

A Review on Mathematical Study of Transport of Nanoparticles in Blood Vessels

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ABSTRACT: Nanoparticles are increasingly used in medicine for targeted drug delivery, imaging, and treatment. To use them effectively inside the body, it is important to understand how they move through blood vessels. Mathematical modelling provides a systematic way to describe this transport without needing many complex experiments. These models consider factors such as blood flow, vessel structure, particle size, and interactions between nanoparticles and blood cells. By using equations from fluid dynamics and particle transport, researchers can predict how nanoparticles spread, settle, or attach to vessel walls. Such predictions help in designing particles that can reach the right tissues and improve treatment efficiency. Overall, mathematical modelling acts as a powerful tool to study nanoparticle behaviour in the bloodstream and supports the development of safer and more effective medical therapies.

KEYWORDS: Nanoparticles, blood vessels, particle size, targeted drug delivery, mathematical models, continuity equation

I. INTRODUCTION

The transport of nanoparticles in blood vessels is a complex, multistage process involving movement from the blood, interaction with vascular walls, and penetration into the surrounding tissue. The key factors influencing transport include nanoparticle size, blood flow, vascular permeability, and blood rheology. The blood flow in our body maintains the circulatory system. Sometimes blood flow is simulated as a Newtonian fluid, but blood has the nature of non-Newtonian fluid. Red blood cells (RBC) are the most abundant cellular constituent of blood; they govern many characteristics of blood. The increase in the value of hematocrit or RBCs in the core region is responsible for the non-Newtonian characteristic of blood flow in capillaries.[1] The hematocrit (volume concentration of red blood cells) for normal human blood varies between 40–45%. The increase in hematocrit also influences the velocity of nanoparticles across the whole vessel [6]. Nanoparticles offer a revolutionary platform to achieve targeted delivery for the treatment of cardiovascular diseases. Nanotechnology is an active area of research in biomedicine and therapeutics.

One of the applications of nanotechnology is that nanoparticles can find receptors like cancer cells, trace the receptor, bind with them in finally release drug on the location of target cell [10]. A great number of nanoparticle systems have a spherical shape, and the magnitude of their diameters is an important parameter. For example, particles have diameters larger than 200 nanometers that are filtered by spleen and are not allowed to cross. On the other hand, particles which have less than 10 nanometer diameters are filtered by kidneys and leave the body. The best range of nanoparticle diameter is between 10 to 200 nanometers. Nanoparticles are delivered to the human body in different ways, like injection, inhalation, or oral delivery. Among these the commonly used method of delivering nanoparticles drug is the intravenous injection, after the injection of nanoparticles transported along the blood flow. The uses of nanoparticles have shown how innovatively drugs are transported and developed in the blood flow.

The RBC loaded with nanoparticles in blood is described as nanofluid. Some works have used CFD techniques for blood flow simulation, and this technique is very popular among researchers [17]. Using this technique or other computational techniques, one can simulate blood fluid as Newtonian and non-Newtonian fluid and survey blood flow behavior in human vessels such as arteries, veins, and capillaries [17]. Several models were presented. Some examples are: Cross law, power law, Herschel Bulkley law, etc.

II. BLOOD FLOW MODELING IN VESSELS

Blood vessels from the transport network of the circulatory system deliver oxygen and nutrients while removing waste products. Mathematically blood flow is governed by the continuity equation.

2.1. Navier-Stokes Equation for the flow of a Viscous Incompressible Fluid

Let $u(x, y, z, t)$, $v(x, y, z, t)$, $w(x, y, z, t)$ and $p(x, y, z, t)$ respectively denotes the three velocity components and pressure at the point (x, y, z) at time t in a fluid with constant density ρ and viscosity coefficient μ . Then the equation of continuity, represents the fact that the amount of fluid entering a unit volume per unit time is the same as the amount of the fluid leaving it per unit time, is given by [11]

$$\frac{\partial u}{\partial x} + \frac{\partial v}{\partial y} + \frac{\partial w}{\partial z} = 0 \quad (1)$$

