Modelling the polymer migration phenomena in DNA-laden flows

Matyas BENKE, Evgeniy SHAPIRO, Dimitris DRIKAKIS*

* Corresponding author: Tel.: 44 (0) 1234 754796; Email: d.drikakis@cranfield.ac.uk
Department of Aerospace Sciences, Cranfield University, UK

Abstract: Cross-stream migration of macromolecules transported in a fluid flow is typically encountered in microfluidic applications. This experimentally observed phenomenon leads to a decrease of the near-wall macromolecule concentration which can be detrimental in applications relying on a high intensity of polymer reactions in the near-wall zone, such as DNA-based bio-sensors. Despite a significant body of experimental, theoretical and numerical research, there is no consensus regarding the nature of this phenomenon. In this paper a meta-modelling approach for macromolecule motion in the flow is presented. It is demonstrated that the hydrodynamic interaction resulting from the incorporation of Saffman lift force, together with Faxen correction to Stokes drag causes migration of DNA molecules towards the middle of a pressure driven micro-flow, which is in agreement with experimental observations. The results suggest that the migration can occur due to macromolecule-flow rather than macromolecule-wall interaction.

Keywords: multi-scale modelling, meta-modelling, DNA transport, polymer migration

1. Introduction

Fluidic transport of large organic and artificial molecules occurs in a variety of application areas including petrol chemistry, organic chemistry, food processing, pharmaceutics and various biomedical applications, such as bio-analysis (Lim et al. 2005, Shi et al. 1999, Simpson et al. 2000) and drug delivery (Pasas et al. (2002), Fanguy and Henry (2002)) systems. A vast majority of the previously listed applications is operating with dilute macromolecular solutions. Since the 1970s, a significant amount of experimental, theoretical and computational investigations have been carried out to understand and describe the features of dilute polymer solutions. The experimental observations indicate the tendency of macromolecules to migrate across streamlines in dilute solutions similarly to molecular diffusion in concentrated solutions. However, contrary to the action of molecular diffusion, the migration observed in dilute solutions can result in the focusing rather than spreading of the macromolecule concentration field.

Cross-streamline migration of polymers in micro-flows has been observed experimentally by a number of researchers, which in turn prompted development of theoretical models of this phenomenon. Radial migration of DNA in cylindrical Couette flows has been observed experimentally by Uhlenhopp and a simple analytical model has been presented based on the streamline curvature (See, for example Shafer et al. (1974)). Dill and Zimm (1979) observed inward radial migration of DNA molecules in the experiments with dilute DNA solutions in a flow field generated between a rotating upper and a static lower cone. Ausserre et al. (1986) conducted experiments with dilute, initially homogeneous solution of rod-like, stiff xanthen molecules. The results indicated the existence of a depletion layer near nonadsorbing solid surfaces, even in the absence of flow. The thickness of the observed depletion layer was comparable to the macromolecular radius of gyration. More recently, DNA migration in channel flows has been investigated by Stein et al. (2006) and Fang et al. (2007). In the former study pressure-driven transport of labelled individual DNA molecules was measured in wide micro-fluidics with

rectangular cross-section. The results indicated that larger molecules tend to spend more time in the high-velocity region of the flow. As a result the DNA concentration profile reaches a maximum at the channel centreline. In the latter study a similar tendency of DNA molecules to migrate towards the middle of the micro-channel was observed using fluorescence microscopy.

Various, and to some degree, contradictory explanations of the physical mechanism responsible for the cross-stream migration have been proposed in the past. For example, Dill and Zimm (1979) attributed the observed behaviour of DNA to radial inward tension forces acting on the molecules due to the stretching of the molecules by the flow field. On the other hand the formation of depletion layer in absence of the flow observed by Ausserre et al. (1986) indicates that the wall-DNA interaction plays an important role.

Aubert and Tirrell (1980) and Aubert et al. (1980) constructed an analytical model based on a linearly elastic dumbbell representation of a macromolecule suspended in fluid. The theory predicted cross-stream migration of macromolecules in curvilinear flows due to non-uniformity of the flow velocity gradient. However the theory failed to explain the experimentally observed polymer migration in rectilinear flows (Ausserre et al. (1991)). Later Sekhon et al. (1982) and Brunn (1983) enhanced Aubert's theory by including hydrodynamic interactions between the beads, leading to the prediction of cross stream migration in rectilinear flows.

