Segmentation of Rat Cardiac Ultrasound Images with Large Dropout Regions

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Abstract

Short-axis rat cardiac ultrasound images contain especially large regions of dropout which make it very difficult to segment the endocardium. Previous strategies, such as using shape priors, are not effective with such large dropout regions. This paper proposes a dropout modeling strategy, which can bridge large dropout regions and segment the endocardium when used along with shape priors. The segmentation is formulated as an active contour in a Maximum-A-Posteriori (M.A.P.) framework with explicit priors for the dropout function and shape. Further, the active contour is evolved by a strategy called tunneling descent. Tunneling descent is a deterministic evolution strategy which can escape from local minima. The combination of dropout modeling and tunneling descent gives active contours which can successfully segment rat cardiac ultrasound images. Experimental results comparing the performance of the new algorithm with manual segmentation and classical active contours are provided.

1. Introduction

Rats are commonly used to study cardiac function and ischemic remodeling. Rat hearts are usually imaged with ultrasound or ultra-high-field MR; and (semi-)automated segmentation of such rodent cardiac images is highly desirable.

In ultrasound images, rat hearts have a very different appearance when compared to human hearts: They are smaller and their effective resolution is lower. Further, the myocardium in rat heart images is not uniformly bright. Instead, it appears as a dark band between two bright rings, which are the endocardium and epicardium. The contrast in the endo- and epicardial rings is variable and can occasionally be quite low. Finally, large signal dropout regions are often present in rat heart images, and they are manifest as big dark holes in the endocardium (see figure 1 for an example). This makes segmentation in ultrasound rat heart images quite challenging.

Two problems are particularly vexing. First, the dropout regions in these images are so large that the usual strategy of bridging the holes using active contours with shape priors does not work. Active contours continue to leak out of the holes. Second, to get good segmentation in rat cardiac images, active contours have to be initialized close to the true boundary. Because a typical rat experiment can produce hundreds of images, initialization close to the boundary is manually taxing. Successful segmentation with distant initialization is highly desirable.

In this paper, we report a dual strategy for overcoming these problems. First, we observe that dropout in cardiac images tends to occur in predictable regions of the images and that dropout reduces - rather than eliminates - the signal amplitude. By learning and using an appropriate prior for the dropout, we show that it is possible to detect and bridge large holes [13]. Second, we use a strategy called tunneling descent for curve evolution. Tunneling descent, which is an alternative to gradient descent, can evolve the active contour into, and subsequently out of, spurious local minima [17]. An active contour evolved with tunneling descent can be initialized far away from the boundary for successful segmentation.

Using this strategy we segment the endocardium with active contours. The energy for our active contour is obtained from a Maximum-A-Posteriori (M.A.P.) formulation. Preliminary experiments are provided demonstrating the performance of the algorithm. We report segmentation of 2 sequences of rat ultrasound cardiac images (82 images in total). All segmentations are achieved without tweaking numerical parameters.

This paper is organized as follows: Section 2 has a brief
2. Literature Review

Many approaches to ultrasound segmentation can be viewed as attempts to reduce the amount of speckle or to use features of the image that are relatively independent of speckle. In the first category falls research in speckle suppression [2, 3]. In the second category lies the work on using local phase information [5]. Some researchers also integrate spectral properties to improve the results [1].

Speckle has a strong effect on active contour energy functions – it introduces many spurious local minima in their energy functions. To escape from spurious local minima, multi-resolution strategies have been proposed [10]. Also, extra forces, such as balloon forces [8], are often introduced to control the evolution. One problem with these approaches is that the amount smoothing and the proper balloon force has to be manually chosen to get the correct segmentation, and the proper amount often varies from image to image.

Data dropout is a serious problem in ultrasound segmentation because active contours tend to leak through dropout holes. The usual technique is to introduce shape priors in active contours to bridge the holes, e.g. [7, 12, 14, 15].

Ultrasound dropout has been modeled following ideas for bias field estimation for MR images by Wells [18] and Brady [9]. Xiao et. al [19] model ultrasound inhomogeneity in breast segmentation.

