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Generalized Geometric Analysis of Blood Vessel Subdivisions and Fluid Mechanics

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Abstract: This study proposes simplified geometric analyses of the subdivisions of blood vessels and extends the fluid-mechanical analysis to derive generalized equilibrium solutions. Departing from the traditional emphasis on symmetrical subdivisions in which one vessel splits into two, we delve into a broader scenario in which a single vessel divides into multiple branches. This exploration advances our understanding of blood vessel fluid mechanics and extends its application to biomechanical contexts. Methodologically, we integrate principles from physics, physiology, geometry, and optimality analysis. The results reveal generalized optimal solutions for the original radius of the vessel compared to bifurcated radii and optimal solutions for bifurcated angles. These findings play a significant and pivotal role in evolution, improving our comprehension of vascular mechanics and paving the way for further applications in understanding hemodynamics and the evolutionary processes of vascular systems in various animals.

***Keywords*:** evolution of blood vessels, blood vessel subdivisions, fluid mechanics, biomechanics, generalized equilibrium solutions, optimal solutions

MSC: 92-10, 92C05, 76Z05, 53Z05, 53Z10, 49Q12

1. Introduction

Understanding the complex dynamics of blood vessel subdivisions is crucial in biomedical engineering and clinical applications. Rosen [1] delineated the geometric shapes of vascular subdivisions, establishing the important foundation for the geometric analysis of the vasculature. However, previous research has primarily focused on subdivisions where one vessel divides into two, but the practical implications of this analysis were limited to this specific scenario. Furthermore, to date, the evolutionary reasons behind vascular development in biomedical science remain unclear. Therefore, the motivation of this study is to understand the directional orientation and caliber issues that arise from the evolution of the vascular system. If we can comprehend these aspects in the future, biomedical science will make further advancements, with research results expected to have significant practical implications.

The purpose of this study is to generalize the geometric expansion model beyond the analysis of bifurcations into two vessels. Through fluid dynamics, it seeks to minimize the energy consumed by blood flow within vessels and

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investigate the distribution of vessel radii and subdivision angles, respectively, exploring symmetric and asymmetric vessel subdivisions to elucidate the evolutionary process of vasculature. For convenience of analysis, this study establishes a simpler model through simplified geometric analyses of the subdivisions of blood vessels. It extends the fluid-mechanical analysis to derive generalized equilibrium solutions.

Rosen's [1] most important contribution was proposing the bifurcation geometry of blood vessels. It also showed how interpretations of state proximity vary between descriptions. It exemplified bifurcation sets by scrutinizing states where minor changes under one description become significant under another. Within his framework, a bifurcation point denotes inherent disparities in the information conveyed. Subsequently, he explored statistical mechanical representations as alternatives to microscopic depictions, confirming the existence of bifurcation points between descriptions.

Ren and Zhou [2] delved into the fluid-mechanics analysis of blood vessels, providing valuable insights into blood flow mechanics within bifurcations. However, their focus remained on bifurcations involving a single vessel dividing into two branches.

West et al. [3] demonstrated that allometric scaling, including the 3/4 power law that governs metabolic rates, is a fundamental principle in biological systems. Their model, grounded in fractal branching networks, describes material transport under the assumptions of minimal energy dissipation and invariant terminal tube dimensions. Their framework extends to various biological transport systems, including cardiovascular and vascular networks. A notable similarity between their study and ours is the use of simplified assumptions, particularly the minimization of energy dissipation while disregarding turbulence and other complexities. However, our model refines this approach by incorporating vessel tapering and non-linear effects and other considerations, which their framework does not account for.

Aracil [4] discovered that modelling complex systems within dynamical systems, particularly in 'soft' systems, involves traversing diverse theoretical frameworks explaining system component interactions. His study uses qualitative dynamical systems theory to explore the relationship between the emergence of new behavioral patterns and the incidence of bifurcations in models.

Nguyen et al. [5] uncovered the initial stages of vascular development, highlighting the pivotal role of mechanical adaptation in the formation of the arteries. However, current numerical simulations may not accurately predict vascular patterns. To address this, they proposed a theoretical model focusing on key factors like side branch disconnection and tissue expansion, enhancing vessel modelling. Furthermore, the model accurately forecasts mechanical outcomes, shedding light on flow-driven vascular branching morphogenesis.

Contarino et al. [6] used implicit solutions to solve the junction-generalized Riemann problem. They also used new global explicit methods, but only partially implicit methods, to solve Arbitrary high-order DERivatives (ADER), and this processing can just solve the problem of stiff sources. Therefore, they could use this technology in the analysis of blood vessel networks. They simplify the nodes of blood vessels to have three subdivisions for analysis and study the convergence of the entire system.

Olufsen et al. [7] studied blood flow in the arteries. They used the Navier-Stokes equation to analyze arterial flow and pressure, which is also applicable to the conical. The analysis of blood vessels aims to predict arterial blood flow, pressure equations, and boundary conditions. They derived an equation for the root impedance of the structural tree by modelling the smaller arteries and arterioles as a structural birch tree and using linearized versions as assumptions. This allows the flow and pressure of large and small arteries to be predicted.

