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Biomedical Advance Studies Involving CFD Models, Specially In Human Anatomy

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ABSTRACT

Biomathematics is the branch of Mathematics where we study those mathematical formulations which are applicable in the field of life sciences. Several biomathematical models have been applying in the field of life sciences for solving complicated and complexioned problems on ecology, growth, viral diseases, cardiovascular diseases etc. Computational Fluid Dynamics (CFD), which is a branch of Mathematics, presently, an important section of Biomathematics, providing Mathematical Models in the studies on human anatomy and human physiology specially related to liquid flow and gaseous flow in human body. In this context, we will discuss about the application of CFD in diagnosis of diseases related to artery (atherosclerosis) circulation of blood through heart valves means heart functioning and further the mathematical design will be studied and investigated in certain circumstances of calculations.

Keywords: *Biomathematics, Cardiovascular diseases, haemolysis, Newtonian and non-Newtonian models, Shear rates.*

1. INTRODUCTION

Recently, several researches has been conducted and several researches are carrying on for developing Mathematical Models (design) in the field of life sciences and also we study them in a known branch of Mathematics called 'Biomathematics'. The topic 'Biomathematics' initiated by Dr William Moses Feldman(Russian Biomathematician, initially he was an expert physician in London Hospital further worked as an astronomer in 1923 (Tripathee, S. M. et al. 2024), published a book entitled 'Biomathematics' in 1935). Today, after completion of 100 years of Biomathematics, this branch became highly relevant and applied discipline for the development of such as bio-informatics, bio-statistics, human physiology and computational biology and also, in the present time, Biomathematics has become the priority-based choice for Mathematical as well as biological academicians and researchers. Biomathematics are being used, now days, in investigations of several sub-branches of biological sciences that includes human genome, population growth, genetical issues, cancer cells, Blood circulation, ecological invasive species, human immune system etc.(Segel, L. A., 1980). The human body is itself, one of the most significant bio-mechanical system, in which, physiological fluid dynamics as well as gaseous flow plays very crucial role during several bio-rheological process and investigations. Physiological fluid dynamics systems is an emerged multi-disciplinary and multi-variational field, developed through enter-collaboration of scientist and researchers of several fields namely engineering, mathematical, statistician and medical science. Tosio Kitagawa (1974) worked on cell spaces using Mathematical formulations of Biomathematics and shown its applicability in cell space can have some connections with biological problems and thus, could be a theoretical framework in the field of biological science. Further, he discussed various biological problems related to birth, growth, death, breakdown, disintegration and ecosystem problems.

Zvia Agur, an Israel Biomathematician explored ideas of modelling disease progression. We analyse the effect of a drug against a particular disease and further testing the efficacy of the drug through several attempts on patient populations and then by using probability of the drug efficiency, a formula of medicine against a particular disease thus prepared. Mathematical modelling in life science can impact on other clinical technologies through several diagnostic devices. In the present time, there are several available diagnostic options in proteomics technology which analyse the cellular pathological events. During the last five decades, progress in biomathematics has been observed as the important period of its development. In this period, biomathematics were applied in the field of drugs, ecology, growth problems, DNA, and infectious diseases on populations, study of liquid and gaseous flow in human bodies, developing several diagnostic devices

and also some little in cancer and its control. In present time, the most advanced technology in the field of biomathematics is CFD (Computational fluid dynamics). CFD, in recent, emerging in biomedical application because of its multiple complexity in the study of human anatomy and human body fluid flow behaviour. Since the importance on studies of body fluids flow and system components are to perform. Further, the study and investigations of bio-fluid physiology on human bodies has been developing for some years, now, resulted the advancement of biomedical practices and technology on this topic has been stimulated. The biomedical researches on this topic, with the inclusion of CFD software and techniques, is still emerging which now, incorporated the systems of physiology and pathophysiology of the cardiovascular system and respiratory system through simulation (Basri, E. I. et al., 2016).