3. MAP Formulation

Our goal is to segment the endocardium by an active contour in a maximum-a-posteriori (MAP) framework. We assume that the endocardium is a closed curve and model the gray levels in the neighborhood of the endocardium as random variables whose parameters depend on the location of the endocardium. This gives the likelihood of observing the image as a function of the curve. Combining this with priors for signal dropout and shape of the endocardium, we get the posterior likelihood of the endocardium and dropout for the given image. Finding the curve that maximizes this likelihood gives the MAP estimate of the endocardium.

There are several decisions to be made in this model:

[1] What is the appropriate model for the gray level distributions? B-mode ultrasound images contain speckle, which is a non-Gaussian stochastic process. Empirical modeling of cardiac images [16] suggests several alternative probability models as equally suitable. We choose the log-normal probability model, because it gives a very natural way of modeling dropout by a multiplicative function. According to the log-normal model, the density of observing a value \( g \) is proportional to \( \exp\{-\log g - \mu)^2/\sigma^2\} \), where \( \mu \) is the mean of the density and \( \sigma \) the variance. We model the gray levels in the ultrasound images as independent random variables with a spatially varying mean \( \mu \). Higher values of the mean imply brighter regions and lower values imply darker regions.

[2] What neighborhood of the endocardium should be modeled? Because the endocardium appears as a bright ring whose thickness varies across images, we choose to model the bright ring and the dark regions on either side of it (the dark region inside the bright ring is the blood pool, while the dark region outside the bright ring is the myocardium).

The model for the ring and the dark regions is as follows:

The endocardium is taken to be a curve which is the zero level set of a signed distance function \( \Phi \). The sign of the distance function is chosen to be negative in the blood pool and positive in the myocardium. We take the bright ring around the endocardium to be a region of uniform width defined as the set of all points \( u \) in the plane for which \( \Phi(u) \geq 0 \) and \( \Phi(u) \leq \Delta \) for some width \( \Delta > 0 \). Define a piecewise constant function \( I_0 \) to take the value 1 outside the ring and the value \( \exp \rho > 1 \) inside the ring (the reason for using the \( \exp \) will be clear shortly). Then, \( I_0 \) depends on the endocardium and, up to a multiplicative factor \( I_0 \) can be the spatially varying mean to model the bright ring.

Multiplying \( I_0 \) by a smooth function \( f \) gives a function which models smooth deviations from the piecewise constant model. In particular, low values of \( f \) model dropout. We call \( f \) the dropout function.

As mentioned above, we assume that the gray level \( g \) of any pixel is a log-normally distributed random variable so that the density of observing the gray level is

\[
p(g) \propto \exp\{-\log g - \log(I_0 \times f)\} / \sigma^2\}
\]

\[
= \exp\{-\log g - \log I_0 - \log f\} / \sigma^2\}
\]

Note that \( \log I_0 \) is equal to \( \log \exp \rho = \rho \) when \( g \) is a pixel inside the bright ring (this is reason for using \( \exp \rho \)), and is equal to \( \log 1 = 0 \) when \( g \) is a pixel outside the bright ring. Thus \( p(g) \) is

\[
p(g) = \begin{cases} p_1(g) & \text{for } g \text{ inside ring,} \\ p_2(g) & \text{for } g \text{ outside ring,} \end{cases}
\]

where \( p_1(g) \propto \exp\{-\log g - \log f - \rho\} / \sigma^2\} \) and \( p_2(g) \propto \exp\{-\log g - \log f\} / \sigma^2\}. \) Assuming that the pixels are independent gives the complete likelihood of the image.

The calculation is given in detail below.
Dropout and Shape Priors

Because dropout tends to occur in predictable regions of the image, we create and use priors on log \( f \) in the image space. Finally, to span the dropout regions correctly we use shape priors on the level set function \( \Phi \). The shape priors are defined in a separate template space which is mapped onto image by a similarity transform \( T \) whose scaling, rotation, and translation are denoted as \( \{s, \theta, t_x, t_y\} \).

The relationship between these variables \( (\Phi, f, \rho, \Delta, T) \) is illustrated in figure 2.

