately 1.1 mm.

Velocity Imaging and Data Analysis

The blood samples were sheared in the couette flow cell at two rotational frequencies where the velocities at the inner rotating wall were 1.96 mm/s and 3.92 mm/s. The pulsed gradient spin echo (PGSE) pulse sequence, Figure 3.8, was employed to obtain transverse velocity images with the following experimental parameters: repetition time (TR) = 3000 ms, echo time (TE) = 24 ms, $\delta = 1$ ms and $\Delta = 9$ ms. Gradient values g were 100 and 700 mT/m for the lower rotation rate and 100 and 400 mT/m for the higher rotation rate. The velocity experiments were averaged over a slice

thickness of 5 mm in the longitudinal (z) direction and had a field of view (FOV) of 10 x 10 mm over 256 x 64 pixels resulting in a spatial resolution of 34 x 156 $\mu\text{m}/\text{pixel}$. The duration of each experiment was approximately 13 minutes, so the measured velocities are a stationary average over this time period.

Figure 5.3 shows a map of the y-component of the velocity v_y for a slice in the z-direction. By analyzing a single center line of data in the high resolution direction spanning the entire image, see the dotted line in Figure 5.3, 30 velocity points with 34 μm spatial resolution were collected across the gap width for each side.

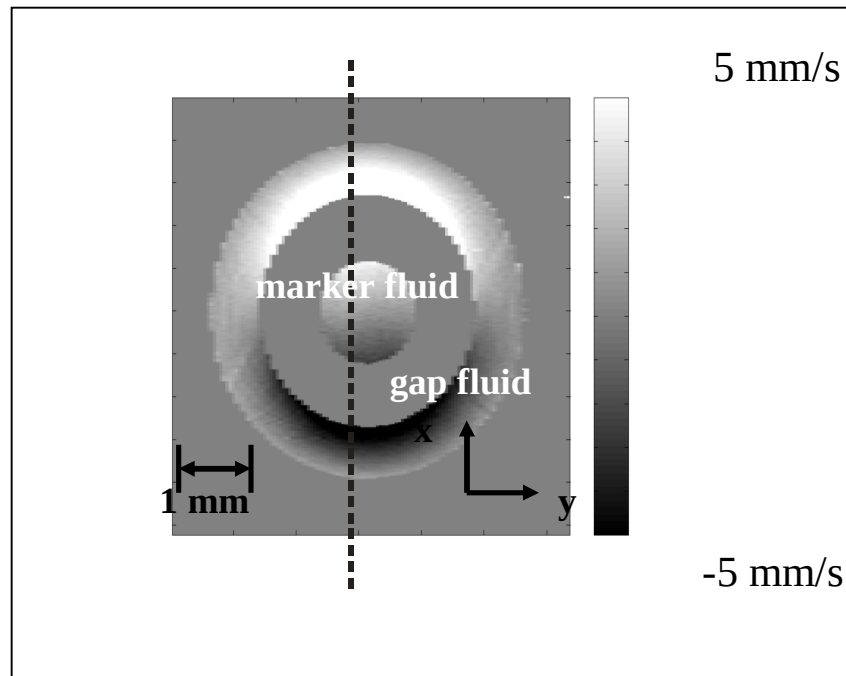


Figure 5.3. Map of the y-component of velocity v_y for the slice area shown in Figure 5.2. White for the positive velocity indicates left to right radial flow while black for negative velocity indicates right to left radial flow for both the gap fluid and center marker fluid.

From the solid body rotation of the glycerol within the inner tube, the rotational velocity of the inner cylinder wall was calculated. This allowed for normalization of the two sets of velocity data and provides an experimental check of the rotation rate set on the stepper motor. By averaging the normalized radius and velocities from each side of the Couette, one set of smoothed data was obtained. A cubic spline interpolation was performed on the data in Matlab, expanding the averaged data set to 60 points of velocity across the fluid gap.

When initially normalizing and plotting the velocity profiles from the images, an artifact became apparent. There was blurring around the edges of the velocity images and when the single line of velocity data was pulled from across the image, the data from the glycerol at the center of the inner rotating cylinder was offset. This gave the appearance that either the inner glass cylinder was not perfectly aligned or the glycerol did not perfectly represent solid body rotation. Neither of these options was truly probable, leading to the realization that a chemical shift artifact was to blame. Since the two fluids in the couette, the blood sample and the solid body rotation calibration glycerol, each have their own individual chemical spectra; their Larmor frequencies are separated by approximately 350 Hz. When imaging, signal is obtained from both these peaks and the resulting images are overlaid on top of each other and slightly offset by this chemical shift, causing blurring. In the case of the blood experiments, the 350 Hz phase shift between blood and glycerol resulted in a spatial offset of approximately 2.4 pixels. When the glycerol data is shifted by the 2.4 pixels represented by the 350 Hz phase difference between spectral peaks, the data becomes symmetric. Without correction, two

different highest possible velocities are predicted by the glycerol solid body rotation and the two sets of data taken from either sides of the Couette cannot be normalized by the same factor. By shifting the glycerol data, this artifact is corrected and accurate data is obtained. In the future, these artifacts would be prevented by widening the bandwidth of the experiment. This has the consequence of bringing the separate peaks closer together and minimizing the spatial offset in the velocity images. Essentially, a greater range of frequencies is being looked at and that translates into a smaller spatial offset.

Hematocrit Calculations

The calculation of the hematocrit, H , distribution across the Couette-flow gap utilized the Quemada Equation[12]. The Quemada equation is

$$\eta_r = \frac{\eta_a}{\eta_o} = (1 - 0.5kH)^{-2} \quad (5.1)$$

where

$$k = \frac{k_o + (k_{inf})\gamma_r^{0.5}}{1 + \gamma_r^{0.5}} \quad (5.2)$$

and

$$\gamma_r = \frac{\gamma}{\gamma_c} \quad (5.3)$$

k_o , k_{inf} , and γ_c are coefficients which are properties of the particular suspension being studied, η_o is the suspending medium viscosity, η_a is the apparent viscosity, η_r is the relative viscosity and γ is the shear rate. This is a 3-coefficient (k_o , k_{inf} , and γ_c)

constitutive equation, with the coefficients for an RBC suspension being dependent on hematocrit, and in the case of γ_c , also on temperature[108].

The Quemada coefficients are represented by polynomial expressions of the form

$$\ln(\text{coefficient}) = A + BH + CH^2 + DH^3 \quad (5.4).$$

Literature constants were used for both the RBCs in isotonic saline containing 0.5% albumin and RBCs in unaltered plasma[108], while for the suspension with Dextran 110, literature constants had to be extrapolated to lower shear rates than was available. Literature values for RBCs suspended in saline containing Dextran were also used in the extrapolation, although the two sets of data were not exactly contiguous. The data used in evaluating the coefficients of the Quemada Equation were collected for suspensions with hematocrits ranging from 0.15 to 0.85, over a shear rate range from 0.08 s^{-1} to 1500 s^{-1} . The values of the Quemada equation coefficients are shown in reference[108]. While the Quemada equation is generally associated with bulk blood measurements, the coefficients calculated are also valid for point locations in blood flow due to the fact that their values were extrapolated back to zero time using a technique outlined in reference[106]. Extrapolating to zero time negates the fact that at low shear rates the torque measured in a concentric-cylinder viscometer is not initially steady due to inertial effects at very short times after startup, but increases with time to a peak value. The RBC syneresis effect also causes the torque to decrease before and after the peak. These effects are accounted for by extrapolating the torque back to zero time. The most accurate torque value in the absence of these effects was then available for calculation of the

coefficients. For the Dextran containing suspension, the k_0 and k_{inf} were the same as for normal human blood. In the case of γ_c , the following relationship was developed:

$$\ln \gamma_c = -7.551 + 25.42 H - 18.17 H^2 \quad (5.5).$$

The Couette flow system used in the MR magnet did not have provision for measuring the torque generated by the Couette flow. Consequently, the following procedure was used to calculate the local hematocrit distribution across the concentric flow region:

- 1) By differentiation of the v/r versus radial position r curve, the shear rate $\gamma = r \frac{d}{dr} \left(\frac{v}{r} \right)$ at each radial position r can be determined.
- 2) Since the overall average hematocrit $H_{average}$ of the suspension in the flow chamber is known, it is initially assumed that this hematocrit value is the local value at the midpoint radial position, $H_{initial} = H_{average}$. From the Quemada equation with the coefficients determined using $H_{initial}$ and the appropriate polynomial relationships, the relative apparent viscosity at this midpoint position is calculated using equations (5.1)-(5.3). The shear stress τ and torque per unit rotor length T/L are then determined (using the appropriate suspending medium viscosity),

$$\tau = \eta_a \gamma \quad (5.6)$$

$$T = 2\pi r^2 L \tau \quad (5.7)$$

$$\frac{T}{L} = 2\pi r^2 \eta_a \gamma \quad (5.8)$$

where T is the torque and L is the length of the surface on which T is measured.

- 3) At any other radial position r , the apparent viscosity η_a can be calculated from equation (5.8) since the torque per unit rotor length T/L is a constant throughout the flow region by the Conservation of Angular Momentum Principle and the shear rate $\gamma = r \frac{d}{dr} \left(\frac{v}{r} \right)$ has been determined from the experimental data.

- 4) Since the values of apparent viscosity and shear rate at a chosen position r can be calculated, one can estimate a hematocrit value H_{est} and use this estimated value to calculate values for k_0 , k_{inf} , and γ_c from the appropriate polynomial equations (5.4). Next, k can be calculated from equation (5.2) and used in equation (5.1) to calculate a value for the hematocrit H_{calc} . If H_{calc} does not agree with H_{est} , one must iterate H until the values do agree. This determines the hematocrit concentration at the chosen position $H(r)$.
- 5) Once all the H values have been determined at each experimental point, the average hematocrit in the flow space can be calculated from:

$$\overline{H} = \frac{\int_{r_i}^{r_o} 2\pi r H \, dr}{\int_{r_i}^{r_o} 2\pi r \, dr} \quad (5.9).$$

This value of average hematocrit is then compared to the known experimentally determined average value. If these values do not agree, one must iterate H_{initial} and repeat steps (2) – (5) until agreement is reached.

One then has determined the hematocrit distribution across the Couette gap from the experimental v/r vs r data. The crucial step of fitting the experimental v/r vs r data was performed on the computer by fitting polynomial equations to data[109]. In some cases, the data were fit with several polynomial equations with the fits constrained to converge using multiple overlapping points. In order to check these fits and the computer based iterative calculation procedure outlined above, the procedure was performed by hand for a few cases using a french curve. In all cases tested, the hand-derived and computer-derived calculations were in agreement.

Results and Discussion

Blood Velocity and Hematocrit Profiles

Figure 5.4 shows normalized velocity versus normalized gap radius for a glycerol standard and RBCs in 3 different suspending media. The maximum velocity at the inner wall was 1.96 mm/s, which corresponds to a nominal shear rate of -2.20 s^{-1} .

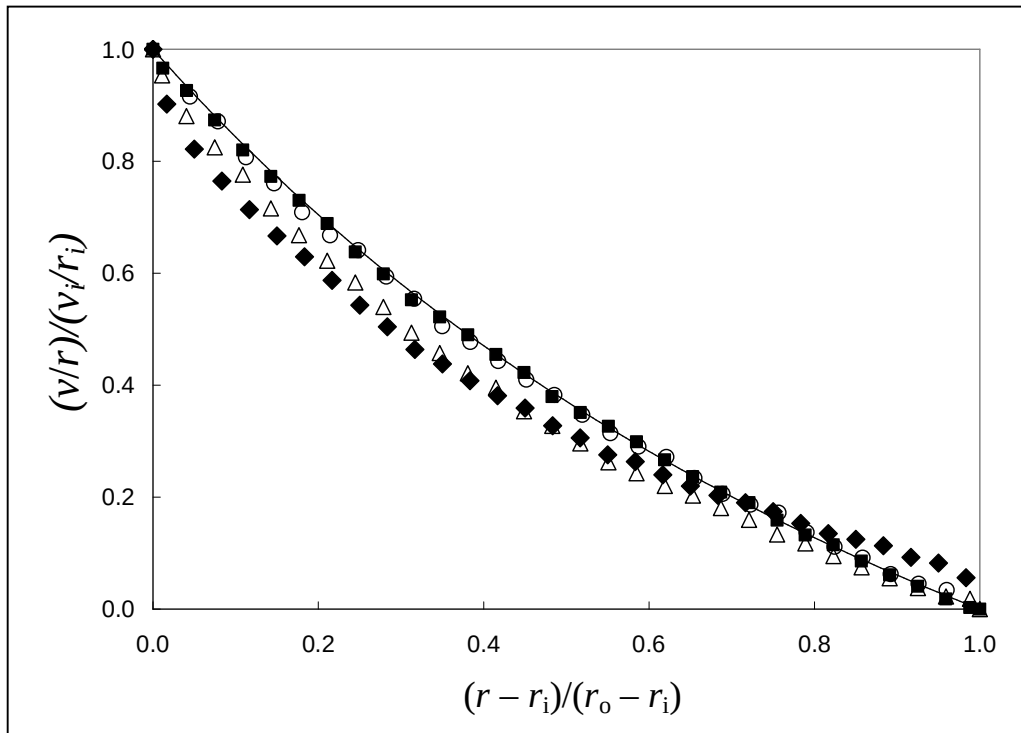


Figure 5.4. Normalized velocity divided by radius as a function of normalized fluid gap radius. The solid line was calculated from theory for a Newtonian fluid based on the viscosity of a 60% glycerol in water solution (open circles). The RBC suspension in albumin-containing isotonic saline (closed squares) behaves as a Newtonian fluid, shown by the slightly decreasing shear rate as the radial position increases. The non-Newtonian behavior of RBCs in plasma (open triangles) and plasma containing Dextran (closed diamonds) is indicated by line shape deviation from Newtonian theory while the higher shear rates at the walls indicates thin layers of erythrocyte depletion.

