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A model for predicting magnetic drug targeting of multifunctional drug carrier for Caputo-Fabrizio fractionalized blood flow through a microvasculature

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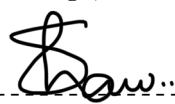
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Abstract

Biofluid mechanics play a major role in the cardiovascular system and blood as a whole, therefore, it may help in detecting and designing a treatment for some blood related diseases and understanding them better. The aim of this thesis is to study the trajectories of nanoparticles during magnetic drug targeting for treatment of cancer and cardiovascular disorders in a fractionalized blood flow. Nanoparticle (NP)-based drug delivery systems have shown many advantages in cancer and cardiovascular treatment. In the present study, magnetic drug targeting which is one of the major drug delivery when treating cancer and cardiovascular diseases was used due to its noninvasiveness, high targeting efficiency and minimized toxic side effects on healthy cells and tissues. Firstly the impact of Reynolds number, pulsatile frequency, magnetic field strength and the Darcy number in a fractionalized blood flow through a permeable vessel was analyzed. We assumed that the blood vessel segment is a rigid cylindrical tube and blood along with magnetic particle flowing through the vessel shows Newtonian behaviour with a constant viscosity. Lastly, we have used a two phase model where the radius of the microvessel is divided into two parts. The flow nature at the clear region is defined by non-Newtonian Jeffrey fluid and the peripheral region is defined by Newtonian fluid. The wall of the microvessel is considered as permeable. We have analyzed and discussed the effects of the time relaxation to retardation ratio, Jeffrey parameter, pulsatile frequency, magnetic field strength and the Darcy number on the trajectories of the drug carrier during magnetic drug targeting. The fractional parameter boost up the motion of radial motion of the drug carrier particles, while restricting the axial motion of the carrier particles as observed in the study through graphs plotted with fractional parameter as a contributing factor. All parameters except the pulsatile frequency accelerated the radial motion of the drug carrier particles as observed in the results. The theory developed can be used to determine the optimum size of the carrier particle for treating a tumor with a given size and location within the body.

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Nomenclature

A_0	amplitude of body acceleration
$\mathbf{B}$	total magnetic field
B_0	external magnetic field
B_i	Bingham number
b_0	amplitude of the pulsatile component of the pressure gradient
b_1	amplitude of pulsatile component which gives rise to systolic and diastolic pressure
C_D	drag coefficient (non -dimensional)
$\mathbf{Da}$	Darcy number
$\mathbf{d}$	distance between the axis of the microvessel and the centre of the magnet
d_{cp}	diameter of the carrier particle
d_v	diameter of the vessel in micron
$\mathbf{E}$	the electric field at any point
F_f	fluidic force on the carrier particle
F_{fr}	fluidic force along the radial direction
F_{fz}	fluidic force along the axial direction
F_m	magnetic force on the carrier particle
F_{mr}	magnetic force along the radial direction
F_{mz}	magnetic force along the axial direction
f_b	frequency of the body force
$\mathbf{H}_a$	applied magnetic field intensity at the center of the particle
H_D	the hematocrit of the blood
$\mathbf{J}$	current density
J_0	zero order modified Bessel function of first kind
$\mathbf{K}$	permeability of the fluid
$\mathbf{k}$	constant
$\mathbf{M}$	Hartmann Number
M_s	magnetization of the magnet
m_p	mass of the carrier particle
$\mathbf{p}$	Fluid pressure
$\mathbf{Q}$	volumetric flow
$\mathbf{Re}$	Reynolds number
R_{cp}	radius of the carrier particle
R_{mag}	radius of the magnet
R_0	radius of the artery
(r, θ, z)	cylindrical coordinates of the axis
r_0	initial position of the carrier particle in the radial direction
$\mathbf{t}$	time
$\mathbf{u}$	the velocity of the fluid

u_f	mean velocity of the fluid
V_{mp}	volume of the magnetic particle
$v_{cp,r}$	velocity of the carrier particle in the radial direction
$v_{cp,z}$	velocity of the carrier particle in the axial direction
z_0	initial position of the carrier particle in the axial direction

Greek letters

β_{vf}	volume fraction parameter
$\dot{\gamma}$	shear rate
η	effective viscosity of the fluid
λ	rigidity modulus
λ_1	Time relaxation-to-retardation ratio
λ_2	Retardation time of Jeffrey fluid
μ	apparent viscosity
μ_0	permeability of the vacuum
μ_f	permeability of the fluid
μ_{plasma}	permeability of the plasma
ν	dynamic viscosity
ρ	density of the fluid
σ	electrical conductivity of the fluid
τ_y	yield stress
ϕ_0	phase angle
χ_f	susceptibility of the fluid
χ_p	susceptibility of the magnetic nano-particle
ω	pulsatile frequency

Subscripts

0	initial
cp	carrier particle
f	component for fluidic force
fr	component of fluidic force along the radial direction
fz	component of fluidic force along the axial direction
m	component of magnetic force
mr	component of magnetic force along the radial direction
mz	component of magnetic force along the axial direction
mag	magnet
r	along radial direction
v	vessel
z	along axial direction

1. Introduction

1.1 Basic Introduction

The flow behavior of biological fluids in living organisms play a crucial role in determining the state of the tissue through which they flow. Biofluid mechanics, which is the study of the fundamentals of biological fluid flow, has been recognized to be extremely important for understanding how changes in the flow behavior within living tissue may affect both the fluid and the tissue. Thus, it studies the movement and balance of forces in resting fluids and fluids in motion. It plays a major role in the cardiovascular system and it is very important to understand the forces and movement of blood cells as well as the interaction between blood cells and the vessel wall. According to Fung [1], for an organism, biomechanics help us to understand its normal function, predict changes due to alterations and propose methods of artificial intervention. Thus, diagnosis, surgery, prosthesis and etc. are closely associated with biomechanics.

Therefore, this is a field whose significance to the field of bioengineering has increased over the last decades as pharmaceuticals, biomaterials, non-invasive diagnostic and surgical procedures create changes in the mechanics of biofluid. Biofluid mechanics is a field including one of the most important areas of the study of blood flow and dispersion of drug delivery to cure cancer and cardiovascular diseases. It have been shown that hemodynamics may have a strong influence on the creation of aneurysms, varicose veins and vessel wall structure. In preliminary studies, it has been demonstrated that geometry of the vessel, elasticity of vessel walls, diameter of the vessel etc. help to determine the flow behavior. High velocity fluctuations indicate flow disturbances that should be avoided (Hennerici et al. [2]). Health care practitioners must understand fluid dynamic factors such as pressure, velocity, flow rate, shear stress on the wall, blood cells and flow behavior.

Blood can be considered as homogeneous in large blood vessels, but in small tubes the rheology shows considerable non-homogeneous behavior. Due to the particulate nature of red blood cells, there is an almost cell-free layer of plasma near the vessel wall according to Gentile and Decuzzi [3]. The major effect of this layer is to decrease the apparent viscosity or resistance (the Fahraeus-Lindqvist effect and Fahraeus effect), especially in medium to moderately small blood vessels. It is also noted that at various positions and situations blood behaves as a Newtonian fluid or non-Newtonian fluid.

It is very crucial to have knowledge of the rate at which different materials that disperse in the circulatory system since some medications are therapeutic at low concentration, but toxic at high concentration. However, blood is a complex biological fluid made up of components

such as Red Blood Cells (RBCs), monocytes, platelets etc.. The nature of blood flow through a microvessel is affected by microscopic properties of blood such as deformation of blood cells, interaction of plasma, blood cells and the blood vessel wall.

Drug delivery has many advantages in various fields such as chemical, environmental and biomedical engineering (Bali et al.[4]). Studying nanoparticles has shown a great significance in biofluid mechanics, specifically during targeted drug delivery. This is due to their high precision, effectiveness and that they are rapidly internalized by the target cells. Also, the longitudinal transport of passive species in a fluid flow is of fundamental importance in different fields such as in medical field for the delivery of nanoparticles carrying therapeutic and imaging agents.

As nanoparticle based drug delivery continued to be researched as a better and improved method of drug delivery, there was a new factor introduced in the process, the fractional calculus. Fractional calculus is one of the generalizations of the classical calculus and it has been successfully used in various fields of science and engineering. It provides more accurate models of the physical systems than the ordinary calculus in areas such as mechanics, chemistry, bioengineering etc.

1.2 Equations Governing Fluid Motion

These are equations that provides a mathematical model of motion of blood in an artery.

Conservation of mass equation

$$\frac{\partial \rho}{\partial t} + \rho \nabla \cdot \mathbf{v} = 0, \quad (1.1)$$

ρ is the fluid density, $\nabla = \hat{i} \frac{\partial}{\partial r} + \hat{j} \frac{\partial}{\partial \theta} + \hat{k} \frac{\partial}{\partial z}$ and $\mathbf{v} = v_r \hat{i} + v_\theta \hat{j} + v_z \hat{k}$ is the velocity vector of the fluid flow and (r, θ, z) are the cylindrical coordinates.

For a fluid whose density is constant (incompressible flow) i.e $\rho = 0$,

$$\begin{aligned} \nabla \cdot \mathbf{v} &= 0, \\ \nabla \cdot \mathbf{v} &= \frac{\partial v_r}{\partial r} + \frac{\partial v_\theta}{\partial \theta} + \frac{\partial v_z}{\partial z} = 0. \end{aligned} \quad (1.2)$$

The momentum equation for the incompressible flow with external force yields;

$$\rho \left(\frac{\partial \mathbf{v}}{\partial t} + \mathbf{v} \nabla \cdot \mathbf{v} \right) = -\nabla p + \eta \nabla^2 \mathbf{v} + \mathbf{F}, \quad (1.3)$$

where $\nabla^2 = \frac{1}{r} \frac{\partial}{\partial r} \left(r \frac{\partial}{\partial r} \right) + \frac{1}{r^2} \frac{\partial^2}{\partial \theta^2} + \frac{\partial^2}{\partial z^2}$, η, p, t are the viscosity of the fluid, pressure and time respectively.

With the components of the velocity vector given by $\mathbf{v} = (v_r, v_\theta, v_z)$, the continuity equation is given by;

$$\frac{\partial v_r}{\partial r} + \frac{v_r}{r} + \frac{1}{r} \frac{\partial v_\theta}{\partial \theta} + \frac{\partial v_z}{\partial z} = 0 \quad (1.4)$$

and the momentum equations based on Newton's law for moving fluids looking at the fact that in biofluid dynamics we deal with incompressible fluid flow, the basic governing equations are given as follows (changing the stresses to velocities) by Waite and Fine [?] as;

$$\rho \left(\frac{\partial v_r}{\partial t} + v_r \frac{\partial v_r}{\partial r} + \frac{v_\theta}{r} \frac{\partial v_r}{\partial \theta} + v_z \frac{\partial v_r}{\partial z} - \frac{v_\theta^2}{r} \right) = -\frac{\partial p}{\partial r} + \eta \left(\nabla^2 v_r - \frac{v_r}{r^2} - \frac{2}{r^2} \frac{\partial v_\theta}{\partial \theta} \right) + F_r, \quad (1.5)$$

$$\rho \left(\frac{\partial v_\theta}{\partial t} + v_r \frac{\partial v_\theta}{\partial r} + \frac{v_z v_\theta}{r} + \frac{v_\theta}{r} \frac{\partial v_\theta}{\partial \theta} + v_z \frac{\partial v_\theta}{\partial z} \right) = -\frac{1}{r} \frac{\partial p}{\partial \theta} + \eta \left(\nabla^2 v_\theta - \frac{v_\theta}{r^2} + \frac{2}{r^2} \frac{\partial v_r}{\partial \theta} \right) + F_\theta, \quad (1.6)$$

$$\rho \left(\frac{\partial v_z}{\partial t} + v_r \frac{\partial v_z}{\partial r} + \frac{v_\theta}{r} \frac{\partial v_z}{\partial \theta} + v_z \frac{\partial v_z}{\partial z} \right) = -\frac{\partial p}{\partial z} + \eta \nabla^2 v_z + F_z, \quad (1.7)$$

where $\nabla^2 = \frac{\partial^2}{\partial r^2} + \frac{1}{r} \frac{\partial}{\partial r} + \frac{1}{r^2} \frac{\partial^2}{\partial \theta^2} + \frac{\partial^2}{\partial z^2}$ and F_r, F_θ, F_z are the respective components of the external force in the radial, transverse and along the axis of the cylinder.

The above momentum equations are known as the Navier-Stokes equations named after Claude-Louis Navier (1823) and George Gabriel Stokes (1845). Their solutions can be physically determined given the boundary and initial conditions. In the case of the viscous fluid, the condition of no-slip on solid boundaries must be satisfied i.e., on the wall both the normal and tangential components of the velocity must be zero.

1.3 Non-Newtonian Fluids

The Newtonian law of viscosity states that the shear stress is directly proportional to the rate of shear strain or the velocity gradient. However, non-Newtonian fluids does not follow this law of viscosity as their viscosity varies (increases or decreases) based on the applied force or stress.

1.3.1 Governing Equations of Non-Newtonian Fluid Models

In the small blood vessels, blood behaves as a non-Newtonian fluid and the constitutive equations are as follows;

1. Time Independent non-Newtonian Fluids

These are fluids for which the shear rate, γ at any point is determined only by the value of the shear stress at that certain point. However, there is a non-linear relationship between the shear stress and shear rate which can be written as;

$$\tau = f(\gamma) \quad (1.8)$$

. A Newtonian fluid is a special case of non-Newtonian fluid where the function $f(\gamma)$ is

linear. The power law fluid (Waele and Ostwal-de[5]), Bingham fluid (Bingham [6, 7]), Herschel-Bulkley fluid (Hershel and Bulkley [8]), Casson fluid (Casson [9]) and bi-viscosity fluids are examples of this class. A rheological model of the non-Newtonian fluid is given in Fig. 1.1.

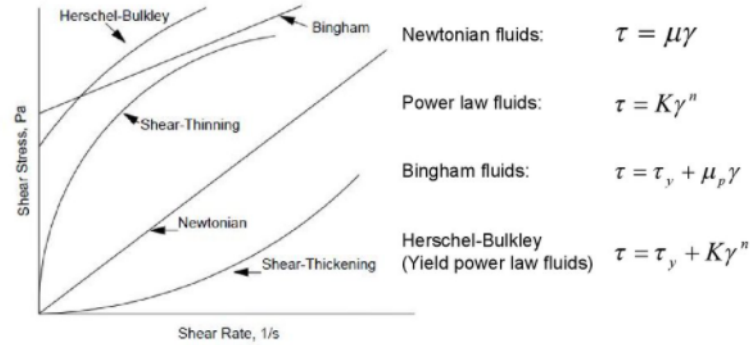


Figure 1.1: Flow curves of different time-independent fluids (<http://www.en.ppt-online.org>)

2. Viscoelastic Fluids

A viscoelastic fluid is a fluid that possesses both viscous and elastic properties at the same time. They show incomplete elastic recovery upon the exclusion of a deforming stress and have the ability to store, recover and release energy. Examples of such fluids are multi-grade oils, paints, polymer melts and liquid detergents etc.. Many different mathematicians have worked a formula needed for a better interpretation of non-Newtonian fluid behavior, such as the Jeffrey's fluid model. Jeffrey fluids unlike other models have a different and more sophisticated way of describing the properties of non-Newtonian fluids. It has two generalized parameters, namely the ratio of retardation over the relaxation time parameter λ_1 and the retardation time parameter λ_2 . Due to the viscoelastic characteristics, Jeffrey fluid has widespread applications in the industry and medical fields.

Because of its extraordinary properties and abilities, various studies have been investigated by different researchers like Ge-JiLe et al. [10] who studied the two-phase flow of Jeffrey fluid in the presence of porous media. Multi-phase flow of Jeffrey Fluid was investigated by Mubbashar Nazeer et al. [11]. Other researches of Jeffrey fluid flow is shown from Rao and Sreenadh [12] - Ramesh et al. [15].

1.4 Boundary Conditions

Boundary conditions are constraints necessary for the solution of a boundary value problem. Boundary conditions are divided into three types namely Dirichlet boundary condition, Neumann boundary condition and Mixed boundary condition.

1.4.1 Dirichlet Boundary Condition

This is a type of boundary condition named after Peter Gustav Lejeune Dirichlet (1805-1859). This boundary condition specifies the value that the unknown function needs to take on along the boundary of the domain. In biofluid mechanics, it consists of the value of velocity and/or dispersion to be taken by a certain nodes.

Continuity of velocity:

$$\begin{aligned} u(r, 0) &= 0, \quad \text{at } t = 0, \quad r \in [0, 1] \\ u(1, t) &= 0, \quad t > 0. \end{aligned} \tag{1.9}$$

The slip condition which is a dirichlet boundary condition specifies that the velocity of a fluid at the wall of the channel is non-zero and the no slip condition specifies that at the wall the velocity is equal to zero, i.e the fluid at the wall will have the same velocity as the velocity of the wall.

1.4.2 Neumann Boundary Condition

This type of boundary condition is named after Carl Neumann (1832-1925). When applied in ordinary or partial differential equations, it specifies the values that the derivative of a solution is going to take. For example:

$$\frac{\partial u(0, t)}{\partial t} = 0, \quad \text{at } t > 0 \tag{1.10}$$

1.4.3 Mixed Boundary Condition

It is named after Victor Gustave Robin (1855-1897). Mixed boundary condition is a combination of the Dirichlet boundary condition and Neumann boundary condition, consisting of linear/ non-linear combination of the values of the field.

1.5 Blood Rheology

1.5.1 Cardiovascular System

The cardiovascular system is part of the large circulatory system which circulates fluids throughout the body. The circulatory system is a network of organs and vessels that are responsible for blood flow, flow of nutrients, hormones, oxygen and other gases in and out of the cells. There have been numerous significant contributors to biomechanics research by many physicians such as Harvey [16] who discovered the nature of blood circulation in the cardiovascular system. His clear description of circulatory system is considered as the first step on the path to modern cardiovascular physiology. The cardiovascular system consists of the heart, blood vessels, and the approximately 5 liters of blood that the blood vessels transport. It protects the body from infections, blood loss and helps regulate body temperature, fluid balance and blood pH. The transport medium, blood, is circulated throughout the body in a network as shown in Figure 1.2.

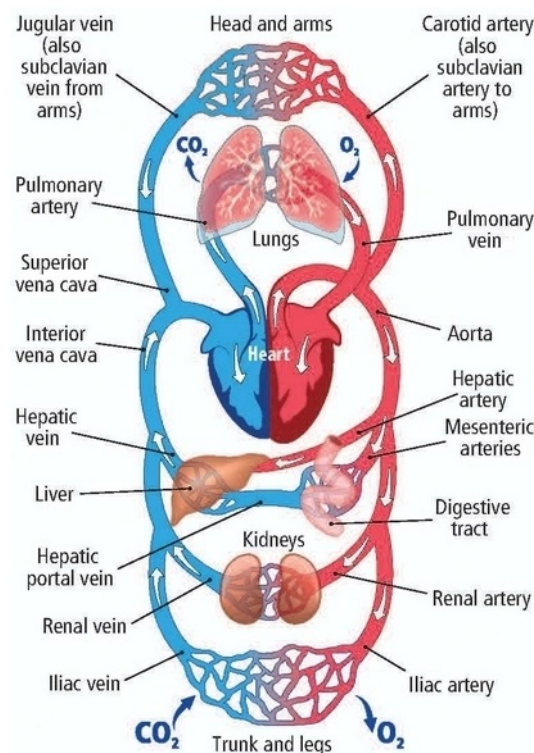


Figure 1.2: The diagram of the human circulatory system (<http://www.tutorvista.com>).

Blood flow in the circulatory system can be divided into two main sections: (i) the pulmonary and (ii) systematic circulatory systems.

