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Universal Atrial Coordinate (UAC) for Wall Motion Deep Learning

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Abstract

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Atrial fibrillation (AF), the most common persistent arrhythmia, increases stroke risk through altered left atrial (LA) wall motion and blood stagnation in the left atrial appendage (LAA). Standard scores like CHA₂DS₂-VASc overlook patient-specific motion patterns, while AF's episodic nature and anatomical variability hinder consistent analysis. This thesis presents a standardized framework for left atrium (LA) wall motion analysis using 4D cardiac CT in both sinus rhythm (SR) and AF. LA geometries were segmented, temporally aligned via Coherent Point Drift (CPD) registration, and mapped to a 2D Universal Atrial Coordinate (UAC) system. Wall motion, quantified from Signed Distance Fields (SDF) and decomposed via fast Fourier transform (FFT), showed coordinated low-frequency contraction in SR and reduced amplitude with higher frequency content in AF. The framework enables anatomy-independent motion comparison and has the potential to predict AF signatures using SR data alone.

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Chapter 1: Introduction

1.1 Stroke and Its Clinical Burden

Stroke is one of the leading causes of mortality and long-term disability worldwide [1]. Often referred to as a "brain attack," it occurs when the blood supply to a region of the brain is interrupted, either due to an obstruction or the rupture of a blood vessel, disrupting the delivery of oxygen and essential nutrients to brain tissue. This deprivation triggers a cascade of cellular injury that can result in permanent neurological damage or death. In addition to direct ischemic injury, surrounding brain cells may suffer secondary damage from swelling, bleeding, or inflammation caused by the initial vascular event [2]. The brain is supplied by an extensive network of blood vessels, and a disruption in any region can have wide-ranging consequences. Since different parts of the brain control specific functions, the effects of a stroke vary depending on its type, location, and severity. Outcomes can range from mild and temporary to severe and permanent impairments.

Notably, some stroke risk factors are unique to women, primarily due to hormonal fluctuations associated with pregnancy, childbirth, and menopause. Although the annual incidence of stroke in women of childbearing age is relatively low (approximately 1 in 10,000), pregnancy increases this risk nearly threefold. This elevation is linked to increased blood clotting tendencies and complications such as infections, preeclampsia (hypertension with fluid retention), or underlying conditions like chronic hypertension and diabetes. The majority of pregnancy-related strokes occur in the early postpartum period, driven by sudden hormonal shifts and changes in blood volume. Similarly, menopause contributes to an elevated stroke risk, which emphasizes the value of recognizing gender-specific risk factors in stroke prevention and management [2].

Similar to a cardiac arrest, a stroke is a severe and extremely delicate medical emergency that requires prompt attention. Stroke was the second most common cause of death and the third most common cause of disability among NCDs in 2022, contributing to almost 7 million deaths worldwide, according to the Global Burden Disease (GBD), as illustrated in Figure 1.1. [3]

Stroke can be broadly classified into two main types: ischemic and hemorrhagic. As introduced earlier, ischemic stroke occurs when a blood vessel supplying the brain becomes blocked, typically due to a thrombus (a blood clot formed locally) or an embolus (a clot that travels from another part of the body). This obstruction reduces the delivery of blood and oxygen to brain tissue, leading to cellular injury and potentially irreversible damage. In contrast, hemorrhagic stroke results from the rupture of a weakened blood vessel, causing bleeding within or around the brain.

This accumulation of blood increases intracranial pressure, which can severely damage surrounding brain tissue and impair neurological function. Out of all stroke types, about 85% are ischemic strokes—caused by reduced or blocked blood flow to the brain [4]. This high prevalence provides a strong rationale for focusing the present study primarily on ischemic stroke.

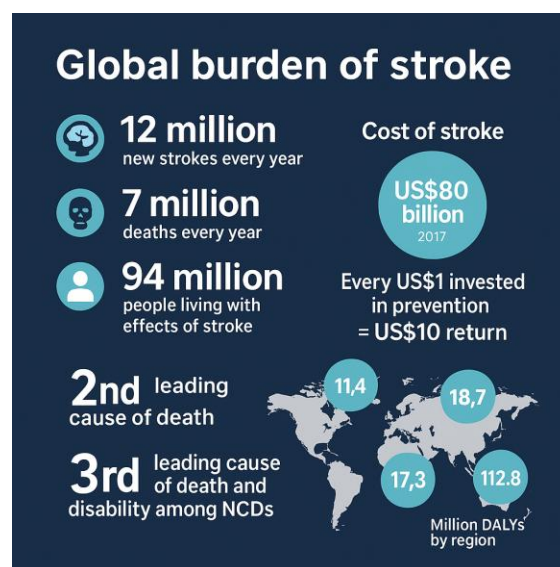


Figure 1.1: Leading causes of death worldwide due to stroke [3]

1.2 Role of Atrial Fibrillation in Stroke Risk

Atrial Fibrillation (AF) is the most prevalent sustained cardiac arrhythmia, affecting approximately 38 million individuals globally [5]. It originates in the atria, the upper chambers of the heart, particularly the left atrium (LA), and is characterized by disorganized and rapid electrical impulses. This erratic activity prevents the left atrial myocardium, the muscular wall of the LA, from contracting effectively, leading to a loss of coordinated atrial contraction. As a result, blood flow within the LA becomes turbulent and stagnant, especially in the left atrial appendage (LAA), a small, muscular, pouch-like extension located on the anterior wall of the LA. Due to its narrow neck and irregular structure, the LAA is especially prone to blood stasis, a major contributor to thrombus (clot) formation, consistent with Virchow's Triad: stasis, hypercoagulability, and endothelial injury (explained later) [6].

When a thrombus dislodges from the LAA, it may enter the systemic circulation through the left ventricle and subsequently travel via the aorta to the cerebral arteries, potentially causing a cardioembolic ischemic stroke. These strokes often involve large cerebral vessels, such as the middle cerebral artery (MCA), leading to sudden and severe neurological impairments [7].

Compared to strokes caused by large-artery atherosclerosis, where plaque buildup narrows extracranial or intracranial arteries, cardioembolic strokes are associated with greater infarct size, higher recurrence rates, increased disability, and elevated mortality [7], [8]. The anatomical relationship of AF in the LA, and the LAA is therefore of paramount importance in understanding stroke risk and guiding therapeutic interventions.

1.3 Electrical Dysfunction in AF: Sinoatrial Node and Rhythm Disruption

Before introducing Sinus Rhythm (SR) in detail, it is important to first understand the role of the sinoatrial (SA) node, as it serves as the heart's natural pacemaker and is fundamental to both the initiation of normal cardiac rhythm and the pathological deviations seen in AF.

As seen in Figure 1.2, the sinoatrial node is a specialized cluster of pacemaker cells situated in the right atrium's top wall, close to the intersection of the superior vena cava, a sizable vein that transports deoxygenated blood from the upper body to the heart. These pacemaker cells have the unusual capacity to produce action potentials, which are spontaneous electrical impulses that travel through the atria and cause them to contract, forcing blood into the ventricles [9]. In addition to pacemaker cells, the SA node also contains a variety of non-pacemaker cells, such as telocytes, peripheral glial cells, and interstitial cells. These cells might be involved in promoting intercellular communication and pacemaker activity. A strong internal regulation mechanism is demonstrated by the SA node's ability to produce action potentials without the assistance of external autonomic inputs [10].

This well-organized conduction system keeps the heart's regular rhythm, or SR, which normally ranges between 60 and 100 beats per minute, stable in a healthy heart [11]. However, this ordered procedure is disrupted by situations such as AF. Rapid and erratic electrical signals coming from several ectopic foci, especially in the vicinity of the LA's PV ostia, are a hallmark of AF. Particularly in the LAA, these chaotic impulses dominate the pacemaking activity of the SA node, resulting in inefficient atrial contractions and encouraging blood stasis [12]. Knowing the structure and function of the SA node is essential to understanding the pathophysiology of arrhythmias such as AF and emphasizes how vital it is to maintain SR for efficient cardiac function.

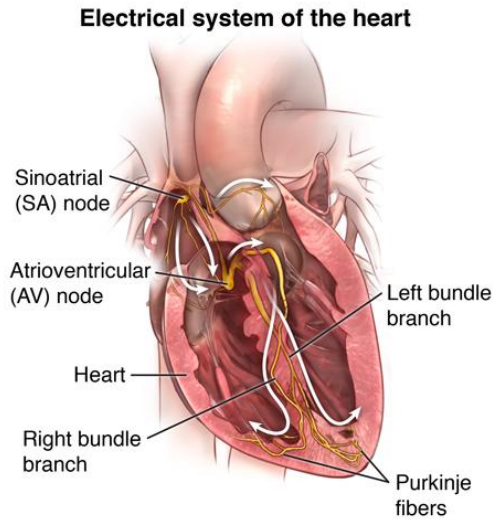


Figure 1.2 Electrical System of Heart [9]

Clinicians can recognize and distinguish between different heart rhythms by measuring the electrical activity of the atria using an electrocardiographic (ECG) diagnostic instrument. The ECG shows regular P waves in a healthy heart, i.e., during SR, with a P wave indicating atrial depolarization preceding each heartbeat. Normal conduction from the atria to the ventricles is indicated by the PR intervals, which show the time interval between the beginning of the P wave and the beginning of the QRS complex. A steady and regular heart rate is also shown by the constant R-R gaps between subsequent QRS complexes. Adults with these traits usually have a heart rate between 60 and 100 beats per minute. The absence of identifiable P waves and uneven R-R intervals during AF, on the other hand, indicate chaotic and disordered atrial activity as shown in Figure 1.3. The heart rate might vary greatly, and the QRS complexes happen at random times [13], [14].

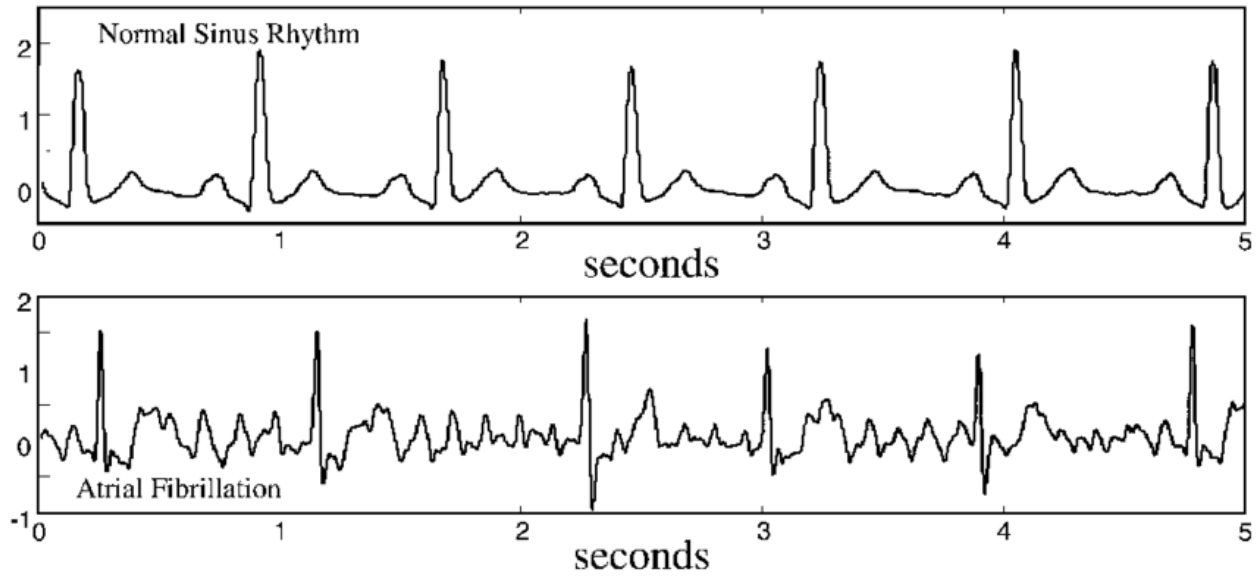


Figure 1.3 ECG of SR and AF [10]

1.4 Treatments for AF using Ablation

The most prevalent prolonged cardiac arrhythmia, AF, is linked to a higher risk of heart failure, stroke, and all-cause death [15]. According to studies, it greatly increases cardiac morbidity and fivefold the risk of stroke. Therefore, prompt and efficient therapy is crucial for both symptom management and averting long-term issues [17].

The treatment methods for AF can be broadly classified into three categories: rate control, rhythm control, and anticoagulation therapy [11]. Rate control focuses on managing the ventricular response using beta-blockers or calcium channel blockers, while rhythm control attempts to restore and maintain SR through drugs, cardioversion, or ablation [12]. Stroke prevention with anticoagulants—typically direct oral anticoagulants (DOACs) or warfarin—remains the cornerstone for patients with high-risk stratification scores.

Among rhythm control options, catheter ablation has become particularly popular. The procedure involves electrically isolating arrhythmogenic foci—most commonly localized at ostia of the

pulmonary veins (PVs)—from the rest of the LA structure. Figure 1.4. The cornerstone of modern ablation is pulmonary vein isolation (PVI), which prevents ectopic PV activity from initiating reentrant circuits responsible for AF. The consistency and safety of the procedure have improved due to advances in electroanatomic mapping systems, real-time imaging (e.g., intracardiac echocardiography), and energy modulation techniques [13].

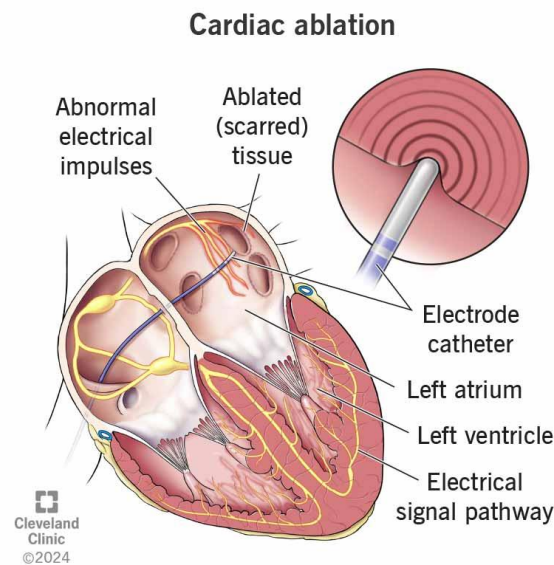


Figure 1.4 Catheter Ablation [13]

Success rates for catheter ablation are highly encouraging, with single-procedure freedom from AF approaching 70-80% and multiple-procedure outcomes exceeding 90% in experienced centers. Catheter ablation, by directly targeting the electrophysiological substrate of AF, circumvents these issues and offers the potential for a durable cure in appropriately selected patients [13].

Ablation is important in this investigation because it offers a unique opportunity to acquire imaging data from the same patient in both AF and SR. This paired dataset minimizes the confounding effects of inter-patient anatomical heterogeneity while allowing for direct, patient-specific assessment of wall motion patterns across beats.

1.5 Current Risk Stratification: CHA₂DS₂VASc

AF patients are typically diagnosed with anticoagulation therapy to reduce the clotting risk [14]. However, anticoagulation treatment itself carries significant risks, most notably an increased risk of bleeding complications, including gastrointestinal bleeding and intracranial hemorrhage [15]. The challenge in clinical practice, therefore, lies in balancing the benefit of stroke prevention against the risk of serious events.

Given this therapeutic dilemma, there is a critical need for a reliable metric that can predict an individual's risk of thromboembolism and guide anticoagulation decisions. Current tools, such as the CHA₂DS₂ – VASc score, aim to fulfill this need by providing a standardized method to stratify patients based on clinical risk factors. However, these tools are primarily statistical and epidemiological, relying on the presence of comorbidities rather than direct mechanistic insights into clot formation [14], [15], [16].

A popular scoring method for determining a patient's risk of stroke in the setting of AF is the CHA₂DS₂-VASc score [21]. The acronym represents: Congestive heart failure, hypertension, age ≥ 75 years, diabetes, prior stroke or TIA, vascular disease, age 65–74 years, and sex category (female) are all represented by the acronym CHA₂DS₂-VASc. Decisions about the start of anticoagulation are guided by the total score, which is calculated by giving each component a defined weight. Clinicians calculate the patient's yearly risk of stroke based on their CHA₂DS₂-VASc score, and if the score is higher than the specified threshold, they suggest anticoagulation. Patients classified as high-risk by this scoring method have been shown to benefit from anticoagulation medications like warfarin and DOACs. Nevertheless, the CHA₂DS₂-VASc score has significant limitations in spite of its widespread acceptance. Atria-specific biological and

anatomical data, such as the degree of atrial remodeling, fibrosis, or other pathophysiological alterations that are known to increase the risk of thrombus formation, are not included.

Emerging evidence suggests that many CHA₂DS₂-VASc components are not only associated with increased stroke risk statistically, but are also linked to biological changes in atrial tissue, particularly fibrosis. For instance, congestive heart failure ('C') promotes fibrotic remodeling of the myocardium, creating a substrate for AF. Similarly, stroke history ('S₂'), increasing age ('A₂', 'A'), and female sex ('Sc') correlate with more extensive fibrosis. This fibrotic remodeling not only facilitates AF persistence but also promotes blood stasis and thrombus formation, offering a potential mechanistic bridge between clinical risk factors and biological thromboembolic propensity. Thus, while the CHA₂DS₂-VASc score remains a cornerstone for clinical risk assessment, integrating biological markers like atrial fibrosis quantification may enhance future models, allowing for a more personalized and mechanistic prediction of stroke risk in AF patients [17], [18], [19], [20].

Many studies indicate that fibrosis is related to AF and increases stroke risk [17], [21], [22]. Nevertheless, clinical scoring systems do not factor in fibrosis when evaluating a patient's risk. One reason fibrosis is not included is that measuring it typically needs advanced imaging, such as MRI with late gadolinium enhancement, which is not routinely done in all patients. Another reason could be that scientists don't fully understand how fibrosis leads to clot (thrombus) formation in the atria. The relationship is recognized, but the exact mechanisms are unclear. In fibrotic regions, the normal heart muscle cells (cardiomyocytes) are replaced with scar-like tissue or excess extracellular matrix. This causes changes in the electrical signal travelling through the heart and also changes the heart tissue mechanically [28]. The tissue becomes stiffer and hypercontractile, reducing the heart's ability to pump blood smoothly [31]. When fibrosis impairs how well tissue

moves, it leads to sluggish blood flow in certain areas. This can increase the risk of thrombosis. Although these effects are observable, we don't know how much each individual factor (e.g., stiffness, electrical delay, loss of contraction) contributes to clot risk. We also lack knowledge to fully understand how fibrosis-induced changes in muscle movement affect hemodynamics in the atria, especially in a mechanistic, patient-specific way [25].

1.6 Virchow's Triad in AF

As mentioned earlier, the CHA₂DS₂-VASc score is an effective tool to estimate stroke risk in patients with AF; however, it is only based on clinical comorbidities and not directly on mechanistic insights like blood hypercoagulability, fibrosis, or endothelial injury. It does not capture the actual biological changes happening in the atrium due to AF. According to Ding et al. [26] AF leads to a prothrombotic (promoting blood clot) state by fulfilling conditions of Virchow's Triad: hypercoagulability (abnormal blood constituents), endothelial injury (vessel wall abnormalities) and blood stasis (abnormal blood flow). Figure 1.5. AF alone (even without other diseases) can create a prothrombotic environment. Short episodes of AF can trigger platelet activation and thrombin generation. AF and endothelial dysfunction strongly contribute to clot formation. Reduced blood flow in the atria during AF further promotes clot risk, seen as spontaneous echo contrast in echocardiography.

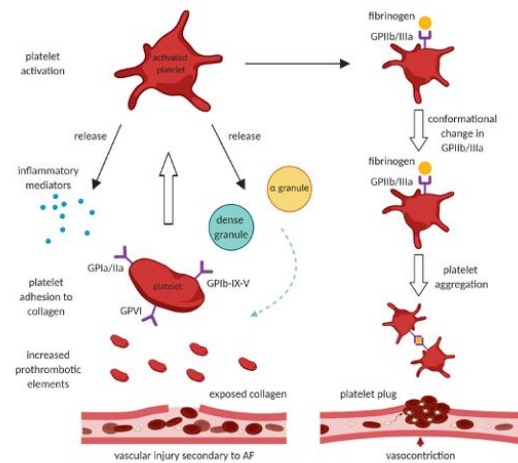
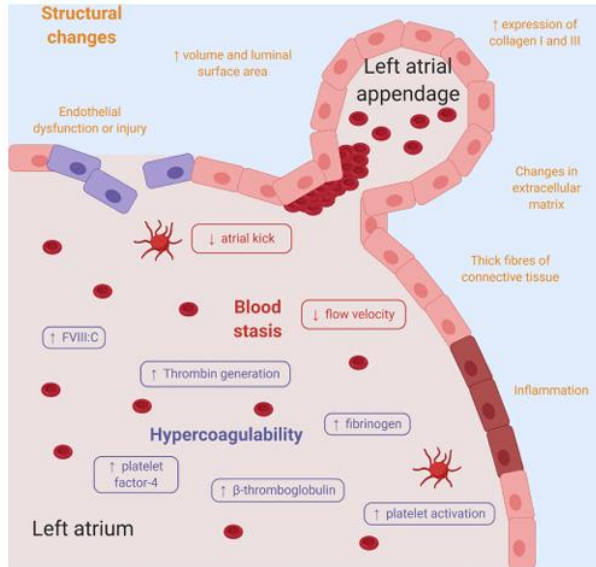


Figure 2 Interaction between vascular injury in atrial fibrillation and the initiation of clot formation in the presence of increased prothrombotic elements.

Figure 1.5 Virchow's Triad [26]

Ding et al. [26] explain that vascular injury in AF triggers clot formation. The atrial wall, when damaged (structural remodeling, fibrosis, endothelial dysfunction), exposes collagen underneath the endothelium, acting like a “sticky trap” for platelets. These activated platelets release dense granules and alpha granules that amplify clotting and release inflammatory mediators. This local inflammation makes blood even more prone to clotting.

Blood stasis represents the final component of Virchow’s Triad and plays a major role in thrombus formation as a direct consequence of AF. The reduction in blood flow can appear on echocardiography as an echogenic, smoke-like swirl within the atria. This sluggish flow results from atrial dilation, increased fibrosis, and the loss of effective atrial systole. Additionally, MRI studies have demonstrated that AF is associated with decreased mean and peak left atrial (LA) flow velocities, along with increased blood stasis within the LA.

1.7 Computational Methods for AF Risk Assessment

Instead of depending just on universal risk factors, there is a strong therapeutic need to move toward individualized care based on patient-specific cardiac activity. Despite extensive demographic studies showing a high correlation between AF and stroke, little is known about the underlying molecular mechanisms, including thrombus development and fibrosis [27]. The ability of contemporary imaging methods (such as LGE-MRI and CT scans) to detect and measure atrial fibrosis allows researchers to investigate the relationship between atrial fibrosis, hemodynamic thrombosis, and AF. Improving stroke prediction relies heavily on this relationship. Since studying the effects of electrical conduction and fibrosis in live patients or animal models is dangerous or impractical, computational simulations provide a potent substitute by combining multiple physics domains, including fluid dynamics, tissue mechanics, and electrophysiology, to precisely and safely study these conditions in detail. Researchers can monitor the evolution of physiological processes thanks to the spatial and temporal data generated by these models. This makes it possible to precisely analyze electrical signal propagation, tissue mechanics, and blood flow [25]. Numerous research teams have developed integrated 3D models that more accurately replicate human cardiac activity by combining hemodynamic and electromechanical computational frameworks. Electrical activity, tissue contraction, and hemodynamics are all simulated using different mathematical techniques. There are various methods for linking these systems, including strong (complete) coupling and loose (weak) coupling. Although loose coupling requires less computing power, its precision is lower. Strong coupling, on the other hand, guarantees tighter system integration, leading to more realistic simulations at the penalty of higher computational costs. The anatomical geometry of these models varies as well; they include representations that are idealized, realistic, and image-based. While realistic models are physically precise but not patient-specific, idealized models make use of simplified geometric shapes. The greatest degree of

customization for subject-specific simulations is provided by image-based models, which are based on real patient scans [28], [29].

A 3D multiscale, multi-physics model of the left ventricle that combines fluid dynamics, tissue mechanics, and electrical activity was first developed by Watanabe et al. [30]. The model's accuracy in simulating genuine blood pressure and aortic flow patterns served as validation. Later, this work was improved to create UT-Heart, a comprehensive solver that uses a monolithic model with tight couplings across all physical domains. Applications of UT-Heart include cardiac resynchronization therapy, a treatment for heart failure, and surgical planning [31]. The first full-heart simulation was carried out by Vigmond et al. [32] to examine how bundle branch blocks affect valve flow dynamics, cardiac pumping efficiency, and myocardial cell response to mechanical stretching. Multi-physics computational models of simplified left ventricles were first shown by Quarteroni et al. [33] and progressively enhanced to replicate accurate left and entire heart anatomy. This illustrates how theoretical or idealized models give way to realistic, patient-specific anatomy. In order to examine how AF and valve leakage impact blood flow in the LA and LAA, all of which are crucial for clot formation and stroke risk, Feng et al. [34] examined the combined effects of the mitral valve and LA. Using anatomy taken from a medical atlas, Viola et al. [35] presented a computational solution that combines fluid–structure interaction with electrophysiology. This work was then expanded by Bucelli et al. [36], who ran simulations on a statistically averaged left heart model. Choi et al. [37] created electromechanical and blood flow models using MRI data from canine hearts. They demonstrated how diseased situations change flow patterns by comparing heart failure cases with healthy hearts using these models. A digital twin, a highly realistic, patient-specific simulation of the human heart, was provided by Viola et

al. [38], [39] in their most recent work. This model is used to investigate the effects of electrical diseases, like left bundle branch block, on cardiac function.

