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Advanced Numerical Algorithms for Simulating Transient Biofluid Flows in Complex Biological Geometries

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Abstract

Recent advances in computational fluid dynamics have enabled unprecedented capabilities for simulating transient biofluid flows in intricate biological geometries, though significant challenges persist in balancing accuracy, stability, and computational cost. This review critically examines state-of-the-art numerical algorithms developed for modeling pulsatile flows, viscoelastic fluids, and fluid-structure interactions in anatomically complex domains. Key methodologies are analyzed through the lens of their mathematical foundations, including high-order discontinuous Galerkin schemes, immersed boundary techniques, and data-driven closure models. The discussion highlights innovations in handling moving boundaries, nonlinear rheology, and multiscale phenomena while identifying persistent limitations related to high-dimensional parameter spaces and experimental validation. Comparative evaluations reveal that hybrid Eulerian-Lagrangian approaches coupled with tensor-reduced constitutive models achieve 25–40% faster convergence than traditional finite volume methods for cardiovascular flows. Emerging trends in physics-informed machine learning and adaptive mesh refinement are assessed for their potential to overcome resolution bottlenecks in clinical-scale simulations.

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Contents

1. Introduction

The numerical simulation of biofluid dynamics in physiological geometries has become an indispensable tool for understanding, predicting, and ultimately improving clinical interventions for a broad spectrum of medical conditions [1]. From the coronary circulation responsible for delivering oxygenated blood to the myocardium, to cerebrospinal fluid flow in the ventricles of the brain, the physical processes that govern these phenomena exhibit a complex interplay of nonlinear rheology, large deformations of biological tissues, and significant multiscale interactions ranging from cellular to organ-level structures. [2]

Although classical Navier-Stokes solvers proved valuable in early biofluid applications, their limitations became evident as researchers encountered the non-Newtonian and viscoelastic properties of real biological fluids. For instance, whole blood can exhibit shear-thinning viscosity (often modeled by the Carreau-Yasuda or Cross law) and viscoelastic effects under high-shear conditions near vessel stenoses or artificial heart valves [3]. Moreover, biological boundaries—the inner walls of arteries, cardiac valves, alveolar sacs in the lungs—are rarely rigid; their deformation can change flow characteristics and lead to phenomena such as flow instabilities, oscillatory shear, and localized recirculation zones. [4]

Over the last decade, considerable effort has been expended to develop numerical methods capable of capturing these complexities while maintaining both computational feasibility and numerical stability. Researchers have pursued four principal directions: [5]

- **High-Order Discretization Schemes.** Spectral element and high-order discontinuous Galerkin (DG) formulations offer polynomial accuracy and minimal numerical diffusion, making them particularly well-suited for transitional and turbulent bioflows in complex vascular networks.
- **Immersed Boundary and Fictitious Domain Methods.** These strategies circumvent the need for body-fitted meshes around deforming or moving biological structures, thereby facilitating simulations of heart valve closure, vocal fold vibration, and ciliary-driven flow in respiratory airways.
- **Advanced Constitutive and Multiscale Modeling.** Enhanced rheological laws (e.g., Oldroyd-B with shear-thinning modifications) and tensor-decomposition approaches address the high computational burden posed by viscoelastic stress evolution at large Weissenberg numbers. Concurrently, multiscale frameworks couple molecular or cellular-scale physics (platelet aggregation, RBC membrane elasticity) to macroscopic flow fields.
- **Machine Learning and Data-Driven Acceleration.** Emerging physics-informed neural networks (PINNs), reduced-order modeling (ROM), and hybrid data-driven closures aim to reduce computational overhead by approximating subgrid-scale phenomena or by rapidly predicting flow statistics in real-time clinical settings.

This review synthesizes the most salient developments in these areas, paying special attention to the mathematical and algorithmic underpinnings that enable robust, accurate, and scalable biofluid simulations [6]. We focus on the theoretical foundations underlying each method, the interplay of spatial and temporal discretization strategies, and the challenges of implementing these schemes in large-scale or clinical contexts where parameter uncertainties, boundary conditions, and model validation come to the forefront [7]. We also emphasize open challenges such as the need for more comprehensive experimental benchmarks, robust coupling with tissue models, and better integration of machine learning with first-principles physics.

2. High-Order Discretization Schemes

One of the most prominent trends in contemporary biofluid simulations is the adoption of high-order methods that achieve increased accuracy per degree of freedom compared to low-order finite volume or finite element methods [8]. Among these, discontinuous Galerkin (DG) and spectral element methods (SEM) have received particular attention due to their favorable dispersive and dissipative properties. [9]

2.1 Discontinuous Galerkin Formulation

In the DG approach for the incompressible or low-Mach-number Navier-Stokes equations, the computational domain Ω is partitioned into a set of non-overlapping elements $\{\Omega_e\}$. Within each element, one seeks a polynomial approximation of degree p for velocity and pressure (or for velocity alone in velocity–pressure mixed formulations). A typical strong-form DG discretization for the momentum equation can be written as: [10]

$$\int_{\Omega_e} \left(\frac{\partial \mathbf{u}_h}{\partial t} + \nabla \cdot \mathbf{F}(\mathbf{u}_h) \right) \phi_h \, d\mathbf{x} = \oint_{\partial \Omega_e} \hat{\mathbf{F}} \cdot \mathbf{n} \, \phi_h \, ds \quad \forall \phi_h \in V_h^p(\Omega_e),$$

where $\mathbf{F}(\mathbf{u}_h)$ includes both convective and diffusive fluxes, and $\hat{\mathbf{F}}$ represents the numerical flux at element boundaries. The choice of flux function affects stability and accuracy; common selections include Rusanov, Roe, and HLLC fluxes. For biofluid flows at moderate Reynolds numbers, a local Lax-Friedrichs or Rusanov flux is often preferred for its simplicity and robust damping of oscillations. [11]

A key advantage of DG is its inherent locality: each element's approximation can be evolved independently, with inter-element coupling handled through fluxes on shared faces [12]. This property lends itself well to parallelization on modern architectures. However, naive DG for incompressible

flows can require sophisticated Lagrange multiplier formulations or penalty terms to enforce the divergence-free constraint [13]. Hybridized DG (HDG) variants have been developed to reduce inter-element communication for large-scale, high-order simulations. Notably, for geometries with complex boundaries—such as branching coronary arteries—DG's element-wise approach accommodates unstructured meshes with minimal overhead. [14]

2.2 Spectral Element Methods and Exponential Convergence

Spectral element methods (SEM) can be seen as a high-order finite element technique where polynomials are collocated at Gauss–Lobatto–Legendre (GLL) or Gauss–Radau–Legendre (GRL) quadrature points within each element [15, 16]. The basis functions are typically Lagrange polynomials that interpolate these nodal points. SEM exhibits exponential convergence for sufficiently smooth solutions, an attribute particularly valuable in laminar or transitional flows such as those found in certain respiratory or vascular contexts. [17]

A canonical SEM approach for arterial flows uses expansions of velocity and pressure in tensor-product polynomial bases on hexahedral elements: [18]

$$\mathbf{u}_h(\xi,\eta,\zeta) = \sum_{i,j,k=0}^{N} \mathbf{u}_{ijk}\ell_i(\xi)\ell_j(\eta)\ell_k(\zeta),$$

where $\ell_i(\xi)$ are Lagrange polynomials. High geometric flexibility is attained by mapping each element in the reference domain $[-1,1]^3$ to a curved physical domain with isoparametric transformations, capturing tortuous vessel shapes [19]. Time-stepping schemes like semi-implicit backward differentiation (BDF2) or Adams–Bashforth–Crank–Nicolson (AB-CN) are then applied to handle the stiff inertial and viscous terms.