2. APPLICATIONS OF CFD IN LIFE SCIENCES

Computational Fluid Dynamics(CFD) is recently emerged and widely adopted computational methodology (Mathematical Models) in order to solve complicated problems in biomedical field. CFD is now become an important component in the advancement of updated designs and optimization through computational models resulting in lower the operating costs with better efficiency. Biomedical applications are now referencing to the complexity of fluid and air flow behaviour within the human anatomy likely human body. The recent applications of CFD models in biomedical applications are more practicable because of its availability of highly performing hardware and software models with updated advanced technologies in computer sciences. Several simulations and clinical consequences have been used for the investigations in biomedical applications specially for blood flow and nasal airflow in human body. The study of human body blood flow includes the circulation of blood in ventricle function, heart valves and coronary artery. The nasal airflow investigations in human body compiled with the basic airflow through human nose and its distribution under drug delivery improvement, food necessity and virtual surgery needs. CFD study plays an important and decision-oriented role in prior support to execute a real commitment towards any medical design(models) alterations and provide the right direction to develop medical interventions and right medications (Basri, I. E. et al. 2016).

In the 21st century, Cardiovascular diseases are accepted as the most common death factor (Amini, M. et al., 2021) and mostly, cardiovascular diseases resulted from atherosclerosis which involves the heart and cardiovascular of human body. Atherosclerosis commonly caused by day-to-day life activities like unhealthy diet, hypertension, smoking, diabetes and less physical activity and this diseases caused depositing cholesterol in blood flowing vessels that reduced its cross-sectional area which leads to increase in local blood flow velocity and shear stress on erythrocytes. The increase in shear stress in the areas of blood flow vessel narrowing increases the risk of haemolysis. Jędrzejczak, K., et al. (2023) have used CFD models to estimate the risk of haemolysis in arteries. According to them, Haemolysis can occur in the stenosed artery areas of high shear stress. The CFD models provide the information on the distributions of vessel shear stress and blood velocity. Various models have been used in different levels of stenosis. On research, Tomographic analysis software (model) were preferred to provide basic information on haemolysis risk which doesn't require highly sophisticated analysis including costly hardware and software, highly power consumption for the diagnosis of clinical patient health. CFD simulation techniques has been widely utilizing in the modelling and designing of several medical conditions, specially in the case of paravalvular leaks(Kozłowski et al., 2022), which generates a risk of haemolysis because of high shear stress, near leaks(Jędrzejczak, K., et al. 2023). Shear stress value, near about the threshold value, is considered as dangerous to patients because the exceedance of the threshold value, indicating towards blood haemolysis in the atherosclerotic stenosis (Antonowicz et al., 2023). Therefore, based on the analysis of the blood-flow field, which is obtained through the µPIV measurements, a possible CFD simulations could be verified for blood-flow in the geometries of narrowing of vessels(Jędrzejczak, K., et al. 2023).

3. CFD FORMULATIONS BEHIND BIOMATHEMATICAL MODELS

Jędrzejczak, K., et al. (2023) have analysed a 3D models based on computed tomography scans of arteries with stenoses. Geometries preparation were arranged through the CAD software which was implemented in the ANSYS software programming package like Design-Modeler and Space-Claim. The blood-inlet and blood-outlet of the vessel were made neat and clean. A rectangular design was prepared for conducting 3D printing in which the blood vessel volume was subtracted. The resulting channel was available for µPIV testing fluids. For carrying comparative analysis, the µPIV calculations and CFD simulations, Mathematical Model(a Newtonian model) was employed. This Mathematical model was conducted using a liquid which was equivalent in viscosity and density to the liquid utilized in the calculations in the µPIV.,

The discussion of Mathematical formulation in this Model (Newtonian) followed through

$$\eta = \varphi(\gamma) = \mu_\infty + (\mu_0 - \mu_\infty)[1 + (\pi\gamma)^\alpha]^{\frac{n-1}{\alpha}} \quad \dots\dots\dots\dots\dots (1)$$

This equation is popularly known by Carreau-Yasuda Model. The symbols in (1), for the liquid, has the following meaning,

