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CFD Characterization of Flow Pattern around Endothelial Cell in Dengue Infection with Plasma Leakage

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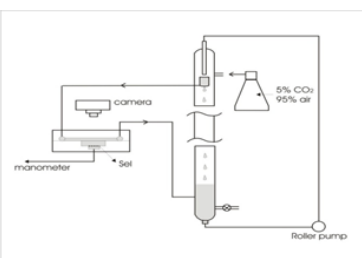
Graphical abstract



Abstract

Plasma leakage is the pathological hall mark in dengue infection and may cause fatal condition to the patients. In this paper, the CFD (computational fluid dynamic) model is adopted to characterize the flow on the endothelial cells surface with plasma leakage based on in vitro experiments of HUVEC (human umbilical vein endothelial cell) culture on the permeable membrane. The computational domain used is a simplified model of single cell. At the leading edge of the domain and among the membranes, the gaps are modeled as a representation of cell-cell junction breakdown caused by dengue virus infection. The result shows that at the leading edge , the fluid starts to move more quickly and increases to the maximum value at the middle of the cell and then drops to zero at the trailing edge. From the physical point of view, this result describes that there is a variation of the values of the wall shear stress due to the velocity gradient. These results can be considered as a first step to develop the ways of the prevention of the dengue infection through manipulation the shear stress to reduce the potency of dengue virus to attach the cell surface.

Keywords: CFD (Computational fluid dynamic); endothelial cell; dengue; wall shear stress

1.0 INTRODUCTION

Dengue infection is still an unsolved problem in more than 100 tropical and sub tropical countries. In many cases, the death in dengue is characterized by plasma leakage caused by the increase of acute vascular permeability due to disfunction of endothelial cells infected by dengue virus [1]. Cardier et al [2] reported the presence of circulating endothelial cells in the peripheral blood as the evidence of vascular damage in DHF patients. Wall shear stress (WSS) is a hemodynamic force that occurs when blood flow over and shear the endothelial cells surface [3].

WSS plays a significant role in endothelial homeostasis. It highly depends on the velocity, blood viscosity and integrity of endothelial cell structure [4]. Other molecules expressed and have strong correlation to the interaction of WSS and endothelial cells are the cell matrix and cell-cell junction molecules including integrin, PECAM-1, VE-cadherin, tyrosine kinase, caveolin-1 and glycocalix [5].

Mitchell and King [6] found that WSS can be used to control the cancer cell COLO 205 and prostate cancer cell PC-3 by inducing the interaction of cancer cells with apoptotic agent such as tumor necrosis factor apoptosis-inducing ligand (TRAIL). Another research by Chiu et al. [7] found that shear stress can be used to inhibit adhesion molecules expression in vascular endothelial cells, like VCAM and ICAM that have strong correlation to dengue infection.

Flow profiles and characterization of cells with respect to the dengue infection is very attracted to the researchers subject to the explanations of many unsolved problems in dengue pathology. In vivo and in vitro experiments are very complex and have many limitations when applied to explore the velocity and shear stress in dengue infection. Along with experimental investigations, CFD (computational fluid dynamic) approaches have been applied to the study of endothelial cells. The aim of the present work is to apply CFD to the investigation of the phenomena affecting the pressure distribution and the velocity profiles in endothelial cells with plasma leakage. CFD is a valuable means for understanding the physics, since it gives an insight into details of the flow which are difficult to obtain experimentally.

2.0 METHOD

2.1 Governing Equations

The general mathematical statements of fluid flow are the conservation equations: mass, momentum and energy. Since the blood flow in arterial segments is adiabatic, the energy equation can be ignored, leaving the continuity and momentum equations as the governing relations for flows of interest in the present study.