There are many significant advances that simulate electrophysiology, mechanics, and hemodynamics, but almost none have considered how fibrosis—the stiffening of heart tissue—affects blood flow inside the heart. Only one simulation study incorporated fibrotic effects on intracardiac flow. Paliwal et al. [40] employed computational fluid dynamics (CFD) to investigate the impact of fibrosis on hemodynamic patterns in the LA. Their study revealed that patients with greater fibrotic burden exhibited abnormal flow characteristics, including reduced flow velocities and elevated thrombotic markers such as low wall shear stress. These findings are significant, as they establish a direct link between atrial fibrosis and increased thrombotic risk. However, their model did not explicitly simulate left atrial (LA) motion resulting from fibrosis. Instead, it employed an idealized approximation by varying the LA volume over time, without incorporating localized stiffening or contractile impairment caused by fibrotic remodeling. While the study provided valuable insights, it did not capture the complex, region-specific mechanical effects of fibrosis on atrial biomechanics.

In a significant advancement towards personalized cardiac modelling, Gonzalo et al. [41] present a multi-physics, multi-scale computational framework that couples electrophysiology (EP), myocardial biomechanics, and CFD to analyze the hemodynamic impact on atrial fibrosis. The authors applied this framework to simulate LA contraction in four subjects with varying degrees of fibrotic remodeling. The simulations revealed that subjects with higher fibrosis burden exhibited greater impairment in atrial wall motion, which led to reduced emptying fractions (EF) in both the LA and LAA. This reduced EF corresponded to lower kinetic energy within the LAA and hence increased the risk of thrombosis.

To deepen mechanistic insight, they also introduced a methodology to isolate the effects of tissue stiffening and loss of contractility due to fibrosis, both individually and in combination. This allowed the researchers to distinguish how each component contributes to the observed biomechanical and hemodynamic disturbances. Overall, it represented an important step towards developing patient-specific atrial models that account for regional myocardial structure and function with the potential to support clinical decision-making and guide therapeutic strategies.

1.8 Aim of the Project

The primary aim of this research is to establish a standardized and interpretable framework for the analysis and comparison of left atrial (LA) wall motion among patients in SR and AF. Considering that AF is an episodic disorder and clinical imaging frequently records patients in SR, there is a necessity for techniques that may derive patient-specific motion signatures and correlate them with AF-related changes. This system aims to address the difficulties associated with significant anatomical diversity and extensive, intricate CFD datasets, facilitating uniform analysis and the training of machine learning (ML) models.

A primary goal is to develop a Universal Atrial Coordinate (UAC) system that facilitates the projection of three-dimensional left atrial motion data onto a standardized two-dimensional parameter space. This mapping diminishes geometric variability among patients and establishes a unified framework for region-specific motion analysis. The methodology guarantees the preservation of both anatomical and functional integrity in the analysis pipeline through precise segmentation, superior meshing, temporal alignment, and motion quantification based on Signed Distance Fields (SDF).

The study ultimately seeks to facilitate accurate detection and comparison of rhythm-specific motion patterns, hence enabling predictive modeling of AF signatures from SR data. This work establishes a platform for future applications in patient-specific risk assessment, treatment planning, and extensive multimodal studies by developing an ML-ready dataset that amalgamates anatomical and functional information, including hemodynamic and electrophysiological characteristics.

Chapter 2: Methodology

In the previous chapter, we discussed the elevated risk of ischemic stroke associated with AF and introduced various clinical and imaging-based metrics commonly used for AF diagnosis and risk stratification. While these metrics, such as the CHA₂DS₂-VASc score, LA volume index, and flow-based assessments—offer useful insights, they exhibit several limitations, including insufficient patient specificity and limited sensitivity to dynamic hemodynamic changes. To address these shortcomings, recent advancements have leveraged computational approaches, particularly CFD, patient-specific atrial modeling, and atrial structural remodeling. These methods provide high-resolution spatial and temporal analyses of blood flow, wall motion, and thrombus formation risk.

However, one of the major obstacles in translating such simulations into clinical practice lies in handling anatomical variability—both between different patients and within the same patient under varying cardiac rhythms (e.g., SR vs. AF). This variability complicates model standardization and hinders meaningful cross-patient comparisons of simulated hemodynamics.

To mitigate this issue, Roney et al. [42] introduced the Universal Atrial Coordinate (UAC) system—a standardized framework that maps complex three-dimensional atrial anatomy onto a common two-dimensional coordinate system defined by α (alpha) and β (beta) axes. This geometric mapping allows for consistent visualization and direct comparison of flow features, wall motion, and structural metrics across patient-specific atrial models. The UAC framework builds upon the earlier Universal Ventricular Coordinate (UVC) system proposed by Bayer et al., which employed a similar approach for ventricular anatomy. By reducing inter- and intra-patient anatomical differences, UAC significantly improves the generalizability and interpretability of computational results across diverse atrial geometries.

In our approach, we integrate CFD with the UAC system to create a unified framework for visualizing and classifying patients in SR and AF. This framework not only enables detailed analysis of atrial flow and motion patterns but also standardizes data across anatomically diverse patients. The final goal is to develop a dataset that feeds into a deep learning model capable of predicting AF using only SR data, as outlined in later sections of Chapter 1. In this study, we acquired data from three patients, each recorded in both SR and AF states.

The adopted workflow is as follows:

- **Patient Imaging Data Acquisition:** Time-resolved cardiac CT scans of patients in both AF and SR (post-ablation) are used as the starting point. These scans capture dynamic changes in atrial geometry across the cardiac cycle.
- **Patient-Specific Model Generation:** The left atrial geometry is segmented from the imaging data to generate 3D anatomical models that capture individualized atrial structure for each patient and time frame.
- **Wall Motion Tracking:** Atrial wall motion is extracted by tracking surface displacements over time. This motion is critical for assessing mechanical function and wall-induced flow effects.
- **Boundary Condition Specification:** Inflow and outflow conditions, such as PV velocities and mitral valve profiles, are defined based on clinical measurements or estimated from imaging data. These serve as inputs for the CFD solver.
- **CFD Simulation:** Blood flow within the patient-specific atrial geometry is simulated using CFD to compute spatial and temporal velocity fields, pressure distributions, vorticity, and residence time (RT).

- **UAC:** Mapping the 3D atrial surfaces and associated flow features are projected onto a standardized 2D (α - β) domain using the UAC system. This enables consistent comparison across patients by aligning anatomical landmarks and minimizing variability.
- **SDF Computation:** SDFs are computed to describe the spatial proximity of internal points to the atrial wall, assisting in tracking wall motion, identifying interior flow patterns, and interpolating values across domains.
- **Data Analysis and Structuring:** All features—including wall motion and velocity—are interpolated onto the UAC grid and organized into a structured dataset. These feature maps are used to classify patients into SR or AF states and serve as inputs for training deep learning models focused on AF prediction using only SR-derived data.

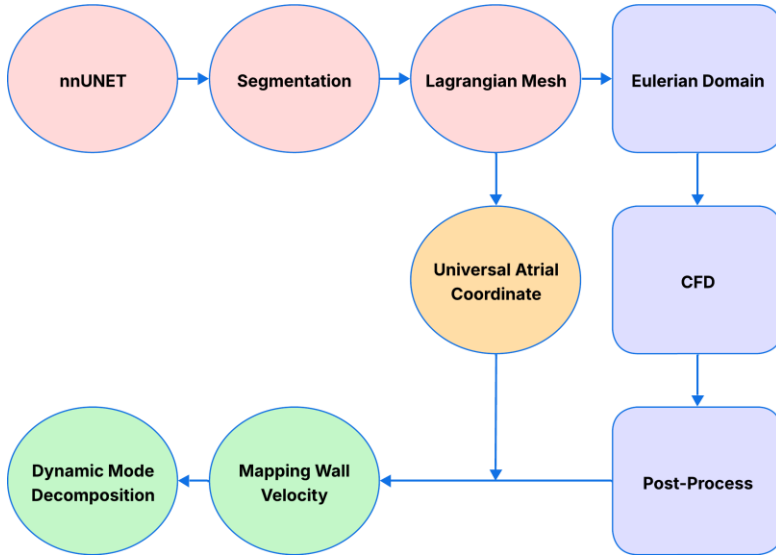


Figure 2.1: General outlined followed in this study

2.1 Segmentation Methodology Using nnU-Net and ITK-SNAP

U-Net is a type of convolutional neural network designed for image segmentation, especially in medical imaging. It has a U-shaped structure with two parts: an encoder that captures important

features from the input image and a decoder that uses those features to create a segmentation mask. This helps automatically identify and separate regions of interest in medical images, reducing the time and effort needed for manual segmentation.

nnU-Net (short for "no-new-Net") is a software framework that builds on U-Net and automatically adjusts itself to work with different types of medical image datasets. It selects the best version of U-Net (2D, 3D, or a combination) and sets up all the steps—such as image resizing, training, and final prediction—based on the data it receives. The entire process is automatic and does not need manual setup [43]. Since the technical details of nnU-Net are not the focus of this thesis, a detailed explanation is beyond its scope. Here, it is simply used as a reliable tool for medical image segmentation.

Although nnU-Net provides a robust and self-configuring framework for biomedical image segmentation, it is not entirely free from limitations. In certain cases, the generated segmentation masks may exhibit artifacts, such as discontinuities, holes, or incomplete boundary definitions, particularly in anatomically complex or low-contrast regions. Workflows that use the output to construct patient-specific anatomical meshes for simulations or structural analysis critically concern these segmentation imperfections. If not addressed properly, such artifacts can lead to the generation of irregular or non-manifold surface meshes, which in turn may degrade the quality of CFD simulations, wall motion tracking, or surface-based coordinate mapping (such as the UAC system). Low-quality meshes can introduce numerical instabilities, distort geometric features, and ultimately compromise the accuracy and reliability of hemodynamic predictions.

Therefore, all segmentation outputs require manual inspection and quality control, and in some cases, post-processing corrections such as morphological operations, hole-filling, or mesh

smoothing must be applied. To ensure high-quality segmentation suitable for mesh generation and simulation, we employed ITK-SNAP, an open-source software widely used for medical image segmentation. Anatomical structures of the LA were manually segmented based on geometric type and functional relevance. Distinct anatomical regions were assigned unique color labels to assist in identification and processing during meshing.

The temporal alignment of anatomical boundaries is a crucial factor in this process, especially at crucial intersections like the PV inlets, MV annulus, and LAA base. The boundary edges of these regions need to be topologically and geometrically matched over successive frames in order for surface mesh registration to be reliable and consistent. When one frame has more or fewer surface elements than the next, misalignment in these areas may result in non-physical deformations, surface folding, or discontinuities in the calculated wall motion. Consequently, this impairs the precision of CFD simulations' residence time computations, wall shear stress measurement, and velocity interpolation.

2.2 Mesh Generation Pipeline

After completing manual segmentations for a given patient across all time points of the cardiac cycle, the next phase involves generating a Lagrangian surface mesh using MATLAB that accurately represents the dynamic motion of the LA. These segmentations—labeling the LA body, PVs, MV, and LAA—serve as the foundation for building time-resolved anatomical models. To ensure geometric consistency and continuity across frames, the segmented volumes are first smoothed using a 4D Gaussian filter. This step significantly reduces noise and temporal artifacts that could otherwise result in poor mesh quality. The resulting Lagrangian mesh sequence is used

for immersed boundary CFD simulations, allowing blood flow to be simulated within a moving wall domain. By capturing surface motion across the entire cardiac cycle, this mesh enables detailed analysis of intra-atrial flow dynamics, wall shear stress, residence time, and other physiologically relevant metrics. The Lagrangian mesh is thus a critical output of the pipeline, bridging medical imaging with simulation-based analysis.

2.2.1 Smoothing

The first and most critical preprocessing step before generating a Lagrangian mesh is segmentation smoothing. This stage is essential for eliminating noise, artifacts, and discontinuities commonly present in raw volumetric segmentations, particularly those created manually. In this project, smoothing is performed using a four-dimensional Gaussian filter with a stencil size of $[N, N, N, T]$ —where the first three dimensions correspond to spatial axes (x, y, z) and the fourth (T) to time. The Gaussian smoothing is combined with a level-set method to further refine boundary surfaces, ensuring that anatomical regions are both geometrically accurate and topologically clean across time. The primary goal of this smoothing step is to produce a consistent and high-quality representation of anatomical boundaries throughout the entire cardiac cycle. This is especially important for time-resolved CT data, where any frame-to-frame inconsistency can lead to significant errors in downstream mesh generation, wall motion tracking, or CFD simulations. By applying smoothing across all time frames, the method ensures that anatomical changes—such as the expansion and contraction of the LA—are captured smoothly and continuously.

2.2.2 Surface Meshing

After segmentation volumes are smoothed across all time frames, the next major step in the LA motion analysis pipeline is surface meshing. This process converts voxel-based segmentation data

into a continuous triangular mesh representation, enabling geometry-based motion tracking, CFD simulations, and biomechanical analysis.

A reference frame, typically the one with the largest LA volume, is selected, as it generally represents the most expanded and structurally well-defined geometry. This frame serves as a stable baseline for subsequent steps such as mesh registration. A triangular surface mesh is then extracted from each frame using iso-surface extraction algorithms such as marching cubes.

The raw meshes are post-processed to improve quality. Key steps include smoothing to remove voxelization artifacts, vertex reduction to optimize computational efficiency, and boundary conditioning to maintain smooth, planar openings at anatomical junctions like the PVs and MV.

Two important parameters govern this step:

1. **Mesh Keep Ratio** – controls how much of the original mesh detail is retained after simplification.
2. **Face Cylinder Threshold**—determines how strictly PV and MV openings are forced into a circular, planar shape.

Table 2.1: Key parameters for surface meshing and their practical guidelines

Parameter	Role in Meshing	Rule of Thumb	Impact of Increasing Value	Impact of Decreasing Value
Mesh Keep Ratio	Controls the percentage of original mesh vertices retained after simplification, balancing anatomical detail with computational efficiency.	Higher values preserve more detail but increase mesh size; lower values reduce file size but may lose fine geometry.	Preserves fine anatomical features and improves simulation fidelity but increases processing/memory cost.	Produces lighter meshes and faster processing but risks loss of clinically relevant detail.
Face Cylinder Threshold	Controls how strictly openings at PVs and MV are fitted to circular, planar shapes during boundary conditioning.	Decrease if openings are jagged/irregular; increase if over-constrained or distorted.	Allows more natural, relaxed fitting for irregular or noisy segmentations.	It produces tighter, more circular openings, which are useful for clean and regular boundary conditions.

2.2.3 Registration of Meshes Across Time Frames

Once surface meshes have been generated for each frame of the cardiac cycle, the next crucial step is registration. This refers to the process of establishing spatial correspondence between meshes over time—specifically, mapping how each anatomical point on the left atrial (LA) surface deforms throughout the cardiac cycle. Although each frame provides an accurate snapshot of LA at a given moment, the meshes are not naturally linked across time. Without registration, there is no assurance that a point on the LA surface in frame i corresponds to the same anatomical location in frame $i+1$. This lack of continuity makes it impossible to compute smooth wall motion, displacement, and velocity or to apply consistent boundary conditions in CFD simulations. To address this, the pipeline performs registration using a combination of Coherent Point Drift (CPD) for non-rigid alignment, spline interpolation for temporal smoothing, and Fourier decomposition to ensure physiologically realistic motion over the cardiac cycle.

2.3.3.1 Coherent Point Drift

Coherent Point Drift (CPD) is a probabilistic technique designed for non-rigid point set registration, aiming to align a template point set with a reference set that may have experienced intricate, nonlinear deformations [44]. CPD represents the template point set as the centroids of a Gaussian Mixture Model (GMM) and considers the reference points as samples extracted from this distribution. The registration is formulated as a Maximum Likelihood (ML) estimation problem, where the template points are iteratively adjusted to optimize the likelihood of the reference data under the GMM, constrained by a smoothness condition that promotes coherent motion. In contrast to conventional rigid or affine registration techniques, CPD accommodates

highly flexible non-rigid deformations such as stretching, bending, and warping, without requiring an explicitly defined transformation model like thin-plate splines. Instead, CPD enforces spatial smoothness through a motion coherence constraint derived from the Motion Coherence Theory (MCT), which assumes that neighboring points tend to move in a coordinated, smooth, and physically plausible manner. This constraint is implemented by regularizing the velocity field of the transformation using a variational approach, resulting in a kernel-based motion field where each template point's displacement is described as a weighted sum of Gaussian radial basis functions.

The optimization is carried out using the Expectation-Maximization (EM) framework. In the E-step, CPD computes posterior probabilities that softly associate each reference point with each GMM component (that is, each template point), producing probabilistic correspondences between the point sets. In the M-step, these probabilities guide the update of template point positions by minimizing an energy function that balances GMM log-likelihood with motion coherence regularization. To improve convergence and reduce sensitivity to local minima, CPD employs deterministic annealing by gradually decreasing the variance (σ^2) of the Gaussian components, enabling a coarse-to-fine registration strategy.

One of CPD's key advantages is its robustness to noise, outliers, missing data, and partial overlap between datasets. It does not require explicit point correspondences, and the resulting deformation remains continuous, smooth, and biologically meaningful. By encouraging coherent motion, where neighboring points deform together rather than independently, CPD avoids unrealistic or abrupt local distortions. These properties make it particularly suitable for registering anatomical surfaces

that undergo complex yet smooth deformations, such as the dynamic motion of the left atrial wall throughout the cardiac cycle.

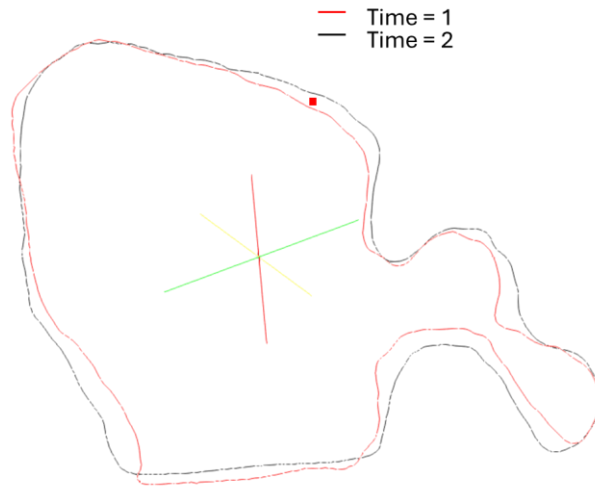


Figure 2.2: Misalignment between two time points of the left atrial (LA) geometry

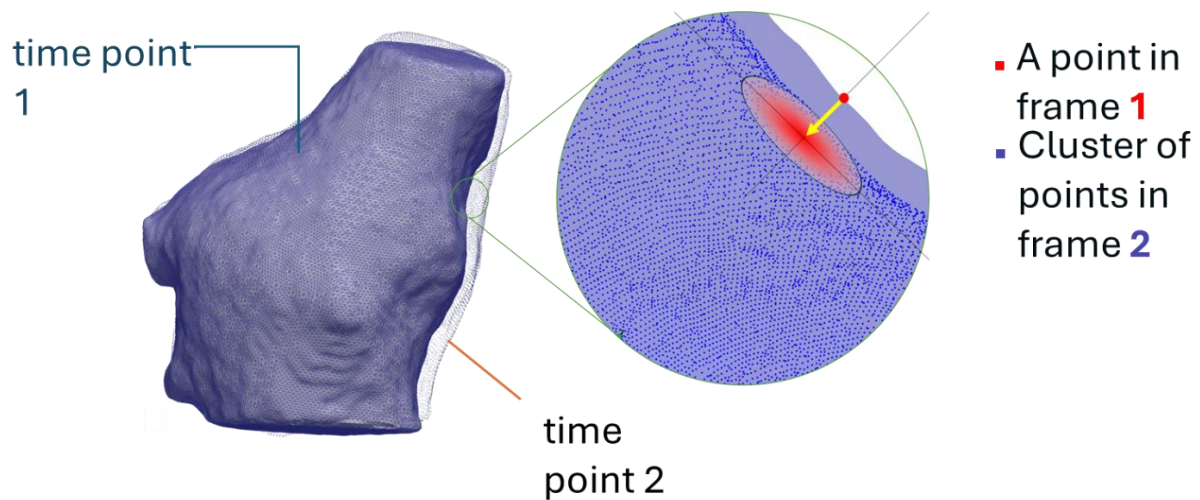


Figure 2.3: Illustration of Coherent Point Drift (CPD) registration, which shows the correspondence between a single point at time point 1 (red) and its matched cluster of points at time point 2 (blue) on the left atrial surface mesh.

In summary, CPD provides a flexible, kernel-based, and fully probabilistic framework for non-rigid registration. Its combination of soft correspondence estimation, motion coherence regularization, and EM-based optimization has established it as a powerful and widely used tool in shape matching and medical imaging applications [44].

2.3 Computational Fluid Dynamics

To simulate patient-specific hemodynamics within the LA, we employ the Immersed Boundary Method (IBM), which enables the accurate coupling of complex, time-varying anatomical geometries with a fixed Cartesian fluid domain. In this framework, the LA wall is represented as a Lagrangian surface embedded within a three-dimensional Eulerian grid of size $256 \times 256 \times 256$. The velocity components are defined at cell faces and pressure at cell centers using a staggered mesh arrangement. The interaction between the moving wall and the surrounding fluid is resolved through interpolation and spreading operations, enabling force and velocity exchange between the Lagrangian and Eulerian fields. The Lagrangian wall motion is prescribed using temporally smoothed Fourier mode representations, allowing compact and physiologically realistic deformation over multiple cardiac cycles.

Blood is modeled as an incompressible, shear-thinning non-Newtonian fluid using the Carreau–Yasuda viscosity model, which adapts dynamic viscosity based on the local shear rate. This formulation is particularly important in accurately capturing physiological flow features in regions exhibiting both jet-like flow (e.g., at pulmonary vein inflows) and stagnation (e.g., near the left atrial appendage). The kinematic viscosity $\nu(\dot{\gamma})$ is given by:

$$\nu(\dot{\gamma}) = \nu_{\infty} + (\nu_0 - \nu_{\infty}) \times [1 + (\lambda\dot{\gamma})^a]^{\frac{n-1}{a}} \quad (2.1)$$

Where $v_0 = 0.64 \text{ cm}^2/\text{s}$ is the zero-shear viscosity, $v_\infty = 0.04 \text{ cm}^2/\text{s}$ is the infinite-shear viscosity, $\lambda = 11.77$ is the time constant, $a = 46.59$ is the Yasuda exponent and $n = 0.3$ is the power-law index.

2.4 Post Process

After completing the CFD simulation, various hemodynamic quantities were extracted to evaluate flow behavior and quantify physiological relevance. These include the residence time (RT) and its variance (RT²), velocity vector fields, and kinetic energy localized within predefined regions of interest (ROIs). These metrics offer clues about transport dynamics, vortex structures, and potential zones of blood stasis within the LA. A critical post-processing step involves capturing the wall motion of the LA as embedded in the Eulerian simulation domain. This is accomplished using a Signed Distance Function (SDF), which encodes the LA geometry implicitly as a scalar field. In this formulation, the SDF is zero on the LA wall, negative inside the atrial cavity, and positive outside. This continuous representation enables sub-voxel resolution of the moving boundary and provides a natural way to mask the wall region in the Eulerian domain.

By computing the temporal derivative of the SDF and projecting the velocity field onto its gradient, we obtain the normal component of wall velocity, which characterizes the local expansion and contraction of the atrial surface over time. This is especially important for accurately tracking wall deformation and dynamic behavior in the UAC framework. The resulting normal wall motion can then be mapped onto the UAC space for spatially uniform analysis, comparison across patients, or input to data-driven modeling pipelines

2.4.1 Signed Distance Field

Signed Distance Functions (SDFs) are spatial models that represent the distance from any point in space to the nearest surface of an object. They implicitly define the object's surface as the set of points where the SDF value equals zero—this is known as the zero-level set. Unlike explicit representations like meshes, SDFs do not directly store the surface geometry. One key advantage of SDFs is that they are often smooth and differentiable, making them well-suited for gradient-based optimization methods. Additionally, for certain types of shapes, SDFs offer a more compact representation compared to explicit mesh models [45].

Z. Lai et al. [46] employed Signed Distance Functions (SDFs) within an Immersed Boundary Method (IBM)-based CFD framework to simulate multiphase fluids and arbitrarily shaped particles, effectively capturing fluid–particle interactions. Inspired by their approach, we adopt SDFs in our simulation framework to compute the velocity of atrial wall motion [47].

In our approach, the SDF defines the left atrial (LA) surface as a decision boundary that separates space-time coordinates (x_k, t_k) into regions inside and outside the anatomical structure. Each (x_k, t_k) point is assigned a signed distance value ϕ , which facilitates both velocity estimation and LA surface reconstruction (Figure 2.4) [48]. In this study, we leverage the SDF to extract wall motion by computing the velocity of each point across time frames and embedding this information within the UAC framework.

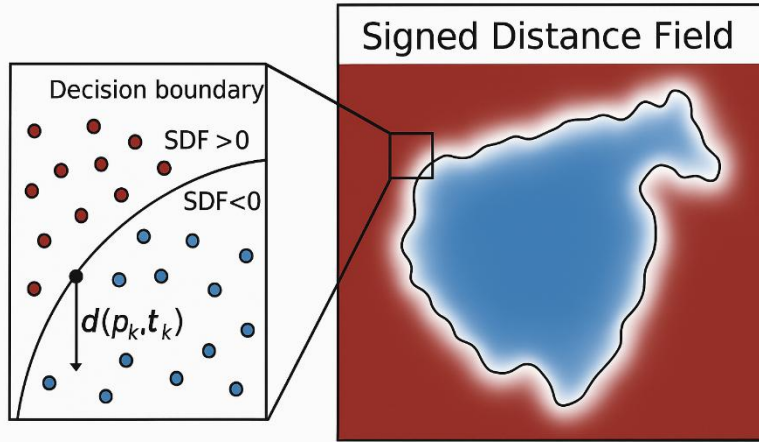


Figure 2.4: Illustrates the concept of an SDF, showing the zero-level set as the anatomical surface, positive values outside, and negative values inside.