1. The Pulmonary Circulatory System

The pulmonary circulation is the path the blood take to send oxygen-depleted blood away from the heart through the pulmonary artery to the lungs to collect oxygenated blood back to the heart through the pulmonary vein. Thus, it provides a gaseous exchange function.

2. Systematic Circulatory System

This circulation system supplies the oxygenated blood from the heart to all body tissue but not the lungs. The systemic circulation is a network of blood vessels that transport blood from the heart and service the body cells .

1.5.1.1 The Heart

It is an organ in the circulatory system responsible for pumping blood to all parts of the body. It is a key organ in the circulatory system and propel blood through the circulatory system. The heart includes a distribution, dispersion and collection systems. It is divided into a right heart, which delivers blood to the pulmonary circulation and a left heart, which supplies blood to the systematic circulation. The schematic diagram of the heart is given in Fig. 1.3. A detailed description about the heart and its functions are given by Fung [17] - Bianco[18].

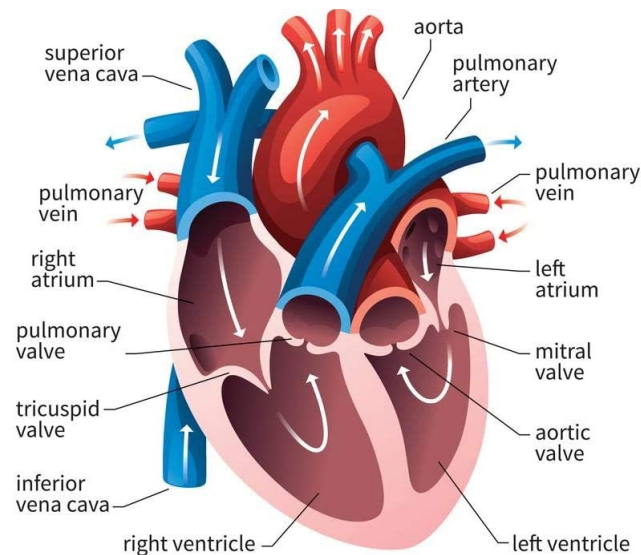


Figure 1.3: Blood flow through the heart (<http://www.nhlbi.nih.gov/health>)

1.5.1.2 Blood Vessels

The cardiovascular system is a complex branched networks of tubes which are called blood vessels. Blood vessels are channels of blood transportation in human body. Blood vessels are divided into three groups;

- Arteries $\Rightarrow$ They transport blood to all parts of the body from the heart.
- Capillaries $\Rightarrow$ Smallest blood vessels, they convey blood between arterioles and venules.
- Veins $\Rightarrow$ They transport blood to the heart from different parts of the body.

1.5.1.3 Blood

Blood is a constantly circulating fluid providing the body with nutrients, oxygen, and waste removal. The average person has about 5 liters (more than a gallon) of blood. It is made up of a suspension of red blood cells (erythrocytes) which transport oxygen in the blood through hemoglobin, white blood cells (leukocytes) and platelets in an aqueous solution (plasma). The density of the erythrocytes is 1.1 gm/cm^3 , while whole blood density is $1.05\text{-}1.06 \text{ gm/cm}^3$. The plasma is a transparent, slightly yellowish fluid and its density is about 1.035 gm/ml . It is responsible for the transportation of substances that can be found dissolved in the plasma such as glucose, oxygen, carbondioxide, nutrients and cellular waste products throughout the body. However, platelets play an important role in the formation of blood clots which may severely interfere with the blood flow.

1.5.2 Microcirculation

Blood flows differently depending on the channel it is flowing in. The flow can be in a closed circulatory system (arteries, veins, capillaries) or an open circulatory system (heart etc). Thus, microcirculation is the circulation of blood in small blood vessel. Nanda and Basun Mallik[19] found out that blood behaves like Newtonian fluids in large blood vessels while in narrow blood

vessels behaves like Non-Newtonian fluids as explained before. For human blood, the vessel diameter is $\leq 1000\mu m$. The diameter of capillaries is $\leq 5\mu m$ and these are permeable in nature. There are parameters that affect microcirculation. They are temperature, systemic blood pressure, general status (stress, food, medication, smoking etc.), mental activity physical activity and age.

1.6 Magnetohydrodynamics

Magnetohydrodynamics (MHD) is the discipline that study magnetic properties and behavior of electrically conducting fluids in the presence of an externally applied magnetic field. Examples of such magneto-fluids include plasmas, liquid metals, salt water, and electrolytes.

1.6.1 Governing Equation of Magnetohydrodynamics

The set of equations that describe MHD are a combination of the Navier-Stokes equations which describes the flow of fluids (fluid dynamics), Newtons second law of motion and Maxwell's equations of electromagnetism. These differential equations can be solved simultaneously, either analytically or numerically. Let us consider a cylindrical tube with an electrically conducting fluid flowing with velocity v in the presence of an applied magnetic flux B , electric field E , magnetic permeability μ_0 electrical conductivity σ , mass density ρ and pressure p varying with time t . Then the Maxwell's equation is given by

$$\begin{aligned}\nabla \times \mathbf{E} &= -\frac{\partial \mathbf{B}}{\partial t} \\ \nabla \times \mathbf{B} &= \mathbf{J}\end{aligned}\tag{1.11}$$

It satisfies the following conditions

$$\nabla \cdot \mathbf{J} = 0 \quad \text{and} \quad \nabla \cdot \mathbf{B} = 0\tag{1.12}$$

where $\mathbf{J}$ is the current density given by the Ohm's law as

$$\mathbf{J} = \sigma[\mathbf{E} + \mathbf{v} \times \mathbf{B}].\tag{1.13}$$

Then the system of MHD equations are given as

$$\begin{aligned}\frac{\partial \mathbf{v}}{\partial t} + (\mathbf{v} \cdot \nabla) \mathbf{v} &= -\frac{\nabla p}{\rho} + \mathbf{v} \nabla^2 \mathbf{v} + \frac{1}{\rho} \mathbf{J} \times \mathbf{B}, \\ \nabla \times \mathbf{v} &= 0.\end{aligned}\tag{1.14}$$

The Lorentz force term $\mathbf{J} \times \mathbf{B}$ expanded using the Ampère's law is

$$\mathbf{J} \times \mathbf{B} = \frac{(\mathbf{B} \cdot \nabla) \mathbf{B}}{\mu_0} - \nabla \left(\frac{\mathbf{B}^2}{2\mu_0} \right). \quad (1.15)$$

1.6.2 Applications of Magnetohydrodynamics

Applications of MHD have been studied extensively across multiple disciplines such as petroleum industries, MHD power generators (Marquis [20]), plasma studies (Wie [21]), automotive engineering (Gourdine [22]), cooling of nuclear reactors, boundary layer control in aerodynamics, biomedical studies (Hamid et al. [23]), biological studies (Saman et al. [24]) etc. In medical applications, it is often noted that the prevention and rational therapy of arterial hypertension are closely connected with the mechanism of its origin and development. The flow of blood can be controlled during surgeries by the application of an external magnetic field. It has also important applications in the development of magnetic devices for cell separation (Yousef et al. [25]), controlling the blood flow velocities in surgical procedures, and evaluating the effect of strong magnetic fields on the human circulation system, targeted transport of magnetic particles as drug carriers etc.

Various researchers studied the applications of magnetohydrodynamics in blood flow for various goals. Sud et al. [26] performed an analysis on a blood pump by means of a non-invasive circulatory assist device using the principle of magnetohydrodynamics. Mustapha et al. [27] studied unsteady magnetohydrodynamic blood flow through an artery in the presence of irregularly shaped pair stenosis. Mizra et al. [28] investigated the blood flow along with magnetic particles through an arterial stenosis with the influence of magnetic field, a magnetohydrodynamic approach of non-Newtonian blood flow with magnetic particles in stenosed artery.

1.7 Drug Delivery

Drug delivery is an important aspect in pharmaceuticals as it describes the method and approach to delivering drugs or pharmaceuticals to their site of action within an organism, with the goal of achieving a therapeutic outcome. Selecting the channels or routes for administering drugs has a significant effect on the efficacy of the drug. Drugs can be delivered in the body in many different ways such as invasive and noninvasive. Invasive delivery involve intravenous delivery and noninvasive includes oral, transdermal, mucosal and nasal. The routes of administration of drugs was further studied by Lansdowne [29] and Nayak [30].

In the last decades, methods of drug delivery have been changed dramatically and even much greater changes are expected in the future. Among the new drug delivery systems, nanotechnology-based drug delivery systems are currently been studied and will facilitate the advanced systems of drug delivery. Corporate investments on nanotechnology for drug delivery diagnostics increased year by year and nanotechnology based drug delivery has already been commercialized by many reputable companies (Wang et al. [31]).

Nanotechnology-based drug delivery is very advantageous as it has the ability to deliver the drugs at the targeted area without the toxicity or the negative effects of the drug affecting other healthy cells in the body. Different type of carrier particles are used in the targeting of nanotechnology-based drug delivery systems, some of them are pH-sensitive carriers, thermally responsive carriers, photochemically controlled delivery system, magnetic targeted drug delivery of nanocarriers, ultrasound-mediated drug delivery and targeting. In the present analyses we mainly focus on the magnetic targeted drug delivery of nanocarriers in a fractionalized blood flow.

1.7.1 Drug Targeting

Drug targeting is the principle by which distribution of drugs in the organism is maneuvered in a manner such that the concentration of the drug at the disease site is high, while its concentration in non-target organs and tissues is low, i.e. below certain minimal level so as to prevent any toxic effect (Maiti and Sen [32]). Targeted drug delivery systems can help improve the outcome of chemotherapy where roughly 99% of the drugs administered do not reach the tumor site (Trafton [33]) by allowing

- the maximum fraction of the delivered drug molecule to react exclusively with the cancer cells without adverse effects to normal cells.
- preferential distribution of drug to the cancer cells.

There are various classifications of drug targeting as shown in the Figure 1.4 below. A detailed description on this can be found in the cited article.

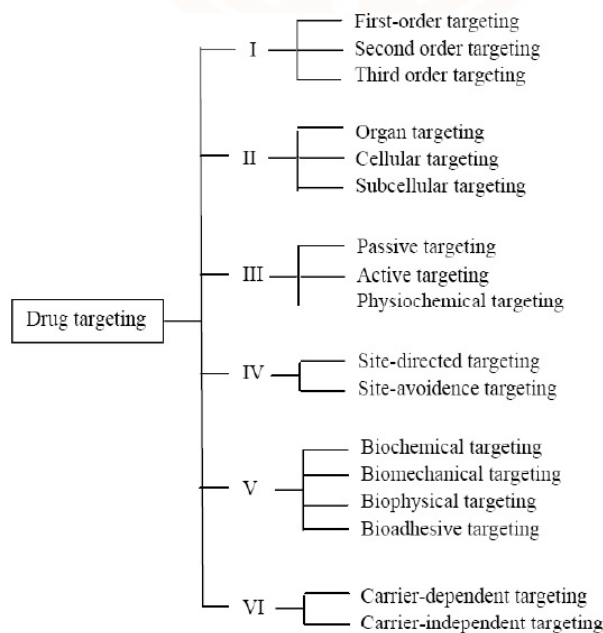


Figure 1.4: Different types of drug targeting (Lubbe et al.[34])

1.7.2 Magnetic Drug Targeting

Magnetic drug targeting is a method whereby magnetic drug carriers in the body are manipulated by external magnetic fields to reach the target area. This method is one of the major drug delivery methods which are used for treatment of diseases like cancer, cardiovascular and endovascular diseases due to its noninvasiveness, high targeting efficiency and minimal negative side effects on healthy cells and tissues (Liu et al. [35]). During application of this method of drug delivery, the therapeutic agent is either encapsulated into a magnetic carrier particle or conjugated on its surface. The magnetic particles with bound drug molecules will be injected into the blood stream where they will be guided by an externally applied magnetic field to the target site as shown in Figure 1.5.

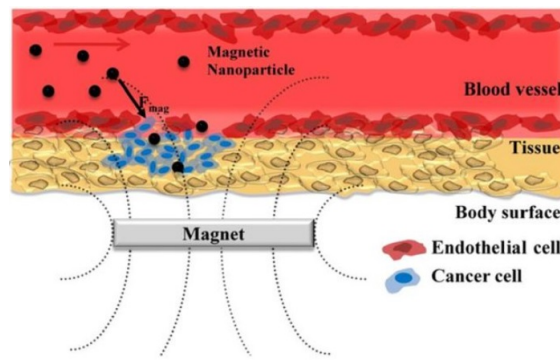


Figure 1.5: Schematic representation of magnetic drug targeting (Park et al. [36])

The effectiveness of the carrier particles accumulation depends on various parameters such as intensity of magnetic field, the rate of blood flow and the surface characteristics of the carrier particles. Upon magnetic particles accumulation at the target site, drug molecules are then released from the carrier particles by changing physiological conditions such as pH, osmolality, temperature, or different enzymatic activity (Molema and Meijer [37]). This will result in higher dosage of the drug at the target site, thus an effective treatment as the drug molecules are localized at the target site (Speziale et al. [38]).

1.8 Fractional Calculus

Fractional calculus deals with the study of fractional order integrals and derivatives and their diverse applications. It has attracted interest of researchers in several field such as mathematics, physics, chemistry, engineering, and even finance and social sciences (Gorenflo and Mainardi [39]) as it provides more accurate models of the physical systems than the ordinary calculus. Fractional Calculus was introduced after the French mathematician L'Hôpital asked for the notation of differentiation of non integer of order $\frac{1}{2}$ to the Leibniz, in 1695 (Ishteva et al. [40]). Leibniz (1695–1697) mentioned a possible approach to fractional order differentiation, in a sense that for non-integer (n) the definition could be following. Since then, many contributions to theory and its applications come up from different famous mathematicians (Gorenflo [41]). Further studies and applications of fractional calculus can be found from Kisela [42] - Zheng [46].

1.8.1 Fractional Derivative and Its Properties

Fractional order systems, or systems containing fractional derivatives have been studied by many in engineering and science field (Heaviside [47], Bush [48]). There are growing number of physical systems whose behavior can be compactly described using fractional calculus system theory. These are electrochemical process (Ichise et al. [49]), dielectric polarization (Sun et al. [50]), viscoelastic materials (Bagley and Calico [51]) and chaos (Hartley et al. [52]), and electromagnetism fractional poles (Engheta [53]).

A fractional derivative is defined using a fractional integral. Suppose that f is a function defined in an open interval $(0, a)$, then the fractional order derivative of f is given as:

$$\frac{1}{\Gamma(\alpha)} \int_0^x (x-t)^{\alpha-1} f(t) dt. \quad (1.16)$$

There are lot of literature on different definitions of fractional derivatives. However, there are only a few of which the researchers such as Thabet Abdeljawad [54] are more focused on and they are

1. Riemann- Liouville fractional derivative

It is the generalization of the derivative for theoretical purpose and it is based on Cauchy's formula for calculating iterated integrals. It is given as (Ross [55] - Machado et al. [57])

$$D^\alpha f(x) = \frac{1}{\Gamma(n-\alpha)} \frac{d^n}{dx^n} \int_0^x \frac{f(t)}{(x-t)^{\alpha+1-n}} dt. \quad (1.17)$$

2. Caputo fractional derivative

Unlike the Riemann-Liouville fractional derivative, it is not necessary to define the fractional order initial conditions when using the Caputo fractional derivative to solve differential equation. The Caputo fractional derivative also allows the use of the initial and boundary conditions when dealing with real-world problems. It is customary in groundwater investigations to choose a point on the centerline of the pumped borehole as a reference for the observations and therefore neither the drawdown nor its derivatives will vanish at the origin. It is also used during magnetic drug delivery during treatment of cancer and cardiovascular disorders. Thus, the Caputo derivative is the most appropriate fractional operator to be used in modeling real-world problem. It is defined by Caputo [58]- Kilbas [60] as

$${}_a^C D_t^\alpha f(t) = \frac{1}{\Gamma(n-\alpha)} \int_a^t \frac{f^{(n)}(\tau) d\tau}{(t-\tau)^{\alpha+1-n}}. \quad (1.18)$$

1.9 Fractional Blood Flow

Fractional blood flow has been investigated by many researchers recently as they wanted to differentiate the difference and its purpose from the normal blood flow or the usual blood flow. Ali et al. [61] have investigated the effect of magnetic fields and their applications in the human body, specifically in blood with the application of a fractional model for two-phase flow. Bansi et al. [62] have studied the fractional blood flow in oscillatory arteries with thermal radiation and magnetic field effects. Ali et al. [63] have explored the Casson fluid model for blood flow in a horizontal cylinder using the fractional derivatives approach. Later, researchers attempted many problems to discuss the blood flow through the artery by using the Caputo-Fabrizio fractional order time derivative (Yang et al. [64] - He et al. [69]).

Khan [70] investigated partial slip effects on the oscillatory flows of a fractional Jeffrey fluid in a porous medium. The oscillatory rotating flows of a fractional Jeffrey fluid filling a porous medium was discussed by Hayat et al. [71]. A non-linear problem of generalized Jeffrey and generalized second grade fluid in terms of (Atangana–Baleanu) AB fractional derivative was modeled by Saqid et al. [72]. Alotta et al. [73] studied a fractional nonlocal approach to nonlinear blood flow in small-lumen arterial vessels and a fractional relaxation time derivative on blood flow in arteries with magnetic and thermal radiation was studied by Yakubu et al. [74]. Farhad Ali et al. [75] theoretically investigated the natural convection blood flow as a Brinkman-type fluid with uniformly distributed magnetic particles in a circular cylindrical tube with the applied external magnetic field. They generalized the blood flow by using the definition of Caputo time-fractional derivative.

1.10 Problem Statement

Cancer and cardiovascular diseases such as atherosclerosis, stenosis, thrombosis and many more are causing havoc all over the world as it deprives people of their social and health lives, especially people from low and middle income countries. Millions of people are dying due to this non-communicable diseases. It has also come to attention that blood flow in the aortic bifurcation is of great clinical interest both with respect to genesis and the diagnostic of these diseases. Therefore, in order to conquer this arterial diseases, traditional drug delivery, a common method was suggested. This method involves injecting drugs in the blood stream that will go throughout the circulatory system. However, this method of drug delivery is inappropriate when treating targeted regions as much dosage of the drug will be needed for the required amount of drugs to reach the target or the diseased area. Thus, the toxicity and the negative effects of the medication will affect and harm other healthy cells in the body due to the dispersion characteristics of blood during drug delivery (Rekhar et al. [76]).

In 2022, 1,918,030 new cancer cases and 609,360 cancer deaths were projected in the United States, including approximately 350 deaths per day from lung cancer, the leading cause of can-

cer death. Therefore, during treatment of cancer and cardiovascular diseases, it is necessary to have the skills or the ability to direct medication to the site where the disease is situated.

Treatment methods such as chemotherapy, surgery, radiation, targeted therapy and stem cell transplant used for cancer and cardiovascular diseases damages normal cells and cause many side effects like deterioration of the patient health. For example, during chemotherapy, less percentage of the drugs go to the tumor cells, with the remaining percentage going to the healthy cells, causing systemic toxicity and negative effects (blood-forming cells in the bone marrow, hair follicles, anaemia, changes in the skin, fatigue etc.). Due to these side effects, the doctors or those who are in charge of the patient end up giving the patient the dosage they can physically withstand rather than what is needed to treat the tumor cells. By doing so, they will be violating the the basic principles of drug management which stipulates that the required amount of drugs should reach the diseased area in the body.