Studies comparing SEM to low-order finite volume methods in patient-specific aneurysm models have shown that high-order expansions significantly reduce spurious oscillations near the aneurysm dome, enabling more accurate capture of vortex structures and shear-layer instabilities [20]. Such improvements are critical for computing clinically relevant metrics, such as wall shear stress and oscillatory shear index. [21]

2.3 Stabilization and Large Eddy Simulation

Although many bioflows are laminar or transitional at small-to-moderate Reynolds numbers (e.g., Re < 1000 in cerebral arteries), some domains—like the larynx or large-diameter vessels—may display turbulent flow features. Direct Numerical Simulation (DNS) at full resolution is infeasible for large Reynolds numbers in anatomically realistic domains. As a compromise, Implicit Large Eddy Simulation (ILES) with high-order methods has emerged as a viable alternative [22]. Here, the intrinsic numerical dissipation of the upwinding scheme in DG or the spectral filter in SEM acts analogously to a subgrid-scale model [23]. This approach has been applied successfully to the pulsatile flow in large catheters and cannulas, providing physically meaningful predictions of turbulent structures at significantly lower cost than DNS.

In some cases, explicit subgrid-scale (SGS) models, such as the dynamic Smagorinsky model, are embedded within DG or SEM frameworks [24]. One approach is to compute the elementwise solution gradient to identify regions of steep velocity gradients or incipient turbulence. A Smagorinsky-type viscosity term can then be added locally [25]. Entropy-stable or positivity-preserving flux modifications ensure the stability of these high-order simulations, even in the face of steep velocity and shear gradients. [26]

Overall, high-order discretization has become a linchpin of advanced biofluid simulation, enabling refined resolution of complex boundary layers, transitional flow phenomena, and subtle rheological variations—capabilities vital for capturing the physiologically relevant details of cardiovascular and respiratory flows.

3. Immersed Boundary and Fictitious Domain Methods

Biological tissues and organs often exhibit intricate, time-evolving boundaries that are prohibitively expensive to mesh or remesh if one relies on body-fitted approaches [27]. Immersed boundary (IB) and fictitious domain methods have therefore gained prominence, allowing one to treat irregular or moving structures embedded within a fixed (or adaptively refined) Eulerian grid.

3.1 Classical Immersed Boundary Formulation

The seminal IB method introduced by Peskin was designed originally for cardiac simulations, embedding flexible heart valve leaflets in a uniform Cartesian mesh [28]. The fluid momentum equation is: [29]

$$\rho\left(\frac{\partial \mathbf{u}}{\partial t} + \mathbf{u}\cdot\nabla\mathbf{u}\right) = -\nabla p + \mu\nabla^2\mathbf{u} + \mathbf{f},$$

where $\mathbf{f}(\mathbf{x},t)$ is a forcing term encoding structural elasticity. If $\mathbf{X}(s,t)$ denotes the position of a material point labeled by s on the immersed boundary, and $\mathbf{F}(s,t)$ is the force density on this material point, then $\mathbf{f}(\mathbf{x},t)$ is obtained by spreading $\mathbf{F}(s,t)$ using a discrete Dirac delta function:

$$\mathbf{f}(\mathbf{x},t) = \int_\Gamma \mathbf{F}(s,t)\,\delta\big(\mathbf{x}-\mathbf{X}(s,t)\big)\,ds.$$

In turn, the immersed boundary moves with the local fluid velocity:

$$\frac{\partial \mathbf{X}}{\partial t}(s,t) = \int_\Omega \mathbf{u}(\mathbf{x},t)\,\delta\big(\mathbf{x}-\mathbf{X}(s,t)\big)\,d\mathbf{x}.$$

This approach obviates the need to mesh the moving structure, instead using interpolation and spreading operations to couple

fluid and solid states [30]. Modern IB variants incorporate advanced regularization kernels and spectral deferred correction to improve the accuracy of delta-function approximations, reducing spurious fluxes across the immersed boundary. [31, 32]

3.2 Fictitious Domain and Distributed Lagrange Multipliers

The fictitious domain (FD) method broadens the IB principle by embedding a solid (possibly rigid or deformable) into a larger "fictitious" domain, then enforcing constraints (e.g., no-slip) via Lagrange multipliers. A typical FD-LM system for a rigid object moving in a viscous fluid can be formulated as: [33]

$$\rho\left(\frac{\partial \mathbf{u}}{\partial t}+\mathbf{u}\cdot\nabla\mathbf{u}\right)=-\nabla p+\mu\nabla^2\mathbf{u}+\lambda,$$
$$\mathbf{u}=\mathbf{V}_s \quad \text{in the solid domain,}$$

where λ is a distribution of Lagrange multipliers that enforces $\mathbf{u}-\mathbf{V}_s=0$ in the solid region. For a moving solid with velocity $\mathbf{V}_s(\mathbf{x},t)$, one can solve for the multipliers in a coupled manner. Recent improvements incorporate robust block preconditioners and multilevel solvers, making FD-LM methods scalable to large 3D problems, such as simulating multiple interacting prosthetic heart valves or stent deployment in arterial flows.

3.3 Extensions for Nonlinear Structures and Contact

More advanced immersed approaches account for the complex rheology of biological tissues [34]. For example, leaflets in heart valves or cartilage surfaces in articulating joints can exhibit hyperelastic or poroviscoelastic behavior [35]. The resulting PDE system might introduce nonlinear solid stress terms of the form:

$$\mathbf{F}(s,t)=-\frac{\delta}{\delta\mathbf{X}(s,t)}\int_{\Gamma_s}W(\mathbf{E}(\mathbf{X}))\,dS-\kappa\nabla_s(\nabla_s\cdot\mathbf{X}),$$

where $W(\mathbf{E})$ is a strain energy functional, $\mathbf{E}$ is the Green–Lagrange strain tensor, and the second term might impose inextensibility or thickness constraints. Immersed finite element (IFE) methods have also gained attention, meshing the structure in its own Lagrangian coordinates and embedding it in an Eulerian fluid mesh, thus bridging classical finite element solid modeling with the IB concept. [36]

In cases of contact or near-contact (e.g., valve leaflets closing or RBCs colliding), robust numerical treatment becomes crucial [37]. Penalty-based approaches or constraint-based collision handling can be introduced into IB or FD frameworks, though these significantly complicate the underlying linear algebra and time-stepping strategies.

3.4 Applications and Performance

Applications range from simulating the fluid-structure interplay in heart valves (mitral, aortic, or tricuspid) to cilia-driven flows in respiratory epithelial surfaces [38]. Benchmark studies indicate that for large amplitude deformations, the IB approach offers an order-of-magnitude improvement in CPU time relative to repeated mesh regeneration required by body-fitted methods. Nevertheless, one must still address potential artifacts such as smearing of the boundary interface, loss of volume conservation, and inaccurate shear stress near immersed boundaries—especially for flow regimes with high Reynolds numbers or strong pressure gradients. [39]

Overall, immersed boundary and fictitious domain methods have demonstrated substantial versatility in addressing the dynamic, deformable boundaries that characterize many biofluid problems, often achieving a harmonious balance between geometric flexibility and numerical tractability. [40]

4. Constitutive Modeling and Tensor Decompositions

Accurate predictive simulations of biofluid flows hinge on realistic constitutive models that capture the fluid's rheological response under the range of shear and strain rates found in vivo. Blood, synovial fluid, and pulmonary mucus, for example, can exhibit non-Newtonian, thixotropic, and/or viscoelastic properties. [41]

4.1 Generalized Newtonian Models

A commonly used approach for blood at moderate shear rates is a generalized Newtonian model:

$$\tau=2\mu(\dot\gamma)\,\mathbf{D},\quad \mathbf{D}=\frac{1}{2}(\nabla\mathbf{u}+\nabla\mathbf{u}^T),$$

where $\dot\gamma=\sqrt{2\mathbf{D}:\mathbf{D}}$ is the scalar shear rate, and $\mu(\dot\gamma)$ might follow Carreau–Yasuda:

$$\mu(\dot\gamma)=\mu_\infty+(\mu_0-\mu_\infty)\left[1+(\lambda\dot\gamma)^2\right]^{\frac{n-1}{2}}$$

or Casson-type yield stress models [42]. These laws capture shear-thinning but ignore elastic effects and time-dependent structural rearrangements of RBC aggregates. Yet for many large-vessel hemodynamics applications ($\mathrm{Re}\approx 200-1000$), such a generalized Newtonian approach provides an acceptable first approximation. [43] [44].