2.5 Universal Atrial Coordinate (UAC)

2.5.1 UAC Background & Motivation

To address the anatomical complexity and variability of the LA, which poses challenges for both visualization and cross-patient comparison, several techniques have been developed to project the 3D LA surface onto a 2D domain. Bisbal et al. [49] introduced Left Atrial Sphericity (LASP) as a morphological metric derived from 3D cardiac MRI to predict AF recurrence after ablation. Their work highlighted the significant shape variability across patients and its clinical impact. Building on this need for standardized representations, Karim et al. [50] proposed a conformal and authalic flattening method to map the LA onto a square domain, enhancing regional visualization while minimizing distortion near pulmonary veins. Williams et al. [51] introduced a schematic unfold map that divided the LA into 24 anatomical regions but required assumptions like a fixed number of pulmonary veins. Roney et al. [52] later developed a distance-preserving flattening approach for electrophysiological mapping but noted limitations in standardization across patients.

To overcome these challenges, Roney et al. [42] introduced the Universal Atrial Coordinate (UAC) system, which provides a reproducible and automated method for mapping the LA surface into a standardized alpha-beta coordinate space. The UAC system enables the mapping of a left atrial (LA) surface mesh onto a unit square, providing a standardized framework for spatially consistent analysis and visualization. After mesh preprocessing, key anatomical landmarks and boundary curves are extracted to define the coordinate system. These include the MV annulus, pulmonary vein ostia, and the atrial roof, which together serve as physiologically meaningful references for computing the UAC. This parameterization allows for uniform data representation across patients and supports downstream tasks such as regional flow quantification, atlas mapping, and machine learning-based analysis.

2.5.2 Concept & General Methodology

UACs were computed by solving Laplace’s equation with Dirichlet boundary conditions on the left atrial (LA) surface mesh. This formulation, also known as the Laplace–Beltrami equation, was solved twice: once to obtain a longitudinal coordinate (α_{LA}) and once for a transverse coordinate (β_{LA}). The approach is analogous to mapping a globe using latitude and longitude, where the resulting coordinate system is smooth and orthogonal. The mathematical formulation is summarized below, where the Laplace’s equation defines the harmonic scalar fields, and the Dirichlet boundary conditions set the coordinate values at two opposing anatomical boundaries:

- Laplace’s Equation:

$$\nabla_s^2 u = 0, \quad \nabla_s^2 v = 0$$

- Dirichlet Boundary Conditions:

$$u = 0 \text{ at } \Gamma_0, \quad u = 1 \text{ at } \Gamma_1$$

$$v = 0 \text{ at } \Gamma_0, \quad v = 1 \text{ at } \Gamma_1$$

For the LA, the α_{LA} coordinate spans from the septal to lateral wall, while β_{LA} extends from the posterior to the anterior portion of the MV annulus. This orthogonal parameterization provides a consistent and anatomically meaningful framework for regional analysis and data mapping across subjects.

These directional choices for the UACs were made to align with the standard clinical orientation used in 2D visualizations of biatrial basket catheter data. In electroanatomic mapping systems commonly used during AF procedures (e.g., CARTO or EnSite), the LA is typically displayed with the septal wall on the left, the lateral wall on the right, the posterior region (near the pulmonary veins) at the bottom, and the anterior MV region at the top. By defining the longitudinal coordinate α_{LA} from the septal to lateral wall and the transverse coordinate β_{LA} from the posterior to anterior mitral annulus, the UAC system replicates this clinically familiar layout. This design ensures that the flattened UAC representation of the LA is directly comparable to standard catheter-based 2D electrogram maps, facilitating the integration of simulation data with clinical mapping for interpretation, visualization, and analysis.

The left atrial (LA) surface mesh was used to first identify important anatomical markers in order to establish the bounds of the septal–lateral coordinate, α -LA. The largest connected collection of boundary edges was identified as the MV ring. Mesh nodes shared by the LA and corresponding PV areas were found to be the right and left superior pulmonary vein (RSPV and LSPV)

connections with the LA body. The shortest geodesic path from the RSPV–LA junction to the MV ring was determined to be the septal boundary of α -LA. To maintain anatomical consistency, the path has to pass via the user-defined fossa ovalis (FO) point. The shortest geodesic route between the LSPV–LA junction and the MV ring, which is located posterior to the LAA, was used to calculate the lateral boundary (Figure 2.5). The algorithm appropriately oriented the LAA on the anterior side in the final coordinate system by assigning the LAA and the left inferior pulmonary vein (LIPV) to opposite walls in the UAC map in order to enforce this posterior constraint. On the LA surface, geodesic pathways were calculated using a fast-marching technique.

The posterior–anterior coordinate β_{LA} was computed by solving Laplace’s equation on the left atrial surface with Dirichlet boundary conditions (Figure 2.5). The MV ring was assigned a value of zero, and the atrial roof boundary was assigned a value of one. The roof boundary was defined as the geodesic path connecting user-defined points at the posterior-anterior transition of the RSPV–LA and LSPV–LA junctions, along with the posterior components of their junctions with the atrial body. Restricting the boundary to the posterior portions of the superior veins ensures anatomically consistent separation between posterior and anterior regions, allowing for clear identification of the pulmonary veins in the UAC framework. To identify the posterior segments of the superior pulmonary vein–left atrium (PV–LA) junctions, four anatomical markers were automatically detected at key transition points along the RSPV and LSPV boundaries. These markers subdivided each vein opening into anterior and posterior segments. Since the segment orientation was initially ambiguous, the posterior components were automatically selected based on their topological mapping in the UAC system. Specifically, the segment that resulted in the superior veins (RSPV and LSPV) being placed on the anterior wall of the UAC map—relative to

the location of the LAA—was selected as the posterior path. This ensured consistent and anatomically accurate coordinate assignment across subjects.

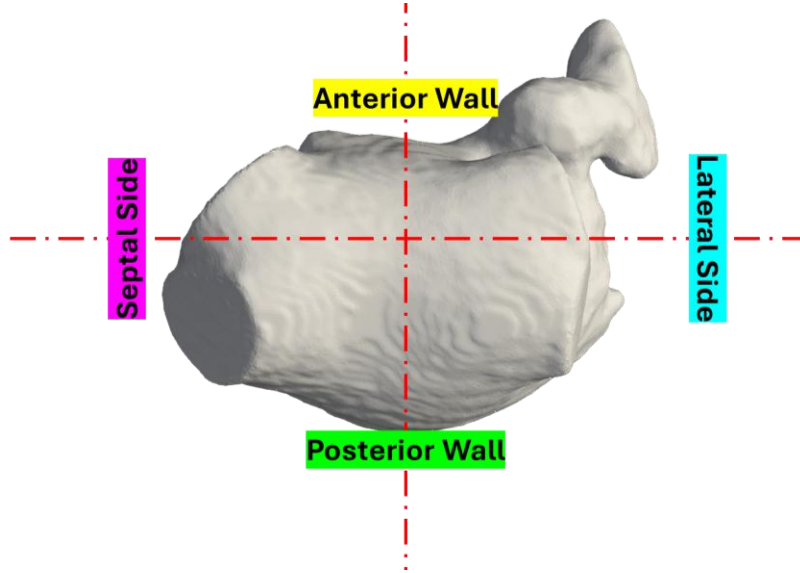


Figure 2.5: Anatomical orientation of the left atrium showing anterior, posterior, septal, and lateral walls.

To ensure consistent coordinate assignment along the septal and lateral boundaries of the LA (corresponding to $\alpha_{LA}=0$ and $\alpha_{LA}=1$), boundary nodes were duplicated and associated elements were renumbered to preserve topological continuity. To account for inter-patient anatomical variation, the α_{LA} coordinate was rescaled based on the physical geometry of the LA. This was achieved by identifying a geodesic path along the posterior wall that followed a constant β_{LA} value. The distance along this path was used to normalize the α_{LA} , creating a mapping between the raw Laplace solution and the true anatomical length of the LA wall. This rescaling ensured that the final α_{LA} coordinate reflected comparable anatomical regions across different patient geometries, improving consistency in subsequent regional analysis and visualization as shown in Figure 2.6.

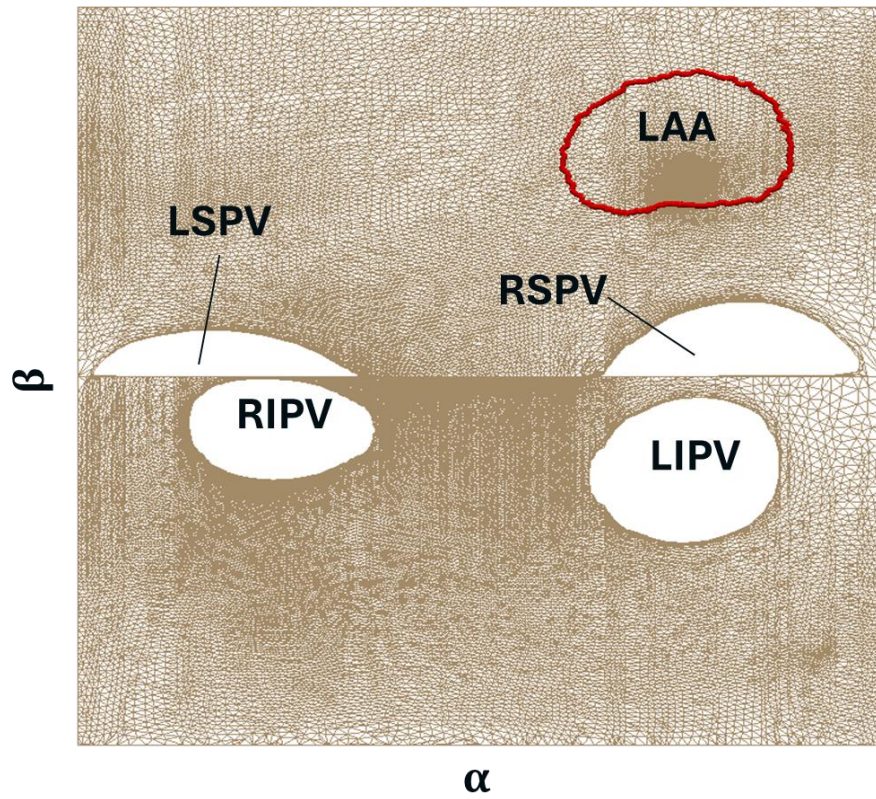


Figure 2.6: 2D UAC map of the left atrium showing pulmonary vein (PV) openings and left atrial appendage (LAA) boundary

Chapter 3: Computational Framework

3.1 Anatomical Segmentation from nnU-Net Outputs

Baseline volumetric images were obtained from the CT scans of two patients. These scans were used as input to the nnU-Net framework, an automated and self-configuring deep learning model designed for biomedical image segmentation. The framework produced predictive three-dimensional segmentation masks along with anatomical labels for key structures within the LA, including the PVs, MV, and LAA. Each of these structures plays a critical role in atrial physiology and disease modeling.

Table 3.1 shows the CT scan dataset with corresponding patient identifiers. For simplicity and consistency, we refer to each dataset by its assigned case number (Case 1, Case 2, and Case 3) throughout this study.

Table 3.1 CT scan dataset used in this study

Case ID	Clinical Case
44243	Case 1
48343	Case 2
CVC	Case 3

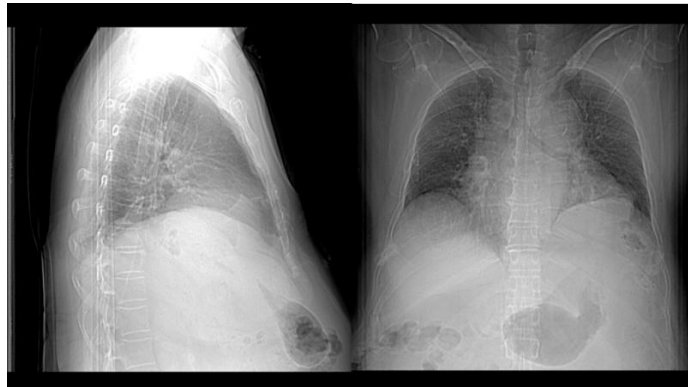


Figure 3.1: Sagittal (left) and coronal (right) CT scan views of human thorax Case 1 patient

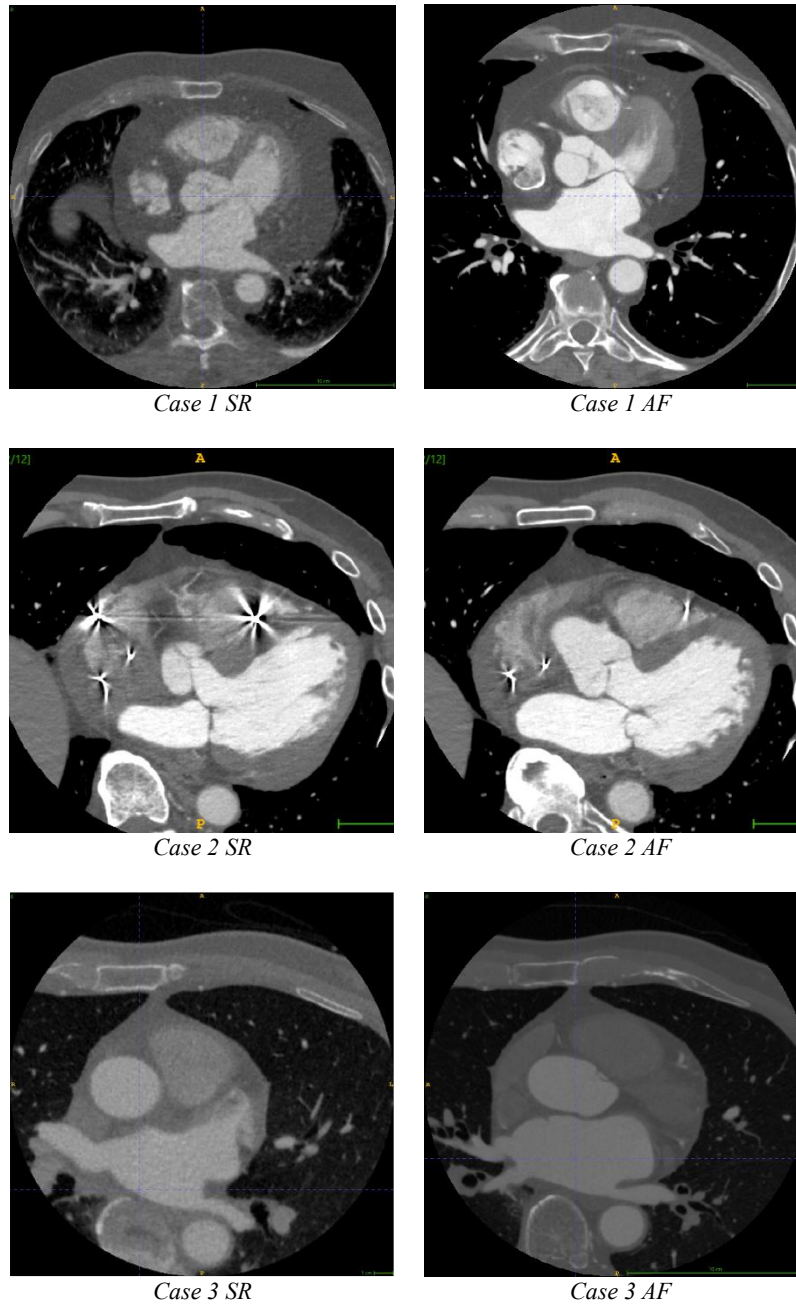


Figure 3.2: Baseline CT images in DICOM format for different patients

As shown in Figure 3.1 and Figure 3.2, the original medical imaging data is provided in DICOM (Digital Imaging and Communications in Medicine) format, which is the standard format used by CT scanners and other medical imaging systems. While DICOM is widely adopted in clinical

environments, it is not directly compatible with many research-focused image processing pipelines or deep learning models.

The DICOM files are first converted to NIfTI (Neuroimaging Informatics Technology Initiative) format. NIfTI is commonly used in research settings because it supports multidimensional image data, preserves spatial orientation, and allows for more efficient data handling. This conversion step ensures that the images meet the format and structural requirements of nnU-Net, including uniform voxel spacing and consistent volume orientation. Once converted, the NIfTI images are processed by the nnU-Net model to generate a predictive segmentation at the region of interest (ROI), as illustrated in Figure 3.3. The model produces a three-dimensional anatomical mask of the LA, including key structures such as the PVs, MV, and LAA with color codes shown in Table 3.2. The color-coded labeling system allows the meshing pipeline to distinguish between different atrial subregions, enabling tailored operations such as smoothing, voxel cleanup, and boundary refinement

Table 3.2: Color labelling for segmentation

Anatomical Structure	Color Label	RGB Value
Left Atrium Body (LA)	Green	(0, 255, 0)
Left Ventricular Body	Red	(255, 0, 0)
Left Atrial Appendage (LAA)	Blue	(0, 0, 255)
Right Superior Pulmonary Vein (RSPV)	Pink	(255, 0, 255)
Left Superior Pulmonary Vein (LSPV)	Yellow	(255,255,0)
Right Inferior Pulmonary Vein (RIPV)	White	(255, 239, 213)
Left Inferior Pulmonary Vein (LIPV)	Cyan	(0, 255, 255)
Aorta	Purple	(0, 0, 205)

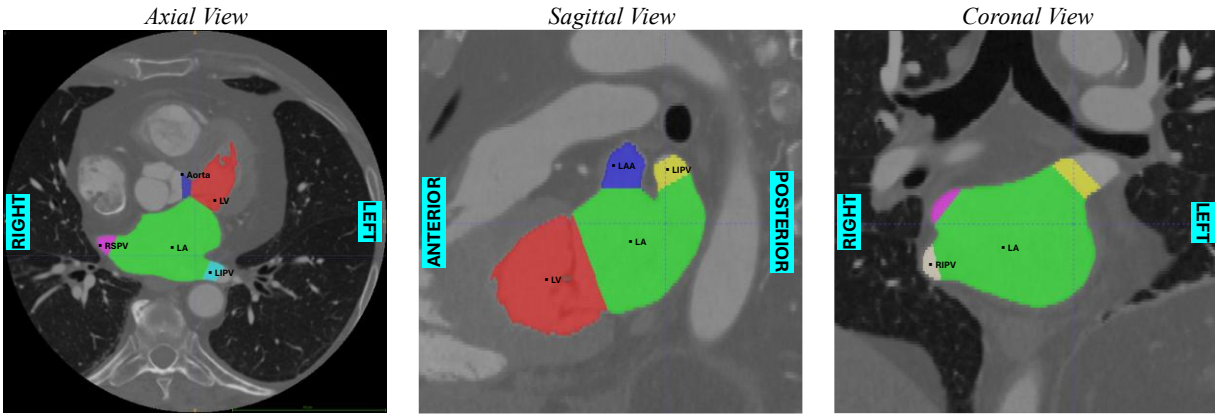
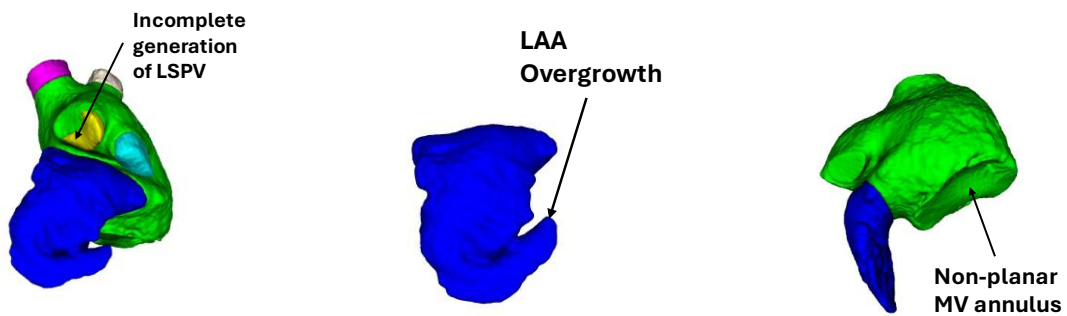


Figure 3.3: nnUNet-generated segmentations of the ROI shown from multiple views for Case 1

Despite the robustness of nnU-Net, its outputs often contain artifacts that require correction before the segmented geometries can be used in CFD simulations. These issues typically arise from variations in image quality, limited training data, or the inherent complexity of atrial anatomy, which can challenge even advanced segmentation algorithms. Common defects include incorrect labeling of anatomical regions, the presence of holes or discontinuities in the segmented surfaces, and partial or missing anatomical structures. These issues compromise the creation of watertight, smooth, and physiologically accurate models needed for CFD analysis.

Case 2 SR:



Case 2 AF:

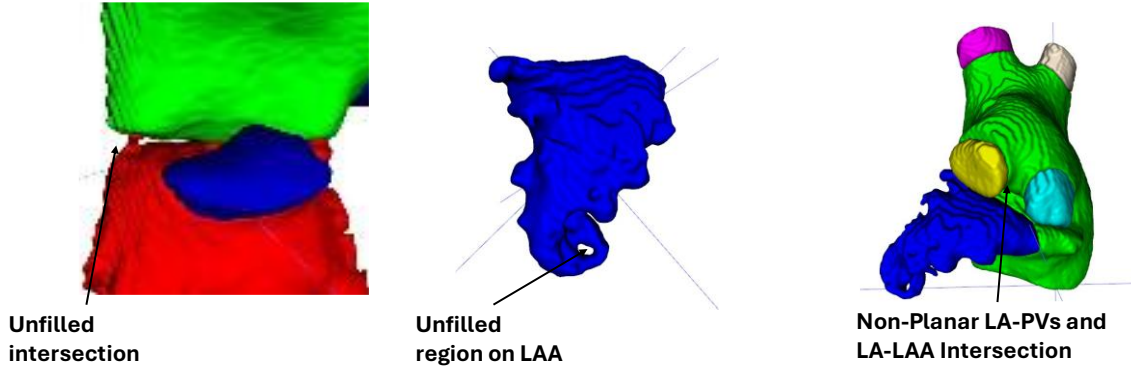


Figure 3.4: Artifacts Generated in nnU-Net Segmentations

As shown in Figure 3.4, several artifacts were observed in the nnU-Net segmentations for patient Case 2 in both AF and SR cases. While the figure highlights these issues in a single frame, similar artifacts may be present in other frames as well. One common issue is the presence of unfilled regions at the intersection of the LA and left ventricle (LV), particularly around the MV annulus. Additionally, the LAA often exhibited surface irregularities and unsegmented internal spots, resulting in undefined or incomplete geometry. Another significant artifact is the lack of geometric planarity across key anatomical regions. The PVs, LAA, and LA body were sometimes misaligned or oriented in a non-planar fashion, which can affect the structural realism and downstream processing required for computational simulations. This misalignment needs to be resolved in each frame to ensure temporal consistency. The positions and orientations of the PVs, MV annulus, and LAA must remain consistent across all time frames. To address these problems, we used ITK-SNAP, a widely adopted software tool for medical image visualization and editing, to refine the predicted segmentation masks. This post-processing step involved a detailed manual inspection and correction of each anatomical region. The primary tasks included fixing mislabeled or incorrectly merged structures, filling small holes and unsegmented areas, removing noise or disconnected components, and smoothing boundaries to ensure that the geometry was closed and

continuous. Upon correcting all segmentation artifacts, a finalized anatomical model is produced and used in downstream processing steps, as shown in Figure 3.6.

