Heart disease is a major cause of mortality worldwide. Detecting/diagnosing such diseases in their early stages is critical, and heavily depends on non-invasive imaging methods, e.g., computed tomography (CT) and magnetic resonance imaging (MRI). High resolution cardiac CT imaging technology has the resolution to reveal the complex endocardial structures of the left ventricle, such as the trabeculae and the papillary muscles. However, the development of suitable methods for the quantitative analysis of these dense data sources has lagged greatly behind the development of the imaging methods themselves. As a result, in clinical practice, and in much of the research that uses these imaging data, the quantitative analysis of cardiac function has largely been confined to the calculation of simple measures of global function, such as the ejection fraction, while local function being just qualitatively assessed. Therefore there is a large amount of the functional information potentially available from cardiac images essentially untouched.

In this thesis, for the first time, we extract clinical meaningful endocardial information of the left ventricle (LV) from high resolution CT images. The reconstructed result captured the fine detailed structures, which are extremely challenging to segment due to their delicate and complex nature in both geometry and topology. Our
algorithm is especially designed to segment those structures, by calculating the potential missing topological structures. Using techniques from computational topology, e.g. persistent homology, our algorithm finds topological handles which are likely to be the true signal. Each handle is evaluated independently based in its saliency, rather than absolute intensities. The final segmentation with handles restored, leads to high quality segmentation of the complex structures. The initialized model was then deformed to other frames to reconstruct the 4D motion. Based on the reconstructed results, we study both the morphology and motion of the trabeculae and the papillary muscles. Proposed measurements have been clinically evaluated.
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Dedication

This dissertation is dedicated to my husband, my sister and my parents, for their endless love and support.
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Chapter 1
Introduction

Cardiovascular disease (CAD), also called heart disease, is one of the leading causes of mortality worldwide. According to the most recent statistics updates of the Centers for Disease Control and Prevention of the National Center for Health Statistics (CDC/NCHS), on the basis of 2010 death rate data, > 2150 Americans die of CAD each day, an average of 1 death every 40 seconds. 34% of deaths attributable to CAD occurred before the age of 75 years, which is before the current average life expectancy of 78.7 years [38]. The prevention, diagnosis and treatment of all forms of heart disease are of great importance to human life quality, and remain active fields of research.

1.1 Background

Medical imaging is the technique that produces images of the internal structures of the body noninvasively. It provides information about human body structures that helps radiologists to visualize and study the anatomy of the structures, localize pathologies and evaluate the need for radiotherapy or surgeries. Nowadays, there are a number of techniques available for cardiac imaging which provide qualitative and quantitative information about morphology, dynamic structure and function of the heart and the blood vessels. The developments of these techniques in cardiac imaging techniques provide 3-D information with continuously increasing spatial and temporal resolution. The recent advanced technologies have been used a lot in guiding clinical diagnosis, treatment, and follow-up of cardiac diseases. Spatio-temporal imaging is a valuable research tool to study cardiac motion and perfusion, and their relationship with stages of disease.

Each modality presents advantages and limitations that influence the achievable
imaging accuracy. Most frequently used 3-D clinical investigation of the heart include Echocardiography, Computed Tomography (CT) and Magnetic Resonance Imaging (MRI).

Echocardiography uses Doppler ultrasound to create images of the heart. It is one of the most widely used diagnostic tests in cardiology. It provides noninvasive assessment, including left ventricular mass, chamber volume, contractive function [2], pumping capacity, myocardial perfusion [82] and the location and extent of any tissue damage.

Cardiac MRI is now an established, although still rapidly advancing technique providing information on morphology and function of the cardiovascular system [41]. Advantages of cardiac MRI include providing both anatomical and functional information about the heart, multiple imaging planes and high soft tissue contrast discrimination between the flowing blood and myocardium without the need for contrast medium or invasive techniques. MR tagging was introduced independently by Zerhouni [103] and Axel [3]. This technique is able to create and track material points over time, such that the myocardial deformation can be studied.

Successive generations of CT technology have been applied to cardiac imaging beginning in the early 1980s with conventional CT, electron beam CT (EBCT) in 1987, and multi-detector CT (MDCT) in 1999. Cardiac CT uses natural contrast within air and different tissue [10]. Compared with other imaging modalities, CT images have a much higher spatial resolution and is able to show detailed anatomic structures within the cardiac chambers [79]. Recent developments on cardiac CT allow a 320 multi-detector CT scanner to successfully capture the detailed endocardial structures, including the papillary muscles and trabeculae in a whole cardiac cycle at a resolution which has not been reached before.

These advances have led to an increasing need for effective and efficient algorithms to plan 3-D acquisitions, automate the extraction and analysis of clinically relevant parameters, and provide tools for their visualization. Among those, the extraction and analysis of clinically meaningful parameters is an important step for diagnosis and to provide scientific evidence for studying causes of diseases and functions of the heart.
However, the development of suitable methods for the quantitative analysis of these dense data sources has lagged greatly behind the development of the imaging methods themselves. As a result, in clinical practice, and in much of the research that uses these imaging data, the quantitative analysis of cardiac function has largely been confined to the calculation of simple measures of global function, such as the overall volumetric mass and ejection fraction. Local features are simply qualitatively evaluated as being normal or hypokinetic. A large amount of the functional information potentially available from cardiac images is essentially untapped. The lack of efficient and effective analysis tools is a significant limitation in the application of cardiac imaging methods in clinical practice. Specifically speaking, the quantified measurements, and function of the left ventricle endocardial structures have not been fully investigated.

1.2 Medical Terminology and Heart Anatomy

The heart is a vital muscular organ in humans and many other animals, which provides the body with oxygen and nutrients, as well as removing metabolic waste by pumping blood around the body through the blood vessels of the circulatory system.

The heart is located in the chest. It is divided into four main chambers: the upper left and right atrium, and the lower left and right ventricles. The left and right heart is separated by the septum. The left ventricle is the major pumping chamber for the circulatory system. The muscular layer is much thicker in the left ventricle compared to the right.

The flow of blood is controlled by heart valves. The left ventricle ejects blood into the aorta through the aortic valve. When the ventricles begin to contract, pressure within the ventricles rises and blood flows toward the atria through aortic valve. This backflow causes the mitral valve to close. The valve are tied to the papillary muscles by chordae tendineae. As the myocardium of the ventricle contracts, so do the papillary muscles. This creates tension on the chordae tendineae, helping to hold the cusps of the valves and preventing them from being blown back into the atria. During the relaxation phase of the cardiac cycle, the papillary muscles are also relaxed and the tension on the
chordae tendineae is light. The mitral valve is open and the aortic valve is closed. The atria contract to pump blood into the ventricle.

Two important structures on the left ventricle are the papillary muscles and the trabeculae. There are two papillary muscles on the left ventricle. The function of the papillary muscles are known to control the opening and closing of the valves. The walls of the ventricle are lined with trabeculae carneae, ridges of cardiac muscle covered by endocardium. The function of the trabeculae carneae is still an open questions.

![Left ventricle anatomy](image)

Figure 1.1: Left ventricle anatomy, picture from Anatomy of the Human Body [39].

1.3 Problem Statement

Specifically, in this thesis, we work on the problem of better evaluation and understanding of the endocardial surface of the left ventricle from various aspects. We focus on extracting valuable information from the papillary muscles and the trabeculae. The goal of this research is to fill in the gap between potentially useful information in high resolution CT images and the clinically valuable parameters characterizing heart diseases. Quantitative analysis of the endocardial structures requires accurate segmentation of the detailed structures and registration between neighboring frames during a cardiac cycle. The reconstructed left ventricle models are then used to analyze the geometric
measurements, local motion and its impact on blood flow. By performing the quantitative assessment of the regional fine scale of the left ventricle, their morphological and functional parameters are provided and previous unknown differences among healthy and diseased hearts have been discovered and quantified.

1.4 Main Contributions

The main contributions of this thesis are summarized as following:

1. The papillary muscles and the trabeculae have the structures of topological handles, where their ends are connected to the heart wall and can be freely moved in the middle. We propose a topological method to explicitly detect and restore the missing handle structures. Our algorithm evaluates each handle independently based on its saliency. Our approach is generic and could be applied to other topologically complicated segmentation problems, such as blood vessels and lung airways.

2. We study the morphology of the complex structures after the topologically accurate segmentation. We represent the structures accurately and concisely using curve skeleton, and measure these structures using topological and geometric features. Distribution pattern of the trabeculae are described in both healthy and diseased hearts.

3. For the first time, we capture the left ventricle motion using deformable model. First of all, the heart model is developed using the method of topological accurate segmentation at the most expanded frame, which captures the endocardial structures most clearly. The cardiac motion is reconstructed by deforming the heart model to other time frames. Since we are using the same model during the deformation, one-to-one correspondence achieved simultaneously.

4. Analysis of the left ventricle motion and the impact of trabeculae structures on patient-specific cardiac blood flow simulations are investigated. Our results
demonstrate that the incorporation of these detailed trabeculae structures affect the intraventricular hemodynamics.

1.5 Organization

The remainder of this thesis is organized as follows.

Chapter 2 reviews the relevant work both in general segmentation and registration methods. We follow the development of existing methods and point out the limitations of previous algorithms on this research problem.

Chapter 3 introduces the proposed segmentation algorithm in detail, including the problem formulation, the theoretical proof and the algorithm performances. Several experiments are performed on synthetic datasets to demonstrate its effectiveness. The proposed method was applied on the real cardiac left ventricle dataset.

After the topologically accurate segmentation from high resolution CT images, Chapter 4 provides several morphological indices to characterize the trabeculation structures. We describe the distribution pattern of the trabeculae and provide the differences in healthy and diseased hearts.

We describe an algorithm to reconstruct the 4D motion of the endocardial surface for a full cardiac cycle in Chapter 5. For the first time, the reconstruction motion allows us to quantitatively investigate their possible functional significance in health and disease.

In Chapter 6, we study the interactions between blood flow and trabeculae motion using the model reconstruction in Chapter 5. Some measurements on the cardiac motion are also provided.

Finally, Chapter 7 summarized the contributions of this work, along with a discussion of limitations and future work.
Chapter 2

Relevant Work

In this chapter we review both general segmentation, registration methods in medical imaging and the recent development on heart modeling and analysis.

2.1 Segmentation

Image segmentation is one of the most interesting and challenging problems in computer vision generally and medical imaging applications specifically. Segmentation is the partition of an image domain $I$ into nonoverlapping, connected regions, being homogeneous with respect to some signal characteristics. This characteristics can be low level, such as coherence criteria on the brightness, color, texture or motion within each region. Or equally important is the knowledge in mid-level and high-level, such as statistics on the shape and appearance of objects that appear in the image.

Medical image segmentation is an essential part of any computer-aided diagnosis (CAD) system, and functionality of the system depends heavily on segmentation accuracy. However, accurate segmentation of medical images has many challenges, such as the common presence of image noise, cluttered objects, nonuniform object texture, variations in lighting, and various other artifacts in natural or medical images. To address these challenges, many segmentation techniques have been developed over years. Various approaches of different accuracy, speed and degree of complexity have been proposed for each practical CAD problem.

Model-based methods have been extensively studied and widely used, with considerable success because of their ability to integrate high-level knowledge about object shape and appearance properties with low-level image processing. Deformable models are curves or surfaces that deform under the influence of internal smoothness and
external image forces to delineate object boundary [50, 89, 21, 11, 58]. Compared to low-level edge detection methods, deformable models have the advantage of estimating boundary with smooth curves or surfaces.