4.2 Viscoelastic Models and the High Weissenberg Number Problem

More sophisticated modeling is required when elasticity plays a prominent role, such as in microcirculation or near large shear gradients [45, 46]. Oldroyd-B, Giesekus, FENE-P, and Phan–Thien–Tanner (PTT) fluids are frequently used in blood flow research. A typical Oldroyd-B equation for the polymeric stress τ_p reads:

$$\tau_p + \lambda \overset{\triangledown}{\tau}_p = 2\eta_p \mathbf{D},$$

where $\overset{\triangledown}{\tau}_p$ is the upper-convected derivative:

$$\overset{\triangledown}{\tau}_p = \frac{\partial \tau_p}{\partial t} + (\mathbf{u}\cdot\nabla)\tau_p - (\nabla\mathbf{u})^T\cdot\tau_p - \tau_p\cdot(\nabla\mathbf{u}).$$

In the presence of large relaxation times λ and high flow speeds, the Weissenberg number $\mathrm{Wi} = \lambda\dot{\gamma}$ can become large, leading to numerical instabilities such as artificial stress growth or unphysical negative eigenvalues in τ_p. This issue is commonly known as the "High Weissenberg Number Problem" (HWNP). [47]

4.3 Log-Conformation and Stabilized Approaches

Log-conformation transformations address the HWNP by rewriting the conformation tensor $\mathbf{c} = \mathbf{I} + \frac{1}{\eta_p}\tau_p$ in terms of a matrix logarithm: $\blacksquare = \log \mathbf{c}$. The evolution equation in $\blacksquare$ space enforces positivity of $\mathbf{c}$ by construction, mitigating blow-up in standard Oldroyd-B formulations. For instance,

$$\frac{D\blacksquare}{Dt} = \mathbf{G}(\blacksquare,\mathbf{u}) + \mathbf{S}(\blacksquare),$$

where $\mathbf{G}$ and $\mathbf{S}$ are carefully designed to preserve symmetry and positive definiteness. Numerical experiments show that log-conformation methods can stably simulate $\mathrm{Wi} > 100$ in certain benchmark flows, far exceeding the typical $\mathrm{Wi} < 1-10$ limits of classical formulations.

4.4 Tensor Decomposition and Reduced Representations

For 3D viscoelastic simulations in large domains, storing and evolving the conformation or stress tensor at every degree of freedom poses a heavy memory and computational burden [48]. Tensor decomposition strategies, such as the canonical polyadic decomposition (CPD) or hierarchical Tucker (HT) decomposition, approximate $\tau_p(\mathbf{x},t)$ or $\mathbf{c}(\mathbf{x},t)$ with a low-rank expansion:

$$\mathbf{c}(\mathbf{x},t) \approx \sum_{\alpha=1}^{R} \psi_\alpha^1(x)\otimes\psi_\alpha^2(y)\otimes\psi_\alpha^3(z)\otimes\phi_\alpha(t).$$

This representation allows large-scale simulations with far fewer parameters, provided the stress/conformation tensors are not pathologically "full rank." Such methods have demonstrated up to 70% reductions in memory usage and speedups of similar magnitude in HPC contexts, enabling more refined or extended spatiotemporal simulations of clot formation or viscoelastic lubrication in joints [49].

4.5 Coupling with Wall Models and Hemodynamics Indices

Practitioners often require not only velocity and stress fields but also clinically relevant indices such as wall shear stress (WSS), oscillatory shear index (OSI), or relative residence time (RRT) [50]. In non-Newtonian flows, these indices can vary significantly depending on the chosen rheological law and local shear rates [51]. Incorporating advanced viscoelastic models can change computed WSS distributions by 20–50% in regions of recirculation, with direct implications for assessing atherosclerotic plaque progression or thrombus risk.

Hence, a thorough approach to biofluid modeling demands robust constitutive equations that capture essential rheological behaviors without overwhelming computational resources [52]. Tensor decomposition, log-conformation transformations, and stabilized numerical formulations each represent crucial developments enabling accurate, high-fidelity simulations of viscoelastic biofluids in anatomically realistic domains.

5. Multiscale and Machine Learning Accelerators

Biological systems often span disparate length and time scales, from cellular (micrometers, microseconds) to organ-level (centimeters to meters, seconds to hours) [53]. Capturing such multiscale interactions can be paramount, for instance, when modeling platelet aggregation (micro-scale) that leads to clot formation altering large-artery flow fields (macro-scale). [54]

5.1 Heterogeneous Multiscale Methods (HMM)

HMM-type schemes couple macroscopic PDEs (e.g., incompressible Navier-Stokes) with on-the-fly microscopic solvers (e.g., dissipative particle dynamics or direct RBC-based modeling) in small subdomains:

$$\mathbf{u}_{\mathrm{micro}}(\mathbf{y},t) \;=\; \mathbf{u}_{\mathrm{macro}}(\mathbf{x}_0,t) + \nabla\mathbf{u}_{\mathrm{macro}}|_{\mathbf{x}_0}(\mathbf{y}-\mathbf{x}_0),$$

where $\mathbf{x}_0$ is a macroscopic "representative point," and $\mathbf{y}$ spans the microscopic domain. The micro-scale simulation provides closure information, such as effective viscosity or particulate stress, which is then fed back into the macro-scale PDEs [55]. This approach is beneficial for microcirculation in capillary beds or for RBC-laden flows with local shear-thinning characteristics. However, computational cost can balloon if many macroscale cells require embedded microscale solvers [56]. Adaptive sampling strategies and surrogate modeling can alleviate these costs by updating micro-scale simulations only when local conditions deviate substantially from known reference states. [57]

5.2 Reduced-Order Models and Surrogate-Based Modeling

To further mitigate cost, reduced-order models (ROMs) employ projection-based techniques (proper orthogonal decom-

position, dynamic mode decomposition) or low-rank expansions to represent flow solutions in a much smaller subspace. For example, in a large vessel simulation, the velocity field might be well-approximated by a combination of 10–50 modes derived from a reference simulation or set of training snapshots: [58]

$$\mathbf{u}(\mathbf{x},t) \approx \sum_{m=1}^{M} a_m(t)\,\Phi_m(\mathbf{x}).$$

During online predictions, only the coefficients $a_m(t)$ are evolved via a reduced system of ODEs. Such ROMs, while extremely fast, can suffer from poor robustness if the real-time operating conditions differ significantly from those in the training data (e.g., higher Reynolds numbers or changed boundary conditions) [59]. Hybrid approaches combine ROM with local recourse to a full solver in critical regions or time intervals.

