

Article

Numerical Simulation of Cerebral Arterial Blood Conductivity Response to Hypertensive Progression and Stroke Risk

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Abstract

Hypertension is a major risk factor for primary stroke; however, reliable noninvasive physiological biomarkers for early stroke warning in hypertensive patients remain elusive. To characterize the dynamic evolution of cerebral arterial blood conductivity—from the earliest hypertensive stages through to imminent stroke onset—we developed four physiologically grounded numerical models: normotension, borderline hypertension, established hypertension, and pre-stroke hypertension. These models were constructed based on empirically validated correlations between in vivo cerebral arterial blood conductivity and key hemodynamic parameters. All input physiological data were rigorously sourced from peer-reviewed clinical studies. Each model was coupled with standardized geometries constructed using population-averaged templates. Using the finite element method, we simulated blood conductivity across a full cardiac cycle under realistic in vivo physiological conditions. Crucially, we performed quantitative decomposition analysis to isolate and assess the individual contributions of specific physiological parameter changes—such as systolic pressure, dynamic viscosity of blood, hematocrit, and blood flow velocity—to the observed shifts in conductivity during hypertensive progression. Results revealed a biphasic, stage-dependent evolutionary pattern: conductivity initially rises slightly in borderline hypertension, then declines markedly as hypertension advances toward the pre-stroke stage. Relative to the normotensive baseline, conductivity in the pre-stroke model decreased by 17.61%—a reduction strongly associated with hypertension-induced reductions in cerebral blood flow velocity and concurrent increases in hematocrit. Comprehensive mesh independence and time-step sensitivity analyses confirmed the numerical robustness and computational reliability of all simulations. Collectively, these findings demonstrate that cerebral arterial blood conductivity undergoes quantifiable, pre-symptomatic deviation prior to stroke onset, establishing it as mechanistically grounded. The research findings demonstrate substantial theoretical significance and translational potential, grounded in a rigorously validated modeling framework and serving as a robust basis for generating and refining novel scientific hypotheses.



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1. Introduction

Stroke is an acute cerebrovascular disorder resulting from sudden occlusion or rupture of cerebral vessels, leading to cerebral ischemia, hypoxia, and irreversible neuronal injury. Its high incidence, disability burden, case fatality, and recurrence rates render stroke

a leading global public health challenge. Robust epidemiological and clinical evidence consistently identifies hypertension as the predominant modifiable independent risk factor for stroke [1,2]. Globally, hypertension contributes to 58.08% of stroke-related deaths and 57.25% of stroke-attributable disability-adjusted life years (DALYs). Stroke attributable to essential hypertension is associated with significantly higher mortality and disability rates [3]. An estimated 1.28 billion adults live with hypertension, representing a substantial at-risk population for stroke [4]. Early risk stratification and targeted prevention are therefore critical to reducing stroke incidence and improving long-term survival. However, conventional neuroimaging modalities detect only established, structural cerebrovascular lesions and lack sensitivity for pre-symptomatic risk assessment—rendering them unsuitable for primary stroke prevention. Digital subtraction angiography (DSA) remains the reference standard for definitive diagnosis of structural cerebrovascular abnormalities. However, it lacks utility in identifying individuals at elevated stroke risk prior to the emergence of such abnormalities. As an invasive procedure requiring intra-arterial contrast administration, DSA entails substantial clinical and economic burdens: patients incur significant exposure to ionizing radiation, alongside elevated risks of contrast-induced nephropathy and acute hypersensitivity reactions [5]. These inherent limitations—namely invasiveness, procedural risk, high cost, and absence of predictive capability—preclude DSA's use in population-level stroke risk screening, leaving a critical gap in the early identification of hypertension-related cerebrovascular vulnerability. Consequently, there is an urgent need to define robust, noninvasive biomarkers that dynamically reflect hypertensive vascular remodeling and predict incident stroke. To fill this research gap, this study constructs and validates a concise, clinically interpretable risk assessment biomarker for hypertension-related stroke, which allows early warning prior to the formation of structural vascular lesions and supports risk stratification of high-risk populations in routine primary care.

Emerging evidence indicates that conventional blood pressure measurements, particularly isolated elevation in systolic or diastolic values, fail to reliably quantify cerebrovascular involvement or end-organ damage in patients with essential hypertension. The earliest manifestation of cerebral arterial injury in hypertension is hemodynamic dysregulation, which consistently precedes detectable structural remodeling of cerebral arteries [6–9]. However, individual hemodynamic parameters (e.g., cerebral blood flow velocity, pulsatility index, resistance index) exhibit complex, interdependent fluctuations across physiological states, rendering them insufficiently robust for individual-level stroke risk prediction. In contrast, cerebral arterial blood conductivity—a biophysically grounded metric integrating pressure, flow, and vascular impedance—represents a synergistic readout of integrated cerebrovascular hemodynamic function. We therefore hypothesize that dynamic alterations in cerebral blood conductivity quantitatively reflect hypertension-driven hemodynamic perturbations, signal subclinical cerebral arterial dysfunction prior to structural lesion formation, and constitute a clinically actionable predictive biomarker for incident stroke.

A robust body of evidence demonstrates that tissue-specific electrical conductivity—rooted in fundamental biophysical principles governing ion mobility and cellular membrane integrity—serves as a noninvasive, quantitative functional biomarker for assessing physiological homeostasis and stratifying risk of end-organ damage in chronic diseases. Shen et al. [10,11] integrated the Ling–Atabek local flow theory with the Maxwell–Fricke conductivity model to develop a biomechanically informed elastic tube hemodynamic framework. Using this model, they systematically quantified how arterial wall distensibility and pulsatile centerline blood velocity jointly modulate cerebral arterial blood conductivity. Simulation results demonstrated that arterial wall motion—driven by pressure-induced cyclic strain—is a dominant biophysical determinant of conductivity in flowing arterial blood. They further decoupled the individual contributions of arterial

radius and centerline flow velocity to both electrical conductivity and impedance in physiologically realistic pulsatile flow within the human common carotid artery. Model validation against high-fidelity computational fluid dynamics (CFD) simulations confirmed that centerline flow velocity exerts a robust, dose-dependent regulatory effect on blood electrical conductivity—accounting for >65% of its dynamic variance under hypertensive flow conditions. Morega et al. [12,13] developed a coupled biophysical model integrating aortic hemodynamics, flow-dependent blood conductivity, and electric field generation—thereby establishing a quantitative link between aortic pulsatile flow patterns and the spatial distribution of thoracic bioelectric potentials underlying electrocardiographic (ECG) signals. Concurrently, they systematically evaluated the sensitivity of thoracic electrical bioimpedance (TEB) to key hemodynamic parameters—including stroke volume, arterial compliance, and systemic vascular resistance—using variance-based global sensitivity analysis. Building on this foundation, they formulated and numerically solved a fully coupled fluid–electric field model for the brachial artery, explicitly incorporating the nonlinear dependence of arterial blood conductivity on local flow velocity, wall shear stress, and hematocrit. Their simulations demonstrated that brachial arterial impedance measurements provide spatially localized, flow-sensitive functional information complementary to standard ECG, enabling concurrent assessment of regional vascular function and integrated cardiac–vascular coupling. Reinbacher-Köstinger et al. [14] developed a numerical simulation model to quantify changes in electrical conductivity associated with aortic dissection, thereby demonstrating the feasibility of bioimpedance technology for its detection. Badeli et al. [15] measured transthoracic impedance signals across a single cardiac cycle to detect and quantify dynamic shifts in intrathoracic blood conductivity. Their simulations further revealed that severe structural disruptions—such as those induced by aortic dissection—lead to pronounced alterations in both aortic blood conductivity and impedance cardiogram (ICG) waveforms. Jafarinia et al. [16] developed an anisotropic model of blood electrical conductivity and conducted a systematic hemodynamic analysis. Their findings confirmed that spatially inhomogeneous and temporally unsteady reorientation and deformation of red blood cells (RBCs) govern blood conductivity variations. Anand et al. [17,18] performed bioimpedance simulation experiments on human forearm tissue, explicitly demonstrating the modulatory influence of pulsatile blood flow on impedance characteristics. Crucially, their study established that both electrical conductivity and impedance spectroscopy are sensitive to flow-induced changes in arterial parameters—highlighting their strong potential as non-invasive, real-time tools for clinical hemodynamic monitoring. Sel et al. [19] employed the finite element method to perform frequency-domain electric field simulations and map current distribution within the wrist anatomical region. Leveraging these simulations, they systematically optimized both operating frequency and electrode configuration to maximize sensitivity and specificity for pulsatile blood flow signal acquisition—achieving high-precision detection of hemodynamic variations. Shash et al. [20] developed mathematical models to characterize vascular impedance across a spectrum of pathological conditions and experimentally measured impedance values associated with distinct vascular states. Their simulations confirmed that hallmark vascular pathologies—including stenosis, occlusion, and aneurysm—induce significant, distinguishable alterations in vascular impedance spectra, thereby establishing a quantitative theoretical foundation for bioimpedance-based lesion screening. Zhang [21] developed a closed-loop, multiscale computational modeling framework for the entire cerebrovascular system, offering an efficient and robust platform to investigate the complex pathophysiological mechanisms underlying hypertension-induced alterations in hemodynamics and arterial wave dynamics. Kizhisseri et al. [22] focused on branch vessels of the internal carotid artery to examine

the association between blood pressure variability and stroke risk, as well as its hemodynamic determinants. Their work comprehensively characterized the hemodynamic profiles of major intracranial arteries and demonstrated that blood pressure fluctuations, time-resolved flow parameters, and fractional flow reserve collectively enhance the diagnostic specificity for assessing arterial stenosis severity. Samavaki et al. [23,24] proposed a coupled fluid–exchange model linking large arteries and penetrating arterioles. Leveraging Archie’s law—which governs fluid transport in porous media—they established a quantitative, physiologically grounded relationship between cerebral tissue electrical conductivity and local volumetric blood concentration. By solving the Navier–Stokes equations to obtain pressure and velocity fields in large vessels, and subsequently mapping spatially resolved cerebral conductivity distributions via Archie’s law using region-specific blood concentration data, their integrated framework enables simultaneous, quantitative estimation of dynamic regional cerebral blood flow and associated conductivity patterns.

Bioimpedance and tissue conductivity are fundamentally interrelated core parameters in bioelectromagnetic sensing. A growing body of research has leveraged bioimpedance measurements to quantitatively characterize the physiological and pathophysiological properties of cerebral vasculature. Everitt et al. [25] demonstrated the clinical utility of bioimpedance monitoring for detecting intracerebral hemorrhage and diffuse cerebral edema, successfully differentiating high-impedance ischemic lesions from low-impedance hemorrhagic lesions—a distinction grounded in their contrasting tissue composition and ionic microenvironments. This capability supports broader applications in monitoring diverse cerebrovascular pathologies. Siegman et al. [26] conducted high-fidelity simulations using anatomically realistic head models to evaluate the feasibility of bioimpedance-based detection of arterial stenosis, systematically quantifying detection sensitivity across multiple electrode configurations. Chen et al. [27] introduced a bioimpedance-derived method for cerebral blood flow assessment and established a mechanistic link between cerebral autoregulation dynamics and time-resolved impedance changes, thereby providing a physiologically validated theoretical basis for noninvasive cerebral perfusion monitoring. Xu et al. [28] employed magnetic induction phase shift spectroscopy to track dynamic variations in brain conductivity and cerebral impedance, enabling sensitive detection of altered cerebrovascular compliance during the early phase of cerebral ischemia. Bronk et al. [29] optimized electrode placement strategies for stroke detection using subject-specific finite element models, experimentally validating that such computational guidance significantly enhances spatial specificity and diagnostic accuracy—thereby strengthening the translational potential of bioimpedance for clinical stroke identification.

Bioimpedance techniques provide noninvasive, real-time acquisition of cerebral electrical signals, whereas machine learning algorithms enable data-driven stroke risk prediction by extracting and integrating discriminative physiological features from high-dimensional multimodal datasets. Consequently, a substantial body of research has developed intelligent, interpretable predictive models for stratified stroke risk assessment. Zhi et al. [30] constructed a machine learning–based stroke prediction framework incorporating clinical, demographic, and bioimpedance-derived features; their evaluation demonstrated that the random forest classifier achieved superior diagnostic performance—evidenced by higher AUC (0.92), sensitivity (86.4%), and cross-validated generalizability—compared with support vector machines and gradient boosting machines. Akinwumi et al. [31] conducted a systematic benchmarking of supervised learning algorithms on the publicly available Kaggle stroke dataset, identifying age, mean blood glucose concentration, and BMI as the top three feature importances for stroke classification. Chirchi et al. [32] introduced a multi-

modal machine learning pipeline for multiclass cerebrovascular risk stratification, training and validating both gradient boosting and convolutional neural network architectures; feature attribution analysis consistently ranked age, hypertension status, systolic/diastolic blood pressure, fasting blood glucose level, and BMI among the most influential predictors across both models. Collectively, these approaches support rapid, scalable, and cost-effective preclinical stroke screening. However, current machine learning models remain complementary to gold-standard modalities: they cannot substitute structural or functional neuroimaging, nor replace direct intracranial physiological monitoring (e.g., ICP, cerebral blood flow velocity); rather, they serve as robust, evidence-informed adjuncts to conventional clinical evaluation.