Piccioli et al. [8] proposed a blood flow model with augmented fluent-structure interaction to study viscoelastic blood vessel-related research and node issues. They believed that the past literature lacks and ignores the contribution of nodes to viscoelasticity and that it tends to use the local elasticity method. Therefore, they innovatively studied the influence of viscoelasticity on boundary conditions, used the standard linear solid model to interpret the viscoelasticity of blood vessels, and constructed a method closely related to the nodes, that is, to build a technique related to the inlet and outlet boundaries of the blood vessels.

Reymond et al. [9] considered one-dimensional arterial tree models to be a preferred option to explore pressure and blood flow propagation in arteries. Accordingly, they used an arterial tree model to analyze the main arteries of the body and obtain the sum of the flow and pressure of the arterial tree. To verify the model's predictability, in addition to human experiments, they also included other actual measurement data, reflecting the consistency between the theory of the one-dimensional model and the empirical results of human experiments.

The first study on bifurcations in cylindrical vessels was published in Young [10]. The first study of bifurcations in trees was published in Roux [11]. Hess [12, 13] and Murray [14, 15] presented two similar models for blood bifurcations that led to a famous "Hess-Murray law" according to which $r_{j+1}/r_j = 2^{-1/3}$. The law was compared to the experimental results and several authors suggested changes. Sherman [16] and Sciubba [17, 18] commented on the state-of-the-art. Bejan [19] proposed a novel model called "Constructal Theory" that may be regarded as an extension of the Hess-Murray law. Experimental evidence published by Huang et al. [20], Seymour et al. [21], Uylings [22], and others demonstrated that the Hess-Murray law can be considered as a first approximation valid for laminar flow, rigid walls, and no-wall suction. Recently, although entropy and exergy models have become popular, they do not use optimal solution exploration.

Singh and Singh [23] believed that blood is a non-Newtonian fluid because blood contains other complex components in addition to red blood cells. In their article, they conducted a numerical analysis of non-Newtonian pulsating blood flow. They used four non-Newtonian models to simulate blood flow and compared the results with Newtonian models. Their study found that using a moderate viscosity model is more meaningful, especially when the average wall shear stress is minor. In addition, they found that the Quemada model produced the highest average wall shear stress among the four models.

Pan et al. [24] believed that the geometry of blood vessels is one of the causes of arteriosclerosis and that this relationship is related to wall shear stress. Therefore, they directly explored the effect of blood vessel geometry on wall shear stress. They found that the blood flow velocity in the basilar arteries is positively related to wall shear stress. The smaller the wall shear stress, the greater the influence of the vascular radius on the basilar arteries. In addition, they found that the length and curvature of the blood vessels do not affect the wall shear stress.

Triebold and Barber [25] believed that the proportion of oxygen carried by red blood cells is more significant in large blood vessels than in the microvasculature. This uneven distribution is primarily due to the bifurcation of blood vessels. Therefore, they focused on studying the effect of vessel wall coating on blood vessel bifurcations. They found that interactions between cells resulted in a more uniform distribution of oxygen and enhanced the influence of the coating of the vessel wall.

Chu et al. [26] studied the issue of blood vessels dividing into two. The main difference between their research and ours is that we generalized the situation to blood vessels dividing into a generic n. They used simulation and fluid dynamics to explore non-Newtonian blood in symmetric and asymmetric blood vessels. Their study found that non-Newtonian fluids have higher values when comparing wall shear stress than Newtonian fluids. Furthermore, when the angle of subdivision of the blood vessel is greater, the shear stress on the wall is also more considerable. They also discovered that when the blood flow velocity is low, the non-Newtonian properties of the blood cannot be ignored.

This study seeks to bridge these gaps by extending the analysis to encompass more general cases of blood vessel subdivisions. By broadening the scope to scenarios where one vessel divides into multiple branches, we aim to provide a comprehensive understanding of fluid mechanics in blood vessel networks. Moreover, our aim is to explore the application of these principles in biomechanics, thereby expanding the practical utility of our findings.

Through a multidisciplinary approach integrating principles from physics, physiology, geometry, and optimality analysis, this study seeks to derive generalized equilibrium solutions for blood vessel subdivisions. By doing so, we hope to contribute to a deeper understanding of blood vessel dynamics and facilitate advancements in biomedical research and clinical practice.

2. Foundational model and analysis

The theoretical framework of this study draws on a multidisciplinary approach that includes principles of physics, physiology, geometry, and optimality analysis to elucidate the dynamics of blood vessel subdivisions. To facilitate the analysis, this study established a simpler model through a simplified geometric analysis of blood vessel subdivisions to analyze the evolution of blood vessels, including changes in the subdivision angle and radius of blood vessels before and after subdivision.

This study extends Rosen [1] by generalizing the geometry of blood vessels from 2 bifurcations to n subdivisions. It adopts the method of extracting and using blood flow in the vessel, which operates with minimal energy, to find the optimal radius ratio and angle of the blood vessel subdivision. Why adopt minimal energy-consuming blood flow? That is, in physiology, all bodily operations have evolved to function in the most energy-efficient way. Therefore, this study assumes the least energy consumption, as described in Equations (1) and (24).

To simplify the model, this study does not delve into complex physiology but instead focusses on two types of energy consumption during blood flow.

1. Blood overcomes resistance to viscous fluids.
2. Blood that nourishes the wall of the vessel.

Regarding the resistance of blood to viscous fluid, according to the laws of fluid mechanics, the resistance experienced by a viscous fluid flowing in a rigid tube is proportional to the square of the flow rate and inversely proportional to the fourth power of the radius of the pipe. This leads to item 13 in the definition of variables in Sections 2.1 and 2.2. Furthermore, this force multiplied by the distance from the blood flow forms energy, which is why the energy in Equations (1) and (24) can be obtained. In other words, in physics, work (or energy) is defined as the product of the applied force and the displacement in the direction of that force. Specifically, work = Force × Displacement in the direction of the force.