η −viscosity (a function of γ), γ −shear rate, μ_∞ −viscosity at infinite shear rate, μ_0 −viscosity when shear rate 0, and n, α & γ are coefficients of materials. For blood, when its density is 1060 kg/m^3 values of following symbols, according to Weddell, J. C. (2015) are as given

$\mu_\infty = 3.45 \times 10^{-3}\ Pa.s$ and $\mu_0 = 5.6 \times 10^{-2}\ Pa.s$ and the coefficients are

$$\pi = 1.902\ s, n = 0.22, \alpha = 1.25.$$

In this case of Newtonian Model (Jędrzejczak, K., et al. 2023), the mathematical representation of viscosity of the utilized liquid is given by

$$\eta = R(\xi)\mu_0 \quad \ldots\ldots\ldots\ldots\ldots \quad (2)$$

μ_0 were determined 6.99×10^{-4} Pa.s and $R(\xi)$ is the relative viscosity of blood which is further defined through the connection

$$R(\xi) = \frac{R_0(\xi) + Pe.R_\infty(\xi)}{1 + Pe} \quad \ldots\ldots\ldots\ldots\ldots \quad (3)$$

Where $R_0(\xi)\ and\ R_\infty(\xi)$ are relative blood viscosity at lowest and highest shear rates respectively, calculated by the formulae

$$R_0(\xi) = (1-\xi)^{-5/2} - \mathrm{K}\left\{\left(1 - \frac{\xi}{\xi^*}\right)^{-2} - \sum_{j=0}^{2}(1+j)\left(\frac{\xi}{\xi^*}\right)^j\right\} \quad \ldots\ldots\ldots\ldots\ldots \quad (4)$$

and

$$R_\infty(\xi) = (1-\xi)^{-5/2} + \mathrm{H}\left\{\ln\left[1 - \left(\frac{\xi}{\xi^*}\right)^{1/3}\right] + \sum_{j=1}^{6}\frac{1}{j}\left(\frac{\xi}{\xi^*}\right)^{j/3}\right\} \quad \ldots\ldots\ldots\ldots\ldots \quad (5)$$

where the symbols $\xi\ and\ \xi^*$ providing the effective apparent volume fraction of RBC and the maximum apparent volume fraction (which is taken 0.695) respectively. K and H are equation constants whose values are taken 1.3 and 2 respectively.

Further, *Pe* is the Peclet number, which is defined by the formula

$$Pe = \frac{\dot{\gamma}\alpha^2}{D_M(\xi)} \quad \ldots\ldots\ldots\ldots \quad (6)$$

Where the symbols $\dot{\gamma}$ stand for shear rate, α stand for the 'characteristic particle size' for the entire population, which is equal to the volume-weighted mean of particle size and D_M stand for the effective diffusion coefficient of molecular diffusion.

Similar analysis were conducted through non-Newtonian Model by Trejo-Soto, C. and Hernández-Machado, A. (2022) by utilizing healthy blood and measured velocity, viscosity, density and pressures through microfluidic channel, using a pressure-driven flow, the effective viscosity were characterised by a function of the blood plasma (non-Newtonian model) as well as the shear rate for the sample blood. The pressure were formulated by $\Delta P_{eff} = \rho g H - P_{cap}$. They observed that the differences in the viscosities of the utilized blood samples depending upon their red- blood cells concentration and further the viscosity curves determines the collapse of the 38% and 25% found hematocrit, while, the 48% was recorded slightly off. Finally they discussed that their normalization processes, in diagnosis, could be applied to differentiate between the healthy and the diseased blood samples.

The Mathematical formulation in this Model (non-Newtonian) followed through

The viscosity formula

$$\eta\big(\dot{\gamma}(\xi)\big) = m\dot{\gamma}(\xi)^{n-1} \quad \ldots\ldots\ldots\ldots\ldots \quad (7)$$

Where m is consistency index and n is specific blood constant. Shear rate $\dot{\gamma}$ is defined by

$$\dot{\gamma}(\xi) = \frac{\partial v_x(\xi)}{\partial \xi} \quad \ldots\ldots\ldots\ldots\ldots \quad (8)$$

For $v_x(\xi)$ be the velocity of blood sample varies on its vertical position ξ in microchannel.