5.3 Machine Learning for Subgrid-Scale Closure

Deep neural networks have recently emerged as universal function approximators for capturing complex closure relationships that are difficult to encode analytically [60, 61]. One approach is to treat subgrid stresses or non-Newtonian closures as unknown functions: [62]

$$\tau_{\mathrm{SGS}} = \mathscr{N}_\theta(\nabla\mathbf{u}, p, \mathrm{Re}, \mathrm{Wi}),$$

where $\mathscr{N}_\theta$ is a neural network with parameters θ. This network is trained on high-fidelity simulation data or experimental velocity fields. Alternatively, physics-informed neural networks (PINNs) incorporate PDE residuals into their loss function, allowing the network to learn flow solutions in a continuous domain: [63]

$$\mathscr{L}(\theta) = \sum_{i=1}^{N_{\mathrm{data}}} \left|\mathbf{u}_\theta(\mathbf{x}_i) - \mathbf{u}_i^{\mathrm{ref}}\right|^2 + \beta \int_\Omega \left\|\nabla\cdot\mathbf{u}_\theta\right\|^2 d\mathbf{x}.$$

PINNs have demonstrated promise in reconstructing flow fields from sparse clinical measurements, such as Doppler ultrasound or MRI velocity profiles [64]. When integrated into a PDE solver, these networks can replace or augment classical closure terms, accelerating computations without losing significant accuracy. GPU-based parallelization often enables near-real-time inference, making these methods attractive for interactive or patient-specific simulations. [65]

5.4 Applications to Hemodynamics and Respiratory Flows

Machine learning accelerators have been explored for multi-parameter sensitivity analyses of arterial flow, where the uncertain parameters might be vessel stiffness, inflow waveforms, or viscosity. By training neural surrogates on a small ensemble of full solutions, clinicians can rapidly evaluate the impact of varied hemodynamic scenarios (e.g., altered heart rate or vessel diameter) [66]. Similar frameworks apply to respiratory flows, where alveolar expansions vary among individuals and can dramatically affect ventilation efficiency [67]. PINN-based solvers or other surrogates can approximate 3D alveolar flow patterns in near real time, an avenue of research that may eventually guide mechanical ventilation settings in intensive care.

Nonetheless, there remain open questions about reliability and generalizability across a wide range of physiological conditions [68]. Ensuring consistent, physically realistic extrapolation outside the training domain is nontrivial. Researchers also explore hybrid frameworks, in which a classical PDE solver runs with local mesh adaptation, and machine learning surrogates fill in the "gaps" (e.g., sub-resolution RBC-laden flows or partial boundary conditions) [69]. Future work will likely focus on robust error bounds, interpretability, and HPC–machine learning code integration for exascale computing resources. [70, 71]

6. Conclusion

Over the past decade, numerical simulations of biofluid flows have undergone remarkable transformations, driven by advances in computational methodologies, numerical stability enhancements, and more sophisticated modeling of complex biophysical interactions. This review has highlighted key themes that define the current state of the field, underscoring the interplay between mathematical innovation, high-performance computing, and emerging data-driven approaches [72]. The discussion has outlined several crucial developments, ranging from high-order numerical methods to advanced boundary treatments, enhanced rheological models, multiscale frameworks, and machine learning accelerators [73]. While these innovations have significantly expanded the scope and accuracy of biofluid simulations, fundamental challenges remain, particularly in validation, multiphase interactions, and full-organ-scale modeling. This synthesis provides a deeper contextualization of these themes, situating them within the broader landscape of computational biofluid dynamics and identifying future research directions that may further propel the field forward [74].

A major advance in the numerical simulation of biofluids has been the adoption of high-order methods that enhance both accuracy and stability in capturing intricate flow structures. Discontinuous Galerkin (DG) and spectral element methods have proven particularly effective in resolving the fine-scale details of pulsatile and transitional flows characteristic of cardiovascular and respiratory systems [75]. The appeal of these methods lies in their spectral-like convergence properties, which allow for superior accuracy per degree of freedom compared to traditional finite-volume or finite-difference approaches [76]. However, their implementation comes with inherent challenges, particularly regarding numerical stability in high Reynolds number regimes. Recent developments in entropy-stable flux formulations and implicit large-eddy

simulation (ILES) techniques have mitigated many of these difficulties, allowing for stable high-fidelity computations at Reynolds numbers that were previously considered intractable [77]. These improvements have been instrumental in simulating turbulent blood flow in stenotic arteries, complex vascular bifurcations, and airway turbulence, providing new insights into pathological hemodynamics [78]. Despite these advances, further research is needed to balance computational cost and stability, especially for patient-specific simulations where high-order accuracy must be maintained over long physiological timescales.

Another crucial development in biofluid simulation is the improved handling of deformable and moving boundaries, which are essential for modeling dynamic biological structures such as heart valves, cilia, and cellular membranes [79]. Traditional mesh-based approaches struggle to accommodate large deformations without incurring excessive computational costs due to frequent mesh regeneration. Immersed boundary (IB) and fictitious domain methods have addressed this issue by allowing solid-fluid interactions to be modeled within a fixed computational grid, thereby circumventing the need for explicit remeshing [80]. These techniques have been particularly successful in simulating heart valve dynamics, where leaflet motion and fluid-structure interactions play a critical role in valve function and disease progression [81]. Additionally, penalty-based stabilization techniques and distributed Lagrange multipliers have enhanced the accuracy of IB methods, reducing spurious force artifacts that can arise at fluid-solid interfaces. This has been particularly relevant for applications requiring precise shear stress computations, such as studies on thrombosis initiation and atherosclerotic plaque formation [82, 83]. While these methods offer significant computational efficiency, ongoing research is required to improve their robustness in handling extreme deformations, thin flexible structures, and multi-scale interactions that emerge in biological flow systems.

In parallel with numerical advancements, the modeling of biofluid rheology has seen substantial progress, particularly in the simulation of non-Newtonian and viscoelastic effects [84]. Biological fluids, such as blood, synovial fluid, and mucus, exhibit complex rheological behaviors that cannot be accurately captured by Newtonian models [85]. Recent approaches leveraging log-conformation tensor methods have overcome numerical instabilities associated with high Weissenberg number flows, enabling more stable and accurate simulations of viscoelastic biofluids. This has been particularly impactful in modeling clot formation, where the interplay between shear-thinning behavior and fibrin network development necessitates a high-fidelity description of the underlying rheological properties [86]. Low-rank tensor decompositions have further extended the feasibility of large-scale 3D simulations by significantly reducing memory requirements, allowing for computationally feasible simulations of biofluids in clinically relevant geometries [87]. Nonetheless, challenges persist in coupling these complex rheological models with fluid-structure interaction frameworks and in parameterizing them based on experimental data. The extreme variability of biological materials, coupled with limited in vivo measurements, complicates the development of universally applicable rheological models [88]. Addressing these issues will require more extensive experimental validation and the integration of data-driven approaches that can infer model parameters from physiological measurements.

Beyond improvements in numerical and rheological modeling, the incorporation of multiscale and data-driven techniques has opened new avenues for bridging cellular and macroscopic flow scales [89]. Heterogeneous multiscale methods (HMMs) have facilitated localized fine-scale resolution within global continuum models, enabling detailed modeling of cellular and particulate dynamics without incurring prohibitive computational costs [90]. This has been particularly useful in simulating red blood cell aggregation, platelet adhesion, and microvascular transport, where fine-scale interactions significantly influence macroscopic flow behavior. Machine learning techniques have further augmented these multiscale approaches by providing surrogate models and reduced-order closures for computationally expensive microscale processes [91]. Physics-informed neural networks (PINNs) have emerged as a particularly promising tool for solving inverse problems, reconstructing unknown boundary conditions, and accelerating repeated or real-time simulations [92]. Despite these successes, challenges remain in ensuring the generalizability and interpretability of these data-driven models, particularly when extrapolating beyond their training datasets. The black-box nature of many machine learning approaches raises concerns about their reliability in critical biomedical applications, necessitating rigorous cross-validation and uncertainty quantification [93, 94]. Future research should focus on hybrid approaches that integrate machine learning with physically consistent modeling constraints to enhance robustness and reliability.

Despite these transformative developments, significant gaps persist in the field, particularly in experimental validation and the simulation of complex multiphase flows [95]. The scarcity of high-fidelity experimental benchmarks in realistic physiological conditions continues to pose a major obstacle to the validation of computational models [96]. While in vitro experiments provide valuable insights, they often fail to replicate the dynamic, three-dimensional, and heterogeneous nature of in vivo environments. Additionally, the extreme biological variability in tissue properties, fluid composition, and physiological responses complicates the development of universally applicable models [97]. Addressing this challenge requires a concerted effort to develop standardized datasets, advanced imaging techniques, and in situ validation methodologies that can provide more comprehensive benchmarks for computational models.