Theoretical and experimental investigations of polymer migration in dilute solutions were systematically reviewed by Agarwal et al. (1994). One of the points highlighted was that there is a disagreement between different theories, even with regard to the predicted direction of macromolecule migration in simple flows.

With the increase of computational power, a number of numerical approaches have been developed capable of modelling the behaviour of dilute DNA solutions. Brownian dynamics simulations of Nitsche and Hinch (1997) and Schiek and Shaqfeh (1997) predicted weak polymer migration towards the channel walls for a plane Poiseuille flow. However the dissipative particle dynamics model of Fan et al. (2003) predicted weak depletion near the walls in a plane Poiseuille flow. Further, Jendrejack et al. (2004) carried out Brownian dynamics simulations of dilute, confined DNA solutions in a plane Poiseuille flow and obtained migration in the presence of wall-DNA interaction. A simple bead-wall repulsive potential was then introduced to force DNA migration away from the channel walls.

An analytical theory has been developed recently by Ma et al. (2005) based on hydrodynamic interaction between the beads of the mechanical polymer model. The theory indicates that the velocity disturbance generated by a single bead can affect its partners and result in migration of the molecule. However the direction of migration which is predicted differs depending on the orientation of the molecule with respect to the surface.

The lack of understanding of the mechanisms responsible for the cross-stream migration of macromolecules prompted the investigation presented in this paper.

While DNA is a relatively complex macromolecule, the meta-modelling approach (Trebotich et al. (2005), Benke et al. (2008)) allows representation of this molecule using a mechanical bead-rod structure with the parameters of the mechanical model derived from the physical properties of the actual macromolecule. The motion of the mechanical model is determined by the hydrodynamic forces acting on individual beads. As early as 1962, the experimental observations of Segre and Silberberg (1962) pointed out the tendency of neutrally buoyant rigid spheres to migrate in channel flows. The observed phenomenon was explained by Saffman (1965), who pointed out that a rigid particle moving in viscous fluid experiences a lift force perpendicular to the flow direction.

In the following sections it is demonstrated that incorporation of the Saffman lift force together with Faxen correction (e.g. Michaelides (2006)) into the meta-model leads

to accurate prediction of cross-stream migration of DNA molecules towards the middle of the channel.

3. Meta-modelling approach

A majority of the reported theoretical investigations was either based on kinetic theory, or resulted from direct simulations using Brownian dynamics or dissipative particle dynamics methods. An alternative approach is provided by meta-models, representing a specific class of multi-scale methods.

Meta-models (Trebotich et al. (2005), Benke et al. (2008)) draw information from the atomic level description of the investigated macromolecule, but the method is essentially continuum-level. This approach can be used to describe transport processes in dilute solutions, where the number density of the solute material is relatively low.

In a meta-model, the investigated large molecules are represented as mechanical structures. The motion of the mechanical structures is governed by forces arising from the interaction between the macromolecules and carrier fluid. While macromolecules of interest are modelled individually and resolved on a fine scale, the motion of the solvent is treated at the continuum level.

The information exchange between the scales of the problem is one-way for the atomic part, which is used to determine the parameters of the mechanical structure representing the macromolecule of interest. The information exchange between the mechanical model and the continuum flow field can be either one-way or two-way, depending on the coupling strategy.

Let us consider representation of a macromolecule as a system of spherical beads connected with rigid rods. The connecting joints are considered to be freely rotating around the spherical particles. This representation is particularly suitable for ssDNA which is a relatively stiff macromolecule (Smith et al. 1996). The motion of individual beads is then governed by the following modified Langevin equation:

$$m_i \frac{d\mathbf{v}_i}{dt} = \mathbf{f}_i = m_i\gamma_i\left(\mathbf{u}(\mathbf{r}_i) - \mathbf{v}_i\right) + \\ + \mathbf{f}_{i,Fax} + \varphi_i(t) + \mathbf{f}_{i,Lift} \tag{1}$$

with $m_i\gamma_i = 6\pi\eta b_i$ friction coefficient arising from Stokes drag. Here m_i and b_i denote mass and radius of bead i respectively; γ_i represents the inverse of the phenomenological relaxation time; η is the viscosity of the carrier fluid; $\mathbf{v}_i$ is the particle velocity; η is the dynamic viscosity and $\mathbf{u}(\mathbf{r}_i)$ is the velocity of the continuum fluid at position $\mathbf{r}_i$.