3.1. MAP estimation

We segment the endocardium by maximizing the log posterior probability of \( \Phi, T, f, \rho, \Delta \) given the image \( I \):

\[
\arg \max_{\Phi, T, f, \rho, \Delta} \log p(\Phi, T, f, \rho, \Delta | I) \tag{1}
\]

\[
= \arg \max_{\Phi, T, f, \rho, \Delta} \log p(I | \Phi, T, f, \rho, \Delta) + \log p(\Phi, T) + \log p(f) + \log p(\rho) + \log p(\Delta),
\]

where \( p(I | \Phi, T, f, \rho, \Delta) \) is the conditional density and the other terms are the priors. Note that \( p(I | \Phi, T, f, \rho, \Delta) = p(I | \Phi, f, \rho, \Delta) \) because the image is completely specified by the curve (i.e. \( \Phi \), \( f \) and \( \Delta \)).

3.2. The \( \log p(I | \Phi, f, \rho, \Delta) \) term

Assuming that the pixels are log-normal independent, \( \log p(I | \Phi, f, \rho, \Delta) \) can be easily computed as

\[
\log p(I | \Phi, f, \rho, \Delta) \propto - \int (\log I - \log f - \rho)^2 (H(\Phi) - H(\Phi - \Delta))
- \int (\log I - \log f)^2 (1 - H(\Phi) + H(\Phi - \Delta)), \tag{2}
\]

where \( H \) is the heaviside function, \( H(0) = 1 \), if \( v \geq 0 \) else \( H(0) = 0 \). This equation shows that in the ring (the region where \( H(\Phi) - H(\Phi - \Delta) \) is not zero) the mean of the log-normal is larger by \( \rho \).

3.3. The prior \( \log p(\Phi, T) \)

Writing \( \log p(\Phi, T) = \log p(\Phi | T) + \log p(T) \), we take \( \log p(\Phi | T) \) to be the shape prior. We use a very simple form for this prior. We simply calculate the average level set function \( \bar{\Phi} = \frac{1}{N} \sum \phi_i \) from the aligned training level set functions \( \{\phi_i\}_{i=1..N} \) and make a compromise between the closeness to the average level set function and smoothness. Thus,

\[
\log p(\Phi | T) \propto -\lambda_1 \int (\Phi - \bar{\Phi})^2 - \lambda_2 \int \delta(\Phi) \|
\nabla \Phi \|, \tag{3}
\]

where \( \Phi \) is the evolving level set; and

\[
\bar{\Phi}'(u) = s \bar{\Phi}(T^{-1} \circ u), \tag{4}
\]

where \( s \) is the scale of the similarity transformation \( T \). This is borrowed from previous work by other authors on shape priors [7, 14].

We further assume that the prior \( p(T) \) is normal and learn its parameters from the training set.

3.4. The prior \( \log p(f) \)

We use Principal Component Analysis to create this dropout function prior. Dropout functions are defined on the whole image domain. By subtracting \( \rho \) from ring-shaped endocardium regions and low-pass filtering the processed training log images, we obtain estimates of the log dropout function \( \log f_i \) in each training image. Then, we write the log dropout function using a linear representation:

\[
\log f = \bar{d} + \sum_j \alpha_j \Psi_j, \tag{5}
\]

where \( \bar{d} = \frac{1}{N} \sum \log f_i \), and \( \{\Psi_j\}_{j=1..M} \) are the principal components of the distribution with \( M < N \) as the dimension of the subspace spanned by the training set. The vector \( \alpha = \{\alpha_1, \ldots, \alpha_j, \ldots, \alpha_M\} \) in (5) parameterizes dropout functions. The dropout prior is expressed as

\[
\log p(f) = \log p(\alpha) \propto -\frac{1}{2} \alpha^T \Sigma^{-1} \alpha, \tag{6}
\]

where the diagonal matrix \( \Sigma_{\alpha} \) is the covariance matrix for \( \alpha \).

3.5. Other priors

We assume that the contrast \( \rho \) follows a normal distribution which we learn from the training set. We assume that \( \Delta \) follows a uniform distribution from 5 pixels to 20 pixels.

3.6. Level set formulation of the model

Maximizing the log posterior probability in (1) is equivalent to minimizing its negative. We define the energy
where $\bar{\rho}$ and $\sigma^2$ are the learned mean and variance of the contrast, and $\lambda_1, \lambda_2, \lambda_3$ are weighting coefficients set empirically and fixed for all the images we segment.