The Navier–Stokes equations were solved over the domain using a finite-volume method with the CFD code. The equations were applied with constant viscosity and density, without body force, while the blood is assumed as incompressible and steady flow. With these properties the Navier–Stokes and the continuity equations can be expressed, respectively,

$$\rho(\mathbf{u} \bullet \nabla)\mathbf{u} = -\nabla p + \eta \nabla^2 \mathbf{u} \quad \text{(Eq. 1)}$$

$$\nabla \bullet \mathbf{u} = 0 \quad \text{(Eq. 2)}$$

2.2 CFD Model

The model developed based on the in vitro experiment exposing dengue infected endothelial cells culture by culture media in parallel plate flow chamber (PPFC). In the in vitro experiment, human umbilical vein endothelial cells (HUVEC) were cultured on the transwell permeable membrane made of polyester (see Figure 1). Based on these conditions, in the present paper the CFD model has been proposed to characterize the flow pattern around the endothelial cell.

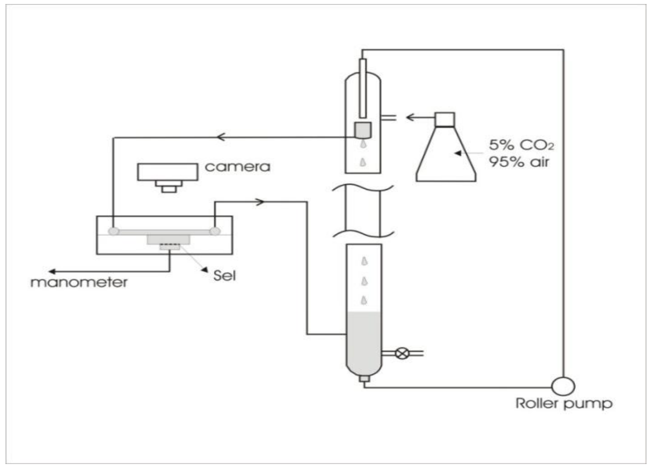


Figure 1 Experimental setup of parallel plate flow chamber using HUVEC

The computational domain was a simplified model of a single cell applied on permeable membrane (see Figure 2). In this work, membrane was represented by numbers of rectangular. The presence of the gap reflects “the pore” of the membrane which allows the fluid enters it and finally falls to the bottom surface. For all following simulations, the geometrical parameters and properties of the computational domain used in this simulation is shown in Table 1.

3.0 RESULTS AND DISCUSSION

Figure 3 shows the prediction of the velocity profile calculated over the HUVEC cell in dengue infection, where some leakages occurred due to cell-cell junction breakdown. It can be observed that at the leading edge of the cell, the fluid starts to move more quickly and increases to the maximum value at the middle position of the cell. Moreover, because there are some leakages of the fluid through the membrane pore, the velocity of the fluid will decrease and finally drops to zero. From the physical point of view, this result describes that there is a variation of the values of the wall shear stress due to the velocity gradient. In addition, this result can also be considered as a way to prevent the infection due to the failure of dengue virus to attach on the cell surface.