The pressure difference function for the coupled system of reservoir–tube microchannel, inside the microchannel is given by

$$\Delta P = \rho g H - \Delta P_t - P_{cap} \quad \ldots\ldots\ldots\ldots\ldots \quad (9)$$

Where ΔP_t denotes the dropped pressure inside the microchannel tube and P_{cap} denotes the capillary pressure inside the microchannel, which is calculated by using the Young–Laplace equation given as

$$P_{cap} = 2T\cos\theta\left(\frac{1}{b} + \frac{1}{\omega}\right) \ldots\ldots\ldots\ldots\ldots \quad (10)$$

Where b be the Averaging of the microchannel depth to obtain the mean shear rate of the front while ω is for tube.

The pressure difference ΔP in terms ofthe averaged velocity $\dot{h}$ of the front is given by

$$\Delta P = \frac{m}{b} 2h \left[\frac{2}{b}\left(2+\frac{1}{n}\right)\right]^n (\dot{h})^n \quad \ldots\ldots\ldots\ldots\ldots \quad (11)$$

And the pressure drop ΔP_t inside tube is determined by

$$\Delta P_t = \frac{2 l_t m}{r^{n+1}} \left[\left(3+\frac{1}{n}\right)\left(\frac{\omega b \dot{h}}{\pi r^2}\right)\right]^n \quad \ldots\ldots\ldots\ldots\ldots \quad (12)$$

Now using (11) and (12) in (9), we obtain

$$\rho g H - P_{cap} = \Delta P + \Delta P_t = 2m\left\{\frac{1}{b} h \left[\frac{2}{b}\left(2+\frac{1}{n}\right)\right]^n + \frac{l_t}{r^{n+1}}\left[\left(3+\frac{1}{n}\right)\left(\frac{\omega b}{\pi r^2}\right)\right]^n\right\}(\dot{h})^n \ldots\ldots (13)$$

Since the resistance for the tube is very larger than comparing to the resistance of the microchannel(Trejo-Soto, C., et al. 2017) which indicates that first part of RHS of (13) can be neglected, then equation (13) reduced to

$$\rho g H - P_{cap} = 2m\left\{\frac{l_t}{r^{n+1}}\left[\left(3+\frac{1}{n}\right)\left(\frac{\omega b}{\pi r^2}\right)\right]^n\right\}(\dot{h})^n \ldots\ldots\ldots\ldots\ldots \quad (14)$$

But we defined the effective pressure $\Delta P_{eff} = \rho g H - P_{cap}$ therefore

$$\Delta P_{eff} = 2m \frac{l_t}{r^{n+1}}\left[\left(3+\frac{1}{n}\right)\left(\frac{\omega b}{\pi r^2}\right)\right]^n (\dot{h})^n \ldots\ldots\ldots\ldots\ldots \quad (15)$$

The flow rate V inside the microchannel, defined by the formula (Trejo-Soto, C. and Hernández-Machado, A., 2022)

$$V = \int_{-b/2}^{b/2} v_x(\xi) d\xi = \frac{2n\dot{\gamma}(\xi)}{2n+1} \omega(\xi)^{\frac{-1}{n}} \left(\frac{b}{2}\right)^{2+\frac{1}{n}} \quad \ldots\ldots\ldots\ldots\ldots \quad (16)$$

4. CONCLUSION

Today, CFD simulations act very important role for several diseases, specially cardiovascular diagnosis, and study the rheological properties of blood samples. It is a numerical modelling(formulation) method, based on solving of equations involving factors pressure, density, viscosity, mass, momentum, energy and certain properties of blood and blood flowing vessels. Further, the diagnosis of diseases can also be carried through relative studies of blood (non-Newtonian model) and a fluid(Newtonian model), behaves blood-like natures and properties. CFD simulations could have more idealised diagnostic methods regarding several flow-matters risk-diseases lesions.

Conflict of interest

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