### 3.7. Gradient Descent

The classic strategy for minimizing the energy in equation (7) is gradient descent, but even a few numerical experiments quickly show that gradient descent works well only when the initialization of $\Phi$ is such that its zero level set is close to the true boundary. When initialized far from the boundary, gradient descent gets trapped by the spurious local minima giving inappropriate solutions. This failure can be seen in figure 6a of section 5.3.

### 4. Tunneling Descent

To overcome entrapment in local minima, we use an alternate evolution strategy called Tunneling Descent. Tunneling descent is based on the idea that when an active contour is initialized within the region whose boundary is sought, it usually finds a local minima within the region and stops before reaching the boundary. This suggests that if the contour is forced to grow while retaining its optimal character, it may be forced out of the local minima and grow towards the true boundary. In tunneling descent, this is achieved by replacing gradient descent with a sequence of constrained minimizations which force the active contour to grow at a non-zero speed. The growth is in a direction that decreases energy when decrease is possible. At a local minimum, the growth is in a direction that causes the least increase in energy. Thus, when the contour is initialized in the blood pool, it continuously expands while descending into and climbing out of local minima. When the contour has expanded sufficiently to cross the endocardium, a stopping rule halts the process. The lowest energy curve in the entire evolution is taken to be the segmentation.

Tunneling descent was first proposed in [17] where it was used to segment human cardiac ultrasound images with active contours. Tunneling descent demonstrated a better performance over gradient descent with human cardiac ultrasound images.

### 4.1. Sequential Minimization

Mathematically speaking, tunneling descent begins with the initialization $\{\Phi_0, T_0, \alpha_0, \rho_0, \Delta_0\}$ and generates from it the sequence $\{\Phi_n, T_n, \alpha_n, \rho_n, \Delta_n\}$ for $n = 1, 2, \ldots$ according to

\[
\Phi_n = \arg \min_{\Phi \in M(\Phi_{n-1})} E(\Phi, T_{n-1}, \alpha_{n-1}, \rho_{n-1}, \Delta_{n-1})
\]

\[
\{T_n, \alpha_n, \rho_n, \Delta_n\} = \arg \min_{T, \alpha, \rho, \Delta} E(\Phi_n, T, \alpha, \rho, \Delta).
\]

Here $M(\Phi_{n-1})$ is the set of all level set functions whose zero level sets have a greater area than the zero level set of $\Phi_{n-1}$ and which are within a small neighborhood of $\Phi_{n-1}$. That is, the set $M(\Phi_{n-1})$ is defined as containing all level set functions $\Theta$ that satisfy:

\[
\int (1 - H(\Theta)) > \int (1 - H(\Phi_n - \Delta_1)), \Delta_1 > 0.
\]

\[
\int (\Theta - \Phi_n)^2 \leq \Delta_2, \Delta_2 > 0,
\]

where $\Delta_1$ and $\Delta_2$ are fixed thresholds. If $\Theta$ and $\Phi_n$ have zero level sets $C$ and $B$ (Figure 3), then the first constraint (9) ensures that the area inside contour $C$ is greater than the area inside $B$. Constraint (10) ensures that $\Theta$ is in a neighborhood of $\Phi_n$. When $\Delta_2$ is small enough, we may replace constraint (9) by its linearized version

\[
\int \delta(\Phi_n - \Delta_1)(\Theta - (\Phi_n - \Delta_1)) \leq 0.
\]

Thus the sequential minimization in equation (8) will produce a sequence of curves with increasing size that minimize the energy. That is, whenever it is possible to decrease the energy while growing, tunneling descent will do so. Further, if the energy can only be increased, then tunneling descent will find the level set function that gives the least increase. This is exactly the strategy we want to escape from spurious local minima.