The solid line represents Newtonian behavior for a fluid with the viscosity of the glycerol standard, as derived from the solution of the equations of motion for the velocity field in a Couette geometry with an inner rotating cylinder. As a Newtonian fluid, the velocity profile for glycerol should and does lie directly atop the solid line. Note that the velocity gradient, or shear rate, across the gap is not constant. Rather, shear stress scales as $1/\gamma$. Deviations from the solid line, and therefore Newtonian fluid behavior, begin to occur in the RBC suspension velocity profiles.

For RBCs suspended in saline, there is only a slight change in the velocity gradient across the gap as compared to the glycerol standard. For normal blood, however, another feature appears in the profile. At the inner rotating wall, there is an indication of slip. The outer wall does not as clearly show this slip layer, but it is possible that a thin layer of plasma exists there. The slight increase in velocity at the last pixel near the outer wall was consistently seen for the normal blood and this effect is in agreement with sub-pixel regions of carrier fluid seen at the walls in paper pulp suspensions studied by MR[60]. An even more extreme deviation of velocity gradient from Newtonian behavior is seen for the RBCs suspended in plasma containing Dextran, as well as slip at both walls. Only one material property differs between the 3 samples that would affect material response: the ability of RBCs to aggregate. Obviously, particle aggregation affects the rheological behavior of the suspension and most likely the particle distribution across the fluid gap. To further analyze what the shape of the velocity profiles are indicating, a shear rate was calculated from the derivative of polynomial fits to the velocity profiles.

Figure 5.5 shows the shear rate as a function of gap radius for each of the RBC suspensions. As indicated by the velocity profiles, the shear rate is not constant across the fluid gap. For the RBCs in saline-albumin, shear rate varies from -2.97 s^{-1} at the inside (rotating) surface, decreasing with radius to -1.69 s^{-1} at the outer wall. Regions of very high shear appear at the inner wall for the RBCs in plasma and at both walls for the RBCs in plasma containing Dextran. The features present in these profiles again allude to the particle migration within the fluid gap. The high shear regions at the walls are an indication of cell-depleted layers of plasma and are present only in the samples where RBCs aggregate. In the saline solution, the RBCs behave as independent particles and so their presence only induces a slight non-Newtonian fluid behavior due to cell deformation.

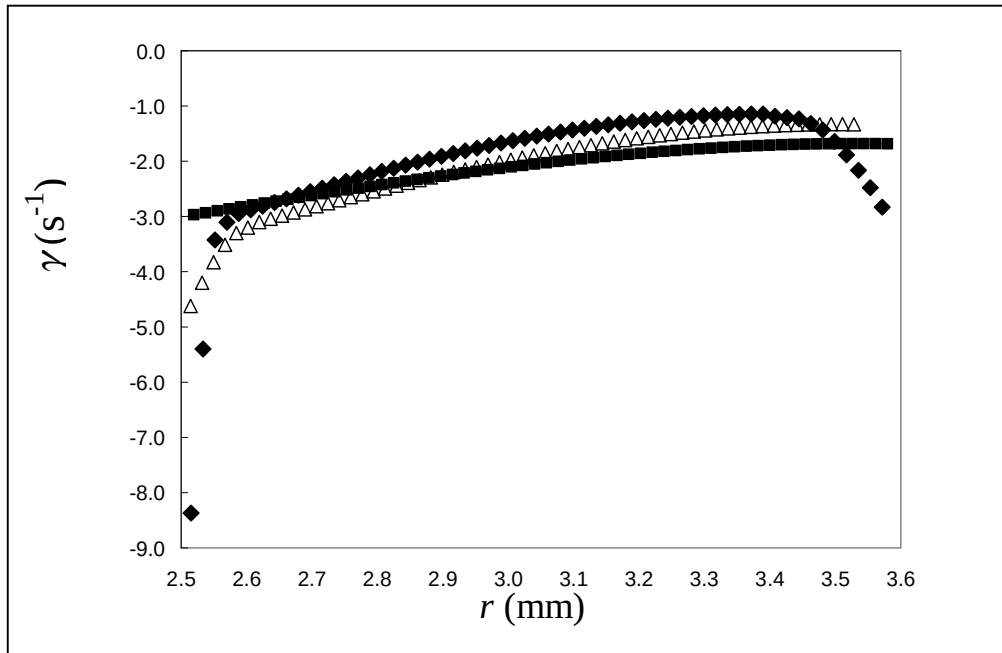


Figure 5.5. Shear rates as a function of radius for each sample calculated from the polynomial fits to the velocity divided by radius curves. The closed squares are RBCs in saline, the open triangles are RBCs in plasma and the closed diamonds are RBCs in plasma containing Dextran 110.

The final step towards obtaining quantitative information about the particle distribution across the gap was the calculation of hematocrit profiles, as outlined in the Calculations section. Figure 5.6 shows Hematocrit versus normalized gap radius for each of the RBC suspensions. The RBCs in saline-albumin, where the cells do not aggregate, showed only a slight inhomogeneity in the particle distribution across the gap. The local hematocrit increased slightly as the shear rate decreased in order to maintain a constant apparent viscosity across the gap. There were no clear cell depleted layers of plasma at the walls, but much smaller layers are possible due to wall exclusion effects or shear induced diffusivity[25]. For the RBCs in plasma, the local hematocrit again increases slightly with decreasing shear rate. At the inner wall where slip was apparent in the velocity profiles, there is also a distinct region of cell depletion about 100 μm thick. The velocity and shear profiles suggest a small layer is possible at the outer wall, where the local hematocrit plateaus and just begins to decrease slightly at the last pixel. Therefore, a partially cell depleted layer, less than the 34 $\mu\text{m}/\text{pixel}$ spatial resolution, develops at the outer wall. These two regional differences are consistent with the previously cited visual evidence of plasma layers at the walls[99, 98]. As expected, the hematocrit profile for RBCs suspended in plasma containing Dextran shows a large, again approximately 100 μm thick, cell-depleted plasma rich layer at the inner wall and a more gradual 100 μm layer at the outer wall as well. The trend of increasing particle concentration with decreasing shear rate continues. In order to maintain the average hematocrit and compensate for the relatively large regions of low cell concentration at the walls, the hematocrit near the center of the gap does increase much more than for the other samples.

The link between particle aggregation and material response via inhomogeneous particle distribution is clearly demonstrated.

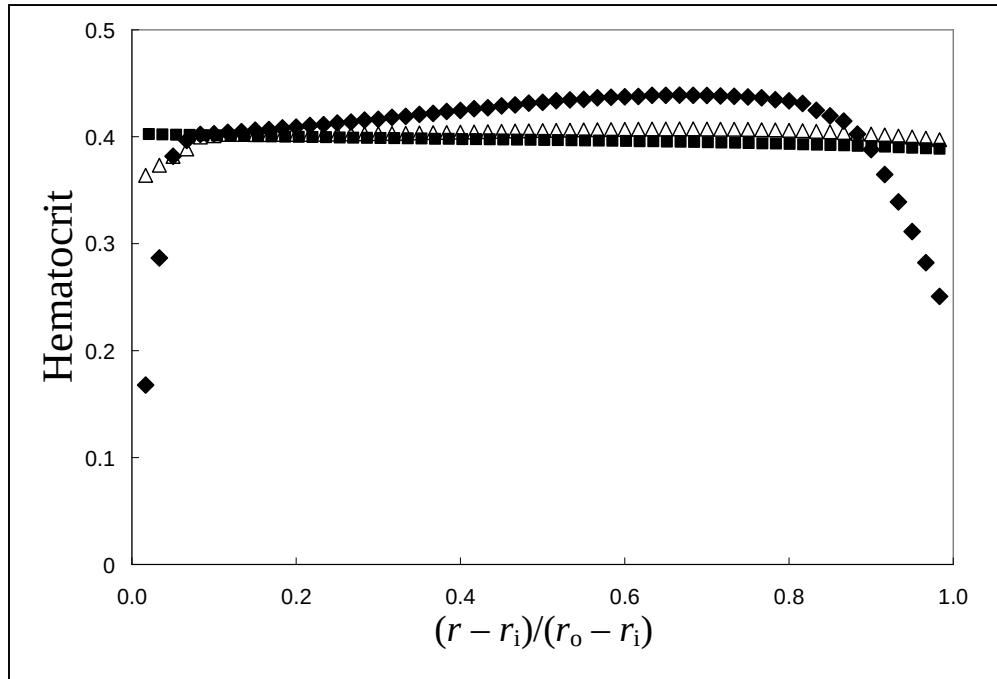


Figure 5.6. Hematocrit profiles as a function of fluid gap radius as calculated from the corresponding velocity profiles in Figure 5.4. For the RBC suspension in the albumin-saline medium (closed squares), aggregation does not occur. Therefore the suspension acts like a Newtonian fluid and hematocrit decreases slowly with increasing radial position. For the RBCs in plasma (open triangles), there is an increase in hematocrit towards the center of the gap as the RBCs pull away from the walls and a thin layer of plasma appears. This plasma layer appears smaller at the outside wall of the gap. For the RBC suspension containing Dextran (closed diamonds), the cell depleted layer is approximately equal at both the inner and outer walls of the gap.

In the case of the RBCs in albumin-isotonic saline, no RBC aggregation occurs at any shear rate and this is reflected as only very slightly non-Newtonian fluid behavior due to RBC deformation changes over a limited shear range. For RBCs in plasma, RBC

aggregation becomes increasingly important as the shear rate is lowered from approximately 10 s^{-1} . Aggregation will happen at 1.93 s^{-1} , within the range of shear rates present in Figure 5.5. Therefore, non-Newtonian fluid behavior starts to occur as is demonstrated in the velocity and hematocrit profiles as wall slip and inhomogeneous particle distributions. The addition of Dextran 110 makes the RBC aggregation markedly increased over that in blood at the same shear rate. The hematocrit profiles shown in Figure 5.6 are therefore reflecting the effect of RBC aggregation on the steady flow patterns in the viscometer. This point is further proven from the data in Figure 5.7a, where the measured normalized velocity profiles in the fluid gap are from RBCs suspended in plasma containing Dextran sheared at two different inner surface rotation rates. The higher rotation rate velocity profile looks closer to that of a Newtonian fluid profile in the central region of the gap and is more regular near the chamber walls than that for the lower rotation rate where aggregation occurs more strongly, again showing that RBC aggregation has an impact on the velocity and hematocrit profiles. Figure 5.7b shows the corresponding hematocrit profiles. Note the significant RBC depletion at the walls for the lower rotation rate. The results clearly indicate that the particle distribution across the gap is not uniform and therefore there must be radial migration of the cells across flow streamlines.

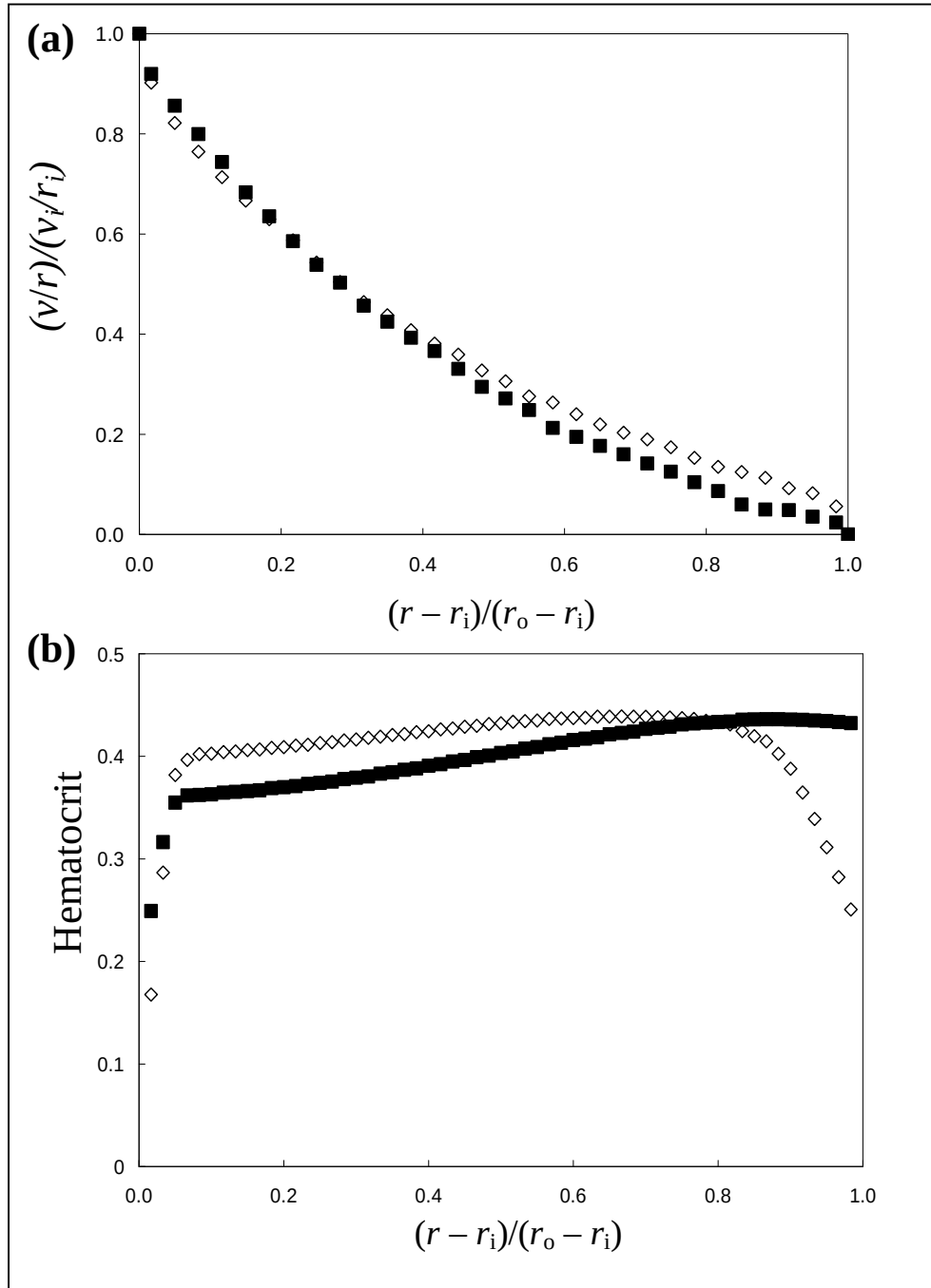


Figure 5.7 (a) Normalized velocity divided by radius as a function of normalized gap radius for RBCs with Dextran at two different rotation rates. The aggregation of RBCs when blood is exposed to the lower shear rate is inferred by the larger variation from Newtonian fluid behavior and greater slip at the walls. (b) Hematocrit as a function of fluid gap radius showing a greater depletion of RBCs at the wall for the blood sample exposed to the lower shear rate.