Responding to the above matter, magnetic drug targeting was proposed. It is a process whereby magnetic particles bounded with drug molecules are injected into the blood stream and guided to the targeted area with the help of an externally applied magnetic fields (Figure 1.5). Magnetic particles were used as transport agents for bio-application because, 1) they are non-toxic and well-tolerated by living organisms when properly synthesized and fractionalized (Safarik and Safarikova[77]), 2) they can be synthesized in sizes that range from a few nanometers to higher ranges with a narrow interval, 3) they can be custom-tailored with surface treatments that enhance biocompatibility and anable coating with affinity biomolecules for highly specific binding with a target bio-material, 4) they show super-paramagnetic behaviour, that is they can be easily be magnetized by an applied magnetic field, but when the field is removed, it reverts back to an unmagnetized state (Furlani [78], Shaw [79]).

1.11 Aim and Objectives

1.11.1 Aim

The aim of this thesis is to study the trajectories of nanoparticles during magnetic drug targeting for treatment of cancer and cardiovascular disorders in a fractionalized blood flow.

1.11.2 Objectives

- To analyze the effect of the fractional parameter during MDT using Caputo-Fabrizio fractional derivative.
- To analyze how various parameters impact treatment of cancer and cardiovascular disorders in a fractionalized blood flow (Parameters influencing drug delivery efficiency).

2. Magnetic Drug Targeting during Caputo-Fabrizio fractionalized blood flow through a permeable vessel

2.1 Introduction

The traditional method of drug targeting involves injection of drugs into the bloodstream, which will be systematically distributed throughout the body. However, when treating a targeted or a specific area, this method of drug targeting is undesirable as much dosage of drugs will be required for treating that particular site. Magnetic drug targeting (MDT) is one of the major drug targeting procedures due to its non-invasiveness, high targeting efficiency and minimal toxic side effects on healthy cells and tissues (Alexiou et al. [80]). Furlani and Ng [81] have presented an analytic model for predicting the transport and capture of magnetic nanoparticles in the microvasculature.

Furlani and Furlani [82] have studied the magnetic targeting of therapeutic carrier particles in microvasculature. In MDT, various forces such as the magnetic force, fluidic force and buoyant force as the dominant forces are acting on the multifunctional carrier particles (Sutradhar et al. [83]). Many researchers have started to work in this direction to understand the influence of the various parameters on the trajectories of the drug carrier by considering different rheology of blood ([84] - [88]), permeability of the blood vessel (Shaw et al. [89]), external magnetic field (Rukshin et al. [90]- Choomphon-anomakhun et al. [91]), two phase blood flow model (Sibanda and Shaw [92]).

As MDT continued to be researched as a better and improved method of drug delivery, there was a new factor introduced in the process, the fractional calculus. Fractional calculus is one of the generalizations of classical calculus and it has been successfully used in various fields of science and engineering. Shah et al. [93] have studied the effects of the fractional order and magnetic field on the blood flow in cylindrical domains by replacing the time derivative of order one with the Caputo fractional derivatives. The fractional derivatives model is obtained by converting the first order time derivatives to Caputo fractional derivatives.

The effect of the magnetic field on the magnetic nanoparticles embedded in blood has been discussed by Ali et al. [94]. They have considered a Caputo-Fabrizio fractional derivative for blood and magnetic particles flowing in a cylindrical domain. A comparison between the ap-

proach of the Caputo-Fabrizio and Atangana-Baleanu fractional derivatives for the blood flow through a cylindrical shaped blood vessel has been discussed by Sheikh et al. [95] and Imtiaz et al. [96]. In the above literature, the authors mainly studied the velocity profile of blood and magnetic particles. However, in the present problem, we have focused on the trajectories of the drug carrier towards the tumor region which gives the capture efficiency of the drug carrier particle at the tumor region. Blood rheology is classified as a Newtonian fluid (Furlani [82]).

The Caputo-Fabrizio fractional time derivative is introduced in the momentum equation with the vibration environment. The velocity profile is solved analytically with the help of the Laplace transform and Finite Hankel transform and the solution is represented in the form of Lorenzo-Hartley and Robotnov-Hartley functions, and convolution of Laplace transform. Fluidic and magnetic force used in the force equilibrium and find the trajectories of the carrier particles. The final axial and radial trajectories of the carrier particles with respect to time and for a fixed time the radial trajectories of the carrier particles with respect to the axial trajectories are shown through graphs. As per the author's knowledge, the present work is unique as it depends on the time parameter and the axial and radial trajectories of the carrier particle are based on the Caputo-Fabrizio fractional time derivative.

2.2 Formulation of the Problem

We have considered blood together with the magnetic nanoparticles embedded in carrier particles flowing through a horizontal cylindrical artery of radius R_0 , where the drug carrier particles are uniformly distributed throughout the blood as shown in Figure 2.1. The coordinates of the artery are defined by a cylindrical coordinate system (r, θ, z) where the z -axis is along the axis of the artery and r is along the radial direction. The blood is considered as a Newtonian fluid, (Pedley [97], Berger and Jou [98]).

The governing momentum equation for fluid flow in cylindrical coordinates is written as (Sharma et al. [65])

$$\frac{\partial \bar{u}}{\partial \bar{t}} = -\frac{1}{\rho} \frac{\partial \bar{p}}{\partial \bar{z}} + \nu \left(\frac{\partial^2 \bar{u}}{\partial \bar{r}^2} + \frac{1}{\bar{r}} \frac{\partial \bar{u}}{\partial \bar{r}} \right) + G(\bar{t}) - \frac{\nu}{K} \bar{u}, \quad (2.1)$$

where $\bar{u}(\bar{r}, \bar{t})$, ρ , ν and K are the respective axial velocity, density, kinematic viscosity of the fluid and the fluid permeability.

The body acceleration $G(\bar{t})$ is written as

$$G(\bar{t}) = \bar{A}_0 \cos(\bar{\kappa} \bar{t} + \phi_0), \quad (2.2)$$

where $\bar{A}_0$ and ϕ_0 denotes the amplitude and lead angle of $G(\bar{t})$, $\bar{\kappa} = 2\pi f_b$ with f_b being the frequency in Hz.

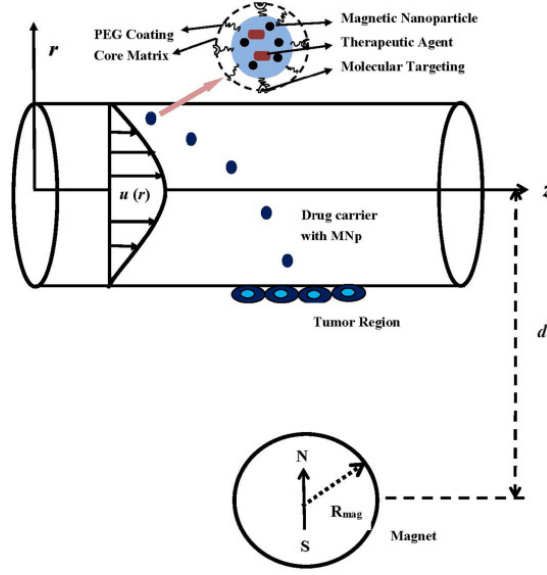


Figure 2.1: Noninvasive magnetic drug targeting in a microvessel with the multifunctional drug carrier. The trajectory of the drug carrier (includes magnetic nanoparticles, therapeutic agents, Molecular targeting, Core matrix, PEG coating) towards the tumor region influenced by the magnetic and fluidic force.

The pulsatile characteristics of the blood originates from the pumping action of the heart and therefore the pressure gradient is written as

$$-\frac{\partial \bar{p}}{\partial \bar{z}} = \bar{b}_0 + \bar{b}_1 \cos(\bar{\omega} \bar{t}), \quad (2.3)$$

where $\bar{b}_0$ is the constant amplitude of the pressure gradient. $\bar{b}_1$ is the amplitude of pulsatile component which gives rise to systolic and diastolic pressure and $\bar{\omega}$ is the pulsatile frequency.

Using equations (2.2) and (2.3) in equation (2.1) yields

$$\frac{\partial \bar{u}}{\partial \bar{t}} = \frac{1}{\rho} (\bar{b}_0 + \bar{b}_1 \cos(\bar{\omega} \bar{t})) + \nu \left(\frac{\partial^2 \bar{u}}{\partial \bar{r}^2} + \frac{1}{\bar{r}} \frac{\partial \bar{u}}{\partial \bar{r}} \right) + \bar{A}_0 \cos(\bar{\kappa} \bar{t} + \phi_0) - \frac{\nu}{K} \bar{u}. \quad (2.4)$$

In order to consider the time-fractional model, we first introduce and multiply equation (2.4) by the factor $\sqrt{\frac{R_0 \rho}{b_0}}$ (Shah et al. [93]) and get

$$\lambda^\alpha D_t^\alpha \bar{u} = \frac{\lambda}{\rho} (\bar{b}_0 + \bar{b}_1 \cos(\bar{\omega} \bar{t})) + \lambda \nu \left(\frac{\partial^2 \bar{u}}{\partial \bar{r}^2} + \frac{1}{\bar{r}} \frac{\partial \bar{u}}{\partial \bar{r}} \right) + \lambda \bar{A}_0 \cos(\bar{\kappa} \bar{t} + \phi_0) - \frac{\lambda \nu}{K} \bar{u}, \quad (2.5)$$

where the derivative

$$D_t^\alpha f(r, t) = \begin{cases} \frac{1}{\Gamma(1-\alpha)} \int_0^{\bar{t}} \frac{1}{(\bar{t}-\tau)^\alpha} \frac{\partial f(\bar{r}, \tau)}{\partial \tau} d\tau, & 0 < \alpha < 1, \\ \frac{\partial f(\bar{r}, \tau)}{\partial \tau}, & \alpha = 1 \end{cases} \quad (2.6)$$

is the Caputo fractional derivative operator of order α with $0 < \alpha < 1$ according to Shantanu [99].

The corresponding initial and boundary conditions of equation (2.5) are given as

$$\begin{aligned}\bar{u}(\bar{r}, 0) &= 0, \quad \text{at} \quad \bar{t} = 0, \quad \bar{r} \in [0, R_0] \\ \bar{u}(\bar{R}_0, \bar{t}) &= 0, \quad \frac{\partial \bar{u}}{\partial \bar{r}}(0, \bar{t}) = 0, \quad \bar{t} > 0.\end{aligned}\tag{2.7}$$

The initial condition shows that the velocity of the blood is zero at $\bar{t} = 0$. The first boundary condition represents the no-slip condition at the wall of the blood vessel and the second condition shows the axi-symmetric nature of the blood flow about the axis of the microvessel.

Introducing the non-dimensional parameters

$$\begin{aligned}r &= \frac{\bar{r}}{R_0}, \quad t = \frac{\bar{t}}{\lambda}, \quad u = \frac{\bar{u}}{u_0}, \quad b_0 = \frac{\lambda \bar{b}_0}{u_0}, \quad b_1 = \frac{\lambda \bar{b}_1}{u_0}, \quad \omega = \lambda \bar{\omega}, \quad \kappa = \lambda \bar{\kappa}, \\ A_0 &= \frac{\lambda \bar{A}_0}{u_0}, \quad z = \frac{\bar{z}}{R_{mag}}, \quad M_s = \frac{\bar{M}_s}{M_0}, \quad d = \frac{\bar{d}}{R_{mag}}, \quad R_{cp} = \frac{\bar{R}_{cp}}{R_0}, \quad R_{mp} = \frac{\bar{R}_{mp}}{R_0}.\end{aligned}\tag{2.8}$$

Using the above non-dimensional parameters, the governing equation becomes

$$D_t^\alpha = [b_0 + b_1 \cos(\omega t)] + \frac{1}{Re} \left(\frac{\partial^2 u}{\partial r^2} + \frac{1}{r} \frac{\partial u}{\partial r} \right) + A_0 \cos(\kappa t + \phi_0) - \frac{1}{Da} u\tag{2.9}$$

and the initial and boundary conditions are written as

$$\begin{aligned}u(r, 0) &= 0 \quad \text{at} \quad t = 0, \quad r \in [0, 1], \\ u(1, t) &= 0 \quad \frac{\partial u}{\partial r}(0, t) = 0, \quad t > 0,\end{aligned}\tag{2.10}$$

where the Reynolds number Re and Darcy number Da are given as

$$Re = \frac{R_0^2}{\lambda \nu}, \quad Da = \frac{K}{\lambda \nu}.\tag{2.11}$$

2.2.1 Solution Procedure

Applying the Laplace transform based on the time variant to equation (2.9) yields

$$s^\alpha u(r, s) = \frac{b_0}{s} + \frac{b_1 s}{s^2 + \omega^2} + A_0 \left[\frac{s \cos \phi_0 - \kappa \sin \phi_0}{s^2 + \kappa^2} \right] - \frac{u(r, s)}{Da} + \frac{1}{Re} \left[\frac{\partial^2 u(r, s)}{\partial r^2} + \frac{1}{r} \frac{\partial u(r, s)}{\partial r} \right].\tag{2.12}$$

Now, applying the Hankel transform of zero order in equation (2.12), we get

$$\begin{aligned}s^\alpha u_H(r_n, s) &= \left[\frac{b_0}{s} + \frac{b_1 s}{s^2 + \omega^2} + A_0 \left[\frac{s \cos \phi_0 - \kappa \sin \phi_0}{s^2 + \kappa^2} \right] \right] \frac{J_1(r_n)}{r_n} - \frac{u_H(r_n, s)}{Da} \\ &\quad + \frac{1}{Re} [-r_n^2 u_H(r_n, s)],\end{aligned}\tag{2.13}$$

where $u_H(r_n, s) = \int_0^1 ru(r, s)J_0(rr_n)dr$ is the finite Hankel transform of the function $u(r, s)$ and $r_n, n = 1, 2, \dots$ are positive roots of the equation $J_0(\chi) = 0$ with J_0 as the Bessel function of the first kind and zero order.

Rearranging and simplifying equation (2.13) results as

$$u_H(r_n, s) = \left[b_0 \left(\frac{s^{-1}}{s^\alpha + a_n} \right) - A_0 \sin \phi_0 \left(\frac{\kappa}{s^2 + \kappa^2} \right) \left(\frac{1}{s^\alpha + a_n} \right) \right] \frac{J_1(r_n)}{r_n} + \left[b_1 \left(\frac{s}{s^2 + \omega^2} \right) \left(\frac{1}{s^\alpha + a_n} \right) + A_0 \cos \phi_0 \left(\frac{s}{s^2 + \kappa^2} \right) \left(\frac{1}{s^\alpha + a_n} \right) \right] \frac{J_1(r_n)}{r_n}, \quad (2.14)$$

where $a_n = \frac{Re + Dar_n^2}{ReDa}$.

Applying the Inverse Laplace transform in equation (2.14) yields

$$u_H(r_n, t) = \left[b_0 \mathcal{L}^{-1} \left(\frac{s^{-1}}{s^\alpha + a_n} \right) - A_0 \sin \phi_0 \mathcal{L}^{-1} \left\{ \left(\frac{\kappa}{s^2 + \kappa^2} \right) \left(\frac{1}{s^\alpha + a_n} \right) \right\} \right] \frac{J_1(r_n)}{r_n} + \left[b_1 \mathcal{L}^{-1} \left\{ \left(\frac{s}{s^2 + \omega^2} \right) \left(\frac{1}{s^\alpha + a_n} \right) \right\} + A_0 \cos \phi_0 \mathcal{L}^{-1} \left\{ \left(\frac{s}{s^2 + \kappa^2} \right) \left(\frac{1}{s^\alpha + a_n} \right) \right\} \right] \frac{J_1(r_n)}{r_n}, \quad (2.15)$$

We have used the Robotnov and Hartley's ($F_\alpha(.,.)$), and Lorenzo and Hartley's ($R_{\alpha,v}(.,.)$) functions and they are respectively defined as (Pries et al. [100])

$$\mathcal{L}^{-1} \left\{ \frac{1}{s^\alpha + m} \right\} = F_\alpha(-m, t) = \sum_{n=0}^{\infty} \frac{(-m)^n t^{(n+1)\alpha-1}}{\Gamma((n+1)\alpha)}, \quad \alpha > 0, \quad (2.16)$$

$$\mathcal{L}^{-1} \left\{ \frac{s^{-1}}{s^\alpha + m} \right\} = R_{\alpha,v}(-m, t) = \sum_{n=0}^{\infty} \frac{(-m)^n t^{(n+1)\alpha-1-v}}{\Gamma((n+1)\alpha - v)}, \quad Re(\alpha - v) > 0. \quad (2.17)$$

Using equations (2.16) and (2.17) on equation (2.15), we get

$$u_H(r_n, t) = [F_{1n}(t) + F_{2n}(t) - F_{3n}(t)] \frac{J_1(r_n)}{r_n}, \quad (2.18)$$

where

$$\begin{aligned} F_{1n}(t) &= b_0 R_{\alpha,-1}(-a_n, t), \\ F_{2n}(t) &= (b_1 \cos(\omega t) + A_0 \cos \phi_0 \cos(kt)) * F_\alpha(-a_n, t), \\ F_{3n}(t) &= A_0 \sin \phi_0 \sin(kt) * F_\alpha(-a_n, t), \end{aligned} \quad (2.19)$$

and $f * g$ represents the Laplace convolution of the functions f and g .

The velocity profile after using inverse Hankel transform on equation (2.18) result as

$$u(r, t) = 2 \sum_{n=1}^{\infty} \frac{J_0(rr_n)}{r_n J_1(r_n)} [F_{1n}(t) + F_{2n}(t) - F_{3n}(t)], \quad (2.20)$$

where

$$u(r, t) = \mathbf{H}_0^{-1} u_H(r_n, t) = 2 \sum_{n=1}^{\infty} \frac{J_0(rr_n)}{r_n J_1^2(r_n)} u_H(r_n, t). \quad (2.21)$$

The volumetric flow rate is written as

$$\begin{aligned} Q &= 2\pi \int_0^1 u(r, t) r dr \\ &= 4\pi [F_{1n}(t) + F_{2n}(t) - F_{3n}(t)] \sum_{n=1}^{\infty} \frac{J_1(r_n)}{r_n^2 J_1(r_n)}. \end{aligned} \quad (2.22)$$

Using equation (2.22), we get the average velocity of the fluid as

$$\begin{aligned} \hat{u}_f &= \frac{Q}{\pi} \\ &= 4 [F_{1n}(t) + F_{2n}(t) - F_{3n}(t)] \sum_{n=1}^{\infty} \frac{1}{r_n^2}. \end{aligned} \quad (2.23)$$

2.2.2 Velocity Profile for Ordinary Fluid

The fluid behaves as an ordinary fluid for $\alpha = 1$, which simplifies equations (2.16) and (2.17) into

$$\begin{aligned} F_1(-m, t) &= e^{-mt}, \\ R_{1,v}(-m, t) &= \frac{1 - e^{-mt}}{m}, \end{aligned} \quad (2.24)$$

and the velocity profile (from equation 2.20) is written as

$$u(r, t) = 2 \sum_{n=1}^{\infty} \frac{J_0(rr_n)}{r_n J_1(r_n)} [G_{1n}(t) + G_{2n}(t) - G_{3n}(t)], \quad (2.25)$$

where

$$\begin{aligned}
G_{1n}(t) &= b_0 \frac{1 - e^{-a_n t}}{a_n}, \\
G_{2n}(t) &= (b_1 \cos(\omega t) + A_0 \cos \phi_0 \cos(kt)) * e^{-a_n t}, \\
G_{3n}(t) &= A_0 \sin \phi_0 \sin(kt) * e^{-a_n t}.
\end{aligned} \tag{2.26}$$

The volumetric flow rate is given by

$$Q = 4\pi [G_{1n}(t) + G_{2n}(t) - G_{3n}(t)] \sum_{n=1}^{\infty} \frac{1}{r_n^2}, \tag{2.27}$$

and the average velocity of the fluid written as

$$\hat{u}_f = 4 [G_{1n}(t) + G_{2n}(t) - G_{3n}(t)] \sum_{n=1}^{\infty} \frac{1}{r_n^2}. \tag{2.28}$$

2.2.3 Effective Viscosity

The viscosity of the blood depends on the hematocrit of the blood which appears due to the presence of the Red Blood Cells (RBCs). We have followed the experimentally determined analytical formula developed by Pries et al. [100] and it is written as

$$\mu = \mu_{plasma} \left[1 + (\mu_{0.45} - 1) \frac{(1 - H_D)^c - 1}{(1 - 0.45)^c - 1} \left(\frac{d_v}{d_v - 1.1} \right)^2 \right] \times \left(\frac{d_v}{d_v - 1.1} \right)^2, \tag{2.29}$$

where $\mu_{plasma} = 0.0012 N.s/m^2$ is the viscosity of the blood plasma (without the blood cells and platelets), d_v is the diameter of the blood vessel in micron, H_D is the hematocrit (normally 0.39 - 0.45) of the blood, $\mu_{0.45} = 6e^{-0.085d_v} + 3.2 - 2.44e^{-0.06d_v^{0.645}}$ and $C = (0.8 + e^{-0.075d_v}) \left(\frac{1}{1+10^{-11}d_v^{12}} - 1 \right) + \frac{1}{1+10^{-11}d_v^{12}}$.