The energy sequence produced by tunneling descent $E(\Phi_n, T_n, \alpha_n, \rho_n, \Delta_n)$ will have subsequences where the energy is decreasing and subsequences where the energy is increasing. Define

\[
\Gamma_n = \Phi_k, \text{ where } k = \arg \min_{i=1, \ldots, n} E(\Phi_i, T_i, \alpha_i, \rho_i, \Delta_i).
\]

That is, $\Gamma_n$ is the level set function with the least energy till the $n$th iteration. Hence, the zero level set of $\Gamma_n$ is the best estimate of the boundary at the $n$th iteration.
4.2. Stopping Rule

The stopping rule is a logical OR of two criteria. The first criteria arises from the zero level set, and the second criteria arises from the likelihood ratio test. Both criteria are based on the level set function as follows:

1. **Zero Level Set Criteria:**
   - Let $\Phi_n$ denote the zero level set of $\Phi_n$.
   - Let $\Gamma_n$ denote the level set function $\Gamma_n$.
   - Set $n$ to 0.

2. **Likelihood Ratio Test Criteria:**
   - For some positive threshold $\tau$, the test is applied.

The stopping rule is then given by:

$$
\Phi_n \cap \Omega_n^c = \Phi_n \cap \Omega_n^c \cup \Omega_n^c \cap \Omega_{n-1}^c
$$

for some positive threshold $\tau > 0$. This can be written in terms of the level set functions as:

$$
\int_{\Omega_n^c \cap \Omega_{n-1}^c} \log \frac{p_1(g)}{p_2(g)} dA > \tau.
$$

In all our experiments, $\tau$ was set to 80. If the area test or the likelihood ratio test is successful at $n$, then the region between $C_n$ and $B_n$ contains tissue, and the sequence is terminated and $C_n$ declared to be the boundary. Else the sequence continues to $n+1$ and the test is applied again.

To sum up, tunneling descent works as follows:

1. Initialize a level set function $\Phi_0$ with its zero level set, $C_0$, in the blood region. Set $n = 0$.
2. Set $n = n + 1$. Generate $\Phi_n$ using equation (8).
3. Apply the stopping rules: If the rule passes, terminate with the level function $\Gamma_n$ with its zero level set $B_n$ as the boundary. Else go to 2.

4.3. Comments on numerical techniques

It is easy to show that $M( \Phi_n )$ is a convex set for all $n$. Thus the minimization in equation (8) is a constrained optimization problem over a convex set. We use the gradient projection method [4] for the numerical minimization. The gradient projection step itself is done by using Dykstra’s Algorithm [11]. Details are borrowed from [17].

Finally, we approximate the heaviside function and delta function by $H_\varepsilon(z) = \frac{1}{2}[1 + \frac{1}{\pi} \arctan(\frac{z}{\varepsilon})]$ and $\delta_\varepsilon(z) = \frac{\varepsilon}{\pi(z^2 + \varepsilon^2)}$. This too is standard [6].

5. Experiments

We now turn to reporting preliminary experimental results. Two short-axis rat cardiac image sequences were obtained. There were a total of 82 images in both sequences. Of these, we selected 20 images as the training set.

The training set was used to obtain the priors in the following way: The endocardium was manually segmented in the training set. The manual segmentations were aligned in a global template coordinate system. Then the average level set and variance of shapes were computed by PCA. This created the shape prior.

Portions of the endocardium that did not have dropout were manually identified and the prior for the contrast $\rho$ between the blood pool and the endocardial ring constructed. Then, focusing on the remaining portion of the endocardial ring (which contained the dropout), we selected 15 pixels as the training thickness of rings and subtracted the contrast from those regions. The resulting images were low-pass filtered and analyzed with PCA to find the average dropout function and the set of basis functions for the dropout function prior.

5.1. Segmentation

With the prior in hand we used the MAP active contour with tunneling descent for segmentation. Three sets of experiments were carried out. The goal of the first was to demonstrate the need for using both shape and dropout priors, the goal of the second was to show the necessity of escaping from local minima, and the goal of the third was to evaluate the accuracy of segmentations. In all of the following experiments, we set $\lambda_1 = 0.04$, $\lambda_2 = 0.0031$, and $\lambda_3 = 0.04$.

5.2. The advantage of modeling dropout

We implemented 3 segmentation algorithms: 1) The standard Chan-Vese algorithm [6]; 2) Chan-Vese with a shape prior; and 3) Our algorithm. The original Chan-Vese model assumes a normal distribution with piecewise constant means and thus the first two of these algorithms provide segmentations with using a normal distribution for log gray levels with and without shape priors.
For all 3 models, we used tunneling descent to evolve the level set functions. All models were initialized from the same curve.