The most significant difference between the three suspensions is the varying ability of RBCs to aggregate. The RBCs in saline do not aggregate at all. In this case, studies have been conducted experimentally and theoretically for small individual particles, both rigid and flexible, moving across streamlines for Poiseuille flow in a right-circular cylindrical tube and for Couette flow[7,16]. For concentrated non-colloidal suspensions, experiments and theory predict shear induced particle migration from regions of high shear to those of low shear[25]. Karnis and Mason[110] experimentally tracked the radial movement of a single deformable drop of a Newtonian fluid suspended in a miscible Newtonian fluid. They showed that the drop tended to migrate towards the center of the Couette fluid gap and that the characteristic time to reach this position was over 100 minutes. Theoretically, Chan and Leal[111] derived equations predicting that the motion of a single deformable drop in Couette flow, for the conditions of the Karnis and Mason experiments, would have an equilibrium position of 0.48 of the way across the gap (from the inner wall). For our conditions, and taking the RBC to be a drop whose interior is a Newtonian fluid of viscosity 10.1 mPa s (that of a 35% hemoglobin solution at 23 C [112]) and the suspending fluid viscosity as 1.21 mPa s, the equilibrium position is predicted to be at about 0.09 of the way across the fluid gap. The hematocrit distribution for the suspension of RBCs in albumin-isotonic saline is slightly non-uniform across the Couette flow space (Figures 5.6), with a maximum concentration near the inner wall that slowly decreases from 0.41 to 0.39 as the radial position moves towards the outer wall. From [110], we can anticipate that the distribution was not at equilibrium over the experimental observation time of 13 minutes and with additional shearing

(sedimentation and thermal degradation effects precluded this) the hematocrit distribution would have evolved further. Nevertheless, our results are consistent with what would be expected from hydrodynamic effects causing radial particle migration, even when we take into account that our RBC suspension did not contain just a single drop, the RBC unstressed shape is not spherical, and it has a viscoelastic membrane as its outer surface. The features which support these expectations are that the maximum concentration occurs near the inner wall and decreases with increasing radius even though the shear rate is slightly increasing with radius.

For the RBCs in plasma, an additional force impacts the particle distribution—the ability of the RBCs to aggregate, or stick together upon collision into doublets, triplets and even large aggregates such as rouleaux. In plasma, the cells aggregate due to the protein fibrinogen and the extent of aggregation is dependent upon shear rate, occurring at shears below 10 s^{-1} . The increased aggregation is reflected in the steady state sedimentation rate of the suspension: for $H \sim 0.40$ at room temperature and in a vertical tube of diameter 1 mm the RBCs in 0.5% albumin-isotonic saline settle at a rate of 0.32 mm/hr. The RBCs in plasma, however, settle much faster at 4 mm/hr[99]. An additional effect is that the suspension should reach equilibrium particle distribution much more quickly than for the RBCs in saline, well within the experimental observation time. The torque reading from a GDM viscometer supports this assertion, since it reaches a steady value after approximately 7 minutes of Couette flow. The interparticle force at work causing aggregation would also cause the RBCs near the walls to have unbalanced forces on themselves, which would instigate a collapse of the RBCs upon themselves and leave

the regions near the walls to be very deficient in cells. The forces near the center of the gap, however, would be much more symmetrically distributed in the radial direction and so the hematocrit should be more uniform. Experimental observations cited earlier also indicate a RBC-deficient region near the walls. Our data for the RBCs in plasma support these expectations and it appears that the RBC-deficient region at the inner wall is larger and more deficient in RBCs than the sub-pixel region near the outer wall.

When Dextran 110 is added to the suspending plasma, aggregation increases due to enhanced interparticle attraction induced by the Dextran molecules. For instance, RBCs in saline containing 1% Dextran 110, diluted 10% with plasma has a sedimentation rate of 50 mm/hr[99], much faster than the sample with plasma alone. Although the faster sedimentation rate would cause the RBC interface at the top of the suspension to fall about 8 mm by the end of the data gathering time, the data is obtained over a 5 mm slice at the center of the MR coil 15 mm below the air interface and so the measured velocity is in the fan region of the sedimenting suspension. The velocity is measured below the clear region at the top and above the compacted sediment at the bottom, providing data at the initial bulk concentration throughout the experiment. As with the RBCs in plasma, the particle distribution can be assumed to be at equilibrium. With increased aggregation, no new forces are introduced, but effects from interparticle interactions should be amplified. This is indeed the case, with the hematocrit distributions showing enlarged regions of cell-depletion at both the inner rotating and outer stationary walls of the Couette. As a consequence of this wall cell depletion, the cell concentrations near the center of the gap are higher. One particularly interesting

feature of the hematocrit distributions when comparing RBCs in plasma to RBCs with Dextran are that the maxima fall at the same spatial location, $r-r_i/r_o-r_i = 0.683$, within the gap in spite of the difference in depletion zones near the walls. Figure 5.7 demonstrates the shear rate dependence of aggregation. At a higher shear rate, the velocity and hematocrit profiles become very similar to those for normal blood. This is because the nominal shear rate of 2.20 s^{-1} is near the upper limit for aggregate formation in normal blood, causing the regions of cell depletion to be small and for there to be less of a variation in particle distribution. When RBCs in plasma containing Dextran are exposed to their upper shear rate limit, where aggregates are more likely to be broken apart and cannot become as large, the cell depleted regions become smaller as well.

Ultimately, the noninvasive MRM data gives a clear connection between the spatial distribution of the RBCs and the spatially dependent material response. Figure 5.4 clearly shows the spatial dependence of shear rate for complex fluids in low Re flows in small channels, calling into question the assumption of nearly uniform shear rates for complex fluid flows in narrow gap Couette devices.

Conclusions

For the three suspensions studied, all samples exhibited some degree of non-Newtonian fluid behavior due to the presence of the red blood cells. With isotonic saline as a suspending medium, the small amount of shear thinning was mainly due to the deformability of the cells, which can become elliptical and elongated with increasing shear. There was a slight difference in our results for the preasymptotic regime studied

versus the theoretical analysis for a single deformable drop because there is more than a single particle in the suspension. The effective radial migration is retarded due to the high frequency of particle collisions in the suspension. By suspending the RBCs in plasma, and therefore adding fibrinogen, aggregation becomes the primary mechanism for shear thinning at low and moderate shear rates. Aggregation is a function of shear rate and the concentration of the macromolecules which enable aggregation. This dependence was demonstrated via the addition of the aggregation enhancing macromolecule Dextran to plasma and exposing it to varying shear rates. The velocity profiles clearly reflect the material response as a function of position across the fluid gap of the Couette. Studies extending these results have the potential to increase predictive modeling of particle distributions and increase understanding of classical Couette rheology, which has importance in both engineering and physiology. In engineering applications, understanding the dependence of particle distribution on aggregation and shear rate would enhance models for such applications as the design of microfluidic cell sampling and transport devices. Understanding RBC distribution inhomogeneity and wall depletion in the microvasculature has importance in physiology, especially as related to the Fåhræus effect[113]. Further MRM studies probing particle distributions in even narrower gap geometries could provide insight as to the impact of shear and RBC aggregation on transport issues in cardiovascular physiology.

IRREVERSIBILITY AND PARTICLE MIGRATION IN DILUTE SHEARED BROWNIAN SUSPENSIONS

Introduction

The dynamics of Brownian suspensions exposed to shear have been the subject of numerous experimental and simulation studies[114, 43, 115, 6, 8, 116-118]. However, these studies mostly track the particle phase[119, 9, 8], generally through optical methods, and are therefore limited by opacity or geometry. The unique ability of MRM to non-invasively obtain spectrally resolved particulate and suspending fluid time-dependent displacement data, as well as spatially resolved bulk velocity, makes it a novel and ideal method that can relate transport issues and microstructure in opaque colloidal suspensions[100, 13, 120]. Here, pulsed gradient spin echo (PGSE) magnetic resonance (MR) techniques are applied to provide direct and simultaneous measurement of the propagator of motion[39, 3] and the diffusivity[55] of both the particle and suspending fluid phase in a dilute ($\phi < 0.10$) Brownian hard sphere model suspension undergoing shear flow in a 1 mm diameter capillary. The use of “MR active” 2.44 μm diameter model hard sphere core-shell particles, which consist of a liquid hexadecane core and a hard outer poly(methylmethacrylate) (PMMA) shell[58, 7, 61, 65], allowed differentiation between the particulate and fluid phases of this multi-phase flow system due to the spectral resolution achievable with PGSE techniques. To our knowledge, no such measurements have been reported before. The results indicate the presence of particle migration inward towards the center of the capillary due to the combination of

the probability of displacement, the propagator, showing an increased probability of finding the colloidal particles at higher velocities and MR velocity imaging showing a parabolic or nearly parabolic bulk velocity profile characteristic of Poiseuille flow where the highest velocity streamlines are located at the centre of the capillary[6]. In addition, dispersion coefficients measured via flow-compensated PGSE as a function of observation time for the Brownian particles indicate the onset of irreversible dynamics with increasing total strain[6]. Particle migration and irreversible dynamics are generally not expected to occur in dilute Brownian suspensions and are therefore not considered in the modeling of flow systems. Particle migration is expected in concentrated non-colloidal systems[42, 25, 29] and recently optical experiments have indicated this effect occurs in concentrated, and possibly even dilute, Brownian suspensions as well[8, 118]. The presence of chaotic particle dynamics leading to irreversibility has been observed in only concentrated non-Brownian suspensions[9, 37]. Evidence of these effects, as indicated by the data presented, exhibits the importance of many body hydrodynamics in dilute Brownian suspensions and shows the applicability of chaos theory and non equilibrium statistical mechanics methods to model these systems.

Residence Time Distributions

In the context of chemical engineering, transport and mixing in reactors are of particular interest, especially bioreactors which are complicated by the presence of cells that are generally on the μm radius size order of a colloidal particle. The transport in many chemical reactors is dependent upon advection dominated mixing, which in turn controls the mass flux through the reactor. In practice, non-ideal behavior is often

exhibited, due to inadequate mixing and non-ideal flow patterns, which impact the reactor efficiency and performance. This non-ideality leads to there being a distribution of residence times. The residence time distribution statistically characterizes the mixing in the reactor and gives a measure of the degree of non-ideality. Traditionally, the RTD is measured through the introduction of a tracer into the system, and it can be difficult finding a tracer which will adequately model the true behavior of the reactant. The tracer must be non-reactive, easily detectable, and soluble in the reacting mixture with similar physical properties. However, the propagator has a convenient connection to the residence time distribution (RTD) of a chemical reactor[121] and with NMR, the tracer is the molecule itself. If the velocity distribution does not change with time, the propagator has a direct correlation to the RTD.

$$N(L,t)dt = \bar{P}(v_z, \Delta)dv_z \quad (6.1)$$

Where L is the reactor length and is considered to be the mean distance traveled by the spins over the observation time.

$$L = v_{z,ave}\Delta \quad (6.2)$$

The residence time of the spin t is related to the velocity through,

$$t = v_{z,ave} \Delta / v_z \quad (6.3).$$

Therefore, as long as the velocity is steady during the observation time Δ , MRM can provide information about mixing in reactors in the language of traditional chemical engineering residence time distributions[122].

Materials and Methods

Colloid Construction/ Sample Preparation

The core-shell latex particles were constructed using the method of Loxley and Vincent[58]. Hexadecane, poly(methylmethacrylate) (PMMA) MW 350,000, and poly(vinyl alcohol) (PVA) MW 95,000, 95% hydrolyzed were purchased from Fisher Scientific. Dichloromethane and acetone of analytical quality were used, as well as deionized water. An oil phase containing 3.0 g of the polymer PMMA, 60 ml of the volatile solvent for the polymer dichloromethane, 3.8 ml of another volatile solvent acetone and 5 ml of the poor solvent hexadecane was prepared. The oil phase was added dropwise to 80 ml of a 2% aqueous solution of PVA. Under constant high shear stirring, an oil-in-water emulsion was created. The speed of the mixing during this step determines the size of the oil droplets and therefore the final size of the microcapsules. As the volatile solvent starts to evaporate from the system, phase separation of the polymer occurs within the oil droplets and the polymer-rich phase migrates to the droplet interface. The dichloromethane continues to evaporate from the polymer-rich phase at the interface and a hard PMMA shell results. Figure 6.1, redrawn from [58] diagrams the encapsulation process.

A Heidolph Silent Crusher M homogenizer was used in the emulsification. To get the desired particle size of 2.5 μm diameter a shear rate of 12,000 rpm was used for a period of one hour. The suspension was then mixed with additional 120 ml of PVA solution and allowed to stir gently overnight under a fume hood, ridding the suspension of any remaining solvent. The resulting microspheres are short range repulsive due to the

residual presence of the short chain PVA molecules adhered to the surface of the hard shell and exhibit a hard sphere type behavior, as demonstrated in [65] where the volume fraction dependence of the diffusion coefficient was found to be roughly consistent with the hard sphere model, $D_{app} = D_o(1 - k\phi)$ with k found to be 1.6. The theoretical particle fraction of the resulting suspension is by weight $\phi = 0.04$.