Numerical simulation provides a mechanistically grounded, integrative approach to modeling how hemodynamic forces collectively modulate cerebral arterial blood electrical conductivity—a key biophysical parameter intrinsically linked to RBC morphology, plasma composition, hematocrit distribution, and microcirculatory integrity. By capturing spatiotemporal hemodynamic patterns with high fidelity, such simulations strengthen both the physiological interpretability and temporal resolution of disease risk prediction. To date, numerous studies have combined numerical modeling with clinical validation to systematically characterize hypertension- and stroke-associated cerebrovascular hemodynamic abnormalities. Predominantly, prior work has centered on classical macro-scale hemodynamic metrics—including pulsatile blood flow velocity, wall shear stress distributions, intravascular pressure gradients, and geometric remodeling of large arteries—to elucidate mechanisms of hypertensive cerebrovascular injury. Nevertheless, critical knowledge gaps persist. Cerebral arterial blood conductivity is not merely a passive electrical property; it functions as a dynamic, composition-sensitive biomarker that quantitatively reflects microenvironmental perturbations—such as RBC aggregation, plasma viscosity shifts, and capillary perfusion deficits—often preceding overt structural or functional deterioration. Despite its pathophysiological significance, this parameter remains underexplored: few studies have rigorously isolated, quantified, or dynamically modeled its behavior *in vivo*. Crucially, no existing work has established a systematic, physics-informed numerical framework to track the progressive evolution of cerebral arterial blood conductivity across stages of hypertensive vascular remodeling, nor has any study quantitatively linked deviations in conductivity—derived from first-principles biophysical models—to stratified stroke risk. This omission constrains the development of a comprehensive, multi-scale mechanistic paradigm for hypertension-induced stroke that bridges hemodynamics, microvascular biophysics, and clinical neurology.

Addressing this critical gap, the present study pioneers a biophysical perspective on cerebrovascular pathophysiology by centering cerebral arterial blood electrical conductivity—not as a secondary surrogate, but as a primary, compositionally sensitive functional biomarker—thereby transcending the descriptive limitations of conventional hemodynamic analysis. In contrast to prior work focused predominantly on macro-scale hemodynamic metrics (e.g., flow velocity, wall shear stress), this study establishes cerebral arterial blood conductivity as the principal quantitative endpoint for evaluating hypertensive cerebrovascular remodeling and associated stroke risk. Leveraging the Maxwell–Fricke equation—a well-validated theoretical framework linking hematocrit, RBC morphology, and plasma conductivity to bulk blood conductivity—we develop a physics-informed, hemodynamically coupled numerical model. This model explicitly quantifies how progressive hypertension-induced alterations in pressure, flow pulsatility, and vascular geometry dynamically modulate cerebral arterial blood conductivity across disease stages, enabling stage-resolved, mechanistic assessment of microvascular dysfunction and its prognostic implications for stroke.

The study comprises three tightly integrated methodological components. First, leveraging anatomically validated cerebral arterial geometric models from prior literature [33], we define high-fidelity computational domains encompassing local cerebral arteries. Within these domains, a coupled fluid–structure interaction (FSI) framework—integrated with the Maxwell–Fricke equation—is implemented via the finite element method to simulate hemodynamic behavior in the circle of Willis under physiologically realistic normotensive and hypertensive conditions, explicitly accounting for pulsatile flow, vascular wall compliance, and autoregulatory feedback. Second, we perform mechanistic analysis of RBC morphological adaptation to pathological shear stress gradients, quantifying how shear-induced deformation, aggregation, and orientation alter bulk blood conductivity—thereby bridging microscale cellular biophysics with macroscale electrical properties. Third, by integrating FSI-derived hemodynamic fields with RBC-conductivity coupling, we reconstruct the spatiotemporal evolution of cerebral arterial blood conductivity across the continuum from normotension through progressive hypertension to the pre-stroke phase. Finally, a stage-specific quantitative mapping is established, linking distinct stages of hypertension development to corresponding values of local cerebral arterial conductivity.

The core innovation of this study lies in the development of a biophysically grounded analytical framework for the quantitative assessment of hypertensive cerebrovascular injury. This framework centers on cerebral arterial blood conductivity as a key variable, establishing it as a dynamic, composition-sensitive functional biomarker. At the mechanistic level, the framework establishes an intrinsic causal link between progressive hypertension and the temporal evolution of vascular physical properties—including RBC deformability and heterogeneity of hematocrit—and systematically elucidates the complete pathway through which sustained hemodynamic load simultaneously induces structural remodeling and electrophysiological dysfunction in cerebral arteries. The findings reveal the dynamic evolution of cerebral arterial blood conductivity throughout the progression from hypertension-related cerebrovascular injury to stroke, demonstrating that these changes are not driven by any single factor in isolation, but rather represent an integrated cascade spanning multiple scales, encompassing hemodynamics, cellular biomechanics, and hemorheology. On this basis, this study provides a solid theoretical foundation for the early detection, physiology-based risk stratification, and noninvasive auxiliary diagnosis of hypertension-related stroke. Furthermore, it establishes a systematic theoretical and technical basis for subsequent biophysical simulation of cerebral electrical impedance and related translational medical research.

2. Materials and Methods

2.1. Hemodynamic Control Equations

In this study, cerebral arterial blood flow was modeled using a continuum-mechanics framework in which blood is treated as a homogeneous, incompressible Newtonian fluid and the arterial wall as an isotropic, linearly elastic solid. The hemodynamic behavior was governed by the coupled Navier–Stokes equations for fluid motion and the equilibrium equations for elastic deformation—complemented by mass conservation (continuity equation) and appropriate boundary conditions [34]. Given the axisymmetric geometry of the cerebral arterial segments under investigation and the negligible influence of gravitational forces at the cerebral scale, the governing system was reduced to a two-dimensional axisymmetric formulation.

$$\frac{\partial u}{\partial t} + v \frac{\partial u}{\partial r} + u \frac{\partial u}{\partial x} = -\frac{1}{\rho} \frac{\partial p}{\partial x} + \mu \left(\frac{\partial^2 u}{\partial r^2} + \frac{1}{r} \frac{\partial u}{\partial r} + \frac{\partial^2 u}{\partial x^2} \right) \quad (1)$$

$$\frac{\partial v}{\partial t} + v \frac{\partial v}{\partial r} + u \frac{\partial v}{\partial x} = -\frac{1}{\rho} \frac{\partial p}{\partial r} + \mu \left(\frac{\partial^2 v}{\partial r^2} + \frac{1}{r} \frac{\partial v}{\partial r} + \frac{\partial^2 v}{\partial x^2} - \frac{v}{r^2} \right) \quad (2)$$

$$\frac{\partial v}{\partial r} + \frac{v}{r} + \frac{\partial u}{\partial x} = 0 \quad (3)$$

When the vessel diameter is smaller than the pulse wave propagation velocity, Equations (1) and (2) can be simplified to the following forms [35].

$$\begin{aligned} \frac{\partial u}{\partial r} \Big|_{r=0} &= 0, \quad v|_{r=0} = 0 \\ u|_{r=R} &= 0, \quad v|_{r=R} = \frac{\partial R}{\partial t} \end{aligned} \quad (4)$$

where ρ denotes blood density; u and v represent the axial and radial flow velocities of blood, respectively; P refers to blood pressure; x and r are the axial and radial coordinates within the vessel; t is time; and R is the vertical distance from the central axis to the inner wall of the blood vessel.

Although cerebral arteries exhibit intrinsic curvature, a short vascular segment can be approximated as a cylindrical tube. Let L denote the length of the blood-filled cylindrical segment and μ represent the dynamic viscosity of blood. The blood pressures at the two ends of the blood vessel are defined as P_1 and P_2 , respectively, yielding a net force of $\pi r^2 (P_2 - P_1) = \pi r^2 \Delta P$. The shear stress $\tau(r)$ induced by the velocity gradient is then given by:

$$\tau(r) = \frac{r(p_1 - p_2)}{2L} = \frac{r\Delta p}{2L} = -\mu \frac{dv(r)}{dr} \quad (5)$$

When the dynamic viscosity μ is constant, $\tau(r)$ varies linearly with the blood flow velocity gradient. The blood flow velocity exhibits a typical parabolic distribution, with the minimum velocity gradient occurring at the vascular central axis. Specifically, $\tau(r)$ equals zero at $r = 0$. By contrast, the velocity gradient peaks at the vascular wall, leading to the maximum magnitude of $\tau(r)$ at this position. Assuming that the vessel wall is axially stationary and has a Young's modulus of E and a wall thickness of h , the radial incremental deformation Δr induced by a blood pressure increment ΔP can be defined by the following formula.

$$\frac{\Delta r}{r} = \frac{3\Delta p}{4E} \cdot \frac{r}{h} \quad (6)$$

Unlike the structurally intact arterial wall in normotensive physiology, sustained elevation of intravascular pressure initiates maladaptive vascular remodeling—a hallmark pathological process in hypertension [36]. Chronic hypertensive loading induces concentric arterial wall thickening and progressive luminal narrowing, as quantitatively demonstrated in Figure 1.

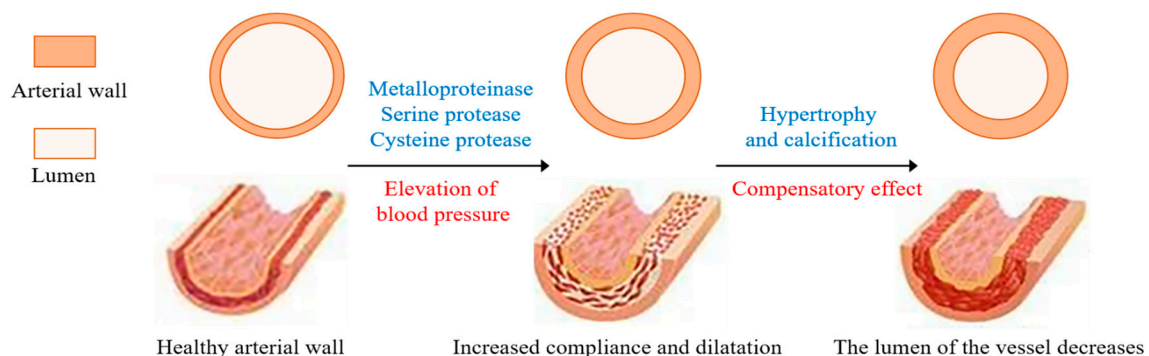


Figure 1. Hypertension-induced arterial remodeling: structural and functional consequences of sustained intravascular pressure elevation.

2.2. The Electrical Conductivity of Arterial Blood Flow

Blood is modeled as a dilute suspension of deformable, elliptical particles—predominantly RBCs—dispersed in a conductive plasma medium. Plasma exhibits constant and isotropic electrical conductivity. At frequencies below 3 MHz, RBCs display negligible intrinsic conductivity relative to plasma and behave as soft, highly deformable ellipsoids; under hemodynamic shear stress, their membranes undergo reversible shape deformation and preferential alignment along the flow direction [37]. Consequently, the effective bulk electrical conductivity of whole blood is governed predominantly by RBC volume fraction (hematocrit) and shear-induced morphological changes—including membrane stretching, axial elongation, and orientation angle distribution. In this model, RBCs are idealized as prolate spheroids with a minor semi-axis of length a_0 and two equal major semi-axes of length b_0 . Their shear-dependent orientation and deformation dynamics are schematically illustrated in Figure 2.