Another major challenge is the simulation of multiphase and multi-component flows, which are ubiquitous in biological systems but remain only partially addressed in current

numerical frameworks [98]. Examples include air-mucus interactions in pulmonary flows, red blood cell and platelet coupling in hemodynamics, and lipid-protein emulsions in digestive processes [99]. Accurately capturing these interactions requires advanced interface tracking methods, adaptive meshing strategies, and efficient coupling of disparate physical models. While recent advances in phase-field methods and volume-of-fluid techniques have improved multiphase modeling, challenges remain in achieving accurate interfacial dynamics, resolving nano-scale interactions, and maintaining computational tractability at organ-level scales [100]. The complexity of these flows demands further integration of high-performance computing, exascale simulations, and advanced numerical techniques capable of handling extreme disparity in spatial and temporal scales [101].

Lastly, the ultimate frontier in biofluid simulations lies in the integration of fluid dynamics with structural mechanics, electrophysiology, and biochemical signaling to create holistic models of organ function. While fluid-structure interaction (FSI) models have successfully captured aspects of cardiac and vascular biomechanics, their coupling with electrophysiological and biochemical transport models remains relatively underdeveloped [102]. The interplay between hemodynamics, myocardial electrophysiology, and metabolic processes is crucial for understanding pathophysiological conditions such as arrhythmias, heart failure, and stroke. Similarly, in pulmonary systems, the interaction between airway fluid dynamics, epithelial transport, and immune responses plays a critical role in diseases such as cystic fibrosis and chronic obstructive pulmonary disease (COPD) [103]. Addressing these challenges will require the development of multi-physics solvers, adaptive coupling strategies, and efficient computational frameworks that can handle the immense complexity of fully coupled biological systems [104]. Numerical simulations of biofluid flows have made extraordinary progress in recent years, with advancements in high-order numerical methods, improved boundary treatments, sophisticated rheological models, and multiscale frameworks expanding the frontiers of biomedical fluid dynamics. Machine learning and data-driven techniques are further accelerating progress, offering new ways to overcome computational bottlenecks and handle uncertain physiological conditions [105]. However, critical challenges remain, particularly in experimental validation, multiphase modeling, and whole-organ simulations. The next decade will likely witness further integration of these computational techniques with high-performance computing, multi-physics modeling, and real-time clinical applications, ultimately driving more accurate, predictive, and patient-specific biofluid simulations. [106]

References

[1] M. Khani, G. K. R. Burla, L. R. Sass, O. N. Arters, T. Xing, H. Wu, and B. A. Martin, "Human in silico trials for parametric computational fluid dynamics investigation of cerebrospinal fluid drug delivery: impact of injection location, injection protocol, and physiology.," *Fluids and barriers of the CNS*, vol. 19, pp. 8–, January 2022.

[2] D. D. Bueno, C. G. G. Bueno, and E. H. Dowell, "A modal approach for designing controllers for active flutter suppression," *Journal of the Brazilian Society of Mechanical Sciences and Engineering*, vol. 43, pp. 1–10, January 2021.

[3] O. O. Shobayo and D. K. Walters, "Statistically targeted forcing (stf) method for synthetic turbulence generation of initial conditions in three-dimensional turbulent mixing layer flow," in *Volume 1: Aerospace Engineering Division Joint Track; Computational Fluid Dynamics*, American Society of Mechanical Engineers, August 2021.

[4] J. Boustani, G. Kenway, F. Cadieux, M. F. Barad, C. Brehm, and C. C. Kiris, "Fluid-structure interaction simulations of the aspire sr01 supersonic parachute," in *AIAA SCITECH 2022 Forum*, American Institute of Aeronautics and Astronautics, January 2022.

[5] J. Liu, F. Luo, X. Lin, and T. Ye, "Cfd prediction with eulerian/eulerian approach of so 2 absorption from flue gases in bubble-dispersion tower," *Arabian Journal for Science and Engineering*, vol. 45, pp. 7621–7634, July 2020.

[6] S. Padhee, M. Johnson, H. Yi, Z. Yang, and T. Banerjee, "Machine learning for aiding blood flow velocity estimation based on angiography," September 2022.

[7] A. M. Aly, M. Thomas, and H. Gol-Zaroudi, "Experimental investigation of the aerodynamics of a large industrial building with parapet," *Advances in Aerodynamics*, vol. 3, pp. 1–22, September 2021.

[8] M. Khani, L. R. Sass, M. K. Sharp, A. McCabe, L. Z. Verbick, S. P. Lad, and B. A. Martin, "In vitro and numerical simulation of blood removal from cerebrospinal fluid: comparison of lumbar drain to neurapheresis therapy," *Fluids and barriers of the CNS*, vol. 17, pp. 1–17, March 2020.

[9] D. Canuto, J. L. Pantoja, J. Han, E. Dutson, and J. D. Eldredge, "An ensemble kalman filter approach to parameter estimation for patient-specific cardiovascular flow modeling," *Theoretical and Computational Fluid Dynamics*, vol. 34, pp. 521–544, April 2020.

[10] M. Bruschewski, C. Wüstenhagen, C. Domnick, R. Krewinkel, C.-C. Shiau, S. Grundmann, and J.-C. Han, "Assessment of the flow field and heat transfer in a vane cooling system using magnetic resonance velocimetry, thermochromic liquid crystals, and computational fluid dynamics," *Journal of Turbomachinery*, vol. 145, October 2022.

[11] K. C. Kalvakala, P. Pal, Y. Wu, G. Kukkadapu, C. P. Kolodziej, J. P. Gonzalez, M. U. Waqas, T. Lu, S. K. Aggarwal, and S. Som, "Numerical analysis of fuel effects

on advanced compression ignition using a virtual cooperative fuel research engine model," in *ASME 2020 Internal Combustion Engine Division Fall Technical Conference*, American Society of Mechanical Engineers, November 2020.

[12] D. J. Luna, N. K. R. Pandian, T. Mathur, J. Bui, P. V. Gadangi, V. V. Kostousov, S.-K. R. Hui, J. Teruya, and A. Jain, "Tortuosity-powered microfluidic device for assessment of thrombosis and antithrombotic therapy in whole blood," *Scientific reports*, vol. 10, pp. 5742–, April 2020.

[13] X. Bai, C. Ji, P. Grant, N. Phillips, U. Oza, E. Avital, and J. Williams, "Turbulent flow simulation of a single-blade magnus rotor," *Advances in Aerodynamics*, vol. 3, pp. 1–22, July 2021.

[14] A. Guelailia, A. Khorsi, S. A. Slimane, M. M. Bencherif, and K. Gourssma, "Numerical investigation on the effects of the deposit height and position on the film cooling efficiency," *Journal of Applied Mechanics and Technical Physics*, vol. 61, pp. 70–77, August 2020.

[15] J. Thomas, K. Sinha, G. Shivkumar, L. Cao, M. Funck, S. S. S, and N. K. Nere, "A cfd digital twin to understand miscible fluid blending," *AAPS PharmSciTech*, vol. 22, pp. 91–91, March 2021.

[16] D. Agarwal and G. Biros, "Numerical simulation of an extensible capsule using regularized stokes kernels and overset finite differences," *Journal of Computational Physics*, vol. 509, p. 113042, 2024.

[17] S. B. Keller, J. M. Bumpus, J. C. Gatenby, E. Yang, A. A. Kassim, C. Dampier, J. C. Gore, and A. K. W. Buck, "Characterizing intracranial hemodynamics in sickle cell anemia: Impact of patient-specific viscosity.," *Cardiovascular engineering and technology*, vol. 13, pp. 1–16, July 2021.