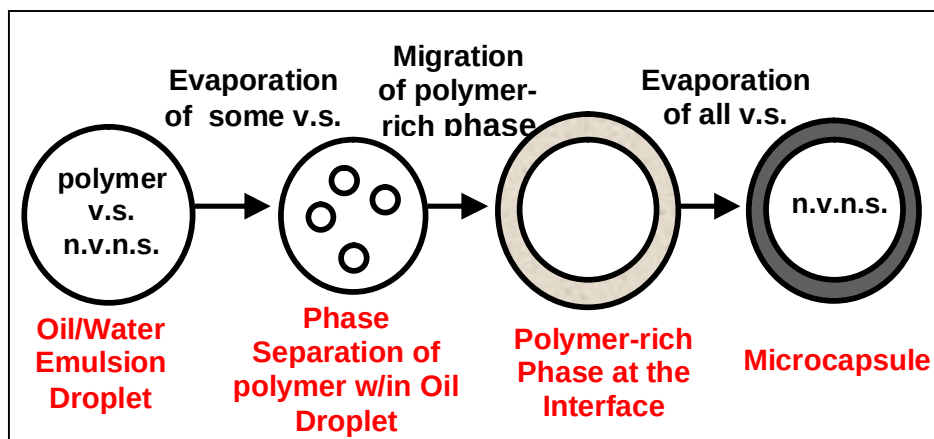


Figure 6.1. Schematic of the steps involved in the encapsulation process: n.v.n.s. is a non-volatile, non-solvent and v.s. is a volatile solvent.

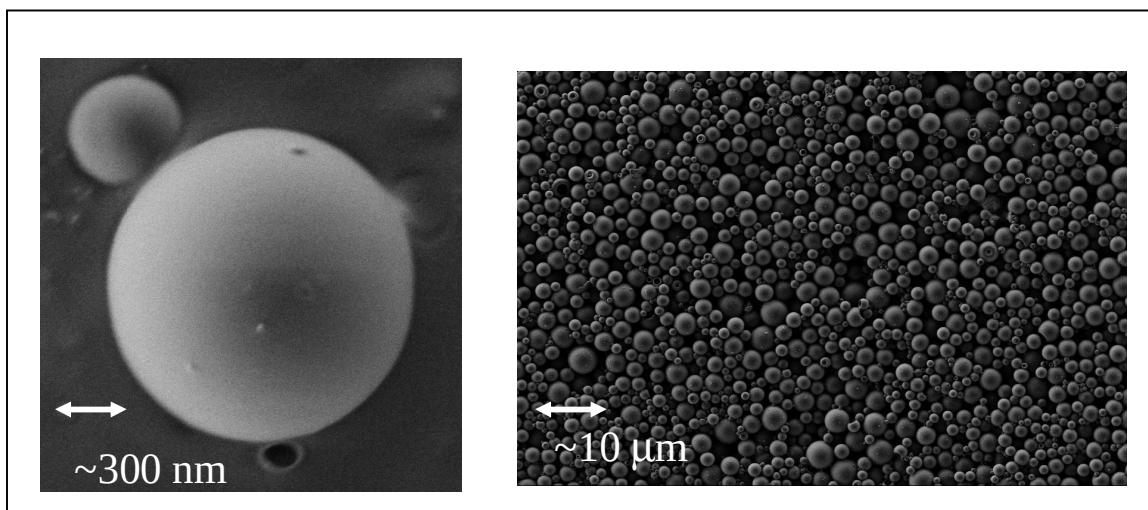


Figure 6.2. Field Emission Microscope (FEM) images of core-shell particles with a hexadecane core and a poly(methyl methacrylate) hard shell. The average particle diameter is $2.43 \pm 0.32 \mu\text{m}$ [courtesy of E.O. Fridjonsson].

This suspension was then centrifuged with a Sorvall RC 5C high speed centrifuge at 3,000 rpm for 10 minutes and 8,000 rpm for another 10 minutes. Since the particles have a slightly lower density than the suspending fluid, half of the lower dilute phase can be removed and the remaining concentrated upper particle phase re-suspended to produce a final particle fraction of $\phi = 0.08$ by weight. The resulting suspension had an average diameter of $d = 2.44 \pm 0.32 \mu\text{m}$ and the particle size distribution is shown in Figure 6.3.

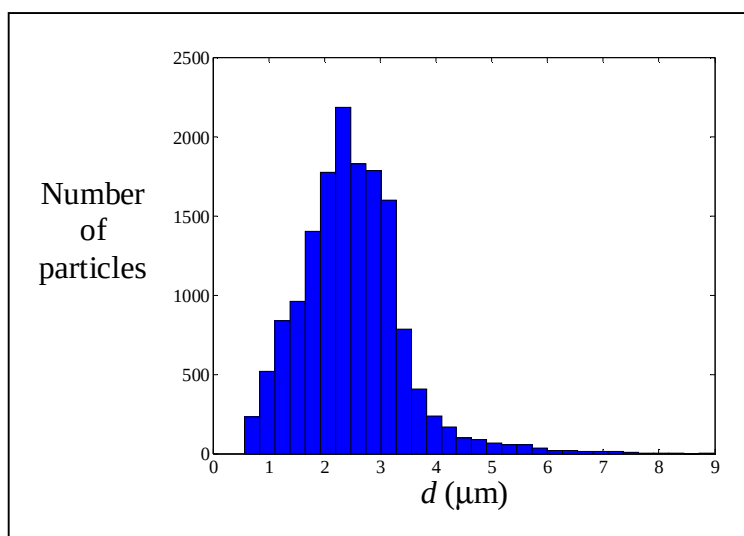


Figure 6.3. Core-shell particle size distribution showing an average diameter of $d = 2.44 \pm 0.32 \mu\text{m}$

The very small fraction of the MRM signal that actually arises from the hexadecane core oil due to the small volume fraction of particles in suspension, as well as the small resonant frequency difference between the oil and water (~ 750 Hz) causes the spectral peak of the suspending water to overwhelm the oil peak. To overcome this difficulty, a paramagnetic spin-lattice relaxation (T_1) enhancing agent, Magnevist, was added at a concentration of 0.0117 ml/1 ml of suspension, causing the suspending water to have a T_1 relaxation time much shorter than that of the oil. Due to the hard shell of the

model colloidal particles, the relaxation enhancing agent does not affect the oil relaxation. During the experimental observation time Δ of the MR PGSE sequence used to measure probability of displacement, most of the water signal disappears due to relaxation while the oil signal remains unaffected. The oil spectral peak is therefore no longer obscured and the dynamics of both the oil and the water may be probed simultaneously. The suspension was then de-gassed under vacuum overnight with constant stirring to remove any entrained air which would disrupt the MRM measurements by introducing susceptibility effects and altering the flow dynamics. The particle density is slightly less than the fluid density, causing a slow creaming. Since the timescale of the creaming is the order of days and would therefore have negligible effect on the experimental measurements, no attempt was made to density match the particle to the fluid, but the suspension was well-mixed before being pumped into the flow loop.

Capillary Flow System

The capillary flow system consisted of a glass capillary with a 1 mm diameter ID and a 10 cm length. The capillary was fixed inside a 5 mm thick-walled NMR tube which stabilized the flow system during loading and unloading from the magnet and eliminated vibration artifacts from the MR measurements. The capillary attached directly at each end to a length of tubing which then fitted to a syringe pump. The capillary was centered within the homogeneous magnetic field region of a 5 mm radio frequency coil, approximately 30 mm from the capillary to tubing connection.

MRM Methods

The MRM experiments were performed on a Bruker Avance DRX spectrometer attached to 250 MHz superconducting magnet. Gradient amplifiers, a Bruker Micro5 gradient probe, producing magnetic field gradients with a maximum strength of 1.7 T/m, and a 5 mm internal diameter radio frequency coil was used for all experiments. The Bruker software package Paravision acquired all of the MR data, while data analysis was conducted using Matlab® and Prospa® software.

The velocity image was acquired using a standard imaging pulse sequence superimposed with a PGSE bipolar gradient pair, which encodes for displacement within each pixel of the image (see Chapter 3, Figure 3.8). Due to acquisition of the echo signal under influence of a position encoding magnetic field gradient, the read gradient G_{rd} , spectral resolution is lost. The resulting image shows a composite velocity of both the oil and the water signal and represents the bulk velocity for the suspension. Three PGSE pulse sequences were also used for this study, a Hahn echo sequence (see Chapter 3, Figure 3.7), a stimulated echo sequence and a flow compensated stimulated echo sequence (see Figure 6.4a and b, respectively). The stimulated echo sequence is often used for samples with a short T_2 relaxation time or where T_2 relaxation greatly affects the signal, as for long diffusion times Δ . Due to the restriction of the core oil within the hard PMMA shell of the particle, the oil T_2^* was quite short. Therefore, most of the experiments were conducted using the stimulated echo sequence. For some experiments where Δ was shorter, the spin echo was used, yielding similar results. The PGSE

sequences retain spectral resolution which allows for the measurement of both the particle core oil and the suspending fluid dynamics.

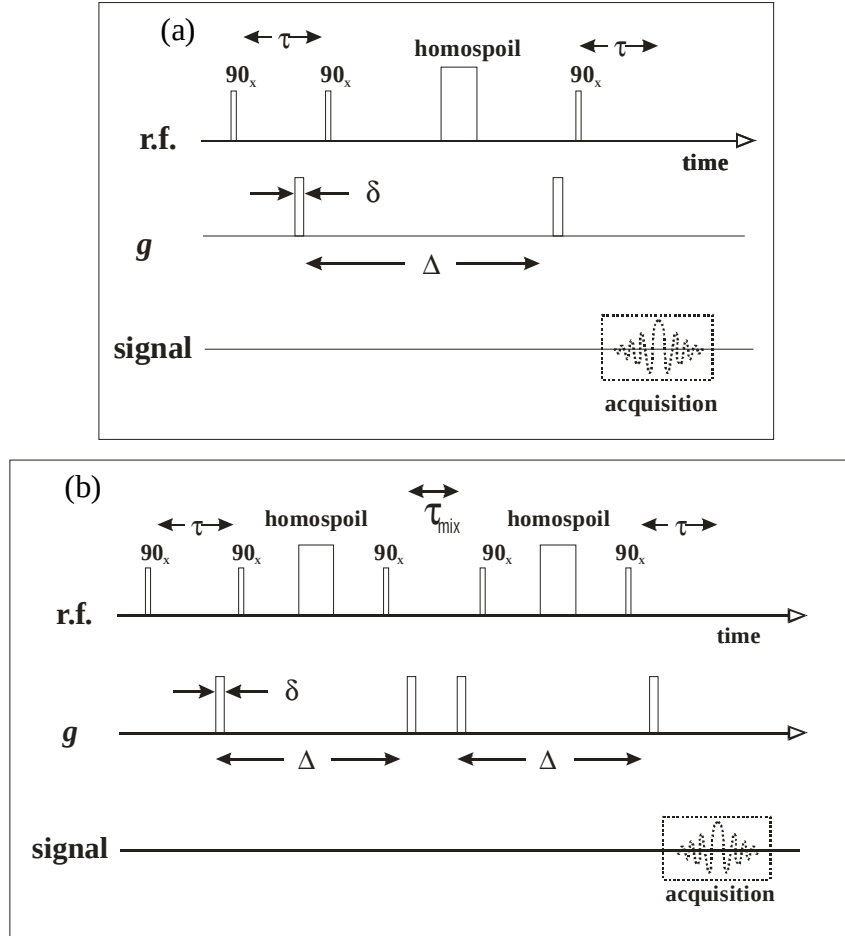


Figure 6.4. (a) Pulsed gradient spin echo pulse sequence with a stimulated echo. (b) Flow compensated PGSE sequence with a stimulated echo.

Six flow rates were studied, corresponding to particle Reynolds numbers

$$Re_p = \frac{\rho_f a^2 \langle \dot{\gamma} \rangle}{\mu_f} \text{ ranging from 3.4 to 11.5, particle Peclet numbers}$$

$$Pe_p = \frac{a^2 \langle \dot{\gamma} \rangle}{D_{SE}} \text{ ranging from 24 to 79, tube Reynolds numbers } Re_t = \frac{\rho_f R \langle v \rangle}{\mu_f} \text{ of 0.53}$$

to 1.77 and tube Peclet numbers $Pe_t = R\langle v \rangle / D_w$ ranging from 227 to 556, where the average shear rate for flow in a capillary of diameter R is $\langle \dot{\gamma} \rangle = \frac{3}{4} \frac{V_{\max}}{R}$. Full propagators, or probabilities for spin displacement, were acquired, but the bulk of the experiments utilized the relationship between the first 30% of the echo attenuation and mean squared displacement to return a dispersion coefficient as a function of Peclet number, strain or observation time Δ .

Results and Discussion

The velocity image in Figure 6.5 shows the composite velocity profile for a $\phi = 0.08$ core-shell suspension flowing in a 1 mm diameter capillary. The composite velocity is the bulk fluid velocity, a combination of the particle and suspending fluid velocities.

$$V_c = (1 - \phi)V_f + \phi V_p \quad (6.4)$$

Due to acquisition of the data under the presence of the read gradient, a standard MR technique to obtain spatial resolution termed frequency encoding shown in Chapter 1, Figure 3.8, the core oil and suspending water are not spectrally resolved. It is possible to obtain spectrally resolved images via Chemical Shift Imaging[3] using pure phase encoding, but not only is the method time-consuming, it was actually desired to obtain the bulk or composite suspension velocity. The corresponding velocity profile can then be fitted theoretically to determine the macroscopic rheological response of the suspension.