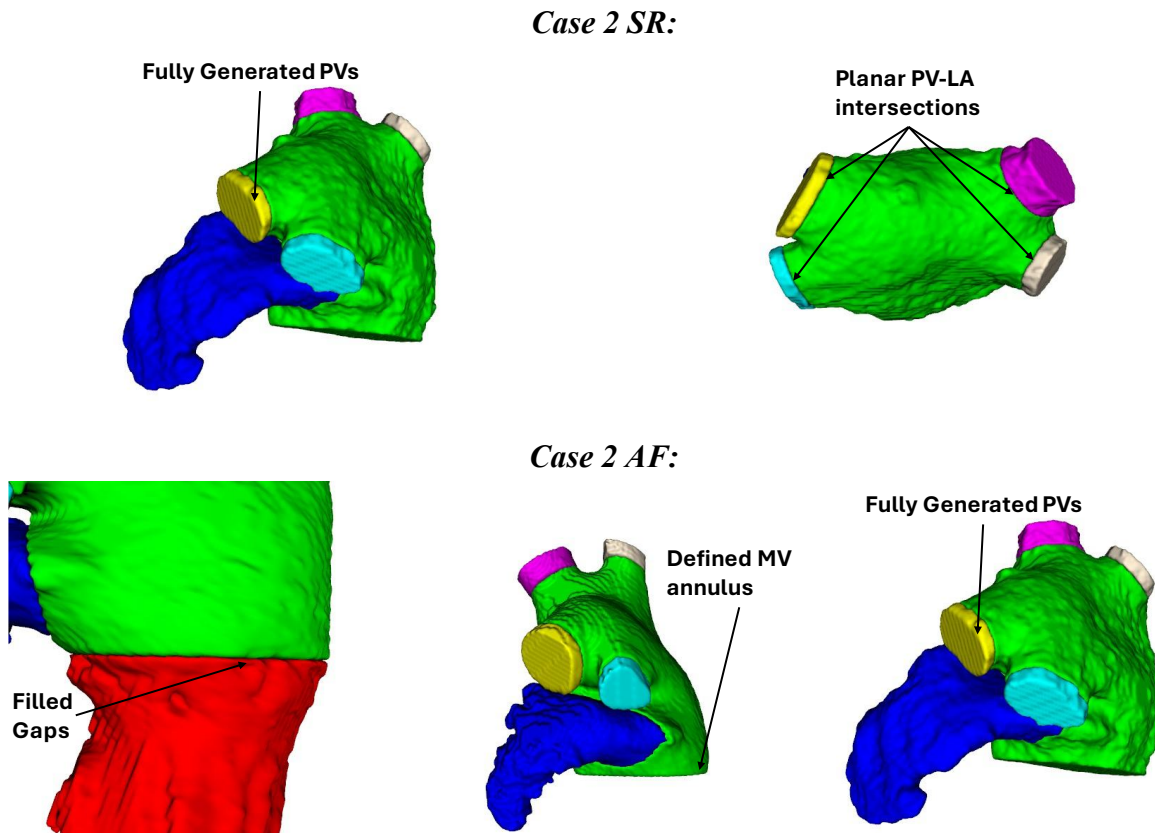


Figure 3.5: Manual Reconstruction of Segmentations using ITK-Snap

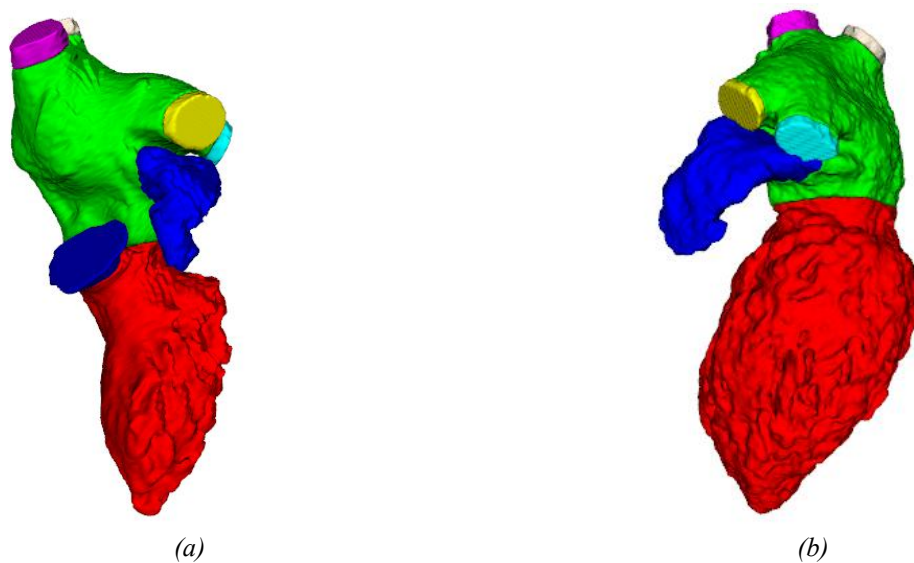


Figure 3.6: Reconstructed segmentation for patient (a) Case 2 SR and (b) Case 2 AF

3.2 Lagrangian Mesh Generation

3.2.1 Computing Segmentation Time

After completing the manual correction of segmentations for both AF and SR cases, a surface mesh is generated using a custom MATLAB script. This script takes as input the segmented NIfTI files and the corresponding time points for each frame in the cardiac cycle. Since the goal is to generate a mesh representing one full cardiac cycle (covering both contraction and relaxation phases), it is important to assign accurate time values to each segmented frame. These time points are recalculated based on the CT acquisition protocol, with the cardiac cycle starting at the R-wave peak of the ECG and ending just before the next R-wave peak, as shown in the Figure 3.7

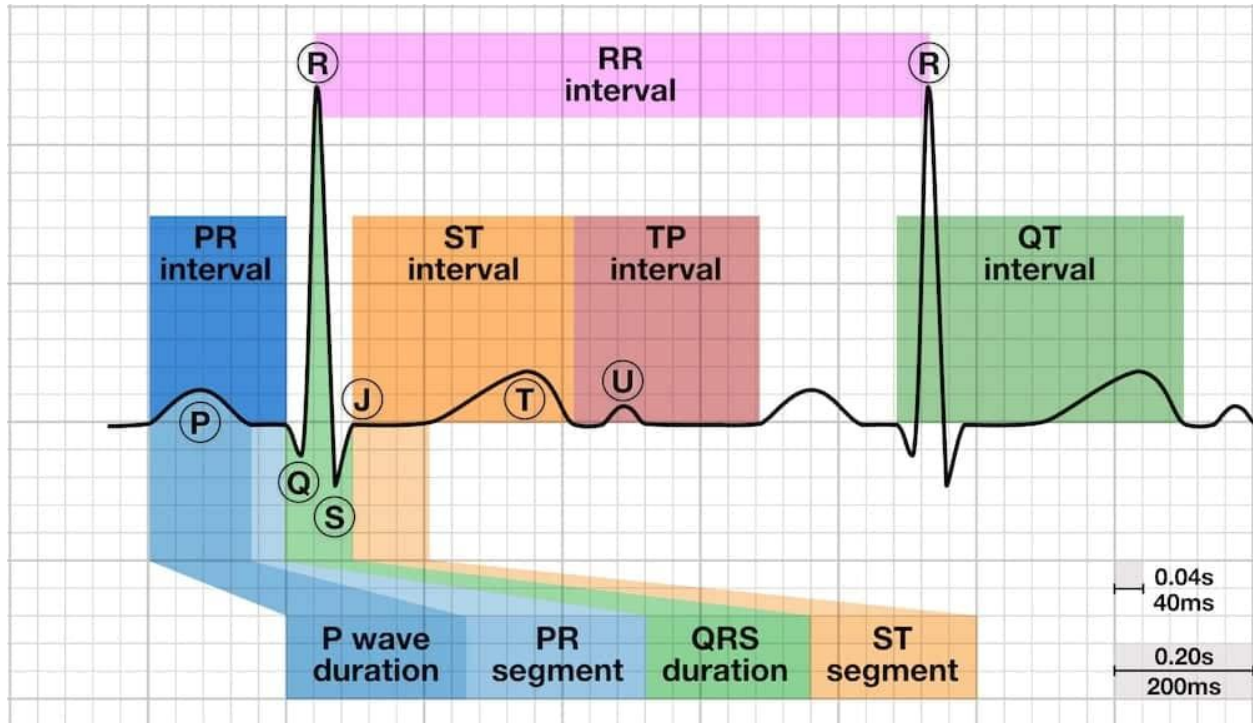


Figure 3.7: An annotated ECG waveform delineating essential segments and intervals (PR, QRS, ST, QT, TP), all quantified inside a single cardiac cycle between two successive R-peaks (RR interval). Temporal markers denote duration in seconds and milliseconds.

In SR cases, the segmentation intervals are typically well-distributed and periodic, aligning with the predictable characteristics of SR. For instance, Case 2 SR features frames distributed at consistent intervals of 10 ms (e.g., 0, 10, 20, ..., 90 ms), whereas Case 3 SR offers a more refined resolution at 6 ms intervals. This regularity is achievable due to the distinctly delineated P and R waves in the SR ECG, facilitating reliable retrospective gating in accordance with the cardiac cycle. In contrast, AF cases exhibit irregular segmentation time points owing to the disorderly characteristics of the condition, characterized by the absence of P waves and high variability in R-R intervals. Case 1 AF contains negative time values (e.g., -27, -18 ms), signifying frames captured prior to the R-peak. Case 3 AF exhibits segmentation periods both preceding and succeeding 0 ms, indicating irregular cardiac cycles. In Case 2, AF exceeds 1 second, with segmentation durations reaching 195 ms, suggesting either an extended cardiac cycle or the recording of numerous partial cycles inside a single sequence.

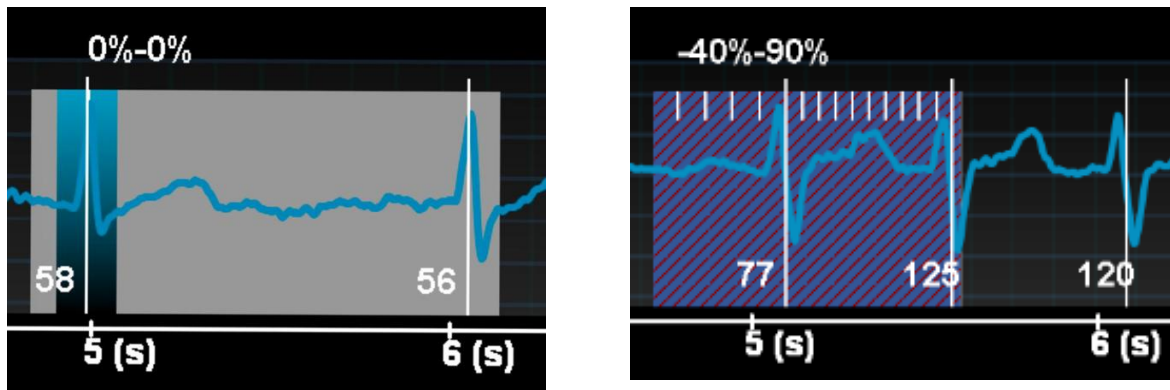


Figure 3.8: Cardiac phase identification and gating for Patient 44243 based on CT-derived ECG signals for Case 1

To provide uniform temporal analysis across all patients and rhythms, segmentation frames have been adjusted or filtered to incorporate only values ranging from 0 to 100 ms. This fulfills two objectives:

- Negative data (preceding the R-peak) are omitted as mechanical events such as cardiac contraction and blood flow predominantly transpire after the R wave.
- Values exceeding 100 ms are excluded to standardize the cardiac cycle length among patients and maintain consistent temporal resolution. This threshold approximates a standard 1-second RR interval at 60 beats per minute.

Therefore, temporal binning is applied only to segmentation frames within the 0–100 ms range, enabling consistent comparisons between SR and AF conditions across all patient cases. The adjusted and filtered AF segmentation times are shown with original segmentation times in Table 3.3 and Table 3.4

Table 3.3: Original segmentation time points (ms) across one RR interval for SR and AF conditions

Case ID	Raw Segmentation Times [ms]	Total Frames
Case 1 SR	[0 10 30 35 40 50 60 70 80 90]	10
Case 1 AF	[-27 -18 -9 0 15 30 35 44 59 73 88]	11
Case 2 SR	[0 10 20 30 35 40 50 60 70 80 90 95]	12
Case 2 AF	[1 22 43 64 85 104 119 135 150 165 180 195]	12
Case 3 SR	[0 6 12 18 24 30 36 42 48 54 60 66 72 78 84 90 95]	17
Case 3 AF	[-18 -11 -6 0 7 14 21 28 35 42 49 56 63 70 77 84 89]	17

Table 3.4: Adjusted segmentation time points (ms) in AF

Case ID	Adjusted Segmentation Times [ms]	Total Frames
Case 1 AF	[0 15 30 35 44 59 73 88]	8
Case 2 AF	[4 19 35 50 65 80 95]	7
Case 3 AF	[0 7 14 21 28 35 42 49 56 63 70 77 84 89]	14

3.2.2 Reference Geometry Selection

Before beginning meshing, the first important preprocessing step is the precise identification of the left atrial (LA) body from the delineated region of interest (ROI). This procedure is directed by color-coded labeling executed during the segmentation phase, which facilitates the precise identification of the LA. Structures irrelevant to the investigation, like the aorta and other neighboring anatomical regions, are omitted from the domain to maintain a focus exclusively on the LA body in the simulations.

To define the computational Eulerian fluid domain, a reference geometry is established by determining the maximum volume of the LA across all temporal frames for each scenario. This maximal volume forms the foundation for creating a coherent and anatomically accurate simulation domain. It guarantees that the domain can support dynamic wall motion during the cardiac cycle, maintains mesh quality, and establishes standardized spatial bounds for inter-case comparison. The precise selection of this reference geometry is thus a crucial step in establishing a dependable CFD pipeline. Table 3.5 below enumerates the maximum LA volumes calculated for each patient case and rhythm state, which were utilized to delineate the simulation domain boundaries.

Table 3.5: Minimum and maximum LA volumes and corresponding emptying fraction (EF) for SR and AF cases

Case ID	Minimum LA Volumes (mm^3)	Maximum LA Volumes (mm^3)	Emptying Fraction (EF)
Case 1 SR	1.0180×10^5	1.3336×10^5	0.24
Case 1 AF	1.1318×10^5	1.3216×10^5	0.14
Case 2 SR	1.2991×10^5	1.9617×10^5	0.34
Case 2 AF	1.2752×10^5	1.7198×10^5	0.26

Case 3 SR	1.6108×10^5	2.1445×10^5	0.25
Case 3 AF	15068×10^5	1.7649×10^5	0.15

3.2.3 Segmentation Volume Smoothing

The next step after assigning segmentation time in the script is to smooth the segmented geometry, as described in Section 2.2.1. This smoothing step is essential for reducing residual noise and eliminating small discontinuities that may persist even after manual correction. To achieve this, a Gaussian filter is applied to the 4D segmentation data (3D space over time). Gaussian filtering is chosen for its ability to suppress high-frequency noise while preserving the overall anatomical structure.

To control the degree of smoothing, a stencil [5, 5, 5, 3] is applied where the first three values correspond to the spatial dimensions (x, y, z) and the fourth to the temporal dimension (t). This means smoothing is performed over a 5-voxel neighborhood in each spatial direction and across 3 consecutive frames in time. A temporal window of 3 offers a good tradeoff, as it reduces frame-to-frame noise while preserving meaningful motion. Larger windows risk over smoothing and may mask true physiological variations like the irregular wall motion seen in AF, while smaller windows can leave excessive jitter and lead to poor mesh consistency across frames. The chosen stencil provides a balanced approach to reducing noise while maintaining clinically relevant atrial dynamics.

3.2.4 Surface Mesh Generation from Segmentation Volumes

In this study, surface meshing was applied to all time frames of each case using the preprocessed segmentation volumes. For Case 1, the marching cubes algorithm was used to extract the initial triangular surface mesh for each frame of the cardiac cycle. The generated meshes were refined

through Gaussian smoothing to minimize voxel-level noise and mesh keep ratio adjustments to balance anatomical detail with computational efficiency. Parameter selection followed the general guidelines outlined in Table 3.5, with specific values chosen for each case and rhythm based on segmentation quality and anatomical clarity.

Boundary conditioning was applied to produce smooth, circular, and planar openings at the PVs and MV. The face cylinder threshold was adjusted per case to ensure consistent boundary shapes while accommodating variations in segmentation quality. Table 3.6 summarizes the exact parameter values used for each case and rhythm in this study.

Table 3.6: Mesh keep ratio and Face cylinder threshold for each case and rhythm

Case ID	Mesh Keep Ratio	Face Cylinder Threshold
Case 1 SR	0.6	0.8
Case 1 AF	0.8	0.8
Case 2 SR	0.8	0.6
Case 2 AF	0.8	0.6
Case 2 SR	0.7	0.6
Case 2 AF	0.6	0.5

The result was a time-resolved sequence of high-quality, anatomically consistent surface meshes for each cardiac cycle. These meshes formed the Lagrangian representation of LA motion used for subsequent wall motion extraction, frequency-domain analysis, and CFD simulation.

3.2.5 CPD-Based Non-Rigid Alignment of Segmented LA Meshes

Following the generation of surface meshes from the segmented volumes, Coherent Point Drift (CPD) registration is applied to align all frames temporally. This process leverages the

probabilistic framework of a Gaussian Mixture Model (GMM), as detailed in Section 2.3.3.1. CPD treats one mesh as a fixed reference and iteratively moves the remaining meshes to achieve optimal alignment by minimizing the distance between corresponding points. This non-rigid registration ensures that anatomical features are coherently tracked across frames, which is essential for accurately interpolating the motion of the Lagrangian mesh and capturing physiologically meaningful deformation throughout the cardiac cycle.

3.2.6 Temporal Interpolation of Wall Motion

After spatial alignment of the segmented frames by CPD registration, the next step is creating a temporally dense representation of LA motion by interpolating between the segmented time points. As indicated in Table 3.3 and Table 3.4, the original segmentation is performed at sparse time intervals across the cardiac cycle. To better resolve the dynamic deformation of the LA wall and reduce temporal jitter, we interpolate intermediate geometries between each pair of registered frames.

In this study, cubic-spline interpolation is employed to estimate the motion trajectory between adjacent frames. This approach results in a total of 40 uniformly spaced frames per cardiac cycle, corresponding to a temporal resolution of $\Delta t = 0.025$ seconds. The choice of 40 frames is based on prior studies and empirical testing, which showed that this sampling rate provides a favorable balance between capturing physiological motion and maintaining computational efficiency in downstream CFD analysis. These interpolated frames are later used to compute SDFs and map wall motion onto the UAC system for further hemodynamic modeling.

3.3 Computational Fluid Dynamics Setup

In this study, blood flow within the LA is modeled using the incompressible Navier–Stokes equations, enhanced with an Immersed Boundary Method (IBM) to incorporate patient-specific, time-resolved wall motion derived from cardiac imaging. While the fluid domain is defined on a fixed Eulerian grid, the atrial wall is represented using a moving Lagrangian mesh. The IBM enforces wall motion by applying a body force in the momentum equation, effectively embedding the moving boundary within the static computational domain. The governing equations consist of the momentum equation and the incompressibility conditions:

$$\frac{\partial \mathbf{u}}{\partial t} + \mathbf{u} \cdot \nabla \mathbf{u} = -\frac{1}{\rho} \nabla p + \nu \nabla^2 \mathbf{u} + \mathbf{f}$$

Here, $\mathbf{u}$ is the velocity vector, p is pressure, ρ is fluid density, ν is kinematic viscosity, and $\mathbf{f}$ is the IBM body force that enforces the prescribed wall motion. These equations are discretized using a Finite Difference Method (FDM), except for the advection term, which is excluded from the pressure-velocity coupling to simplify the incompressibility enforcement.

To assess blood stasis and thrombotic risk in AF patients, a scalar transport equation is solved to compute the residence time (RT) of blood particles:

$$\frac{\partial RT}{\partial t} + \mathbf{u} \cdot \nabla RT = D \nabla^2 RT + 1$$

In this equation, RT denotes the accumulated time spent by blood elements in the domain, and D is a small scalar diffusivity that promotes numerical stability while approximating near-Lagrangian transport. The RT equation is solved using a fifth-order Weighted Essentially Non-Oscillatory (WENO) scheme, which maintains high resolution and suppresses non-physical oscillations near

steep flow gradients. Time integration is carried out using an explicit Runge–Kutta scheme. The IBM force f is computed iteratively to enforce velocity boundary conditions on the moving Lagrangian mesh.

Following flow simulation, wall motion is extracted from the converged cycle using a Signed Distance Function (SDF). The SDF assigns a scalar value to every point in the domain, representing its shortest distance to the wall: zero at the wall, negative inside the wall, and positive outside. In 3D, this allows for precise localization of the interface and facilitates consistent projection of wall velocities onto surface-based coordinate systems like the UAC. This framework enables physiologically realistic modeling of blood flow in the LA, supporting analysis of wall shear stress, vortex structures, and regions of potential thrombogenesis.

3.4 Universal Atrial Coordinate (UAC) Mapping

After generating the time-resolved Lagrangian surface meshes, the computational workflow proceeds along two complementary paths. The first path involves conducting fluid simulations using an Eulerian solver embedded with an immersed boundary method to analyze intra-atrial blood flow. The second path focuses on establishing a universal, surface-based coordinate system to enable consistent geometric and functional comparisons across patients and time frames. While the CFD route offers comprehensive details about flow structures and hemodynamics, the UAC mapping facilitates standardized post-processing and rhythm-based feature analysis.

Once the 3D Lagrangian mesh is generated, the next essential step is to map each mesh point onto the UAC system. This mapping process enables the standardized spatial representation of left atrial

geometry across time frames and individuals. In this study, UAC mapping is performed for all 40 time points, spanning one complete cardiac cycle for all three cases. The UAC system was constructed for each patient case to provide a standardized spatial framework for mapping left atrial (LA) wall motion. The process consisted of five main steps: lid removal, landmark identification, α -mapping, β -mapping, and coordinate rescaling.

3.4.1 Lid Removal

Artificial caps at the PV ostia and the MV ring were removed (shown in Figure 3.9) to open the anatomical boundaries needed for UAC computation. This step ensured that the PV and MV boundaries were represented as true anatomical openings, allowing accurate boundary condition assignment in the Laplace–Beltrami equation



Figure 3.9: Illustrates the lid removal for Case 1 SR, showing (a) geometry before lid removal and (b) geometry after lid removal.

3.4.2 Landmark Identification

Anatomical landmarks were identified on the surface mesh (Figure 3.10), including the PV ostia, MV annulus, and fossa ovalis (FO). The MV annulus was defined as the largest connected

boundary loop. Through surface connectivity analysis, we located the right and left superior PV (RSPV, LSPV) junctions, as well as the right and left inferior PV (RIPV, LIPV) junctions. The FO point was manually placed to guide the septal boundary of α_{LA} . Geodesic paths were later computed between these landmarks to define coordinate boundaries.

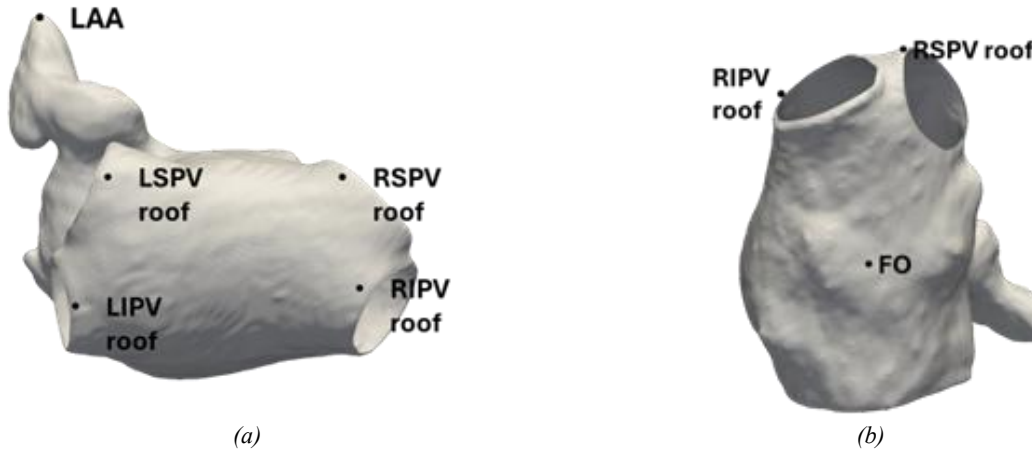


Figure 3.10: Identification of anatomical landmarks for Case 1 SR, which shows (a) the left atrial appendage (LAA) and pulmonary vein (PV) roofs, and (b) the fossa ovalis (FO) along with the right pulmonary vein (RPV) roofs.

PV boundary points were placed slightly inward from the vein openings to avoid ambiguity in hole detection while preserving anatomical fidelity. Landmark selection for the first frame (Frame 1) was performed manually in Blender 4.4, and the coordinates of five anatomical landmarks were exported in .txt format. Because the Lagrangian mesh maintained consistent point indexing across frames, these indices were used to track landmarks throughout the cardiac cycle. A custom MATLAB script automated coordinate extraction for all 40 frames, ensuring consistent landmark tracking. The extracted landmarks were then used in the UAC mapping code to compute α - β coordinates for each mesh point, producing standardized spatial representations of the LA geometry for subsequent analysis.

3.4.3 Alpha Mapping

The longitudinal coordinate, α_{LA} , was computed by solving the Laplace–Beltrami equation:

$$\nabla_s^2 \alpha_{LA} = 0$$

The Dirichlet boundary conditions are defined as follows: $\alpha = 0$ along the septal boundary and $\alpha = 1$ along the lateral boundary, as illustrated in Figure 3.11. The septal boundary was defined as the shortest geodesic path from the RSPV–LA junction to the MV annulus passing through the FO, while the lateral boundary was the shortest geodesic from the LSPV–LA junction to the MV annulus located posterior to the LAA. This ensured correct anterior–posterior orientation of the LAA in the final map.

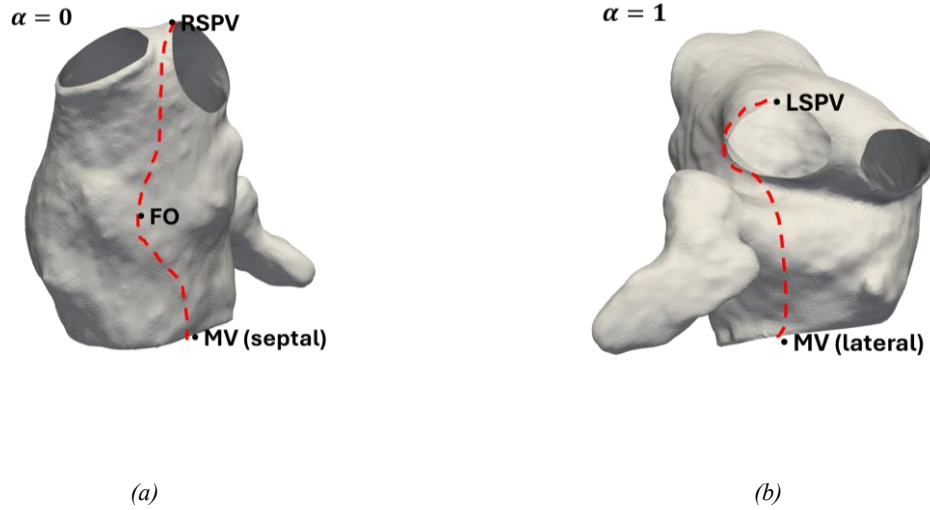


Figure 3.11: α_{LA} boundaries for Case 1 SR showing (a) septal path ($\alpha = 0$) and (b) lateral path ($\alpha = 1$) paths from PV-LA junctions to the MV annulus

3.4.4 Beta Mapping

The transverse coordinate, β_{LA} , was computed by solving:

$$\nabla_s^2 \beta_{LA} = 0$$

In Figure 3.12, $\beta = 0$ is assigned to the posterior boundary at the atrial roof, while $\beta = 1$ is assigned to the anterior MV annulus. The atrial roof boundary was defined as a geodesic path connecting posterior aspects of the RSPV–LA and LSPV–LA junctions. The posterior PV segments were identified using automatically detected anatomical markers and validated to ensure consistent placement of PVs relative to the LAA in the flattened coordinate system.

