Kinematic analyses of a cross-slot microchannel applicable to cell deformability measurement under inertial or viscoelastic flow

Ju Min Kim*,**,†

*Department of Chemical Engineering, Ajou University, Suwon 443-749, Korea
**Department of Energy Systems Research, Ajou University, Suwon 443-749, Korea

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Abstract—A cross-slot microchannel has been harnessed for a wide range of applications, such as label-free measurements of cell deformability and rheological characterization of complex fluids. This work investigates flow kinematics in a cross-slot microchannel used for the measurements of cell deformability utilizing finite element method (FEM)-based numerical simulation. In a cross-slot microchannel, the cell is stretched near the stagnation of the cross-slot channel, and cell deformation is significantly affected by its trajectory. Two passive methods, inertia- and viscoelasticity-based, which do not rely on any external force such as an electric field, have been applied to focus particles along the channel centerline so that the cell trajectories are unified. However, it is not well understood how the flow kinematics inside the cross-slot channel is altered by the inertial or viscoelastic effect when these two methods are employed. This work demonstrates that the flow kinematics such as the distributions of flow type and strain rate is notably changed with an increase in the Reynolds number when an inertia-based method is employed. On the other hand, flow kinematics does not significantly deviate from that of an inertia-less Newtonian fluid irrespective of the Weissenberg numbers when a viscoelasticity-based method is used. The current work will be helpful for the design and operation of a cross-slot microdevice for measuring cell deformability.

Keywords: Cross-slot Microchannel, Cell Deformability, Particle Focusing, Numerical Simulation

INTRODUCTION

Live cells are deformed under external fields such as an optical or hydrodynamic force [1-4]. The cell deformability represents the pathophysiological conditions of the human body or cell itself [5,6]. For instance, the deformability of red blood cells (RBCs) is significantly altered when the human body contracts malaria or diabetes [7]. Thus, cell deformability measurements have been efficient biomarkers for the diagnosis of diseases or cell health [3,8-10], which is attractive because it requires neither a complicated nor expensive labeling procedure [5]. Further, the deformability of the cells can be measured by optical microscopy in a high throughput manner, which guarantees a fast but accurate measurement of their deformability [8-10]. Microfluidics-based deformability measurements have recently attracted significant attention because the flow can be precisely controlled, and the procedures for a deformability measurement can potentially be automated [5]. The design of a microchannel shape, which generates flow fields to deform the cells, is a key technology in such microfluidics-based approaches.

As previously discussed by Cha et al. [3], the planar extensional flow generated by a cross-slot microchannel has been used for the deformation of materials such as cells [2,3,8] and DNA [11] because its affine deformation increases exponentially as the strain experienced by a deformable particle increases [12]. Further, its flow type does not include any rotational components [13]. Thus, the deformation of the materials by an extensional flow field is larger compared to the deformation in a shear flow, which is relevant in a pressure-driven channel flow [13]. A shear flow is a weak flow in which the affine deformation of a deformable particle is linearly increased with an increase in the strain [12], and the particle deformation is significantly hindered by the rotational motion [13]. In a cross-slot microchannel, as shown in Fig. 1(a), a deformable particle such as an RBC, which emanates from the inlets (top and bottom channels), is stretched near the stagnation point (central point) and then moves toward the outlets (right and left channels). However, the deformability of a cell can be measured differently according to its spatial trajectory irrespective of its intrinsic physical properties because the flow kinematics, such as the local strain rate and flow type in a practical device, is not spatially homogeneous [3,14]. Thus, unification of the cell trajectory prior to a deformability measurement is an essential step for an accurate deformability measurement [3,5].

Particles migrate laterally toward positions of equilibrium under channel flows when a fluid flow is inertial (still laminar) [15] or viscoelastic [16]. Recently, such phenomena have been extensively exploited to manipulate particles in a microfluidic channel [17-28]. Researchers have also engineered such phenomena to focus the particles along the channel centerline to unify particle trajectories [2,3]. The two passive methods of inertial and viscoelastic particle focusing are attractive because they do not require any external force such as an electric field despite the particles being tightly focused along the channel centerline through a purely hydrodynamic effect.
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Flow kinematics was investigated utilizing FEM-based numerical simulations with a constitutive modeling (upper convective Maxwell (UCM) model [29]) for a viscoelastic fluid. The flow kinematics inside a cross-slot channel is shown to be significantly different according to whether an inertial or viscoelastic particle focusing method is used. The current study is expected to provide useful information and insight into the design and analysis of a microdevice for cell deformability measurements.

GOVERNING EQUATIONS AND BOUNDARY CONDITIONS

The cell deformability has been measured under the inertial Newtonian and inertia-less viscoelastic flow conditions. A poly(vinylpyrrolidone) (PVP) mixture in a buffered solution, i.e., phosphate-buffered saline (PBS), was used as a viscoelastic fluid with nearly constant shear viscosity [33], which can be modeled as a UCM model [3,19]. The cross-slot geometry considered in this work is shown in Fig. 1(b). The mathematical modeling for such a fluid flow is composed of continuity, momentum balance, and constitutive (UCM) equations. This study considers a two-dimensional steady problem, and the dimensionless forms of the governing equations can be represented as follows:

\[ \nabla \cdot \mathbf{u} = 0 \]  
\[ \text{Re}(\mathbf{u} \cdot \nabla \mathbf{u}) = -\nabla p + \nabla \cdot \boldsymbol{\tau} \]  
\[ \tau + \text{Wi}[\mathbf{u} \cdot \nabla \mathbf{u} - (\nabla \mathbf{u})^T - (\nabla \mathbf{u})] = [((\nabla \mathbf{u}) + (\nabla \mathbf{u})^T) \]  

where \( \mathbf{u} \) is the velocity vector, \( p \) is the pressure field, and \( \tau \) is the extra stress tensor, and all of the variables are dimensionless. In the equations, ‘.’ denotes a dot product and \( (\cdot) \) is the transpose of tensor \( (\cdot) \). In addition, Re and Wi are defined by \( \text{Re} = \frac{u h}{\nu} \) and \( \text{Wi} = \frac{\lambda}{\nu} \), respectively (note that the current definition of Wi is equivalent to twice the Deborah number (De) defined by Cha et al. [3]), \( h \) is half of the channel width, \( <u> \) is the average velocity in the channel cross section, \( \rho \) is the fluid density, and \( \mu \) and \( \lambda \) are the shear viscosity and relaxation time of a fluid, respectively. In the equations, the length of scale was normalized using \( h \), velocity \( \mathbf{u} \) was non-dimensionalized using \( <u> \), and \( p \) and \( \tau \) were scaled using \( \mu <u>/h \). The UCM model is reduced to a Newtonian fluid case when Wi is set to zero [29].

In the computational domain shown in Fig. 1(b), a fully developed velocity was imposed on the inlet and outlets, a no-slip boundary condition was imposed on the channel wall, and a fully developed boundary condition of extra stresses was imposed on the inlet. In addition, a symmetric boundary condition was imposed along the symmetric line shown in Fig. 1(b). Note that this geometrical shape (Fig. 1(b)) and the symmetric flow conditions at both the inlets and outlets are equivalent to that used by Cha et al. [3].

NUMERICAL METHODS

The governing equations presented in the previous section were solved using a standard mixed finite element formulation, and the numerical procedures applied in this work are identical to those of a previous work [34]. Thus, the numerical methods were briefly introduced to explicitly define the problems considered. The numer-