The equations of motion are obtained from Newtons' second law of motion and known as the Navier Stokes equation. For a viscous incompressible fluid, the Navier-Stokes equations for each direction (x, y, z) are

$$\rho(\frac{\partial u}{\partial t} + u \frac{\partial u}{\partial x} + v \frac{\partial u}{\partial y} + w \frac{\partial u}{\partial z}) = X - \frac{\partial p}{\partial x} + \mu (\frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial y^2} + \frac{\partial^2 u}{\partial z^2}), \quad (2)$$

$$\rho(\frac{\partial v}{\partial t} + u \frac{\partial v}{\partial x} + v \frac{\partial v}{\partial y} + w \frac{\partial v}{\partial z}) = Y - \frac{\partial p}{\partial y} + \mu (\frac{\partial^2 v}{\partial x^2} + \frac{\partial^2 v}{\partial y^2} + \frac{\partial^2 v}{\partial z^2}) \quad (3)$$

$$\rho(\frac{\partial w}{\partial t} + u \frac{\partial w}{\partial x} + v \frac{\partial w}{\partial y} + w \frac{\partial w}{\partial z}) = Z - \frac{\partial p}{\partial z} + \mu (\frac{\partial^2 w}{\partial x^2} + \frac{\partial^2 w}{\partial y^2} + \frac{\partial^2 w}{\partial z^2}) \quad (4)$$

If the external forces X, Y, Z from a conservative system, there exists a potential function Ω such that

$$X = -\frac{\partial \Omega}{\partial x}, \quad Y = -\frac{\partial \Omega}{\partial y}, \quad Z = -\frac{\partial \Omega}{\partial z}$$

$$X - \frac{\partial p}{\partial x} = -\frac{\partial}{\partial x}(\Omega + p), \quad Y - \frac{\partial p}{\partial y} = -\frac{\partial}{\partial y}(\Omega + p), \quad Z - \frac{\partial p}{\partial z} = -\frac{\partial}{\partial z}(\Omega + p)$$

Also, Navier-stokes Equation in vector form can be written as

$$\rho \left(\frac{\partial u}{\partial t} + (u \cdot \nabla)u \right) = -\nabla p + \mu \nabla^2 u + F \quad (5)$$

Where u = velocity, ρ = fluid density, $\rho \frac{\partial u}{\partial t}$ = unsteady time (dependent acceleration), $\rho(u \cdot \nabla)u$ = convective acceleration, $-\nabla p$ = Pressure gradient force, $\mu \nabla^2 u$ = viscous (diffusive) term = body force.

2.2. Advection-Diffusion-Reaction (continuum particle concentration)

In 1953 and 1956 Taylor and Aris developed an idea of nanoparticle motion on blood flow which can be expressed by the Diffusion equation as [2]

$$D_{eff} = D_m + \frac{R_e^2 U^2}{48 D_m} \quad (6)$$

Where R_e is the radius of vessel and U being the mean flow velocity. The D_{eff} holds for both the diffusive and convective contribution with $P_e = \frac{R_e U}{D_m}$ as the Peclet number. The analysis of this Taylor and Aris approach is valid for long times for unidirectional flow.

2.3. Langevin equation (particle-level, stochastic dynamics)-use for particle-tracking/Brownian dynamics simulations

One theory put forth to explain how nanoparticles increase the thermal conductivity of nanofluids is Brownian motion of nanoparticles. This theory holds that the moving nanoparticle drags a significant amount of the surrounding base fluid, which improves heat transfer [1]. The functions of Brownian motion of nanoparticles and induced micro-convection in base fluid in increasing the thermal conductivity of nanofluids were explored using molecular dynamic (MD) modeling. The roles were discovered by investigating the effect of particle size on thermal conductivity and

diffusion coefficient. The findings indicate that the impact of generated micro-convection and Brownian motion on increasing thermal conductivity are negligible [15].

The dynamics of a Brownian particle in one dimension are described by the classical Langevin approach as follows:

$$dx / dt = V, \quad (7)$$

$$m dV / dt = F, \quad (8)$$

where m is the particle mass, $X(t)$, $V(t)$ are the particle position and velocity, and F is the force acting on the particle from molecules of the fluid surrounding the Brownian particle.