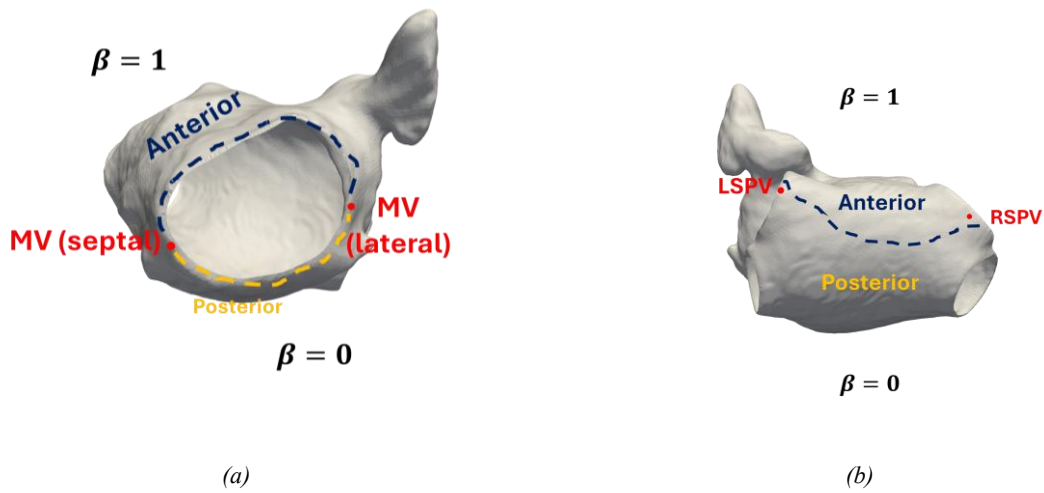


Figure 3.12: β_{LA} boundaries for Case 1 SR showing (a) anterior ($\beta = 1$) and posterior ($\beta = 0$) limits on the MV annulus and (b) corresponding posterior–anterior separation across the superior PVs.

3.4.5 Coordinate Rescaling

Finally, α_{LA} values were rescaled to account for the true anatomical length of the posterior wall at constant β_{LA} . This normalization ensured that comparable α – β coordinate pairs corresponded to equivalent anatomical locations across all cases. The rescaled coordinates were then used to generate the final 2D UAC maps for projecting wall motion and frequency data.

3.5 Wall Velocity Projection on UAC

After computing the UAC system for all time frames, the next step involves mapping the dynamic changes in the left atrial wall motion onto this standardized coordinate space. In this study, the wall motion is extracted from CFD simulations, which model the interaction between blood flow and the deforming left atrial wall. During the CFD simulation, the motion of the atrial wall is captured in 3D Lagrangian space. This 3D motion data provides the deformation of the left atrial mesh across time, driven by the pressure and flow field of the blood.

To extract quantitative wall motion from the CFD output, we focus on a converged cardiac cycle—a complete, periodic loop in which the flow and wall motion behavior is stable and repeatable. From this cycle, we retrieve the 3D coordinates of mesh points (or voxels) for each of the 40 time frames. However, to accurately quantify how the wall moves over time, especially at the boundary of the left atrial cavity, we utilize a SDF approach.

The SDF is a scalar function defined in 3D space and time that, for any given point, returns the shortest distance to the surface of the left atrial wall. The sign of the value indicates the point's location relative to the wall:

The SDF is a scalar field denoted by $\phi(x, t)$ which provides the shortest distance from any spatial point x to the LA surface at time t , along with a sign that indicates whether the point lies inside or outside the anatomical domain. Specifically, $\phi(x, t) = 0$ if the point lies exactly on the LA wall, $\phi(x, t) > 0$ if the point lies outside the atrial body, and $\phi(x, t) < 0$ if the point lies inside the tissue.

This field serves as a powerful tool to estimate the velocity of the atrial wall in the direction normal to the surface, denoted as v_n . Because the LA wall moves over time due to contraction and expansion, the location of the surface changes, and so does the value of ϕ at a given spatial point. However, the defining feature of the wall, the zero level set of the SDF, is conserved in time as it moves with the material surface. Therefore, the material derivative of the SDF along the wall satisfies:

$$\frac{D\phi(x, t)}{Dt} = \frac{\partial\phi(x, t)}{\partial t} + v \cdot \nabla\phi(x, t) = 0$$

Here $\phi(x, t)$ is the SDF and v is the velocity vector of the wall. This equation states that as the wall moves, the zero level set of the SDF (i.e., the wall itself) is advected by the velocity field without changing its value. Thus, the dot product $v \cdot \nabla\phi$ corresponds to the normal component of the wall velocity v_n . Rearranging the material derivative, we obtain:

$$\frac{\partial\phi(x, t)}{\partial t} = -v_n$$

This equation indicates that the rate of change of the SDF in time at a point on a surface is directly proportional to the negative of the wall's normal velocity. Therefore, we can compute the normal velocity by measuring how the value of ϕ changes over time at a fixed spatial location.

Assuming that the temporal change is small between two consecutive frames, we can approximate the time derivative using a finite difference scheme as shown below:

$$\frac{\partial\phi(x, t)}{\partial t} \approx \frac{\phi(x, t + 1) - \phi(x, t)}{\Delta t} = \frac{\phi(x, t + 1)}{\Delta t} = v_n$$

By restricting this analysis to the surface at time t , $\phi(x, t) = 0$. Thus, the normal velocity of the LA body wall can be approximated from the SDF computed at each frame, using only the current and next time steps. This velocity is computed at every point on the LA surface across all frames and subsequently mapped to the UAC space for standardized analysis. The method is illustrated visually using the SDF field where regions inside the atrial body have negative values, regions outside have positive values, and the surface itself corresponds to the zero-level set. This technique enables frame-by-frame computation of wall motion with high spatial and temporal resolution, making it ideal for studying cardiac surface dynamics during the atrial contraction cycle.

3.6 Fourier Analysis of Velocities for Neural-Net

The Signed Distance tool (SDF) data derived from the CFD simulations is interpolated and projected into a uniform α - β grid of dimensions 100×100 using MATLAB's mesh grid tool. Mapping the SDF data onto this grid improves visualization and facilitates direct comparison of wall motion characteristics in both SR and AF scenarios.

To examine localized wall dynamics more thoroughly, the 100×100 UAC mesh is subdivided into 16 equal quadrants (4×4 subregions). This region segmentation facilitates the isolation of particular areas of the LA wall, enabling a more efficient analysis of spatial changes in motion patterns and velocity fluctuations in different parts of the LA, like PVs and MV.

To enhance the analysis of localized wall dynamics, the 100×100 UAC mesh is partitioned into 16 equal quadrants, creating a 4×4 grid of subregions as shown in Figure 3.13. This segmentation facilitates targeted analysis of specific features of the left atrial wall, including the PVs and the

MV, thereby enhancing the ability to identify spatial shifts in motion patterns and velocity fluctuations across different anatomical regions. Employing the Nyquist frequency threshold, we examine the predominant frequencies and energy levels in each area. Comparing the frequency spectra of SR and AF examples reveals distinct differences in periodic behavior, frequency content, and energy localization. These region-specific frequency profiles function as significant attributes for later machine learning models. This technique ultimately converts spatial-temporal velocity data into compact frequency-domain characteristics for each of the 16 regions. This decreases data dimensionality and encapsulates physiologically significant dynamics, facilitating input into a neural network for classification or prediction tasks concerning atrial health.

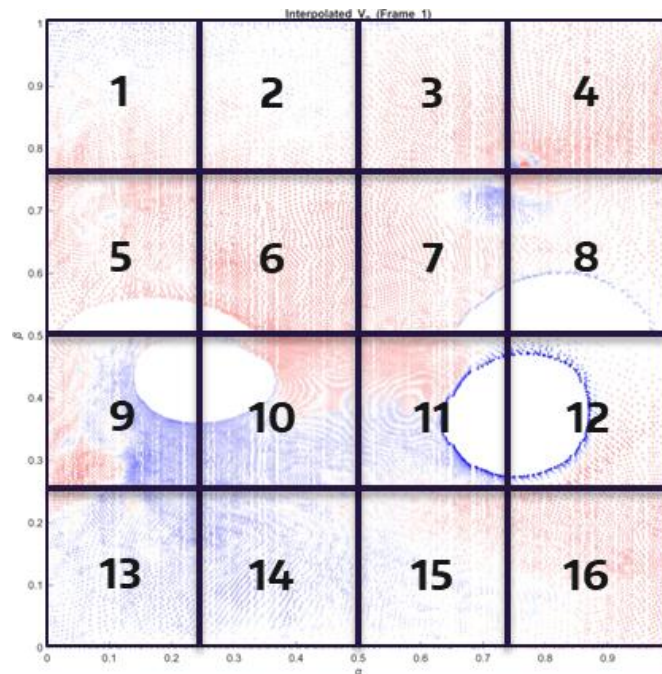


Figure 3.13: Case 1 SR UAC space divided into 16 spatial blocks for regional wall motion analysis

Chapter 4: Results and Discussion

4.1 Meshing and Preprocessing Results

4.1.1 Segmentation quality and corrections

After using nnU-Net segmentations, we obtained a reasonably accurate anatomical reconstruction of the LA. The initial results captured the overall geometry of the PVs, MV annulus, and LAA to a satisfactory extent. However, several adjustments were necessary to refine these structures and ensure consistency across temporal frames.

In particular, the LA body boundaries and PVs exhibited segmentation artifacts and irregular edges that could impact downstream meshing and simulation quality. Therefore, we performed manual corrections in ITK-Snap to refine the PV inlets, clean the MV annulus, and isolate the LAA more precisely. These refinements improved anatomical fidelity, reduced stair-stepping artifacts on the boundaries, and enhanced the mesh compatibility with CFD solvers.

As discussed in Section 3.1, this manual intervention ensures the structural accuracy necessary for simulating physiologically relevant wall motion. Below in Figure 4.1, we present one representative case showing the initial nnU-Net prediction and the final manually corrected segmentation used for meshing and flow simulation.

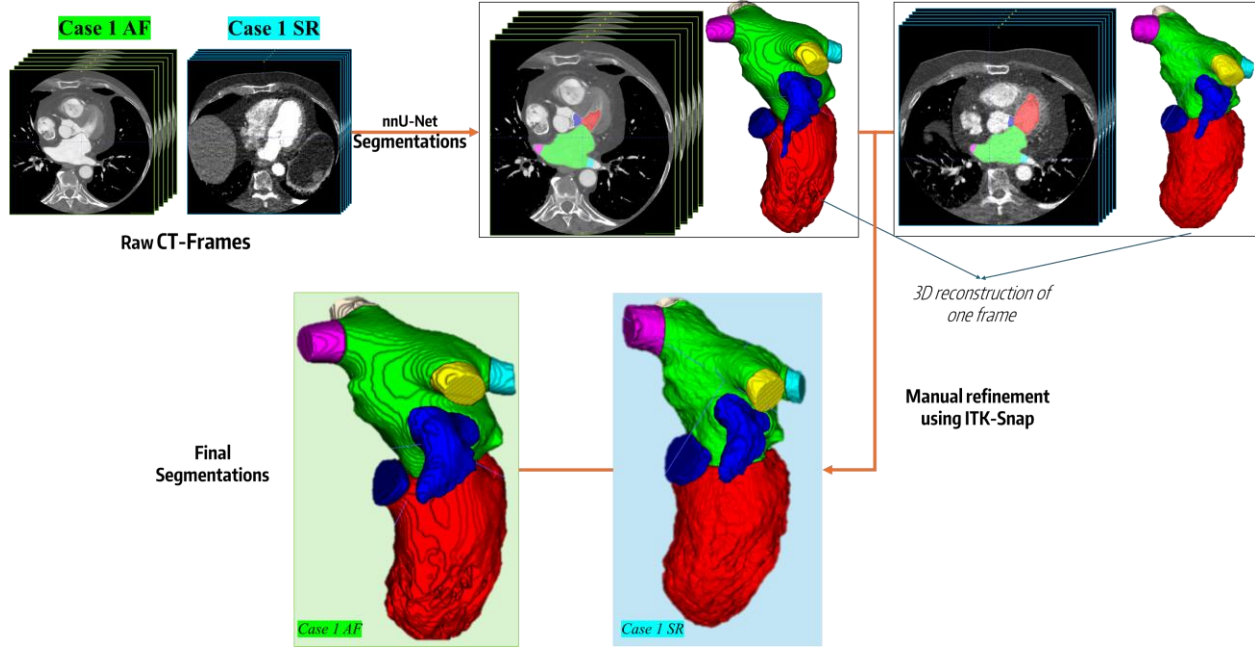


Figure 4.1: Workflow of LA segmentation for subject Case 1 (AF and SR cases). Raw CT frames from AF and SR cases were input into the nnUNet model to generate segmentations of ROI. A 3D reconstruction from one representative is shown. The outputs were further manually refined using ITK-Snap to ensure anatomical accuracy. The final segmentations for both AF and SR cases are shown at the bottom.

4.1.2 Temporal Smoothing and Noise Reduction

To enhance the anatomical accuracy of the segmented geometry, a level-stencil-based smoothing technique using a Gaussian filter was applied. As shown in **Error! Reference source not found.** The unsmoothed surface displays stair-step artifacts and jagged edges, particularly on the LA surface and LAA structure. These irregularities can lead to numerical instabilities during mesh generation and CFD simulations. After smoothing, the left atrial wall appears significantly more continuous and anatomically realistic. The LAA, which previously had a non-uniform and distorted shape, now exhibits a smoother and more consistent structure.

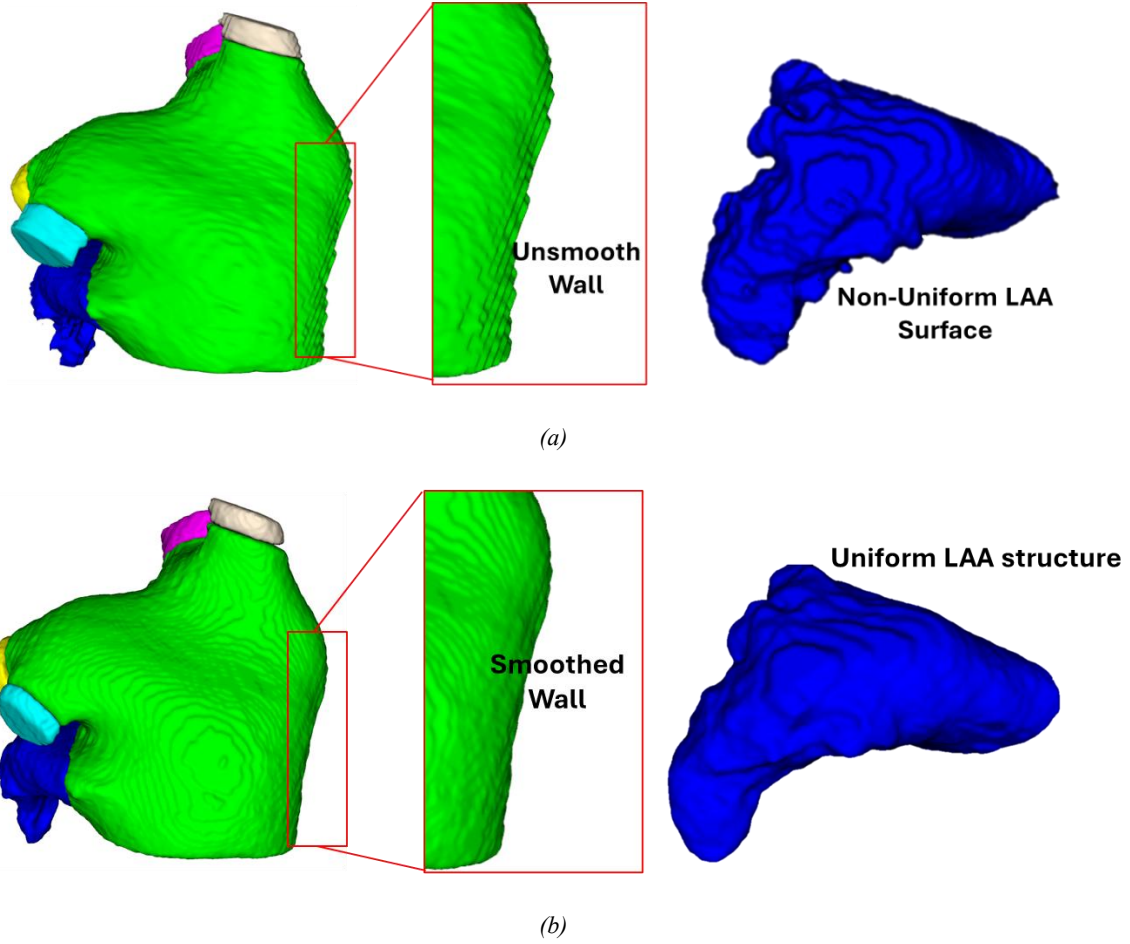


Figure 4.2 Effect of surface smoothing on LA and LAA geometry: (a) Unsmooth LA wall with non-uniform LAA surface, and (b) smoothed LA wall with uniform LAA structure, improving geometric consistency for further analysis.

4.1.3 Surface mesh generation from segmented volumes

Following segmentation and smoothing, a triangular surface mesh was generated for the left atrial (LA) geometry, as shown in Figure 4.3 and Figure 4.4. A histogram of the characteristic lengths of mesh triangles is presented in Figure 4.5. The distribution indicates that most triangles fall within the range of 0.025–0.045 cm, with a peak around 0.035 cm for both AF and SR cases. A red vertical line at 0.05 cm marks the mesh size threshold used for quality control, and only a small fraction of triangles exceeded this limit. The carefully controlled resolution not only preserves

anatomical accuracy but also ensures numerical stability, particularly in the LAA and PV regions, where capturing flow separation and recirculation is essential for physiological modeling.

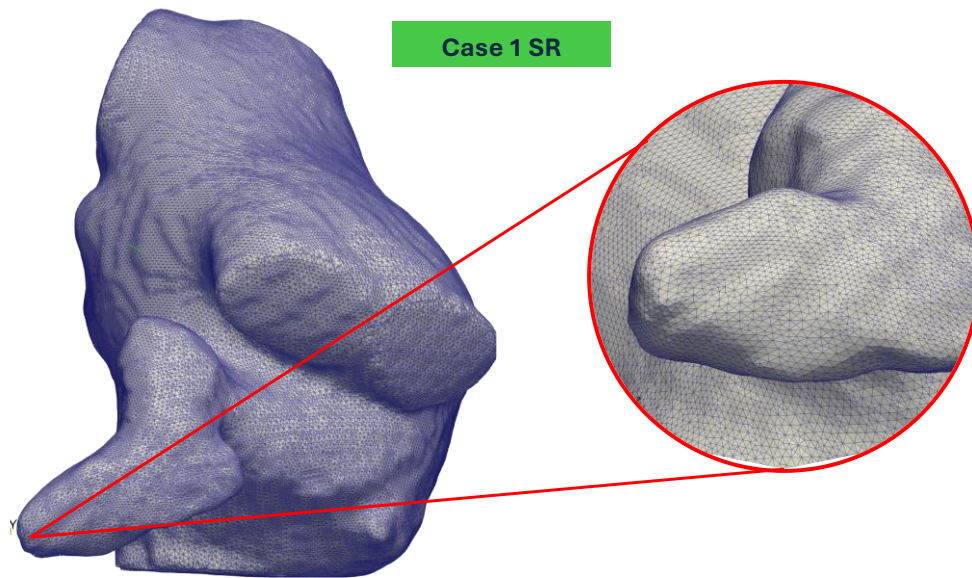


Figure 4.3 Surface mesh for Case 1 SR

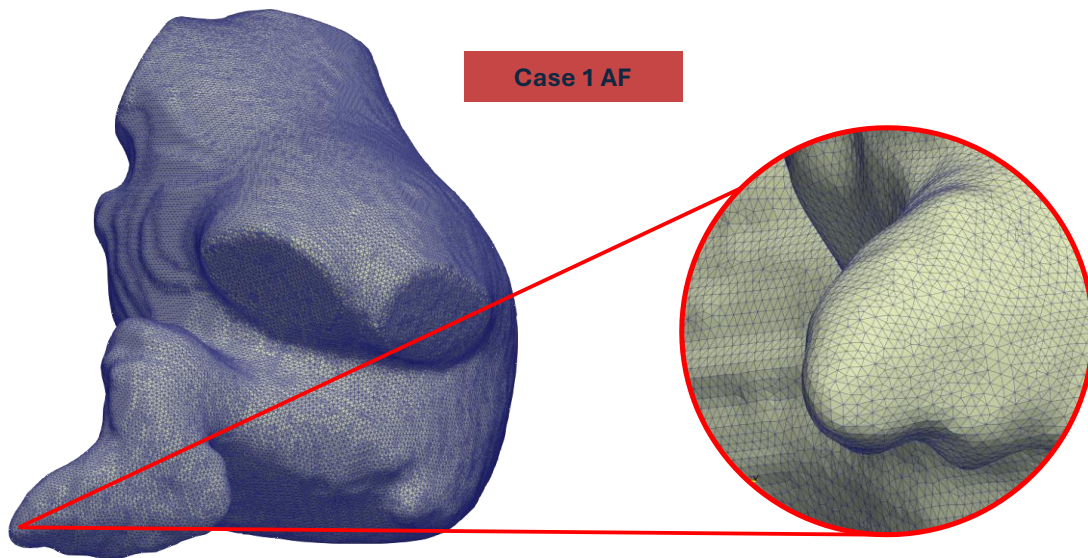


Figure 4.4: Surface mesh for Case 1 AF

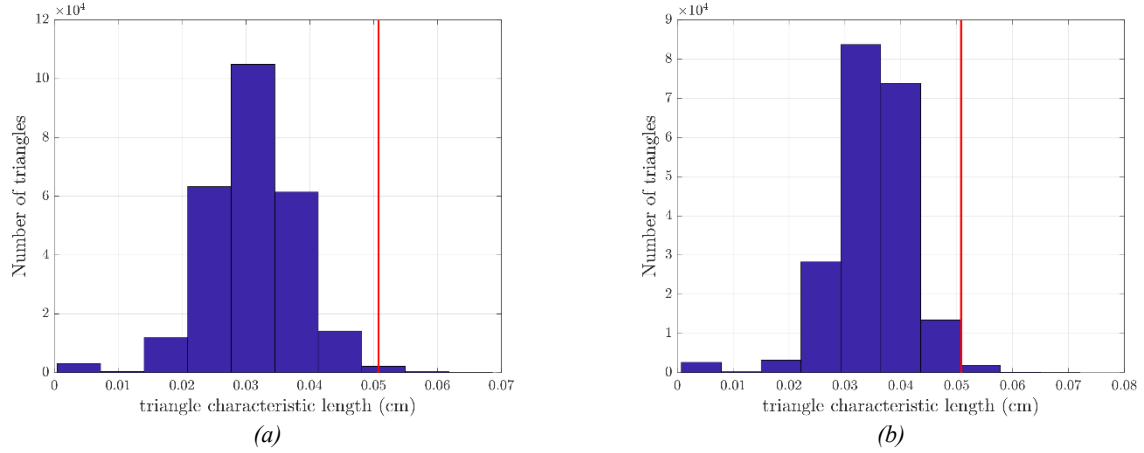


Figure 4.5: Mesh quality (a) Case 1 SR and (b) Case 1 AF

4.1.4 Temporal mesh registration and wall motion interpolation

To achieve a temporally smooth and physiologically accurate representation of left atrial (LA) wall motion, CPD registration was first applied to align the segmented surface meshes across all time points. This ensured non-rigid, anatomically consistent correspondence and minimized frame-to-frame jitter. Spline-based interpolation was then used to generate intermediate frames, increasing the temporal resolution to 40 frames per cardiac cycle. Cubic B-splines preserved the smoothness and continuity of wall motion while capturing meaningful physiological deformation.

Following interpolation, cork particles were generated and tracked across the interpolated surfaces to define the Lagrangian motion of the mesh. These corks maintained consistent vertex correspondence across frames and enabled accurate application of wall velocity in the CFD solver. As shown in Figure 4.6, the interpolated frames demonstrate gradual and continuous expansion and contraction of the 3D LA surface. The combined use of CPD registration, spline interpolation, and cork tracking resulted in high-quality, artifact-free motion suitable for simulating dynamic left atrial blood flow.

Table 4.1 below summarizes the number of vertices and faces for each case in both SR and AF after registration.

Table 4.1: Total Number of vertices and faces

Case ID	Number of Vertices	Number of Triangles
Case 1 SR	135545	261822
Case 1 AF	107668	207388
Case 2 SR	124060	240460
Case 2 AF	159267	309890
Case 3 SR	154245	308486
Case 3 AF	155717	302329

The Eulerian geometry for CFD analysis was generated using the Immersed Boundary Method (IBM) on a uniform Cartesian grid to ensure numerical stability and compatibility with the structured solver. Grid spacing was chosen to balance spatial resolution and computational cost, and each simulation domain was sized to fully enclose the deforming atrial wall throughout the cardiac cycle. CFD simulations were carried out using a finite difference method (FDM) framework. The FDM was used to solve the governing equations for velocity and pressure, while a high-order WENO scheme was applied to the transport equation for residence time (RT), enabling accurate resolution of sharp gradients and minimizing numerical diffusion. The Eulerian grid resolution used for each case is summarized below in Table 4.2.

Table 4.2: Eulerian Grid Resolution for each case

Case ID	Eulerian Grid Resolution
Case 1 SR	256x256x256
Case 1 AF	256x256x256
Case 2 SR	256x270x256
Case 2 AF	256x280x256
Case 3 SR	256x288x270
Case 3 AF	256x274x264

Wall motion within the Eulerian grid was captured using a Signed Distance Function (SDF)-based approach. The SDF was computed at each time point of the cardiac cycle, where a value of zero represents the atrial wall surface, positive values indicate points outside the wall, and negative values correspond to regions inside the wall. This implicit representation enabled smooth tracking of the dynamically deforming atrial surface on the fixed Cartesian grid. By interpolating SDFs across frames, the wall position and velocity were accurately reconstructed and imposed within the Immersed Boundary framework. The figure below illustrates the temporal evolution of the atrial wall as represented by the SDF across multiple phases of the cardiac cycle, highlighting the contractile behavior and regional deformation patterns. Notably, a greater range of distance values is observed in SR compared to AF, reflecting stronger and more synchronized wall contractions in SR and reduced or disorganized motion in AF. This will be used further for projecting normal wall velocity onto UAC.