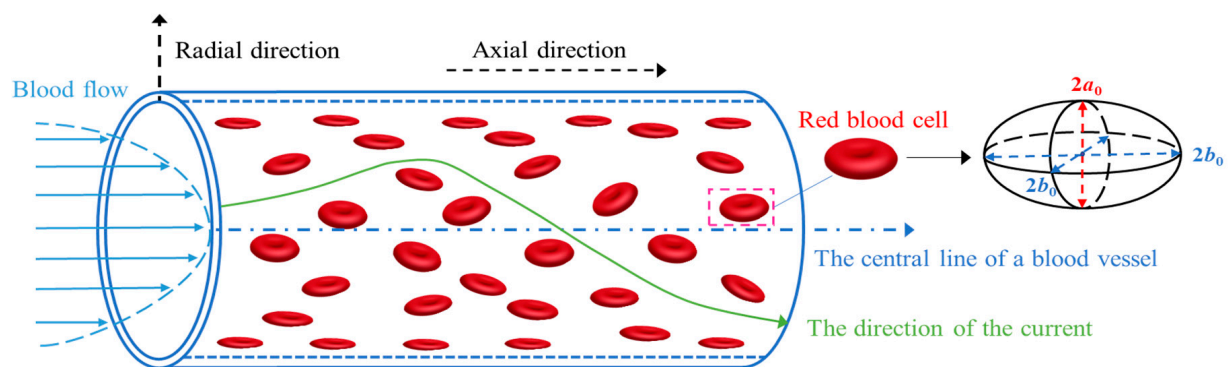


Figure 2. Diagram of Electrical Conduction in Blood Flow.

The blood flow domain is partitioned into three coaxial cylindrical subregions—designated S_L (low-shear), S_M (medium-shear), and S_H (high-shear)—ordered radially by increasing magnitude of wall-normal shear stress $\tau(r)$. These subregions are color-coded orange, green, and blue in Figure 3, respectively. This stratification is grounded in the theory of hemodynamic–electromagnetic coupling: shear stress governs RBC membrane deformation and preferential orientation, thereby modulating the effective electrical conductivity of whole blood [38]. Each subregion is defined by physiologically and rheologically justified shear stress thresholds. In the S_L subregion ($\tau(r) < 0.03$ Pa), the velocity gradient and shear stress are minimal; RBCs undergo negligible shape distortion and exhibit isotropic rotational diffusion, with no preferred alignment of their major or minor axes—yielding the lowest effective conductivity. In the S_H subregion ($\tau(r) > 0.1$ Pa), adjacent to the luminal wall, shear stress is maximal; RBCs experience pronounced axial elongation and near-complete alignment parallel to the flow direction, resulting in the highest effective conductivity. The transitional S_M subregion ($0.03 \text{ Pa} \leq \tau(r) \leq 0.1 \text{ Pa}$) exhibits intermediate mechanical loading: RBCs cease tumbling, adopt moderate elongation, and progressively align along the flow axis—producing an effective conductivity intermediate between S_L and S_H . Critically, these region-specific microstructural states directly determine spatially heterogeneous conductivity, necessitating distinct constitutive relations for each subregion in subsequent electromagnetic modeling.

A rectangular element with length L , width $2\pi r/k$, and height Δr is constructed inside the blood vessel, as shown in the upper part of Figure 3. This element is located at a radial distance r from the vessel's central axis. Here, k denotes the number of such rectangular elements distributed along each annular region of radius r [39,40]. The element is filled with homogeneously mixed blood consisting of a single red blood cell (RBC) and the surrounding plasma, and the RBC is placed at the geometric center of this element. The

electrical conductivity of this unit (σ_c) can be calculated via the Maxwell mixing theory and the Fricke equation [41]:

$$\frac{\sigma_c}{\sigma_p} = \frac{1-H}{1+(C_{od}-1)} \quad (7)$$

$$C_{ods} = \frac{1}{3}(C_{oda} + 2C_{odb}) \quad (8)$$

where C_{oda} and C_{odb} denote the orientation and deformation coefficients corresponding to the minor axis $2a_0$ and major axis $2b_0$ of RBCs aligned along the blood flow direction, respectively.

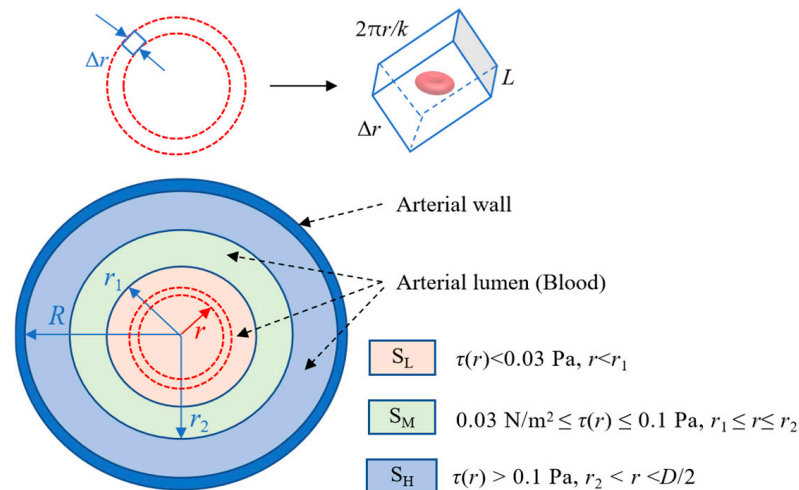


Figure 3. Intraluminal shear stress distribution and regional division of the vessel.

In physiologically realistic pulsatile flow conditions, the influence of shear stress in pulsatile blood flow cannot be ignored. Under its cyclic compressive and elongational action, RBCs undergo deformation, and their deformed minor and major axes are denoted as $2a_d$ and $2b_d$. The orientation angle φ_d of RBCs is correlated with the combined orientation and deformation coefficient C_{od} , as expressed below:

$$\varphi_d(r) = \arccos\left(\frac{a_d(r)}{b_d(r)}\right) = \arccos\left(\frac{a_0}{b_0}\left(1 + \frac{b_0 \cdot \tau(r)}{4\mu}\right)^{-3}\right) \quad (9)$$

$$C_{od}(r) = \frac{\varphi(r) - \frac{1}{2}\sin(2\varphi(r))}{\sin^3(\varphi(r))} \cos(\varphi(r)) \quad (10)$$

The electrical conductivities in the S_L , S_M , and S_H regions are denoted as σ_L , σ_M , and σ_H , respectively. These three regions form concentric cylinders, and the bulk electrical conductivity of the composite cylindrical structure is defined as σ_{bi} .

$$\sigma_{bi} = \frac{1}{2R^2} \left(\int_0^{r_1} \sigma_L(r) r dr + \int_{r_1}^{r_2} \sigma_M(r) r dr + \int_{r_2}^R \sigma_H(r) r dr \right) \quad (11)$$

The combined orientation and deformation coefficients for each region are C_{odL} , C_{odM} , and C_{odH} , which are derived from the Maxwell–Fricke equation.

$$C_{odL}(r) = \frac{1}{2}(C_{odb}(r) + C_{odr}(r)) \quad (12)$$

$$C_{\text{odM}} = \frac{C_{\text{odb}} + \frac{\tau(r) - \tau(r_2)}{\tau(r_1) - \tau(r_2)} \cdot C_{\text{odr}}(r)}{1 + \frac{\tau(r) - \tau(r_1)}{\tau(r_1) - \tau(r_2)}} \quad (13)$$

$$C_{\text{odH}}(r) = C_{\text{odb}}(r) \quad (14)$$

The three-dimensional elastic artery is divided into N coaxial cylindrical segments of equal length along the vessel centerline. In the numerical simulation, the electrical conductivity obtained at the middle cross-section of each cylinder is adopted to represent its overall conductivity. The relationship between the bulk electrical conductivity $\sigma_{\text{bl}}(t)$ of the entire artery and the conductivity $\sigma_{\text{bi}}(t)$ of each cylinder is described as follows:

$$\frac{1}{\sigma_{\text{bl}}(t)} = \sum_{i=1}^N \frac{1}{\sigma_{\text{bi}}(t)} \quad (15)$$

2.3. Models and Properties

2.3.1. Geometry

Given the axial symmetry of the geometric model, the arterial segment encompassing the Circle of Willis—including the terminal bifurcation of the internal carotid artery (ICA) and the origins of the middle cerebral artery (MCA) and anterior cerebral artery (ACA)—is selected as the computational domain for arterial blood conductivity analysis. This anatomically defined region constitutes a hemodynamic and pathological hotspot: it exhibits elevated oscillatory shear index and is clinically recognized as the most frequent site of hypertensive intracranial hemorrhage and small-vessel stroke. The mean luminal diameters of the reconstructed ICA, MCA, and ACA segments are 4.59 mm, 2.75 mm, and 2.45 mm, respectively. Arterial wall thickness is uniformly prescribed as 0.275 ± 0.025 mm, and the total intraluminal blood volume within the domain is 197.74 mm^3 . All geometric parameters align quantitatively with high-resolution *in vivo* morphometric data from postmortem and 7T MRI studies of human cerebral arteries [42].

The inset box in Figure 4a indicates the intracranial positioning of the arterial geometric model, centered within the supratentorial compartment of the human brain. Figure 4b illustrates the computational domain geometry, comprising two physically distinct subdomains: the arterial wall (solid phase, rendered in gray) and the intraluminal blood volume (fluid phase, rendered in blue). Blue arrows denote the blood flow inlet, and red arrows represent the blood flow outlets. In this model, the arterial wall is defined as a linearly elastic material, while blood is treated as an incompressible Newtonian fluid. Gravitational body forces and thermal conduction are omitted, consistent with the dominant hemodynamic timescales and negligible temperature gradients in cerebral pulsatile flow. The terminal internal carotid artery (ICA) is prescribed as the velocity inlet boundary, while the middle cerebral artery (MCA) and anterior cerebral artery (ACA) branches are assigned as pressure outlets. Owing to the anatomically realistic, highly irregular geometry—particularly at bifurcations and curvatures—volume mesh optimization was performed using Materialise 3-Matic 12.0 software. Automated mesh generation with targeted local refinement at geometric singularities ensured high-fidelity discretization. The final conformal meshes for the solid and fluid domains are shown in Figures 4c and 4d, respectively, comprising 334,070 tetrahedral volume elements and 29,071 triangular boundary elements.

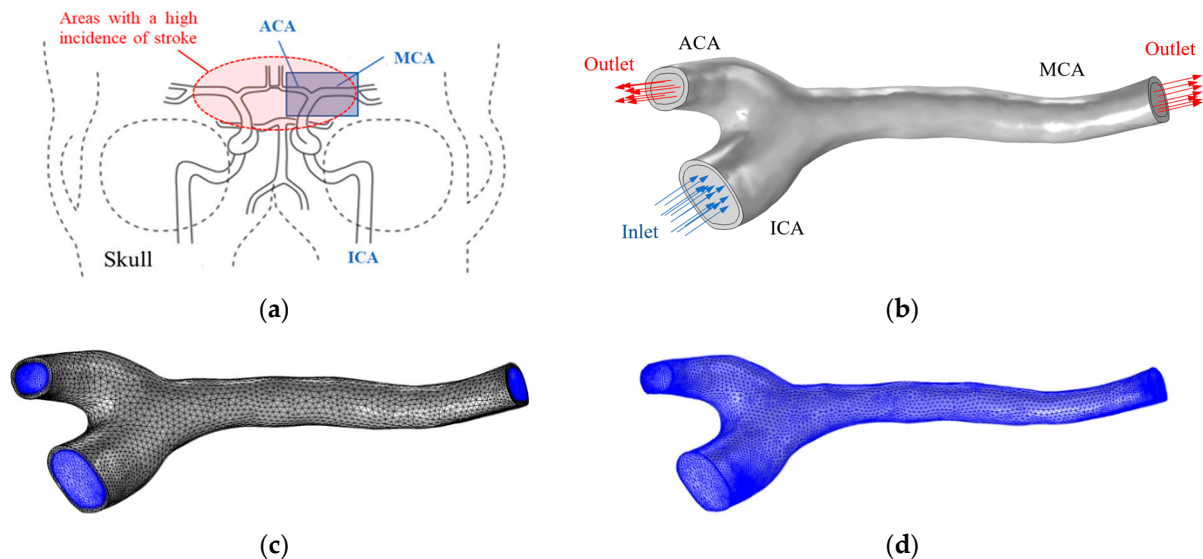


Figure 4. Geometric reconstruction and computational mesh of the cerebral arterial model: (a) Anatomical localization of the Circle of Willis within the supratentorial brain compartment, highlighting its status as a hemodynamic and clinical hotspot for hypertensive small-vessel stroke; (b) Three-dimensional geometric model of the arterial domain, encompassing the terminal internal carotid artery (ICA), middle cerebral artery (MCA), and anterior cerebral artery (ACA); (c) Conformal tetrahedral mesh of the arterial wall (solid domain); (d) Conformal tetrahedral mesh of the intraluminal blood volume (fluid domain).

2.3.2. Model Development

To systematically investigate the progressive modulation of cerebral blood electrical conductivity across the pathophysiological continuum—from normotension through chronic hypertension to the pre-stroke hemodynamic instability phase—four physiologically calibrated numerical models were developed in this study.