Statistical shape and appearance models are learned a priori from examples to capture variations in the shape and appearance of an object of interest in images [24, 23, 56, 108]. When applied to segmentation, the models deform toward object boundary but with constraints to deform only in ways characteristic of the object they represent. These statistical models encode high-level knowledge in a more specific manner and are often more robust for image interpretation. However, those methods require more efforts collecting training data and the registration of training examples.

In both types of models, integrating region statistics constraints, such as the appearance statistics into shape based models has been proposed for more robust models in segmentation. Region-based strategies have been proposed to dynamically estimate intensity/texture statistics of the region inside a deformable model using parametric (e.g. Gaussian, Mixture-of-Gaussian) or nonparametric methods, and to ensure the statistical coherence inside the model [111, 70, 99, 44, 76, 17]. Both region and edge forces work complementarily to aid the model overcome local minima due to spurious edges, and to prevent the model from leaking at boundary gaps. For statistical prior models, a generalization to statistical appearance models also integrate the interior region information [23, 107], and enables registration of a target object with the learned prior model. Being complementary to each other, the integration of statistical shape and appearance models results in a powerful image analysis paradigm.

Another category of segmentation is the integration of topological prior knowledge, which is closely related to the our concern during the segmentation. Geometric deformable models designed using topology-preserving level set method has achieved topology preservation by applying the simple point concept from digital topology [42, 5]. Zeng et al. [102] introduce TopologyCuts, a topology preserving variant of GraphCut that is inspired by level set methods. After initialization with a coarse presegmentation of correct topology, TopologyCuts iteratively minimizes the energy function while preserving the topology, converging to a local minimum of the energy. Chen et al. [16]
introduced TopoCut, a method to integrate knowledge about topological properties into random field image segmentation model. In previous methods, that use either random field energy models (MRF and CRF) \cite{69} or level set models \cite{91}, topological priors such as connectivity or handle-free are enforced as a segmentation constraint.

### 2.2 Registration

Registration is the process of establishing point-by-point correspondences between images of a scene or shapes of an object captured from different view points. Image/Shape registration can be applied to the same subject acquired by different imaging modalities (multi-modal image registration) or at different time points (serial image registration). For that purpose, parameters of global transformation and/or local deformation models are to be recovered to geometrically transform a moving image/shape to achieve high spatial correspondence with a fixed image/shape.

The shape registration problem has been widely studied because of its applications in computer vision and medical image analysis. Global registration, also known as shape alignment, is designed to recover a global transformation that matches a source shape to a target shape as close as possible. Shape alignment has extensive uses in as object recognition, tracking and shape retrieval. Nonrigid local registration is required to further establish dense correspondences between shapes. Local registration has been used a lot in medical imaging, such as building statistical shape models, training examples need to be registered to extract statistical features \cite{43}, intra-subject or atlas registration of 2D/3D anatomical structures.

There has been a lot of previous work on the shape registration problem, as well as on similar problems such as shape matching, and point set matching. These algorithms approach the shape registration problem in the following aspects. Shape can be represented as clouds of points \cite{6, 20, 8}, parametric curves/surfaces \cite{25, 61}, conformal mapping \cite{40, 101, 37}, fourier descriptors \cite{51} and implicit distance functions \cite{71, 45}.

Transformation refers to the global or local transformation, which is used to transform the source shape to the target shape. Global transformation is applied to the
entire shape, such as rigid, similarity, affine and perspective. Local transformation refers to pixel-wise deformations that deform a shape locally and non-rigidly, such as displacement vector field [94], Thin Plate Splines [6, 9], Radial Basis Functions [30], and Free Form Deformation [80, 77].

Registration criterion is the approach used to recover the optimal transformation parameters given a shape representation and a transformation model. The existing approaches can be categorized into two classes: The first is to recover the transformation parameters using the explicit geometric feature correspondences [6]. The second is to estimate the transformation parameters through optimization of energy functions [20].

2.3 Heart Modeling

Cardiac imaging is routinely applied for assessment and diagnosis of cardiac diseases. Computerized image analysis methods are now widely applied to cardiac segmentation and registration in order to extract the anatomy and contractile function of the heart [32, 96, 93]. Modeling of the cardiac shape, motion and physical structure have played a major role in the development of the image analysis algorithms. In terms of cardiac imaging modalities, previous work can be categorized on echocardiography segmentation [68], cine MR segmentation [73] or Tagged MRI [4]. In terms of cardiac modeling techniques, there are three classes: surface models [87, 72, 44, 90], volume models [72, 86] and deformable models [54, 1, 7].

The shape of the cardiac ventricles is considered known, the prior shape knowledge has been incorporated into the segmentation process. Unfortunately, the rich endocardial information of the chambers, which is patient specific, is usually discarded by using the generic smooth surface model. Although segmenting the papillary muscles and the trabeculae is of high interest to doctors, limited work has been proposed to quantitatively characterize those structures.
Chapter 3

Segmenting the Papillary Muscles and the Trabeculae through Restoration of Topological Handles

This chapter introduces an algorithm for segmenting the high resolution CT images of the left ventricle, particularly the papillary muscles and the trabeculae. This problem is difficult because of the detailed information and complicated topological structures. Our algorithm computes the potential missing topological structures of a given initial segmentation. These proposals are measured by the saliency and confidence from a trained classifier. Handles with high scores are restored in the final segmentation, leading to high quality segmentation results of the complex structures.

3.1 Introduction

Most of the existing methods to perform cardiac segmentations [18, 109, 57] model the inner heart wall as a smooth surface, which does not include the papillary muscles and the trabeculae at all. Zheng et al. [109] proposed an algorithm to automatically segment the four chambers of the heart in four seconds. Ecabert et al. [28] presented a learning-based approach based on active shape model (ASM) for the segmentation of four chambers and major vessel trunks. Other models include, but are not limited to graph cut [33], atlas based segmentation [46] and local deformation [48].

These methods, although proven to be successful in various situations, are not designed to accurately segment smaller, complex structures such as the papillary muscles and the trabeculae. Previous attempts [18, 88, 36] were able to capture the papillary muscle, but could not segment trabeculae with satisfying quality. Although their method focused on preserving the fine structures during the deformation, it only enforced consistency of geometry [84], not of topology. Accurately segmenting the complex
structures of the papillary muscles and the trabeculae is still a challenging task. The reason is threefold. 1) The detailed structures are complex and small, making them hard to be distinguished from noise. 2) Some trabeculae go through the ventricle cavity and are very thin. Existing methods often fail to segment them due to the smoothness prior. 3) Such complex structures have a very different nature from other parts such as free wall and septum. Furthermore, trabeculae have a large variety of geometry and intensity even within the same cardiac image. This requires the segmentation method to be extremely adaptive in terms of parameters, making full automation very difficult.

Figure 3.1: (a) Left ventricle anatomy, picture from [39]. (b) Segmentation results represented as a 3D triangle mesh successfully captured the papillary muscle and the trabeculae.

Accurately segmenting the papillary muscles and the trabeculae is very important and of high interest to doctors for several reasons. First, left ventricular (LV) mass and ejection fraction have been widely used in diagnosis and therapy. Inclusion or exclusion of these structures significantly affects quantification of LV volume and mass [97]. Second, the functions of the papillary muscles and the trabeculae have still not been fully understood. Left ventricle anatomy is show in Fig. 3.1. The papillary muscles are attached to the valves via chordae tendineae. The trabeculae project from the inner surface of both ventricles of the heart. Some are completely attached to the wall of the heart. Others are fixed at both ends to either the ventricular wall or septum, but the intermediate section is freely mobile within the cavity, forming topological handles. There are a number of functional hypotheses for the trabeculation of the heart
wall. High quality segmentations of such structures are useful for further investigating their functions, the mechanics of the heart [52] and geometrical properties of cardiac structures [57].

In this chapter, we propose a topological method to restore missing structures of a given segmentation, generated by any existing segmentation tool. It proposes hypotheses of where and how topological handles should be reestablished. On the basis of those topological proposals, a two-step screening is performed to select handles with higher confidence for structure restoration. Our algorithm evaluates each handle independently based on its saliency, rather than absolute intensities. Explicitly restoring selected handles makes the restoration adaptive to each trabecula, thus avoiding a universal threshold in the whole domain. Furthermore, such explicit restoration is not affected by the smoothing prior of segmentation models. Fig. 3.1 shows the improvements of our algorithm, with restored trabeculae highlighted. Quality of restored handles can be verified by comparing with the intensity function in Fig. 3.2.

Using topological information in image segmentation has been studied in both computer vision [16] and medical imaging [81]. As far as we know, in all previous methods, that use either random field energy models (MRF and CRF) [69] or level set models [91], topological priors such as connectivity or handle-free are enforced as a segmentation constraint. In this paper, instead of enforcing the final segmentation to have an upper bound of the number of components or handles, we restore topological features, as long as we have high confidence in them.

3.2 Methodology

The algorithm flow is illustrated in Fig. 3.2. An initial segmentation is applied on the image and then we compute handles that need to be restored. Each handle is delineated by a thickened cycle, as illustrated in Fig. 3.2 (c). The segmentation is fixed accordingly, by enforcing these cycles to appear in the final segmentation.

In this section, we first state the desired properties for the cycles that we should use for handle restoration. Next, we build a connection to a theory of persistent homology
in the computational topology community. The output of persistent homology is a set of dots corresponding to handles that appear when we threshold the domain using a function value. Based on such theory, we design an algorithm to compute proposal cycles, each of which delineates one handle. We conclude this section by explaining how to choose the promising candidates from all these proposals so that they satisfy the desired properties.

![Figure 3.2](image)

Figure 3.2: A two-dimensional slice of the data on which we illustrate the workflow. (a) CT image. (b) Initial segmentation. (c) Proposed fixing cycles (partially occluded). (d) Final segmentation with handles restored.

### 3.2.1 Intuition and the Desired Properties of Cycles for Handle Restoration

![Figure 3.3](image)

Figure 3.3: (a) A given cycle is sealed by two different patches (pink and green). (b) The sum of two cycles is sealed by a tube shaped patch (pink), which delineates a way to deform between the two. (c) The mod-2 sum of two cycles, and a sealing patch.

We start by introducing some terminology. A closed curve is called a *cycle*. The mod-2 sum (exclusive or) of a set of cycles is also called a *cycle*. A 2-manifold with boundary is called a surface *patch*. A patch *c seals* a cycle *z* if its boundary is *z*, formally, \( \partial(c) = z \). When the sealed cycle is the sum of two cycles, the patch could be considered as the area swept through when we smoothly deform the first cycle into
the second. In a 3D image, there could be infinitely many patches that seal a given cycle, and thus infinitely many ways to deform between cycles. See Fig. 3.3(a)-(c) for illustration.

Given a function defined on the image domain \( f : \Omega \to \mathbb{R}, \Omega \subseteq \mathbb{R}^3 \). To restore missing handles based on the image \( f \), the two blue cycles in Fig. 3.4 are natural choices.