4.2 Universal Atrial Coordinate Results

4.2.1 UAC Generation for SR and AF

The UAC system was successfully generated for the segmented LA geometry in both SR and AF cases, across all time frames of the cardiac cycle. The β and α coordinates were computed to represent the circumferential and longitudinal directions, respectively. Figure X (top row) shows the β coordinate distribution, which varies smoothly from 0 (blue) to 1 (red) across the atrial surface. This smooth gradient confirms that the circumferential mapping preserved anatomical continuity around the LA body and appendage, enabling consistent orientation across all surface points. Figure 4.6 presents the α coordinate after rescaling, demonstrating a uniform progression from the MV annulus (low values) to the left atrial appendage tip (high values). The coordinate field maintained smooth transitions even in regions with high curvature, such as around the pulmonary vein inlets, indicating robust parameterization over complex geometries.

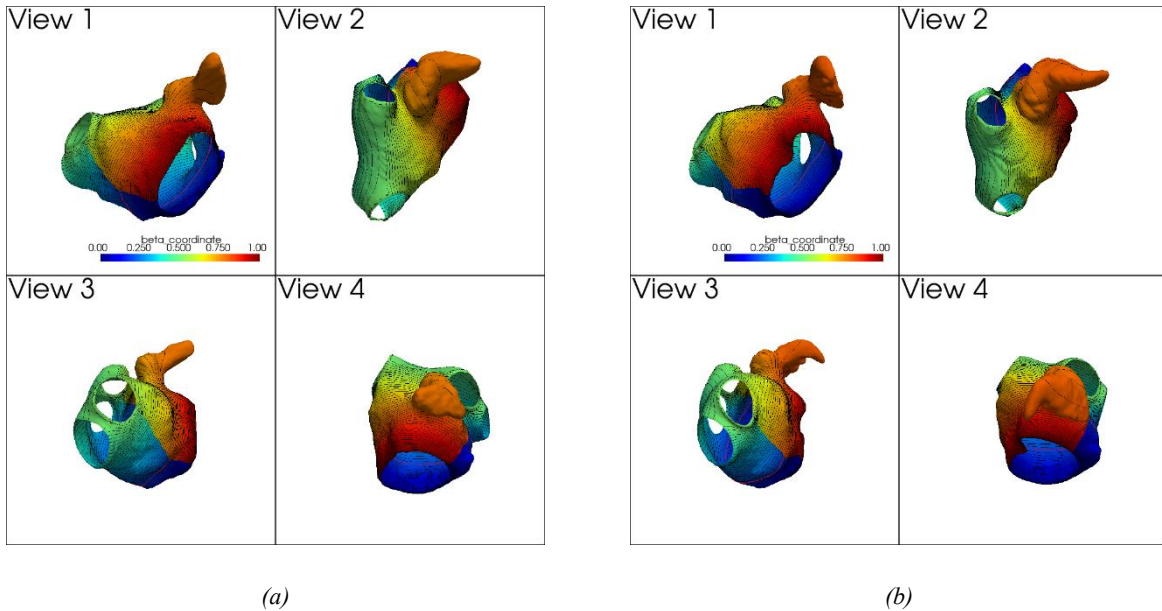


Figure 4.6 Four views of the left atrium at frame 1 showing β -coordinate mapping for (a) Case 1 SR and (b) Case 2 AF. Colors range from anterior (blue) to posterior (red).

The α -coordinate mapping for case 1 was evaluated in both SR and AF geometries before and after rescaling Figure 4.7. In both SR and AF, the α -coordinate showed a smooth progression from the MV annulus (blue) to the left atrial appendage tip (red). After rescaling, the coordinate distribution became more uniform across the atrial surface, maintaining consistent gradients along the longitudinal direction in the UAC system.

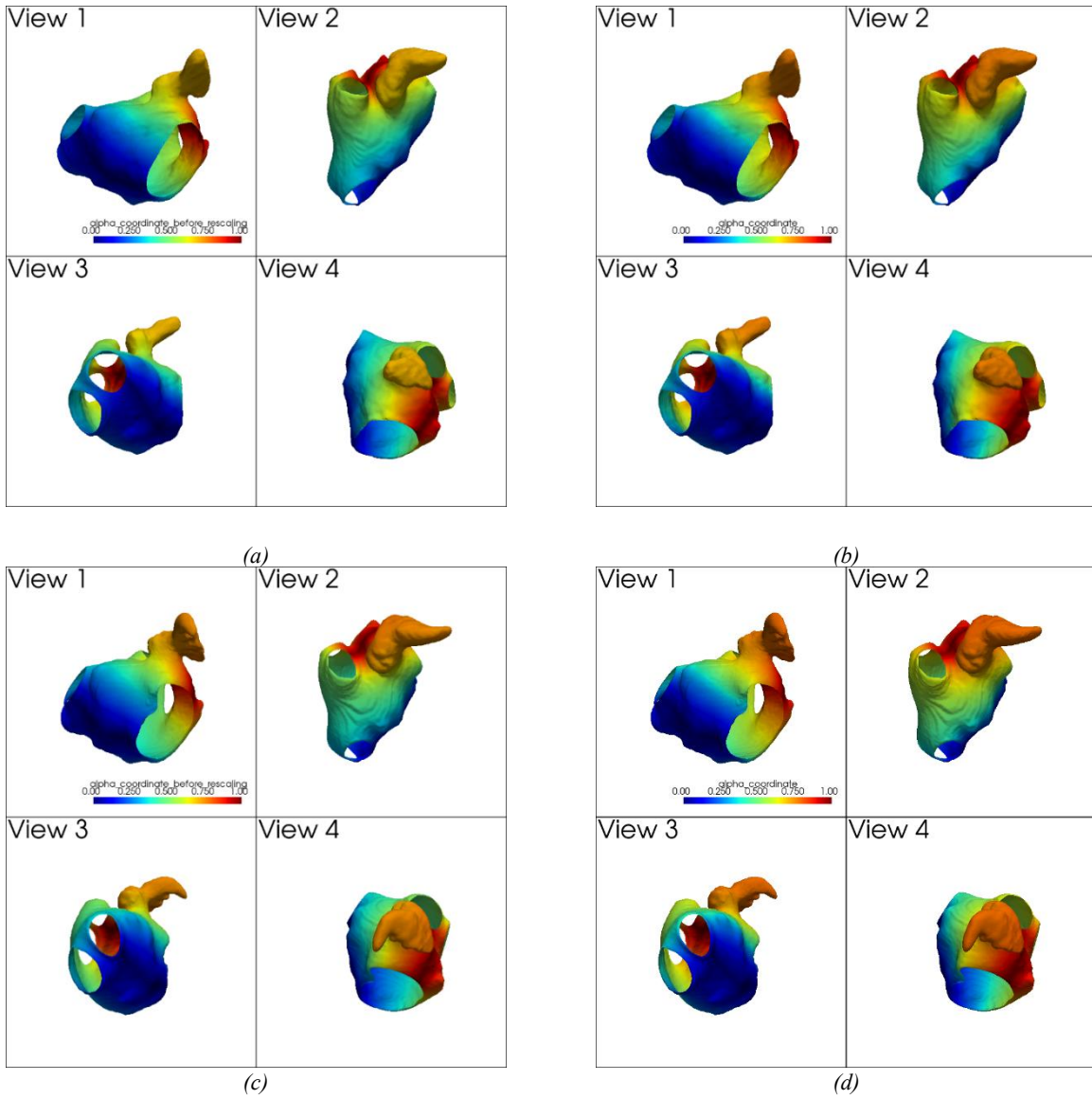


Figure 4.7: Four views of the left atrium showing α -coordinate mapping at frame 1 for case 1. (a) SR before rescaling, (b) SR after rescaling, (c) AF before rescaling, and (d) AF after rescaling. Colors range from the mitral valve annulus (blue) to the left atrial appendage tip (red), representing the longitudinal direction in the UAC system.

The LAA was segmented from the LA geometry to assess the extent and quality of its capture. Figure 4.8 presents four views of the segmented LA, with the LAA highlighted in green and the remaining LA body in gray. The segmentation successfully identified the LAA's origin from the anterior-superior region of the LA and preserved its general orientation relative to the pulmonary veins and MV annulus. However, the distal lobes and finer morphological details were only partially captured, indicating incomplete representation of the full anatomical structure. This partial capture provides sufficient information for basic anatomical referencing in the UAC framework but may limit detailed morphological analyses or applications that rely on full appendage geometry.

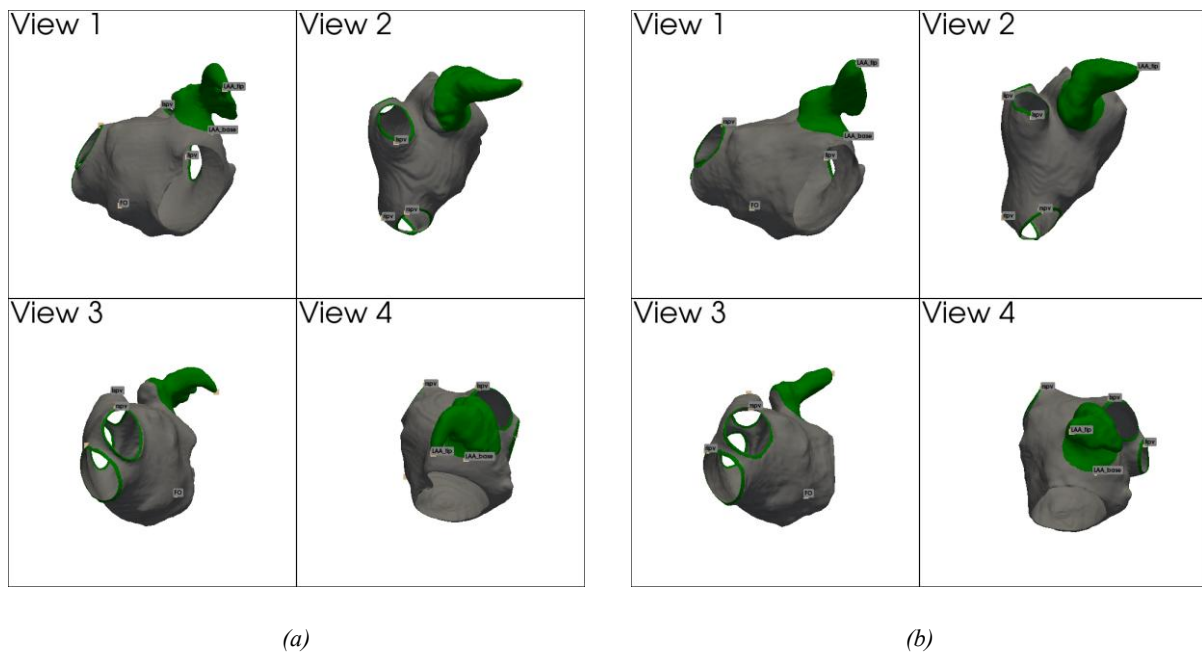
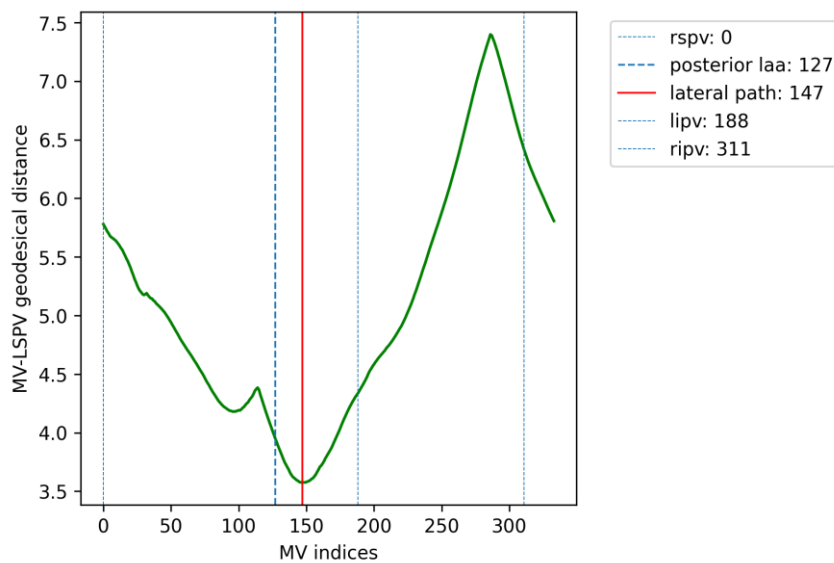


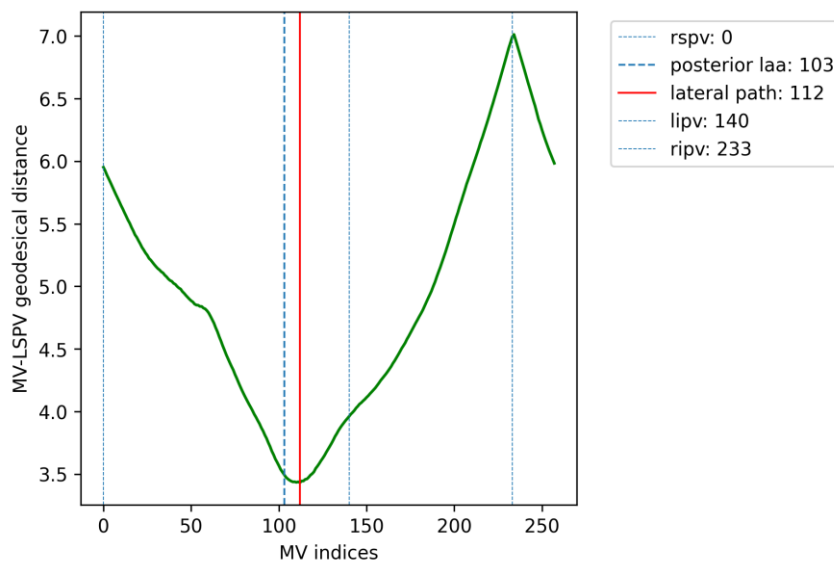
Figure 4.8: Four views of the segmented LAA (green) for case 1 in (a) SR and (b) AF. The LAA's origin, orientation, and partial morphology are visible relative to the LA body (gray)

The sanity assessment for the UAC system was performed by plotting the geodesic distance from the MV to the LSPV across MV indices for both SR and AF geometries (Figure 4.9). In both cases, the curve exhibits a distinct valley, corresponding to the shortest path between the MV and LSPV along the atrial surface. This valley occurs between the posterior LAA and lateral path landmarks,

aligning with the expected anatomical location of the direct MV–LSPV connection. The presence of a single, well-defined valley in both SR and AF confirms that the circumferential ordering of MV indices is correct and that the β -coordinate parameterization preserves anatomical continuity.



(a)



(b)

Figure 4.9: MV–LSPV geodesic distance for case 1 in (a) SR and (b) AF, with the valley indicating correct anatomical ordering.

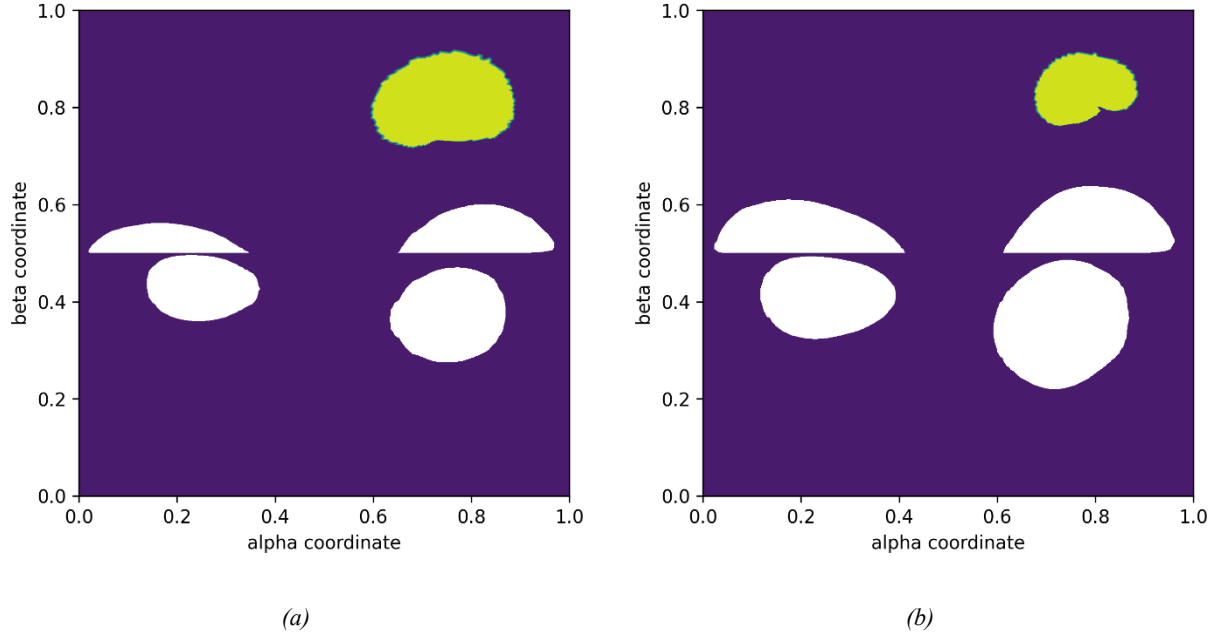


Figure 4.10: Final UAC framework for Case 1 (a) SR and (b) AF at frame 1.

Figure 4.10 shows the final UAC framework for case 1 in SR and AF at frame 1, with both α - and β -coordinates normalized between 0 and 1. The framework clearly maps the atrial surface to a structured 2D coordinate space, where anatomical regions such as the pulmonary veins and left atrial appendage (highlighted in yellow) are distinctly localized. This mapping provides a consistent spatial reference across the atrial surface, enabling direct comparison between SR and AF geometries. The same procedure was applied to all 40 frames for each patient, ensuring temporal continuity in coordinate mapping throughout the cardiac cycle.

4.2.2 UAC-based wall velocity projection and Fourier analysis

The velocity field was projected onto the UAC framework using the computed SDF after the CFD simulation. Specifically, the normal component of the wall velocity was extracted at the zero-level set of the SDF to represent surface motion. This mapping enabled the transformation of complex

3D wall dynamics into a structured 2D (α , β) coordinate space, facilitating consistent comparison across time points and patient cases.

The SDF representations in the Eulerian domain for the LA geometry illustrate the spatial configuration of the chamber surface in SR and AF prior to the projection of wall motion onto the UAC system, as shown in Figure 4.11. The SDF clearly captures the chamber boundaries with smooth gradients from the endocardial surface (zero-level set) to the surrounding domain, enabling accurate delineation of wall locations for subsequent velocity mapping. While both SR and AF geometries preserve the overall anatomical topology, subtle differences in shape and curvature are visible, particularly along the left atrial appendage and posterior wall. The SDF color bar limits directly reflect the extent of motion captured in each case, with SR showing a larger range that indicates greater wall displacement and AF showing a narrower range that is consistent with reduced wall motion. By establishing a consistent geometric basis through the SDF, this stage ensures that the subsequent UAC projection captures true spatial correspondence rather than being confounded by mesh or alignment discrepancies.

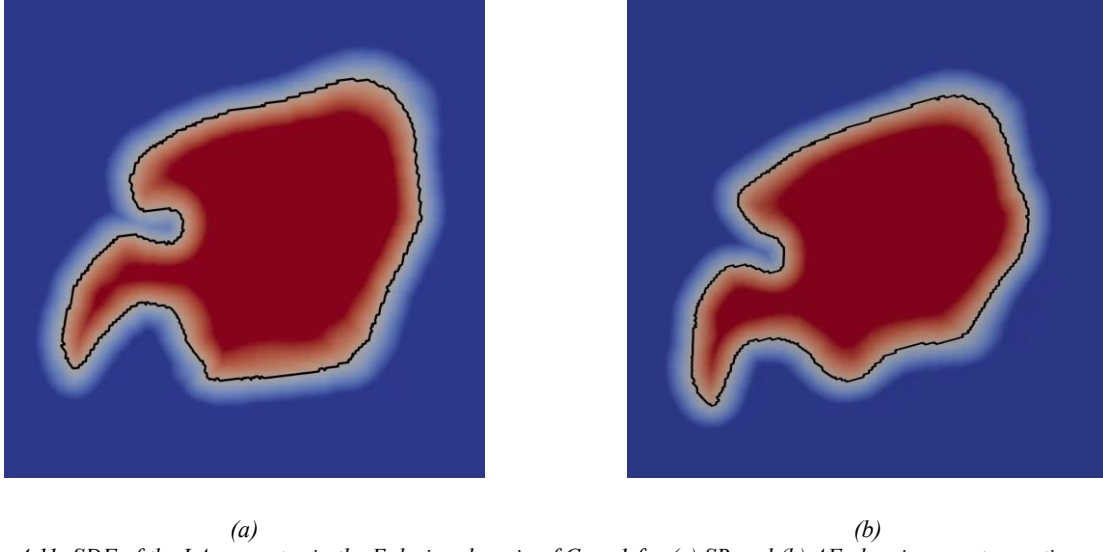


Figure 4.11: SDF of the LA geometry in the Eulerian domain of Case 1 for (a) SR and (b) AF, showing greater motion range in SR as indicated by the broader colorbar limits.

The projection of wall-normal velocity V_n the UAC for Case 1 (Figure 4.12) highlights distinct spatiotemporal patterns between SR and AF across the cardiac cycle. In SR, higher velocity magnitudes and clearer large-scale flow structures are observed, particularly at early (0%) and mid-diastolic (25%) phases, with more organized red–blue regions indicative of coherent inflow and outflow jets. In contrast, AF exhibits markedly reduced peak velocities and more spatially fragmented patterns, reflecting weaker and less synchronized wall motion. The late-diastolic (80%) phase in AF shows diminished velocity gradients compared to SR, suggesting impaired contractile efficiency. Notably, the magnitude range in AF is consistently lower, which may limit the ability to capture subtle yet clinically relevant differences in wall dynamics when using velocity projection alone. This reduced dynamic range underscores a methodological limitation—while UAC-based mapping standardizes spatial comparison, the attenuated AF velocities may approach the noise floor in regions of low motion, potentially affecting interpretability in quantitative analyses.

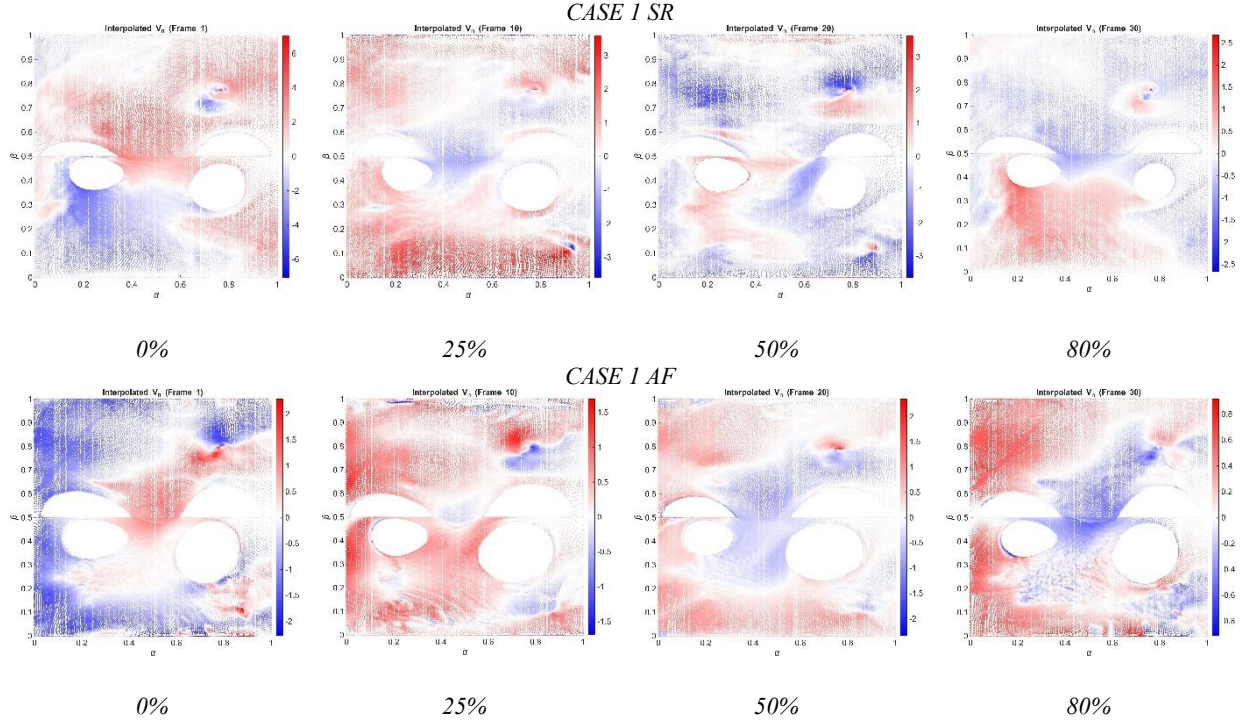


Figure 4.12: Wall-normal velocity (V_n) projected on UAC for Case 1 showing reduced magnitude and coherence in AF compared to SR across cardiac phases.

Figure 4.13 presents the variation of average normal wall velocity (V_n) over one cardiac cycle for SR and AF in cases 1, 2, and 3. Across all cases, SR geometries exhibit larger fluctuations in V_n with distinct peaks and troughs, reflecting the coordinated contraction and relaxation sequence of a healthy atrial cycle. AF cases, in contrast, display dampened and irregular velocity profiles with reduced peak magnitudes and diminished periodicity, indicative of impaired and asynchronous wall motion. The timing of peak velocities shifts between SR and AF for each case, highlighting differences in contraction onset and relaxation phases under arrhythmic conditions. Notably, SR profiles show sharp, well-defined peaks followed by rapid deceleration phases, while AF curves are more flattened and prolonged, suggesting weaker contractile efficiency. Although the overall pattern of higher and more coordinated velocities in SR compared to AF is consistent across all three cases, inter-patient variability is evident in both amplitude and temporal alignment of the curves, likely reflecting differences in individual atrial anatomy and remodeling extent.