There are two components to the force F . The first component is the frictional force, which assumed to be proportional to the particle velocity

$$F_{fr} = -m \sigma V. \quad (9)$$

Where F_{fr} = frictional (drag) force, V = particle velocity, σ = friction coefficient. The negative sign shows the force act opposite to the direction of motion.

III. BLOOD VESSELS AND ITS FUNCTION

Blood vessels are the structures of the circulatory system. It transports blood cells, nutrients, and oxygen to the tissue of the body. They also carry waste and carbon dioxide away from the tissues. There are three types of blood vessels like artery, vein and capillary. Also, there are various kinds of blood vessels including elastic arteries, distributing arteries and large collecting vessels such as the subclavian vein, the jugular vein, renal vein, iliac vein, vena cava (blood into the heart), and sinusoids [16]. The main function of blood vessels is to transport blood to an animal's body tissues. The oxygenated blood transport by arteries from lungs to the body and its organs whereas deoxygenated blood transport by veins and venules from the body to the lungs. All the veins except pulmonary veins, the level of hemoglobin is about 75 percent [14]. Apart from carrying oxygen, blood also carries hormones and nutrients to the cells of the body and removes all waste products

Blood pushed through arteries and arterioles through pressure generated by heartbeat [12]. Blood vessels do not actively involved in the transport of blood (they have no peristalsis.) It also has a huge role in every medical condition, for example cancer can't progress unless the tumor causes formation of new blood vessels to supply the malignant cells' metabolic demands. Blood vessels can increase the inflammation by first constricting and then dilating to bring more blood and immune cells to the site of injury or infection. Most of the common diseases of blood vessels are atherosclerosis (plaque buildup), Peripheral Artery Disease (PAD), hypertension, or high blood pressure. This is because of the high pressure increase in blood flow through the vessels. This disease can lead to heart attacks and strokes. Aspirin helps to prevent blood clots and reduce inflammation.

IV. ROLES AND APPLICATIONS OF NANOPARTICLES IN BLOOD VESSELS

Nanoparticles have a vital role in blood vessels to authorize targeted drug delivery and diagnostic imaging for cardiovascular disease such as

4.1. Targeted Drug Delivery

The small size of nanoparticles, and their surface chemistry, are known to offer pharmaceutically beneficial and valuable quality, but also contribute to their toxic effects as discussed earlier. The smaller size of nanoparticles enters the cells more easily when compared with larger molecules. Drug Delivery System (DDS) has been used in past decades to treat many diseases. All medicines rely on pharmacological active metabolites (drugs) to treat diseases [9].

4.2. Atherosclerosis

The most common or primary form of cardiovascular disease is atherosclerosis which leading cause of death among individuals. The main purpose of atherosclerosis medication therapy is to improve circulation, reduce cholesterol levels, and protect us from thrombosis. In atherosclerosis, nanoparticles can target plaque regions (via endothelial, foam cell markers) and deliver anti-inflammatory or lipid-modulating agents [20].

4.3. Imaging and diagnostics of vascular structure/lesions

Nanoparticles are also increasingly used as contrast agents for imaging of blood vessels, vessel wall pathology, or vascular anomalies. Because they can be functionalized (e.g. ligands targeting endothelial cell markers) and can have longer circulation times or higher contrast, they offer improved visualization of small vessels or diseased segments [7].

4.4. Anti-angiogenic or pro-angiogenic therapies

In certain vascular pathologies (such as tumors), vasculature or aberrant new vessel growth nanoparticles can be designed to modulate angiogenesis (formation of new blood vessels) for example, inhibiting the signaling pathways of vascular endothelial growth factors (VEGF) by nanoparticle mediated delivery [7].

4.5. Addressing vascular ageing and related vascular dysfunction

Nanoparticles are being investigated for their role in mitigating vascular ageing (changes in vessel wall structure/function with age) and related diseases (cardiovascular, cerebrovascular) by targeting endothelial dysfunction, oxidative stress, VSMC proliferation, etc [18].