The set of cycles we select should satisfy the following properties. First, we require a high saliency for each selected cycle. A selected cycle \( z \) needs to go through points with relatively low function values, and any surface patch sealing this cycle has to have some points with relatively large function values. We measure the saliency of the cycle using the minimal difference between the maximal function value of the cycle and the maximal value of a sealing patch,

\[
Saliency(z) = \min_{c : \partial(c) = z} \max_{p \in c} f(p) - \max_{p \in z} f(p)
\]  

(3.1)

In Fig. 3.4, the blue and red cycles have high saliency, but green ones do not.

Second, we should not select several cycles that in fact correspond to the same trabeculae/handle. Any two selected cycles are required to have a large dissimilarity, i.e., the saliency of their sum,

\[
\text{Dissimilarity}(z_1, z_2) = Saliency(z_1 + z_2)
\]
The dissimilarity between a cycle and zero is its saliency. In Fig. 3.4, there is a small dissimilarity between each blue cycle and the red cycle surrounding it. We should only select one of them.

Third, we should exhaustively select all possible salient cycles. Any given cycle $z$ should have a small dissimilarity from the set of selected cycles, $Z$, which is defined as

$$\text{Dissimilarity}(z, Z) = \min_{z_1, \ldots, z_n \in Z} \text{Dissimilarity}(z, \sum_i z_i)$$

Note that this quantity lowerbounds the saliency of $z$ itself since we allow $n$ to be zero. Thus the dissimilarity is small if $z$ has small saliency.

3.2.2 Persistent Homology

![Figure 3.5: (a) Synthetic function. (b)-(e) Sublevel sets $\Omega_\ell$ at time $b_1 < b_2 < d_2 < d_1$. Bottom row: 2D slices of the sublevel sets. We also show the intensity inside the sublevel sets.](image)

In order to compute cycles that serve our purpose, we use persistent homology. The input of the tool is a topological space and a scalar function, e.g., the image domain $\Omega$ and the image function $f$. The output is a set of dots on $\mathbb{R}^2$ corresponding to a set of features.

For a given scalar value $\ell$, we call the set of points with function value no greater than $\ell$ a sublevel set, formally, $\Omega_\ell = \{x \in \Omega \mid f(x) \leq \ell\}$. We study the topological changes of sublevel sets $\Omega_\ell$ as the parameter $\ell$ increases from $-\infty$ to $+\infty$, during which the sublevel set grows from empty to the whole domain $\Omega$. For convenience, we say a
topological event happens at time $\ell_0$ if it happens when we grow the sublevel set from $\Omega_{\ell_0-\epsilon}$ to $\Omega_{\ell_0}$.

In this chapter, we focus on a specific kind of topological feature, handle. In Fig. 3.5, at time $b_1$, a new handle (delineated by the cycle $z_1$) is created. This handle is destroyed (becomes trivial) at time $d_1$. The two corresponding function values are called the birth time and death time of this topological feature. At time $b_2$ and $d_2$, another handle (delineated by the cycle $z_2$) is created and destroyed. For each handle, the difference between its death time and birth time is called the persistence.

![Persistence diagram of the synthetic function $D_f$.](image)

All topological features are recorded in a persistence diagram. Each handle corresponds to a dot in $\mathbb{R}^2$, whose $x$ and $y$ coordinates are the birth and death times. The vertical or horizontal distance of a dot from the diagonal $x = y$ is its persistence. Fig. 3.6 is the persistence diagram of the synthetic function, with the two handles corresponding to two blue dots.

A justification of using the persistence diagram as a signature of functions is its stability with regard to perturbations of the function [22]. Formally, the bottleneck distance between the diagrams of a function and the same function with added noise is upperbounded by the $L_\infty$ norm of the noise, formally,

$$\text{dist} (D_f, \hat{D}_f) \leq \| f - \hat{f} \|_\infty = \| e \|_\infty,$$

where $\hat{f} = f + e$.

In Fig. 3.7, after introducing noise $e$ into the synthetic function, the persistence diagram could have many new dots with small persistence ($\leq \| e \|_\infty$). However, no
large persistence dots are introduced or removed. The large persistence dots only move in the diagram by at most $2\|e\|_{\infty}$. In other words, noise in the image only introduces spurious handles that are destroyed right after creation. The stability theorem gives us the rational of selecting dots corresponding to the true signal by thresholding the persistence. We will utilize this as the first step of screening proposed handles.

In order to compute the persistence diagram, we first discretize the image domain into a cubical complex whose basic elements are simplices of dimension zero to four, i.e., vertices, edges, squares and cubes, respectively. The set of vertices corresponds to the set of all voxels in the image. We assign function values to all simplices. A vertex has the value of its corresponding voxel. A simplex has the maximal value of all its vertices.

Simplices are indexed proportionally to their function values. We build the boundary matrix of dimension $d$, whose columns and rows correspond to $d$-dimensional simplices, i.e., $d$-simplices and $(d - 1)$-simplices respectively. Columns and rows are indexed from left to right and from top to bottom respectively. An entry of the matrix is set to 1 if the corresponding $(d - 1)$-simplex belongs to the boundary of the corresponding $d$-simplex, and 0 otherwise. The one-dimensional boundary matrix is, in fact, the adjacency matrix of the underlying graph. In Fig. 3.8(a), we show an example complex, with values of vertices specified. The sorted simplices, and one-and-two-dimension boundary matrices are given in Fig. 3.8(b) Each column vector of the two-dimensional boundary matrix is a cycle, and the boundary of a 2-simplex is a square. Since we use mod-2 addition, the
sum of any set of columns is a cycle and the boundary of a patch which is the sum of
the set of corresponding 2-simplices. Columns of the boundary matrix span the space
of all possible cycles of the discretized image domain $\Omega$.

![Diagram](image.png)

Figure 3.8: (a) Example cubical complex, with function values given. (b) Boundary
matrices of dimension one and two. (c) Reduced matrix $R$.

To compute the one-dimensional persistence diagram, which records features cor-
responding to handles, we apply a matrix reduction on the two-dimensional boundary
matrix. All additions are mod-2. We reduce columns of the matrix from left to right.
For each column, we only use the columns on its left to reduce it. We start from the row
index of the lowest nonzero entry of column $i$, called $\text{low}(i)$. If this row index is equal
to $\text{low}(j)$ for some column $j$ that has been reduced, we add column $j$ to $i$, and thus
reduce $\text{low}(i)$. We repeat until $\text{low}(i)$ is not the lowest nonzero entry of any column
$j < i$, or column $i$ becomes zero. In the former case, this reduced column corresponds
to a handle in the persistence diagram, whose birth (resp. death) time is the function
value of the simplex $\text{low}(i)$ (resp. the simplex $i$). One property of the reduced matrix
is that the $\text{low}(\ast)$s for all columns are unique. See Fig. 3.8(c) for an example of the
reduced matrix, denoted by $R$. The edge $\text{low}(i)$ and the square $i$ are where the handle
is created and destroyed, called the creator and destroyer.

**Algorithm 1** Persistent Homology Computation

```plaintext
R ← D; L ← [0, ..., 0]
for $j = 1, \ldots, n_2$ do
    while $R_j \neq 0 \land L[\text{low}(R_j)] \neq 0$ do
        $R_j ← R_j + R_L[\text{low}(j)]$
    end while
    if $R_j \neq 0$ then $L[\text{low}(R_j)] ← j$
end for
return $R$
```
The pseudo-code for computing persistence is given in Algorithm 1. The input is the 2-dimensional boundary matrix $D$, whose columns and rows are sorted according to the function values. The output is $R$, the reduced matrix. Denote by $n_1$ and $n_2$ the numbers of 1-cells and 2-cells, and thus the numbers of rows and columns of $D$. The vector $L$ has length $n_1$ and is initialized to be a zero vector. Entry $L[i]$ is a positive integer $j$ if and only if $i = \text{low}(j)$, and 0 otherwise.

### 3.2.3 Computing Proposal Cycles

We first compute one proposal cycle for each handle from the persistence diagram. For a handle that is born at time $b$ and dies at $d$, we take a cycle that goes through the handle and lies within the sublevel set $\Omega_b$. Furthermore, we choose a cycle which is sealed by a patch with the maximum function value $d$. For example, in Fig. 3.5, we choose $z_1$ for the handle born at $b_1$. For the handle born at $b_2$, we choose $z_2$ instead of $z_3$, because it is sealed up by a patch with the maximum value $d_2$. We say the computed cycle delineates the corresponding handle. We denote by $\tilde{Z}$ the set of all proposal cycles, delineating all handles that appeared in some sublevel sets. How to choose from them the salient ones will be discussed later.

To compute elements of $\tilde{Z}$, we reuse the output of the algorithm for the persistence diagrams, in particular, the reduced matrix $R$ (Fig. 3.8(c)). To compute a cycle for the handle corresponding to column $i$, collect the set of columns $R(\ast, j)$ on $R(\ast, i)$’s left such that $\text{low}(j) < \text{low}(i)$, e.g., the three marked columns in Fig. 3.8(c). These columns form a new matrix, $\hat{R}^i$. The following theorem shows that any cycle that is the sum of the $i$-th column and a set of columns in $\hat{R}^i$ is a valid cycle representing the handle corresponding to column $i$.

**Theorem 1.** $\forall x, y = R(\ast, i) + \hat{R}^i x$ is a cycle delineating the corresponding handle.

**Proof.** Since $y$ is the sum of a set of columns of the boundary matrix, it is a boundary, and thus a cycle. By definition of $\hat{R}^i$, the lowest nonzero entry of $y$ is still $\text{low}(i)$. $y$ contains the edge $\text{low}(i)$ where the handle is created. Furthermore, $y$ only contains edges of function values no greater than edge $\text{low}(i)$. Therefore, $y$ is a cycle going
through the handle and is contained within the sublevel set at the birth time.

What is left is to show that $y$ is sealed up by a patch within the sublevel set at the death time. The persistence algorithm reduces the boundary matrix $D$ from left to right. For each column, only columns from the left are used for reduction. The reduction stops when the unique lowest entry is found. We note that $R(\ast, i)$ belongs to the space spanned by the first $i$ columns of $D$, but not the first $i - 1$ columns. This can be trivially extended to $y$. In other words, $y$ is a cycle that is sealed up at the function value of the square $i$, not before.

A delineating cycle may have freedom to wiggle within a handle, as long as it contains the creator edge $\text{low}(i)$. Thus we prefer computing a cycle with simple geometry. This leads to the problem of computing the shortest cycle among all candidates.

**Problem 1.** Compute $y = R(\ast, i) + \hat{R}^j x$ with the minimal number of nonzero entries.

Unfortunately, this problem is not only NP-hard, but also NP-hard to approximate within any constant.

**Theorem 2.** Problem 1 is NP-hard to approximate within any constant factor.

**Proof.** Our proof is for two-dimensional persistent homology. It suffices to construct a strict reduction from the homology localization problem [15]: given a complex $K$, and a nonboundary cycle $z_0$, compute the shortest cycle homologous to $z_0$.

We construct a new complex $\tilde{K}$ as follows: construct a suspension of $K$. Replace one of the new vertices by a 2-simplex, $\sigma$. Add a 3-dimensional patch $c_0$ sealing up the 2-cycle formed by $z_0$ and the suspension. We assign function value 0 to all simplices in the suspension except for $\sigma$, which is assigned value 1. Assign the patch $c_0$ value 2.