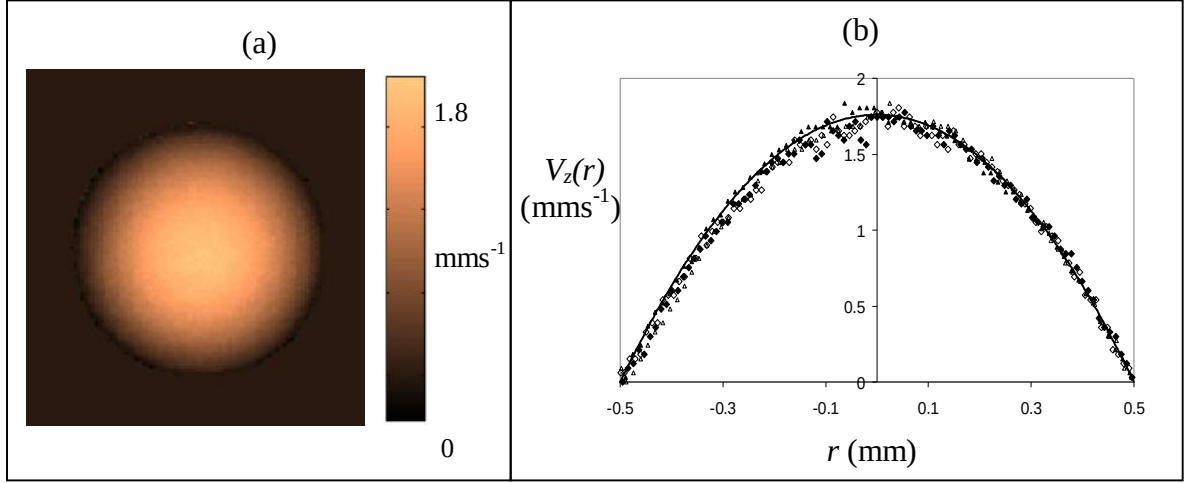


Figure 6.5. Composite axial velocity $V_z(r)$ for $\phi = 0.08$ core-shell particle suspension flow in a 1 mm diameter capillary with an average velocity $V_{ave} = 0.88 \text{ mm s}^{-1}$ ($Re_t = 0.88$, $Re_p = 5.7$). (a) Image of the spatial distribution of velocity in the plane perpendicular to flow with $\sim 14 \times 14 \text{ } \mu\text{m}$ resolution. (b) Velocity as a function of radius across various capillary diameter (symbols) and the parabolic velocity profile $V_z(r) = V_{\max} \left(1 - \frac{r^2}{R^2}\right)$ for Poiseuille flow (black line).

Figure 6.5 demonstrates that a parabolic velocity profile, expected for Poiseuille flow in a capillary, fits the data in a reasonable manner.

$$V(z) = V_{\max} \left(1 - \frac{r^2}{R^2}\right) \quad (6.5)$$

There is a possibility of seeing power law behavior $V(z) = V_{\max} \left(1 - \left(\frac{r}{R}\right)^{\left(\frac{1}{n}\right)+1}\right)$ in more

concentrated hard sphere colloidal suspensions, and preliminary experiments have shown signs of this in core-shell suspensions at higher volume fractions. At these dilute concentrations, however, this behavior is not seen and the suspension has been determined to behave as a Newtonian fluid.

Turning now to the ability of PGSE NMR to retain spectral resolution, the probability of displacement, or propagator, for both the core oil and the suspending fluid was measured simultaneously, as shown in Figure 6.6a.

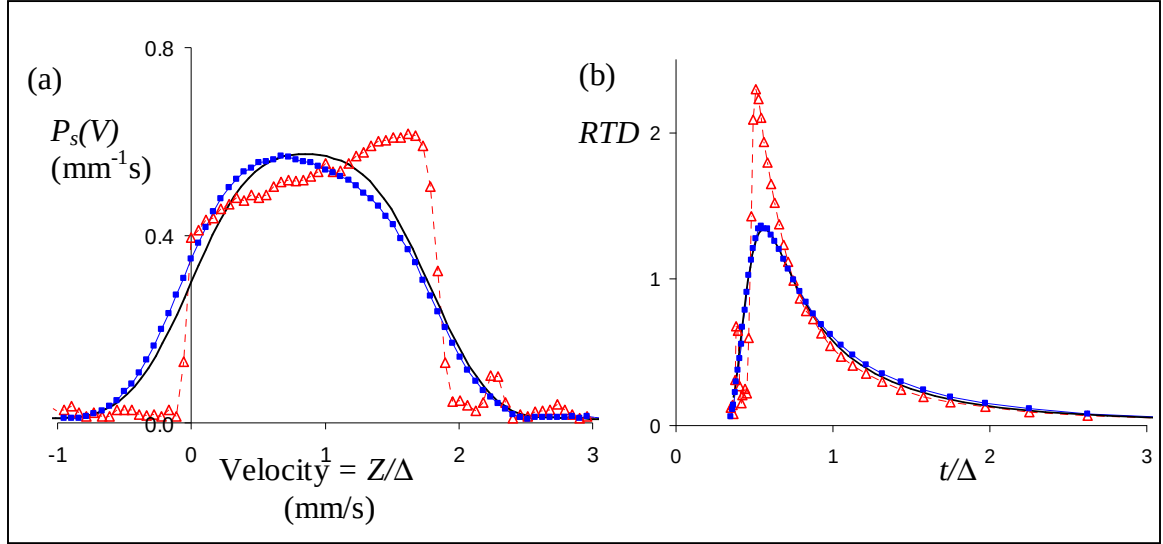


Figure 6.6. (a) Propagators for water (black line) and $\phi = 0.08$ suspension (blue closed squares are the suspending water and red open triangles are the core oil) flowing at $V_{ave} = 0.88 \text{ mms}^{-1}$ ($Re_t = 0.88$, $Re_p = 5.7$, $Pe_t = 376$, $Pe_p = 39$) over an observation time $\Delta = 30 \text{ ms}$. The order of magnitude differences in D_w and D_{SE} gives the particle propagator much sharper edges. (b) The corresponding residence time distributions.

A propagator was also measured for pure water flowing in the capillary (the black line) and is a hat function, as expected for Poiseuille flow since there is an equal probability for every velocity from 0 to v_{max} . Due to diffusion occurring during the finite observation time, the edges are softened and the final shape is the convolution of the velocity probability distribution hat function and the molecular diffusion probability distribution Gaussian. In contrast, the propagator for the suspending fluid, which is also water, is slightly skewed towards slower velocities. The widths of the propagators are very similar, indicating that a similar amount of water molecular diffusion is occurring. The

particle oil propagator however is strikingly different. The edges of the propagator are much sharper due to several reasons: the slower self-diffusion of hexadecane $D_o = 4.6 \times 10^{-10} \text{ m}^2 \text{ s}^{-1}$, the restriction of the oil within the hard shell of the particle and the small Stokes-Einstein diffusivity for 2.44 μm diameter particles.

$$D_{SE} = \frac{kT}{6\pi\mu a} = 1.76 \times 10^{-13} \text{ m}^2 \text{ s}^{-1} \quad (6.6)$$

The observation time Δ was 30 ms for these experiments, which is short enough that the largest impact is most likely from restricted diffusion of the oil molecules within the particles[65]. In addition, the particle oil propagator appears to be much noisier than the suspending water propagator. This can be explained by realizing that within the flow field, the particles are constantly fluctuating about their average value, due to hydrodynamic and interparticle interactions while the velocity fluctuations in the continuous suspending phase are more damped by viscosity over the measurement scale. The most dramatic observation however is the skewing of the particle oil propagator towards higher velocities. There is a higher probability of finding an oil molecule at a higher velocity. The root cause of this shape can be extracted by realizing that the width of the propagator, when taking into account the different diffusion properties, implies that the range of velocities of the particle oil phase and the suspending water phase is the same. The skewing of the propagator towards higher velocities is therefore due to the spatial position of the particles on their streamlines. Since the higher velocities are known to occur near the center of the capillary, as demonstrated by the parabolic velocity profile in Figure 6.5, it is clear that the particles have undergone shear-induced migration towards the center of the capillary. Shear-induced particle migration is well documented

for non-colloidal and concentrated suspensions in systems where a varying shear rate is present[2, 29, 42, 123, 124]. Normal stresses cause a preferential distribution of particles in the shear field[38, 29, 125]. The dynamics of dilute Brownian suspensions however is not extensively covered in the literature. Only recently has experimental evidence from optical studies shown particle migration for Brownian systems[8, 118] and for non-colloidal dilute suspensions[35]. In order to compare our results directly with these existing studies, the propagator was combined with the velocity imaging data to obtain a particle concentration profile as a function of radial position as shown in Figure 6.7.

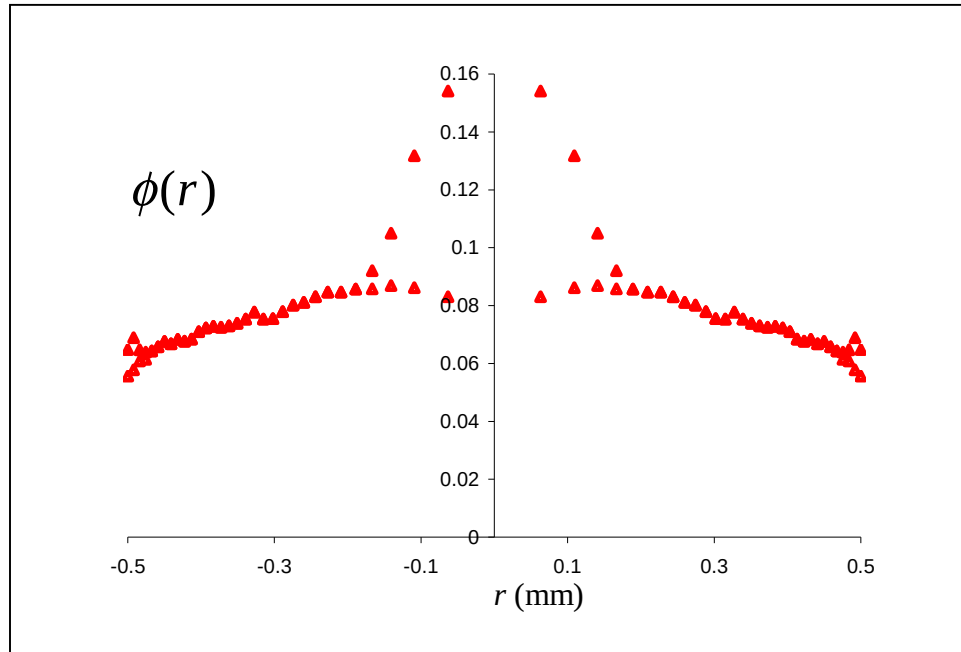


Figure 6.7. Volume fraction of core oil as a function of radial position, $\phi(r)$ for a core-shell suspension with an average volume fraction $\phi_{ave} = 0.08$ flowing in a 1 mm diameter capillary at $V_{ave} = 0.88 \text{ mm s}^{-1}$. The volume fraction was mapped to radial position using the data in Figures 6.5 and 6.6a. The open triangles are for the unaltered propagator in Figure 6.6a, while the closed triangles account for propagator signal above the maximum velocity and below zero as analyzed in the text and shown in Figure 6.8.

Since the velocity field is known, the radial position of each velocity measured in the propagator can be calculated. In addition, the area of the propagator is normalized to one during the data analysis to be consistent with the definition of a statistical normalized probability distribution, and represents the total amount of oil signal present. Since a fixed $\phi = 0.08$ suspension is being pumped through the system, the average amount of particle oil present per volume is known and the area under the propagator can be rescaled to represent a volume fraction. The volume fraction at each velocity was then mapped to each radial position.

Due to the geometry of the cylindrical capillary and the resulting quadratic dependence of velocity on radius (6.5), velocity resolution achieved in the propagator is not equivalent to the radial spatial resolution. The spatial resolution was the coarsest near the center of the capillary, making it difficult to discern the exact extent of peaking which occurs there. Since diffusion causes the propagator to register velocities that are higher than dictated according to the known volumetric flowrate, some signal has been lost near the maximum velocity causing a misregistration of the particle concentration near the center of the capillary, where the fastest velocity occurs as indicated by the open triangles in Figure 6.7. Particle oil appears to be traveling faster than the maximum allowable velocity due to the broadening of the probability distribution by the oil diffusion. While this signal cannot be assigned to a radial position by solving (6.5), it must be accounted for in order to retain the full average volume fraction. The area missing from the rounded edges of the propagator due to diffusive broadening should be the same as that above the average velocity and below zero respectively. Therefore the area of the

propagator which was faster than maximum velocity and slower than zero velocity due to diffusion was reflected back into the bulk propagator. To test this process, it was applied to the pure water propagator, where it is known theoretically that without diffusion a hat function should and does occur as can be seen from the dashed line in Figure 6.8.

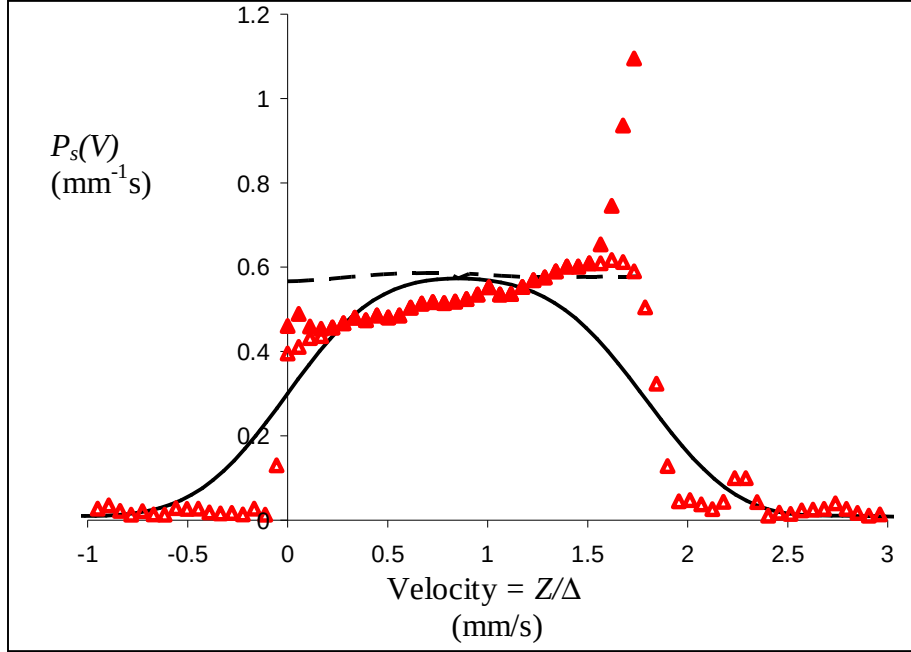


Figure 6.8. Propagators for water (black line) and particle oil of a $\phi = 0.08$ suspension (red open triangles) flowing at $V_{ave} = 0.88$ mm s^{-1} over an observation time $\Delta = 30$ ms. Altered propagators where signal registered as moving at a velocity faster than the maximum from the known flowrate and slower than zero has been reflected back into the bulk propagator for water (dashed black line) and particle oil (closed red triangles). The water shows the expected return to a hat function for Poiseuille flow in the absence of diffusion, indicating that this method should be valid for use on the particle oil propagator even though its exact shape is not known a priori.