Regarding the blood that feeds the vessel wall, from a physiological perspective, it is a function of the thickness and radius of the vessel wall. For simplicity, this study assumes that the thickness of all vessel walls is similar. From physiology, it is known that the resistance produced by the blood that feeds the vessel wall is a function of the radius to a power, where a is bounded between 1 and 2. This force multiplied by the distance from which the blood flows form energy.

The four concepts of the research methods of this study are as follows.

First, physics principles are applied to understand the resistance encountered by a viscous fluid flowing through a rigid pipe. This aspect is crucial to comprehend the behavior of blood flow within blood vessels, where viscosity plays a significant role in determining resistance.

Second, insights from physiology are leveraged to recognize the physiological necessity for blood to support the resistance exerted by the tube wall during its flow. Understanding the interplay between blood flow dynamics and the mechanical properties of the walls of blood vessels is essential to elucidate the underlying mechanisms that govern the subdivisions of blood vessels.

Third, geometry is used to analyze the intricate spatial configurations of the blood vessel networks. Trigonometric functions are used to mathematically model the phenomenon of one-to-many blood vessels, allowing a comprehensive examination of vascular branching patterns and their implications on blood flow dynamics.

Fourth, optimality analysis is used to identify equilibrium solutions that minimize the total energy required to overcome resistance and supply the wall of the tube. By optimizing energy efficiency, these equilibrium solutions provide insights into the adaptive strategies employed by biological systems to ensure efficient blood flow within blood vessel networks. This study is a simplistic model, so its objective is to remove unnecessary complexity to grasp the key points of vascular evolution without getting bogged down by mastering all the details and not being able to draw any conclusions. It is well known that blood is non-Newtonian and that flow in larger blood vessels can be turbulent, with each split potentially bringing additional local resistance. To simplify the hypothesis, this study adopts the principles of fluid mechanics.

In summary, this theoretical framework integrates diverse disciplines to provide a comprehensive understanding of blood vessel subdivisions, encompassing both structural and functional aspects of vascular dynamics.

This study will conduct an analysis using two types of models. First, we will construct and analyze a symmetrical model of blood vessel subdivision. This model encompasses parameters such as blood flow volume, vessel radius, length of the pathway traveled by the vessel post-subdivision, angle between the vessel and the pre-subdivision extension line (midline), and perpendicular distance of the furthest endpoint of the vessel to the midline, all assumed to be uniform across different subdivisions. Second, we will construct and analyze an asymmetrical model of blood vessel subdivision, where we relax the assumption of symmetry.

2.1 *Symmetrical modeling and analysis of blood vessels*

The variables in our theoretical framework are defined as follows:

1. The Subdivision Number into which a Blood Vessel Branches: n represents the subdivision number after a blood vessel splits into n branches.

2. Fluid Resistance Coefficient: K represents the fluid resistance coefficient.

3. Blood Flow Volume: f represents the blood flow volume.

4. Vessel Radius before Subdivision: r represents the radius of the blood vessel before subdivision.

5. Vessel Radius after Subdivision: r_1 represents the radius of the blood vessel after subdivision.

6. The Coefficient of the Resistance when Nourishing the Vessel Wall: b is the coefficient of the resistance when nourishing the vessel wall.

7. Length of Blood Vessel before Subdivision: l represents the distance of blood flow before subdivision.

8. Length of Blood Vessel after Subdivision: l_1 represents the distance of blood flow after subdivision.

9. Horizontal Distance of Blood Flow before and after Subdivision: The total horizontal distance of blood flow along the original vessel pathway (midline) before and after subdivision is denoted as L. The horizontal distance serves as the reference distance in the model and can be used to calculate the vascular length associated with the displacement in the direction of the force before and after branching.

10. Perpendicular Distance between the Vessel Endpoint after Subdivision and Extension Pathway before Subdivision: The perpendicular distance between the farthest end point of the vessel after the subdivision and the forward extension direction of the vessel pathway before the subdivision is denoted as H.

11. Angle between the Vessel after Subdivision and Extension Pathway before Subdivision: The angle between the direction of the vessel after subdivision and the forward extension direction of the vessel pathway before subdivision is denoted as θ. This investigation is three-dimensional, which means that the overall vascular branching is distributed in a 360-degree manner. However, when considering the angle relationship between a vessel before branching and a single branch after bifurcation, the relationship, expressed as $(180° - \theta)$, resembles a two-dimensional spatial configuration.

12. Exponent of the radius in the resistance of the nourishing vessel wall: a represents the exponent of the radius in the resistance of the nourishing vessel wall, where $1 \leq a \leq 2$. This assumption is based on physiological principles and, along with other model parameters, can be empirically validated through physiological experiments. Accurate determination of the value of a remains a critical avenue for future research.

13. Blood Resistance within Blood Vessels: The resistance of a viscous fluid within a rigid pipe is denoted as $K\ f^2/r^4$ before and $K\ (f/n)^2/{r_1}^4$ after branching.