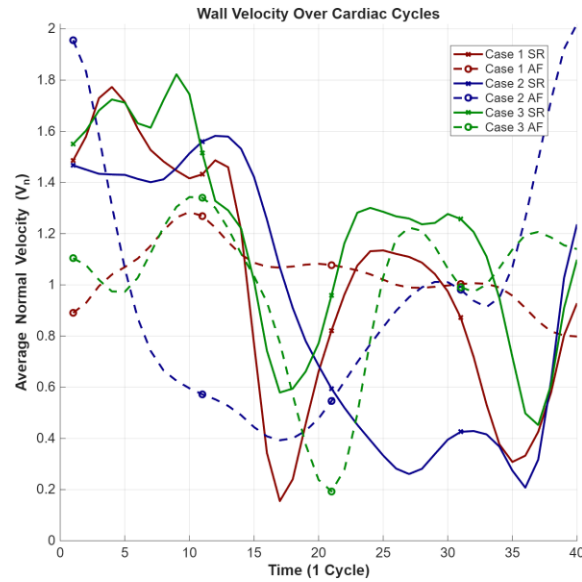


Figure 4.13 Average normal wall velocity (V_n) over one cardiac cycle for SR and AF in cases 1-3

Fourier Transform (FFT) was applied to analyze the energy distribution of wall motion over the whole atrial domain for SR and AF in cases 1–3, with the spectra normalized by the maximum energy value across all harmonics for each case (Figure 4.14). Overall, SR cases show higher energy than AF at low frequencies, indicating more coherent and organized wall motion during SR. In contrast, AF cases display elevated energy in the higher frequency range (>8 Hz), reflecting the irregular and rapid fluctuations characteristic of arrhythmic contraction. Among the three cases, clinical case 3 demonstrates the highest overall motion energy in both SR and AF, suggesting stronger anatomical variation and greater rhythm intensity compared to the other cases.

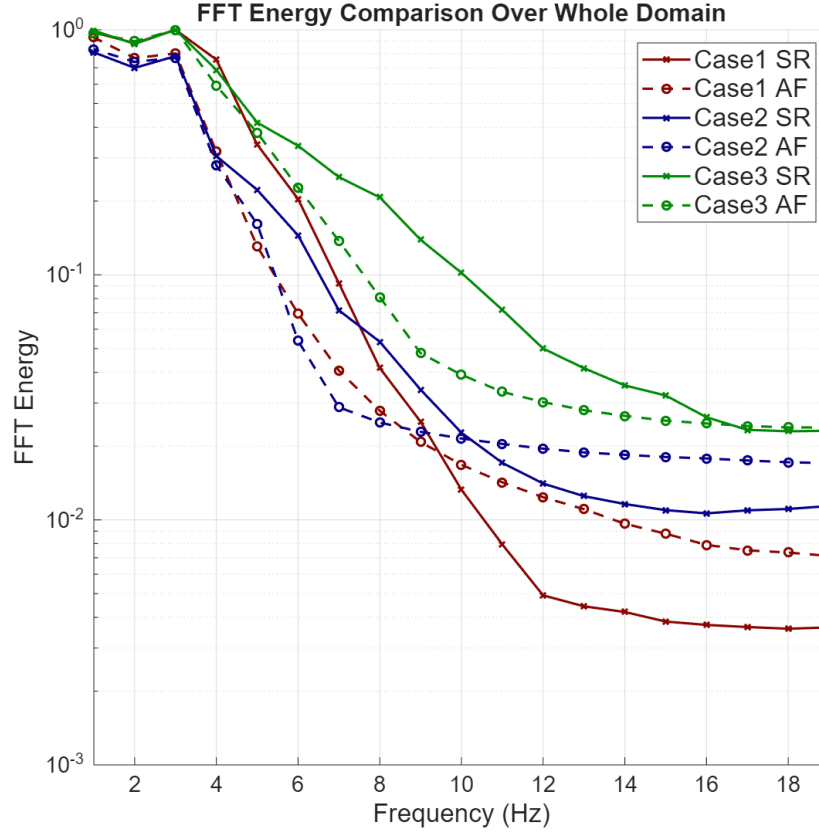


Figure 4.14: FFT energy distribution of wall motion for SR and AF in cases 1–3 over the whole atrial domain.

To analyze local rhythm signatures across LA surfaces, FFT was applied to 16 anatomical regions (blocks) for SR and AF in cases 1, 2, and 3, with spectra normalized by the maximum energy value across all harmonics for each block (Figure 4.15). In the anterior regions, particularly blocks 1, 2, 3, 4, and 7, which include the LAA and adjacent anterior wall, AF cases exhibit noticeably higher energy in the high-frequency range (>8 Hz), reflecting rapid and irregular wall motion patterns. SR cases in these regions show stronger low-frequency energy, indicating more coherent and organized contraction. The difference between SR and AF is most pronounced in block 3, where AF maintains a relatively flat decay at higher frequencies, suggesting persistent rapid motion components.

In the posterior regions, represented exclusively by blocks 12, 15, and 16, the spectral differences between SR and AF are still evident but less dramatic. SR cases maintain higher low-frequency energy, consistent with synchronized posterior wall motion, whereas AF cases show slightly elevated mid-frequency content, indicating residual irregularities even in these regions. Overall, these patterns reveal that AF is associated with stronger high-frequency local rhythm signatures near the LAA and anterior wall, while SR consistently exhibits low-frequency dominance across the LA surface, with posterior regions showing a subtler separation between rhythms.

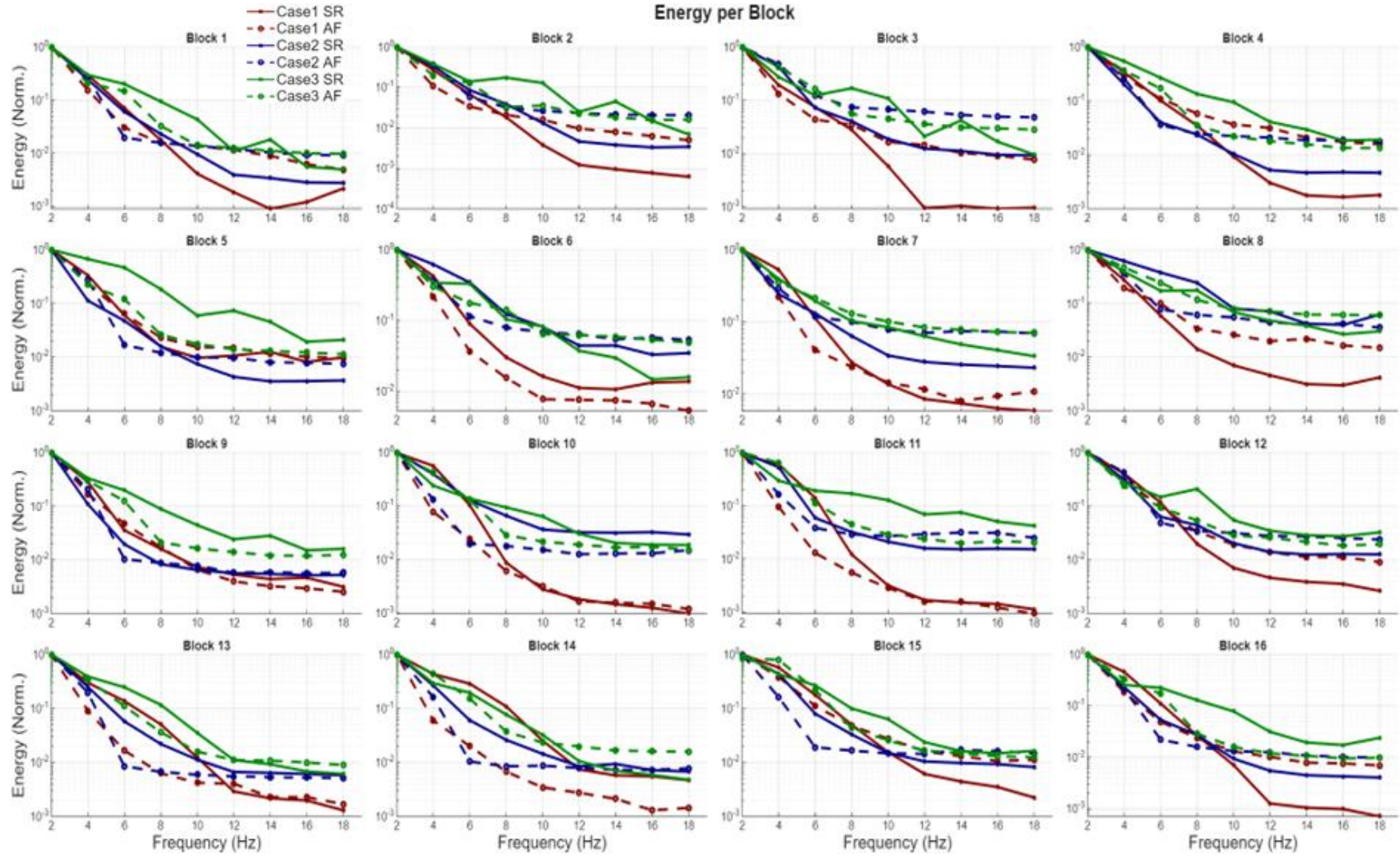


Figure 4.15: Normalized FFT energy spectra for 16 anatomical regions (blocks) of the LA in SR and AF for cases 1–3. AF shows higher high-frequency energy, especially in anterior regions near the LAA, while SR exhibits stronger low-frequency energy across most regions.

4.2.3 *Regional Variation in Wall Motion Energy*

In Figure 4.16, the plots show the correlation (r) heatmaps between SR and AF FFT energy spectra for 16 anatomical blocks of the LA in cases 1, 2, and 3. Values closer to 1 indicate a high degree of similarity in frequency-domain patterns between the two rhythms, while lower values point to greater divergence in local rhythm signatures. Each cell corresponds to the correlation between SR and AF for a specific block pairing, with warm colors (yellow) representing higher correlation and cooler colors (blue) representing lower correlation. Notably, certain anterior wall and LAA-associated blocks in case 3, such as block 1, show significantly reduced correlation values, indicating substantial differences in spectral content and contraction dynamics compared to SR.

The patterns across the three cases highlight both preserved and disrupted motion regions in AF. In cases 1 and 2, most blocks maintain high correlation values, suggesting that AF modifies the magnitude of frequency components without drastically altering the spectral profile. In contrast, case 3 exhibits more heterogeneous correlation, with specific regions showing marked departures from SR, likely reflecting localized desynchronization or loss of coordinated motion. This spatial variability underscores that AF does not uniformly disrupt LA wall motion but rather affects certain anatomical regions more severely, which could have implications for targeted rhythm assessment and intervention strategies.

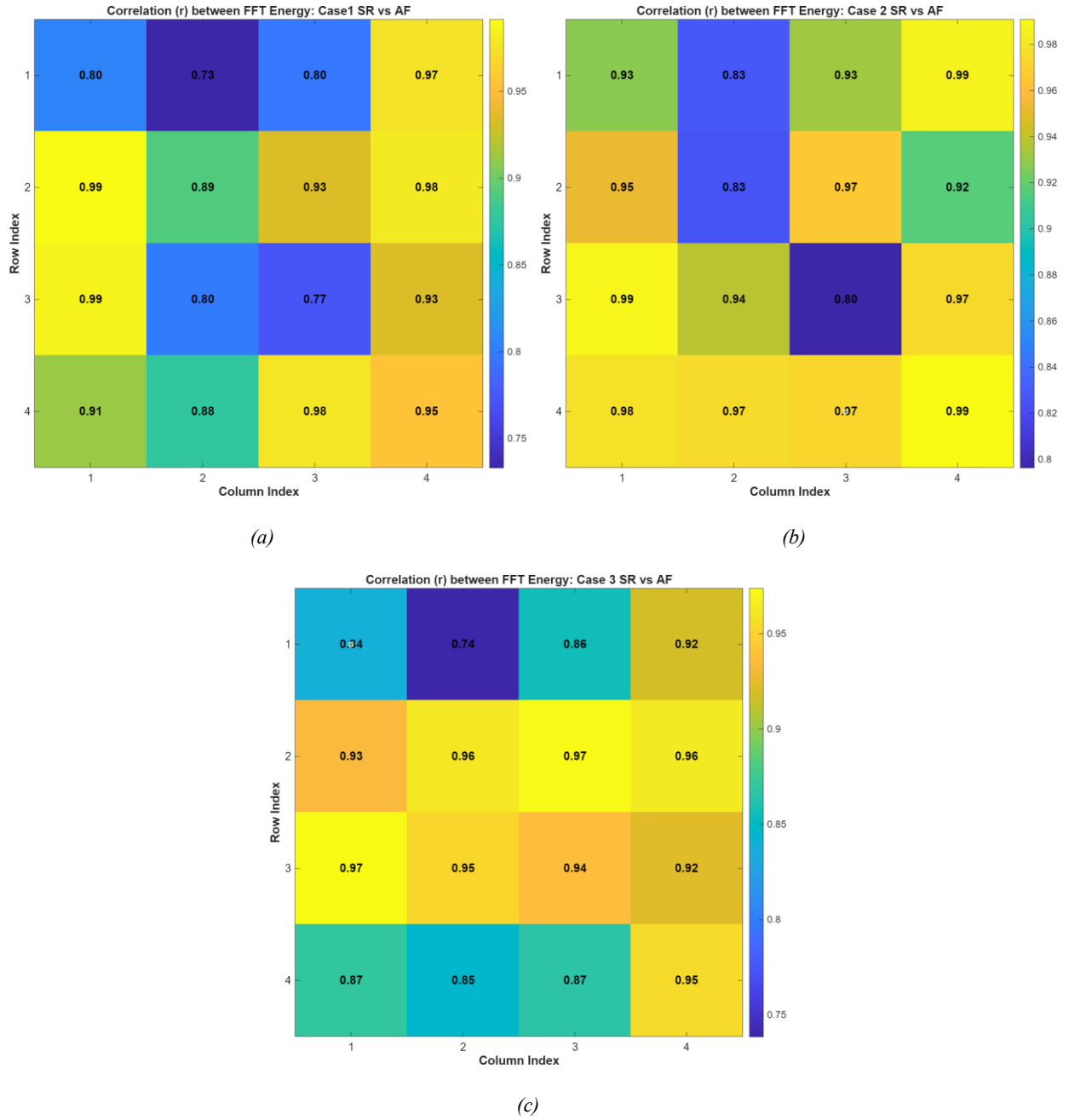


Figure 4.16: Correlation (r) between FFT energy spectra of SR and AF for (a) Case 1, (b) Case 2, and (c) Case 3, computed blockwise across the LA surface.

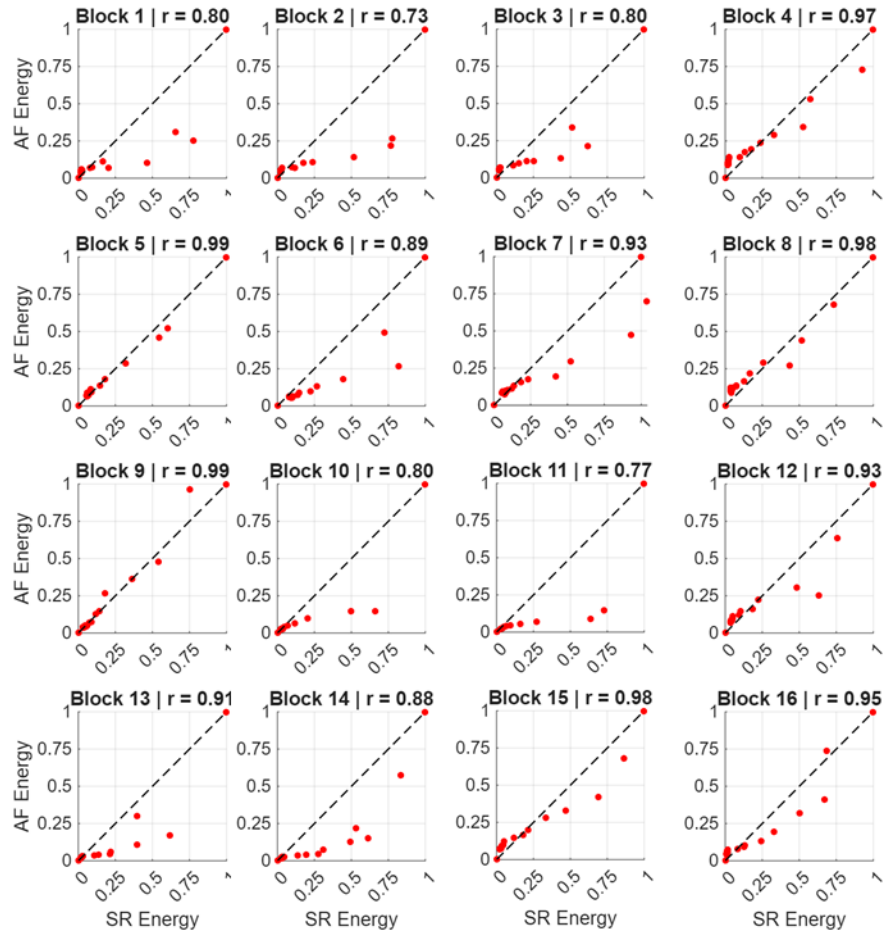


Figure 4.17: Blockwise scatter plots directly comparing normalized FFT energy between SR and AF for Case 1. Each panel shows a specific anatomical block, with the dashed line representing perfect agreement ($r=1$).

Chapter 5: Conclusion and Future Scope

5.1 Conclusion

This work presents a comprehensive, patient-specific computational framework for modeling and analyzing dynamic blood flow in the human LA using time-resolved cardiac CT data. The pipeline integrates segmentation, mesh generation, motion tracking, and frequency-based feature extraction to create a physiologically realistic and simulation-ready LA model. The workflow was applied to three patients, each with paired datasets in both SR and AF, enabling detailed rhythm-wise comparison. Segmentation is performed using a pre-trained nnU-Net model, followed by manual correction to address structural artifacts, particularly near the PVs, MV, and LAA. To reduce voxel-based surface artifacts and ensure continuity, level-set-based Gaussian smoothing is applied prior to surface mesh generation. The resulting triangular meshes, with characteristic lengths between 0.045 and 0.05 cm, offer a balance between anatomical accuracy and computational efficiency.

To model dynamic motion, the segmented surfaces across segmented time points are aligned using Coherent Point Drift (CPD) registration. This non-rigid method minimizes temporal jitter while preserving anatomical fidelity. Spline interpolation is then used to increase temporal resolution to 40 time points per cardiac cycle. Cork particles are seeded and tracked across these frames to define the Lagrangian motion of the surface, enabling the imposition of wall velocity in CFD simulations.

A key strength of the framework lies in the use of the UAC system, generated by solving Laplace-Beltrami equations to produce orthogonal longitudinal (α) and transverse (β) scalar fields. The resulting (α , β) coordinate system provides an anatomically meaningful and standardized mapping

of the LA geometry onto a two-dimensional domain. This enables spatial normalization across patients, simplifies machine learning input generation, and facilitates consistent visualization of motion patterns as 2D heatmaps. The UAC mapping also allows for region-specific analysis and the construction of population-level motion atlases, while improving the interpretability of features derived from complex CFD data.

After CFD simulation, wall velocity was projected onto the UAC domain using SDF. Fast Fourier Transform (FFT) was then applied to the time series of normal wall velocities at each spatial location. This frequency-domain transformation revealed key differences in energy distribution between SR and AF. SR cases were characterized by energy concentrated in low-frequency harmonics, indicative of regular, synchronized contraction. In contrast, AF cases displayed broader and higher-frequency spectra, reflecting disorganized, chaotic wall motion.

Beyond spectral energy, FFT enabled the computation of phase angles at each spatial point, capturing the local timing of wall motion. Phase relationships between SR and AF were explored by plotting AF phase against SR phase across the atrial surface. Regions with steeper positive slopes showed alignment between the rhythms, while shallow or negative slopes indicated phase dispersion and AF-dominant behavior. This desynchronization was particularly pronounced near the LAA and left inferior pulmonary vein (LIPV), regions known to be critical in AF initiation and maintenance. These spatial phase dynamics offer physiologically interpretable features that can enhance machine learning models for rhythm classification or electromechanical coupling analysis.

Ultimately, the FFT-derived features projected in UAC space serve as low-dimensional, structured, and rhythm-sensitive representations of wall motion. Compared to raw CFD outputs,

these spectral maps are better suited for machine learning, improving classification accuracy while enhancing model interpretability. This approach lays the foundation for advanced predictive modeling, including thrombus risk assessment, evaluation of ablation outcomes, and tracking disease progression using patient-specific atrial motion dynamics.

5.2 Limitations

Despite the strengths of the proposed framework, a few limitations remain. Manual refinement of segmentation masks was necessary in anatomically complex regions such as the pulmonary veins and mitral annulus, which limits the scalability and full automation of the workflow. Landmark points for generating the UAC system, including the MV plane and pulmonary vein endpoints, had to be manually selected for each case. This introduces operator dependency and potential variability across datasets. Although the UAC system provides a standardized mapping of the atrial surface, it does not fully capture the intricate geometry of the LAA, particularly due to its peripheral location and high anatomical variability. However, for the purposes of motion analysis and frequency-based feature extraction, the spatial coverage was sufficient. The computational cost of CPD registration, spline interpolation, and time-resolved CFD simulations is considerable, making large-scale or real-time clinical deployment currently impractical.

Another limitation arises from the presence of drift in local motion patterns during AF, where certain regions gradually shift in contraction–relaxation timing or amplitude over the cycle. This drift can influence FFT-based comparisons between SR and AF, potentially lowering correlation values in otherwise structurally similar regions.

The use of FFT assumes periodicity and may not capture transient, non-repetitive features commonly observed in AF. The framework also does not yet incorporate uncertainty quantification, which could be important when extending the model to decision-support systems. Most importantly, the methodology has not been clinically validated against patient outcomes such as thrombus formation or treatment response. This represents a critical next step for translating the research into practical, patient-centered applications.

5.3 Future Scope

This project provides a strong foundation for future advancements in both computational modeling and clinical translation. One immediate extension involves refining the nnU-Net segmentation model. Expanding the training dataset and incorporating more anatomically diverse cases, especially those with complex pulmonary vein and left atrial appendage structures, could improve segmentation accuracy and reduce the need for manual corrections. This improvement would enhance automation and support broader clinical application of the pipeline.

Another promising direction is the use of the Universal Left Atrial Appendage Coordinate (ULAAC) system, developed by Pamplona et al. [53], which captures the geometry of the left atrial appendage more accurately and enables the integration of advanced data analysis tools for improved regional assessment. While this work employed Fast Fourier Transform to extract rhythm-sensitive features, techniques such as Proper Orthogonal Decomposition (POD) or modified Dynamic Mode Decomposition (DMD) could offer deeper insights into spatial-temporal wall motion patterns. These tools may help identify latent deformation modes or transient flow features, adding greater physiological interpretability to machine learning models.

The pipeline can also be leveraged to build predictive models using only SR cases. By learning the normal motion patterns present in SR, machine learning algorithms could be trained to detect early signs of mechanical remodeling that precede the onset of AF. Feeding frequency and phase features extracted in the atrial coordinate space into neural networks may support predictive tasks such as AF risk stratification or recurrence forecasting after treatment.

The UAC framework also allows for the integration of multimodal atrial data, including electroanatomical maps, MRI, or ECG-derived features. This opens the possibility of creating spatially consistent, population-level motion atlases and comparing specific anatomical regions across patients. Future work should include clinical validation to correlate simulation-derived metrics with outcomes such as stroke risk, thrombus formation, or therapeutic response, advancing the framework toward meaningful clinical decision support.

References

- [1] V. L. Feigin *et al.*, “World Stroke Organization (WSO): Global Stroke Fact Sheet 2022,” *Int. J. Stroke*, vol. 17, no. 1, pp. 18–29, Jan. 2022, doi: 10.1177/17474930211065917.
- [2] National Institute of Neurological Disorders and Stroke, “Stroke Overview | National Institute of Neurological Disorders and Stroke,” www.ninds.nih.gov. [Online]. Available: <https://www.ninds.nih.gov/health-information/stroke/stroke-overview>
- [3] V. L. Feigin *et al.*, “Global, regional, and national burden of stroke and its risk factors, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021,” *Lancet Neurol.*, vol. 23, no. 10, pp. 973–1003, Oct. 2024, doi: 10.1016/S1474-4422(24)00369-7.
- [4] John Hopkins Medicine, “Types of Stroke,” John Hopkins Medicine. [Online]. Available: <https://www.hopkinsmedicine.org/health/conditions-and-diseases/stroke/types-of-stroke>
- [5] M. Lamassa *et al.*, “Characteristics, Outcome, and Care of Stroke Associated With Atrial Fibrillation in Europe: Data From a Multicenter Multinational Hospital–Based Registry (The European Community Stroke Project),” *Stroke*, vol. 32, no. 2, pp. 392–398, Feb. 2001, doi: 10.1161/01.STR.32.2.392.
- [6] G. Lippi, F. Sanchis-Gomar, and G. Cervellin, “Global epidemiology of atrial fibrillation: An increasing epidemic and public health challenge,” *Int. J. Stroke*, vol. 16, no. 2, pp. 217–221, Feb. 2021, doi: 10.1177/1747493019897870.
- [7] W. D. Freeman and M. I. Aguilar, “Prevention of Cardioembolic Stroke,” *Neurotherapeutics*, vol. 8, no. 3, pp. 488–502, 2011, doi: 10.1007/s13311-011-0048-y.
- [8] H. J. Lin *et al.*, “Stroke severity in atrial fibrillation. The Framingham Study,” *Stroke*, vol. 27, no. 10, pp. 1760–1764, 1996, doi: 10.1161/01.str.27.10.1760.