There is an one-to-one correspondence between all 1-dimensional cycles of $K$ and all 2-dimensional cycles of the suspension. In such case, let patch $c_0$ be the $i$-th 3-simplex and then $\sigma$ is the $\text{low}(i)$-th 2-simplex. After persistence reduction, the remaining column $R(\ast, i)$ is a cycle homologous to the suspension of $z_0$. Finding the optimal cycle representing this persistent class is equivalent to finding the optimal cycle homologous
to $z_0$ in $K$. Since sizes of the corresponding cycles differ by a constant factor, two, this reduction is a strict reduction.

Alternatively, we propose a heuristic method to compute $y$ as follows. Starting with the $i$-th column $y = R(\ast, i)$. Iterate through the row indices from low($i$) − 1 to 1. For each row index $k$, if $y(k) \neq 0$, and $k = \text{low}(j)$ for some $j < i$, and adding $R(\ast, j)$ to $y$ would reduce the number of nonzero entries, then add $R(\ast, j)$ to $y$.

Over the course of the algorithm, all used columns $R(\ast, j)$ will belong to $\hat{R}^i$. So we always get a valid $y$. Furthermore, the number of nonzero entries of $y$ monotonically decreases. The cycle gets shorter after each addition. In practice, the heuristic algorithm generates cycles that are reasonably simple. Trabeculae usually correspond to thin handles, which leave limited space for cycles to wiggle within.

### 3.2.4 Selecting Proposal Cycles Satisfying Desired Properties

From the set of all proposed cycles, $\bar{Z}$, we select the set of promising ones using a two level screening method. In the first level, we select cycles delineating handles with persistence not less than a threshold $\theta$.

In fact, the saliency of each delineating cycle as defined in Equation (3.1) is equal to the persistence of the handle. To show this, recall that the cycle goes through the creator edge and lies within the sublevel set defined by the birth time. Thus, its maximal function value is equal to the birth time. Since the death time $d$ is when the handle is destroyed, the cycle is sealed by a patch within the sublevel $\Omega_d$. However, there is no such patch within $\Omega_{d-\epsilon}$. Thus the death time $d$ is equal to the first item in Equation (3.1).

We abuse notations and say a proposed cycle has the same birth time, death time and persistence as its corresponding handle. Theorem 3 guarantees that the selected set of cycles, namely, $Z_\theta = \{z \in \bar{Z} \mid \text{persistence}(z) \geq \theta\}$, satisfies the three desired properties we discussed in Section 3.2.1. Although high persistence cycles lead to salient handles that are more likely from trabeculae, in practice, the first screening would inevitable select certain wrong cycles. Therefore, we use a classifier with geometrical features as
The second level screening.

**Theorem 3.** (A) Any cycle in $Z_\theta$ has a saliency at least $\theta$;
(B) The dissimilarity between any two cycles of $Z_\theta$ is at least $\theta$;
(C) For any cycle $z$, its dissimilarity from $Z_\theta$ is at most $\theta$.

**Proof.** (A) is true, as we have shown that the saliency is equal to the persistence.

For any two cycles from $Z_\theta$, their mod-2 sum has a saliency of at least $\theta$. Otherwise, without loss of generality we assume $z_2$ is born after $z_1$. At the birth time of the second handle, $b_2$, if one chooses $z_1 + z_2$ instead of the $z_2$ to delineate the handle, it would be sealed up before time $b_2 + \theta$. This contradicts the fact that the second handle has persistence at least $\theta$, and thus dies at least at time $b_2 + \theta$. Thus, (B) is true.

By the theory of persistence, in the case when $\Omega$ is an image domain with trivial topology, the set $\bar{Z}$ is a basis of all cycles. In other words, any cycle $z$ can be written as the sum of some elements from $\bar{Z}$, $z_1, \ldots, z_n$. Assume only the first $m$ of them belong to $Z_\theta$. The dissimilarity between $z$ and $Z_\theta$ is at most the saliency of $z + z_1 + \ldots + z_m = z_{m+1} + \ldots + z_n$, denoted by $y$. We abuse the notation and say a computed cycle is born and dies at the birth and death time of the corresponding handle. By definition, the birth time of $y$ is the maximum of the birth times of $z_{m+1}, \ldots, z_n$. The death time of $y$ is no greater than the maximum of the death times of $z_{m+1}, \ldots, z_n$. Therefore the saliency of $y$ is no greater than the maximum of the saliency of $z_{m+1}, \ldots, z_n$, which is upperbounded by $\theta$. Thus, (C) is correct.

3.3 Experiments

In this section, we present experiments of using the proposed topological repaired segmentation algorithm. The algorithm was evaluated on two synthetic data and one real data set to show its effectiveness. All the experiments were tested on a 2.40GHZ Intel Core2 Quad computer with 8G RAM.

The proposed algorithm was employed on 6 cardiac CT image at the end diastolic state, where trabeculae structures are separated the most. The CT data were acquired
on a 320-MDCT scanner, using a conventional ECG-gated contrast-enhanced CT angiography protocol. The imaging protocol parameters include: prospectively triggered, single-beat, volumetric acquisition; detector width 0.5 mm, voltage 120 KV, current 200 – 550 mA. The resolution of each time frame is 512 by 512 by 320.

We used the region competition algorithm [111] to initialize the segmentation. In order to focus on restoring the missed trabeculae, we decreased the function value of a voxel to zero if it was already segmented as the heart wall, the papillary muscles or the trabeculae. Handles which correspond to the structures that had been successfully captured would have birth time 0 and appear as dots on the y axis of the diagram. Their cycles were not be used for restoration. Fig. 3.9(a) illustrates the persistence diagram of one cardiac image. To compute the persistence diagram and corresponding cycles, our algorithm was run on a commodity machine in 6 to 8 minutes using 6 to 10 GB memory.

Figure 3.9: (a) Diagram of persistent pairs. The persistence threshold is marked as 80. (b) The relationship of persistence threshold and number of topological repairs. As the threshold moves from 120 to 80, it includes more and more positive pairs.

For all images, proposal cycles for all persistence dots were computed. We used 5 out of 6 images for selecting persistence threshold, and training, and the remaining image for testing. We had human experts carefully examine proposal cycles and mark them as positive and negative, by studying the image function. (For example, the blue cycles in Fig. 3.2(c) are considered positive.) We performed the two level screening to select
promising proposals. We empirically chose the persistence threshold. For illustration, in Fig. 3.9(b) we plotted the number of positive and negative dots with persistence above a threshold, for one training image. We chose $\theta = 80$ so that we included all positive proposal cycles and a reasonable number of negative ones from the training images. In the persistence diagram shown in Fig. 3.9(a), we drew the line $y = x + \theta$. All dots above this line were selected after the first level screening. Dots on the $y$ axis were all positive. Notice the big variation of the birth and death times of positive dots. This implies that it is impossible to detect them using an universal intensity prior.

Next we explain how to train the classifier for the second level. For all six images, we selected 458 positive out of 1095 proposals after persistence screening. Among those selected proposals, we used the ones from the five training images for training and 10-fold cross validation, and the ones belonging to the test image for testing. We used the LIBSVM toolbox [14] to train our classifier. Features used were birth time, death time, persistence, length of the cycle, and the relative position in the ventricle. We achieved 81.69% accuracy in the testing.

![Figure 3.10: (a) Baseline segmentation. (c) Proposed segmentation. (b),(d) Distance map from the pseudo-groundtruth to the baseline segmentation, and the proposed segmentation, respectively.](image)

After promising proposals were selected, we generated the final segmentation by enforcing these cycles to be included. We reused the region competition algorithm with the same parameters so that the remaining parts of the final segmentation are the same as the initial one. Groundtruth is extremely difficult to get for this kind of data using manual segmentation. We generated the pseudo-groundtruth for the testing image by enforcing the human marked positive cycles. We compared the results of our method to
that of a baseline segmentation generated by the region competition method (Fig. 3.10). We showed the distance from the pseudo-groundtruth to the baseline segmentation and to our segmentation. Distance was represented by different colors. Green, red and blue represented accurate segmentation, over segmentation and under segmentation, respectively. The trabeculae missing from the baseline segmentation had greater error and are shown in red and blue colors. Our segmentation, as shown in Fig. 3.10(b), successfully captured more trabeculae. The distance error of the initial segmentation is 0.2108 ± 0.4973 voxel, whereas our proposed segmentation method has distance error 0.1101 ± 0.3679 voxel.
Chapter 4
Morphological Analysis of the Endocardial Surface

Clinically meaningful parameters are needed for accurate diagnosis. In this chapter, we explain how the segmented results can be used to extract useful parameters to characterize the detailed endocardial left ventricle [35]. We study the morphology of such complex structures. We represent the structures accurately and concisely using curve skeletons, and measure these structures using topological and geometrical features. It is observed both qualitatively and quantitatively that structures at different parts of the endocardial surface have different characteristics. This morphological study sheds light on the potential future use of these complex endocardial structures to study cardiac function and to diagnose cardiac diseases.

4.1 Introduction

Images acquired from various imaging techniques are usually fed into image segmentation algorithms to extract anatomical structures such as left ventricle (LV) and right ventricle (RV) [73]. And then based on the segmentation results, various parameters are extracted and used for analyzing cardiac function and diagnosing cardiac diseases. Global features, such as ejection fraction (EF), ventricular volume and myocardial mass [78] have been used frequently in clinical situations. Some other indices have been proposed to quantify shape and motion features [104]. Regional features such as myocardial strain [96], wall thickness [12] and local contraction of the endocardial surface [75] have also been studied.

Although many measurements have been developed, it is surprising that we still cannot characterize the detailed endocardial surface structures that have been documented
since 1513 \[98\], namely, the *trabeculae* and the *papillary muscles* (TPM). Some trabeculae are completely attached to the wall of the heart, while others are fixed at both ends to the ventricular wall, but the intermediate section is freely mobile within the cavity, forming topological handles. The papillary muscles are attached to the valves via chordae tendineae. They start contracting shortly before the ventricle contraction starts, so valves function properly during a cardiac cycle. The anatomical picture of the heart is illustrated in Fig. 3.1.

The study of these complex structures is very important. A recent study shows that the papillary muscles and the trabecular composes up to 23\% of LV end-diastolic volume in average \[19\]. Therefore, an accurate measurement of TPM is critical for any study using volume-related metrics. Furthermore, an accurate extraction of TPM is the prerequisite for an accurate simulation of blood flow in ventricles \[52\]. In terms of clinical impact, there are hypotheses about correlations between TPM and cardiac diseases like LVH, AS, thrombus and stroke \[95\].

The investigation of the papillary muscles and the trabecule was underdeveloped due to the limitation of traditional imaging modality. The new technology of high resolution CT enables us to capture the fine papillary muscles and the trabecule structures in a higher accuracy. Using new segmentation methods inspired from computational topology, Gao et al. \[36, 34\] accurately reconstructed the fine and complex structure from these high resolution CT images. The acquired TPM structures are used for further analysis. Zhong et al. \[110\] extracted and quantitatively characterized the motion of papillary muscles. Differences between healthy and hypertrophic papillary muscles were observed. Mukhopadhyay et al. \[65\] studied the LV endocardial surface using an isometry-invariant bag-of-words (BOW) feature. They chose descriptors invariant to isometric deformations and achieved effective incidence of coronary arterial stenosis localization. However, the BOW method, as a black box characterization of the endocardial surface, cannot give clinically insightful explanation of the diseased regions or provide specifically effective features.