- **Model 1: Normotension**

Normotension corresponds to the normal physiological state of healthy individuals. All hemodynamic and hemorheological parameters for this model were adopted from datasets of healthy subjects. For adults, the systolic pressure (P_s) ranges from 90 to 120 mmHg, and the diastolic pressure (P_d) is between 60 and 80 mmHg.

- **Model 2: Borderline hypertension**

Borderline hypertension is characterized by elevated blood pressure without organic lesions in cerebral vessels and other tissues, and this condition may further develop into sustained hypertension. Individuals with blood pressure between 140/90 mmHg (P_s/P_d) and 160/95 mmHg are classified as having borderline hypertension, which is a reversible hypertensive state. Except for blood pressure differences, no obvious variations in hemodynamic and hemorheological parameters are observed between Model 1 and Model 2.

- **Model 3: Hypertension**

In accordance with the hypertension diagnostic criteria issued by the World Health Organization (WHO), individuals with P_s above 160 mmHg and P_d above 95 mmHg are diagnosed with hypertension [43]. Approximately 71.5% of patients with borderline hypertension eventually progress to definite hypertension, which is typically a chronic and progressive condition. During this pathological evolution, a series of physiological compensations induce considerable changes in hemodynamic and hemorheological parameters. In addition, the arterial wall undergoes structural remodeling. Consequently,

hypertensive arteries become more vulnerable to rupture and occlusion compared with normal blood vessels.

- Model 4: Pre-stroke hypertension

Model 4 represents the high-risk transitional phase immediately preceding ischemic or hemorrhagic stroke onset in hypertensive patients—defined as the three-month window prior to clinical event manifestation. Physiological parameters were extracted exclusively from prospectively enrolled hypertensive subjects who subsequently experienced a cerebrovascular event within this interval [44]. While systolic and diastolic pressures remain comparable to Model 3 (established hypertension), this phase exhibits quantifiable deterioration in cerebral hemodynamics: decreased blood flow velocity, elevated hematocrit, and reduced arterial lumen diameter. Critically, these alterations are subclinical: they precede structural imaging abnormalities and remain undetectable by conventional angiography or routine MRI, necessitating advanced computational modeling for their identification.

The hemodynamic and hemorheological parameters across the four models are summarized in Table 1 [45–48]. Luminal narrowing—attributable to hypertension-induced arterial remodeling—is observed exclusively in Models 3 (hypertension) and 4 (pre-stroke hypertension), with no structural lumen reduction in Models 1 (normotension) or 2 (borderline hypertension). Consequently, the intraluminal fluid domain volume remains statistically invariant between Models 1 and 2. Based on quantitative morphometric analyses from histopathological studies of hypertensive cerebral arteries [49], the mean luminal diameters of the fluid computational domains in Models 3 and 4 are scaled to 90% and 80% of the Model 1 reference diameter, respectively.

Table 1. Parameters adopted in numerical simulations.

Symbol	Quantity	Model 1	Model 2	Model 3	Model 4
a_0	Minor axis of RBCs				
b_0	Major axes of RBCs				
P_s	Systolic blood pressure	120 mmHg	140 mmHg	165 mmHg	165 mmHg
P_d	Diastolic blood pressure	80 mmHg	90 mmHg	100 mmHg	100 mmHg
$V_{\max}$	Maximum blood flow velocity	59 cm/s	63 cm/s	50 cm/s	41 cm/s
ρ_{bl}	Density of Blood	1050 kg/m ³	1050 kg/m ³	1050 kg/m ³	1050 kg/m ³
H	Hematocrit	0.44	0.46	0.46	0.50
μ_{pl}	Dynamic viscosity of plasma	1.35×10^{-3} Pa·s	1.43×10^{-3} Pa·s	1.46×10^{-3} Pa·s	1.50×10^{-3} Pa·s
μ_{bl}	Dynamic viscosity of blood		$\mu_{pl} (1 + 2.5H + 7.37 \times 10^{-2}H^2)$ Pa·s		
MRBCs	Membrane Shear modulus of RBCs	1.5×10^{-5} N/m	1.5×10^{-5} N/m	1.7×10^{-5} N/m	1.8×10^{-5} N/m
E	Young's modulus of arterial wall	0.6 MPa	0.7 MPa	1.0 MPa	1.1 MPa

2.4. Numerical Methods and Setup

2.4.1. Boundary Conditions

Fluid boundary conditions were configured to replicate physiologically realistic cerebral arterial hemodynamics: the terminal internal carotid artery (ICA) was designated as the velocity inlet, while the anterior cerebral artery (ACA) and middle cerebral artery (MCA) branches served as pressure outlets—mirroring in vivo arterial topology and physiological loading. The directional flow pattern is illustrated in Figure 4b. Hemodynamic simulations employed a transient, pulsatile solver with time-resolved boundary conditions: a clinically validated Womersley-type velocity waveform was prescribed at the ICA inlet, and a corresponding physiological pressure waveform was applied at the ACA and MCA

outlets. For Model 1 (normotension), the inlet velocity waveform (red curve, Figure 5) exhibits a diastolic baseline of 0.162 m/s at $t = 0$ s and a systolic peak of 0.59 m/s; this peak velocity was adopted as the reference magnitude for scaling all model-specific inlet waveforms. The outlet pressure waveform (blue curve, Figure 5) follows a standard clinical profile with systolic pressure $P_s = 120$ mmHg, diastolic pressure $P_d = 80$ mmHg, and an initial pressure of 82 mmHg at $t = 0$ s. All boundary conditions are rigorously aligned with phase-synchronized, high-fidelity in vivo measurements from Doppler ultrasound and intra-arterial catheterization studies [50,51]. Complete parameter specifications for Models 1–4 are tabulated in Table 1 and derived exclusively from peer-reviewed clinical and experimental literature [45–48].

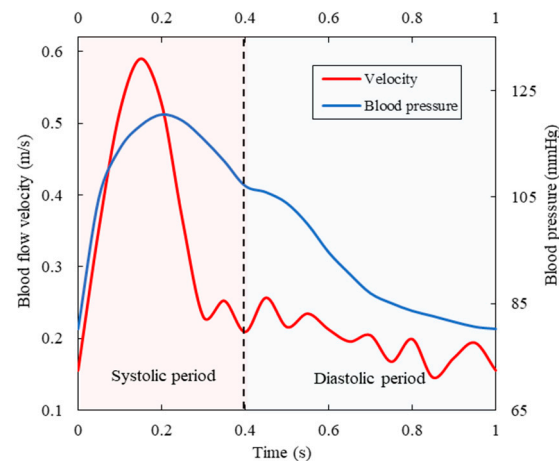


Figure 5. Waveforms of blood flow velocity and blood pressure.

Both flow velocity and blood pressure exhibit synchronous peaks during systole. During diastole, flow velocity declines rapidly to a low baseline level characterized by minimal oscillatory fluctuations. The acceleration phase of the inlet velocity waveform spans from $t = 0$ s to $t = 0.15$ s, followed by a deceleration phase extending from $t = 0.15$ s to the end of the cardiac cycle ($t = 1.0$ s). Critically, both velocity and pressure waveforms are strictly periodic and phase-locked to the cardiac cycle, ensuring physiological fidelity in transient hemodynamic simulation. For all models, a heart rate of 60 beats per minute was adopted—corresponding to a fixed cardiac cycle duration of 1.0 s—consistent with standard resting physiological conditions in healthy adults.

Blood flow was modeled under the axisymmetric assumption, and numerical computations were performed using a pressure-based coupled solver with second-order temporal and spatial discretization. A no-slip boundary condition was rigorously enforced on all arterial wall surfaces to reflect the physiological adherence of blood to the endothelium. Fixed support boundary conditions—representing mechanical anchoring of vessel segments to surrounding brain parenchyma—were applied at the inlet and outlet boundaries of the computational domain to suppress unphysical rigid-body motion and ensure biomechanical stability during transient simulation.

2.4.2. Numerical Methods and Computational Setup

Fluid–structure interaction (FSI) simulations were conducted across all four models to concurrently resolve hemodynamic forces and vessel wall deformation. Under baseline physiological conditions, the previously defined time-resolved inlet velocity and outlet pressure waveforms were applied to each model. Both the fluid domain and the solid domain were discretized using unstructured tetrahedral meshes—a robust strategy for capturing geometric complexity at arterial bifurcations and curvature-induced flow dis-

turbances. FSI coupling was implemented in COMSOL Multiphysics 5.4. A systematic mesh sensitivity analysis was performed using four resolution levels (coarse, medium, fine, extra-fine), with wall shear stress (WSS) and electrical conductivity (σ) at the MCA bifurcation serving as primary convergence metrics. Relative to the fine mesh, the extra-fine mesh yielded WSS and σ deviations of only 2.01% and 0.67%, respectively—well below the 3% threshold for numerical convergence. Given the marginal accuracy gain versus prohibitive computational cost ($11.5\times$ increase in CPU time), the fine mesh was selected as the optimal resolution. Its geometric specifications include: minimum element size = 0.0396 mm, maximum element size = 0.924 mm, maximum element growth rate = 1.35, curvature factor = 0.3, and narrow-region resolution factor = 0.85. As summarized in Table 2, the final cerebral artery mesh comprises 363,141 elements and satisfies stringent quality criteria: average values of skewness, maximum angle, volume-length ratio, and condition number all exceed 0.65—indicating high geometric regularity and numerical stability. The local critical region element quality is slightly below 0.15; however, low-quality elements constitute less than 0.02% of the total mesh volume, and their spatial distribution is highly localized. The minimum element growth rate (0.05) occurs exclusively in hemodynamically critical regions—including vascular bifurcations and curved segments prone to stenosis—where localized mesh refinement is physiologically justified, reflecting the spatial heterogeneity of wall shear stress and electrophysiological responses. Critically, this low-quality element fraction falls well below the validated tolerance threshold for FSI–conductivity coupled solvers; thus, it introduces no measurable numerical error and fully satisfies the quantitative accuracy requirements of the simulation.

Table 2. Mesh quality metrics.

Symbol	Number of Elements	Minimum Element Quality	Average Element Quality	Element Volume Ratio
Skewness	363,141	0.09859	0.6689	1.0103×10^{-4}
Maximum angle	363,141	0.1074	0.7522	1.0103×10^{-4}
Volume vs. length	363,141	0.1224	0.7145	1.0103×10^{-4}
Condition number	363,141	0.1417	0.7716	1.0103×10^{-4}
Growth rate	363,141	0.05	0.5993	1.0103×10^{-4}

Temporal discretization sensitivity was rigorously assessed using four time step sizes: $\Delta t = 0.03$ s, 0.02 s, 0.01 s, and 0.005 s. Wall shear stress (WSS) at the MCA bifurcation—the hemodynamically most vulnerable site—was selected as the primary convergence metric. Relative to the $\Delta t = 0.01$ s benchmark, the absolute relative discrepancies in peak systolic WSS were 1.92% ($\Delta t = 0.03$ s), 1.55% ($\Delta t = 0.02$ s), and 0.88% ($\Delta t = 0.005$ s). As all deviations remained below the 2% numerical convergence threshold and the $\Delta t = 0.01$ s solution achieved optimal balance between temporal resolution and computational efficiency (requiring only $1.7\times$ the CPU time of $\Delta t = 0.02$ s versus $4.3\times$ for $\Delta t = 0.005$ s), this time step was adopted as the final simulation setting.

Bidirectional fluid–structure interaction (FSI) coupling between blood and the arterial wall was implemented within the Fluid–Structure Interaction multiphysics interface of COMSOL Multiphysics 5.4. The transient Navier–Stokes equations for blood flow (modeled as an incompressible Newtonian fluid) and the elastic structural equations for the vessel wall were solved simultaneously using a fully coupled, monolithic Newton–Raphson iterative scheme. Spatial discretization employed first-order Lagrange elements for the fluid domain and second-order quadratic Lagrange elements for both the solid domain and the electrical conductivity submodel—ensuring optimal accuracy for stress/strain gradients and field continuity. Temporal discretization utilized the backward differentiation formula (BDF) with adaptive time stepping, configured with an absolute tolerance of

1×10^{-6} and a relative tolerance of 1×10^{-4} for the transient solver (the latter governing convergence of nonlinear residuals). Boundary conditions were rigorously enforced via COMSOL's built-in coupling features: a normal-velocity inlet condition prescribed the time-resolved waveform (red curve, Figure 5), while pressure-outlet conditions applied the corresponding physiological waveform (blue curve, Figure 5) at the ACA and MCA branches; backflow suppression was activated to prevent unphysical reverse flow at outlets. Critically, the coupling mechanism was defined as fluid load transfer—i.e., pressure and wall shear stress from the fluid solution directly serve as traction boundary conditions on the solid domain—thereby ensuring physically consistent two-way interactions. Nonlinear convergence was achieved when the relative residual norm fell below 1×10^{-4} within a maximum of 25 Newton iterations per time step, a threshold validated against benchmark FSI studies.