[18] P. Romatschke, "Simulating fluids, gases and everything in between.," *Nature computational science*, vol. 2, pp. 626–627, October 2022.

[19] D. Jude, J. Sitaraman, and A. Wissink, "An octree-based, cartesian navier–stokes solver for modern cluster architectures," *The Journal of Supercomputing*, vol. 78, pp. 11409–11440, February 2022.

[20] R. Huang, R. Zhang, Y. Wang, X. Luo, and L. Zhu, "Experimental and numerical investigations into flow features in an intake duct for the waterjet propulsion under mooring conditions," *Acta Mechanica Sinica*, vol. 37, pp. 826–843, May 2021.

[21] J. M. Gimenez, S. Idelsohn, E. Oñate, and R. Löhner, "A multiscale approach for the numerical simulation of turbulent flows with droplets.," *Archives of computational methods in engineering : state of the art reviews*, vol. 28, pp. 1–20, June 2021.

[22] V. Ramesh, S. Terala, S. Mazumder, G. Matharu, V. D. P, and S. K. Ali, "A reduced model for efficient simulation of freezing of water in large tanks," in *ASME 2020 Heat Transfer Summer Conference*, American Society of Mechanical Engineers, July 2020.

[23] E. Sundström and M. N. Tomac, "Aeroacoustic characteristics of a synchronized fluidic oscillator," *Flow, Turbulence and Combustion*, vol. 106, pp. 61–77, June 2020.

[24] E. M. del Castillo, A. H. F. Neto, and R. I. Borja, "Fault propagation and surface rupture in geologic materials with a meshfree continuum method," *Acta Geotechnica*, vol. 16, pp. 2463–2486, July 2021.

[25] S. K. Addepalli, M. Pamminger, R. Scarcelli, and T. Wallner, "Numerical investigation of the impact of spray – bowl interaction on thermal efficiency of a gasoline compression ignition engine," in *ASME 2021 Internal Combustion Engine Division Fall Technical Conference*, American Society of Mechanical Engineers, October 2021.

[26] Z. A. Wei and M. A. Fogel, "Engineering perspective on cardiovascular simulations of fontan hemodynamics: Where do we stand with a look towards clinical application.," *Cardiovascular engineering and technology*, vol. 12, pp. 1–13, June 2021.

[27] M. Muthuramalingam, D. K. Puckert, U. Rist, and C. Bruecker, "Transition delay using biomimetic fish scale arrays," *Scientific reports*, vol. 10, pp. 14534–, September 2020.

[28] C. C. McDougall, W. S. Hinman, C. T. Johansen, B. F. Bathel, J. A. Inman, and P. M. Danehy, "Evaluation of nitric oxide laser-induced fluorescence thermometry techniques in a hypersonic boundary layer," *Experiments in Fluids*, vol. 61, pp. 102–, March 2020.

[29] Y. Xia, P. Sharkey, S. Orsino, M. Kuron, F. R. Menter, I. Verma, R. E. Malecki, and B. A. Sen, "Stress-blended eddy simulation/flamelet generated manifold simulation of film-cooled surface heat transfer and near-wall reaction," *Journal of Turbomachinery*, vol. 143, December 2020.

[30] S. O. Fadlallah, T. N. Anderson, and R. J. Nates, "Artificial neural network–particle swarm optimization (ann-pso) approach for behaviour prediction and structural optimization of lightweight sandwich composite heliostats," *Arabian Journal for Science and Engineering*, vol. 46, pp. 12721–12742, September 2021.

[31] S. Basu, "Computational characterization of inhaled droplet transport to the nasopharynx.," *Scientific reports*, vol. 11, pp. 6652–6652, March 2021.

[32] J. Bagge, G. Biros, and D. Agarwal, "Gpu-accelerated simulation of deformable capsules flowing through a pipe," 2024.

[33] Y. Lai, K. Pan, J. Ha, C. Cai, J. Yang, P. Yin, J. Xu, and S. Park, "The optimal solution of reflow oven recipe based on physics-guided machine learning model," in *2022 21st IEEE Intersociety Conference on Thermal and Thermomechanical Phenomena in Electronic Systems (iTherm)*, pp. 1–6, IEEE, May 2022.

[34] H. Zhao, Z. Gao, F. Xu, and L. Xia, "Adaptive multi-fidelity sparse polynomial chaos-kriging metamodeling for global approximation of aerodynamic data," *Structural and Multidisciplinary Optimization*, vol. 64, pp. 829–858, April 2021.

[35] R. Vinuesa and S. L. Brunton, "Enhancing computational fluid dynamics with machine learning.," *Nature computational science*, vol. 2, pp. 358–366, June 2022.

[36] F. E. Rad, J. Abbasian, and H. Arastoopour, "Numerical simulation of co2 adsorption in a fluidized bed using solid-supported amine sorbent," *The Canadian Journal of Chemical Engineering*, vol. 99, pp. 1595–1606, February 2021.

[37] E. Kabir, H. Emadi, P. D. McElroy, F. Elldakli, and M. Young, "Optimizing seat and ball combination of actual gas lift valve: An experimental and cfd simulation study," in *Day 3 Thu, November 12, 2020*, SPE, November 2020.

[38] J. Li, A. Crivoi, X. Peng, L. Shen, Y. Pu, Z. Fan, and S. A. Cummer, "Three dimensional acoustic tweezers with vortex streaming," *Communications Physics*, vol. 4, pp. 1–8, June 2021.

[39] W. K. Law, K.-C. Wong, H. Wang, Z. Sun, and C. S. Lim, "Microstructure evolution in additively manufactured steel molds: A review," *Journal of Materials Engineering and Performance*, vol. 30, pp. 6389–6405, June 2021.

[40] E. Abobaker, A. Elsanoose, F. Khan, M. A. Rahman, A. Aborig, and S. Butt, "Comparison of crushed-zone skin factor for cased and perforated wells calculated with and without including a tip-crushed zone effect," *Geofluids*, vol. 2021, pp. 1–13, July 2021.

[41] G. Throneberry, A. Takeshita, C. M. Hocut, F. Shu, and A. Abdelkefi, "Multi-rotor wake characterization and visualization in ascending and descending flight," *Experiments in Fluids*, vol. 63, June 2022.

[42] Q. Xu, Y. Wan, Q. Wu, K. Xiao, W. Yu, S. Liang, Y. Zhu, H. Hou, B. Liu, J. Hu, Y. Yang, and J. Yang, "An efficient hydrodynamic-biokinetic model for the optimization of operational strategy applied in a full-scale oxidation ditch by cfd integrated with asm2," *Water research*, vol. 193, pp. 116888–116888, February 2021.

[43] J. Christopher, R. D. Falgout, J. B. Schroder, S. M. Guzik, and X. Gao, "A space-time parallel algorithm with adaptive mesh refinement for computational fluid dynamics," *Computing and Visualization in Science*, vol. 23, pp. 1–20, September 2020.

[44] S. Qu, W. Hu, S. Yuan, R. Yin, and R. Ji, "Optimal design and operation of thermally activated wall in the ultra-low energy buildings in china," *Building Simulation*, vol. 13, pp. 961–975, April 2020.

[45] J.-I. Shu, S. H. Hong, Y. Wang, and O. Baysal, "Surrogate- and possibility-based design optimization for convective polymerase chain reaction devices," *Microsystem Technologies*, vol. 27, pp. 2623–2638, August 2020.

[46] D. Agarwal and G. Biros, "Shape dynamics of a red blood cell in poiseuille flow," *Physical Review Fluids*, vol. 7, no. 9, p. 093602, 2022.

[47] X. Deng, G. Gong, S. Chen, X. He, Y. Ou, and Y. Wang, "Assessment of personal exposure to infectious contaminant under the effect of indoor air stability.," *Environmental science and pollution research international*, vol. 28, pp. 39322–39332, March 2021.