In this chapter, we study the morphology of the trabeculae and the papillary muscles. We design a framework to segment the papillary muscles and the trabecule and then
extract their skeleton, giving us convenient tools for measurement and visualization. A set of features are proposed and computed, which characterize the structures in terms of both topology and geometry. Our analysis reveals that these papillary muscles and the trabecule have different characteristics in different locations.

4.2 Methodology

Our system first accurately segments the structures from high resolution CT images, then extracts skeletons of trabeculae. Finally we compute features based on these skeletons.

4.2.1 Topologically Accurate Segmentation

In order to analyze the papillary muscles and the trabeculae, a high quality segmentation which captures these fine structures is required. Gao et al. [34] proposed a method to segment 3D high resolution CT data by explicitly restoring topological handles, which happen regularly in the detailed structures. The location and geometry of these handles are suggested by a tool from computational topology, namely, persistent homology [29]. Intuitively speaking, a suggested handle should have high saliency, which is defined as the difference between the maximal intensity value along the handle and the maximal value of the best 3D patch sealing the handle up. The method has been proved to be accurate both topologically and geometrically. Fig. 4.2 (left) shows a representative segmentation result.

4.2.2 Skeleton Extraction

Since trabeculae have the shape of tubes, it is natural to represent them using skeletons, namely, pieces of 1-manifolds with boundaries stitched together at vertices. See Figure 4.2 for an illustration. Computed skeletons will be used for our visualization and morphological analysis.

We choose the curve skeleton defined by Dey and Sun [27] because of its numerical stability and robustness. A curve skeleton is a subset of the medial axis of a given 3D
object, which includes the trabeculae and the papillary muscles in our case. The \textit{medial axis} is the set of points each of which is the center of a ball, $B_x$, contained in the 3D object and that touches the surface in at least 2 points. The \textit{medial geodesic function} of a point $x$ in the medial axis is the shortest geodesic distance between the two touching points of $B_x$ within the surface. The curve skeleton is then defined as the singularities, namely, non-differentiable points of this medial geodesic function. One may also use the radius of the ball $B_x$, instead, for the definition. The difference between the two definitions is marginal when the trabeculae are close to tubes.

\section*{4.2.3 Features}

We design and compute several features to describe the morphology of the trabeculae and the papillary muscles. The extracted trabeculae (Fig. 4.2 (left) and Fig. 4.3) are generally in the form of triangular meshes. In order to describe the complexity of such structures, we would like to count the number of handles and tunnels. This can be calculated using a metric from algebraic topology, i.e., the \textit{Betti number}. Beside topological complexity, we also would like to measure the geometry, like how wiggly and how thick these handles are. Therefore we use geometric features like \textit{length} and \textit{diameter}. Next, we define these features in details.

![Figure 4.1](image)

\textbf{Fig. 4.1:} (a) A surface with genus two (two handles). The Betti number is four. (b) The diameter at point $p$ is measured by the perimeter of the intersection disk.

\textbf{One-dimensional Betti number:} The \textit{genus} of an orientable surface is the maximum number of cutting planes that could be applied before cutting the surface into disconnected components. Intuitively, the genus counts the number of handles of a
surface. We could approximately compute the genus of a surface as a half of the one-dimensional Betti number, $\beta_1$ (Fig. 4.1 left). To compute the Betti number, we extract from a mesh of the endocardial surface two boundary matrices, $\partial_1$ and $\partial_2$. The former, $\partial_1$, is the adjacency matrix of the graph, which consists of all vertices and edges of the mesh. The latter, $\partial_2$, is similarly defined, except that each row corresponds to an edge and each column corresponds to a triangle of the mesh. The one-dimensional Betti number is then computed as $\beta_1 = \text{rank}(\text{kernel}(\partial_1)) - \text{rank}(\partial_2)$, where $\text{rank}$ is the rank of a vector space and $\text{kernel}$ is the nullspace of a linear operator \cite{29}.

**Length:** While the one-dimensional Betti number describes the topological complexity of the structure, the total length of a trabecula is used to describe its geometrical complexity. It is measured by calculating the total length of the extracted skeleton.

**Diameter:** The diameter at a particular point of the trabecula is the diameter of the intersection disk of the trabecula and a cutting plane. The cutting plane is selected to be perpendicular to the tangent of the skeleton (Fig. 4.1 right).

### 4.3 Experiments and Discussion

![Figure 4.2](image)

(a) Endocardial surface. (b) Curve skeleton colored by diameter.
4.3.1 Skeleton Extraction Validation

We started our experiments by validating the accuracy of the skeleton extraction. We compared our curve skeleton result to the skeleton computed using the classical morphological operators [55], thinning. Fig. 4.2 shows the left endocardial surface mesh and the curve skeleton extracted from it. To quantitatively evaluate the accuracy of the skeleton extracted, we computed the distance from curve skeleton to thinning and the reverse. The average distances between curve skeleton to thinning skeleton and reverse are $0.52 \pm 0.42$ voxels and $1.02 \pm 1.39$ voxels, respectively. In summary, the curve skeleton gives a good approximation of the true skeleton and can be used for visualization and measuring of trabeculae.

![Figure 4.3: (a) There are three types of trabeculae. Zoomed in views are illustrated in (b)(c)(d) respectively.](image)

### 4.3.2 Morphological Analysis

The segmentation and skeleton extraction algorithms were firstly applied to get a triangle mesh and a skeleton abstraction. We observed the spatial distribution of the trabeculae varies with the location within the LV. Consistent with the standard anatomical description [39], we observed three types of trabeculae (Fig.4.3).

1. Attached to the wall along their entire length and formed as prominent ridges of the heart wall. Located approximately in the left circumflex coronary artery area. These trabeculae are generally thick and have a consistent orientation and diameter.
2. Fixed at their extremities but free in the middle. Located approximately near the two papillary muscles. They have small diameter and inconsistent orientation.

3. Located on the apices of the papillary muscles, which give origin to the chordae tendineae.

We further divided the mesh into 17 segments according to the AHA model as shown in Fig. 4.4 [13] to perform regional shape analysis (Fig. 4.5). Different segments clearly have different trabeculae complexity. This observation is verified quantitatively using the proposed features.

Figure 4.4: Display on a circumferential polar plot of the 17 myocardial segments recommended by AHA.

Figure 4.5: 17 Segments of the LV.
Figure 4.6: One-dimensional Betti number, total length of LV segments. Red line is the median of data, blue box shows the range of 25% to 75% of the data. Black dots represent the range.

Figure 4.7: Bull’s eye visualization of the regional features mean value on normal heart data set. (a) Betti number (b) Total length features
We measured the proposed features on 10 data sets, each of which had been reconstructed and further divided into segments. Fig. 4.6 left shows regional properties of different segments of the LV. We also illustrate the pattern of proposed features in different regions, using a bull’s eye visualization (Fig. 4.7). While the Betti number and length features illustrate apparent differences between different regions, it is difficult to distinguish regions using diameter alone.

The two measurements are both consistent with the qualitative observations discussed in the previous section. While there are fewer trabeculae on the septum (e.g., segments 2,3,8,9), most of the trabeculae are located on the anterolateral segments of the heart (e.g., segments 5,10,11,15). The mid-cavity portions have the most complex structures, compared to the basal and apical portions. The diameter of the structures appear to be consistent through the whole ventricle, ranging around 3 mm.

We performed statistical analysis to measure the significance of the differences in features between different regions, using t-test. We found that the difference between different regions was indeed statistically significant. The p-value of differences between one-dimensional Betti number and total lengths of segment 8 (mid anteroseptal) and segment 11 (mid inferolateral) are $4.8 \times 10^{-4}$ and $1.6 \times 10^{-3}$, respectively. Taking segment 4, using total length feature for example, segments 1, 5, 6, 7, 10, 11, 12, 13, 14, 16 did not reject the null hypothesis, which means those regions are not independent. For segment 8 using one-dimensional Betti number feature, segments 2, 3, 9 did not reject the null hypothesis. Thus, as expected, the septum has quantifiable differences in trabeculation from the free wall.

We also measured the proposed features on an abnormal heart using the exactly same setting as normal data sets. Bull’s eye visualization of the regional features are show in Fig. 4.8. Compared to the distribution of the regional features on normal data set in Fig. 4.7, we have several observations. The pattern of Betti number and total length are similar in normal or abnormal hearts. However, note that the Betti number has a very different color legend, the abnormal heart has a much larger range, which is between 0 and around 150, compared to the range 0 to 30 in normal hearts. This experiment showed that the one-dimensional Betti number has the discriminative power
in distinguishing some diseased hearts from normal.

Figure 4.8: Bull’s eye visualization of the regional feature on an abnormal heart (a) Betti number (b) Total length.

4.4 Conclusion

In this paper, we proposed a method to analyze the complex endocardial structures, namely, the papillary muscles and the trabeculae. There are several directions for the future work. Closely looking at the quantitative features of normal hearts and diseased hearts would also provide insight, once diseased samples are available. This work can also be extended to a full spatio-temporal cardiac image analysis.
Chapter 5

4D Cardiac Reconstruction Using Deformable Model

In this chapter, we present a framework that uses high resolution cardiac CT images to reconstruct the 4D motion of the endocardial surface of the left ventricle (LV) for a full cardiac cycle. This reconstruction framework captures the motion of the full 3D surfaces of the complex anatomical features, which allows us to quantitatively investigate their motion characteristics in healthy and diseased hearts.

5.1 Introduction

For the case of 4D cardiac images, two problems have to be considered simultaneously: 1) a heart wall segmentation problem in each image and 2) a tracking problem of the left ventricle motion given the data set. In [59], Mcinerney et al. proposed a method for 4D cardiac reconstruction, in which the output of the previous time frame is used as the initial guess for the current time frame in order to do a sequential segmentation. They used a finite element surface model which may not be able to handle topology changes. Montagnat et al. proposed an extended deformable framework by introducing time-dependent constraints. Thus, in addition to computing an internal force to enforce the regularity of the deformable model, prior motion knowledge is introduced in the deformation process through either temporal smoothing or trajectory constraints [64]. However, these 4D reconstruction methods do not capture detailed features.

In this chapter, we present a framework for 4D left ventricle (LV) segmentation with inclusion of small scale anatomical features. Semi-automatic segmentation is used to get the initial segmentation from high resolution CT data for an initial (3D) frame of data. This semi-automatic segmentation is time consuming and tedious, so it is not efficient to use it for segmentation of all the frames. The initial high resolution mesh model is
generated as an isosurface of the segmentation. Geometric processing is then applied
to the initial model to get a smooth and regular mesh with an appropriate number
of vertices. Based on the initial model from one time frame, our method deforms it
towards the boundaries on the other frames. During the formation, the topology of
the model is kept unchanged. We can also get the one-to-one correspondence between
frames, as an additional benefit during the segmentation process. With the one-to-one
correspondence, we can easily do interpolation among different time frames to get a
smoother heart cycle animation. We have applied our framework on a whole cardiac
cycle. The results have been validated based on the ground truth segmented by multiple
clinical experts. These novel and powerful methods can extract the full 3D surfaces of
these complex anatomical structures, which allows us for the first time to quantitatively
investigate their possible functional significance [36, 106].

5.2 Methodology

We propose a framework to reconstruct the cardiac model. This framework includes:
initial model construction, deformable model based segmentation, and interpolation be-
tween time frames. The initial model is generated from one time frame of the CT image.
The initial model needs geometry processing, such as decimating, detail-preserving s-
mothing and isotropic remeshing to get high-quality meshes. Based on the initial
model, segmentation of the rest of the CT images is automatically performed using the
deformable model. The segmentation of a sequence of CT images is interpolated in
time to get a higher effective temporal resolution.