14. Blood Resistance when Nourishing the Vessel Wall: Resistance encountered while feeding the vessel wall during its flow. The energy required per unit length of the blood vessel is represented by $b\ r^a$ before and $b\ {r_1}^a$ after branching.

15. Energy Required to Overcome both Viscous Fluid Resistance and Nourish the Vessel Wall: When a blood vessel bifurcates into n, the total energy expended by blood is the sum of the energy required to overcome the resistance of viscous fluid and the energy expended to nourish the wall of the vessel. This total energy expenditure is denoted as $C = (Kf^2/r^4 + b\ r^a)l + [K(f/n)^2/{r_1}^4 + b\ {r_1}^a]n\ l_1$.

The thirteenth item refers to the scenario in which one blood vessel bifurcates into n, representing a generalized exception. This study will investigate the generalized optimal solution for the ratio of the original radius of a blood vessel to the bifurcated radius, as well as the optimal solution for the cosine of the subdivision angle. The generalized model framework of this study will employ trigonometric functions to analyze the mathematical phenomena of one-to-many (n) subdivisions.

The following discussion pertains to the scenario in which a blood vessel bifurcates into n branches, with the blood volume evenly distributed among the n bifurcated vessels.

In this model where a blood vessel is divided into n, the angle between each of the bifurcated vessels and the forward extension direction (also known as the midline) before subdivision is denoted as θ. Additionally, the spatial distribution of each subdivision results in the division of the 360-degree plane formed by the endpoints of the branches into n, resulting in $360/n$ degrees between the endpoints of each subdivision. (This refers to the angular distribution among all vascular branches.) The total energy expenditure is denoted by minimizing the following expression.

$$\begin{aligned}\min_{r,\, r_1,\, \theta} C &= \min_{r,\, r_1,\, \theta}\left\{\left(\frac{Kf^2}{r^4}+\ b\ r^a\right) l+\left[\frac{K\left(\dfrac{f}{n}\right)^2}{{r_1}^4}+\ b\ {r_1}^a\right] nl_1\right\}\\ &= \min_{r,\, r_1,\, \theta}\left\{\left(\frac{Kf^2}{r^4}+\ b\ r^a\right)\left(L-\frac{H}{\tan\theta}\right)+\left[\frac{K\left(\dfrac{f}{n}\right)^2}{{r_1}^4}+\ b\ {r_1}^a\right]\left(\frac{nH}{\sin\theta}\right)\right\}\end{aligned} \tag{1}$$

The following are the first-order necessary conditions for r, r_1, and θ. That is to say, Equation (1) represents the cost-minimization problem of blood flowing through blood vessels. The first-order necessary conditions of Equation (1) are that the partial derivatives of the cost function for r, r_1, and θ are equal to zero. Equations (2)-(4) are obtained, respectively, as follows:

$$\frac{\partial C}{\partial r}=\left(-4Kf^2r^{-5}+b\ a\ r^{a-1}\right)\left(L-\frac{H}{\tan\theta}\right)+0=0 \tag{2}$$

$$\frac{\partial C}{\partial r_1}=0+\left(-\frac{4Kf^2{r_1}^{-5}}{n^2}+b\ a\ {r_1}^{a-1}\right)\left(\frac{nH}{\sin\theta}\right)=0 \tag{3}$$

$$\frac{\partial C}{\partial \theta}=\left(\frac{Kf^2}{r^4}+\ b\ r^a\right)\left(H\csc^2\theta\right)+\left(\frac{Kf^2}{n^2{r_1}^4}+b\ {r_1}^a\right)\left(-nH\csc^2\theta\cos\theta\right)=0 \tag{4}$$

From the rearrangement of Equations (2) and (3) above, we obtain the following two expressions.

$$4Kf^2=\ b\ a\ r^{a+4} \tag{5}$$

$$\frac{4Kf^2}{n^2}=b\ a\ {r_1}^{a+4} \tag{6}$$

Dividing Equation (5) by Equation (6) and rearranging yields the following expression.

$$\frac{r}{r_1}=n^{\frac{2}{a+4}} \tag{7}$$

By rearranging Equation (7), we obtain $r=r_1n^{2/(a+4)}$, which is then substituted into Equation (4). After further rearrangement, we obtain the following expression.

$$\cos\theta=n^{\frac{a-4}{a+4}} \tag{8}$$

In this study, the second-order conditions for the three variables in the cost function problem, represented by the Hessian matrix of second derivatives, are assumed to be positive semidefinite. Therefore, the objective function corresponds to cost minimization.

Proposition 1 If a blood vessel bifurcates into n branches symmetrically after subdivision, it can be analyzed using trigonometric functions, fluid dynamics, and physics. The equilibrium solutions are derived as follows through the application of generalization and building on the foundational points mentioned above. (1) $r/r_1 = n^{2/(a+4)}$, (2) $\cos\theta = n^{(a-4)/(a+4)}$.