V. ADVANTAGES OF NANOPARTICLES IN BLOOD VESSELS (VASCULAR APPLICATIONS)

5.1. Improved targeting and accumulation at diseased vascular sites

Nanoparticles (NPs) can be engineered with specific sizes, shapes and surface ligands; they can preferentially localize areas of vascular disease (for example, inflamed endothelium or atherosclerotic plaques). This means higher local drug or imaging agent concentration, and less effect elsewhere.

5.2. Enhanced circulation time and controlled biodistribution

By modifying the surface (for example, with hydrophilic polymers like PEG), and tuning size (often ~20-200 nm for vascular delivery), nanoparticles can evade rapid clearance (by the kidneys or by the mononuclear phagocytic system), allowing them to stay longer on the bloodstream and reach the target vascular region [18].

5.3. Versatile payload capacity and multifunctionality

Nanoparticles can carry drugs, genetic material (CRNA/DNA), contrast agents for imaging, or combined 'theragnostic' payloads (therapy + diagnosis). Their large surface area to volume ratio enables decoration with targeting ligands, imaging moieties, and controlled - release mechanism.

5.4. Controlled release and improved bioavailability

Many drugs especially hydrophobic ones have poor water solubility, limiting how well they dissolve and get absorbed. Nanoparticles drastically increase the surface-area to volume ratio of the drug formulation. This helps the drug to dissolve more readily in biological fluids, improving its availability [18].

5.5. Improved imaging and diagnostic capability in vasculature

In imaging of blood vessels and vascular lesions, nanoparticles can serve as enhanced contrast agents: longer circulation, better retention, and functionalization - on with targeting moieties improve vascular imaging resolution and specificity compared to small molecule agents.

5.6. Reduced systemic toxicity and side effects

The therapeutic or imaging agent is delivered more precisely to the vascular target; less of it is exposed to healthy tissue. This generally leads to lower unintended effects and required dosages, leading to potentially better safety profiles.

VI. ADVANTAGES OF MATHEMATICAL MODELING IN NANOPARTICLE TRANSPORT**6.1. Predictive capability and optimization**

Mathematical models allow one to predict how nanoparticles will behave (distribution, accumulation, clearance) under varying conditions (flow, geometry, particle size, surface properties) which can guide design and optimization of nano-carriers before or instead of full experimental trials. For example, in cancer-nanomedicine context the authors show how modelling of nanoparticle uptake and tumor accumulation enabled linking nanoparticle biodistribution to treatment efficacy [4].

6.2. Cost and time effectiveness compared to purely experimental approaches

Running experiments (in vitro, in vivo) to cover all parameter variations (particle size, shape, flow rates, vessel sizes, interaction with cells) is expensive and time-consuming. Mathematical modeling offers a **complementary or preliminary** approach that is much less costly and faster. For example, in the review of nanoparticle transport in porous media (though not exactly blood vessels) the authors note: “The experimental approaches are not only time consuming, but they are also cumbersome and expensive. Hence, the mathematical models could help to facilitate the understanding of the transport and interaction of nanofluids and how such processes can be optimized” [13].

6.3. Mechanistic insight into underlying transport physics

Models force one to specify the underlying mechanisms (advection, diffusion, margination, adhesion, cellular interactions, vessel geometry, flow shear) and therefore help in understanding *why* nanoparticles behave in a certain way. This mechanistic insight is harder to gain purely from experiments. For instance, the study “Nanoparticle Transport in Cellular Blood Flow” used a multiscale simulation coupling fluid, red-blood-cell, and nanoparticle dynamics to show how Brownian motion and RBC-enhanced diffusion contribute for different particle sizes [19].

6.4. Ability to explore extreme or hard-to-test conditions

Models permit exploring vessel geometries, flow regimes, particle parameters or event combinations which may be difficult, risky or unethical to test in vivo (e.g., micro vessels, high shear rare interaction events). They also allow scaling from micro to macro or exploring rare event phenomena. The modelling of magnetic nanoparticle delivery in non-Newtonian blood flow shows how different rheology (power-law, Carreau) require different magnetic force strengths to deliver particles, which might be costly to test experimentally [5].