5.2.1 Model Initialization

The model initialization framework is illustrated in Fig. 5.1. We use the method provid-
ed in Chapter 3 to get the initial model. This segmentation process is time consuming
and could not be used to segment all frames. However, once this model has been
generated, it is used to segment the rest of other frames automatically.

Segmentation results are represented as binary images. Isosurface detection is then
applied to generate the the triangle mesh. However, the resulting mesh is usually bulky, noisy and irregular. To get a better initialization model, some geometric processing should be done on that mesh, such as decimating, detail-preserving smoothing and isotropic remeshing.

First, the initial model is too large to readily modify, edge collapses are performed during decimation. After decimation, we get a mesh with much fewer vertices, but that still retains most of the shape details. The meshes have been decimated to about 20,000 vertices. Detail-preserving smoothing is then performed after decimation. The smoothing is restricted to the tangential direction. Instead of moving each vertex towards the centroid of its neighbors, which would smooth out the shape details and sharp features, detail-preserving smoothing ensures higher quality meshes without losing details. Isotropic remeshing is important for the mesh quality. In irregular meshes, the vertices with high valences exert strong internal forces to drag other vertices, which can cause unrealistic results in deformable models [85]. An incremental isotropic remeshing technique is used to remesh the given triangular mesh so that all edges have approximately the same target edge length and the triangles are as regular as possible. This process would generally be iterated several times to get the final results.

After all these geometric processing steps, we finally get a high-quality triangular mesh with an appropriate number of vertices. This mesh is used as an initialization for other frames.
5.2.2 Deformable Model Based Segmentation

We want to deform our model normal to the boundaries during tracking. This process is formulated as an energy minimization procedure. Three energy functions are introduced to control the model deformation and preserve the mesh quality, i.e., model energy, external energy and shape energy. Given a gray level image $I(x, y)$, viewed as a function of continuous position variables $(x, y)$. The model $M_{t-1}$ derived from the previous frame is used to fit the current frame $M_t$. The energy function we want to minimize is defined as follows:

$$E(M_t, I_t, M_{t-1}) = E_{\text{ext}}(M_t, I_t) + E_{\text{model}}(M_t, M_{t-1}) + E_{\text{shape}}(M_t). \quad (5.1)$$

The External energy $E_{\text{ext}}(M_t, I_t)$ is designed to move the deformable model towards object boundaries. Model energy $E_{\text{model}}(M_d, M_o)$ reflects the geometric differences between $M_t$ and $M_{t-1}$. It preserves the geometric characteristics during the deformation. By jointly minimizing these two terms, the model will deform to the boundaries of the target and still preserving its geometric characteristics. An additional term Shape energy $M_{\text{shape}}(M_t)$ is designed to ensure that vertices are evenly distributed and shape details are roughly preserved. The quality energy $M_{\text{shape}}$ induced here ensures that the mesh quality is improved during deformation procedure, making the whole model more robust to handle diverse input.

To optimize this energy function, we use an expectation-maximization (EM) type of algorithm. During the “E” step, the model energy and external energy are minimized. Thus the source surface is deformed to fit the target one, although this deformation may degrade mesh quality and not be accurate. In the “M” step, the mesh quality is improved by minimizing the shape energy. As we show in Sec. 5.2.2, this step is formulated as a least square problem and solved efficiently. Two procedures are alternately performed to robustly register the source surface to the target surface. In the following sections, we will introduce the details of different energies as well as the optimization algorithms.
**External Energy**

External energy is designed to move the deformable model toward an object boundary. The minimization of external energy $E_{ext}$ is fairly standard. First, distance transform is applied to $M_t$ to obtain a binary distance 3D image $I_t$, which is the implicit embedding space of the target mesh. Then the deformed mesh $M_d$ is placed in the embedding space $I_t$. Standard gradient on $M_d$ vertices is computed from $I_t$. The gradient force drives $M_d$ to be close to $M_t$ on the boundaries. The details of $E_{model}$ and $E_{quality}$ are introduced in the next two subsections.

$$E_{ext}(M_d, M_t) = E_{ext}(M_d, I_t) = -|\nabla I|^2,$$

(5.2)

where $\nabla$ is the gradient operator.

**Model Energy**

Model energy measures the geometric differences between the original model and its deformed version. It is designed to maintain the geometric characteristics of the source surface while it is deforming to the target one. Model energy is defined by the differences of geometric attribute vectors. An attribute vector is attached to each vertex of the model, which reflects the geometric structure of the model from a local to global level. For a particular vertex $V_i$ in 3D, each attribute is defined as the volume of a tetrahedron on that vertex. The other three vertices form the tetrahedron are randomly chosen from the $l$th level neighborhood of $V_i$. Smaller tetrahedrons reflect the local structure near a vertex while larger tetrahedrons reflect a more global information around a vertex. The attribute vector, if sufficient enough, uniquely characterizes the different anatomical structures along a surface. Denote the volume of a tetrahedron as $f_l(V_i)$, the attribute vector of a vertex is defined as:

$$F(V_i) = [f_1(V_i), f_2(V_i), ..., f_{R(V_i)}(V_i)],$$

(5.3)

where $R(V_i)$ is the neighborhood layers we want to use around $V_i$. 
The model energy term reflects the differences of attribute vectors between the original and the deformed surface. Mathematically, it is represented as:

\[ E_{\text{model}}(M_d, M_o) = \sum_{i=1}^{N} \sum_{l=1}^{R(V_i)} \delta_l (f_{d,l}(V_i) - f_{o,l}(V_i))^2, \] (5.4)

where \( f_{d,l}(V_i) \) and \( f_{o,l}(V_i) \) are components of attribute vectors of the deformed surface and surface at vertex \( V_i \), respectively. \( \delta_l \) here denotes the importance of the \( l \)th neighborhood layers. \( R(V_i) \) is the number of neighborhood layers around vertex \( V_i \).

The proposed algorithm is optimized iteratively. In each iteration, a neighborhood of a vertex has been examined and the point in the neighborhood with the minimum model energy would be chosen as the new location of the vertex. The iterations continue until the energy converges. During the deformation, we suggest moving a surface segment as a whole, rather than a single vertex. This would avoid the risk of getting trapped in a local minimum, and also speed up the convergence. Let \( V_i \) be the vertex to be deformed during a particular iteration. The first to \( R(V_i) \)th neighborhood layers are about to move together as a surface segment. Suppose \( V_i \) is to move to \( V_i + \Delta \) as a tentative position. Then the new position of each vertex \( \text{nbr}_{l,m}(V_i) \), the \( m \)th vertex on \( l \)th neighborhood layer, is set to move to:

\[ \text{nbr}_{l,m}(V_i) + \Delta \cdot \exp(-\frac{l^2}{2\delta^2}), \] (5.5)

where \( \delta \) is a parameter determining the locality of the transformation. We make the deformation unchanged on the boundary of the surface segment, such that the continuity has been maintained.

The parameter \( R(V_i) \) that determines the locality if the deformation is chosen to be large in the initial iteration, and is then gradually reduced to 1. Therefore, initially there are more vertices involved in the deformation. More global features are used in deformation. In later stages, more local deformations are performed.
Shape Energy

Shape energy is used to smooth the shape without losing the important details. Usually there is a tradeoff between the smoothness and keeping shape details. We extend the Laplacian coordinate to achieve this. Let the mesh $M$ of the shape be described by a pair $(\mathcal{V}, \mathcal{E})$, where $\mathcal{V} = \{v_1, ..., v_n\}$ describes the geometric positions of the vertices in $\mathbb{R}^3$ and $\mathcal{E}$ describes the connectivity. The neighborhood ring of a vertex $i$ is the set of adjacent vertices $\mathcal{N}_i = \{j | (i, j) \in \mathcal{E}\}$ and the degree $d_i$ of this vertex is the number of elements in $\mathcal{N}_i$. Instead of using absolute coordinates $\mathcal{V}$, the mesh geometry is described as a set of differentials $\Delta = \{\delta_i\}$. Specifically, coordinate $i$ will be represented by the difference between $v_i$ and the weighted average of its neighbors:

$$\delta_i = v_i - \sum_{j \in \mathcal{N}_i} w_{ij} v_j$$

(5.6)

where $w_{ij}$ is computed from cotangent weights [74] (Fig. 5.2). Assume $V$ is the matrix representation of $\mathcal{V}$. Using a small subset $\mathcal{A} \subset \mathcal{V}$ of $m$ anchor points, a mesh can be reconstructed from connectivity information alone. The $x$, $y$ and $z$ positions of the reconstructed object ($V'_p = [v'_1, ..., v'_m]^T$, $p \in \{x, y, z\}$) can be solved for separately by
minimizing the quadratic energy:

\[
E_{\text{shape}}(M_d, L_o) = \|M_d - L_o\| = \|L_u V'_p - \Delta\|^2 + \sum_{a \in A} \|v'_a - v_{ap}\|^2,
\]  

(5.7)

where \(L_u\) is the Laplacian matrix from uniform weights, and the \(v_{ap}\) are anchor (landmark) points. \(\|L V'_p - \Delta\|^2\) tries to smooth the mesh when keeping it similar to the original shape, and \(\sum_{a \in A} \|v'_a - v_{ap}\|^2\) keeps the anchor points unchanged. The cotangent weights approximate the normal direction, and the uniform weights point to the centroid. By minimizing the difference of these two (i.e., \(L_u V'_p\) and \(\Delta\)), the vertex is actually moved along the tangential direction. Thus the shape is smoothed without significantly losing the detail. With \(m\) anchors, (5.7) can be rewritten as a \((n + m) \times n\) overdetermined linear system \(AV'_p = b:\)

\[
\begin{bmatrix}
L \\
I_{ap}
\end{bmatrix} V'_p = \begin{bmatrix}
\Delta \\
V_{ap}
\end{bmatrix}
\]

(5.8)

This is solved in the least squares sense using the method of normal equations \(V'_p = (A^T A)^{-1} A^T b\). The conjugate gradient method is used in our system to efficiently solve it. The first \(n\) rows of \(AV'_p = b\) are the Laplacian constraints, corresponding to \(\|L V'_p - \Delta\|^2\), while the last \(m\) rows are the positional constraints, corresponding to \(\sum_{a \in A} \|v'_a - v_{ap}\|^2\). \(I_{ap}\) is the index matrix of \(V_{ap}\), which maps each \(V'_a\) to \(V_{ap}\). The reconstructed shape is generally smooth, with the possible exception of small areas around anchor vertices. Different from [105], we use cotangent weights instead of uniform weights. Thus the movement along the normal direction is prevented, and shape details can be better preserved.

Although this method is able to improve mesh quality during runtime, it may still have difficulty to handle very dense and degenerated initial meshes. Furthermore, the computational efficiency can also be adversely affected by such dense meshes. Thus, we can also improve the mesh quality in the preprocess step, as shown in Fig.5.3. Usually mesh decimation can be employed to decrease the number of vertices, and this shape energy can be used to smooth the mesh.
Figure 5.3: Illustration of geometry processing methods, including decimation and detail preserve smoothing. After these operations, the mesh still has similar geometric characteristics with certain level of details, while the mesh quality is highly improved.