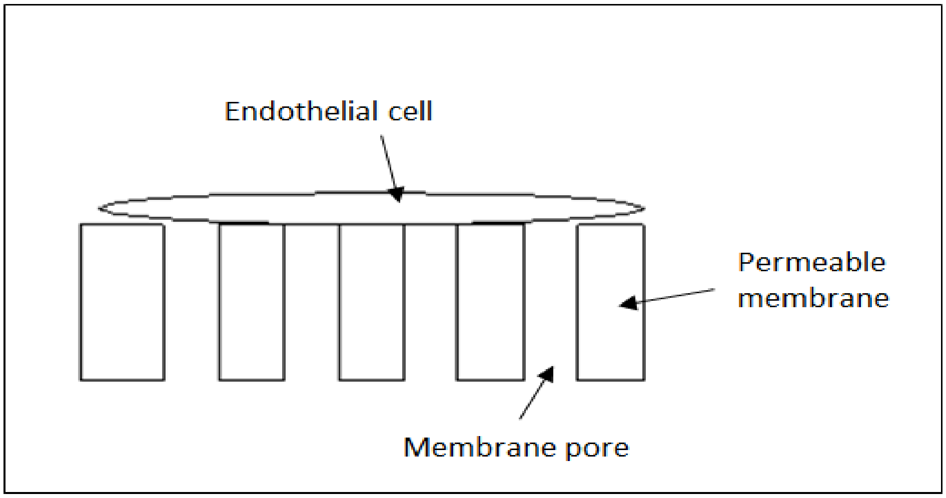


Figure 2 Model of endothelial cell on the permeable membrane for simulation

Table 1 Physical value for the model

Properties	Value	Unit
Height of computational domain domain	10	[μm]
Length of computational domain	1000	[μm]
Thickness of HUVEC cell	2	[μm]
Length of HUVEC cell	30	[μm]
Length of capillary	1000	[μm]
Diameter of capillary	10	[μm]
Permeable membrane		
Pore size	3	[μm]
Thickness	10	[μm]
Diameter	24	[mm]
Pore density	2.10^6	[pores/cm^2]

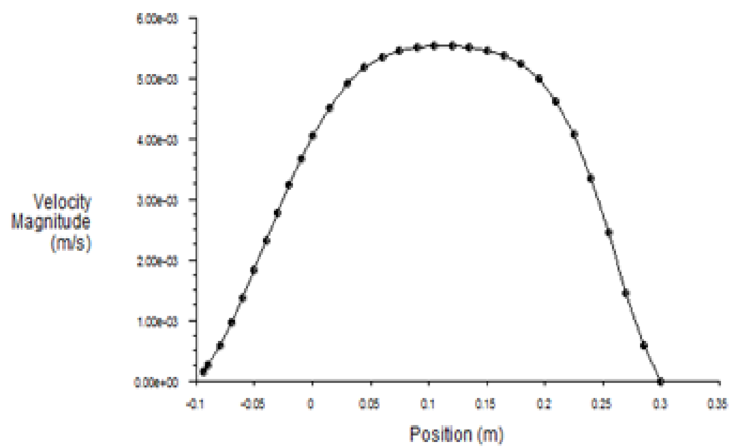


Figure 3 Velocity profile over the HUVEC cell

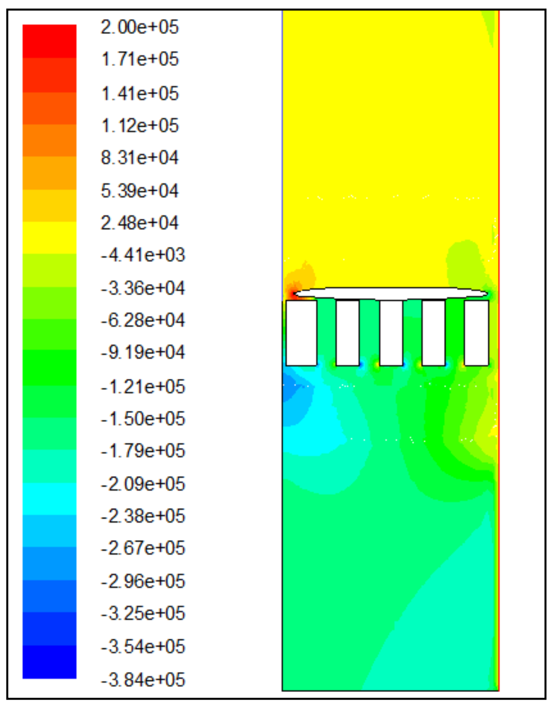


Figure 4 Pressure distribution over the HUVEC cell cultured on the permeable membrane

In order to investigate the profile of velocity gradient as discusses before, Figure 4 depicts the pressure distribution which may affect the fluid movement. As illustrated in this figure, at the leading edge of the cell, the high pressure can be observed, but at the outlet, the pressure has a lower value. This is as expected, because the change of geometry, due to the curve of the cell and the presence of the first pore, makes the fluid struggles to enter that gap. When the pressure is high, the velocity is low, and it seems the simulation matches well with the theory reported in the literature.

4.0 CONCLUSION

In this work, CFD was applied to characterize the flow pattern for endothelial cells in dengue infection with plasma leakage. The pressure distribution and the velocity profile over the cell have been shown and the characterization of cell has been described. This study can be considered as a first step to develop the ways of the prevention of the dengue infection through manipulation the shear stress to reduce the potency of dengue virus to attach the cell surface and inhibit the expression of adhesion molecules.

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