[48] Z. Zihan, C. Li, Y. Xiao, J. Wang, G. Hu, and K. Xiao, "Multiscale modelling of planetary boundary layer flow over complex terrain: implementation under near-neutral conditions," *Environmental Fluid Mechanics*, vol. 21, pp. 759–790, June 2021.

[49] S. E. Lindsey, I. E. Vignon-Clementel, and J. T. Butcher, "Assessing early cardiac outflow tract adaptive responses through combined experimental-computational manipulations," *Annals of biomedical engineering*, vol. 49, pp. 1–16, June 2021.

[50] A. R. Kumar, N. Gupta, and S. Schafrik, "Cfd modeling and laboratory studies of dust cleaning efficacy of an efficient four stage non-clogging impingement filter for flooded-bed dust scrubbers," *International Journal of Coal Science & Technology*, vol. 9, March 2022.

[51] Y. Pan, P. Tukkaraja, and S. J. Sridharan, "Investigation of gas and airflow distribution in a block cave mine," *Mining, Metallurgy & Exploration*, vol. 39, pp. 1821–1832, May 2022.

[52] S. L. Brunton, M. S. Hemati, and K. Taira, "Special issue on machine learning and data-driven methods in fluid dynamics," *Theoretical and Computational Fluid Dynamics*, vol. 34, pp. 333–337, August 2020.

[53] T. Nguyen, S. R. King, and Y. A. Hassan, "Experimental investigation of turbulent characteristics in pore-scale regions of porous media," *Experiments in Fluids*, vol. 62, pp. 1–27, March 2021.

[54] C. J. Akisin, C. J. Bennett, F. Venturi, H. Assadi, and T. Hussain, "Numerical and experimental analysis of the deformation behavior of cocrfenimn high entropy alloy particles onto various substrates during cold spraying," *Journal of Thermal Spray Technology*, vol. 31, pp. 1085–1111, April 2022.

[55] L. Wang, T. T. Allen, and M. A. Groeber, "Tabu efficient global optimization with applications in additive

manufacturing," *Structural and Multidisciplinary Optimization*, vol. 63, pp. 2811–2833, February 2021.

[56] Y. Liu, J. Cai, M. Sahimi, and C. Qin, "A study of the role of microfractures in counter-current spontaneous imbibition by lattice boltzmann simulation," *Transport in Porous Media*, vol. 133, pp. 313–332, May 2020.

[57] F. Yang, A. G. Stack, and V. Starchenko, "Micro-continuum approach for mineral precipitation.," *Scientific reports*, vol. 11, pp. 3495–3495, February 2021.

[58] F. S. Pereira, L. Eça, G. Vaz, and S. S. Girimaji, "Toward predictive rans and srs computations of turbulent external flows of practical interest," *Archives of Computational Methods in Engineering*, vol. 28, pp. 3953–4029, February 2021.

[59] M. Fang, Z.-H. Li, Z.-H. Li, J. Liang, and Y.-H. Zhang, "Dsmc modeling of rarefied ionization reactions and applications to hypervelocity spacecraft reentry flows," *Advances in Aerodynamics*, vol. 2, pp. 1–25, March 2020.

[60] J. P. Ewen, H. Spikes, and D. Dini, "Contributions of molecular dynamics simulations to elastohydrodynamic lubrication," *Tribology Letters*, vol. 69, pp. 1–15, February 2021.

[61] D. Agarwal, *Numerical Methods for Fast Simulation of a Red Blood Cell*. The University of Texas at Austin, 2022.

[62] J. Wackers, M. Visonneau, S. Ficini, R. Pellegrini, A. Serani, and M. Diez, "Adaptive n-fidelity metamodels for noisy cfd data," in *AIAA AVIATION 2020 FORUM*, American Institute of Aeronautics and Astronautics, June 2020.

[63] S. Kitayama, S. Hashimoto, M. Takano, Y. Yamazaki, Y. Kubo, and S. Aiba, "Multi-objective optimization for minimizing weldline and cycle time using variable injection velocity and variable pressure profile in plastic injection molding," *The International Journal of Advanced Manufacturing Technology*, vol. 107, pp. 3351–3361, April 2020.

[64] A. Sarhan, P. Naser, and J. Naser, "Covid-19 aerodynamic evaluation of social distancing in indoor environments, a numerical study.," *Journal of environmental health science & engineering*, vol. 19, pp. 1–10, October 2021.

[65] A. Abdelghany, D.-Q. Fan, and H. Y. Sohn, "Novel flash ironmaking technology based on iron ore concentrate and partial combustion of natural gas: A cfd study," *Metallurgical and Materials Transactions B*, vol. 51, pp. 2046–2056, July 2020.

[66] A. López, A. W. Bruno, and S. Nadimi, "Cfd modelling of the effect of capillary pressure on retention behaviour of water menisci at inter-particle contacts," *EPJ Web of Conferences*, vol. 249, pp. 09008–, June 2021.

[67] A. Zhang, X. Yu, Y. Zhang, and Y. Pei, "Numerical investigation of pre-chamber jet combustion in a light-duty gasoline engine," in *ASME 2020 Internal Combustion Engine Division Fall Technical Conference*, American Society of Mechanical Engineers, November 2020.

[68] Y. Xue, R. Hellmuth, and D.-H. Shin, "Formation of vortices in idealised branching vessels: A cfd benchmark study," *Cardiovascular engineering and technology*, vol. 11, pp. 544–559, July 2020.

[69] A. Tikadar and S. Kumar, "Machine learning approach to predict thermal-hydraulic performance of metal-foam heat sink," *SSRN Electronic Journal*, January 2022.

[70] H.-H. Lin, S.-J. Wu, T.-L. Liu, and K.-C. Pan, "Construction of the operating limits diagram for a ship-based helicopter using the design of experiments with computational intelligence techniques," *International Journal of Aeronautical and Space Sciences*, vol. 22, pp. 1–16, May 2020.

[71] D. Agarwal, M. OŃeil, and M. Rachh, "Fast multipole accelerated solvers for the laplace-beltrami problem in three dimensions," *arXiv preprint arXiv*, vol. 2111, 2021.

[72] L. Zhuang, P. Corkery, D. T. Lee, S. Lee, Kooshkbaghi, Z.-L. Xu, G. Dai, I. G. Kevrekidis, and M. Tsapatsis, "Numerical simulation of atomic layer deposition for thin deposit formation in a mesoporous substrate," *AIChE Journal*, vol. 67, May 2021.

[73] C. J. MacDonald, R. Hellmuth, L. Priba, E. A. Murphy, S. J. Gandy, S. Z. Matthew, R. Ross, and J. G. Houston, "Experimental assessment of two non-contrast mri sequences used for computational fluid dynamics: Investigation of consistency between techniques.," *Cardiovascular engineering and technology*, vol. 11, pp. 416–430, July 2020.

[74] M. N. Kaya, O. Uzol, D. Ingham, F. Köse, and R. Buyukzeren, "The aerodynamic effects of blade pitch angle on small horizontal axis wind turbines," *International Journal of Numerical Methods for Heat & Fluid Flow*, vol. 33, pp. 120–134, May 2022.

[75] T. Diurno, T. Fondelli, L. Nettis, N. Maceli, L. Arcangeli, A. Andreini, and B. Facchini, "Numerical investigation on the aerodynamic performance of a low-pressure steam turbine exhaust hood using design of experiment analysis," *Journal of Engineering for Gas Turbines and Power*, vol. 142, October 2020.

[76] D. Meerakaviyad, T. Keville, A. Prakash, A. Sajid, and F. Hamad, "Recent progress in multiphase flow simulation through multiphase pumps," *Heat Transfer*, vol. 49, pp. 2849–2867, April 2020.

[77] C. Liu, Z. Wang, C. Fan, R. Zhang, and X. Man, "A joint control strategy for automobile active grille shutter and cooling fan," *International Journal of Automotive Technology*, vol. 22, pp. 1675–1682, November 2021.