Apart from the Stokes drag force, the forces include $\mathbf{f}_{i,Fax}$ is the Faxen correction factor of the Stokes drag, defined as: $\mathbf{f}_{i,Fax} = \eta\pi b_i^3\left(\nabla^2\mathbf{u}(\mathbf{r}_i)\right)$. In a fully developed Poiseuille flow, an approximation of the Faxen correction is given by $\mathbf{f}_{i,Fax} = \eta\pi b_i^3\left(\frac{2\mathbf{u}_{\max}}{H^2}\right)$, with denoting H half channel height. The random force $\varphi_i(t)$ possesses Gaussian distribution around a zero mean and with the variance of $\langle\varphi_i(t)\varphi_i(t')\rangle = 2m_i\gamma_i k_B T\delta(t-t')$, where k_B is the Boltzmann constant, T is the temperature and $\delta(t-t')$ is the Dirac function. $\mathbf{f}_{i,Lift}$ represents the Saffman lift force acting on the spherical beads of the meta-model, which is given by

$$\mathbf{f}_{i,Lift} = \frac{1.615(2b_i)^2\sqrt{\rho\eta}\left(\mathbf{u}(\mathbf{r}_i) - \mathbf{v}\right)\times\omega}{\sqrt{\omega}}, \tag{2}$$

where ω is the vorticity of the flow.

It is worth noticing that when the macromolecule is in equilibrium with the carrier fluid flow, the lift force disappears. However there is always a lag between the transported particles velocity and the fluid flow due to the Faxen correction term. The resulting relative velocity difference gives rise to the Saffman lift force.

Complete description of the macromolecule transport requires information exchange

between the concerning scales. This is achieved by tight coupling of the governing equations of macromolecule motion to the continuum level fluid flow equations. Data transfer between the mechanical structures and the continuum field is implemented through force-based coupling (e.g. Benke et al. (2008)). However since the effect of a small quantity of DNA molecules on the fluid flow can be considered negligible in most cases, in this paper we will consider carrier flow velocity $\mathbf{u}(\mathbf{r}_i)$ to be given by the expression for Poiseuille flow in a channel.

In order to complete the mathematical model, numerical formulation of the bond length criteria is necessary:

$$\left\|\mathbf{r}_{i+1} - \mathbf{r}_i\right\| = a \qquad (3)$$

where a corresponds to prescribed bond lengths and index i runs from 1 to $N-1$ in case of N particles. Geometric constraints are implemented as additional restrictions imposed on calculated particle positions.

During the numerical calculations, bead positions are determined using a predictor-corrector type algorithm. In the predictor stage, unconstrained bead coordinates are calculated by numerical integration of the governing equation (1), neglecting the bond length criteria. The second, corrector stage is implemented in order to ensure prescribed bond lengths. During this stage, beads are re-positioned to meet the geometric requirements. In the calculations presented in this paper, Fast Linear Corrector (FALCO) (Benke et al. (2008)) has been used in order to implement bond length constrains.

4. Results and discussion

In the numerical simulations presented here, the transport of individual DNA molecules was considered in a fully developed parabolic channel flow. Parameters of the micro-channel and flow rates were chosen to represent the conditions encountered in typical bio-sensor applications (Stone et al. 2004). The channel height was equal to 75 μm and the Reynolds number based on bulk velocity and channel height was 0.075. Water was chosen as a carrier liquid with dynamic viscosity of 10^{-3} Pa·s and density of 10^3 kg/m^3. In order to demonstrate the migration effect, individual DNA molecules were distributed uniformly along the channel height at the inlet section of the channel. 100 individual molecules were tracked for 300 seconds. Each molecule consisted of 160 beads, parameters of the bead-rod models were obtained from the mesoscopic model of 48 kbp lambda-DNA molecules leading to the bead radius of 6.47 nm and rod length of 86.57 nm (Doi 1986).