2.2.4 Fluidic Force

In the present problem, we have considered blood as a Newtonian fluid and the carrier particle is spherical in shape (Furlani and Furlani [82]). The fluidic force is predicted by using the Stokes' approximation and is written as

$$F_f = -6\pi\mu R_{cp}(v_{cp} - u(r, t)), \tag{2.30}$$

where v_{cp} and R_{cp} are the reference velocity and radius of the carrier particle, respectively.

Now, the fluidic force in the component form in the $r - z$ plane is written as

$$F_{fr} = -6\pi\mu R_{cp}v_{cp,r}, \tag{2.31}$$

$$F_{fz} = -6\pi\mu R_{cp}(v_{cp,z} - \hat{u}_f). \tag{2.32}$$

2.2.5 Magnetic Force

The magnetic force on the carrier particle can be written as [81]

$$F_m = \mu_f \bar{V}_{mp} \frac{3(\chi_p - \chi_f)}{(\chi_p - \chi_f) + 3(\chi_f + 1)} (\mathbf{H}_a \nabla) \mathbf{H}_a, \quad (2.33)$$

where $\mu_f, \chi_p = \frac{\mu_p}{\mu_0} - 1, \chi_f = \frac{\mu_f}{\mu_0} - 1$ and $\mathbf{H}_a$ are the permeability of the fluid, susceptibility of the particle and fluid, and the externally applied magnetic field intensity at the center of the particle, respectively. μ_p and μ_0 are the respective permeability of the particle and the permeability of the air. The volume of a spherical magnetic particle is considered as $\bar{V}_{mp} = \frac{4\pi}{3} \bar{R}_{mp}^3$. We preferred the non-invasive magnetic targeting, where the distance of the drug carrier from the axis of the magnet ($\bar{d}$) is much larger than the diameter of the blood vessel i.e., $R_v \ll \bar{d}$. Further, the material of the magnet nanoparticle e.g., magnetite (Fe_3O_4) is biocompatible. These two assumptions simplified the magnetic force and it is written in the component form in the $r - z$ plane (Furlani and Ng [81]) as

$$F_{mr}(r, \bar{z}) = -3\mu_0 \bar{V}_{mp} \bar{M}_s^2 R_{mag}^4 \frac{d}{2(\bar{d}^2 + \bar{z}^2)^3} \quad (2.34)$$

and

$$F_{mz}(r, \bar{z}) = -3\mu_0 \bar{V}_{mp} \bar{M}_s^2 R_{mag}^4 \frac{\bar{z}}{2(\bar{d}^2 + \bar{z}^2)^3}, \quad (2.35)$$

where $\bar{M}_s, R_{mag}$ and $\bar{z}$ are the magnetization of the magnet, the radius of the magnet and the axial distance of the carrier particle, respectively.

Using equation (2.8), equations (2.34) and (2.35) can be written as

$$F_{mr}(r, z) = -L \beta_{vf} R_{cp}^3 M_s^2 \frac{d}{(d^2 + z^2)^3} \quad (2.36)$$

and

$$F_{mz}(r, z) = -L \beta_{vf} R_{cp}^3 M_s^2 \frac{z}{(d^2 + z^2)^3} \quad (2.37)$$

with $L = \frac{2\pi\mu_0 R_0^3 M_0^3}{R_{mag}^2}$.

2.2.6 Equilibrium Force

The particle motion can be anticipated using Newton's law, which is given by

$$m_p \frac{dv_p}{dt} = F_m + F_f, \quad (2.38)$$

where m_p, v_p are the mass and velocity of the drug carrier particle, F_m and F_f are the magnetic and fluidic forces, respectively. By ignoring the inertial term as it is sufficiently small for the blood vessel with a small radius, we obtain the particle motion on a simple force balance as

$$F_m + F_f = 0. \quad (2.39)$$

2.2.7 Noninvasive Procedure on the Trajectories of the Drug Carrier Particle

A noninvasive procedure is a safer medical procedure where no break in the skin is created and there is no contact with the mucosa, or skin break, or internal body cavity beyond a natural or artificial body orifice. Based on the non-invasive condition, the implemented condition is

$$\frac{L\beta_{vf}R_{cp}^2M_s^2}{6\pi\mu} \ll 1. \quad (2.40)$$

Implementing the non-invasive condition (equation 2.40) in equation (2.39) with equations (2.31) and (2.36), and equations (2.32) and (2.37), the velocity components of the drug carrier particle in the $r - z$ plane are written as

$$v_{cp,r} = \frac{dr(t)}{dt} = \frac{L\beta_{vf}R_{cp}^2M_s^2}{6\pi\mu} \frac{d}{(d^2 + z^2)^3} \quad (2.41)$$

and

$$v_{cp,z} = \frac{dz(t)}{dt} = \frac{L\beta_{vf}R_{cp}^2M_s^2}{6\pi\mu} \frac{z}{(d^2 + z^2)^3} + \hat{u}_f. \quad (2.42)$$

The axial position of the carrier particle is given by

$$z = z_0 + \hat{v}_{cp}t. \quad (2.43)$$

Assume that the average axial velocity of the carrier particle ($\hat{v}_{cp}$) equals the average fluid (blood) velocity, i.e,

$$\hat{v}_{cp} = \hat{u}_f \quad (2.44)$$

By coupling equations (2.41) and (2.42) with equations (2.43) and (2.44), we get the trajectories of the drug carrier particles $r(t)$ and $z(t)$ as

$$\frac{dr(t)}{dt} = \frac{L\beta_{vf}R_{cp}^2M_s^2}{6\pi\mu} \frac{d}{(d^2 + (z_0 + \hat{u}_{cp}t)^2)^3} \quad (2.45)$$

and

$$\frac{dz(t)}{dt} = \frac{L\beta_{vf}R_{cp}^2M_s^2}{6\pi\mu} \frac{z_0 + \hat{u}_{cp}t}{(d^2 + (z_0 + \hat{u}_{cp}t)^2)^3} + \hat{u}_f. \quad (2.46)$$

2.3 Results and Discussion

The average velocity of the fluid is determined by equations (2.23) and (2.28). The positive roots of the equation $J_0(x) = 0$ was calculated numerically and took the least positive root. The trajectories of the carrier particles for different parameters was determined from the solutions of equations (2.45) and (2.46). Since the governing equations are highly coupled, we have used the fourth-order Runge-Kutta method to solve the differential equations with the initial conditions $z(t = 0) = z_0$ and $r(t = 0) = -1$.

A comparison is made with the work of Furlani and Furlani [82] for a steady Newtonian blood flow through the vessel with $\alpha = 1, Da \rightarrow \infty, A_0 = b_1 = 0$ and the results are displayed in Figure 2.2. The results show a good agreement with the referenced or cited work. The effects of the Reynolds number (Re), the pulsatile frequency ω , magnetic strength parameter (Ms) and Darcy number (Da) on the radial and axial trajectories are studied for different values of the fractional-order parameter.

For the rest of the calculations, the parameter values are considered as $b_0 = 0.5, b_1 = 0.6, A_0 = 0.05, \phi_0 = 0.4, \kappa = 0.1, Da = 0.1, Ms = 1$ and $Re = 5$. The corresponding results are recorded graphically in Figures 2.3-2.13.

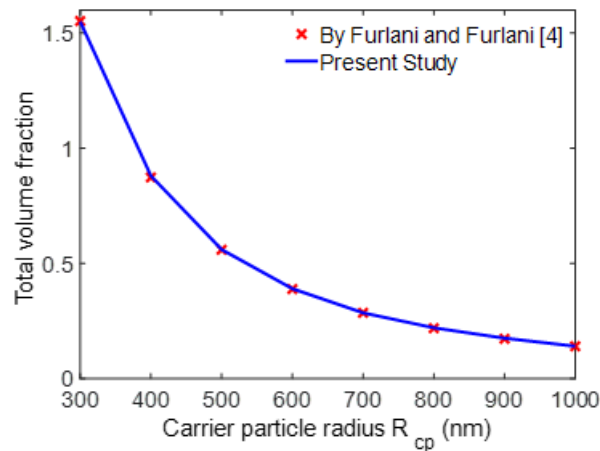


Figure 2.2: A comparison of the present work with Furlani and Furlani [82]

2.3.1 Effect of Fractional Parameter

The impact of the fractional parameters on the radial and axial trajectories of the carrier particle are observed in all the Figures 2.3 - 2.13. All figures contain four sub figures which plot for different values of the fractional parameters. Four different values of the fractional parameters are considered as 0.6, 0.8, 0.9 and 1. It is noted that for $\alpha = 1$, the governing equation behaved as a general differential equation. In all figures, it is observed that the radial movement of the carrier particle is downward with an increase in the value of α . It implies that the carrier particle is more easily captured by the fluid following the general derivatives than that of the fractional

derivatives.

In general, it is observed that the radial velocity of blood decelerates with an increase in the values of α (Abdullah et al. [101]). Hence, the impact of the magnetic force shows to be more significant and effective, which helps the carrier particle to move towards the downward direction, close to the tumor position (see Figures 2.3, 2.6, 2.8 and 2.11). For a similar reason, the axial motion of the carrier particle is observed as a slow movement with an increase in the values of α (see Figures 2.4, 2.7, 2.9 and 2.12).

The carrier particle feels a resultant force from the fluidic force and the magnetic force. With an increase in the value of α , the magnetic force puts more impact on the carrier particle than the fluidic force and hence the resultant trajectories of the carrier particle are observed downward and reach easily close to the tumor region (see Figures 2.5, 2.10 and 2.13). The fractional parameter shows a significant influence in the trajectories of the drug carrier particle with respect to time. Thus, the time dependent memory effect should not be neglected while developing a new drug targeting treatment to optimize the path of the drug carrier particle.

2.3.2 Effect of the Reynolds Number

The impact of the Reynolds number on the trajectories of the carrier particle in the x and z -directions with respect to time and with a fixed time is shown in Figures 2.3-2.5. Figures 2.3 and 2.4 depict the radial and axial trajectories of the carrier particle with respect to time, respectively, while Figure 2.5 depicts the trajectories of the particles for $r(t)$ versus $z(t)$. With small values of Re , the blood flow is calm and fashionable layered (Berger and Jou [98]). In this study, we restricted the Reynolds number to a lower value and chose the values of Re is 1, 3, 5 and 7. It is observed that with an increase in the Reynolds number, the radial trajectories of the carrier particles decreases. However, an opposite phenomenon is observed for the axial trajectories of the carrier particles. With an increase in the Reynolds number, the axial velocity of the fluid increases and it boosts up the axial velocity of the carrier particles.

According to our study, the velocity of the carrier particle is equal to the average of the fluid velocity. With an increase in axial velocity, the fluidic force on the carrier particle increases and it influences the carrier particle to move away from the tumor region, as observed with an increased value of z , in Figure 2.4. Figure 2.5 depicts the resultant trajectories of the carrier particles for different Re , which are essentially the trajectories of the carrier particles in the radial direction with respect to the axial direction. It observed that the carrier particle went far away from the capture point for a higher value of Re . This is because, the Reynolds number enhanced the axial velocity of the carrier particle, which restricted the radial downward movement of the carrier particle towards the tumor position.

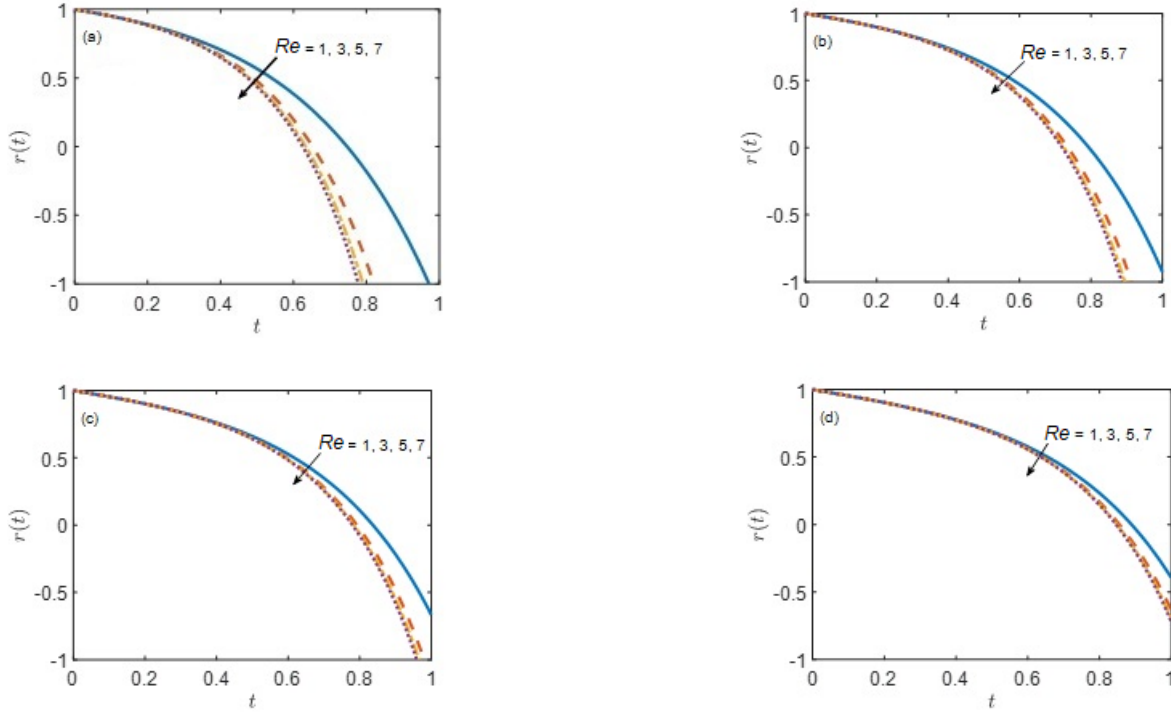


Figure 2.3: Radial trajectories of the carrier particle ($r(t)$) as a function of time for different Re with (a) $\alpha = 0.6$, (b) $\alpha = 0.8$, (c) $\alpha = 0.9$ and (d) $\alpha = 1$.

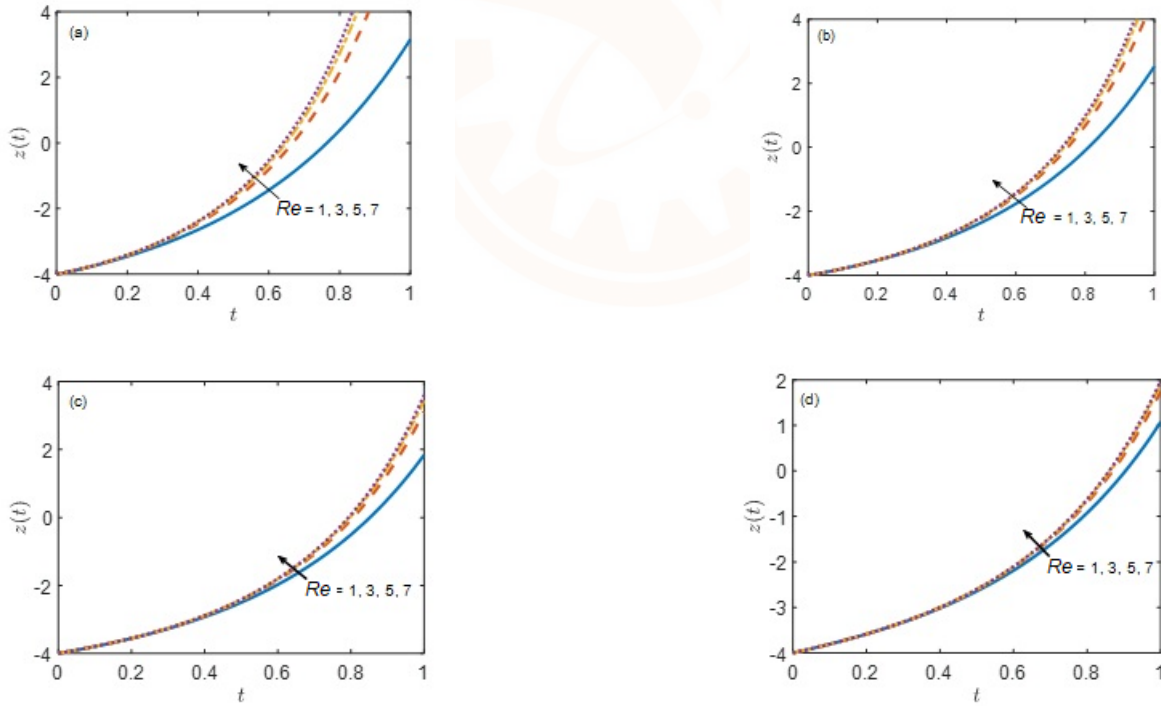


Figure 2.4: Axial trajectories of the carrier particle ($z(t)$) as a function of time for different Re with (a) $\alpha = 0.6$, (b) $\alpha = 0.8$, (c) $\alpha = 0.9$ and (d) $\alpha = 1$.

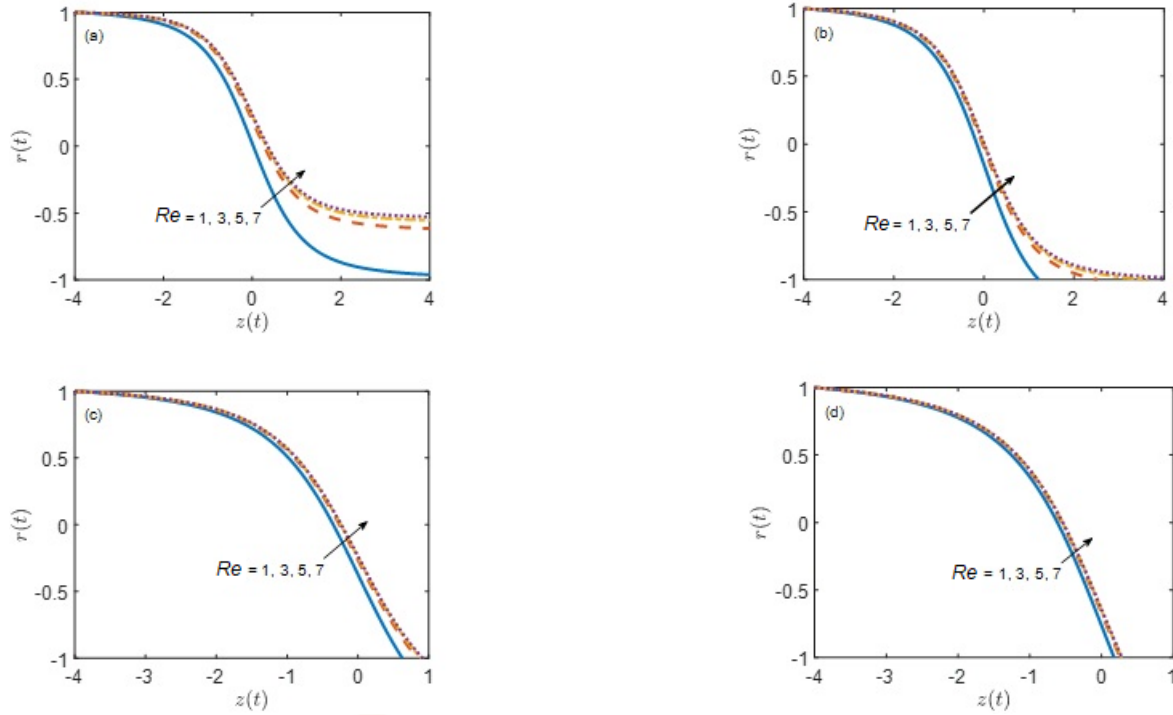


Figure 2.5: Radial trajectories with respect to the axial trajectories ($r(t)$ vs. $z(t)$) for different Re with (a) $\alpha = 0.6$, (b) $\alpha = 0.8$, (c) $\alpha = 0.9$ and (d) $\alpha = 1$.

