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Synthesis of Cervical Tissue Second Harmonic Generation Images Using Markov Random Field Modeling

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Abstract- This paper presents a statistical image modeling approach based on Markov random field to synthesize cervical tissue second harmonic generation (SHG) images. Binary images representing fiber and pore areas of the cervix tissue are first obtained from SHG images using an image processing pipeline consisting of noise removal, contrast enhancement and optimal thresholding. These binary images are modeled using a Markov random field whose parameters are estimated via the least squares method. The parameters are then used to synthesize fiber and pore areas of cervical tissue in the form of binary images. The effectiveness of the synthesis is demonstrated by reporting the classification outcome for two classes of cervical SHG images collected from mice at two different stages of normal pregnancy. The developed synthesis allows generation of realistic fiber and pore area binary images for cervical tissue studies.

Index Terms – Biomedical image synthesis, Markov random field modeling, Second Harmonic Generation imaging, statistical image modeling.

1. INTRODUCTION

During normal pregnancy, flexibility of the cervix - a rigid tissue at the mouth of the birth canal that helps to hold the fetus in the womb - increases throughout gestation and there is a gradual decline in stiffness of the cervix reaching its lowest point at the time of birth. These changes are primarily due to progressive changes in strength, shape and organization of extracellular matrix of collagen fibers, the main structural component of the cervix. The primary determinant of cervical rigidity is fibrillar collagen type I which can be captured via SHG imaging. This imaging modality is a new non-invasive laser-based imaging modality that permits capturing images of collagen fiber type I present in cervical tissue [1-2].

Mouse animal experiments are informative because of the similarity between mouse and human cervix. By investigating the changes in the structure of fibrillar collagen type I in mouse pregnancy, which lasts a short gestation of 19 days, via SHG imaging, a step is taken towards a non-invasive pregnancy diagnostic tool for human subjects.

Considering the difficulty associated with obtaining SHG cervical images, this paper provides a statistical modeling approach to synthesize fiber and pore areas seen in SHG images of cervical tissue under normal birth conditions. Synthesized images if close to real images can be used for medical training purposes or for carrying out cervical tissue studies. In this paper, the SHG images of collagen fibers are first modeled using Markov Random Field (MRF). The MRF parameters are then used to achieve image synthesis. The effectiveness of the synthesis is established by reporting the classification outcome based on three porosity features extracted from synthesized images.

The rest of the paper is organized as follows: Section 2 outlines the image processing pipeline that is used to extract porosity image features from the SHG images for normal birth studies. In section 3, the statistical image modeling of SHG images using MRF is provided followed by the synthesis technique for generating synthesized images. A classification experiment is reported in section 4 to demonstrate the effectiveness of the developed image synthesis. Finally, the conclusion is stated in section 5.

2. POROSITY FEATURES

Figure 1 shows two sample SHG images of a mouse cervix, one corresponding to the gestation day 12 and the other to the gestation day 18. As reported in [3-5], porosity features extracted from such SHG images are used for studying the pore changes from day 12 to day 18. These features reflect the characteristics of the pores and thus the morphological characteristics of collagen fiber. To extract porosity features, first a binary image representing pore areas is formed out of an SHG image. This is done by thresholding which is done either manually or automatically. The binary image is then used for the extraction of porosity features.

These features include number of pores, pore space, and pore area. The number of pores (*PN*) feature is computed by obtaining the 4-neighboring connected components of the areas more than 7 pixels in size:

$$PN = \#\ of\ pore\ area > 7 \qquad (1)$$

The pore spacing (*PS*) feature reflects the average distance between pores. A region-of-interest (ROI) is considered and the number of pores in that area is calculated. The pore spacing feature is then computed as follows:

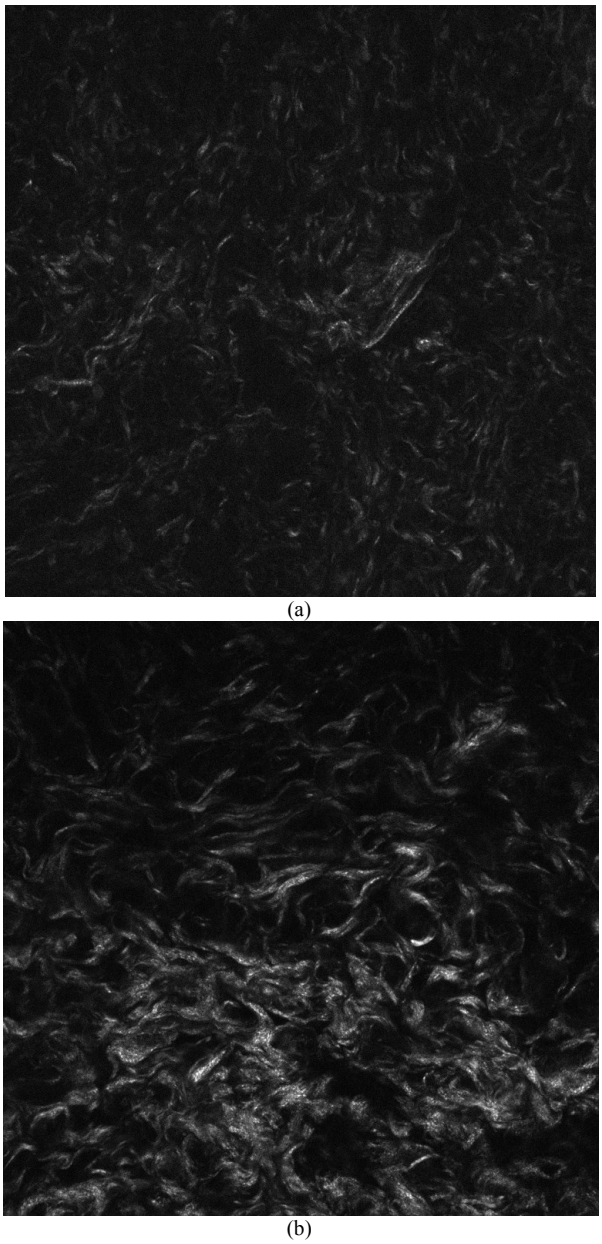

Fig. 1. Sample SHG images of mouse cervix: (a) gestation day 12, and (b) gestation day 18

$$PS = \sqrt{\frac{size(ROI)}{number\ of\ pores}} \tag{2}$$

Finally, the pore area (PA) feature is computed as follows:

$$PA = \frac{size(total\ pore\ area)}{size(ROI)} \times 100 \tag{3}$$

3. MARKOV RANDOM FIELD MODELING AND IMAGE SYNTHESIS

In this section, we present a statistical modeling of the binary SHG images based on Markov Random Field (MRF). MRF constitutes a powerful tool for statistical modeling of pixel interactions in images [10]. A random field $\mathcal{F}$ is MRF with neighborhood $N_{i,j}$ if it satisfies the following conditions [6]:

$$P(F) > 0 \quad \forall F \in \mathcal{F} \tag{4}$$

$$P\left(f_{i,j}|F - \{f_{i,j}\}\right) = P(f_{i,j}|f_{N_{i,j}}) \tag{5}$$

where $P(F)$ denotes the probability of pattern F occurring, $f_{i,j}$ intensity at a pixel (i,j), $N_{i,j}$ a small neighborhood (typically the first order or second order neighbors consisting of the 4 or 8 nearest neighbors is considered). The positivity condition in Equation (4) ensures that the probability exists for every configuration, while the second condition in Eq. (5) specifies the interaction of a pixel with its neighboring pixels.

MRFs are equivalent to Gibbs Random Fields (GRFs) as per the Hammersley-Clifford theorem [7]. A Gibbs distribution takes the following form:

$$p(F) = Z^{-1}exp\left(-U(F)\right) \tag{6}$$

$$Z = \sum_{F \in \Omega} exp\left(-U(F)\right) \tag{7}$$

where Z is a normalization constant called partition function, Ω is the sample space consisting of all possible patterns of F, U is an energy function indicating interaction between pixels defined based on a number of clique potential functions V_C as follows:

$$U(F) = \sum_{c} V_C(F) \tag{8}$$

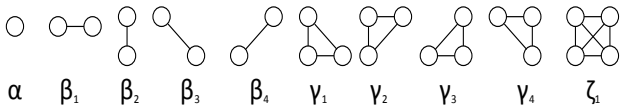

Fig. 2. Neighboring clique configurations (circles represent pixel locations)

The energy function is typically considered to be of low order. Figure 2 illustrates some clique configurations of the neighboring pixels. These clique potentials are regarded as the MRF parameters. Based on Equation (5), one can write:

$$P\left(f_{i,j}|F - \{f_{i,j}\}\right) = \frac{P(F)}{\sum_{f_{i,j}} P(F - \{f_{i,j}\})} \tag{9}$$