The following discussion will undertake a comparative static analysis of the two equilibrium solutions.

$$\frac{\mathrm{d}\dfrac{r}{r_1}}{\mathrm{d}n} = \frac{\mathrm{d}\, n^{\frac{2}{a+4}}}{\mathrm{d}n} = \frac{2}{a+4}\, n^{-\frac{a+2}{a+4}} > 0 \tag{9}$$

$$\frac{\mathrm{d}^2 \dfrac{r}{r_1}}{\mathrm{d}n^2} = \frac{\mathrm{d}\, \frac{2}{a+4}\, n^{-\frac{a+2}{a+4}}}{\mathrm{d}n} = -\frac{2(a+2)}{(a+4)^2}\, n^{-\frac{2a+6}{a+4}} < 0 \tag{10}$$

$$\frac{\mathrm{d}\cos\theta}{\mathrm{d}n} = \frac{\mathrm{d}\, n^{\frac{a-4}{a+4}}}{\mathrm{d}n} = \frac{a-4}{a+4}\, n^{-\frac{8}{a+4}} < 0 \tag{11}$$

$$\frac{\mathrm{d}^2\cos\theta}{\mathrm{d}n^2} = \frac{\mathrm{d}\, \dfrac{a-4}{a+4}\, n^{-\frac{8}{a+4}}}{\mathrm{d}n} = -\frac{8(a-4)}{(a+4)^2}\, n^{-\frac{a+12}{a+4}} > 0 \tag{12}$$

Since the model parameter is constrained within the range $1 \le a \le 2$, it follows from Equations (9) and (10), it can be observed that r/r_1 is an increasing and concave-downward function of n. Equation (9) seems intuitive, as it suggests that the ratio of radii increases with the subdivision number. However, Equation (10) presents an interesting resilience phenomenon in vessels post-subdivision. It implies that with an increase in the subdivision number, the vessels after the subdivision become progressively narrower, albeit to a diminishing extent.

Equations (11) and (12) reveal that cosine is a decreasing and concave upward function of n, while the angle θ, derived from cosine, is an increasing and concave downward function of n. From Equations (11) and (12), it is evident that as the subdivision number increases, the subdivision angle also increases. However, as the angle θ approaches 90 degrees, its increment decreases. As n tends to infinity, cosine tends to 0, and the angle θ tends to 90 degrees. This suggests that post-subdivision vessels do not exhibit a reversal phenomenon but rather extend forward, with a maximum divergence of approximately 90 degrees.

Some vessels terminate at a certain subdivision, whereas others continue to bifurcate further into micro-vessels. However, as long as some vessels continue to bifurcate, we will investigate the optimal vessel ratio as outlined below. If r_i denotes the radius of the vessel at the i^{th} subdivision and n_i represents the subdivision number at the i^{th} subdivision, and θ_i denotes the angle between the blood vessel after the subdivision and the midline, where $i = 0, 1, 2, 3, \ldots, N$, then the optimal radius ratio and conditions involving cosine are as follows:

$$\frac{r_0}{r_1} = n_1^{\frac{2}{a+4}} \tag{13}$$

$$\frac{r_1}{r_2} = n_2^{\frac{2}{a+4}} \tag{14}$$

$$\frac{r_2}{r_3} = n_3{}^{\frac{2}{a+4}} \tag{15}$$

$$\vdots$$

$$\frac{r_{N-1}}{r_N} = n_N{}^{\frac{2}{a+4}} \tag{16}$$

By inference from Equations (13)-(16), the following expression can be obtained:

$$\frac{r_0}{r_N} = (n_1 n_2 n_3 \cdots n_N)^{\frac{2}{a+4}} \tag{17}$$

Equation (17) above elucidates that as blood vessels branch out more, the vessels become finer. This elucidates a physiological phenomenon, in which blood vessels only become finer with increased branching, without exhibiting a sudden thickening after branching.

$$\cos\theta_1 = n_1{}^{\frac{a-4}{a+4}} \tag{18}$$

$$\cos\theta_2 = n_2{}^{\frac{a-4}{a+4}} \tag{19}$$

$$\cos\theta_3 = n_3{}^{\frac{a-4}{a+4}} \tag{20}$$

$$\vdots$$

$$\cos\theta_N = n_N{}^{\frac{a-4}{a+4}} \tag{21}$$

By multiplying Equations (18) through (21) and then rearranging, we obtain Equation (22). Additionally, Equation (23) is obtained by applying the conditions of Equation (17). The results obtained by Equation (21) are different from the cosine formula obtained by Murray [15] because the settings and assumptions of the model are different.

$$\cos\theta_1 \cos\theta_2 \cos\theta_3 \cdots \cos\theta_N = (n_1 n_2 n_3 \cdots n_N)^{\frac{a-4}{a+4}} \tag{22}$$

$$\frac{r_0}{r_N} = (\cos\theta_1 \cos\theta_2 \cos\theta_3 \cdots \cos\theta_N)^{\frac{2}{a-4}} \tag{23}$$

From Equation (23), it can be deduced that as the angle of each subdivision increases, the cosine value decreases, ultimately resulting in the radius of the original vessel being relatively larger compared to the final micro-vessel.

2.2 *Asymmetrical modeling and analysis of blood vessels*

The aforementioned model involves an analysis of symmetric branching in blood vessels, encompassing parameters such as vessel radius (r_1) post-subdivision, the angle (θ) between the vessels and the midline after branching, the flow distance post-subdivision (l_1), the perpendicular distance (H) from the furthest endpoint to the midline post subdivision and the horizontal distance (L) of blood flow along the original vessel pathway before and after subdivision, all under the assumption of uniform conditions. To better capture the actual phenomenon of asymmetric branching in blood vessels, this study relaxes the aforementioned uniform conditions, as described below.

The definitions of variables in the aforementioned symmetrical model, namely the variables θ_i, r_i, and l_i, differ from those in the symmetrical model, despite sharing the same symbols. These differences will be elaborated upon and introduced in the following.