The work of Frank *et al*[8] experimentally measures the concentration of hard spheres under flow in a rectangular capillary. Despite the fact that our experimental conditions do not exactly match theirs, the general shape of the concentration profiles

appear to agree, with the lowest volume fraction of spheres near the capillary walls, slowly increasing and peaking near the center. The primary difference between the experiments of Frank *et al* and ours is that their particles were slightly smaller at 2 μm in diameter, their lowest Peclet Number was 69 in contrast to the $Pe = 39$ in Figures 6.5 and 6.6, and their volume fractions were $\phi = 0.05, 0.22$ and 0.34 while ours was 0.08 . A later work by Semwogerere *et al*[118] has indicated that the entrance length required for fully developed flow is dependent upon Peclet number when Brownian forces are present. From their analysis, it is clear that our system did not have a sufficient entrance length to be fully developed at the Peclet numbers studied. The ratio of entrance length to channel radius L/a was 68 for our system, while Semwogerere *et al*[118] indicate that fully developed flow for a 0.22 volume fraction suspension occurs within approximately $L/a \sim 800$. Since a more dilute suspension would take even longer to develop, the results here definitely do not show fully developed flow and migration is still occurring. However, in comparison to both studies[8, 118], regardless of volume fraction, entrance length, or Peclet number, the channel positions at which the average volume fraction occurs corresponds to $\sim 25\text{-}30\%$ and $70\text{-}75\%$ of the distance across the channel. Even though our experimental geometry is cylindrical instead of rectangular, the radial positions at which the average volume fraction occurs in our system is $r = \pm 0.275\text{ mm}$, corresponding to 25% and 75% across the channel diameter as shown in Figure 6.7. Our results show that even at a short entrance length, significant migration has occurred and the profile would only develop a stronger peak at the center of the capillary if allowed to evolve further.

It has been noted previously that in dilute Brownian suspensions the viscosity may appear Newtonian due to limitations in measurement sensitivity, but that normal stresses are early indicators of the onset of non-Newtonian behavior[115, 114, 8]. Shear-induced particle migration in a capillary is a symptom of normal stresses. Through the use of spectrally resolved MRM techniques and model core-shell particles, this particle migration represents an experimentally accessible measure of the suspension microstructure. In dilute suspensions, where on the microscale the dynamics are quite complex, the macroscale viscosity may not reflect the true microstructure due to the difficulty of mechanically detecting non-Newtonian behavior. The velocity image in Figure 6.5 is a good example of this, as it appears to fit a parabolic Newtonian profile. However, a power law fit where $n=0.95$ could be said to fit as well. Shear-thinning, due to the microstructure being distorted by the flow faster than Brownian motion can restore it, has not manifest itself macroscopically in the image despite the microscopic forces clearly at work from the propagators in Figure 6.6a. Thus demonstrating that dilute colloidal suspensions qualitatively possess some of the same characteristic non-Newtonian flow behaviors as concentrated suspensions[1]. In fact, shear-induced migration was detected in even more dilute suspensions than the $\phi = 0.08$ suspension in Figure 6.6. Figure 6.9 shows propagators comparing a $\phi = 0.08$ suspension to a $\phi = 0.04$ suspension and the weighting of the particle oil towards higher velocities indicative of particle migration is still clearly evident. The $\phi = 0.08$ suspension propagators for the particle oil and suspending water in Figure 6.9 differ slightly from those in Figure 6.6, since they were measured during a different experimental run.

However, the appearance of the characteristic skewing of the particle oil propagator towards higher velocities demonstrates repeatability of these measurements and consistent observation of particle migration at $\phi = 0.08$.

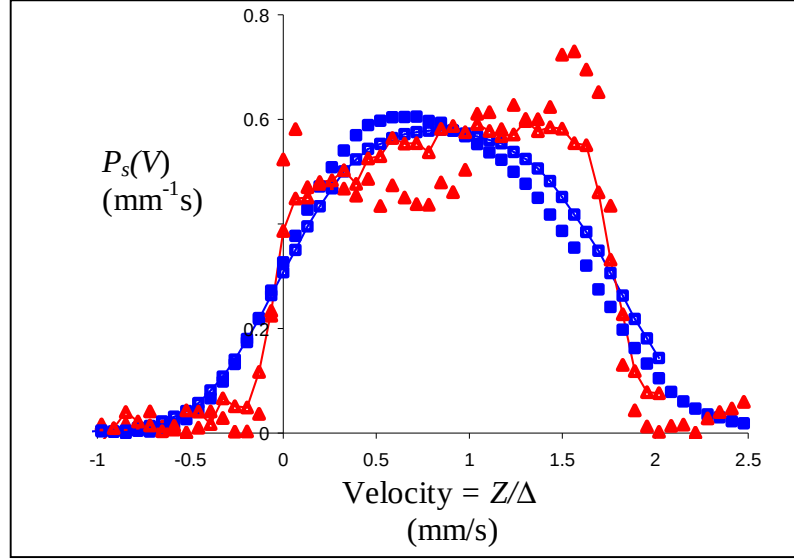


Figure 6.9. Propagators for a $\phi = 0.04$ suspension (open red triangles are the core oil and open blue squares are the suspending water) and a $\phi = 0.08$ suspension (red closed triangles are oil and closed blue squares are suspending water) flowing at $V_{ave} = 0.88$ mm/s ($Re_t = 0.88$, $Re_p = 5.7$, $Pe_t = 376$, $Pe_p = 39$) over an observation time $\Delta = 30$ ms.

The relative importance of hydrodynamic interactions, interparticle forces and Brownian forces differentiates a dilute suspension from a concentrated one and clearly, as our data demonstrates with regard to particle migration, dilute suspensions can exhibit the same macroscopic manifestations of these forces as concentrated suspensions. Various theories have been put forth to model shear-induced particle migration, including diffusive flux models[42, 34], as well as a suspension pressure balance model[29]. In the suspension balance model, the averaged equations of motion are used and include a temperature equation governing velocity fluctuations as discussed in Chapter 2.

However, the constitutive equations modeling the stress due to the presence of the particles is different than that used in Drew[24] and presented in Chapter 2. Despite the range of theoretical approaches in the literature, one generally agreed upon point is that normal stresses arise due to an asymmetry of the pair microstructure[114, 2].

The pair microstructure is represented by the pair distribution function $\xi(r)$ which analyzes the microscale interaction between a pair of particles and the impact such a collision has on particle trajectories. The conditional probability $P(x_o + r|x_o)$ of finding another particle center at $x_o + r$, given that a particle center resides at x_o , is the pair-particle probability distribution function. At large r , the particle positions are completely uncorrelated and $P(x_o + r|x_o)$ becomes the average particle density. The conditional probability is then normalized by the average particle density and is traditionally then called the pair distribution function $\xi(r)$. The form of this probability distribution gives insight as to the exact nature of the two particle collision and what net effect a collision has in reference to macroscopic phenomena such as normal forces. Collision in this context refers to particle interactions that are still mediated by lubrication forces in the thin fluid layers between particles at close contact. Batchelor and Green originally calculated $\xi(r)$ for a dilute suspension undergoing linear shear flow, considering only hydrodynamic interactions between two particles, and found it to be symmetric[32]. For perfectly smooth particles with no surface charge, binary particle interactions are symmetric and therefore completely reversible in time. For the model core-shell colloidal particles used in this study, however, the interparticle interaction is that of a

hard sphere, with short range repulsion due to the presence of a short chain polymer, polyvinyl alcohol, which adheres to the sphere surface during the encapsulation process.

In early experimental work, particle trajectories upon collisions under simple shear were investigated for polystyrene spheres suspended in aqueous glycerol containing various electrolyte concentrations, which controlled the interparticle force[33]. In the case of a slight repulsive force, a collision between a particle approaching a test sphere was shown to result in the sphere's final radial position slightly displaced from its initial position[33, 31]. More recent simulation work[35, 34, 38, 36, 37] analyzing pair distribution function has been in agreement with this conclusion. When a repulsive force is present, even a short range repulsion such as for ideal hard spheres, then particle interactions are no longer symmetric and a net anisotropic stress field is present within the flow field[38]. The same effect has been shown to occur due to roughness, *ie* any spatial irregularities that mar the surface of the smooth sphere[35, 34, 33]. The model core-shell particles used in this work are in general smooth, as can be seen in the Field Emission Microscope images in Figure 6.2, but there is a possibility that roughness could be having an impact. Surface roughness, even down to 10^{-4} of the particle diameter can impact the particle trajectory enough to cause crossing of streamlines upon collision[34]. In the case of $2.44\text{ }\mu\text{m}$ diameter particles, a deviation from surface smoothness of only $0.000244\text{ }\mu\text{m}$ would have an effect. However, FEM images, including those shown in Figure 6.2, indicate a significant degree of uniform smoothness of the particles. In Stokesian Dynamics simulations, roughness and a short range repulsive interparticle force are both modeled through the ad hoc addition of a repulsive force to the Langevin

equation. Either effect results in a depletion of bound pairs of spheres, or primary doublets. Doublets form when a sphere comes close enough to the test sphere so as to be trapped within a closed trajectory streamline at which point the spheres continually orbit each other. The presence of either roughness or a repulsive force precludes the entry of the sphere into these closed orbits, since the spheres never come close enough unless forced through Brownian motion or due to a many body interaction. The impact on $\xi(r)$ is a fore-aft asymmetry[35-37]. Gadala-Maria and Acrivos[123] were the first to provide evidence that concentrated suspensions develop an anisotropic structure when sheared and found $\xi(r)$ to be anisotropic and asymmetric under reversal of flow direction – fore-aft asymmetric. Transient responses have been found in both the normal stress response and the shear stress response for concentrated suspensions upon reversal of flow in a parallel ring geometry[126], indicating that the fore-aft asymmetry in the microstructure is not enough by itself to explain the transient response and some non-hydrodynamic force must also be present. As a sphere approaches a test sphere, its trajectory is not altered and the sphere may get as close as the range of roughness or repulsion will let it. There is therefore a higher probability of finding a sphere near a test sphere on the approaching, or higher velocity, side. Then, as the sphere passes the test sphere, it will not return to its original streamline, again because of the repulsive/roughness force and resulting in the generation of a normal stress. There will also be a decreased probability of finding a particle just on the receding side of the test particle, since most particles will have moved off their original streamline, and therefore the particle interaction has lost symmetry.

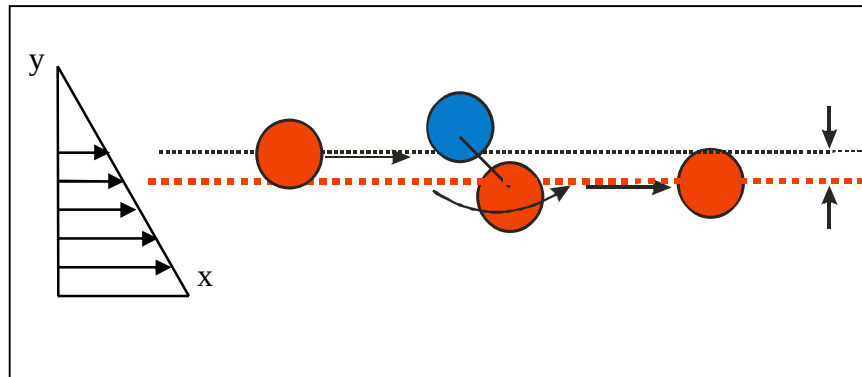


Figure 6.10. Asymmetric two particle interaction showing the net particle displacement in the y -direction that occurs when roughness or a repulsive force is present.

Influence on normal forces of the hard sphere interaction is caused by two factors: one is the depletion of particles downstream from the interaction, the asymmetry, and so there is a decrease in the total normal stress from the region on the receding side of the test sphere. Secondly the repulsive force causes a resistance when a sphere approaches a test sphere, contributing to the normal stress in the approach region. Both effects imply that the particles impart an additional stress on the fluid[38].

The model core-shell particles used in this study were narrowly distributed in size with a variation in diameter of only 14%, but were not perfectly monodisperse as can be seen in Figure 6.3. In capillary flow of a suspension where two different size populations exist, smaller particles can migrate to the edges of the capillary while larger particles occupy the center. For these particles however, there are not two distinct populations, so complete segregation would not be expected to occur. From the particle size distribution, the percentage of particles that are larger than one standard deviation from the mean particle diameter of $2.44 \mu\text{m}$ was found to be 14%. The amount of

propagator signal present at velocities where the oil volume fraction is higher than the average value of $\phi = 0.08$ is 40%. Even if all such larger particles, were to move to the center of the capillary, they would only represent only $(0.14/0.4)*100 \sim 34\%$ of the total particles in this region and so any particle separation due to polydispersity is deemed insignificant. The weighting of the propagator towards higher velocities is not due merely to the presence of the largest particles at the capillary center, but primarily to an increase in particle concentration from shear-induced migration.

The propagator itself contains other interesting information regarding the system dynamics. For example, in averaged transport theory, extra stress terms arise during the averaging process. These terms take into account fluctuations in the particle velocities $v'_p = v_p - \langle v_p \rangle$ or fluid velocities $v'_f = v_f - \langle v_f \rangle$ present in the system, as well as differences between the average velocities of each phase $\langle v_f \rangle - \langle v_p \rangle$ [24]. The form of these terms are akin to Reynolds stresses as seen in turbulent flows [19]. The NMR measurement is inherently an ensemble averaged quantity and the velocities obtained have been averaged over multiple time and length scales. A signal acquisition occurs for each value of the 128 q points collected. Each signal acquisition encodes for a displacement $1/q$ over the observation time $\Delta = 30$ ms and these acquisitions are then repeated 8 times each in order to increase signal to noise. One timescale is the average over the observation time, which corresponds to the measurement of the dynamics of a single spin ensemble with specific initial positions. Since the suspension is flowing, a new ensemble of spins enters the active region of the coil between every acquisition, which occurs on the order of the experimental repetition time, 4 seconds for these

propagators. The entire experimental time is on the order of one hour and since the signals are Fourier transformed in q to obtain the propagator, each velocity point contains data from the entire one hour acquisition. The velocities measured therefore are intrinsically averaged over time, space and realizations of the flow. The width of the water propagator at full width half maximum[3] shows a maximum velocity of 1.76 mm/s, as expected from the set volumetric flowrate delivered by the pump during the experiment. When the slower diffusion of the oil is accounted for, the maximum velocity of oil is also 1.76 mm/s, indicating that both the suspending water and the particle oil phase experience the same range of velocities. Therefore, the differences in average velocities between the fluid and the solid particle phase are merely due to their spatial location and not due to any intrinsic transport which may cause $\langle v_f \rangle - \langle v_p \rangle$ to have a value other than zero. This is a difficult quantity to measure, and to our knowledge has not been reported. Future studies on concentrated suspensions will focus on further elucidating this quantity.