5.2.3 Interpolation

Segmentation for all frames are deformed from one single model, such that not only the topology is consistent, but also we have one-to-one correspondence of different time frames. All the meshes are interpolated in time to get a smooth animation of the cardiac cycle. We use periodic cubic spline interpolation. The last frame is set as the previous frame of the first frame in the interpolation process to get a circular animation of the heart cycle. Periodic cubic spline interpolation makes heart meshes continuous on the second derivatives. The interpolation results are used in simulation of blood flow in the left ventricles.

5.3 Results and Validation

Our reconstruction method successfully captured the papillary muscles and the trabeculae of the left ventricle. Figure 5.4 illustrates the anatomic structure of the papillary muscles and the trabeculae of the left ventricle. The three-dimensional structures, their relationship and their movement during the cardiac cycle are much more readily
Figure 5.4: Reconstruction results of left ventricle at one time frame. Papillary muscles and the trabeculae are clearly captured. (a) The left ventricle from the top, through valves. (b) The trabeculae of left ventricle from the front. (c) Zoom-in view of the papillary muscles and the trabeculae. (d) The papillary muscles and trabeculae being clipped by a user-defined plane.

appreciated from the model than from the original volumetric image data.

We compare our results to the ground truth from the annotations of clinical experts. Figure 5.5 shows the differences of the results from the manual segmentations. The color indicates the distance from each vertex of our results to the manual segmentation.

Figure 5.5(d) shows the quantitative evaluation of the results. The mean distance from every vertex to the semi-automatic segmentation is about one voxel. During the diastolic frames, which are frames 4 to frame 9, there are smaller distances and less distance variations. On the other hand, during cardiac systole, because of large deformations between neighboring frames, the results have larger errors.

The interpolation results have made possible a smooth animation of the full cardiac movement cycle.

5.3.1 Shape Statistics

The one-to-one correspondence is obtained for each vertex among all shapes after shape registration. Then the shape statistics can be computed straightforwardly using generalized Procrustes analysis and hierarchical PCA. Given any two shapes, they can be fitted to each other using a similarity or rigid transformation. Procrustes analysis is used to find the translation, rotation and scaling components. Since there is no mean
Figure 5.5: Differences of the left ventricle to the ground truth. Green colors mean that the distances are within one voxel. Red colors mean under-segmentation while blue colors mean over-segmentation. (a)(b)(c) Different frames of the differences of the left ventricle to the ground truth. (d) Distances distribution of every frame.
shape in the beginning, generalized Procrustes analysis arbitrarily chooses a shape to use as the reference and transforms all the rest to fit it. After that, a mean shape is computed by averaging all transformed shapes. Then, this mean shape is used as a reference shape in the next round. We repeat this procedure until the mean shape converges to a stable state. Note that normalization is necessary, as otherwise the mean shape will degenerate to a single point. After the alignment, each resulting shape is filled into a matrix as a column vector. PCA is applied to get the Point Distribution Model (PDM).

To effectively extract shape statistics from complex shapes, which often have multiple structures, we employ PCA hierarchically. First, RPCA is applied on each structure separately. Thus, shape variation of individual structure can be well discovered even with limited number of samples. Second, their relative locations with respect to the mass centroid are also modeled using PCA. This global statistics is used to place structures. Then local statistics of shapes is employed to select the important “modes” (i.e., eigenvectors corresponding to the largest eigenvalues) to cover more than 80% of the variance. Combining the mean shape and the modes, the PDM is able to summarize and describe the sample shapes concisely and accurately.

Fig. 5.6 shows the reconstruction results of high resolution cardiac CT images. Each shape contains around 20 to 25K vertices in order to capture fine details. The three-dimensional structures, their relationship and their movement during the cardiac cycle are much more readily appreciated from the shape model than from the original volumetric image data. After applying detail preserved smoothing and surface registration, we can simply use linear interpolation to obtain higher temporal resolution.

Fig. 5.7 shows the comparisons between our method and three widely-used shape
Figure 5.7: Comparison of different shape registration methods. We show the results of registered shapes from two time frames (i.e., the first and the fifth frames). Color map has been used to visualize the distance between each result and the ground truth. Green colors mean that the distances are within one voxel. Red colors mean under-segmentation while blue colors mean over-segmentation. From left to right: registered results from 1) Coherent Point Drift (CPD), 2) robust point set registration using Gaussian Mixture Models (GMM), 3) the Thin Plate Spline robust point matching (TPS-RPM), and 4) our proposed method. Top and bottom rows show two different viewpoints of the registered shapes.

registration algorithms: 1) Coherent Point Drift (CPD) [66], 2) robust point set registration using Gaussian Mixture Models (GMM) [47], and 3) the Thin Plate Spline robust point matching (TPS-RPM) [20]. We register the shape at the first frame to the one at the fifth frame, and then use color maps to visualize the distance between the registered shape and the ground truth. Green colors mean that the distances are within one voxel. Red colors mean under-segmentation while blue colors mean over-segmentation. Shape registration is very challenging since there are many shape details in this cardiac data. Large regions of the compared three methods are in blue and red, which means inaccurate local fitting. Compared to the three methods, the proposed method has achieved the best accuracy and preserved most visual details.

Table 5.1 shows the results of quantitative comparisons. We compare the mesh quality measured by the min and mean values of the radius ratio [67], the accuracy of
Table 5.1: Quantitative comparisons of the proposed method and four widely-used methods: 1) Coherent Point Drift (CPD), 2) robust point set registration using Gaussian Mixture Models (GMM), 3) the Thin Plate Spline robust point matching (TPS-RPM), and 4) the original AFDM. We compare the mesh quality measured by the min and mean values of radius ratio ($Q_{\text{mean}}, Q_{\text{min}}$), the accuracy of registration measured by the mean and standard deviation of voxel distances between the target and deformed shapes ($\text{Voxel Distance}$), and the running time ($\text{Time}$).

<table>
<thead>
<tr>
<th></th>
<th>High Resolution Cardiac</th>
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<tr>
<td></td>
<td>$Q_{\text{min}}$</td>
<td>$Q_{\text{mean}}$</td>
<td>$\text{Voxel Distance}$</td>
<td>$\text{Time}$</td>
</tr>
<tr>
<td>CPD [66]</td>
<td>0.00</td>
<td>0.63</td>
<td>2.21 ± 1.99</td>
<td>10′23″</td>
</tr>
<tr>
<td>GMM [47]</td>
<td>0.00</td>
<td>0.68</td>
<td>2.73 ± 2.87</td>
<td>21′5″</td>
</tr>
<tr>
<td>TPS-RPM [20]</td>
<td>0.00</td>
<td>0.52</td>
<td>1.66 ± 1.26</td>
<td>30′12″</td>
</tr>
<tr>
<td>AFMD [83]</td>
<td>0.00</td>
<td>0.73</td>
<td>2.03 ± 0.72</td>
<td>8′37″</td>
</tr>
<tr>
<td>Ours</td>
<td>0.02</td>
<td>0.97</td>
<td>0.47 ± 0.13</td>
<td>7′56″</td>
</tr>
</tbody>
</table>

registration measured by the mean and standard deviation of voxel distances between the target and deformed shapes, and the running time. Usually keeping shape details reduces the mesh quality. However, our proposed method ensures both fine shape details and high mesh qualities, because of the mesh quality term. Furthermore, its computational cost is also comparable to the AFDM, even with this extra energy term. The reason is that shape quality constraint aims to produce evenly distributed vertices, which also speeds up the convergence of the AFDM.

Fig. 5.8 compares the results using different smoothing weights, i.e., cotangent or uniform weights. Using cotangent weights can preserve more details than the uniform weights since the vertices are moved toward the tangential direction.

Fig. 5.9 visualizes the shape variation along the first and second principal directions. Our framework is robust and general enough to handle such complex shapes. The first mode represents the changing of the volume magnitude, and the second mode captures the changing of shape details such as the papillary muscles and the trabeculae. Again, these findings are in accordance with clinical knowledge, which can be used to categorize the cardiac properties.
5.4 Conclusion

In this chapter, we have presented a framework using high resolution CT data to reconstruct 4D motion of the left ventricle for a full cardiac cycle. The framework has been applied to a sequence of cardiac CT volumes. High resolution details, such as papillary muscles and ventricular trabeculae, were successfully captured in this framework. In the future, we plan to use this framework to capture more fine structures of the heart, e.g., the valves and wall surfaces of all the four chambers.
Figure 5.9: Principal modes of variation for an SSM of the cardiac shape. For each row, we show the variation of the largest eigenmode between $-3\sigma$ to $3\sigma$ (from left to right). The first mode (the first row) represents the changing of the volume size. The second mode (the second row) is the changing of shape details such as papillary muscles. For better visualization, please refer to the video sequence in the supplementary materials.
Chapter 6

The Impact of Trabeculae Structures On Patient-Specific Cardiac Blood Flow Simulations

Trabeculae and papillary muscles may have an important role in intraventricular hemodynamics. While recent studies have shown possible interactions between blood flow and trabeculae motion, there has been, until now, no clear evidence that these interactions are significant enough to alter the computed flow fields. In this chapter, we use state-of-the-art techniques to reconstruct the full 4D endocardial surface motion from high-resolution CT imagery of four different patients. We then simplify these models to replicate the smoothed-heart models often used in cardiac blood flow simulations. We use these surfaces as boundary conditions in a Navier-Stokes simulator, and then measure and visualize the average residency times of blood within each heart. Our results clearly demonstrate that the incorporation of these detailed trabeculae structures greatly affect the flow in clinically-interesting ways.

6.1 Introduction

Simulating patient-specific blood flow has recently become an area of great interest to doctors. In patients who experience a heart attack, or in those who suffer from other various cardiovascular diseases, the motion of the heart walls and valves can become disturbed, leading to an abnormal blood flow pattern. If the blood is not being fully circulated within the heart and becomes stagnant, these patients are at high risk of thrombus, leading to stroke. Thus, it is very important for doctors to be able to visualize and understand a patient’s cardiac blood flow. While it is possible to acquire flow data from MRI or Doppler ultrasound imaging, the relatively low quality and resolution of this data severely limits its usefulness to doctors. In particular, these
imaging techniques lose nearly all detail in the apex regions of the left ventricle, where there is heavy trabeculation. Therefore, to visualize and understand the blood flow within the entire left ventricle requires the use of cardiac blood flow simulations.

Early work in ventricular simulations used highly simplified models of the heart walls and structure. Jones et al. [49] were the first to use MRI data to perform patient-specific cardiac blood flow simulations, applying fluid velocity boundary conditions at the valves. In 2010, Mihalef et al. [62] used CT data to simulate left ventricular blood flow, and were able to compare the computed flow fields in healthy and diseased hearts.

More recently, Kulp et al. [52, 53, 60] used a more sophisticated method of extracting the heart and its motion from CT in order to capture the geometry of the trabeculae, and used fluid simulations to determine whether the motion and structure of the trabeculae interacts with the blood flow. While this work did show evidence of such interactions, they were not able to show that these interactions are significant enough to justify the much higher cost of incorporating the trabeculae in blood flow simulations, rather than using more traditional smoothed-heart models. Thus, the purpose of this paper is to fill this gap, by comparing the computed flow fields of simplified and complex versions of four patient-specific heart models, and visually and quantitatively show that these trabeculae structures are critical in developing the best, clinically-useful results.