By further developing Equation (9), canceling the terms that are not dependent on $f(i,j)$ from the nominator and the denominator, and considering pairwise cliques (β-cliques as shown in Fig. 2) for calculating the energy function in Equation (7), we obtain:

$$P\left(f_{i,j}|F-\{f_{i,j}\}\right)=\frac{e^{-\sum_{\{(i,j),(i',j')\}\in clique}\beta_{(i,j),(i',j')}f_{i,j}f_{i',j'}}}{\sum_{f_{i,j}}e^{-\sum_{\{(i,j),(i',j')\}\in clique}\beta_{(i,j),(i',j')}f_{i,j}f_{i',j'}}} \quad (10)$$

where it is assumed that f takes on values in discrete label set $\mathcal{L}=\{-1,1\}$ corresponding to a binary image. To model the pore or fiber characteristics, it is considered that the binary SHG images originate from a MRF specified by Equation (10). Thus, the form of the model is specified.

The next step is to specify the parameters of this model or the β-parameters as stated in Equation (10). There are several ways in the literature to estimate the parameters of a MRF model [8]. The least squares method [9] is used here to extract the parameters of the introduced MRF model.

Cervix tissue samples used in this work were collected from mice at different time points of normal pregnancy. Details of the SHG imaging process are provided in [3-5]. Two datasets are considered here for our synthesis based on the day 12 and day 18 of mice pregnancy. The day 12 dataset consists of 317 and the day 18 dataset consists of 279 images. The images are of size 776×776 pixels with 8-bits per pixel corresponding to cervical tissue slices of 230×230 μm^2 in size.

The image processing pipeline for obtaining the MRF model parameters is as follows (see Fig. 3): A Gaussian filter ($\sigma=0.2$) is first applied for noise reduction. Contrast enhancement is utilized at the next step to enhance the appearance of the pores in the SHG images. Then, segmentation is done by selecting a fixed threshold value (0.25 here) and finally the segmented images are used for the parameter estimation.