- [9] John Hopkins Medicine, “Anatomy and Function of the Heart’s Electrical System,” Johns Hopkins Medicine. [Online]. Available: <https://www.hopkinsmedicine.org/health/conditions-and-diseases/anatomy-and-function-of-the-hearts-electrical-system>
- [10] F. Castells, C. Mora, J. Millet, J. J. Rieta, C. Sánchez, and J. M. Sanchis, “Multidimensional ICA for the Separation of Atrial and Ventricular Activities from Single Lead ECGs in Paroxysmal Atrial Fibrillation Episodes,” in *Independent Component Analysis and Blind Signal Separation*, vol. 3195, C. G. Puntonet and A. Prieto, Eds., in Lecture Notes in Computer Science, vol. 3195. , Berlin, Heidelberg: Springer Berlin Heidelberg, 2004, pp. 1229–1236. doi: 10.1007/978-3-540-30110-3_155.
- [11] C. Gutierrez and D. G. Blanchard, “Diagnosis and Treatment of Atrial Fibrillation,” *Atr: Fibrillation*.
- [12] J. Xu, J. G. Y. Luc, and K. Phan, “Atrial fibrillation: review of current treatment strategies,” *J. Thorac. Dis.*, vol. 8, no. 9, pp. E886–E900, Sept. 2016, doi: 10.21037/jtd.2016.09.13.
- [13] A. Verma and A. Natale, “Why Atrial Fibrillation Ablation Should Be Considered First-Line Therapy for Some Patients,” *Circulation*, vol. 112, no. 8, pp. 1214–1230, Aug. 2005, doi: 10.1161/CIRCULATIONAHA.104.478263.
- [14] S. Ballestri *et al.*, “Risk and Management of Bleeding Complications with Direct Oral Anticoagulants in Patients with Atrial Fibrillation and Venous Thromboembolism: a Narrative Review,” *Adv. Ther.*, vol. 40, no. 1, 2022, doi: 10.1007/s12325-022-02333-9.
- [15] M. A. Crowther and T. E. Warkentin, “Bleeding risk and the management of bleeding complications in patients undergoing anticoagulant therapy: focus on new anticoagulant agents,” *Blood*, vol. 111, no. 10, pp. 4871–4879, 2008, doi: 10.1182/blood-2007-10-120543.

- [16] P. S. Cunha, S. Laranjo, J. Heijman, and M. M. Oliveira, “The Atrium in Atrial Fibrillation - a Clinical Review on How to Manage Atrial Fibrotic Substrates,” *Front. Cardiovasc. Med.*, vol. 9, p. 879984, 2022, doi: 10.3389/fcvm.2022.879984.
- [17] M. Daccarett *et al.*, “Association of Left Atrial Fibrosis Detected by Delayed-Enhancement Magnetic Resonance Imaging and the Risk of Stroke in Patients With Atrial Fibrillation,” *J. Am. Coll. Cardiol.*, vol. 57, no. 7, pp. 831–838, 2011, doi: 10.1016/j.jacc.2010.09.049.
- [18] F. Gramley *et al.*, “Age-related atrial fibrosis,” *Age*, vol. 31, no. 1, pp. 27–38, 2008, doi: 10.1007/s11357-008-9077-9.
- [19] Y. Sun *et al.*, “Finding low CHA2DS2-VASc scores unreliable? Why not give morphological and hemodynamic methods a try?,” *Front. Cardiovasc. Med.*, vol. 9, 2023, doi: 10.3389/fcvm.2022.1032736.
- [20] T. Wynn, “Cellular and molecular mechanisms of fibrosis,” *J. Pathol.*, vol. 214, no. 2, pp. 199–210, 2008, doi: 10.1002/path.2277.
- [21] K. Tandon, D. Tirschwell, W. T. Longstreth, B. Smith, and N. Akoum, “Embolic stroke of undetermined source correlates to atrial fibrosis without atrial fibrillation,” *Neurology*, vol. 93, no. 4, pp. e381–e387, 2019, doi: 10.1212/wnl.0000000000007827.
- [22] P. M. Boyle, J. C. Del Álamo, and N. Akoum, “Fibrosis, atrial fibrillation and stroke: clinical updates and emerging mechanistic models,” *Heart Br. Card. Soc.*, vol. 107, no. 2, pp. 99–105, 2021, doi: 10.1136/heartjnl-2020-317455.
- [23] N. G. Frangogiannis, “Cardiac fibrosis,” *Cardiovasc. Res.*, vol. 117, no. 6, pp. 1450–1488, 2020, doi: 10.1093/cvr/cvaa324.
- [24] P. Kong, P. Christia, and N. G. Frangogiannis, “The pathogenesis of cardiac fibrosis,” *Cell. Mol. Life Sci.*, vol. 71, no. 4, pp. 549–574, 2013, doi: 10.1007/s00018-013-1349-6.

- [25] Å. Telle, C. Bargellini, Y. Chahine, J. C. Del, Nazem Akoum, and P. M. Boyle, “Personalized biomechanical insights in atrial fibrillation: opportunities & challenges,” *Expert Rev. Cardiovasc. Ther.*, vol. 21, no. 11, pp. 817–837, 2023, doi: 10.1080/14779072.2023.2273896.
- [26] W. Y. Ding, D. Gupta, and G. Y. H. Lip, “Atrial fibrillation and the prothrombotic state: revisiting Virchow’s triad in 2020,” *Heart*, vol. 106, no. 19, pp. 1463–1468, Oct. 2020, doi: 10.1136/heartjnl-2020-316977.
- [27] P. Kirchhof *et al.*, “Personalized management of atrial fibrillation: Proceedings from the fourth Atrial Fibrillation competence NETwork/European Heart Rhythm Association consensus conference,” *Europace*, vol. 15, no. 11, pp. 1540–1556, Nov. 2013, doi: 10.1093/europace/eut232.
- [28] D. A. Nordsletten, S. A. Niederer, M. P. Nash, P. J. Hunter, and N. P. Smith, “Coupling multi-physics models to cardiac mechanics,” *Prog. Biophys. Mol. Biol.*, vol. 104, no. 1–3, pp. 77–88, Jan. 2011, doi: 10.1016/j.pbiomolbio.2009.11.001.
- [29] R. Verzicco, “Electro-fluid-mechanics of the heart,” *J. Fluid Mech.*, vol. 941, p. P1, June 2022, doi: 10.1017/jfm.2022.272.
- [30] H. Watanabe, S. Sugiura, H. Kafuku, and T. Hisada, “Multiphysics Simulation of Left Ventricular Filling Dynamics Using Fluid-Structure Interaction Finite Element Method,” *Biophys. J.*, vol. 87, no. 3, pp. 2074–2085, Sept. 2004, doi: 10.1529/biophysj.103.035840.
- [31] S. Sugiura, J.-I. Okada, T. Washio, and T. Hisada, “UT-Heart: A Finite Element Model Designed for the Multiscale and Multiphysics Integration of our Knowledge on the Human Heart,” in *Computational Systems Biology in Medicine and Biotechnology*, vol. 2399, S.

- Cortassa and M. A. Aon, Eds., in *Methods in Molecular Biology*, vol. 2399. , New York, NY: Springer US, 2022, pp. 221–245. doi: 10.1007/978-1-0716-1831-8_10.
- [32] E. J. Vigmond, C. Clements, D. M. McQueen, and C. S. Peskin, “Effect of bundle branch block on cardiac output: A whole heart simulation study,” *Prog. Biophys. Mol. Biol.*, vol. 97, no. 2–3, pp. 520–542, June 2008, doi: 10.1016/j.pbiomolbio.2008.02.022.
- [33] A. Quarteroni, T. Lassila, S. Rossi, and R. Ruiz-Baier, “Integrated Heart—Coupling multiscale and multiphysics models for the simulation of the cardiac function,” *Comput. Methods Appl. Mech. Eng.*, vol. 314, pp. 345–407, Feb. 2017, doi: 10.1016/j.cma.2016.05.031.
- [34] L. Feng, H. Gao, B. Griffith, S. Niederer, and X. Luo, “Analysis of a coupled fluid-structure interaction model of the left atrium and mitral valve,” *Int. J. Numer. Methods Biomed. Eng.*, vol. 35, no. 11, p. e3254, Nov. 2019, doi: 10.1002/cnm.3254.
- [35] F. Viola, V. Meschini, and R. Verzicco, “Fluid–Structure-Electrophysiology interaction (FSEI) in the left-heart: A multi-way coupled computational model,” *Eur. J. Mech. - BFluids*, vol. 79, pp. 212–232, Jan. 2020, doi: 10.1016/j.euromechflu.2019.09.006.
- [36] M. Bucelli, A. Zingaro, P. C. Africa, I. Fumagalli, L. Dede’, and A. Quarteroni, “A mathematical model that integrates cardiac electrophysiology, mechanics, and fluid dynamics: Application to the human left heart,” *Int. J. Numer. Methods Biomed. Eng.*, vol. 39, no. 3, p. e3678, Mar. 2023, doi: 10.1002/cnm.3678.
- [37] Y. J. Choi, J. Constantino, V. Vedula, N. Trayanova, and R. Mittal, “A New MRI-Based Model of Heart Function with Coupled Hemodynamics and Application to Normal and Diseased Canine Left Ventricles,” *Front. Bioeng. Biotechnol.*, vol. 3, Sept. 2015, doi: 10.3389/fbioe.2015.00140.

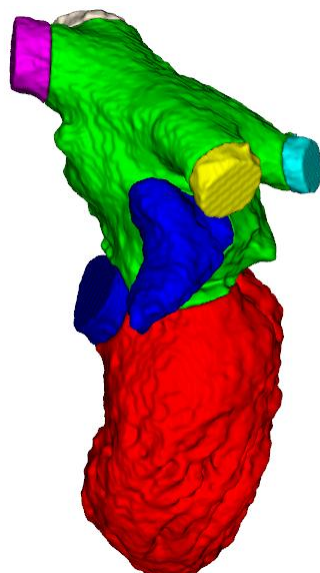
- [38] F. Viola *et al.*, “FSEI-GPU: GPU accelerated simulations of the fluid–structure–electrophysiology interaction in the left heart,” *Comput. Phys. Commun.*, vol. 273, p. 108248, Apr. 2022, doi: 10.1016/j.cpc.2021.108248.
- [39] F. Viola, G. Del Corso, R. De Paulis, and R. Verzicco, “GPU accelerated digital twins of the human heart open new routes for cardiovascular research,” *Sci. Rep.*, vol. 13, no. 1, p. 8230, May 2023, doi: 10.1038/s41598-023-34098-8.
- [40] N. Paliwal *et al.*, “Presence of Left Atrial Fibrosis May Contribute to Aberrant Hemodynamics and Increased Risk of Stroke in Atrial Fibrillation Patients,” *Front. Physiol.*, vol. 12, p. 657452, June 2021, doi: 10.3389/fphys.2021.657452.
- [41] A. Gonzalo *et al.*, “Patient-specific multi-physics simulations of fibrotic changes in left atrial tissue mechanics impact on hemodynamics”.
- [42] C. H. Roney *et al.*, “Universal atrial coordinates applied to visualisation, registration and construction of patient specific meshes,” *Med. Image Anal.*, vol. 55, pp. 65–75, July 2019, doi: 10.1016/j.media.2019.04.004.
- [43] F. Isensee *et al.*, “nnU-Net: Self-adapting Framework for U-Net-Based Medical Image Segmentation,” Sept. 27, 2018, *arXiv*: arXiv:1809.10486. doi: 10.48550/arXiv.1809.10486.
- [44] A. Myronenko and X. Song, “Point-Set Registration: Coherent Point Drift,” 2009, doi: 10.48550/ARXIV.0905.2635.
- [45] “An Eigenshapes Approach to Compressed Signed Distance Fields and Their Utility in Robot Mapping,” *ar5iv*. Accessed: Jan. 02, 2025. [Online]. Available: <https://ar5iv.labs.arxiv.org/html/1609.02462>
- [46] Z. Lai, J. Zhao, S. Zhao, and L. Huang, “Signed distance field enhanced fully resolved CFD-DEM for simulation of granular flows involving multiphase fluids and irregularly shaped

- particles,” *Comput. Methods Appl. Mech. Eng.*, vol. 414, p. 116195, Sept. 2023, doi: 10.1016/j.cma.2023.116195.
- [47] Z. Lai, J. Zhao, S. Zhao, and L. Huang, “Signed distance field enhanced fully resolved CFD-DEM for simulation of granular flows involving multiphase fluids and irregularly shaped particles,” *Comput. Methods Appl. Mech. Eng.*, vol. 414, pp. 116195–116195, 2023, doi: 10.1016/j.cma.2023.116195.
- [48] K. Sørensen *et al.*, “Spatio-temporal neural distance fields for conditional generative modeling of the heart,” July 15, 2024, *arXiv*: arXiv:2407.10663. doi: 10.48550/arXiv.2407.10663.
- [49] F. Bisbal *et al.*, “Left Atrial Geometry Improves Risk Prediction of Thromboembolic Events in Patients With Atrial Fibrillation,” *J. Cardiovasc. Electrophysiol.*, vol. 27, no. 7, pp. 804–810, July 2016, doi: 10.1111/jce.12978.
- [50] R. Karim *et al.*, “Surface flattening of the human left atrium and proof-of-concept clinical applications,” *Comput. Med. Imaging Graph.*, vol. 38, no. 4, pp. 251–266, June 2014, doi: 10.1016/j.compmedimag.2014.01.004.
- [51] S. E. Williams *et al.*, “Standardized unfold mapping: a technique to permit left atrial regional data display and analysis,” *J. Interv. Card. Electrophysiol.*, vol. 50, no. 1, pp. 125–131, Oct. 2017, doi: 10.1007/s10840-017-0281-3.
- [52] C. H. Roney *et al.*, “A technique for visualising three-dimensional left atrial cardiac activation data in two dimensions with minimal distance distortion,” in *2015 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, Milan: IEEE, Aug. 2015, pp. 7296–7299. doi: 10.1109/EMBC.2015.7320076.

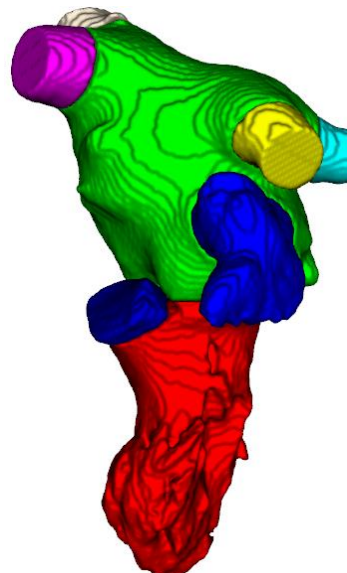
- [53] J. Dueñas-Pamplona *et al.*, “Reduced-order models of wall shear stress patterns in the left atrial appendage from a data-augmented atrial database,” *Appl. Math. Model.*, vol. 130, pp. 713–727, June 2024, doi: 10.1016/j.apm.2024.03.027.

Appendix

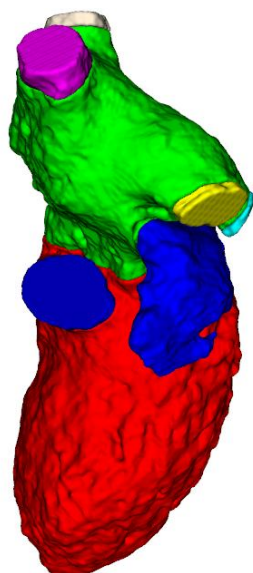
A. Final Segmentations



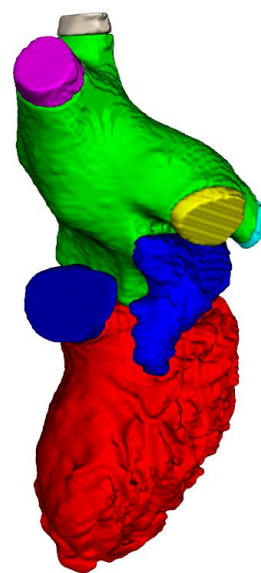
Case 1 SR



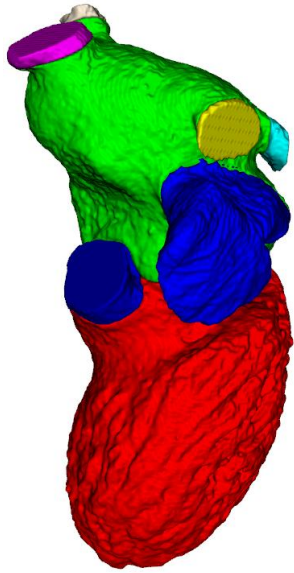
Case 1 AF



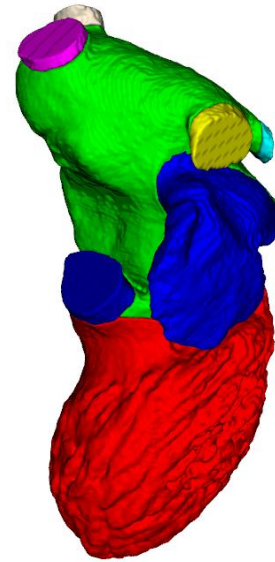
Case 2 SR



Case 2 AF



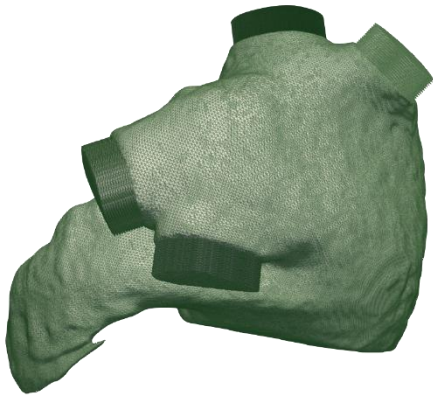
Case 3 SR



Case 3 AF

B. Final Mesh Results

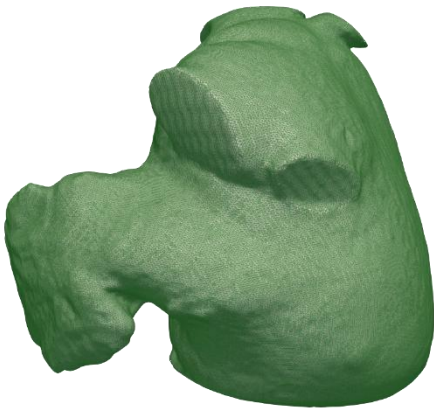
Surface mesh for Case 2 and Case 3



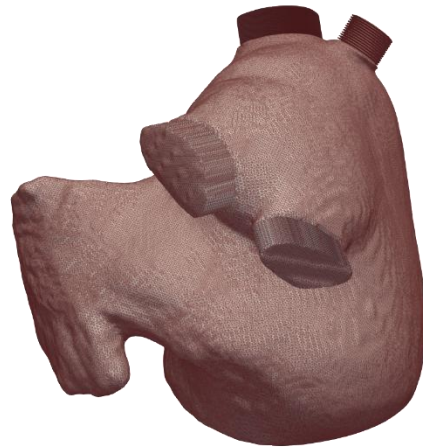
Case 2 SR



Case 2 AF



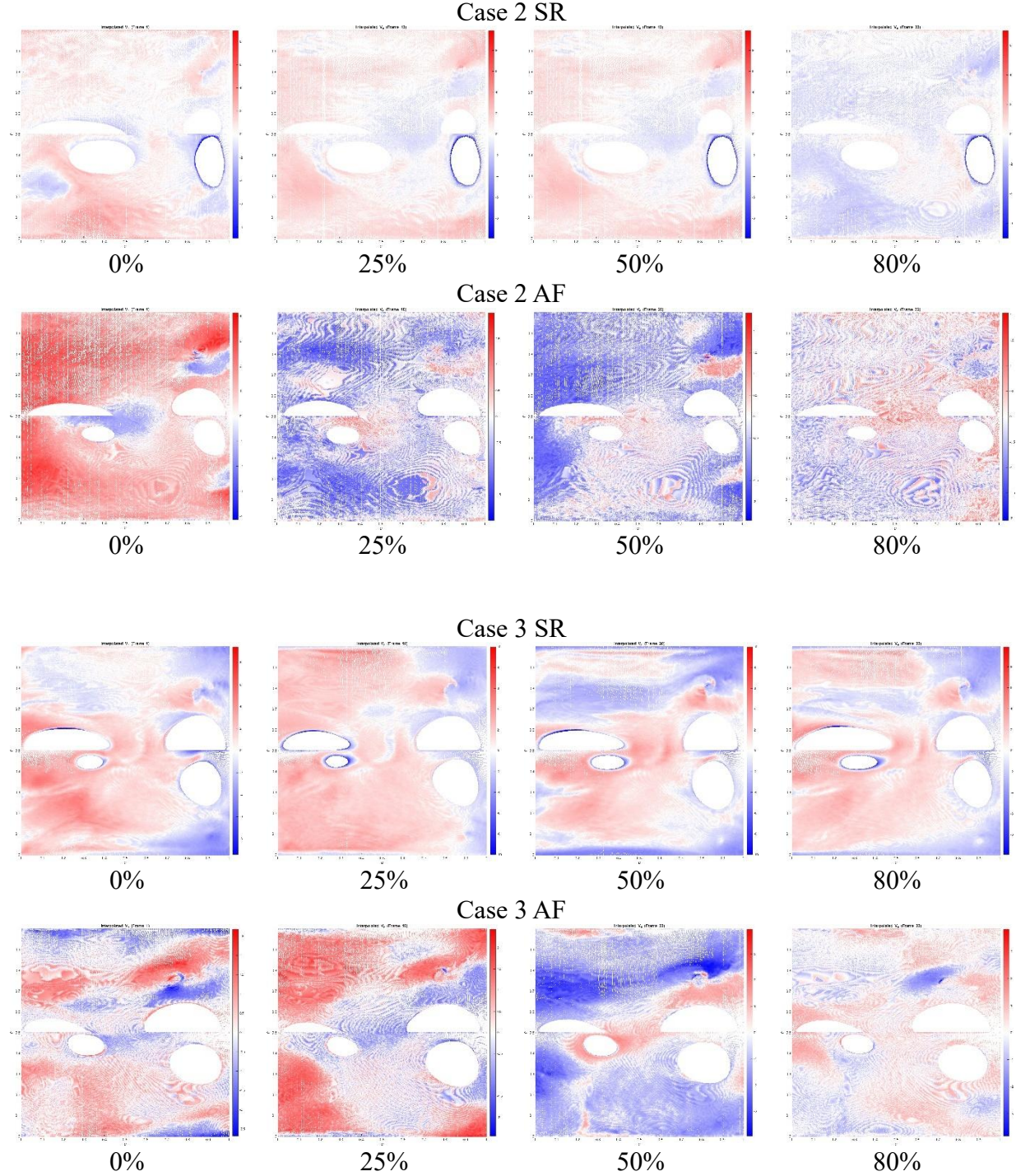
Case 3 SR



Case 3 AF

C. Velocity Interpolation onto UAC

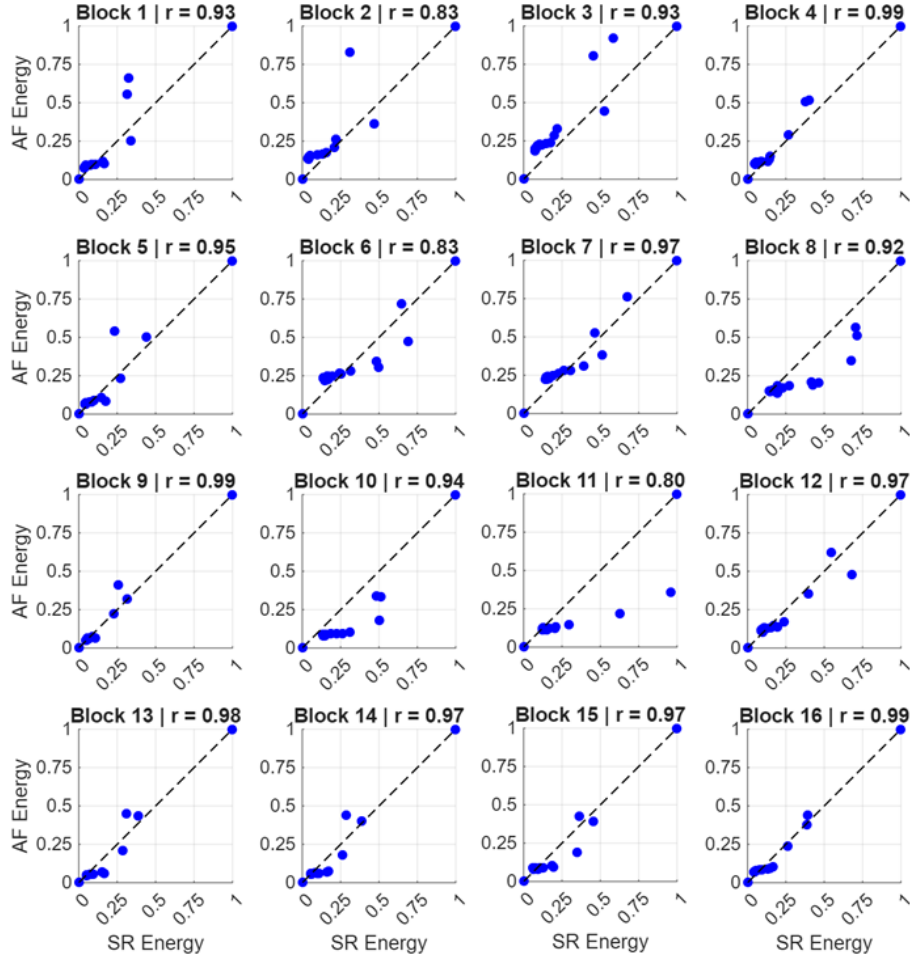
Wall-normal velocity (V_n) projected on UAC for Case 2 and Case 3 showing reduced magnitude and coherence in AF compared to SR across cardiac phases.



D. Localized FFT Energy Results

Block-wise scatter plots directly comparing normalized FFT energy between SR and AF for Case 1. Each panel shows a specific anatomical block, with the dashed line representing perfect agreement ($r=1$).

Case 2 Results



Case 3 Results