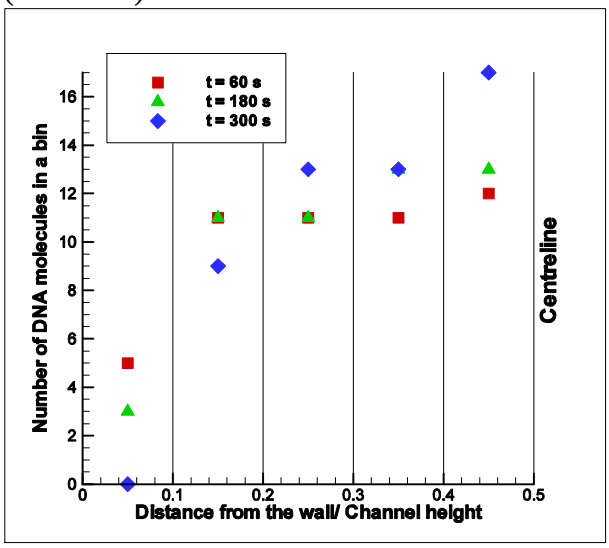

Fig. 1. Variation of DNA molecules number density with distance from the channel wall at t=60 s, 180 s and 300 s.

Figure 1 presents the distribution of the DNA molecules across the channel height at different time instances. In order to obtain the number distribution, the channel height was divided into 10 bins and the DNA molecules distribution was computed according to the position of the centre of mass. The results clearly indicate that the number of molecules present in the near wall zones (at coordinate 0) is decreasing and the number of molecules in the channel mid-plane (at coordinate 0.5) is increasing as time progresses. Figure 2 shows some individual DNA path lines developed along the channel length demonstrating the tendency of molecules to migrate towards the channel mid-plane. It is worth noticing that the curvature

of the centre of mass trajectory varies with the position in the channel, becoming zero for the molecules close to the centreline.

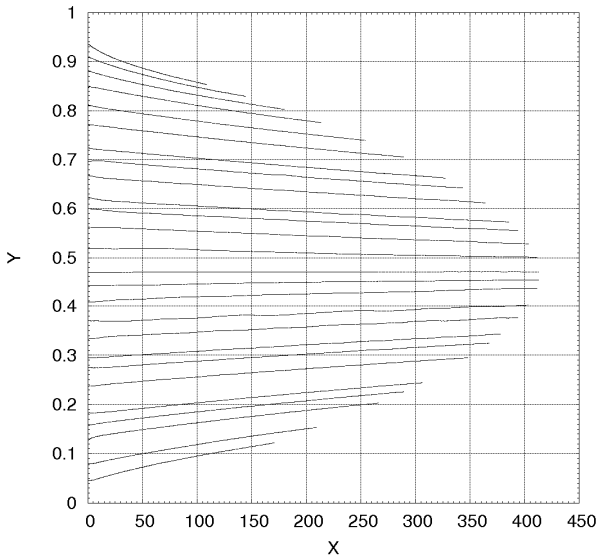

Fig. 2. Centre of mass trajectories of individual DNA molecules, flow direction is horizontal.

The migration time-scale is sufficiently large suggesting that the effect is weak, which is in agreement with experimental observations (Fang et al. 2007). The migration mechanism presented here depends on the macroscopic flow field and is independent of the orientation of the macromolecules.

6. Conclusions

A new hydrodynamic explanation has been proposed for the experimentally observed polymer migration phenomena. The explanation is based on the combination of Saffman lift force and Faxen correction to Stokes drag acting on the individual beads in a mechanical meta-model of DNA. Numerical calculations were carried out to demonstrate the tendency of the investigated macromolecules to migrate towards the position of zero shear stress in a plane Poiseuille flow.

Computation presented demonstrates the physical mechanism, but further research however is required in order to refine the definition of the parameters of the meta-model. In particular, the effective radius of the bead required for the correct representation of the Saffman lift can differ from the hydrodynamic radius used in the Stokes drag force and Faxen correction. Such a refinement can be obtained from large-scale molecular dynamics simulations or carefully constructed experiment.

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