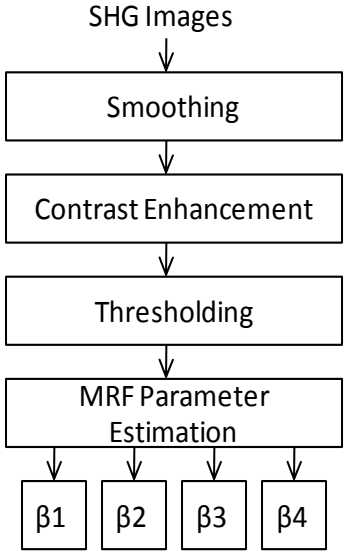

Fig. 3. MRF parameters estimation based on real SHG images

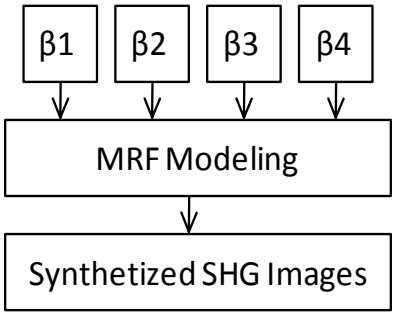

Fig. 4. Generation of synthesized binary images using MRF parameters

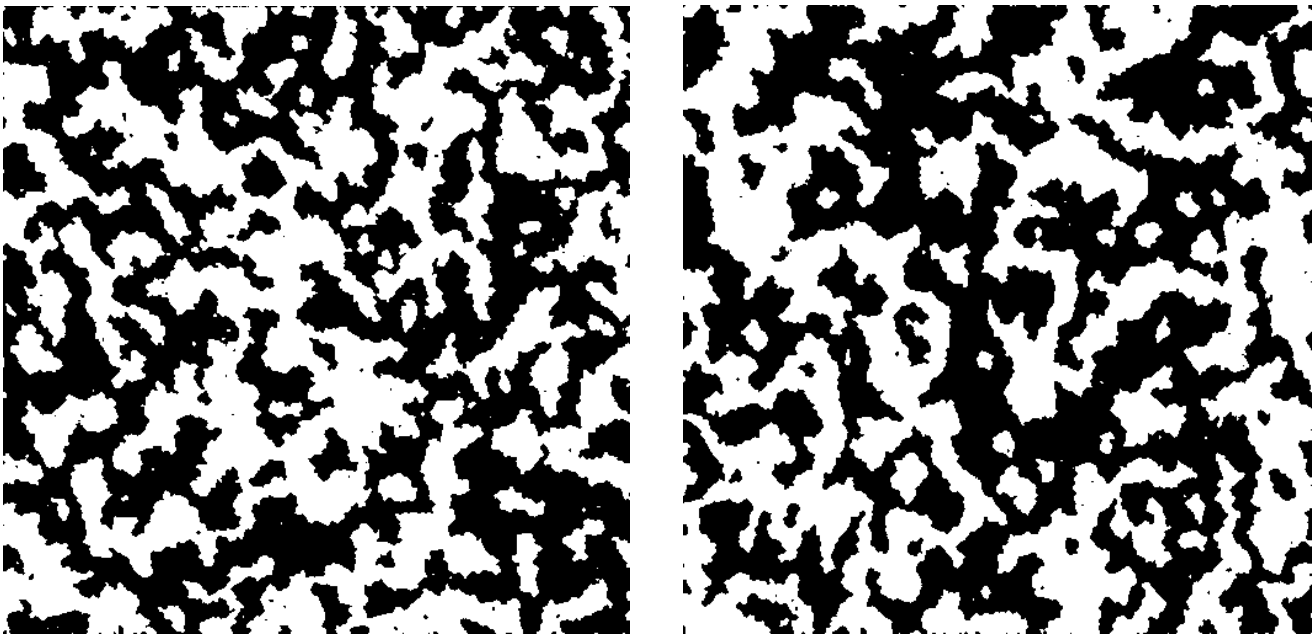

Fig. 5. Synthesized binary SHG images generated using MRF model: left image is generated based on MRF parameters extracted from day 12 images; right image is generated based on MRF parameters extracted from day 18 images

The four parameters $(\beta_1, \beta_2, \beta_3, \beta_4)$ were first extracted from each image of the day 12 and day 18 databases. Then, we considered the model parameters for each database to be the parameter averages for that database. Table 1 shows the MRF parameters for the two databases. In general, these parameters reflect the morphological characteristics of the pores in the SHG images. In Fig. 4, the steps for generating the synthesized binary SHG images are shown and in Fig. 5, sample synthesized images are displayed. In these sample images, the white indicates the fiber areas and the black indicates the pore areas.

4. EFFECTIVENESS OF SYNTHESIS

The classification outcome was used as a mechanism to show the effectiveness of the developed image synthesis. Three porosity features were extracted from each synthesized image. The extracted porosity features were fed into a classifier to distinguish the above two datasets. A Gaussian mixture model (GMM) consisting of two Gaussian distributions was utilized to serve as the classifier.

TABLE 1
MRF MODEL PARAMETERS OF DAY 12 AND DAY 18 DATASETS

Dataset	β_1	β_2	β_3	β_4
Day 12	0.3773	0.4025	0.0878	0.1442
Day 18	0.2683	0.4073	0.1842	0.1853

TABLE 2
CLASSIFICATION OUTCOME

True\Classified	Class 1	Class 2
Class 1 (day 12)	76	3
Class 2 (day 18)	2	68

The features were divided into two non-overlapping sample groups, testing (20%) and training (80%), to avoid bias in the classification. Then, the classifier was trained using the training samples. Afterwards, the testing samples were fed into the classifier. The distance between a sample and the classifier Gaussian mixtures were calculated and used for class assignment. This process was repeated 400 times, every time randomly selecting the test samples and the classification outcomes were averaged. Table 2 shows the averaged classification outcome across the runs. As can be seen, on average, only 5 images out of 149 images were misclassified. The averaged correct classification rate was thus obtained to be around 95%. The classification results show that, in general, day 12 synthesized images can be distinguished from day 18 synthesized images indicating the effectiveness of the developed biomedical image synthesis based on statistical MRF modeling.

5. CONCLUSION

A statistical modeling approach based on MRF has been presented in this paper in order to synthesize cervical tissue binary SHG images representing morphological characteristics of pores and fibers in cervical tissue. Real SHG images from mice cervices were used to extract the MRF parameters and it was shown that the porosity characteristics can be effectively modeled by the MRF model. Considering the difficulty involved with the labor-intensive process of obtaining cervical SHG images, the developed synthesis can be used as a useful tool for pregnancy staging studies or for medical training. The use of more complex models utilizing more parameters and more gray levels is expected to improve the synthesis outcome.

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