6.2 Data Acquisition

CT images were acquired from four patients. Patient 1’s heart is healthy and functions normally. Patient 2 is 49 year old female with nonobstructive coronary artery disease. Patient 3 is a 62 year old patient with obstructive coronary artery disease. Finally, Patient 4 suffers from dysynchronous cardiac function. For each patient, we construct both “smoothed” (less trabeculae) and “complex” (more trabeculae) 4D models of their heart, described below.
Figure 6.1: 3D meshes generated from high-resolution CT imagery. (a)-(d) Patient 1 (Normal); (e)-(h) Patient 2 (Nonobstructive CAD); (i)-(l) Patient 3 (Obstructive CAD); (m)-(p) Patient 4 (Dysynchrony). Column 1: Smoothed version outside left ventricle; Column 2: Smoothed version inside left ventricle pointing at apex; Column 3: Complex version outside left ventricle; Column 4: Complex version inside left ventricle pointing at apex. Note that in all of the complex versions of each patients’ heart, we can clearly see highly detailed trabeculae structures.
6.2.1 Mesh Generation

To compare the impact the trabeculae structures, we also reconstructed the smoothed models with trabeculae. The registration between smoothed models directly would not be reliable because of the limited anatomical information. We first build the correspondence between the smoothed models and complex models. Then using the registration of the complex models between frames, the smoothed models also captures the motion of the LV endocardial surface.

The aortic and mitral valves are thin and move fast, and so the CT data is not currently able to adequately capture these details. We add 3D models of the valves created from ultrasound data to each mesh in the sequence, and open and close the valves at the appropriate time steps.

6.3 Fluid Simulation

In Computational Fluid Dynamics, we seek to numerically solve the Navier-Stokes equations when computing the flow of compressible or incompressible fluids. In this problem, we are interested in the incompressible equations:

\[
\rho \left( \frac{\partial u}{\partial t} + u \cdot \nabla u \right) = -\nabla P + \mu \nabla^2 u, \quad (6.1)
\]

\[
\nabla \cdot u = 0, \quad (6.2)
\]

where \( u \) is the velocity vector field, \( P \) is pressure, \( \rho \) is the fluid density, and \( \mu \) is the coefficient of viscosity. The first equation balances the forces within the fluid and enforces conservation of momentum, while the second maintains conservation of mass.

Foster and Metaxas [31] were the first to develop a fast method of solving the NS equations for graphics applications by applying a staggered grid across the domain and explicitly solving for velocity at the cell faces. They then used successive over-relaxation to solve for pressure and correct the velocities to maintain incompressibility.

Our fluid-solid interaction system uses a “boundary immersed in a Cartesian grid formulation”, allowing for an simple treatment of complex moving geometries embedded
in a closed computational domain. In 2005, Yokoi et al. [100] applied the formulation of Sussman [92] to both graphics and medical simulations. More recently, Zelicourt et al. [26] implemented a similar system that can efficiently deal with complex geometric data, such as a system of blood vessels.

The heart models used here are embedded in a computational mesh of $10^3$ cells on which the full NS equations are solved using FDM. The blood is modeled as a Newtonian fluid, with viscosity of 4mPa·s and density of 1050kg/m$^3$, which are physiologically accepted values for normal human blood [62]. The heart model is given to the solver as a set of meshes with point correspondences, which allows for easy interpolation and also obtaining the velocity of the heart mesh at every point in time. Our system represents the 3D meshes as a Marker Level Set (MLS) [63], where markers are placed on the boundary and are used to correct the level set at every time step. Since markers are only placed on the surface, MLS has been proven to be more efficient and more accurate for complex boundaries. The MLS and its velocity are rasterized onto the Eulerian grid and are used to impose the appropriate boundary conditions in the fluid solver. A simulation of a single cardiac cycle takes about 5 days to complete on a machine with an Intel i7 processor and 16GB of RAM.

6.3.1 Visualizations

![Visualization of streamlines within the healthy heart. (a) Blood flow near apex during diastole. (b) Blood flow during systole at the apex, against the trabeculae.](image)
The streamline visualizations provide detailed information on the trabeculae-blood interaction. Figure 6.2(b), taken during diastole, demonstrates how the complex surface causes the flow to fill the empty spaces between the trabeculae. Then, in Figure 6.2(c), during systole, we see another example of how the blood is expelled out of the spaces between the trabeculae, rather than simply flowing directly towards the aortic valve as older methods with simpler meshes have suggested.

### 6.3.2 Blood Residence Time

In addition to the blood flow velocities, we wish to visualize the residence time of blood within the heart. By doing so, we can quantitatively determine regions of the heart that are at greater risk of thrombus, as slower flows are known to be a significant factor predisposing to thrombus formation.

At the initial time step, ten thousand particles are generated randomly within the heart. At the beginning of each time step, new particles are generated at the valves, allowing fresh blood particles to enter the heart during diastole. Each new particle has an initial age of zero, and this age is incremented at every time step.

At each consecutive time step, we determine a particle’s velocity by interpolation, given the fluid velocities at the center of each cell. Each particle’s new position is calculated using Euler time integration. Then, any particle in a cell exterior to the heart is removed from the system, and the average particle residence time within each cell can then be easily determined. We run this for four cardiac cycles and create volumetric visualizations, as seen in Figure 6.3. Here, blue represent regions in which average residency is less than 1 cardiac cycle, green-yellow represents 1-3 cardiac cycles, and red represents 3-4 cycles.

### 6.4 Results and Discussion

Visualizations of average residency time for each patient after four cardiac cycles can be seen in Figure 6.3. Figures 6.3(a-b) are of Patient 1, smoothed and complex respectively, (c-d) are of Patient 2, (e-f) are of Patient 3, and (g-h) are of Patient 4. Each image was
Figure 6.3: Average residency time visualizations for four blood flow simulations after four cardiac cycles. Blue regions represent areas of fresh blood, red regions represent blood that has been in the left ventricle for about four cycles. (a-b) Patient 1 [Normal] - Smoothed and Complex meshes, respectively; (c-d) Patient 2 [Nonobstructive CAD] - Smoothed/Complex; (e-f) Patient 3 [Obstructive CAD] - Smoothed/Complex; (g-h) Patient 4 [Dyssynchrony] - Smoothed/Complex. We note that in Patients 1 and 2, average residency time appears higher in the smoothed version, but for Patients 3 and 4, residency time is higher in the complex version.
taken during diastole, and both images within a pair were taken from the same angle. We immediately notice large differences between the smooth and complex experiments for all four patients. In Patients 1 and 2, in particular the latter, we see that blood in the complex models have a significantly lower residency times than in the smoothed models. This suggests relatively healthy trabeculae motion and fast blood turnover rates. While Patient 2 does suffer from non-obstructive CAD, hearts with non-obstructive CAD can still function normally when at rest. Therefore, these results are consistent with our expectations.

We then see the opposite effect in Patients 3 and 4. In both cases, the average residency time is much higher in the complex version, suggesting poorly-functioning trabeculae that is severely dampening the intraventricular flow. Since Patient 3 has obstructive CAD, her cardiac function is impaired, even at rest. Even more importantly, we note that in the smoothed cases, Patient 2 and Patient 3 appear to have very similar average residency times. However, in the complex cases, Patient 3 is clearly much worse. If just the simplified models are used in cardiac blood flow simulations, these clinically significant problems would be completely invisible to the physician.

Quantitative analysis corroborates our visual inspection of the particle age fields. In Table 1, we see the median and standard deviation of the average particle ages at the end of four cardiac cycles. We note that in both Patients 1 and 2, there is a significant drop in median residency time as we move from smoothed to complex models. In Patients 3 and 4, we see that the opposite: median residency time sharply increases in the complex case. This, also, suggests that healthy trabeculae helps to circulate residual blood within the ventricle so as to speed up the turnover rate, while poorly-functioning trabeculae of the older/obstructive CAD (Patient 3) or dyssynchronous (Patient 4) heart by acting as a cushion or trap, slowing the blood turnover rate.
<table>
<thead>
<tr>
<th></th>
<th>Median Age (Cycles)</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1 (Smoothed)</td>
<td>1.26</td>
<td>0.93</td>
</tr>
<tr>
<td>Patient 1 (Complex)</td>
<td>1.09</td>
<td>0.94</td>
</tr>
<tr>
<td>Patient 2 (Smoothed)</td>
<td>1.38</td>
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</tr>
<tr>
<td>Patient 2 (Complex)</td>
<td>0.71</td>
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</tr>
<tr>
<td>Patient 3 (Smoothed)</td>
<td>0.87</td>
<td>0.76</td>
</tr>
<tr>
<td>Patient 3 (Complex)</td>
<td>1.20</td>
<td>1.03</td>
</tr>
<tr>
<td>Patient 4 (Smoothed)</td>
<td>1.72</td>
<td>0.79</td>
</tr>
<tr>
<td>Patient 4 (Complex)</td>
<td>2.50</td>
<td>0.97</td>
</tr>
</tbody>
</table>

Table 6.1: Median and Standard Deviation of particle ages after four cardiac cycles.

6.5 Conclusion

In this chapter, we have described our method of determining the impact trabeculae geometry, or lack thereof, can have on the computed flow fields in a cardiac blood flow simulation. For example, in the cases of Patients 2 and 3, while they appear to maintain similar average residency times in simplified heart models, we have seen that by adding the trabeculae to the models, these residency times can significantly change. It is clear that these structures provide an important role in intraventricular hemodynamics, and thus their inclusion in future simulations is critical for the most clinically useful results.
Chapter 7

Conclusions

This dissertation addressed the challenging problem of analyzing clinically useful parameters to describe the endocardial surface of the left ventricle. We proposed a system to topologically accurately segment the papillary muscles and the trabecula, registration of neighboring frames to establish the one-to-one correspondence, and provided some analysis about both the 3D morphological analysis and the interaction between the motion of endocardial surface and blood. Our results have shown the quantification, distribution and impact of the left ventricle endocardial surface.

This work, for the first time, offered understanding about the detailed left ventricle endocardial surface, and provided efficient and effective geometric tools for further scientific discoveries about the functions of the left ventricle, their relations to heart diseases or strokes. Regional features, which were traditionally untouched, have been demonstrated to be able to distinguish diseased hearts from normal.

Beyond the application of medical imaging, our methods are general and can be used in other applications. The algorithm of segmenting the segmenting the trabeculae can be applied to other topologically complicated segmentation problems with complex topological structures. This basic idea of the algorithm, which is to explicitly detect, evaluate and modify the topology property in an image, is a powerful method to study the topology in nature.

Further works go to three directions. First, it is desired to gather a larger data set of both healthy and diseased hearts to study the relationship between some specific diseases and the proposed geometrical and topological features. Our hypothesis is that by performing the quantitative assessment of the regional fine scale of the left ventricle we will be able to discover and quantify previous unknown differences among normal
and diseased hearts.

Second, the proposed segmentation method with topological constraint is general and can be applied to other applications, such as left atrial appendage (LAA), which also has the characteristic of topological handles. Some other applications, such as vessel and lung airway, have the properties of no topological cycles. The proposed algorithms can be modified accordingly to handle specific topological prior knowledge.

Third, during a cardiac systole cycle, some tissue of the left ventricle may have touched each. In those cases, as presented in the CT images, the topology of the cardiac model is changed during the deformation. How to do deformable registration with topological constraint is an interesting yet challenging problem. This is one of our future directions.
References