2.3.3 Effect of the Pulsatile Frequency

The pulsatile frequency is related to the pulsatile nature of the blood flow which is based on the pressure gradient. The pressure gradient is pulsatile in nature due to the presence of periodic function $\cos(\omega t)$ term. In the present problem, we have considered the values of ω as 1, 3, 5, and 7. From Figure 2.6, it is observed that with an increase in the value of ω , the pressure gradient increases, which basically boosts up the fluid velocity in the axial direction. Hence, with an increase in the value of ω , the particle moves away from the tumor region (at $r(t) = -1$). Due to the higher value of the pressure gradient, the axial velocity of the carrier particle increases with time, which influence of the movement of the carrier particle towards the tumor position, thus the tumor cells will be engulfed by the carrier particles as observed in Figure 2.7. As the carrier particles move towards the diseased area, with changes of various physiological parameters once they reach the area, more of the drug will be engulfed by the tumor cells, thus they will be treated faster and in a safe way.

2.3.4 Effect of Magnetization

In the present problem, we have considered the magnetization model for Fe_3O_4 adopted by Takayasu et al. [102]. The field source is considered as a NdFeB magnet with a diameter of 6cm i.e., $R_{mag} = 3cm$ and with a non-dimensional magnetization $Ms = 1$ (while in dimensional form $Ms = 10^6 A/m$). The surface of the magnet is placed at a distance of 2.5cm, which gives the distance between the axis of the magnet and the axis of the blood vessel as $d = 5.5cm$.

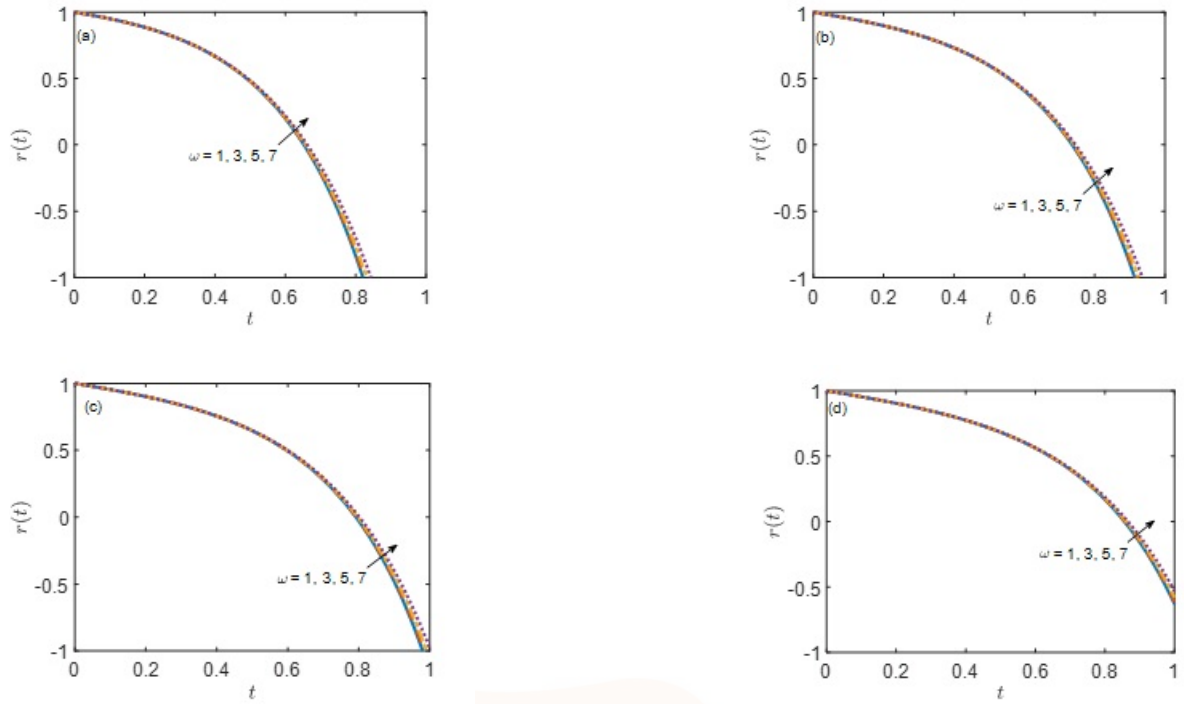


Figure 2.6: Radial trajectories of the carrier particle ($r(t)$) as a function of time for different ω with (a) $\alpha = 0.6$, (b) $\alpha = 0.8$, (c) $\alpha = 0.9$ and (d) $\alpha = 1$.

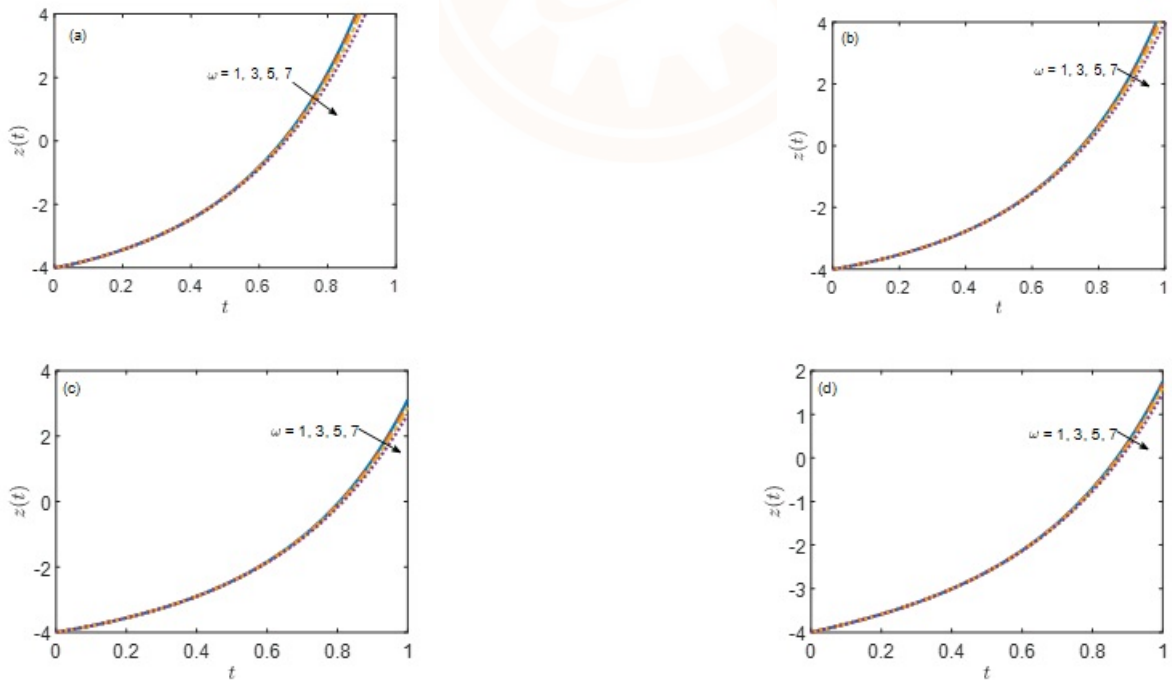


Figure 2.7: Axial trajectories of the carrier particle ($z(t)$) as a function of time for different ω with (a) $\alpha = 0.6$, (b) $\alpha = 0.8$, (c) $\alpha = 0.9$ and (d) $\alpha = 1$.

Magnetization is one of the most important parameters to consider when using the magnetic drug targeting method of drug delivery. Increasing the magnetization of the magnet increases the capture efficiency of magnetic particles and the impact on the trajectories of the carrier particle is shown in Figures 2.8, 2.9 and 2.10.

In the present problem, we have considered the values of Ms as 0.6, 0.8, 1 and 1.2. With an increase in the values of Ms , the magnetic force between the magnet and the magnetic particles (embedded in the carrier particle) increases, which boosts up the radial movement of the carrier particle. The carrier particle moves downward and reaches the tumor position (at $r(t) = -1$). An opposite phenomenon is observed for the axial trajectories of the carrier particle (see Figure 2.9). For a fixed time, the radial movement of the carrier particle with respect to the axial movement is observed in figure 2.10. The particles are observed closure to $z(t) = 0$ with increase in the values of Ms .

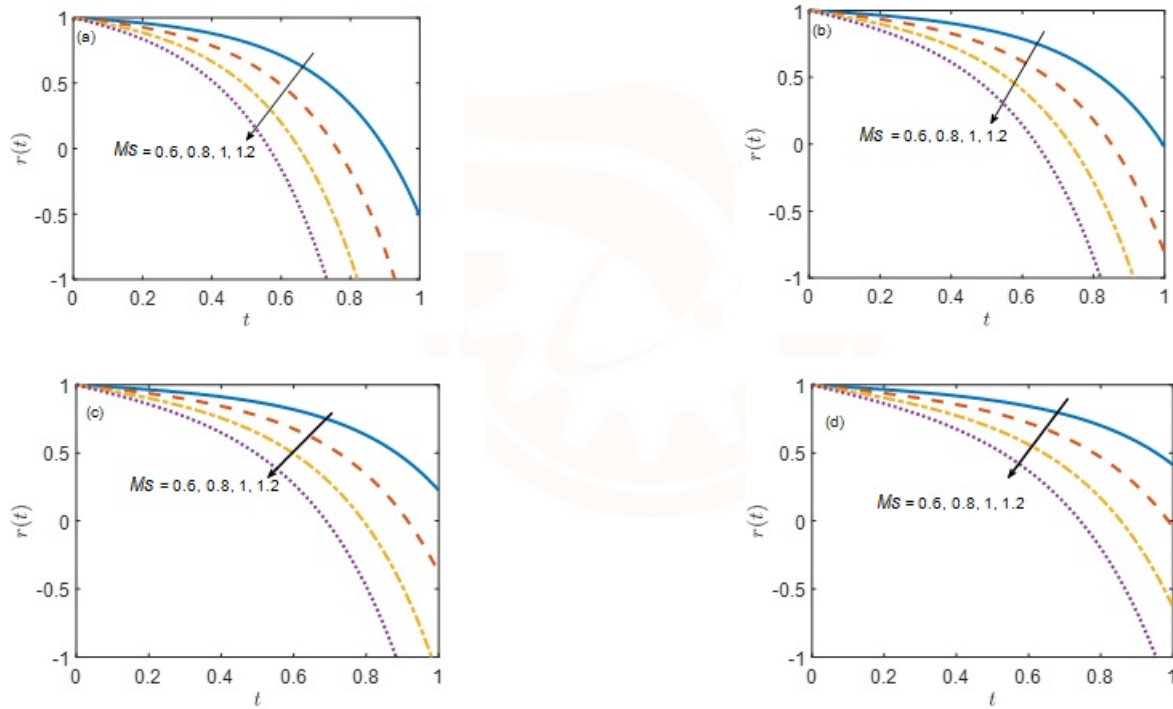


Figure 2.8: Radial trajectories of the carrier particle ($r(t)$) as a function of time for different Ms with (a) $\alpha = 0.6$, (b) $\alpha = 0.8$, (c) $\alpha = 0.9$ and (d) $\alpha = 1$.

2.3.5 Effect of the Darcy Number

The Darcy number represents the porosity of the blood vessel and it highly influences the axial velocity of the blood. The impact of the Darcy number on the trajectories of the carrier particles is shown in Figures 2.11, 2.12 and 2.13. Figures 2.11 and 2.12 displayed the radial and axial trajectories of the carrier particles against time for different values of Darcy number, whereas Figure 2.13 represents the graph of $r(t)$ against $z(t)$ for a fixed time. The Darcy number is proportional to the porosity of the blood vessel. In general, higher porosity disperses the

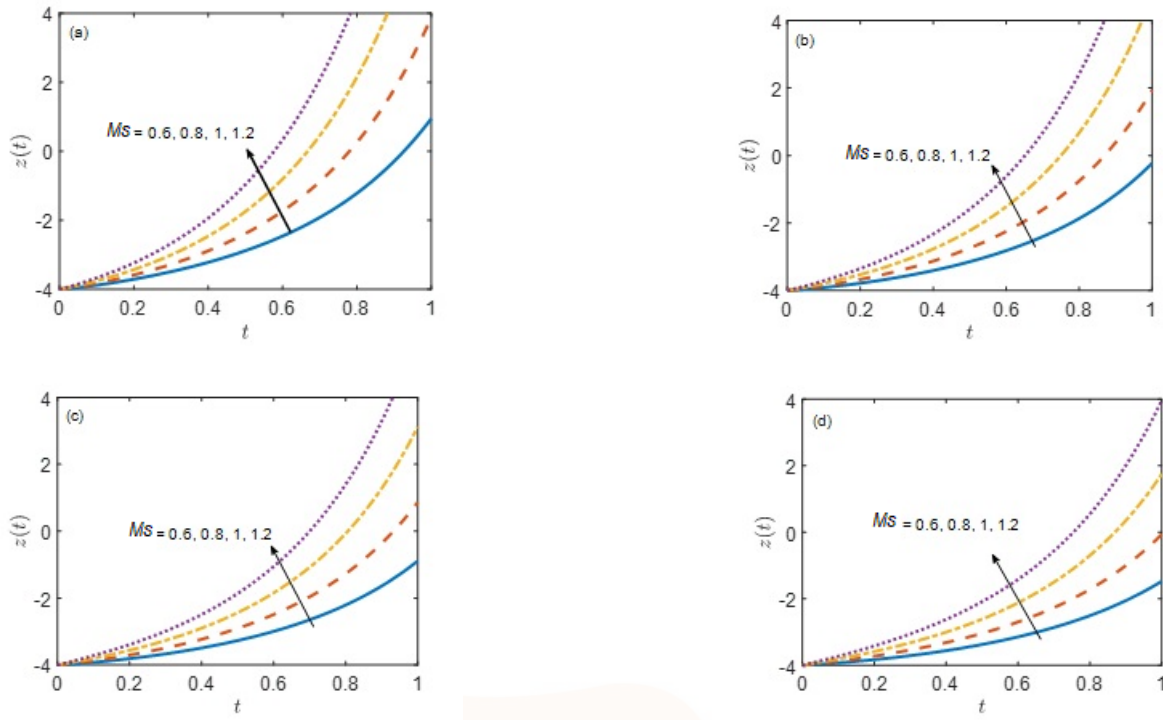


Figure 2.9: Axial trajectories of the carrier particle ($z(t)$) as a function of time for different Ms with (a) $\alpha = 0.6$, (b) $\alpha = 0.8$, (c) $\alpha = 0.9$ and (d) $\alpha = 1$.

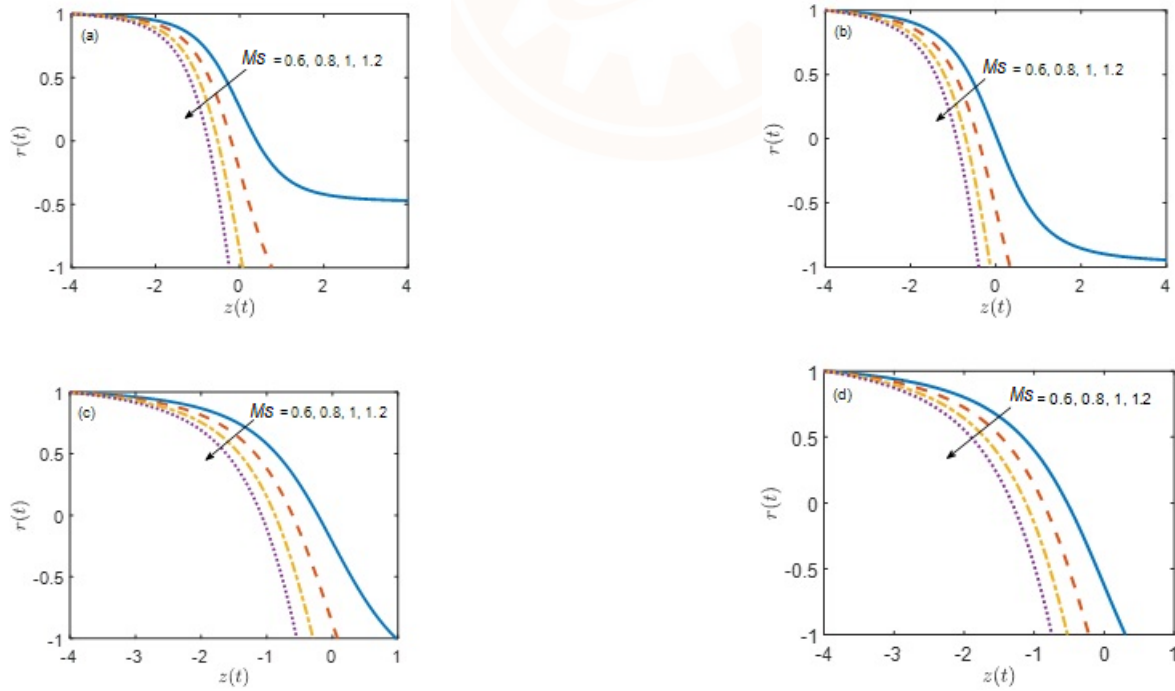


Figure 2.10: Radial trajectories with respect to the axial trajectories ($r(t)$ vs. $z(t)$) for different Ms with (a) $\alpha = 0.6$, (b) $\alpha = 0.8$, (c) $\alpha = 0.9$ and (d) $\alpha = 1$.

nanoparticles (carrier particles) towards the wall of the blood vessel (Fung [1]) and hence, it influences the radial movement of the carrier particles. For that reason, the carrier particles are easily moved downward with an increase in the Darcy number as shown in Figure 2.11.

On the other hand, the higher porosity of the blood vessel restricts the fluid flow towards the axial direction (Marquis [20]). Hence, the axial motion of the carrier particle gears up with an increase in the Darcy number (see Figure 2.12). From the above discussion, it is clear that the resultant motion of the carrier particles is highly influenced by the Darcy number and the resultant motion towards the direction of the magnet is restricted by the increased value of the Darcy number as shown in Figure 2.13. It is also noted that the porosity of the vessel depends on the location of the vessel or organs. It is observed that the porosity of the vessel is higher in the glomerulus of the kidney and lower in the brain. This implies that the magnetic drug targeting is more effective at curing the diseases in the kidney than in the brain. However, it is not the only parameter which influences the trajectories of the drugs embedded in the carrier particles.