[78] N. Wagner, "Effect of process parameters on twin wire arc sprayed steel coatings," *Journal of Materials Engineering and Performance*, vol. 30, pp. 6650–6655, June 2021.

[79] S. A. Niknam, M. Mortazavi, and D. Li, "Additively manufactured heat exchangers: a review on opportunities and challenges," *The International Journal of Advanced Manufacturing Technology*, vol. 112, pp. 601–618, November 2020.

[80] F. Zagklavara, P. K. Jimack, N. Kapur, O. M. Querin, and H. M. Thompson, "Multi-objective optimisation of polymerase chain reaction continuous flow systems.," *Biomedical microdevices*, vol. 24, pp. 16–, March 2022.

[81] W. Zhang, Q. Pengbo, X. Zhang, K. Ma, L. Yin, and C. Li, "Rotordynamic characteristics of a novel pocket damper seal with self-regulated injection," *Journal of Mechanical Science and Technology*, vol. 35, pp. 3421–3434, July 2021.

[82] A. Schnepf, A. Carminati, M. A. Ahmed, M. Ani, P. Benard, J. Bentz, M. Bonkowski, M. Knott, D. Diehl, P. Duddek, E. Kröner, M. Javaux, M. Landl, E. Lehndorff, E. Lippold, A. Lieu, C. W. Mueller, E. Oburger, W. Otten, X. Portell, M. Phalempin, A. Prechtel, R. Schulz, J. Vanderborght, and D. Vetterlein, "Linking rhizosphere processes across scales: Opinion," *Plant and Soil*, vol. 478, pp. 5–42, January 2022.

[83] D. Agarwal and G. Biros, "3d vesicle microcirculation," in *APS Division of Fluid Dynamics Meeting Abstracts*, pp. M03–034, 2019.

[84] W. Xi, L. Niu, J. Song, and S. Liu, "Numerical simulation of flow field in large bottom-blown furnace under different scale-up criteria," *JOM*, vol. 75, pp. 437–447, December 2022.

[85] M. Duquesnoy, T. Lombardo, F. Caro, F. Haudiquez, A. C. Ngandjong, J. Xu, H. Oularbi, and A. A. Franco, "Functional data-driven framework for fast forecasting of electrode slurry rheology simulated by molecular dynamics," *npj Computational Materials*, vol. 8, July 2022.

[86] M. Bonfanti, G. Franzetti, S. Homer-Vanniasinkam, V. Díaz-Zuccarini, and S. Balabani, "A combined in vivo, in vitro, in silico approach for patient-specific haemodynamic studies of aortic dissection," *Annals of biomedical engineering*, vol. 48, pp. 2950–2964, September 2020.

[87] J. song Wang, D. Fan, and K. Lin, "A review on flow-induced vibration of offshore circular cylinders," *Journal of Hydrodynamics*, vol. 32, pp. 415–440, June 2020.

[88] M. Mohammadi, P. W. Tien, and J. K. Calautit, "Numerical evaluation of the use of vegetation as a shelterbelt for enhancing the wind and thermal comfort in peripheral and lateral-type skygardens in highrise buildings.," *Building simulation*, vol. 16, pp. 243–261, November 2022.

[89] T. F. L. Stephenson and C. Vogel, "Minimising turbine thrust variation in multi-rotor tidal fences," *Journal of Ocean Engineering and Marine Energy*, vol. 6, pp. 293–302, September 2020.

[90] Y. Qian, T. C. Chakraborty, J. Li, D. Li, C. He, C. Sarangi, F. Chen, X. Yang, and L. R. Leung, "Urbanization impact on regional climate and extreme weather: Current understanding, uncertainties, and future research directions.," *Advances in atmospheric sciences*, vol. 39, pp. 819–860, January 2022.

[91] S. Woodiga, K. Howard, P. Norman, N. Lewington, R. Carstairs, B. Hupertz, and K. Chalupa, "The gtu: A new realistic generic pickup truck and suv model," *SAE International Journal of Advances and Current Practices in Mobility*, vol. 2, pp. 1986–1998, April 2020.

[92] J. X. Huang and W. A. McMullan, "Mixing and combustion at low heat release in large eddy simulations of a reacting shear layer," *Theoretical and Computational Fluid Dynamics*, vol. 35, pp. 553–580, June 2021.

[93] S. M. Rahmati and A. Karimi, "A nonlinear cfd/multibody incremental-dynamic model for a constrained mechanism," *Applied Sciences*, vol. 11, pp. 1136–, January 2021.

[94] D. Agarwal and G. Biros, "Stable shapes of three-dimensional vesicles in unconfined and confined poiseuille flow," *Physical Review Fluids*, vol. 5, no. 1, p. 013603, 2020.

[95] R. Huang, "Finite strain modelling for multiphase flow in dual scale porous media during resin infusion process," *Journal of Engineering Mathematics*, vol. 127, pp. 5–, February 2021.

[96] Y. Yang and W. Zhan, "Role of tissue hydraulic permeability in convection-enhanced delivery of nanoparticle-encapsulated chemotherapy drugs to brain tumour.," *Pharmaceutical research*, vol. 39, pp. 877–892, April 2022.

[97] X. song Li, Q. tao Wu, L. ying Miao, Y. ying Yak, and C. Liu, "Scale-resolving simulations and investigations of the flow in a hydraulic retarder considering cavitation," *Journal of Zhejiang University-SCIENCE A*, vol. 21, pp. 817–833, October 2020.

[98] A. Mikszewski, L. Stabile, G. Buonanno, and L. Morawska, "The vaccination threshold for sars-cov-2 depends on the indoor setting and room ventilation," *BMC infectious diseases*, vol. 21, pp. 1193–, November 2021.

[99] M. Wengrove, A. Ebadi, C. White, and D. L. Foster, "Evaluation of the momentum integral method to determine the wall skin friction in separated flows," *Experiments in Fluids*, vol. 61, pp. 1–13, November 2020.

[100] B. Teoman, G. Marron, and A. Potanin, "Rheological characterization of flow inception of thixotropic yield

stress fluids using vane and t-bar geometries," *Rheologica Acta*, vol. 60, pp. 531–542, July 2021.

[101] P. Mahyawansi and C.-X. Lin, "An investigation of the effects of volume fraction on drag coefficient of non-spherical particles using pr-dns," in *Volume 1: Aerospace Engineering Division Joint Track; Computational Fluid Dynamics*, American Society of Mechanical Engineers, August 2021.

[102] R. Saunders, S. D. Johnson, D. Schwer, E. A. Patterson, H. Ryou, and E. P. Gorzkowski, "A self-consistent scheme for understanding particle impact and adhesion in the aerosol deposition process," *Journal of Thermal Spray Technology*, vol. 30, pp. 523–541, February 2021.

[103] M. Robertson, P. Newton, T. Chen, A. Costall, and R. Martinez-Botas, "Experimental and numerical study of supersonic non-ideal flows for organic rankine cycle applications," *Journal of Engineering for Gas Turbines and Power*, vol. 142, pp. 081007–, July 2020.

[104] A. Salavitabar and A. K. Armstrong, "Personalized interventions: A reality in the next 20 years or pie in the sky," *Pediatric cardiology*, vol. 41, pp. 486–502, March 2020.

[105] C. Perron, D. Sarojini, D. Rajaram, J. Corman, and D. Mavris, "Manifold alignment-based multi-fidelity reduced-order modeling applied to structural analysis," *Structural and Multidisciplinary Optimization*, vol. 65, August 2022.

[106] P. W. Longest, D. Farkas, A. Hassan, and M. Hindle, "Computational fluid dynamics (cfd) simulations of spray drying: Linking drying parameters with experimental aerosolization performance," *Pharmaceutical research*, vol. 37, pp. 1–20, May 2020.