The novel variables in our generalized theoretical framework are defined as follows: where $i = 1, 2, 3, \ldots, n$ denotes the i^{th} subdivision of vessels post-subdivision, indicating that a single vessel bifurcates into n branches.

The model settings in Section 2.2 for asymmetrical modelling are identical to those in Section 2.1 for symmetrical modelling in terms of the first, second, fourth, sixth, seventh and twelfth parameters. Specifically, the shared parameters include the subdivision number into which a blood vessel branches (n), the fluid resistance coefficient (K), the vessel radius before subdivision (r), the coefficient of resistance when nourishing the vessel wall (b), the length of the blood vessel before subdivision (l), and the exponent of the radius in the resistance of the nourishing vessel wall (a). The aspects in which the model settings in Section 2.2 differ from those in Section 2.1 are detailed as follows:

1. Blood Flow Volume: Variable f denotes the total volume of blood flow. After the vessel bifurcates into n branches, the volume of blood flow of the i^{th} branch is given by $\beta_i f$, where β_i represents the proportion of total blood flow for the i^{th} subdivision. Additionally, $\sum_{i=1}^{n} \beta_i = 1$

2. Vessel Radius after Subdivision: The variable r_i denotes the radius of the i^{th} subdivision of vessel 1 after it bifurcates into n branches.

3. Length of Blood Vessel after Subdivision: The symbol l_i represents the distance travelled by blood flow after subdivision for the i^{th} subdivision of vessel 1 when it bifurcates into n branches.

4. Horizontal Distance of Blood Flow before and after Subdivision: For a vessel 1 that bifurcates into n branches, the total horizontal distance of blood flow along the original vessel pathway (midline) before and after subdivision for the i^{th} branch is denoted as L_i.

5. Perpendicular Distance between the Vessel Endpoint after Subdivision and Extension Pathway before Subdivision: For a vessel 1 that bifurcates into n branches, the perpendicular distance between the farthest end point of the vessel after the subdivision and the forward extension direction of the vessel pathway (midline) before the subdivision for the i^{th} branch is denoted as H_i.

6. Angle between the Vessel after Subdivision and Extension Pathway before Subdivision: For a vessel 1 that bifurcates into n branches, the angle between the direction of the vessel after subdivision and the forward extension direction of the vessel pathway (midline) before subdivision for the i^{th} branch is denoted as θ_i.

7. Blood Resistance within Blood Vessels: The resistance of a viscous fluid within a rigid pipe for the i^{th} branch is denoted as Kf^2/r^4 before and $K(\beta_i f)^2/{r_i}^4$ after branching.

8. Blood Resistance when Nourishing the Vessel Wall: Resistance encountered while feeding the vessel wall during its flow. The energy required per unit length of the blood vessel for the i^{th} branch is represented by br^a before and $b{r_i}^a$ after branching.

9. Energy Required to Overcome both Viscous Fluid Resistance and Nourish the Vessel Wall: When a blood vessel bifurcates into n, the total energy expended by blood is the sum of the energy required to overcome the resistance of viscous fluid and the energy expended to nourish the wall of the vessel. This total energy expenditure is denoted as $C = (Kf^2/r^4 + b\,r^a)l + \sum_{i=1}^{n} [K(\beta_i f)^2/{r_i}^4 + b\,{r_i}^a]l_i$.

The total energy expenditure is denoted by minimizing the following expression. Equation (24) is similar to Equation (1). We can derive the following.

$$\begin{aligned}\min_{r,\,r_i,\,\theta_i} C &= \min_{r,\,r_i,\,\theta_i}\left\{\left(\frac{Kf^2}{r^4}+b\,r^a\right)l+\sum\nolimits_{i=1}^{n}\left[\frac{K(\beta_i f)^2}{{r_i}^4}+b\,{r_i}^a\right]l_i\right\}\\ &= \min_{r,\,r_i,\,\theta_i}\left\{\left(\frac{Kf^2}{r^4}+b\,r^a\right)\left(L_i-\frac{H_i}{\tan\theta_i}\right)+\sum\nolimits_{i=1}^{n}\left[\frac{K(\beta_i f)^2}{{r_i}^4}+b\,{r_i}^a\right]\frac{H_i}{\sin\theta_i}\right\}\\ &= \min_{r,\,r_i,\,\theta_i}\left\{\left(\frac{Kf^2}{r^4}+b\,r^a\right)\left(L_i-\frac{H_i}{\tan\theta_i}\right)+\frac{1}{\beta_i}\left[\frac{K(\beta_i f)^2}{{r_i}^4}+b\,{r_i}^a\right]\frac{H_i}{\sin\theta_i}\right\}\end{aligned}\tag{24}$$

where $L_1-H_1/\tan\theta_1=L_2-H_2/\tan\theta_2=L_3-H_3/\tan\theta_3=\cdots=L_n-H_n/\tan\theta_n$. The following are the first-order necessary conditions for r, r_i, and θ_i. That is to say, Equation (24) represents the cost-minimization problem of blood flowing through blood vessels. The first-order necessary conditions of Equation (24) are that the partial derivatives of the cost function for r, r_i, and θ_i are equal to zero. Equations (25)-(27) are obtained, respectively, as follows:

$$\frac{\partial C}{\partial r}=\left(-4Kf^2r^{-5}+b\,a\,r^{a-1}\right)\left(L_i-\frac{H_i}{\tan\theta_i}\right)+0=0\tag{25}$$

$$\frac{\partial C}{\partial r_i}=0+\frac{1}{\beta_i}\left(-4K{\beta_i}^2f^2{r_i}^{-5}+b\,a\,{r_i}^{a-1}\right)\frac{H_i}{\sin\theta_i}=0\tag{26}$$

$$\frac{\partial C}{\partial\theta_i}=\left(\frac{Kf^2}{r^4}+b\,r^a\right)\left(H_i\csc^2\theta_i\right)+\frac{1}{\beta_i}\left(\frac{K{\beta_i}^2f^2}{{r_i}^4}+b\,{r_i}^a\right)\left(-H_i\csc^2\theta_i\cos\theta_i\right)=0\tag{27}$$

From the rearrangement of Equations (25) and (26) above, we obtain the following two expressions.

$$4Kf^2=\;b\,a\,r^{a+4}\tag{28}$$

$$4K{\beta_i}^2f^2=b\,a\,{r_i}^{a+4}\tag{29}$$

Dividing Equation (28) by Equation (29) and rearranging yields the following expression.

$$\frac{r}{r_i}=\beta_i^{-\frac{2}{a+4}}\tag{30}$$

By rearranging Equation (30), we obtain $r_i=r\beta_i{}^{2/(a+4)}$, which is then substituted into Equation (27). After further rearrangement, we obtain the following expression.

$$\cos\theta_i=\beta_i^{-\frac{a-4}{a+4}}\tag{31}$$

In this study, the second-order conditions for the three variables in the cost function problem, represented by the Hessian matrix of second derivatives, are assumed to be positive semidefinite. Therefore, the objective function corresponds to cost minimization. The inference drawn from Equations (30) and (31) consists in the following proposition.

Proposition 2 In scenarios where a blood vessel bifurcates into multiple (n) branches and exhibits an asymmetric structure post-subdivision, an analysis employing trigonometric functions, fluid dynamics, and physics principles is warranted. By minimizing the work generated by blood flow within the vessels, the following equilibrium can be attained: (1) $r/r_i = \beta_i{}^{-2/(a+4)}$, (2) $\cos\theta_i = \beta_i{}^{-(a-4)/(a+4)}$. As the proportion of total blood flow for the i^{th} subdivision increases, the vessels after the subdivision become progressively wider, albeit to a diminishing extent, and the optimal angle also decreases. This optimal angle is denoted as $\beta_i \uparrow\ \Rightarrow \beta_i{}^{-(a-4)/(a+4)} \uparrow \Rightarrow \cos\theta_i \uparrow \Rightarrow \theta_i \downarrow$.

The following discussion will undertake a comparative static analysis of the two equilibrium solutions. The term "comparative static analysis" refers to the changes in the equilibrium solution when exogenous variables change.

$$\frac{\mathrm{d}\,\dfrac{r}{r_i}}{\mathrm{d}\,\beta_i} = \frac{\mathrm{d}\,\beta_i{}^{-\frac{2}{a+4}}}{\mathrm{d}\,\beta_i} = -\frac{2}{a+4}\,\beta_i{}^{-\frac{a+6}{a+4}} < 0 \tag{32}$$

$$\frac{\mathrm{d}^2\dfrac{r}{r_i}}{\mathrm{d}\,\beta_i{}^2} = \frac{\mathrm{d}\,-\frac{2}{a+4}\,\beta_i{}^{-\frac{a+6}{a+4}}}{\mathrm{d}\,\beta_i} = \frac{2(a+6)}{(a+4)^2}\,\beta_i{}^{-\frac{2a+10}{a+4}} > 0 \tag{33}$$

$$\frac{\mathrm{d}\,\cos\theta_i}{\mathrm{d}\,\beta_i} = \frac{\mathrm{d}\,\beta_i{}^{-\frac{a-4}{a+4}}}{\mathrm{d}\,\beta_i} = -\frac{a-4}{a+4}\,\beta_i{}^{-\frac{2a}{a+4}} > 0 \tag{34}$$

$$\frac{\mathrm{d}^2\cos\theta_i}{\mathrm{d}\,\beta_i{}^2} = \frac{\mathrm{d}\,-\dfrac{a-4}{a+4}\,\beta_i{}^{-\frac{2a}{a+4}}}{\mathrm{d}\,\beta_i} = \frac{2a(a-4)}{(a+4)^2}\,\beta_i{}^{-\frac{3a+4}{a+4}} < 0 \tag{35}$$

Equations (32) and (33) show that r/r_i is a decreasing and convex-downward function of β_i. Equation (32) seems intuitive, as it suggests that the ratio of radii decreases with the proportion of total blood flow for the i^{th} subdivision. Here, i represents an individual vascular branch, meaning that there is no summation on the index i. However, Equation (33) presents an interesting resilience phenomenon in vessels post-subdivision. It implies that with an increase in the proportion of total blood flow for the i^{th} subdivision, the vessels after the subdivision become progressively wider, albeit to a diminishing extent.