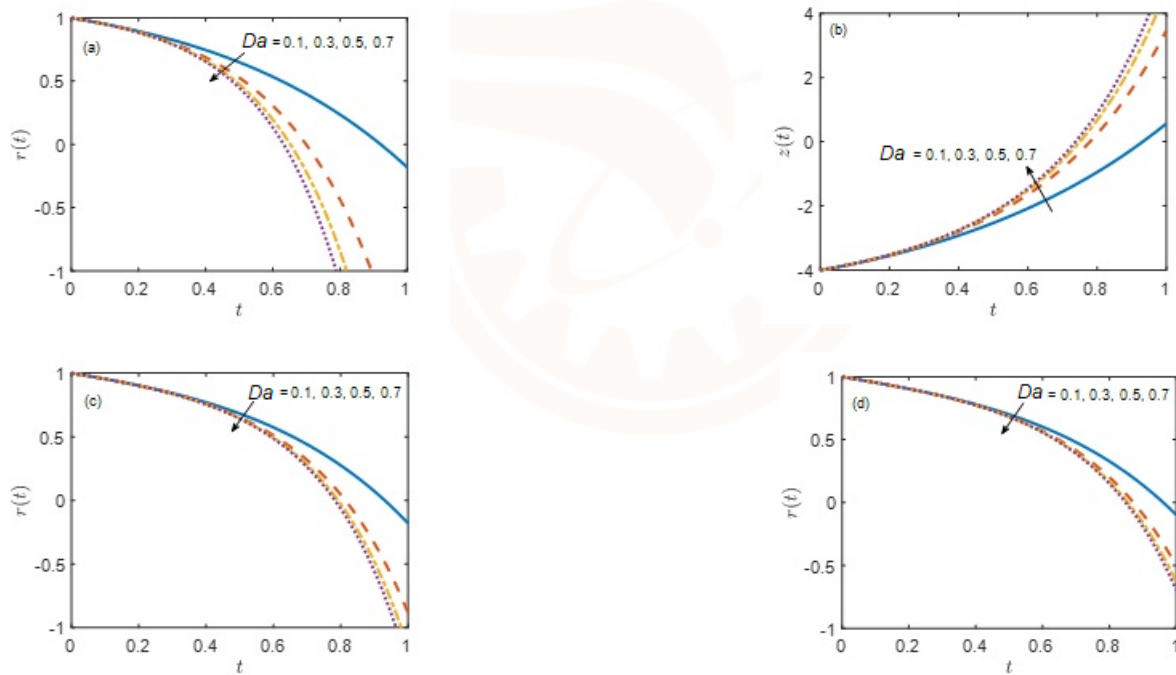


Figure 2.11: Radial trajectories of the carrier particle ($r(t)$) as a function of time for different Da with (a) $\alpha = 0.6$, (b) $\alpha = 0.8$, (c) $\alpha = 0.9$ and (d) $\alpha = 1$.

2.4 Conclusion

The present study is concerned with the trajectories of the carrier particles through a permeable blood vessel under the influence of body acceleration, externally applied magnetic fields considering blood as a Newtonian fluid. Caputo-Fabrizio fractional time derivative considered in the momentum equation and solved by using the Laplace transform and Hankel transform of zero

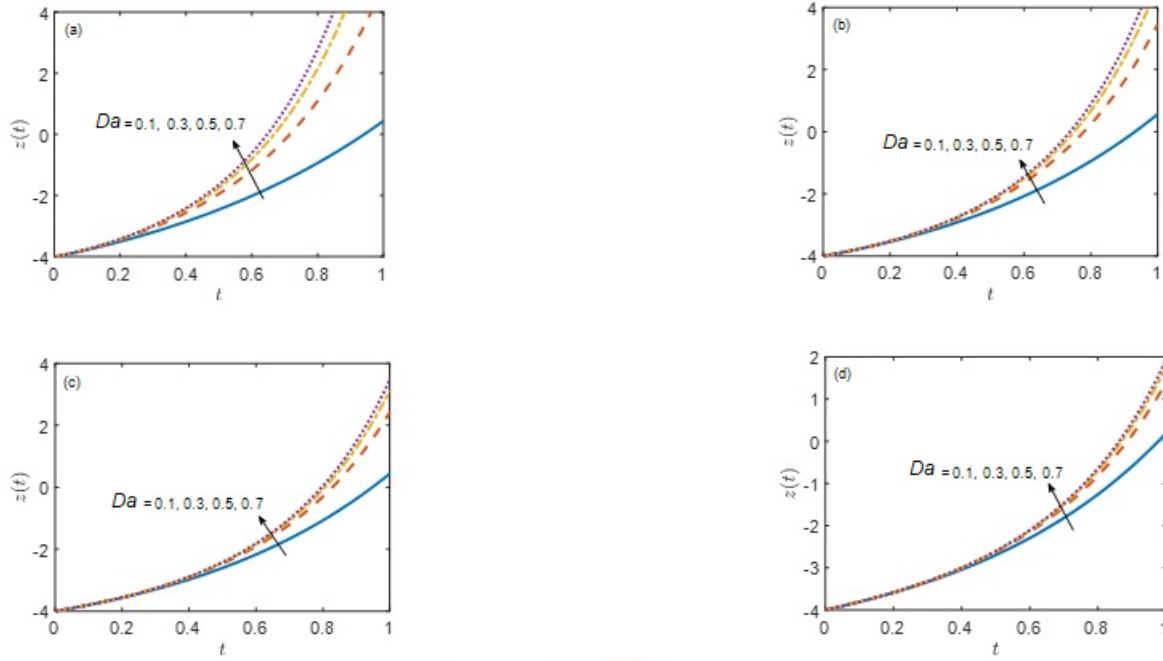


Figure 2.12: Axial trajectories of the carrier particle ($z(t)$) as a function of time for different Da with (a) $\alpha = 0.6$, (b) $\alpha = 0.8$, (c) $\alpha = 0.9$ and (d) $\alpha = 1$.

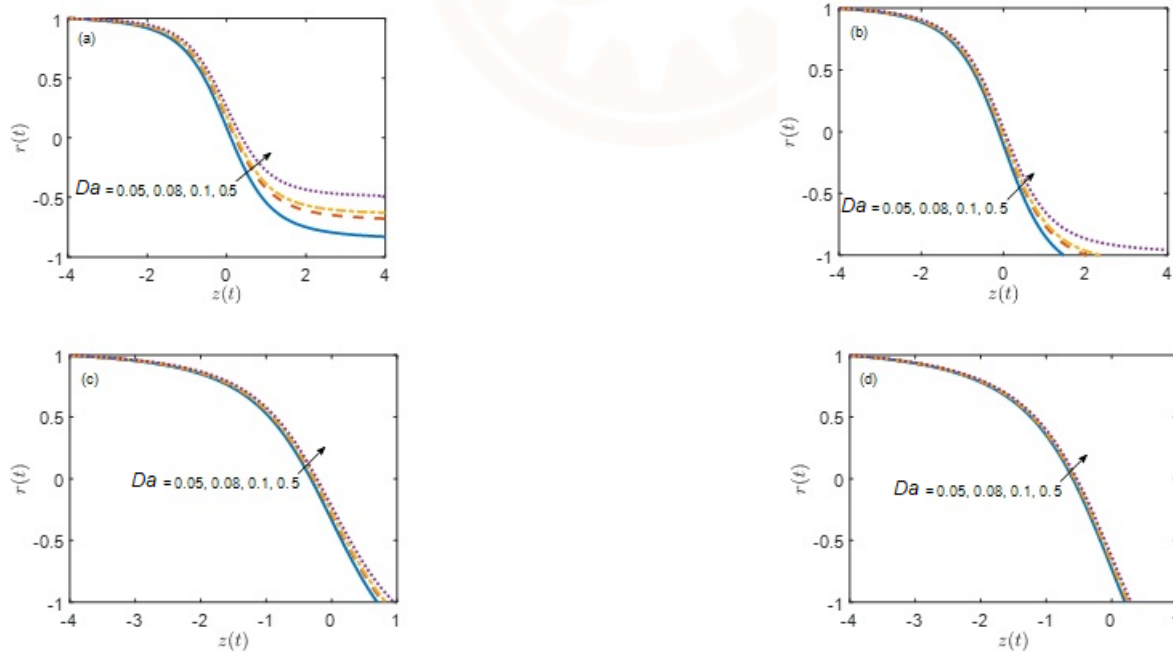


Figure 2.13: Radial trajectories with respect to the axial trajectories $r(t)$ vs. $z(t)$ for different Da with (a) $\alpha = 0.6$, (b) $\alpha = 0.8$, (c) $\alpha = 0.9$ and (d) $\alpha = 1$.

order. Memory effects of the fractional parameter on the trajectories of drug carrier particles have been discussed. The influence of Darcy number, Reynolds number, pulsatile frequency and magnetization have been discussed to understand the trajectories of the drug carrier particles. We found that the fractional parameters boost up the motion of the radial motion of the drug carrier particles, while it restricts the axial motion of the carrier particles.

Further, fractional parameters help the drug carrier particles to capture close to the tumor region. Reynolds number, Darcy number and magnetization of magnet accelerated the radial motion of the carrier particles, while an opposite phenomenon was observed for the axial motion of the drug carrier particle. Pulsatile frequency helps the drug carrier particles to reach towards the tumor region. The theory developed herein can be used to determine the optimum size of the carrier particle for treating a tumor with a given size and location within the body. Thus, these outcomes will be helpful in the new drug-targeting apparatus and treatments.



3. Magnetic Particle Trajectories in a Fractionalized Jeffrey Fluid Model Through a Permeable Microvessel

3.1 Introduction

Non-Newtonian fluids has suddenly became a great interest to researchers because of their extensive utilization and their applicability in various regions such as industries, petroleum, biological sciences and geophysics. Examples of non-Newtonian fluids such as oils, tooth paste, paints, ketchup, liquid polymers and asphalt exhibit some remarkable phenomena due to their viscoelastic nature. These fluids have intriguing applications and are very useful in our lives. Many researchers have proven that such type of fluids have a non-linear relationship between shear rate and shear stress and they are important for industries like polymer processing and making of papers and foods (Jamil and Haleem [103]). The Jeffrey fluid is considered to be one of the simplest type of fluid which describes the rheological effects of viscoelastic fluids. The Jeffrey model is a relatively simpler linear model that uses the time derivatives instead of convected derivatives.

As of recent, the investigation towards this fluid flow is still being studied by many researchers in different aspects either by the implementation of numerical methods or analytical methods. Khan et al. [104] studied the unsteady magnetohydrodynamic flow of Jeffrey fluid through a porous oscillating rectangular duct. Khan et al. [105] examined unsteady flows of Jeffrey fluid between two side walls over a plane wall. Some exact solutions corresponding to three unsteady flow problems of a generalized Jeffrey fluid produced by a flat plate between two side walls perpendicular to the plate using N-Transform was experimented by Khan et al. [106].

Nallapu and Radhakrishnamacharya [107] studied a two-fluid model for the Jeffrey fluid flow in tubes of small diameters. Later they extended their research to a two-fluid model for the Jeffrey fluid flow through a porous medium in the presence of magnetic field in narrow tubes (Nallapu and Radhakrishnamacharya [108]). They studied the influence of different parameters such as effective viscosity, core hematocrit and mean hematocrit on the flow characteristics. The study of an incompressible Jeffrey fluids flow in a porous-walled channel of a narrow width has being studied by Kahshan et al. [109]. Ahmad et al. [110] studied the heat and mass transfer of fractional Jeffrey fluid flow over an infinite vertical plate moving exponentially with variable temperature and mass diffusion. The study of non-Newtonian blood flow of Jeffrey Fluid in an elastic tube was studied by Sreenadh et al. [111]. Many researchers continued to in-

investigate this fluid and their findings can be seen from Agbaje and Leach [112] - Guo et al. [122].

Viscosity is an essential parameter of fluid physical properties for examining the heat transfer when designing a nanofluid system. In 2016, Alvi et al. [123] investigated the peristalsis of nonconstant viscosity Jeffrey fluid with nanoparticles. The effect of temperature dependent viscosity on the peristaltic flow of Jeffrey nanofluid in an asymmetric channel was investigated by Hasona et al. [124]. Transport of a Jeffrey nanofluid through two-dimensional curved channel undergoing peristalsis was theoretically investigated by Narla et al. [125] and the Jeffrey fluid model for peristaltic flow of chyme in the small intestines in the presence of magnetic field was analysed by Akbar et al. [126].

The influence of melting heat transfer and thermal radiation on MHD stagnation point flow of Jeffrey fluid over a stretching sheet with surface slip was numerically investigated by Das et al. [127]. Farooq et al. [128] studied the magnetohydrodynamic peristalsis of variable viscosity Jeffrey liquid with heat and mass transfer. Zeeshan and Majeed [129] investigated the flow and heat transfer of Jeffrey fluid over a stretching sheet with suction /injection and magnetic dipole effect.

In the present paper, a two-fluid model for the flow of fractionalized Jeffrey fluid through a porous medium in tubes of small diameters with magnetic effect has been investigated. It is assumed that the clear region consists of Jeffrey fluid and the peripheral region consists of Newtonian fluid. The fractionalized governing equation of Jeffrey fluid is presented analytically with the help of the Laplace transform, finite Hankel transforms and their inverse techniques. The analytical solution is represented in the form of Lorenzo-Hartley and Robotnov-Hartley functions and the convolution of the Laplace transform. Fluidic and magnetic forces are used in the force equilibrium to obtain the trajectories of the carrier particles. The influence of various pertinent parameters on the trajectories such as the time relaxation parameter, retardation time of Jeffrey fluid, pulsatile frequency, magnetization and the Darcy number has been studied.

Finally, the memory effects on the axial and radial trajectories of the carrier particles with time have been presented graphically. To the best of our knowledge, the present work is unique as it depends on the fractional-order time parameter. The axial and radial trajectories of the carrier particle are obtained based on the Caputo-Fabrizio fractional order time derivative.

3.2 Formulation of the Problem

We considered the following assumptions when solving our problem, i. blood was considered as a fractional model, ii. the fluid was considered as a Jeffrey fluid, iii. magnetic nanoparticles, iv. cylindrical artery of radius R_0 , where the magnetic nanoparticles are uniformly distributed throughout the blood, and lastly v. the velocity of the fluid. We considered the flow of blood through a straight cylindrical artery of radius R_0 , along with the magnetic nanoparticles. The coordinates of the artery is defined by cylindrical coordinate system (r, θ, z) where z -axis is the

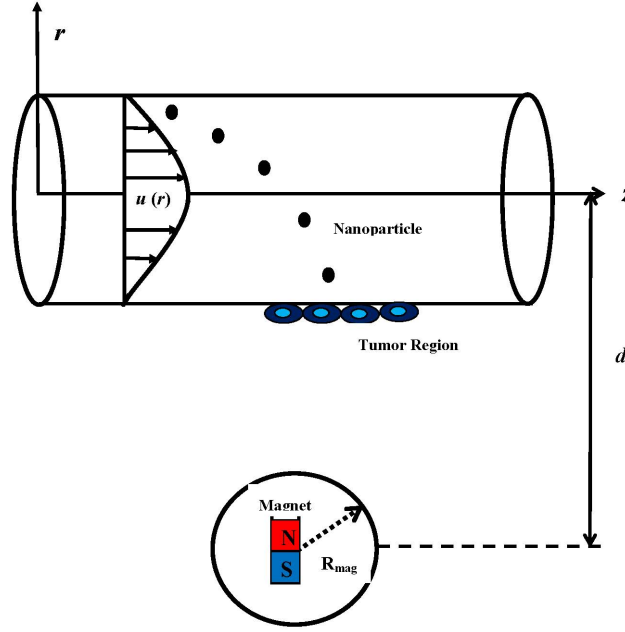


Figure 3.1: The flow geometry

axial direction of the artery and r the radial direction.

The blood and the magnetic nanoparticles are flowing in the axial direction of the artery while the applied magnetic fields acts vertically to the direction of the flow. The whole system is subjected to an external magnetic field as the Reynolds number R_e is very small such that the induced magnetic field has been ignored (Srinivas and Kothandapani [130]). Initially, $t = 0$, the artery, blood and the magnetic nanoparticles are at rest. If a magnetic material like biomagnetic fluid flows in the uniformly applied magnetic field, it experiences an electromotive force which will results to the flow of an electric current. The electromotive force depends on the speed of motion as well as the magnetic flux intensity (Bourhan and Magableh [131]).

The flow in our problem involves Navier-Stokes equations which describes the flow of the fluid, Newtons second law of motion for the particles motion and Maxwell's relations for magnetic field. The Maxwell equations of the electro-magnetic field can be defined as (Sharma et al. [65], Shah et al.[93]);

$$\nabla \cdot \vec{B} = 0, \quad \nabla \times \vec{B} = \mu_0 \vec{J}, \quad \nabla \times \vec{E} = -\frac{\partial \vec{B}}{\partial t}, \quad (3.1)$$

where $\vec{B}$ is the magnetic flux intensity, μ_0 is the magnetic permeability, $\vec{J}$ is the current density, $\vec{E}$ is the electric field intensity, respectively. The density of the electric current is given by

$$\vec{J} = \sigma(\vec{E} + \vec{V} \times \vec{B}), \quad (3.2)$$

where σ is the electrical conductivity and $\vec{V} = \bar{u}(\bar{r}, \bar{t}) \vec{k}$ is the axial velocity vector of the blood

in the vessel.

The electromotive force $\vec{F}_{em}$ can be expressed as

$$\vec{F}_{em} = \vec{J} \times \vec{B} = \sigma(\vec{E} + \vec{V} \times \vec{B}) \times \vec{B} = -B_0^2 \bar{u}(\bar{r}, \bar{t}) \vec{k}, \quad (3.3)$$

where $\vec{k}$ is the unit vector in the z -direction.

The governing momentum equation of the fluid flow in cylindrical coordinates (r, θ, z) is given by Sharma et al. [65];

$$\frac{\partial \bar{u}}{\partial \bar{t}} = -\frac{1}{\rho} \frac{\partial \bar{p}}{\partial \bar{z}} + \frac{\nu}{1 + \lambda_1} \left(1 + \lambda_2 \frac{\partial}{\partial \bar{t}} \right) \left[\frac{\partial^2 \bar{u}}{\partial \bar{r}^2} + \frac{1}{\bar{r}} \frac{\partial \bar{u}}{\partial \bar{r}} \right] + \frac{G(\bar{t})}{\rho} - \frac{\nu}{K} \bar{u} - \frac{\sigma B^2}{\rho} \bar{u} \quad (3.4)$$

where ρ is the fluid density, ν is the kinematic viscosity, p is the pressure, σ and B are the respective electrical conductivity and the intensity of the applied magnetic field, λ_1, λ_2 are the Jeffrey parameters.

The body acceleration is given by;

$$G(\bar{t}) = \bar{A}_0 \cos(\bar{k}\bar{t} + \phi_0), \quad (3.5)$$

and $\bar{A}_0$ denotes the amplitude of the body acceleration. The pulsatile characteristics of the blood originates from the pumping action of heart and hence the pressure gradient is given as follow;

$$-\frac{\partial \bar{p}}{\partial \bar{z}} = \bar{b}_0 + \bar{b}_1 \cos(\bar{\omega}\bar{t}), \quad (3.6)$$

where $\bar{b}_0$ is the constant amplitude of the pressure gradient. b_1 is the amplitude of pulsatile component which gives rise to systolic and diastolic pressures and $\bar{\omega}$ is the pulsatile frequency.