3. Results

3.1. Conductivity of Cerebral Blood Flow

Under physiological in vivo conditions, arterial blood flow is intrinsically pulsatile due to cyclic cardiac ejection. To resolve regional heterogeneity in electrical conductivity, the arterial model was segmented into 407 anatomically consistent vascular segments—each representing a discrete computational unit for localized conductivity mapping. Pulsatile blood conductivity was simulated in an elastic arterial segment under normotension (120/80 mmHg), borderline hypertension (140/90 mmHg), hypertension (165/100 mmHg), and pre-stroke hypertension (165/100 mmHg) pressure conditions, all at a fixed heart rate of 60 beats per minute. Simulations captured full-cycle transient behavior, with instantaneous conductivity distributions visualized as cross-sectional contours in Figure 6.

The temporal evolution of blood electrical conductivity across one cardiac cycle is characterized as follows. All four models exhibit a qualitatively consistent waveform morphology—namely, a systolic rise followed by diastolic decay—with peak conductivity occurring at late systole ($t \approx 0.2$ s), consistently lagging behind the peak blood velocity ($t = 0.15$ s) by 50 ms. This phase lag reflects the finite time required for hemorheological reorganization (e.g., RBC disaggregation and alignment) under pulsatile shear stress. Quantitatively, conductivity amplitude varies significantly with pathological stage: Model 2 (prehypertension) yields the highest instantaneous peak conductivity ($\sigma_{\max} = 1.45$ S/m), exceeding Model 1 (normotension: $\sigma_{\max} = 1.37$ S/m) by 5.84% and Model 3 (established hypertension: $\sigma_{\max} = 1.30$ S/m) by 11.54%. In contrast, Model 4 (pre-stroke hemodynamic instability) exhibits a marked suppression of conductivity ($\sigma_{\max} = 1.18$ S/m), representing a 13.87% reduction relative to Model 1 and an 18.62% decline versus Model 2.

Numerical simulation results demonstrate pronounced spatial heterogeneity in cerebral blood conductivity, characterized by a consistent gradient increase from the central vascular lumen toward the arterial wall. Specifically, conductivity values are elevated at arterial bifurcations and in proximity to the vessel wall, whereas they are comparatively lower along the vascular central axis and within straight vessel segments. This distribution pattern is mechanistically attributable to regional variations in wall shear stress (WSS): elevated WSS at bifurcations and near-wall regions induces significant alignment and morphological deformation of RBCs, thereby enhancing local electrical conductivity. The mean wall shear stress values are 2.96 Pa for Model 1, 3.39 Pa for Model 2, 2.65 Pa for Model 3, and 2.14 Pa for Model 4. The simulated WSS distribution shows good agreement with the clinical measurement data reported in reference [52], corroborating the fidelity and reliability of the present hemodynamic model. Conversely, WSS remains markedly low in the central lumen and straight segments, resulting in minimal influence on RBC morphology and orientation. In these regions, RBCs exhibit random spatial distribution,

which constrains the percolation pathway for electrical current; moreover, the relatively high hematocrit—i.e., volume fraction of cellular components—introduces substantial resistive impedance, ultimately diminishing local conductivity.

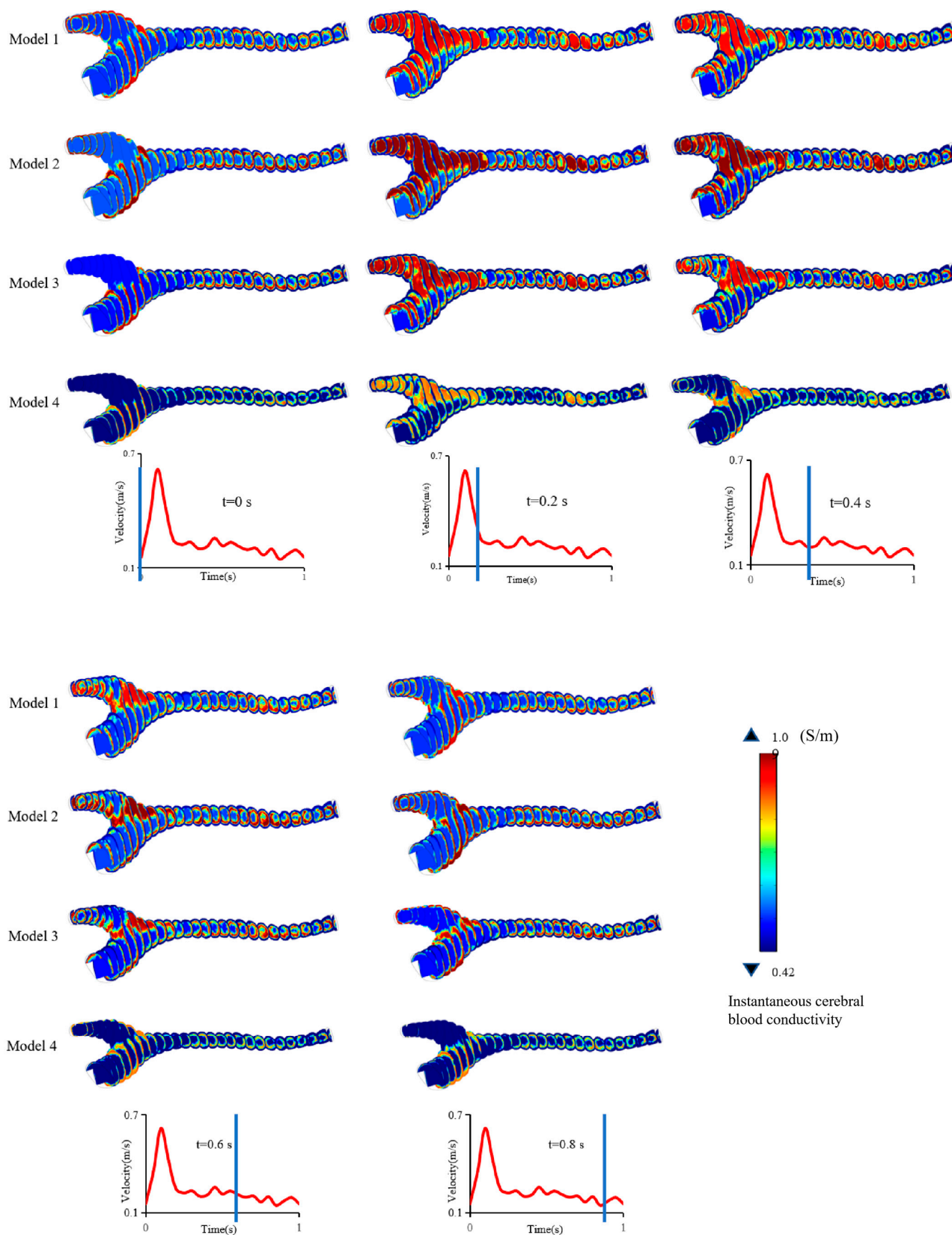


Figure 6. Spatiotemporal distribution of instantaneous cerebral blood conductivity under pulsatile flow conditions.

Figure 7 presents the time-resolved profiles of σ_L , σ_M , and σ_H —corresponding to the green, orange, and yellow dashed lines, respectively—as well as bulk conductivity (blue solid line), under pulsatile hemodynamic conditions for Models 1–4. During systole, σ_L closely follows the temporal profile of blood velocity, whereas σ_M and σ_H exhibit inverse phase relationships with respect to both velocity and σ_L . Bulk conductivity displays a pronounced periodic behavior: it initiates at a low baseline at the onset of the cardiac cycle, peaks at $t = 0.2$ s during mid-systole, undergoes a sharp decline in late systole, and remains suppressed throughout diastole ($t > 0.4$ s), exhibiting only minor fluctuations. Across all time points, the mean bulk conductivity ranks Models 2 > Model 1 > Model 3 > Model 4.

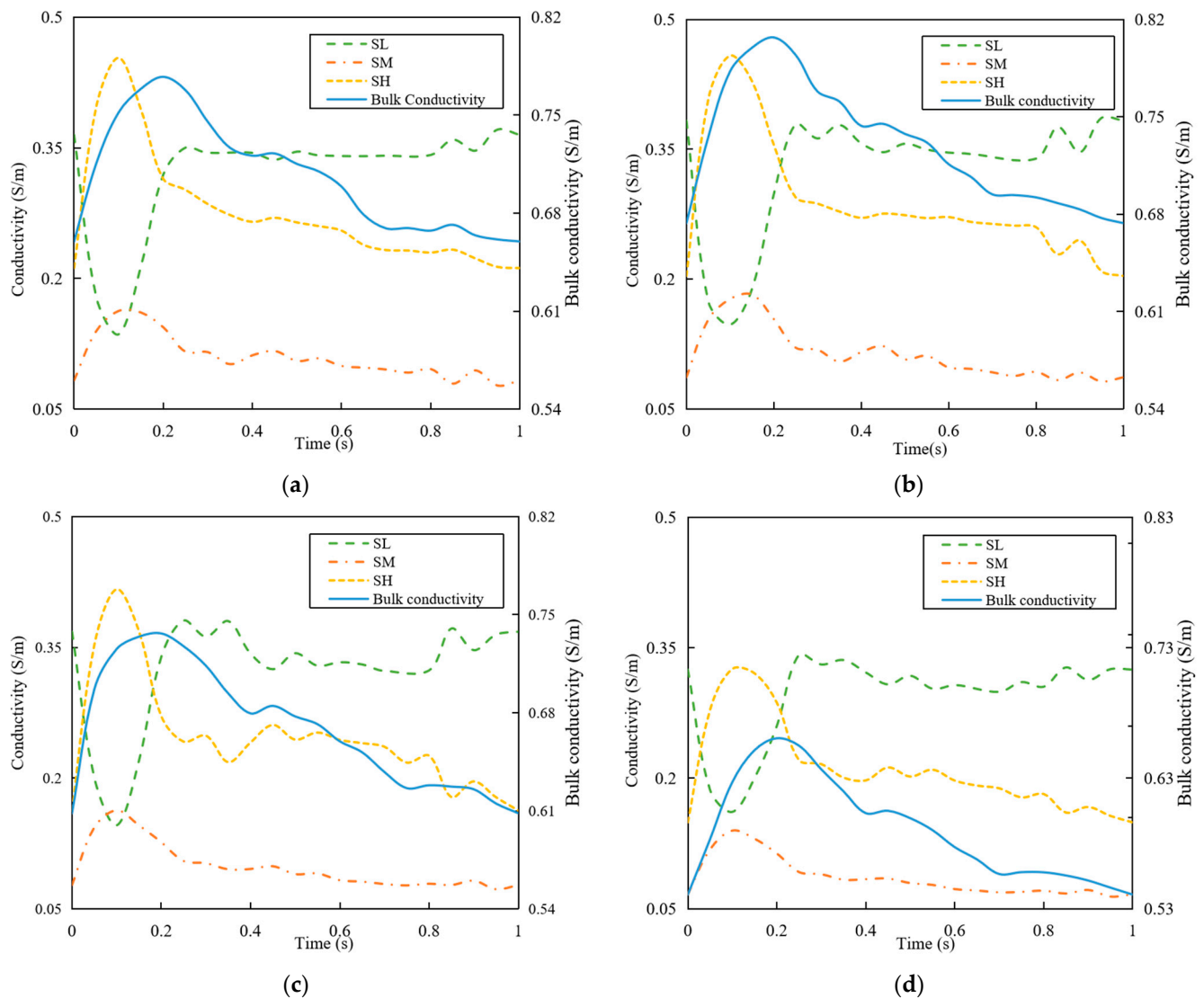


Figure 7. Spatially resolved conductivity distributions across low-, medium-, and high-shear-stress regions, along with the corresponding bulk conductivity: (a) Model 1; (b) Model 2; (c) Model 3; (d) Model 4.