As can be seen in Figure 6.6b, there is a distinct difference between the residence time distribution (RTD) for pure water flow and the suspending water and particle oil in the suspension flow. Higher peaking and a quicker decay around a short time t/Δ indicates that the majority of the oil particles are moving out of the “capillary reactor”, which in this case is the active region of the radiofrequency coil used to excite the sample and detect resulting signal. This corresponds to the skewing of the propagator towards higher velocities and the migration of the particles to the center of the capillary. The presence of inhomogeneous particle concentrations in dilute suspensions which are

expected to be homogeneous obviously changes reactor residence times and could negatively impact reactor efficiency. Such an effect may be of particular significance in sensors in which dilute suspensions flow and require interaction with assays on the channel walls.

Further insight into suspension microstructure can be obtained by looking directly at the echo signal, instead of Fourier Transforming to obtain a propagator, where the low q or first 30% of the echo attenuation holds information about effective diffusion or dispersion. Acquisition of data in the low q regime allows the use of fewer points and a shorter experiment time. The analysis consists of constructing Stejskal-Tanner plots, discussed in Chapter 3, section 3 where the slope of the linear region is the effective diffusion coefficient dependent on the experimental observation time Δ .

Figure 6.11a is the effective diffusion or dispersion coefficient as a function of average shear rate for the single PGSE sequence shown in Figure 6.4a. Both phases, pure water flow and the suspending water and particle oil of the suspension flow, exhibit much the same behavior. A linear dependence on shear rate is as expected for a Brownian suspension and the range of the effective dispersion coefficients is of the order of magnitude of $10^{-8} \text{ mm}^2\text{s}^{-1}$. The calculation of the dispersion coefficient from MR measurements assumes the traditional Einstein relation for the mean squared displacement where D_{eff}^* scales linearly with time. A linear dependence of the effective dispersion coefficient then demonstrates the quadratic dependence on velocity that is seen in the short time limit $t \ll a^2 / D_{SE}$ of Taylor Dispersion where the dispersion coefficient is represented by (2.37) in Chapter 2.

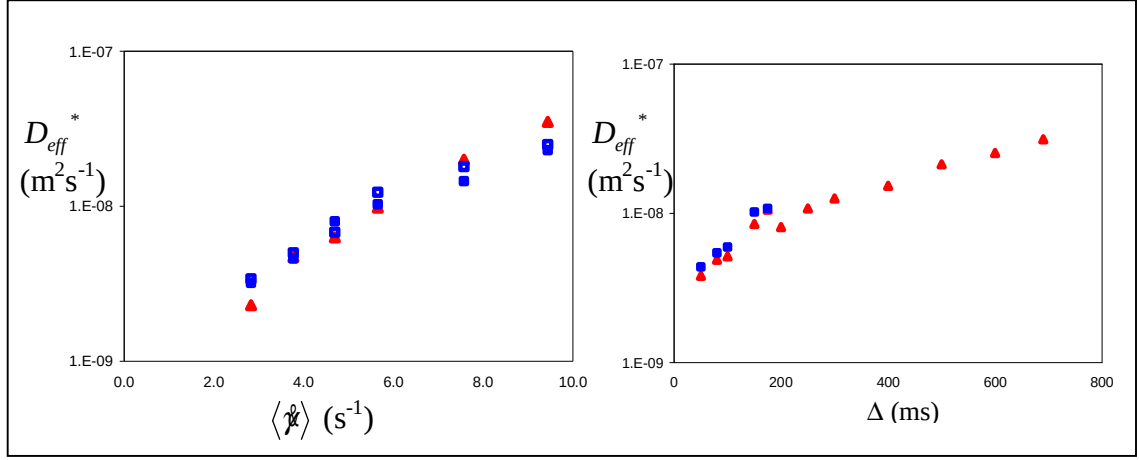


Figure 6.11. Effective diffusion D_{eff}^* for a $\phi = 0.08$ suspension measured using a single PGSE sequence (shown in Figure 6.4a) which is sensitive to the distribution of velocities for a displacement time. (a) D_{eff}^* for the suspending water (blue filled squares) and the particle core oil (red open triangles), as well as pure water (blue open squares) of $\Delta = 100$ ms as a function of average shear rate $\langle \dot{\gamma} \rangle = -\frac{4\langle v_z \rangle}{3R}$ which is directly proportional to Pe . (b) D_{eff}^* for the suspending water (blue filled squares) and the particle core oil (red open triangles) at an average shear rate $\langle \dot{\gamma} \rangle = 4.7$ s^{-1} as a function of Δ .

Figure 6.11b shows the increase of D_{eff}^* as a function of observation time Δ . Notice that due to the extremely short T_1 relaxation time of the highly doped water, values were only available for times up to 200 ms. This is a limitation, but not significant to the present results and discussion. Future experiments will seek to extend this range. The increase of D_{eff}^* with observation time for the single PGSE is again dominated by Taylor Dispersion and the distribution of velocities in the short time limit. The dispersion coefficient should keep increasing to the time independent value of the Taylor dispersion coefficient for this system $D = 2.2E-2$ m^2s^{-1} in the Taylor-Aris limit

$\Delta \ll R^2 / D_{SE} \sim 10^6$ seconds for the particles and $\Delta \ll R^2 / D_w \sim 10^4$ seconds for water, well beyond the MR experimental time limit imposed by T_1 relaxation.

It is difficult to discern any differences in the diffusive behavior of the two phases since the dominant reason for the phase spreading responsible for echo signal attenuation in these measurements is the velocity gradient, or distribution of velocities represented by the hat function of the parabolic Poiseuille velocity profile[95] as shown in the velocity images of Figure 6.5 and the propagators in Figure 6.6a. The use of a flow compensated PGSE sequence cancels the contribution of mean flow to the effective diffusion coefficient by use of two bipolar magnetic field gradient pairs as discussed in Chapter 3. It is as if the fluid were set flowing for a certain amount of time and then the flow reversed for the same amount of time. Any spin that has undergone an incoherent motion will not refocus to its original phase shift and its motion is irreversible. In the absence of flow, the single PGSE and the flow-compensated PGSE sequences (Figure 6.4a and b, respectively) will return the same value for the diffusion coefficient, when the factor of two due to twice the gradient application over time Δ in the flow compensated PGSE experiment is accounted for. Figure 6.12a shows D_{eff}^* as a function of Δ as measured using the flow compensated PGSE pulse sequence of Figure 6.4b in the absence of flow.

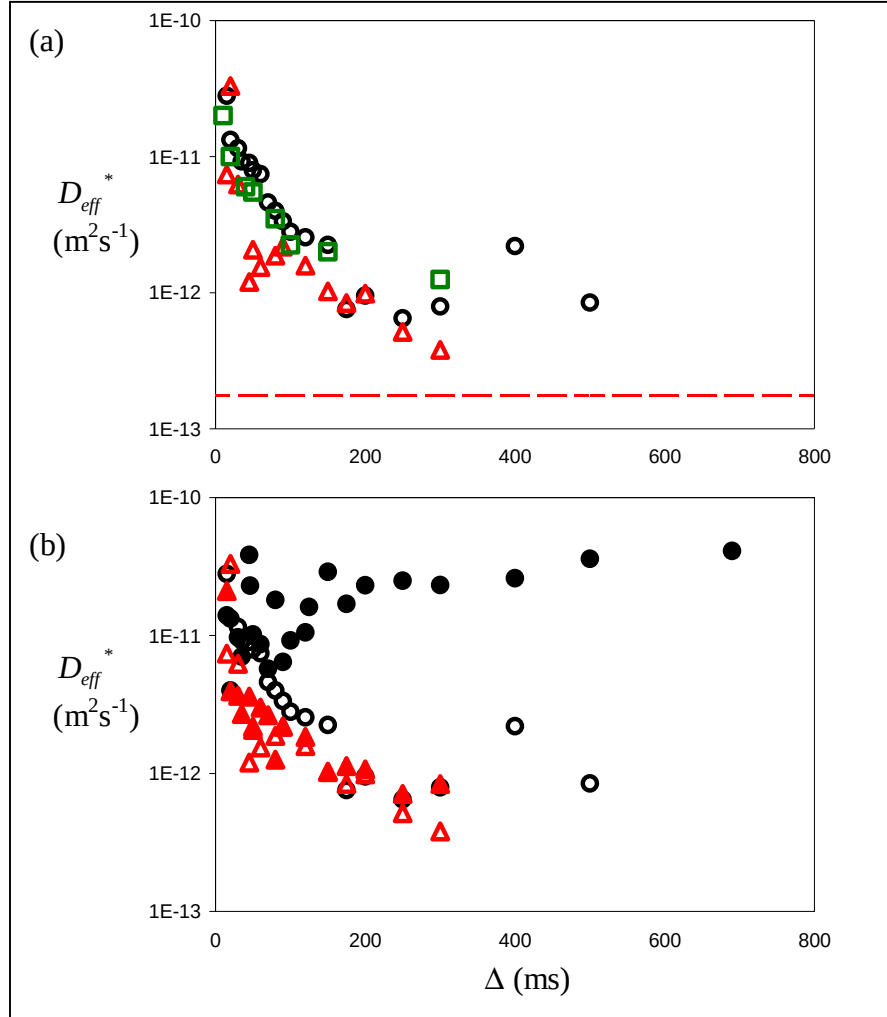


Figure 6.12. D_{eff}^* $\phi = 0.08$ suspension obtained using flow compensated PGSE sequence (Figure 4d), which measures only irreversible stochastic motions. (a) In the absence of flow D_{eff}^* for the particle oil as a function of observation time Δ in the z (black open circles) and y (red open triangles) directions, as well as the results obtained by Wassenius *et al*[65](green open squares), showing excellent agreement. The D_{eff}^* decreases with increasing time due to the dominant impact of oil restriction within the hard shell of the particle and slowly approaches the Stokes-Einstein diffusivity (dotted red line) (b) For an average velocity of 0.88 mm s^{-1} ($Re_p=5.7$, $Pe_p=39$) D_{eff}^* for the particle core oil as a function of observation time Δ in the flow direction z (black closed circles), in the velocity gradient direction y (red closed triangles), and again in the absence of flow.

In the absence of flow, the z and y directions exhibit a decrease in D_{eff}^* with increasing observation time. This is due to the restricted motion of the oil molecules within the hard shell of the sphere[127]. At a short enough time, the oil molecules diffuse freely with the self-diffusion coefficient of hexadecane $D_o = 4.6 \times 10^{-10} \text{ m}^2 \text{ s}^{-1}$. It is not possible to measure the hexadecane self-diffusion coefficient when the oil is confined within micron sized particles, as this would require submillisecond delta times, so such a measurement was made on the pure analytic quality hexadecane. As the observation time is increased, more and more of the molecules' motion is inhibited by the presence of the sphere walls, causing a decrease in the diffusion coefficient[65]. At still longer times, the oil molecules have sampled the entire pore dimension and the random motion of the colloidal particles themselves becomes increasingly important. In Figure 6.12a, D_{eff} slowly approaches the Stokes-Einstein diffusivity for a sphere of radius $d = 2.44 \text{ } \mu\text{m}$. These results compare well with those of Wassenius *et al*[65] using the same type and size of microcapsule as also shown in Figure 6.12a. With the imposition of flow, shown in Figure 6.12b, there is a dramatic change in the behavior of D_{eff}^* with respect to time. In the y direction, which is a combination of the velocity gradient direction r and vorticity direction θ ; $D_{xx,s}^*(\Delta) = D_{rr,s}^* \cos^2 \theta - D_{r\theta,s}^* \cos \theta \sin \theta + D_{\theta\theta,s}^* \sin^2 \theta$; the trend is the same as in the absence of flow. In the z or axial direction, however, D_{eff}^* decreases with Δ only at short times ($< 100 \text{ ms}$). This trend is quite noisy, due in part to particle fluctuations in the presence of a shear field, in stark contrast to the no flow and non-axial data. At 100 ms , D_{eff}^* suddenly begins to increase, indicating that some mechanism has

introduced an amount of irreversibility to the system. A motion which appears random over a timescale of 100 ms is apparent in the response of the particle phase dynamics to pressure driven shear flow. The same effect occurs for slower flowrates as well, as shown in Figure 6.13.

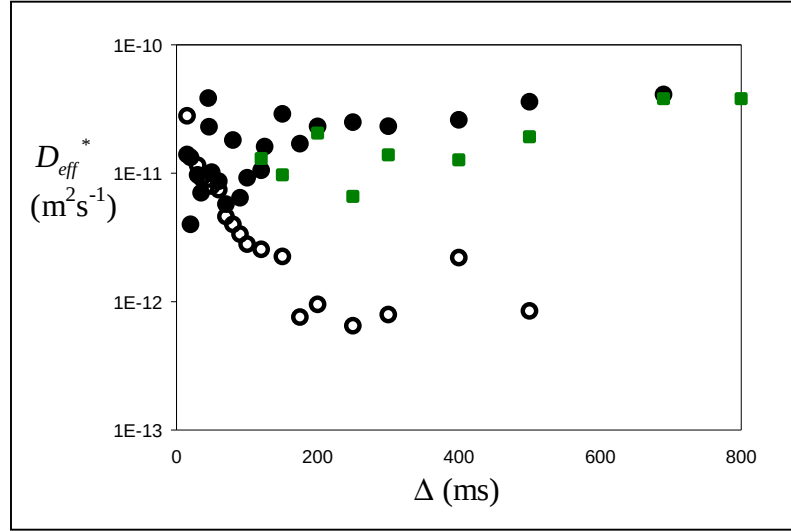


Figure 6.13. D_{eff}^* for the particle oil as a function of observation time Δ in the flow direction z for an average velocity of 0.53 mms^{-1} (green closed squares), for an average velocity of 0.88 mms^{-1} (black closed circles) and in the absence of flow (black open circles).