Then by using equations (3.5) and (3.6) in equation (3.4) gives

$$\begin{aligned} \frac{\partial \bar{u}}{\partial \bar{t}} = \frac{1}{\rho} (\bar{b}_0 + \bar{b}_1 \cos(\bar{\omega}\bar{t})) + \frac{\nu}{1 + \lambda_1} \left(1 + \lambda_2 \frac{\partial}{\partial \bar{t}} \right) \left[\frac{\partial^2 \bar{u}}{\partial \bar{r}^2} + \frac{1}{\bar{r}} \frac{\partial \bar{u}}{\partial \bar{r}} \right] \\ + \frac{1}{\rho} \bar{A}_0 \cos(\bar{k}\bar{t} + \phi_0) - \frac{\nu}{K} \bar{u} - \frac{\sigma B^2}{\rho} \bar{u}. \end{aligned} \quad (3.7)$$

The fractional derivative can be introduced in the momentum equation on the time dimension by firstly introducing and multiplying Eqt. (3.7) by the factor $\lambda = \sqrt{\frac{R_0 \rho}{b_0}}$ and get;

$$\lambda^\alpha D_t^\alpha \bar{u} = \frac{\lambda}{\rho} (\bar{b}_0 + \bar{b}_1 \cos(\bar{\omega} \bar{t})) + \frac{\nu}{1 + \lambda_1} (\lambda + \lambda_2 \lambda^\alpha D_t^\alpha) \left[\frac{\partial^2 \bar{u}}{\partial \bar{r}^2} + \frac{1}{\bar{r}} \frac{\partial \bar{u}}{\partial \bar{r}} \right] + \frac{\lambda}{\rho} \bar{A}_0 \cos(\bar{k} \bar{t} + \phi_0) - \frac{\lambda \nu}{K} \bar{u} - \frac{\lambda \sigma B^2}{\rho} \bar{u}, \quad (3.8)$$

where the derivative;

$$D_t^\alpha f(\bar{r}, \bar{t}) = \begin{cases} \frac{1}{\Gamma(1-\alpha)} \int_0^{\bar{t}} \frac{1}{(\bar{t}-\tau)^\alpha} \frac{\partial f(\bar{r}, \tau)}{\partial \tau} d\tau, & 0 < \alpha < 1, \\ \frac{\partial f(\bar{r}, \tau)}{\partial \tau}, & \alpha = 1 \end{cases} \quad (3.9)$$

is the Caputo fractional derivative operator of order α , with $\alpha \in (0, 1)$ according to Shantanu [99].

The corresponding boundary conditions are;

$$\begin{aligned} u(\bar{r}, 0) &= 0, \quad \text{at } \bar{t} = 0, \quad r \in [0, R_0], \\ u(\bar{R}_0, \bar{t}) &= f \sin(\Omega t), \quad t > 0. \end{aligned} \quad (3.10)$$

Introducing the non-dimensional parameters;

$$\begin{aligned} r &= \frac{\bar{r}}{R_0}, \quad t = \frac{\bar{t}}{\lambda}, \quad u = \frac{\bar{u}}{u_0}, \quad b_0 = \frac{\lambda \bar{b}_0}{\rho u_0}, \quad b_1 = \frac{\lambda \bar{b}_1}{\rho u_0}, \quad \omega = \lambda \bar{\omega}, \quad \kappa = \lambda \bar{\kappa}, \\ A_0 &= \frac{\lambda \bar{A}_0}{u_0}, \quad z = \frac{\bar{z}}{R_{mag}}, \quad M_s = \frac{\bar{M}_s}{M_0}, \quad d = \frac{\bar{d}}{R_{mag}}, \quad R_{cp} = \frac{\bar{R}_{cp}}{R_0}, \quad R_{mp} = \frac{\bar{R}_{mp}}{R_0}. \end{aligned} \quad (3.11)$$

Using the above non-dimensional parameters and taking $\lambda = 1$, the governing equation becomes;

$$\begin{aligned} D_t^\alpha u &= (b_0 + b_1 \cos(\omega t)) + \frac{1}{Re} \frac{1}{1 + \lambda_1} (1 + \lambda_2 D_t^\alpha) \left(\frac{\partial^2 u}{\partial r^2} + \frac{1}{r} \frac{\partial u}{\partial r} \right) \\ &\quad + A_0 \cos(kt + \phi_0) - \frac{1}{Da} u - M^2 u, \end{aligned} \quad (3.12)$$

where the Reynolds number Re , Darcy number Da , Hartmann number M are defined as

$$Re = \frac{R_0^2}{\lambda \nu}, \quad Da = \frac{K}{\lambda \nu}, \quad M = B \sqrt{\frac{\sigma \lambda}{\rho}}, \quad (3.13)$$

and similarly, the boundary initial and boundary conditions can be written as;

$$\begin{aligned}
u(r, 0) &= 0, \quad \text{at } t = 0, \quad r \in [0, R_0], \\
u(1, t) &= f \sin(\Omega t), \quad t > 0 \\
\frac{\partial u}{\partial t}(0, t) &= 0, \quad t > 0.
\end{aligned} \tag{3.14}$$

3.2.1 Solution Procedure

Applying the Laplace transform based on the time variant to equation (3.12) yields;

$$\begin{aligned}
s^\alpha u(r, s) &= \left[\frac{b_0}{s} + b_1 \frac{s}{s^2 + \omega^2} \right] + \frac{1}{Re} \frac{1}{1 + \lambda_1} (1 + \lambda_2 s^\alpha) \left(\frac{\partial^2 u(r, s)}{\partial r^2} + \frac{1}{r} \frac{\partial u(r, s)}{\partial r} \right) \\
&\quad - \frac{1}{Da} u(r, s) + A_0 \left[\cos(\phi_0) \frac{s}{s^2 + k^2} - \sin(\phi_0) \frac{k}{s^2 + k^2} \right] - M^2 u(r, s). \tag{3.15}
\end{aligned}$$

Now, applying Hankel transform of zero order to equation (3.15), we get;

$$\begin{aligned}
s^\alpha u_H(r, s) &= \left(\left[\frac{b_0}{s} + b_1 \frac{s}{s^2 + \omega^2} \right] + A_0 \left[\cos(\phi_0) \frac{s}{s^2 + k^2} - \sin(\phi_0) \frac{k}{s^2 + k^2} \right] \right) \frac{J_1(r_n)}{r_n} + \\
&\quad \frac{1}{Re} \frac{1}{1 + \lambda_1} (1 + \lambda_2 s^\alpha) (-r_n^2 u_H(r_n, s)) - \frac{1}{Da} u_H(r_n, s) - M^2 u_H(r_n, s), \tag{3.16}
\end{aligned}$$

where $u_H(r_n, s) = \int_0^1 r u(r, s) J_0(r r_n) dr$ is the finite Hankel transform of the function $u(r, s)$ and $r_n, n = 1, 2, \dots$ are positive roots of the equation $J_0(\chi) = 0$ with J_0 as the Bessel function of the first kind and zero order.

Simplifying equation (3.16) gives the velocity profile as

$$\begin{aligned}
u_H(r_n, s) &= \left(\left[\frac{b_0}{s} + b_1 \frac{s}{s^2 + \omega^2} \right] \right) \frac{J_1 r_n}{2 r_n} \frac{1}{s^\alpha + a_n} \\
&\quad + A_0 \left[\cos \phi_0 \frac{s}{s^2 + k^2} - \sin \phi_0 \frac{k}{s^2 + k^2} \right] \frac{J_1(r_n)}{x r_n} \frac{1}{s^\alpha + a_n}, \tag{3.17}
\end{aligned}$$

$$\text{with } x = 1 + \frac{r_n^2 \lambda_2}{Re(1 + \lambda_1)}, \quad a_n = \frac{Da r_n^2 + (MDa + 1) Re(1 + \lambda_1)}{x Da Re(1 + \lambda_1)}.$$

Then equation (3.17) becomes

$$u_H(r_n, s) = \left[b_0 \left(\frac{s^{-1}}{s^\alpha + a_n} \right) + b_1 \left(\frac{s}{s^2 + \omega^2} \right) \left(\frac{1}{s^\alpha + a_n} \right) \right] \frac{J_1 r_n}{x r_n} + A_0 \left[\cos \phi_0 \left(\frac{s}{s^2 + k^2} \right) \left(\frac{1}{s^\alpha + a_n} \right) - \sin \phi_0 \left(\frac{k}{s^2 + k^2} \right) \left(\frac{1}{s^\alpha + a_n} \right) \right] \frac{J_1 r_n}{x r_n}. \quad (3.18)$$

Applying Inverse Laplace transform in equation (3.18) with some help from Saha et al. [132],

$$L^{-1} \left\{ \frac{1}{s^\alpha + m} \right\} = F_\alpha(-m, t) = \sum_{n=0}^{\infty} \frac{(-m)^n t^{(n+1)\alpha-1}}{\Gamma((n+1)\alpha)}, \quad \alpha > 0, \quad (3.19)$$

$$L^{-1} \left\{ \frac{s^{-1}}{s^\alpha + m} \right\} = R_{\alpha, v}(-m, t) = \sum_{n=0}^{\infty} \frac{(-m)^n t^{(n+1)\alpha-1-v}}{\Gamma((n+1)\alpha - v)}, \quad \text{Re}(\alpha - v) > 0. \quad (3.20)$$

where $F_\alpha(.,.)$ and $R_{\alpha, \nu}(.,.)$ are Robotnov and Hartley's, Lorenzo and Hartley's functions and m is any integer.

Using the above equations, equation (3.19) and (3.20) on equation (3.18), we get

$$u_H(r_n, t) = [F_{n1}(t) + F_{n2}(t) - F_{n3}(t)] \frac{J_1(r_n)}{x r_n}, \quad (3.21)$$

where

$$\begin{aligned} F_{n1}(t) &= b_0 R_{\alpha, -1}(-a_n, t), \\ F_{n2}(t) &= (b_1 \cos(\omega t) + A_0 \cos \phi_0 \cos(kt)) * F_\alpha(-a_n, t), \\ F_{n3}(t) &= A_0 \sin \phi_0 \sin(kt) * F_\alpha(-a_n, t), \end{aligned} \quad (3.22)$$

where $f * g$ represents the convolution product of the functions f and g .

The velocity profile applying the Inverse Hankel transform on equation (3.21) result as

$$\begin{aligned} u(r, t) &= 2 \sum_{n=1}^{\infty} \frac{J_0(r r_n)}{J_1^2(r_n)} u_H(r_n, t), \\ &= 2 [F_{n1}(t) + F_{n2}(t) - F_{n3}(t)] \sum_{n=1}^{\infty} \frac{J_0(r r_n)}{x r_n J_1(r_n)}, \end{aligned} \quad (3.23)$$

where $H_0^{-1} u_H(r_n, t) = u(r, t) = \sum_{n=1}^{\infty} \frac{J_0(r r_n)}{J_1^2(r_n)} u_H(r_n, t)$.

The volumetric flow rate is written as

$$\begin{aligned} Q &= 2\pi \int_0^1 u(r, t) r dr \\ &= 4\pi [F_{1n}(t) + F_{2n}(t) - F_{3n}(t)] \sum_{n=1}^{\infty} \frac{J_1(r_n)}{xr_n^2 J_1(r_n)}. \end{aligned} \quad (3.24)$$

Using equation (3.24), we get the average velocity of the fluid as

$$\begin{aligned} \hat{u}_f &= \frac{Q}{\pi} \\ &= 4 [F_{1n}(t) + F_{2n}(t) - F_{3n}(t)] \sum_{n=1}^{\infty} \frac{1}{xr_n^2}. \end{aligned} \quad (3.25)$$

3.2.2 Velocity Profile for Ordinary Fluid

When $\alpha \rightarrow 1$, the fluid behaves as an ordinary fluid. Then equations (3.19) & (3.20) becomes

$$F_1(-m, t) = \sum_{n=0}^{\infty} \frac{(-m)^n}{\Gamma(n+1)} = e^{-mt}, \quad (3.26)$$

$$R_{1,v}(-m, t) = \sum_{n=0}^{\infty} \frac{(-m)^n t^{(n+1)-v}}{\Gamma((n+1)1-v)} = \frac{1 - e^{-mt}}{m}, \quad (3.27)$$

which gives the velocity as;

$$u(r, t) = 2 \sum_{n=1}^{\infty} \frac{J_0(rr_n)}{xr_n J_1(r_n)} [G_1(t) + G_2(t) - G_3(t)], \quad (3.28)$$

where

$$\begin{aligned} G_{1n}(t) &= b_0 \frac{1 - e^{-a_n t}}{a_n}, \\ G_{2n}(t) &= (b_1 \cos(\omega t) + A_0 \cos \phi_0 \cos(kt)) * e^{-a_n t}, \\ G_{3n}(t) &= A_0 \sin \phi_0 \sin(kt) * e^{-a_n t}. \end{aligned} \quad (3.29)$$

The volumetric flow rate will be given as

$$Q = 4\pi [G_{1n}(t) + G_{2n}(t) - G_{3n}(t)] \sum_{n=1}^{\infty} \frac{1}{xr_n^2}, \quad (3.30)$$

and the average velocity of the fluid written as

$$\hat{u}_f = 4 [G_{1n}(t) + G_{2n}(t) - G_{3n}(t)] \sum_{n=1}^{\infty} \frac{1}{xr_n^2}. \quad (3.31)$$

3.2.3 Fluidic Force

In the present problem, we have considered blood as a non-Newtonian fluid and the blood flowing in a cylindrical vessel (Furlani and Furlani [82]). The fluidic force is predicted by using the Stokes' approximation and is written as (Bachelor [133])

$$F_f = -6\pi\mu R_{cp}(v_{cp} - u(r, t)), \quad (3.32)$$

where v_{cp} and R_{cp} are the velocity and radius of the carrier particle, respectively.

Now, the fluidic force in the component form in the $r - z$ plane is written as

$$F_{fr} = -6\pi\mu R_{cp}v_{cp,r}, \quad (3.33)$$

$$F_{fz} = -6\pi\mu R_{cp}(v_{cp,z} - \hat{u}_f). \quad (3.34)$$

3.2.4 Magnetic Force

The magnetic force on the carrier particle can be written as (Furlani and Ng [81])

$$F_m = \mu_f \bar{V}_{mp} \frac{3(\chi_p - \chi_f)}{(\chi_p - \chi_f) + 3(\chi_f + 1)} (\mathbf{H}_a \nabla) \mathbf{H}_a, \quad (3.35)$$

where $\mu_f, \chi_p = \frac{\mu_p}{\mu_0} - 1, \chi_f = \frac{\mu_f}{\mu_0} - 1$ and $\mathbf{H}_a$ are the permeability of the fluid, susceptibility of the particle and fluid, and the externally applied magnetic field intensity at the center of the particle, respectively. μ_p and μ_0 are the respective permeability of the particle and the permeability of the air. The volume of a spherical magnetic particle is considered as $\bar{V}_{mp} = \frac{4\pi}{3} \bar{R}_{mp}^3$. We preferred the non-invasive magnetic targeting, where the distance of the drug carrier from the axis of the magnet ($\bar{d}$) is much larger than the diameter of the blood vessel i.e., $R_v \ll \bar{d}$. Further, the material of the magnet nanoparticle e.g., magnetite (Fe_3O_4) is biocompatible. These two assumptions simplified the magnetic force and it is written in the component form in the $r - z$ plane (Furlani and Ng [81]) as

$$F_{mr}(r, \bar{z}) = -3\mu_0 \bar{V}_{mp} \bar{M}_s^2 R_{mag}^4 \frac{1}{2(\bar{d}^2 + \bar{z}^2)^3}, \quad (3.36)$$

and

$$F_{mz}(r, \bar{z}) = -3\mu_0 \bar{V}_{mp} \bar{M}_s^2 R_{mag}^4 \frac{\bar{z}}{2(\bar{d}^2 + \bar{z}^2)^3}, \quad (3.37)$$

where $\overline{M}_s$, R_{mag} and $\bar{z}$ are the magnetization of the magnet, the radius of the magnet and the axial distance of the carrier particle, respectively.

Using equation (3.11), equations (3.36) and (3.37) can be written as

$$F_{mr}(r, z) = -L\beta_{vf}R_{cp}^3M_s^2\frac{1}{(d^2 + z^2)^3}, \quad (3.38)$$

and

$$F_{mz}(r, z) = -L\beta_{vf}R_{cp}^3M_s^2\frac{z}{(d^2 + z^2)^3}, \quad (3.39)$$

$$\text{with } L = \frac{2\pi\mu_0 R_0^3 M_0^3}{R_{mag}^2}.$$

3.2.5 Equilibrium Force

The particle motion can be anticipated using Newton's law, which is given by

$$m_p \frac{dv_p}{dt} = F_m + F_f, \quad (3.40)$$

where m_p , v_p are the mass and velocity of the drug carrier particle, F_m and F_f are the magnetic and fluidic forces, respectively. By ignoring the inertial term as it is sufficiently small for the blood vessel with a small radius, we obtain the particle motion on a simple force balance as

$$F_m + F_f = 0. \quad (3.41)$$

3.2.6 Noninvasive Procedure on the Trajectories of the Drug Carrier Particle

A noninvasive procedure is a safer medical procedure where no break in the skin is created and there is no contact with the mucosa, or skin break, or internal body cavity beyond a natural or artificial body orifice. Based on the non-invasive condition, the implemented condition is

$$\frac{L\beta_{vf}R_{cp}^2M_s^2}{6\pi\mu} \ll 1. \quad (3.42)$$

Implementing the non-invasive condition (equation 3.42) in equation (3.41) with equations (3.33) and (3.38), and equations (3.34) and (3.39), the velocity components of the drug carrier particle in the $r - z$ plane are written as

$$v_{cp,r} = \frac{dr(t)}{dt} = \frac{L\beta_{vf}R_{cp}^2M_s^2}{6\pi\mu} \frac{1}{(d^2 + z^2)^3}, \quad (3.43)$$

and

$$v_{cp,z} = \frac{dz(t)}{dt} = \frac{L\beta_{vf}R_{cp}^2M_s^2}{6\pi\mu} \frac{z}{(d^2 + z^2)^3} + \hat{u}_f. \quad (3.44)$$

The axial position of the carrier particle is given by

$$z = z_0 + \widehat{v}_{cp}t. \quad (3.45)$$

Assume that the average axial velocity of the carrier particle ($\widehat{v}_{cp}$) equals the average fluid (blood) velocity, i.e,

$$\widehat{v}_{cp} = \widehat{u}_f. \quad (3.46)$$

By coupling equations (3.43) and (3.44) with equations (3.45) and (3.46), we get the trajectories of the drug carrier particles $r(t)$ and $z(t)$ as

$$\frac{dr(t)}{dt} = \frac{L\beta_{vf}R_{cp}^2M_s^2}{6\pi\mu} \frac{1}{(d^2 + (z_0 + \widehat{u}_{cp}t)^2)^3} \quad (3.47)$$

and

$$\frac{dz(t)}{dt} = \frac{L\beta_{vf}R_{cp}^2M_s^2}{6\pi\mu} \frac{z_0 + \widehat{u}_{cp}t}{(d^2 + (z_0 + \widehat{u}_{cp}t)^2)^3} + \widehat{u}_f. \quad (3.48)$$

3.3 Results and Discussion

In this study, we used fractional calculus as it proved that for practical purposes it is very useful in areas such as mechanics, bioengineering and science. The fractional calculus provides more accurate models of the physical system as compared to the ordinary calculus. Therefore, the fractional approach is helpful in generalization of complex dynamic of fluid motion.

The governing equation was solved numerically with the help of the Laplace transform and the finite Hankel transform to determine the numerical value of the fluid velocity. By taking only the positive roots of the equation $J_0(x) = 0$ the trajectories of the carrier particles for different parameters was determined. The results of our investigation is discussed in this section with graphical presentation of $r(t)$ and $z(t)/R_{mag}$ which corresponds to the radial and axial trajectories.

In order to discuss the effects of relaxation time (λ_1) of the model, Jeffery parameter (λ_2), magnetic field strength (Ms), the pulsatile frequency (ω) and Darcy number (Da) on the particle trajectories with differing values of the fractional-order parameter have been numerically computed and graphically presented in figures 3.2-3.16. For the rest of the calculations, some of the parameter values are considered as $b_0 = 0.5, b_1 = 0.6, A_0 = 0.05, \phi_0 = 0.4, \kappa = 0.1, Da = 0.1, Ms = 1$ and $Re = 5$.