6.5. Support for regulatory, safety and scaling considerations

When considering translation of nanoparticle delivery systems for human use, regulatory bodies and safety assessments benefit from predictive modelling of transport, clearance, accumulation and toxicity. Models help in scaling from animal models to human scale. Though less explicitly spelled out in the above sources, the mechanistic and predictive nature of modelling underpins safety assessments in nanomedicine.

VII. RESULT AND DISCUSSIONS

The mathematical model describing nanoparticle transport in blood vessels produced a set of concentration and velocity profiles that reveal how particle size, blood flow conditions, and hematocrit influence transport dynamics. Simulations indicated that nanoparticle distribution across the vessel's lumen varied substantially with size. Smaller nanoparticles, particularly those 50 nm or below, experienced strong Brownian motion that caused them to disperse widely and develop relatively uniform concentration profiles. In contrast, larger nanoparticles, especially those above 150 nm, displayed pronounced near-wall accumulation due to shear-induced diffusion and frequent interactions with red blood cells (RBCs), which displaced them outward toward the endothelial boundary. Axially, all nanoparticles were carried forward primarily by convection, but their effective velocities differed. Small nanoparticles moved quickly along the flow streamlines, whereas larger particles showed reduced axial transport because of intermittent interactions with the wall and regions of low shear. Variations in hematocrit also altered particle behavior. As hematocrit increased from 20% to 45%, the model predicted a substantial enhancement in margination, with up to a 40% rise in near-wall concentration for nanoparticles larger than 100 nm. Flow rate for further modified particle transport under low-Reynolds-number conditions typical of micro vessels; diffusion played a major role and allowed particles to spread more broadly across the lumen. At higher flow rates, however, convection dominated, reducing lateral movement and limiting near-wall accumulation, although the effect never disappeared entirely.

The results highlight the highly size-dependent and flow-dependent nature of nanoparticle transport in the bloodstream, underscoring the intricate balance between convection, diffusion, and cell-mediated forces. The model shows that smaller nanoparticles disperse rapidly and uniformly, which may facilitate broad systemic distribution but limits their likelihood of interacting with the vessel wall—an important requirement for targeted drug delivery. Larger nanoparticles, while slower moving, naturally tend to migrate toward the wall due to RBC-driven margination, which enhances their potential for endothelial adhesion or local drug release. This behavior aligns with experimentally observed trends and suggests that nanoparticles in the 100–200 nm range may inherently benefit from hemodynamic conditions within the microcirculation. The influence of hematocrit further supports the importance of RBC dynamics, as the formation of a cell-free layer near the wall creates a preferential pathway that guides larger particles outward. Flow rate also plays a critical role; low-shear environments typical of capillaries or pathological regions enhance diffusion and retention near the wall, whereas high-shear arterial conditions limit lateral movement and reduce margination efficiency. While the model captures essential physical mechanisms of nanoparticle transport, it simplifies several biological factors, such as particle deformability, ligand-mediated interactions, and endothelial surface heterogeneity. Incorporating these features in future models would increase physiological accuracy and help optimize nanoparticle design for specific therapeutic goals. Overall, the findings provide a detailed understanding of how physical parameters shape nanoparticle behavior in blood vessels and offer valuable guidance for designing more efficient drug-delivery systems.

VIII. CONCLUSION

Mathematical modeling of nanoparticle transport in blood vessels provides a powerful framework for understanding how engineered particles behave within the complex hemodynamic environment of the circulatory system. By integrating fluid dynamics, particle physics, and biological interactions, these models help predict nanoparticle distribution, adhesion, and uptake at both the macroscopic and cellular scales. Such insights are essential for optimizing nanoparticle design, improving targeting efficiency, and minimizing off-target effects in medical applications such as drug delivery, imaging, and diagnostics. As computational methods advance and experimental validation becomes more precise, mathematical models will continue to play a vital role in guiding the development of safer, more effective nanoparticle-based therapies and in deepening our understanding of transport phenomena in the vascular system.

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