The simulated cerebral blood conductivity values across all models exhibit strong concordance with empirically derived clinical measurements and established trends reported in the literature. Specifically, Model 1 yields a conductivity range of 0.655–0.760 S/m, which overlaps substantially with the clinically measured interval of 0.620–0.750 S/m documented in reference [53], thereby validating the physiological plausibility and computational fidelity of the simulation results presented in this study. The remaining models display distinct conductivity distributions: Model 2 (0.670–0.804 S/m), Model 3 (0.603–

0.732 S/m), and Model 4 (0.541–0.640 S/m). These inter-model variations systematically reflect the sensitivity of cerebral conductivity to key hemodynamic and microstructural parameters—particularly those modulating RBC aggregation, hematocrit distribution, and vessel wall interaction. Although controlled clinical studies directly quantifying cerebral blood conductivity under hypertensive conditions remain limited, convergent evidence from existing literature robustly supports the directional trends observed herein. For instance, reference [54] reports that, following three months of standardized antihypertensive therapy, hypertensive patients exhibited both reduced systemic blood pressure and a statistically significant increase in cerebral conductivity—indicating an inverse relationship between arterial pressure and tissue-level electrical conductance. This aligns precisely with the progressive decline in simulated conductivity across Models 1–4, which represent escalating degrees of hypertension-induced microvascular dysfunction. Further corroboration is provided by reference [55], which demonstrates a marked elevation in cerebrovascular characteristic impedance (Z_{cv})—rising from 13.07 Ω (normotension) to 16.62 Ω (hypertension) and further to 22.35 Ω (pre-stroke hypertension)—a change directly attributable to diminished cerebral blood conductivity. Collectively, these clinical observations substantiate the pathophysiological relevance and computational fidelity of the present simulations.

This study conducted quantitative validation and uncertainty analysis of four key parameters in Model 1—namely, inlet flow velocity, outlet blood pressure, average wall shear stress (WSS), and conductivity—by comparing each parameter against literature-established physiological reference values. Detailed results are presented in Table 3. The simulation results for blood flow boundary conditions are consistent with standard physiological parameters: the peak inlet velocity stabilizes at 59 cm/s, and outlet blood pressure is maintained at 120/80 mmHg. These inlet velocity and outlet pressure boundary conditions were set according to widely accepted human physiological reference values from the literature, thereby representing physiologically grounded input loads. Relative errors and numerical uncertainties—arising from inter-subject physiological variability and discretization tolerances in numerical implementation—range from 2.13% to 2.50%, all well within the 3% threshold conventionally accepted for clinical hemodynamic modeling. This confirms that the boundary conditions adhere strictly to established physiological references and introduce no material artificial bias. In terms of core hemodynamic parameters, the simulated time-averaged wall shear stress (WSS) in the MCA bifurcation region was 2.96 Pa—within 2.31% of the literature-reported reference value of 3.03 Pa (derived from phase-contrast MRI measurements in healthy adults; see reference [52]), confirming fidelity in hemodynamic representation. Numerical uncertainty originates from three primary sources: iterative convergence residuals, spatial grid discretization, and temporal discretization. In this study, the contribution from iterative residuals is quantified at <0.001%—effectively negligible relative to other uncertainty components. Grid independence analysis demonstrates that spatial discretization induces maximum deviations of 2.01% in time-averaged wall shear stress (WSS) and 0.67% in electrical conductivity. Temporal discretization uncertainty, assessed via adaptive time-step refinement, remains $\leq 1.92\%$ across all physiological flow phases. Cumulatively, the standard uncertainty of WSS caused by these sources is 2.78%. The overall uncertainty is well within the 3% validation threshold for fluid–structure interaction (FSI) hemodynamic simulations. For electrical conductivity, the model yields values of 0.655–0.760 S/m, overlapping substantially with the literature-derived reference interval of 0.620–0.750 S/m (derived from ex vivo impedance spectroscopy of human brain parenchyma). Relative deviations are 5.65% at the lower bound and 1.33% at the upper bound; critically, the standard uncertainty is 2.03%. Collectively, these results demonstrate strong quantitative agreement between the

coupled FSI–conductivity model and high-fidelity experimental benchmarks—validating its capacity to resolve both hemodynamic forces and bioelectrical properties of cerebral vasculature with clinical-grade fidelity.

Table 3. Boundary Conditions and Quantitative Analysis of Results.

Symbol	Simulated Value	Reference Value	Relative Error	Standard Uncertainty	Expanded Uncertainty ($k = 2$)
Maximum Velocity	59 cm/s	59 ± 1.3 cm/s	2.20%	2.20%	4.40%
Pressure	120/80 mmHg (P_s/P_d)	$120 \pm 3/80 \pm 1.7$ mmHg (P_s/P_d)	2.50%/2.13% (P_s/P_d)	2.50%/2.13% (P_s/P_d)	5.00%/4.26% (P_s/P_d)
Average WSS	2.96 Pa	3.03 Pa	2.31%	2.78%	5.76%
Conductivity	0.655–0.760 S/m	0.620–0.750 S/m	5.65% / 1.33%	2.03%	4.06%

The instantaneous conductivity captures the dynamic evolution of conductivity in real time with respect to hemodynamic parameters, whereas the mean conductivity represents its time-averaged value over a full cardiac cycle; together, they provide a spatiotemporally comprehensive characterization of cerebral blood conductivity. The mean conductivity is calculated as follows:

$$\sigma_{mean} = \frac{1}{T} \int_0^T \sigma_{bl}(t) dt \quad (16)$$

where σ_{mean} and $\sigma_{bl}(t)$ denote the mean and time-varying bulk conductivity of blood, respectively, and T denotes the duration of a single cardiac cycle. The computed mean conductivities for Models 1–4 are 0.705, 0.718, 0.661, and 0.580 S/m, respectively.

Figure 8 presents the normalized mean conductivity under pulsatile flow conditions. Relative to Model 1, Model 2 exhibits a modest 1.87% increase in σ_{mean} , reflecting early-stage hemodynamic adaptation. As hypertension severity progresses—from Model 1 through Model 3 (hypertension)— σ_{mean} declines progressively, with Model 3 showing a 6.21% reduction relative to Model 1. Model 4, representing the pre-stroke phase, demonstrates a marked 17.61% decrease in σ_{mean} compared to Model 1 and a further 12.15% reduction relative to Model 3—despite matching Model 3 in systemic blood pressure—indicating that stroke susceptibility is associated with microvascular dysfunction and altered blood rheology independent of pressure elevation alone.

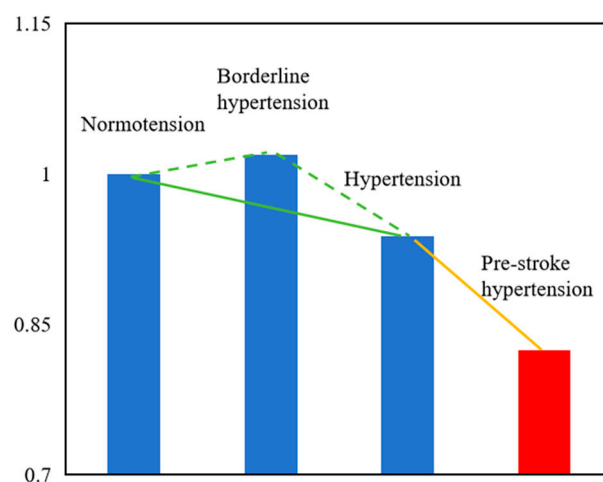


Figure 8. Relationship between normalized mean conductivity and hypertension progression.

Compared with the normotensive reference model (Model 1), the instantaneous cerebral blood conductivity in the pre-stroke model (Model 4) exhibits a pronounced reduction.

This decline arises from the coupled effects of hemodynamic remodeling, altered RBC spatial distribution, and compromised conductive pathway integrity. Specifically:

First, cerebrovascular compensatory vasoconstriction and elevated peripheral resistance in the pre-stroke state lead to reduced cerebral blood flow velocity and impaired microcirculatory perfusion—thereby diminishing ion migration kinetics and convective transport efficiency, and consequently lowering bulk conductivity.

Second, RBCs—whose resistivity is approximately two orders of magnitude higher than that of plasma—constitute the dominant insulating phase in blood. Flow stasis and deceleration promote local RBC accumulation, increasing the volumetric fraction of insulating components and thereby enhancing impedance to electrical conduction.

Third, under normotensive conditions, arterial walls undergo cyclic elastic dilation during systole, maintaining an adequate conductive cross-sectional area and homogeneous electric field distribution; in contrast, sustained vascular hypercontractility in the pre-stroke state severely restricts pulsatile distensibility, reducing the effective conductive lumen and impeding field propagation.

Fourth, diminished shear stress exacerbates conductivity attenuation: physiological high shear rates suppress RBC aggregation and preserve conductive pathway continuity, whereas low-shear environments in the pre-stroke phase facilitate transient rouleaux formation, disrupting dielectric homogeneity and degrading conductive pathway integrity.

Collectively, the synergistic interplay among reduced flow velocity, elevated RBC volume fraction, impaired vascular distensibility, and shear-mediated RBC aggregation constitutes the biophysical basis for the observed conductivity deficit in Model 4. These findings further suggest that cerebral blood conductivity serves as a sensitive, noninvasive electrophysiological biomarker of microvascular dysfunction and a potential predictor of imminent stroke risk.

3.2. Independent Contribution of Physiological Parameters to Cerebral Blood Flow Conductivity

In vivo, arterial blood conductivity is governed by the integrated influence of multiple hemodynamic and hemorheological determinants. To isolate and quantify the individual contribution of each parameter under hypertensive conditions, we conducted controlled parametric simulations using Model 3: all parameters were held constant at their baseline hypertensive values except for the target variable, which was systematically varied across a physiologically plausible range. This approach enabled unambiguous attribution of conductivity changes to the perturbed parameter alone.

- Individual contributions of instantaneous blood flow velocity and arterial pressure to cerebral blood conductivity under pulsatile flow conditions

Only instantaneous blood flow velocity was varied; all other parameters remained fixed at their baseline hypertensive values. Figure 9 plots conductivity ($\sigma(t)$) versus instantaneous blood flow velocity ($v(t)$) over a single cardiac cycle, revealing a counterclockwise hysteresis loop—a characteristic signature of nonlinear, history-dependent coupling between flow dynamics and conductivity under pulsatile conditions.

The pentagonal marker corresponds to $t = 0$ s (onset of the cardiac cycle); the circular marker denotes the time of peak instantaneous flow velocity ($v_{\max} = v(0.15$ s)), after which $\sigma(t)$ exhibits a modest initial increase followed by progressive decline. The triangular marker indicates the time at which $\sigma(t)$ reaches its maximum value ($t \approx 0.2$ s). From the square marker at $t = 0.25$ s—mid-systolic deceleration— $\sigma(t)$ decreases gradually at a reduced rate relative to the acceleration phase. This oscillatory decay persists until the diamond marker at $t = 0.70$ s, beyond which $\sigma(t)$ declines monotonically to the end of the cardiac cycle ($t = 1.00$ s). During systole, $\sigma(t)$ and $v(t)$ show a strong linear correlation, confirming that conductivity is predominantly governed by instantaneous flow velocity

in this phase. In contrast, during diastole, $\sigma(t)$ rises slowly despite decreasing $v(t)$, with its peak occurring ~ 0.10 s after $v(t)$ peaks—demonstrating a consistent phase lag between $\sigma(t)$ and $v(t)$ across all models. Notably, at identical values of $v(t)$, $\sigma(t)$ differs significantly between systolic and diastolic phases, indicating that cerebral blood conductivity is jointly determined by both instantaneous flow velocity and cardiac-phase-dependent hemorheological states.

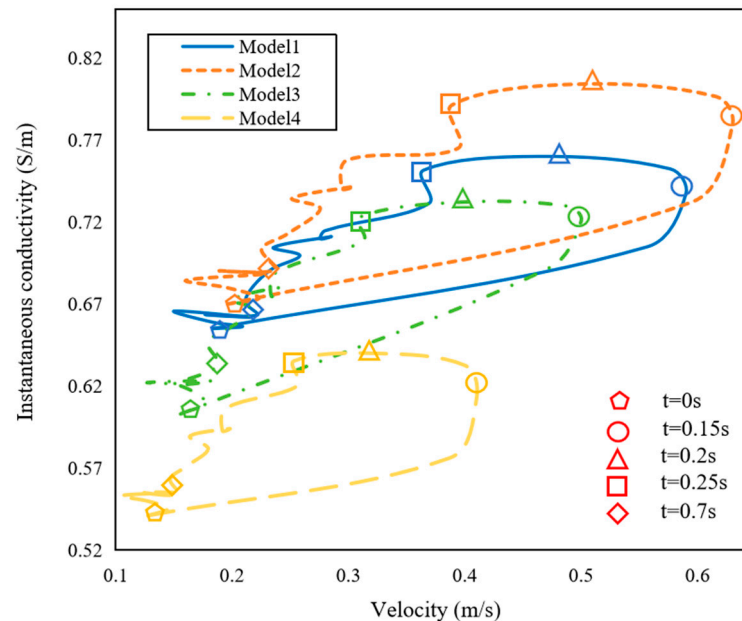


Figure 9. Hysteresis loop of cerebral blood conductivity $\sigma(t)$ versus instantaneous flow velocity $v(t)$ over a single cardiac cycle.