The particle Reynolds number in this case is small, but not less than one based on particle radius. Therefore the Stokes equations still apply which eliminates the nonlinearity in the equation of motion due to inertia and implies reversibility of two body interactions. There are however several sources of irreversibility in colloidal suspensions that are not inertial effects, where particles may be forced to cross streamlines and change their velocity; including Taylor Dispersion, particle roughness, interparticle forces, and many body hydrodynamics.

Experimental diffusivity measurements for suspensions under shear are sparse, especially for dilute Brownian suspensions. Optical methods often have measurement limitations in the direction of flow due to large displacements carrying particles out of the observation window[128]. Simulations offer much insight, but most offer information about the velocity gradient and vorticity directions as they are generally unable to do calculations in the flow direction due to the dominance of the velocity field to the particle displacement[14, 28, 129] and few are for Brownian suspensions[129]. Sierou and Brady[30] are a notable exception, and while their results are for non-Brownian particles, they still offer significant insight. As has become common in Stokesian Dynamics simulations and was previously mentioned, a short range repulsive force has been included which may represent small surface roughness, a hard sphere repulsion or residual Brownian motion.

The longitudinal self-diffusion coefficient in the direction of flow of a colloidal particle undergoing simple shear in terms of the mean squared displacement has been calculated from the solution of the advection-diffusion equation where the diffusing substance is initially considered as a point source by Elrick[130].

$$\langle z(t)z(0) \rangle = 2D_{zz}t + 2D_{zy}\dot{\gamma}^2 + \frac{2}{3}D_{yy}\dot{\gamma}^2t^3 \quad (6.7)$$

Where D_{zz} is the diffusion coefficient in the direction of flow z , D_{yy} is in the velocity gradient direction y , and D_{zy} is a coupling term between the flow direction and the velocity gradient direction. The brackets $\langle \rangle$ indicate an ensemble averaged quantity.

The mean squared displacements are $\langle z(t)z(0) \rangle$, $\dot{\gamma}$ is the shear rate and t is time. The

difficulty in simulation is accounting for the coupling between the flow and velocity gradient directions. Sierou and Brady have derived a slightly different form for calculating the diffusion coefficient in the direction of flow from a master Fokker-Plank equation governing the evolution of a particle probability density[30]. The resulting equation is

$$D_{zz} = \frac{1}{2} \frac{d}{dt} \langle Z^h Z^h \rangle + \left\langle \frac{dZ^h}{dt} \int_0^t \dot{\gamma}(\tau) d\tau \right\rangle \quad (6.8)$$

where Z^h represents the part of the z-direction motion not due to bulk flow. This representation of the diffusion coefficient is applicable at all times whereas often in simulations and experiments, the calculation of the diffusion coefficient is limited to the region where the mean squared displacement increases linearly in time[30, 128]. This can lead to confusion in the literature since the value of the diffusion coefficient depends upon the correct identification of this time domain[14]. The diffusion coefficient of (6.8) is exactly that measured by flow compensated PGSE NMR, where the coherent, or affine[30, 14], motion is cancelled and the overall mean squared displacement intrinsically includes any coupling. The results of Sierou and Brady[30] shown only for a $\phi = 0.35$ non-Brownian suspension indicate a normalized diffusion coefficient

$D_{zz} / a^2 \dot{\gamma}$ that increases with accumulated strain until reaching an asymptotic value at an

accumulating strain of approximately $\dot{\gamma} = 1.5 - 2$. Our data for a dilute Brownian

suspension demonstrates the same quantitative behavior. The difference between a non-

Brownian and a Brownian suspension becomes apparent in the calculation of the last

term on the right hand side of (6.8). The integral is related to the “diffusive” distance[30]

that a particle has traveled in the velocity gradient direction. Brownian particles become uncorrelated more quickly, even at dilute concentrations, due to the additional contribution of random Brownian motion. In our system, this term probably contributes more strongly to the value of the normalized diffusion coefficient and this could be one factor in the order of magnitude increase we've seen of the asymptotic diffusion coefficient D_{zz} . In addition, their simulation method becomes less accurate as $\phi \rightarrow 0$ [30].

Pine *et al*[9] present one of the few existing experimental studies where the external flow field is physically reversed and the longitudinal diffusion coefficient measured is similar to the one measured via flow compensated PGSE MR experiments, where flow reversal is accomplished with the application of two bipolar gradient pairs. Pine *et al*[9]utilize an optical technique, imposing periodic strain in a cylindrical Couette geometry to reverse the flow and record only incoherent displacements. Again, the normalized diffusivity increases with increasing accumulated strain in a qualitative trend with our data in Figure 6.12b, showing an asymptotic behavior at approximately $\dot{\gamma} = 1.5 - 2$. The discrepancy between the magnitude of the normalized diffusivity in the flow direction in our results and other experimental data[9] and simulations[30] could be due to several things. Their measurements were again for a concentrated non-Brownian suspension. In a Brownian suspension, Taylor Dispersion does cause a random sampling of streamlines, which leads to an enhanced dispersion in the axial direction. The quantitative difference in the value of the diffusivity could possibly be attributed to Brownian forces, but the timescale of this phenomena for water is $\Delta \ll R^2 / D_w \sim 10^4$ s

and for the particles is $\Delta \ll R^2 / D_{SE} \sim 10^6$ s, as stated previously. Therefore, within 100 ms, the experimental observation time at which irreversibility appears to occur in the data, Brownian motion causes a $0.2 \mu\text{m}$ displacement across streamlines, resulting in an average change in the velocity of a particle of only 0.4 mm/s . This is not enough of an impact to cause the magnitude of increase of D_{eff}^* that is seen. In addition, D_{eff}^* appears to approach an asymptotic value by 600 ms, much sooner than the Taylor-Aris dispersion limit. The Taylor dispersion coefficient in the asymptotic time limit is $2.2 \times 10^{-2} \text{ m}^2 \text{ s}^{-1}$, as opposed to the value seen here of approximately $4 \times 10^{-11} \text{ m}^2 \text{ s}^{-1}$, so the trend in the diffusivity cannot be attributed to purely Brownian forces. This point is reinforced by the qualitative agreement between the timescales, or accumulated strain, over which the increase in D_{eff}^* occurs in our data and those that occur in simulation[30] and experiment[9] in non-Brownian suspensions. Our studies are also for a dilute suspension, where hydrodynamics are probably more important than the interparticle effects which begin to dominate at larger concentrations. In concentrated suspensions, the particle has less time to “feel” a long range hydrodynamic interaction before it comes into contact with another particle. Finally, PGSE MR measurements are the most intrinsically sensitive to diffusion dynamics and have been utilized for decades as a highly accurate measure of self-diffusion in liquids[55].

As previously discussed, the microscopic origins of irreversibility can also be traced back to the presence of particle roughness or a repulsive force allowing a two body interaction to result in a particle crossing a streamline. The observation of particle migration in this system and the idea that shear-induced particle migration has been

attributed to normal stresses generated when the particle distribution function is asymmetric, implies that binary collisions are causing particles to cross streamlines. However, the question remains as to whether these binary collisions are the major contributor to the increased diffusivity at times greater than 100 ms. Diffusion is possible, even without microscopic imperfections or interparticle forces, due to the nature of long range hydrodynamic interactions, specifically many body interactions. An interaction between three particles is not the same deterministic process as a binary collision. The nonlinear nature of a three body interaction introduces a dynamics to the system, which gradually cause the particles to lose memory of their initial trajectories and motion. Even within a strict hydrodynamic limit, three body collisions would cause an eventual loss in correlation between particles and an increased diffusivity. In the dilute limit, many body hydrodynamic interactions are considered rare and are traditionally neglected in theoretical treatments. This assumption has led to much confusion in the literature as to how irreversibility could arise in a system governed by the linear reversible Stokes equations[131]. In reality, the reversibility of the Stokes equations holds exactly only for two body interactions between particles[26]. Plotting the data of Figure 6.12b with the diffusion coefficient normalized by the characteristic time and length scales present, *ie* the shear rate and particle radius, as a function of accumulated strain $\gamma = \langle \dot{\gamma} \rangle \Delta$, shown in Figure 6.14, the diffusion asymptotes to one. This indicates that the hydrodynamic interactions are a significant mechanism of the irreversibility since $D_{eff}^* \sim a^2 \langle \dot{\gamma} \rangle$ is the scaling for hydrodynamic shear induced diffusivity[2] and the onset

occurs at $\gamma \sim 1$ as for hydrodynamic interactions in concentrated non-colloidal suspensions[9, 30].

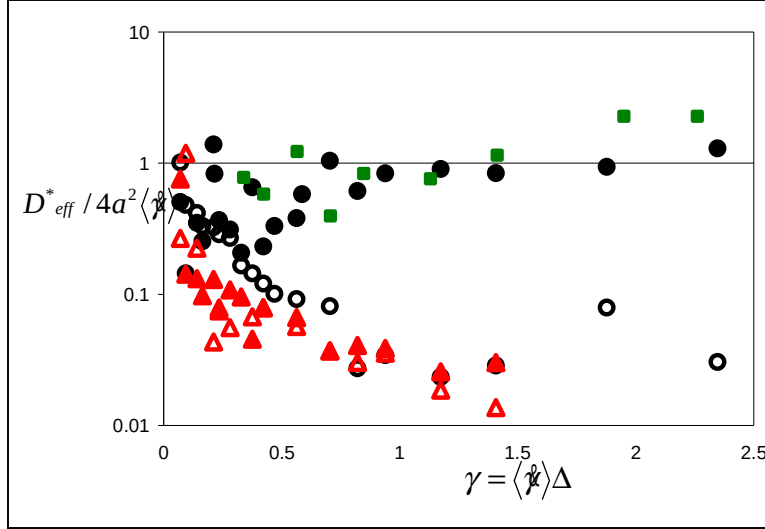


Figure 6.14. D_{eff}^* normalized by the average shear rate $\langle \dot{\gamma} \rangle$ and the square of the particle diameter $4a^2$ as a function of accumulated strain $\gamma = \langle \dot{\gamma} \rangle \Delta$ for an average velocity of 0.88 mm s^{-1} in the flow direction z (black closed circles), in the velocity gradient direction y (red closed triangles), and in the absence of flow in the z (black open circles) and y (red open triangles) directions, as well as for an average velocity of 0.53 mm s^{-1} in the z -direction (green closed squares).

Conclusions

A future experimental test to differentiate the impact of roughness and repulsion in binary collisions from many body hydrodynamics would be a volume fraction study. An increase in diffusivity due to many body hydrodynamic collisions would have a ϕ^2 dependence because the rate of simultaneous interactions of a sphere with two other spheres is proportional to $\langle \dot{\gamma} \rangle \phi^2$ as $\phi \rightarrow 0$ [42]. The lengthscale of particle displacement

is the particle radius, and so the diffusivity should scale as $a^2\phi^2\langle\chi\rangle$. Surface roughness or interparticle forces however would scale linearly with ϕ , since the rate of interaction between two spheres goes as $\langle\chi\rangle\phi$ [37]. In our experimental system, whether or not a linear dependence on volume fraction would occur depends upon the strength of the interparticle force.

Several factors point towards many body hydrodynamics, which introduce a nonlinear component to the momentum conservation, as the root cause of irreversibility in dilute suspensions. In fact, Stokeslets model simulations predict that chaotic particle dynamics occur in viscous flows when only three particles interact hydrodynamically [26], certainly a dilute system. In the light of chaos or dynamical systems theory, irreversible particle dynamics as manifested by an increasing effective dispersion coefficient can be analyzed through the calculation of the Lyapunov exponent. Lyapunov exponents are used in dynamical systems theory as a measure of the stochastic nature of particle trajectories and essentially are a measurement of chaos [17]. They have also been incorporated into definitions of diffusion coefficients using nonequilibrium statistical mechanics [17]. Drazer *et al* [37] calculated the dependence of the Lyapunov exponent on concentration in a non-Brownian suspension and found that it remains finite even as $\phi \rightarrow 0$, indicating that chaotic behavior can be expected even at dilute concentrations. The particle trajectories were not found to separate exponentially immediately, and the time it took to transition to exponential separation increased with decreasing volume fraction [37]. This could possibly be due to smaller number of particle interactions that occur at dilute concentrations and the correspondingly longer time

required for particles to lose memory of their dynamics through many body interactions. Regardless of the transition region, the finite nature of the Lyapunov exponent even in dilute suspensions is a reflection of the long range nature of hydrodynamic interactions. In addition, Lyapunov exponents were calculated from the experimental data of Pine *et al*[9]. They found a strong increase in λ with increasing accumulated strain that qualitatively matched the increase in diffusivity. The suspension appears to become more sensitive to initial conditions as strain is increased, which implies that hydrodynamic interactions are the root cause in the onset of chaos. The simulations of Sierou and Brady[30] noted a ϕ^2 dependence on diffusivity even at $\phi = 0.1$, very near the $\phi = 0.08$ suspension studied here, intimating that the linear dependence of ϕ due to roughness or repulsion in binary collisions may not dominate even at very low concentrations. In fact, it is possible that the irreversibility of two body interactions between particles could lead to a higher probability of having a three body interaction, as could the presence of Brownian forces even at a much shorter time scale than Taylor Dispersion. Regardless, interparticle forces are not necessary to get diffusive behavior even at low volume fractions, due to the chaotic nature of many body hydrodynamics in suspensions[131].

The data presented here provides evidence of both particle migration and irreversible dynamics which are generally not expected to occur in dilute Brownian suspensions and therefore not considered in the modeling of flow systems. The importance of many body hydrodynamics in dilute Brownian suspensions has been

demonstrated, as has the applicability of chaos theory and non equilibrium statistical mechanics methods to model these systems[6].

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