Some examples of the segmentations by the algorithms are shown in figure 4 and figure 5. White circles in the figures are initial contours, the green curves are the results of the algorithms, and the red curves are manual segmentations provided as a guide for evaluating the accuracy of segmentation. As expected, the original Chan-Vese algorithm (the (a) parts of the figures) leaks out in the dropout regions. Chan-Vese with a shape prior does not leak in figure 4 when the dropout is not strong; but it does leak out of the gap in figure 5, showing that just adding a shape prior is not an entirely reliable way of dealing with severe signal dropout. Our algorithm does not leak out in either example (nor in any other images that we tried). It is also the closest segmentation to the manual segmentations.

For the quantitative comparison of the results from three algorithms, we found that the first two leak out in most of our images. The calculation of the indices in section 5.4 is not straightforward because of the leakage; but it is obvious that our algorithm using the dropout model should have better numbers since it leak out in none of our images.

5.3. Tunneling descent overcomes spurious local minima

Figure 6 compares the segmentation results using tunneling descent and gradient descent. As before, initial contours are the white round curves in blood, segmentation results are in green, while manual segmentations are in red. Figure 6a gives the segmentation results by using gradient descent. The active contours are trapped in local minima and have stopped before reaching the endocardium. Figure 6b shows the results of using tunneling descent. These segmentations are closer to manual segmentations. The figures in figure 6c plot the energy function sequences $E(\Phi_n, T_n, \alpha_n, \rho_n, \Delta_n)$ generated by tunneling descent for the segmentation in the first and second rows. Local minima in the energy sequence are marked by vertical lines, and the insert shows the details of the energy function near the local minima. These figures clearly show that the energy functions have a number of spurious local minima and that tunneling descent can escape from them and find the endocardium. We recorded the number of local minima that were overcome by tunneling descent for 62 images (all images other than the 20 training images). The average number of local minima per image was 1.58 with a standard deviation 1.79. This shows the need for a local minima escaping algorithm for evolving the active contour.

5.4. Accuracy

We compared our algorithm segmentations to manual segmentations for all of the 62 images that were not in the training set. Before presenting the comparison we present typical segmentations in figure 7. Algorithm segmentations are in green, manual segmentations in red.
For a quantitative evaluation of accuracy, we calculated the Symmetric Hausdorff Distances (SHD) between manual and algorithm segmentations for 62 images. Hausdorff distance $h(C_1, C_2)$ for closed curves $C_1, C_2$ is defined as

$$h(C_1, C_2) = \max_{u \in C_1} \min_{v \in C_2} \|u - v\|,$$

where $\| \|$ is the Euclidean distance, and the symmetric Hausdorff distance is $\text{SHD} = \frac{h(C_1, C_2) + h(C_2, C_1)}{2}$.

We also computed the percentage of correctly segmented pixels (PTP), percentage of false positives (PFP) and extent of non overlap (ENO). Let $\Omega_{C_1}$ and $\Omega_{C_2}$ represent the inside region of manual and our algorithm segmentations. We define

$$\text{PTP} = \frac{\text{Area}(\Omega_{C_1} \cap \Omega_{C_2})}{\text{Area}(\Omega_{C_2})},$$

$$\text{PFP} = \frac{\text{Area}(\Omega_{C_2}) - \text{Area}(\Omega_{C_1} \cap \Omega_{C_2})}{\text{Area}(\Omega_{C_1})},$$

and

$$\text{ENO} = 1 - \frac{\text{Area}(\Omega_{C_1} \cap \Omega_{C_2})}{(\text{Area}(\Omega_{C_1}) + \text{Area}(\Omega_{C_2})) / 2}.$$
a dropout and a shape prior, our algorithm prevents leakage from boundary “holes” even when the dropout is severe. The tunneling descent level set evolution strategy overcomes spurious local minima. Experiments show that the new algorithm reliably finds the endocardium without tweaking parameters.

This level set formulation can be easily extended to 3-D or 3-D + time problems.

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Figure 8. Cumulative Distribution of Non Overlap with Manual Segmentation