3.3.1 Effects of Fractional Parameter

The impact of the fractional parameter on the particle trajectories is observed in all figures just like in the previous chapter(Chapter 2). All figures are plotted using four different sub figures of the fractional parameter being 0.6, 0.8, 0.9 and 0.1. The governing equation behaved as a general differential equation for $\alpha = 1$. It is observed in all figures that the radial movement of the carrier particles is downward with increasing values of α (see Figures 3.2(a), 3.3(a), 3.4(a), 3.5(a) and 3.6(a)). Thus, the carrier particles are more likely to be swept away from the tumor site by the fluid following the general derivatives than that of the fractional derivatives.

3.3.2 Effects of Time Relaxation-to-Retardation Ratio

Figures 3.2 depicts the influence of λ_1 on the particle trajectories. These figures shows how λ_1 influence the capture of the injected magnetic particles in the blood stream with the influence of the externally applied magnetic field. In physical terms, λ_1 gives rise to viscous forces or increases the non-Newtonian behavior, which will result in the increment of the thickness of momentum boundary layer (a boundary layer is the layer of fluid in the immediate vicinity of a bounding surface where the effects of viscosity are significant). This will cause the decrease of the velocity which will have a significant effect in the capture of the particles at the target site. Figure 3.2(a) shows the influence of λ_1 for $t \in [0, 1]$ in the radial trajectories. For small values of λ_1 , the particles are likely to be swept away during blood flow. However, for larger values of λ_1 , the particles are likely to be captured at large values of t .

Figure 3.2(b) illustrates the influence of λ_1 on the axial trajectories. Just like in Figure 3.2(a), due to the reduced velocity of the blood flow, the particles are easily captured at the target area. With increasing values of λ_1 , the particles becomes vulnerable to capture. Figure 3.2(c) describes the capture of particles in the blood vessel for varying values of λ_1 . Here, the particles are likely to be captured at the edge of the vessel.

3.3.3 Effects of Retardation Time of Jeffrey Fluid

Figure 3.3 (a) depicts the influence of the Jeffrey parameter λ_2 during magnetic drug targeting in a fractionalized Jeffrey fluid. Clearly, the particles are easily captured in all the three cases. Figure 3.3(b) indicates that the particles will be captured in a short period of time. In Figure 3.3(c), the particles are likely to be captured in the center of the blood vessel which displays Jeffrey fluid. In the center or the plug region, the blood particles are experiencing a constant velocity. Therefore, due to the particle-particle interactions, deformation and the rotational movement of Red Blood Cells (RBCs), the particles capture in the plug region becomes difficult to attain.

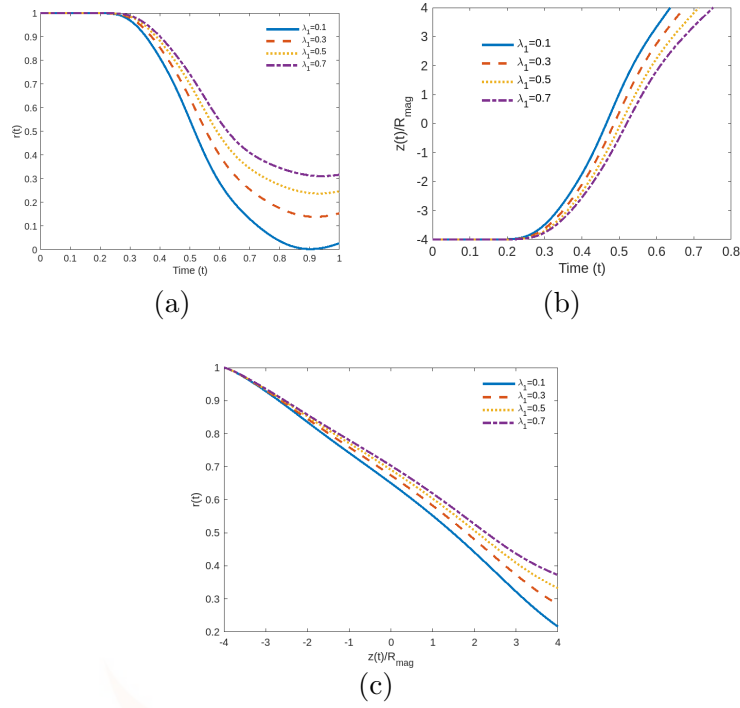


Figure 3.2: Trajectories of drug carrier particles for various values of λ_1 with $\alpha = 1$. (a) Radial trajectories, $r(t)$ of the drug carrier particles as a function of time. (b) Axial trajectories, $z(t)$ of the drug carrier particles as a function of time. (c) Radial trajectories with respect to the axial trajectories ($r(t)$ vs. $z(t)$).

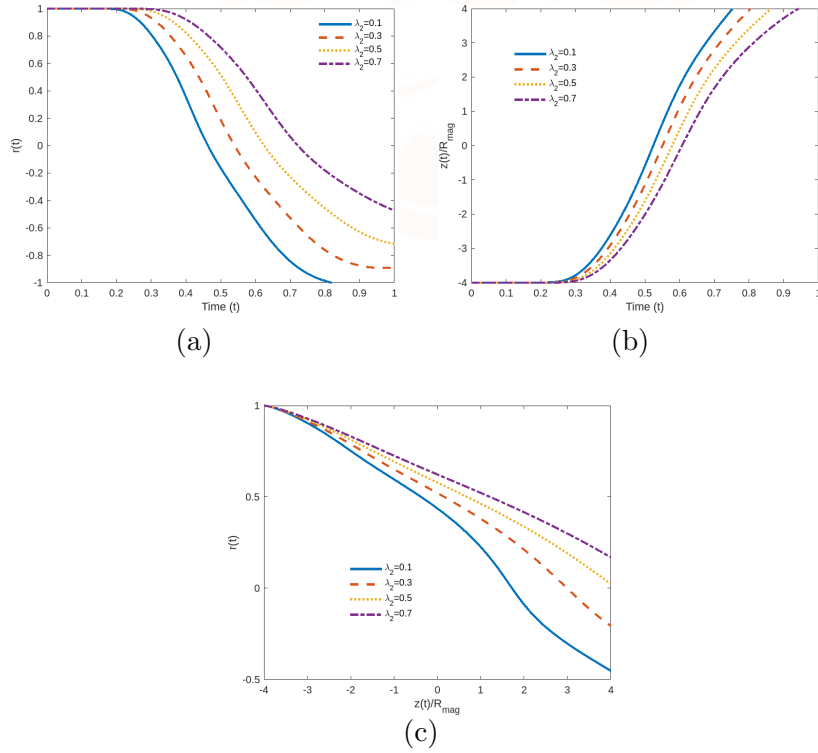


Figure 3.3: Trajectories of drug carrier particles for various values of λ_2 with $\alpha = 1$. (a) Radial trajectories, $r(t)$ of the drug carrier particles as a function of time. (b) Axial trajectories, $z(t)$ of the drug carrier particles as a function of time. (c) Radial trajectories with respect to the axial trajectories ($r(t)$ vs. $z(t)$).

3.3.4 Effects of the Pulsatile Frequency

The pulsatile frequency is related to the pulsatile nature of the blood flow which is based on the pressure gradient. In the present problem, we have considered the values of ω as 1, 3, 5, and 7. From figure 3.4, it is observed that with an increase in the value of ω , the pressure gradient increases, which basically boosts up the fluid velocity in the axial direction. Hence, with an increase in the value of ω , the particles move away from the tumor region. Due to the higher value of the pressure gradient, the axial velocity of the carrier particles increases with time, which influence of the movement of the carrier particles towards the tumor position as observed in figure 3.4(c).

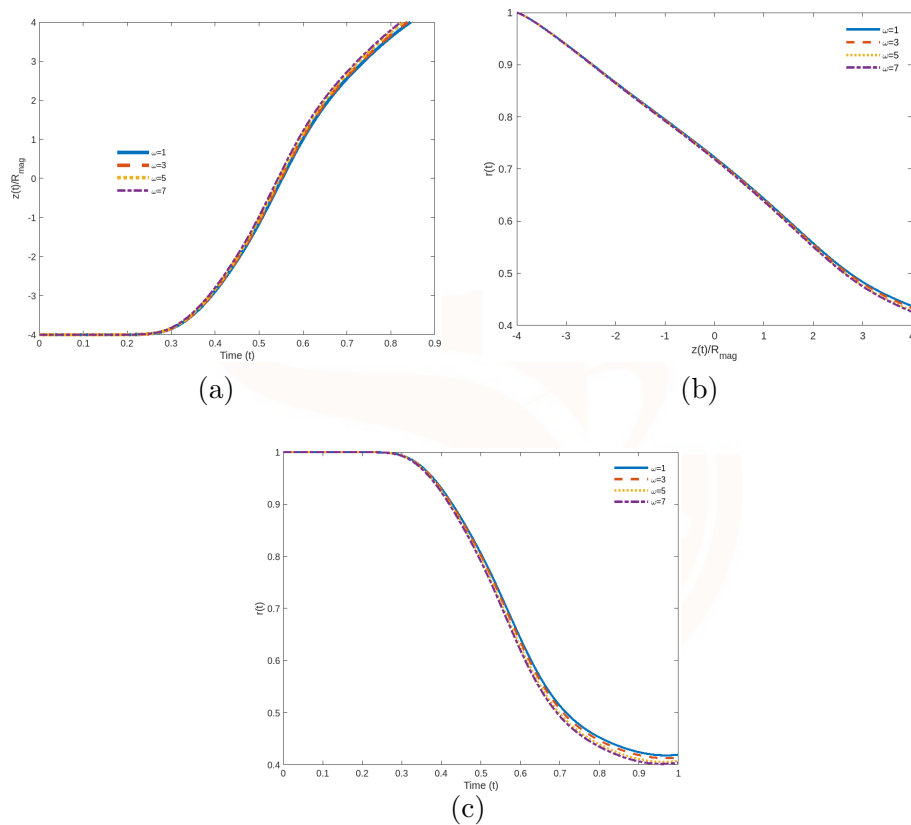


Figure 3.4: Trajectories of drug carrier particles for various values of ω with $\alpha = 1$. (a) Radial trajectories, $r(t)$ of the drug carrier particles as a function of time. (b) Axial trajectories, $z(t)$ of the drug carrier particles as a function of time. (c) Radial trajectories with respect to the axial trajectories ($r(t)$ vs. $z(t)$).

3.3.5 Effects of Magnetization

Magnetic field strength is one of the most important parameter to consider when using the magnetic drug targeting method of drug delivery. Increasing the magnetization of the magnet increases the capture efficiency of magnetic particles and how it impact the trajectories of the carrier particle is shown in Figure 3.5.

In the present investigation, we have considered the values of M_s as 3, 5, 7 and 9. With an

increase in the values of Ms , the magnetic force between the magnet and the magnetic particles increases, which boosts up the radial movement of the carrier particle (figure 3.5(a)). The carrier particles move downward and reaches the tumor position. A similar phenomenon is observed for the axial trajectories of the carrier particles (see Figure 3.5(b)). For a fixed time, the radial movement of the carrier particles with respect to the axial movement is observed in figure 3.5(c). The particles are observed to be closer to $z(t) = 2$ with increase in the values of Ms . Thus, the capture efficiency of the carrier particle is more significant with the increase in the magnetization of the magnet.

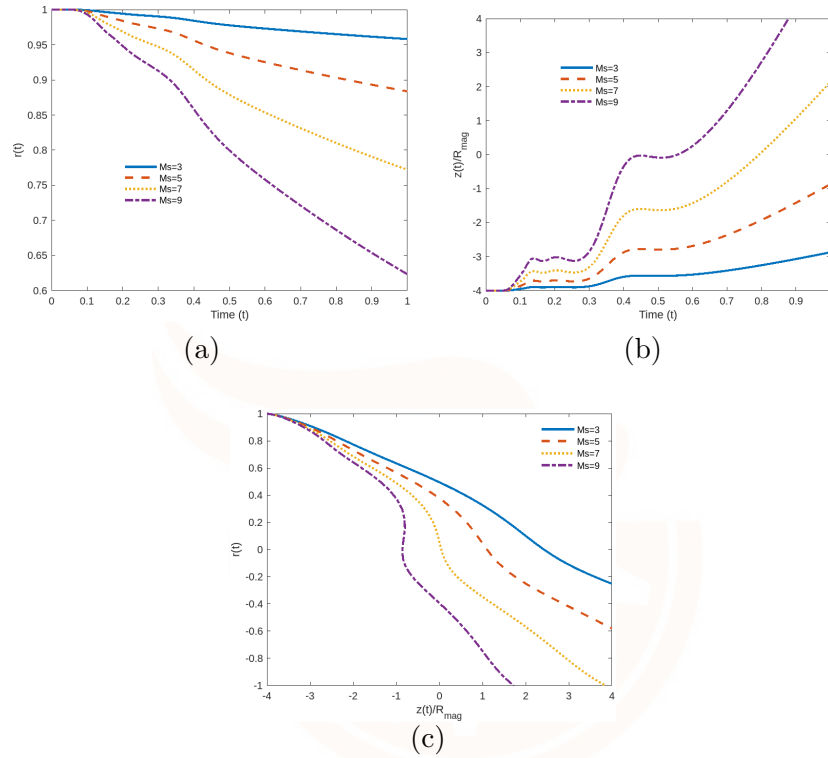


Figure 3.5: Trajectories of drug carrier particles for various values of λ_1 with $\alpha = 1$. (a) Radial trajectories, $r(t)$ of the drug carrier particles as a function of time. (b) Axial trajectories, $z(t)$ of the drug carrier particles as a function of time. (c) Radial trajectories with respect to the axial trajectories ($r(t)$ vs. $z(t)$).

3.3.6 Effects of the Darcy Number

The Darcy number represents the porosity of the microvessel and it highly influences the axial velocity of the blood. The impact of the Darcy number on the trajectories of the carrier particles is shown in Figure 3.6. Figures 3.6(a) and 3.6(b) shows the radial and axial trajectories of the carrier particles against time for different values of the Darcy number, whereas Figure 3.6(c) represents the graph of $r(t)$ against $z(t)$ for a fixed time. Due to the nature of the Darcy number, they help the particle capture at the tumor location by influencing the radial movement of the carrier particle downwards towards the capture site. Figure 3.6(c) shows that with an increase in Da , the carrier particles are likely to be captured at the tumor site as all the trajectories are going downwards.

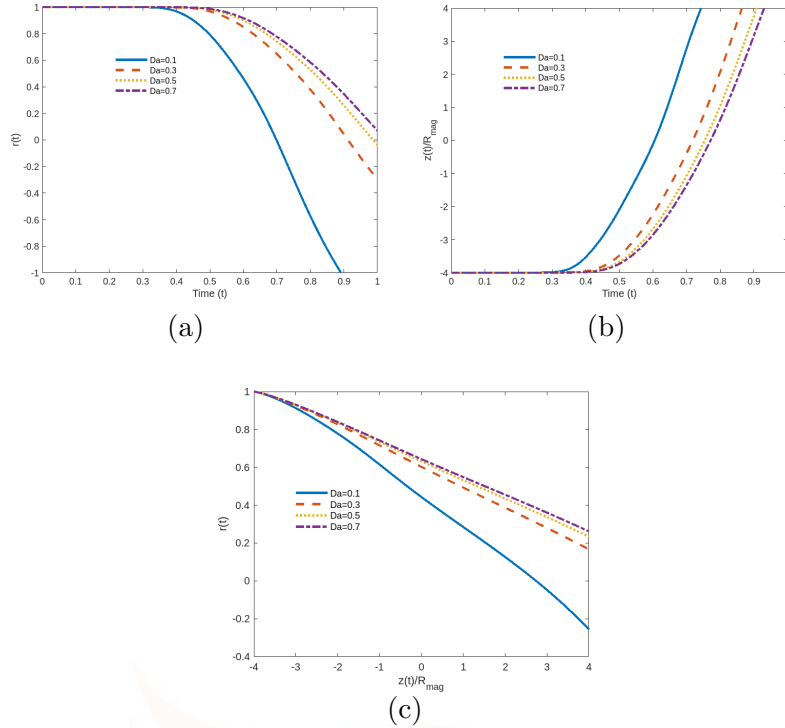


Figure 3.6: Trajectories of drug carrier particles for various values of Da with $\alpha = 1$. (a) Radial trajectories, $r(t)$ of the drug carrier particles as a function of time. (b) Axial trajectories, $z(t)$ of the drug carrier particles as a function of time. (c) Radial trajectories with respect to the axial trajectories ($r(t)$ vs. $z(t)$).

3.4 Conclusion

The current problem deals with the trajectories of the carrier particles in a microvessel under the influence of body acceleration and externally applied magnetic fields. Here the blood is considered as a non-Newtonian Jeffrey fluid. The flow of (Jeffrey fluid) blood mixed with magnetic particles in a circular cylinder (blood vessel) has been modeled with Caputo-Fabrizio Fractional derivative. Both the Laplace transform and finite Hankel transform of zero order have been used to obtain the analytical solutions of the governing fractional partial differential non-linear equations. Numerical models have been generated using numerical analysis and with the help of the Matlab software. The study is helpful and supportive for other practical non-linear problems. The influence of time relaxation parameter, Jeffrey parameter, pulsatile frequency, magnetization and Darcy number have been discussed to understand the trajectories of the drug carrier particles. The fractional parameter helps the drug carrier particles to be more vulnerable to capture at the region where the tumor is located. The time relaxation parameter, Jeffrey fluid, Darcy number and magnetization of the magnet accelerated the radial motion of the carrier particles, whilst an opposite phenomena was observed for the axial motion of the drug carrier particle. Pulsatile frequency helps the drug carrier particle to reach the tumor region. The developed theory can be of help when determining the optimum size of the carrier particle for treatment of tumor with a given size and location in the body.

4. Conclusion and Future Scope

4.1 Conclusion

The first chapter gives the basics and principles of bio-fluid dynamics. The second chapter is based on the trajectories of drug carrier particle during Caputo-Fabrizio fractionalized blood flow through a permeable vessel. The influence of Darcy number, Reynolds number, pulsatile frequency and magnetization are very important and they have been discussed through graphs. The fractional parameter boost up the motion of radial motion of the drug carrier particles, while restricting the axial motion of the carrier particles. All parameters except the pulsatile frequency accelerated the radial motion of the drug carrier particles. The theory developed can be used to determine the optimum size of the carrier particle for treating a tumor with a given size and location within the body. The third chapter is also about the trajectories of drug carrier particles. However, therein the blood was considered as a non-Newtonian Jeffery fluid. The effects of the pertinent parameters such as the time relaxation parameter, Jeffery fluid, Darcy number, pulsatile frequency and magnetization of the magnet have been analyzed and the results are recorded graphically.

4.2 Future Scope

In the present thesis we mainly focused on the effects of the pertinent parameters (time relaxation parameter, Jeffery fluid, Darcy number, pulsatile frequency and magnetization of the magnet) on the trajectories of drug carrier particles through a permeable microvessel considering both non-Newtonian Jeffery fluid flow and ordinary Newtonian fluid flow. Furthermore, the present work can be extended as follows;

1. Both chapters, the study of magnetic drug targeting during Caputo-Fabrizio fractionalized blood flow through a permeable vessel and magnetic particle trajectories in a fractionalized Jeffery fluid model can be extended by changing the flow pattern into an unsteady flow.
2. The artery of the cardiovascular system is not always shaped like a circular straight cylinder. The shape depends on the position at different organs, it may be curved or bifurcated. In future, the present problems can be extended with the above mentioned complex geometries.
3. In the present study we were only focusing on the tumor located on the organs near the surface of the skin and the small blood vessels, therefore the problem can be extended to the larger blood vessels and the ones deep in the body.

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