Equations (34) and (35) reveal that cosine is a decreasing and concave upward function of n, while the angle θ_i, derived from cosine, is an increasing and concave downward function of the proportion of total blood flow for the i^{th} subdivision. From Equations (34) and (35), it is evident that as the proportion of total blood flow for the i^{th} subdivision increases, the subdivision angle also decreases. However, as the angle θ approaches 90 degrees, its increment decreases. As β_i tends to zero, cosine tends to zero, and the angle θ tends to 90 degrees. This also suggests that post-subdivision vessels do not exhibit a reversal phenomenon but rather extend forward, with a maximum divergence of approximately 90 degrees.

Proposition 2 indicates that as the proportion of total blood flow for the i^{th} subdivision increases, the optimal angle between the vessels and the intermediary angle also decreases. Consequently, subdivisions with higher blood volumes are likelier to maintain their flow direction along the original trajectory. This theoretical observation aligns with empirical phenomena, thereby validating the proposition.

Propositions 1 and 2 reveal similarities, demonstrating consistent outcomes, constituting a particularly intriguing phenomenon. Firstly, Proposition 1 suggests that in symmetrical vessel subdivision, as the subdivision number increases, the proportion of blood volume allocated to each subdivision decreases, resulting in a larger optimal angle between the bifurcated vessel and the midline. Secondly, Proposition 2 indicates that in asymmetrical vessel branching, as the proportion of blood volume allocated increases, then the optimal angle between the bifurcated vessel and the midline also decreases. From the implications of these observations, it becomes evident that both symmetric and asymmetric evolutions in vessel branching play a pivotal role in the systemic distribution of blood flow. When certain organs necessitate heightened blood volume, vessels evolve into symmetric or asymmetric subdivisions to provide more smaller angles for oxygen and nutrient delivery, characterized by larger-caliber vessels. Conversely, for long-distance vascular transport needs throughout the body, vessels evolve into symmetric or asymmetric subdivisions with fewer subdivisions, which will be optimally represented by intermediate-caliber vessels. Thirdly, in situations where neither substantial nor moderate blood volume is required, combinations of fine vessels with asymmetric branching and numerous subdivisions of vessels with symmetric branching facilitate oxygen and nutrient supply, with fine vessels representing the subdivision pattern in this context.

3. Conclusions

This study aims to investigate the evolutionary process of blood vessels through scientific inquiry, focusing on two crucial factors: the radius of the vessel and the angle formed between the vessel and the midline. These variables play an essential role in facilitating the body's supply of nutrients and oxygen. Employing methods such as trigonometric functions, fluid dynamics, physics, and work minimization, this research delves into the evolution of vessel radius and branching angles, yielding significant insights. In the future, leveraging the fluid mechanics principles elucidated in this study, researchers can dig into understanding the mechanics of blood cells that flow within vessels and further elucidate the evolutionary trajectory of blood vessels.

Although exhibiting some consistencies, the discoveries from Propositions 1 and 2 also present partial discrepancies. These consistencies and discrepancies are crucial elements in the evolution of blood vessels and contribute significantly to their distribution within the body. The consistent findings across both propositions indicate that as the number of vessel subdivisions increases or the proportion of total blood flow for the i^{th} subdivision decreases, the ratio of vessel radii before and after subdivision tends to increase.

The partial variabilities in the vascular branching manifest in two distinct aspects. This study reveals that an increase in the number of subdivisions in symmetrically branching vessels results in a smaller optimal angle between the branching vessel and the median line. Furthermore, it shows that in vessels with asymmetric branches, the optimal angle between the branching vessel and the median line tends to decrease as the proportion of blood flow allocated increases. These findings highlight the critical role that symmetric and asymmetric vessel branching can play in vascular evolution. When certain organs require an increased blood supply, vascular structures tend to evolve into either asymmetrical subdivisions that accommodate a larger proportion of blood flow or symmetrical subdivisions with fewer branches, both of which must exhibit smaller angles and higher blood volumes to efficiently transport nutrients and oxygen, ultimately leading to the formation of larger-caliber vessels. On the contrary, vessels generally evolve into fewer branches for long-distance blood transport, forming medium-caliber vessels that optimize flow efficiency. In regions where minimal blood volume is required, vascular structures develop into asymmetrically bifurcating vessels with lower blood volume or symmetrically branching vessels with a higher subdivision count, ultimately giving rise to small-caliber vessels.

To understand the evolution of blood vessels, this study had to simplify the model, which also constitutes a limitation of this study. There are still some things worth noting in the direction of future research, including the following three points. First, the metabolic demand of the surrounding tissues dictates the permeated flow rate. Second, the permeated flow rate is not controlled by a "pressure drop" but by the diffusivity through the vessel walls. Third, the amount of permeation decreases the mass flow through the vessel, and the resistance coefficient should be adjusted accordingly.

Since the model of this study is based on simplifying factors and makes strict assumptions, the research limitations of this study are the following: that is, the pressure loss may not be the only objective function. First, the organism spends more energy pumping the blood through smaller vessels but less energy building them. Second, the mass flow rate pumped into the aorta is continuously decreased by wall permeation in the arterioles and capillaries, and the permeation rate in each of these smaller vessels depends on the metabolic needs of the surrounding tissue. To refine the model and enhance its applicability, future research should incorporate additional physiological and biomechanical factors into the optimization framework, ensuring a more comprehensive representation of vascular branching mechanisms.

In addition, this study considers the number of vascular branches as exogenous variables. A promising avenue for future research is to explore the evolutionary optimization of vascular branching to determine whether this optimized state has been universally achieved across species or if certain organisms have yet to reach it.

Conflict of interest

The authors declare no competing financial interest.

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