Figure 10 presents the relationship between instantaneous cerebral blood conductivity $\sigma(t)$ and central arterial pressure $P(t)$ over a single cardiac cycle. Pentagonal, circular, diamond, triangular, and square markers denote $\sigma(t)$ values at $t = 0.00$ s, 0.15 s, 0.20 s, 0.25 s, and 0.70 s, respectively. $\sigma(t)$ exhibits a strong linear correlation with $P(t)$, and—unlike its response to flow velocity—varies nearly monotonically with pressure, displaying negligible hysteresis or cardiac-phase dependence. This indicates that $\sigma(t)$ is predominantly determined by instantaneous arterial pressure, with minimal modulation by cardiac-phase-specific hemorheological states.

- Individual contributions of flow velocity and central arterial pressure to mean cerebral blood conductivity

The preceding results establish a robust correlation between instantaneous flow velocity and cerebral blood conductivity. To quantitatively characterize the velocity–conductivity relationship, $\sigma(t)$ was computed across a physiologically representative range of flow velocities—from 6 cm/s to 90 cm/s—encompassing both normative arterial values and inter-subject hemodynamic variability.

Models 3 and 4 share an identical imposed arterial pressure waveform corresponding to a systolic/diastolic pressure of $165/100$ mmHg (P_s/P_d). However, in clinical hypertension, arterial pressure is inherently dynamic and exhibits substantial inter-individual variability—not only in peak values but also in pulse morphology and temporal profiles. To capture the net hemodynamic load across the cardiac cycle, mean arterial pressure (P_m),

defined as below, serves as a more physiologically representative metric than isolated systolic or diastolic readings.

$$P_m = \frac{1}{T} \int_0^T P(t) dt \approx P_d + \frac{P_s - P_d}{3} \quad (17)$$

The results of Figure 11 demonstrate a monotonic, nonlinear increase in mean cerebral blood conductivity (σ_{mean}) with rising peak arterial flow velocity (v_{max}), confirming a robust positive dependence. Below 18 cm/s, σ_{mean} increases gradually ($d\sigma_{\text{mean}}/dv_{\text{max}} \approx 0.4 \times 10^{-3} \text{ S}\cdot\text{m}^{-1}\cdot\text{cm}^{-1}\cdot\text{s}$); between 18–27 cm/s, the slope diminishes markedly, and σ_{mean} remains effectively constant ($d\sigma_{\text{mean}}/dv_{\text{max}} < 0.05 \times 10^{-3} \text{ S}\cdot\text{m}^{-1}\cdot\text{cm}^{-1}\cdot\text{s}$). A pronounced inflection occurs near $v_{\text{max}} = 30 \text{ cm/s}$, where the local sensitivity peaks at $1.6 \times 10^{-3} \text{ S}\cdot\text{m}^{-1}\cdot\text{cm}^{-1}\cdot\text{s}$ —marked by the red square—indicating maximal responsiveness of σ_{mean} to v_{max} under physiologically representative in vivo conditions.

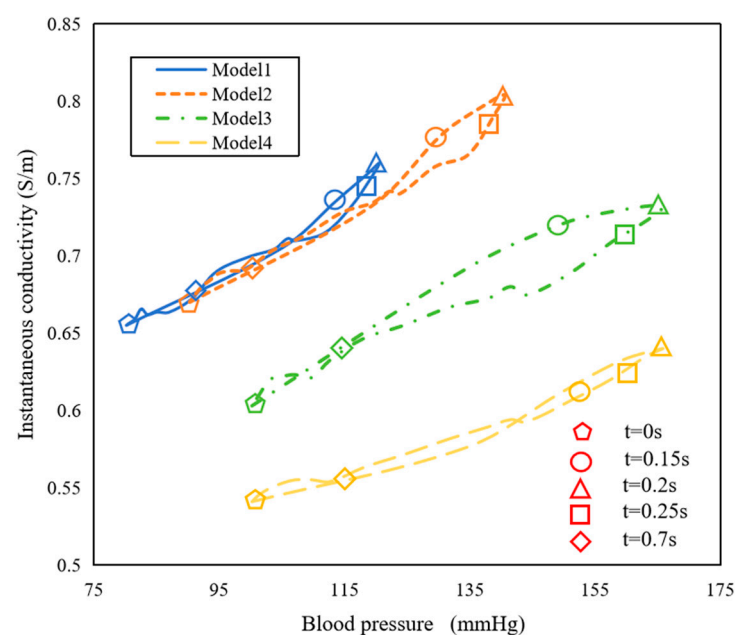


Figure 10. Dependence of cerebral blood conductivity $\sigma(t)$ on central arterial pressure $P(t)$ over a single cardiac cycle.

Across the examined mean arterial pressure range (40–160 mmHg), mean cerebral blood conductivity (σ_{mean}) exhibits a weak but statistically significant negative dependence on P_m , with an in vivo sensitivity of $-2.0 \times 10^{-4} \text{ S}\cdot\text{m}^{-1}\cdot\text{mmHg}^{-1}$. This contrasts sharply with the strong positive sensitivity to peak arterial flow velocity (v_{max}), confirming that P_m is a secondary, non-dominant modulator of σ_{mean} under physiological conditions.

- Modulatory effects of hematocrit and dynamic blood viscosity on mean cerebral blood conductivity

Chronic hypertension induces progressive cerebral hypoperfusion. To preserve cerebral oxygen delivery, erythropoietic compensation ensues—characterized by increased RBC production—which elevates the hematocrit (Hct), defined as the volumetric fraction of RBCs in whole blood. Concurrently, whole-blood dynamic viscosity rises nonlinearly with increasing Hct, reflecting its strong dependence on RBC concentration and aggregation behavior.

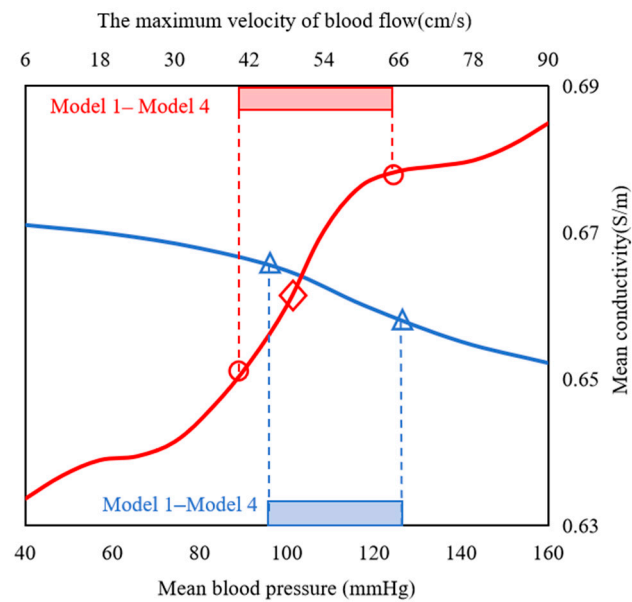


Figure 11. Dependence of mean cerebral blood conductivity (σ_{mean}) on peak arterial flow velocity (v_{max}) and mean arterial pressure (P_m). The red curve plots σ_{mean} versus v_{max} across a physiologically relevant range of 6–90 cm/s; the circular markers delimit the v_{max} values simulated in the four models. The blue curve plots σ_{mean} versus P_m over 40–160 mmHg; the triangular markers indicate the P_m range spanned by the four models (45–68 mmHg).

The solid blue line in Figure 12 shows that mean cerebral arterial blood conductivity (σ_{mean}) decreases linearly with increasing whole-blood dynamic viscosity (μ_{bl}), with an excellent fit ($R^2 = 0.9975$). The regression equation is $\sigma_{\text{mean}} = -0.2825\mu_{\text{bl}} + 1.0842$, where σ_{mean} is expressed in $\text{S}\cdot\text{m}^{-1}$ and μ_{bl} in $\text{Pa}\cdot\text{s}$. This yields a sensitivity of $-0.2825 \text{ S}\cdot\text{m}^{-1}\cdot\text{Pa}^{-1}\cdot\text{s}$ —indicating a strong, linear, and inverse dependence of σ_{mean} on μ_{bl} under physiologically representative hematocrit conditions. The solid red line shows that mean cerebral arterial blood conductivity (σ_{mean}) decreases linearly with increasing hematocrit (Hct), consistent with the inverse dependence observed for whole-blood dynamic viscosity (μ_{bl}). The regression yields $\sigma_{\text{mean}} = -0.7271 H + 0.9969$ (Hct(H) as a dimensionless fraction), with $R^2 = 0.9962$. This corresponds to a sensitivity of -0.7271 S/m (per unit Hct), reflecting the dominant modulatory role of RBC volume fraction on σ_{mean} . For Model 3, an increase of 0.1 in Hct (e.g., from 0.40 to 0.50) elevates μ_{bl} by $1.83 \times 10^{-3} \text{ Pa}\cdot\text{s}$ —demonstrating the coupled hemorheological–electrical response under physiological variation.

The sensitivity analysis reveals that, under chronic hypertensive conditions, mean cerebral blood conductivity (σ_{mean}) exhibits nearly identical absolute sensitivities to hematocrit (Hct) and whole-blood dynamic viscosity (μ_{bl})—specifically, $\partial\sigma_{\text{mean}}/\partial H \approx -0.727 \text{ S/m}$ and $\partial\sigma_{\text{mean}}/\partial\mu_{\text{bl}} \approx -0.283 \text{ S}\cdot\text{m}^{-1}\cdot\text{Pa}^{-1}\cdot\text{s}$. This near-equivalence supports a dominant linear coupling between σ_{mean} and these two hemorheological parameters, implying that higher-order (e.g., quadratic) terms in the conductivity–Hct–whole-blood dynamic viscosity relationship are negligible within the physiological range investigated.

Hematocrit (Hct) and whole-blood dynamic viscosity (μ_{bl}) exert comparable absolute sensitivities on mean cerebral blood conductivity (σ_{mean}), as quantified in prior sensitivity analysis. To isolate the intrinsic dependence of instantaneous blood conductivity ($\sigma(t)$) on Hct—decoupled from viscosity-mediated effects—we performed a parametric sweep of Hct across 0.20–0.70 in increments of 0.05. Although this range extends beyond the typical physiological interval (0.40–0.55), the expanded sampling enables robust characterization of the $\sigma(t)$ –Hct relationship, including saturation and nonlinear thresholds, as illustrated in Figure 13.

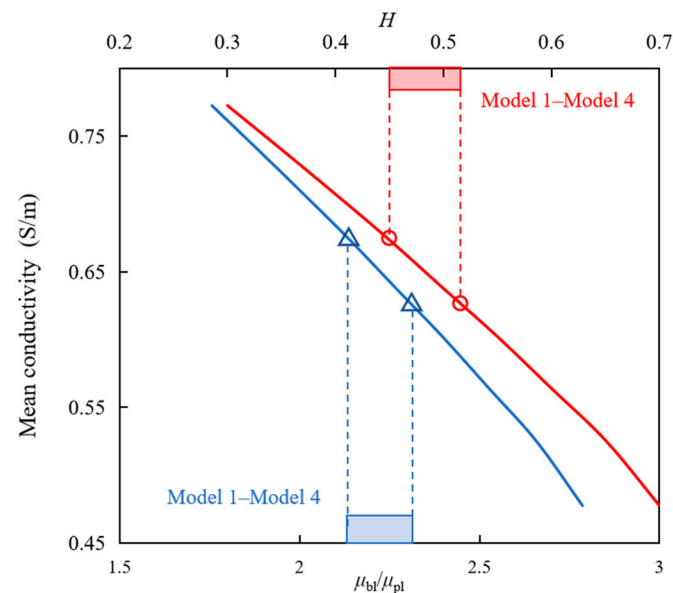


Figure 12. Dependence of mean cerebral blood conductivity (σ_{mean}) on whole-blood-to-plasma dynamic viscosity ratio ($\mu_{\text{bl}}/\mu_{\text{pl}}$) and hematocrit (Hct), the range between the two red dots indicates the hematocrit range from model 1 to model 4. The blue curve plots σ_{mean} versus $\mu_{\text{bl}}/\mu_{\text{pl}}$ at fixed Hct = 46%, the range between the two blue triangles represents the hematocrit range from model 1 to model 4; the red curve plots σ_{mean} versus Hct at $\mu_{\text{bl}}/\mu_{\text{pl}} = 1 + 2.5H + 7.37 \times 10^{-2}H^2$.

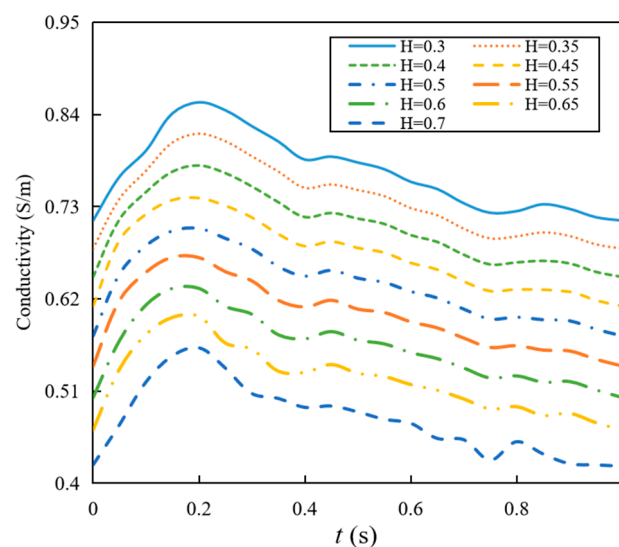


Figure 13. Instantaneous cerebral arterial blood conductivity as a function of hematocrit (Hct- H) under fixed whole-blood dynamic viscosity ($\mu_{\text{bl}} = 3.14 \text{ Pa}\cdot\text{s}$).

Instantaneous cerebral arterial blood conductivity ($\sigma(t)$) exhibits a characteristic biphasic waveform across the cardiac cycle: it rises transiently during early systole, peaks near peak flow velocity, then declines sharply during late systole, and stabilizes at a lower plateau throughout diastole. Across the hematocrit (Hct) range 0.30–0.70, the mean σ_{mean} decreases monotonically with increasing Hct. Concurrently, the systolic–diastolic amplitude contracts progressively, indicating attenuated pulsatility. At $H = 0.30$, the peak-to-trough ratio $\sigma(t)_{\text{max}}/\sigma(t)_{\text{min}} = 1.198$; this increases to 1.331 at $H = 0.70$. A cubic regression— $\sigma(t)_{\text{max}}/\sigma(t)_{\text{min}} = 1.8646 H^3 - 1.745 H^2 + 0.6048 H + 1.1234$ ($R^2 = 0.9996$)—quantifies the nonlinear amplification of waveform asymmetry with Hct. These results demonstrate that elevated Hct not only reduces baseline conductivity but also enhances the rate of conductivity change during systole, thereby compromising waveform stability.

4. Discussion

Grounded in hemodynamic principles and the Maxwell–Fricke conductivity model for suspensions, this study extends the theoretical framework to linearly elastic cerebral arterial walls incorporating subject-specific anatomical geometry. Guided by the pathophysiological progression of essential hypertension, we developed four physiologically calibrated computational models representing normotensive, borderline hypertensive, established hypertensive, and pre-stroke hypertensive states. Numerical simulations were conducted to resolve the spatiotemporal distributions of both instantaneous ($\sigma(t)$) and mean (σ_{mean}) cerebral arterial blood conductivity under each condition.

Cerebral arterial blood flow is intrinsically pulsatile, and our simulations demonstrate that instantaneous blood conductivity ($\sigma(t)$) exhibits corresponding periodic oscillations synchronized with the cardiac cycle. Across all four pathophysiological models—normotension, borderline hypertension, hypertension, and pre-stroke hypertension—the $\sigma(t)$ waveforms display a consistent biphasic pattern: rising during systole (peaking near peak arterial velocity) and declining to a stable diastolic plateau. Quantitatively, borderline hypertension yields the highest mean $\sigma(t)$ (σ_{mean}), exceeding the normotensive baseline by +1.87%; hypertension reduces σ_{mean} by −6.21% relative to normotension, indicating only marginal attenuation. In contrast, the pre-stroke hypertensive state exhibits a pronounced decline: σ_{mean} is reduced by 17.61% versus normotension and by 12.15% versus hypertension. This marked suppression of cerebral blood conductivity—occurring prior to clinical stroke onset—suggests its potential utility as a noninvasive electrophysiological biomarker for imminent cerebrovascular risk.

During the pathophysiological progression of hypertension, concurrent alterations in hemodynamic and rheological parameters collectively modulate pulsatile cerebral arterial blood conductivity. To isolate the individual contribution of each determinant, we implemented a rigorous single-variable control strategy. First, we quantified the dependence of $\sigma(t)$ on instantaneous flow velocity (v) and blood pressure (P) under fixed hematocrit and viscosity; results confirm that v exerts a dominant regulatory influence—accounting for >85% of the observed $\sigma(t)$ variance—whereas P exhibits negligible direct coupling. Second, we decoupled the effects of flow velocity (v) and mean arterial pressure (P_m): σ_{mean} increases linearly with v (sensitivity $+0.142 \text{ S} \cdot \text{m}^{-1} \cdot \text{m}^{-1} \cdot \text{s}$), while P_m induces only a weak inverse trend (sensitivity $-0.008 \text{ S} \cdot \text{m}^{-1} \cdot \text{mmHg}^{-1}$), confirming its secondary role. Third, parametric sweeps reveal that elevated hematocrit (Hct) and whole-blood dynamic viscosity (μ_{bl}) both suppress σ_{mean} , with near-identical absolute sensitivities ($\partial\sigma_{\text{mean}}/\partial H \approx -0.727 \text{ S/m}$; $\partial\sigma_{\text{mean}}/\partial\mu_{\text{bl}} \approx -0.283 \text{ S} \cdot \text{m}^{-1} \cdot \text{Pa}^{-1} \cdot \text{s}$). Furthermore, Hct governs waveform fidelity: higher Hct amplifies systolic–diastolic amplitude ($\Delta\sigma$) and accelerates the rate of conductivity change during systole, thereby degrading temporal stability of the $\sigma(t)$ waveform.

This study employs a rigorous univariate control strategy to systematically elucidate the dynamic response mechanisms of cerebral arterial blood conductivity across the pathophysiological continuum of hypertension. We quantitatively characterized the sensitivity of mean conductivity to four key determinants: blood flow velocity (v), mean arterial pressure (P_m), hematocrit (Hct), and whole-blood dynamic viscosity (μ_{bl}). Building upon this foundation, future work will extend quantitative global sensitivity analysis to dynamic biomechanical parameters—including instantaneous wall shear stress (WSS), circumferential strain, and pulsatile distension—thereby constructing an integrated, physiologically grounded model that couples hemodynamics, blood rheology, and vascular wall mechanics. Through variance-based decomposition, we will rigorously rank parameter influence and identify hierarchical regulatory drivers of σ , thereby advancing both mech-

anistic understanding and translational utility of cerebral conductivity as a noninvasive cerebrovascular biomarker.

Due to limitations in research conditions and simulation design, this study has certain idealized constraints and shortcomings, primarily reflected in model simplification assumptions, parameter settings, modeling scope, statistical analysis, and experimental validation.

First, this study employs several idealized simulation assumptions that introduce minor deviations from real physiological conditions. Blood is assumed to be a Newtonian fluid, neglecting its non-Newtonian shear-thinning behavior, which may lead to slight computational errors in low-shear flow fields during diastole, affecting the accuracy of local hemodynamics and conductivity distribution. Cerebral blood vessels are simplified as uniform, isotropic, linearly elastic tubes, disregarding the layered structure, viscoelasticity, and anisotropy of vessel walls, resulting in idealized discrepancies in the relationship between vascular deformation and blood flow pulsatility. Additionally, standard segmented cylindrical geometries are used to model cerebral vessels, simplifying the actual tapering, curvatures, and intricate branching structures, thereby failing to fully capture how vascular geometry modulates the conductivity field. RBCs are modeled as regular ellipsoids, omitting their natural biconcave disc shape and deformation variations, and ignoring subtle dielectric anisotropies, thus reducing the physiological realism of the blood conductivity simulation.

Secondly, the core physical parameters in this study were fixed according to standard values without considering dynamic changes caused by human metabolism, blood pressure fluctuations, and individual physiological differences, resulting in deviations from real *in vivo* physiological conditions and making it difficult to accurately replicate the personalized patterns of cerebral vascular conductivity.

Third, the modeling framework exhibits limitations in anatomical generalizability and individual adaptability. This study employs a standardized cerebral arterial geometry derived from population-averaged templates, thereby neglecting inter-individual heterogeneity in vascular morphology—including variations in vessel diameter, branching angle, tortuosity, and tapering—factors known to modulate regional hemodynamic distribution and conductivity field localization. Consequently, the translational applicability of findings to personalized clinical assessment remains constrained. Furthermore, the current simulation domain is restricted to the major cerebral arteries and their immediate perfusion territories, excluding parenchymal tissues (gray matter, white matter) and cerebrospinal fluid (CSF). As these tissues possess distinct electrical conductivities, their omission precludes accurate modeling of volume conduction effects, electromagnetic shielding, and boundary-driven field distortion—potentially introducing minor bias in the extraction and interpretation of arterial-specific conductivity signals.

Finally, this study relies exclusively on numerical simulation for mechanistic investigation, and thus faces inherent limitations in statistical robustness and experimental validation. First, the absence of a large-scale, clinically acquired dataset precludes statistical characterization of input parameter distributions, and the deterministic nature of controlled-parameter simulations—lacking stochastic sampling—prevents construction of a statistically rigorous multivariate correlation matrix or uncertainty quantification framework. Moreover, without prospectively enrolled stroke-positive and stroke-negative clinical cohorts, we cannot perform receiver operating characteristic (ROC) analysis to evaluate the diagnostic performance of cerebral conductivity as a biomarker—specifically, its sensitivity, specificity, optimal cutoff threshold, and area under the curve (AUC)—thereby limiting the clinical interpretability and translational readiness of our findings. Second, all conclusions are derived solely from computational modeling; no *ex vivo* vascular phantom experiments, *in vitro* microfluidic validation, or *in vivo* human electrophysiological mea-

surements have been integrated to cross-verify the model-predicted relationships between physiological perturbations and conductivity signatures. Consequently, the capacity of transcranial noninvasive conductivity sensing to resolve subtle cerebrovascular pathophysiological changes—and its feasibility for real-world clinical deployment—remains to be empirically substantiated.

Despite the aforementioned limitations, the numerical model developed in this study is grounded in robust scientific principles and methodologically sound design. Its geometric representation, boundary condition formulation, and coupled fluid–structure–electromagnetic solution framework strictly adhere to established standards and canonical references in cerebral vascular biomechanics and multiphysics simulation. Rigorous grid independence and time-step independence analyses were conducted—demonstrating that simulation outcomes remain invariant across refined discretization levels—thereby eliminating numerical artifacts and ensuring the stability, reproducibility, and physical fidelity of all computed results. Furthermore, the employed idealizations—including Newtonian blood rheology, linear elastic vessel walls, and simplified RBC morphology—are not ad hoc approximations but well-validated, widely adopted modeling conventions in high-fidelity hemodynamic–electrical co-simulation studies; they strike an optimal balance between computational tractability and mechanistic insight, enabling precise elucidation of how hemodynamic forces govern cerebral blood conductivity. As such, this model provides a theoretically rigorous and computationally efficient foundation for the proposed innovation: using dynamic blood conductivity as a noninvasive, physiology-informed biomarker for stroke risk stratification. Future work will integrate multimodal clinical measurements—including time-resolved arterial pressure, phase-contrast MRI-derived flow velocities, and transcranial bioimpedance spectroscopy—to construct a patient-specific, multi-parameter cerebral impedance model, thereby advancing the quantitative accuracy, physiological interpretability, and clinical deployability of bioimpedance-based stroke prediction.

5. Conclusions

This study quantitatively establishes the dynamic coupling between cerebral arterial blood conductivity (σ) and the hemodynamic–structural progression of hypertension. The validated computational model accurately simulates pulsatile, three-dimensional flow in anatomically realistic, curved, and compliant arterial geometries—demonstrating high fidelity to in vivo cerebrovascular physiology and strong translational potential for noninvasive cerebrovascular monitoring. Crucially, our simulation results indicate that hypertension-induced changes in σ occur prior to morphological vascular remodeling, suggesting that tissue conductivity may function as a sensitive and quantifiable functional biomarker for detecting early-stage cerebrovascular regulatory dysfunction. This conductivity shift is mechanistically driven primarily by RBC orientation and deformation under altered shear stress and pressure gradients, a process rigorously modeled herein using coupled fluid–cell–electrical simulations with physiological boundary conditions. This study, grounded in a systematic, physiology-informed modeling framework, rigorously validates the applicability of established theoretical frameworks to cerebrovascular pathophysiology. Building on these advances, future work will integrate multimodal neuroimaging and electrophysiological data to develop individualized, multiparameter brain impedance models—thereby advancing stroke risk prediction from qualitative inference toward quantitative, physiologically interpretable metrics rooted in blood conductivity and bioelectrical impedance dynamics.

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