INCORPORATING USER INPUT IN TEMPLATE-BASED SEGMENTATION

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ABSTRACT

We present a simple and elegant method to incorporate user input in a template-based segmentation method for diseased organs. The user provides a partial segmentation of the organ of interest, which is used to guide the template towards its target. The user also highlights some elements of the background that should be excluded from the final segmentation. We derive by likelihood maximization a registration algorithm from a simple statistical image model in which the user labels are modeled as Bernoulli random variables. The resulting registration algorithm minimizes the sum of square differences between the binary template and the user labels, while preventing the template from shrinking, and penalizing for the inclusion of background elements into the final segmentation. We assess the performance of the proposed algorithm on synthetic images in which the amount of user annotation is controlled. We demonstrate our algorithm on the segmentation of the lungs of *Mycobacterium tuberculosis* infected mice from μCT images.

Index Terms— Registration - Template-based Segmentation - User Input - Diseased Organs

1. INTRODUCTION

Intensity-based segmentation techniques usually fail at segmenting diseased organs due to the presence of lesions. Template registration techniques are commonly employed to overcome this difficulty and produce a segmentation under some shape constraints. Template-based segmentation is omnipresent in medical imaging. It usually relies on a trade-off between the similarity of the target image and the deformed template, and the amount of deformation. The segmentation result is generally reviewed by the user. If it is not satisfactory, the user needs to modify the parameters of the registration algorithm in the hope of improving the final segmentation. It can take several iterations to tune the parameters adequately to the task on hand. It would be easier for the user to highlight regions that have been missed in the segmentation than finding the subtle trade-off between deformation and similarity. Unfortunately template registration algorithms do not generally take user input into account.

In this paper, we present a simple method to elegantly incorporate user input in a template-based segmentation technique for the segmentation of diseased organs. The user provides a partial segmentation - also called *positive segmentation* - of the organ of interest. It will be used to match the template onto the target organ. The user also highlights in what we call the *negative segmentation*, parts of the image that should be excluded from the final segmentation. Since user input is by essence incomplete, the registration algorithm needs to be robust to missing data. We have presented in [1] a simple statistical image model from which we derived a registration algorithm that deals with missing data. This work builds onto the same principles to deal with missing data while taking advantage of the user input.

We demonstrate our segmentation algorithm in the context of inflammation imaging with combined μCT and FDG-PET of *M. tuberculosis* infected mice. The task consists of delineating the lungs from the CT images in the presence of lesions so that the PET activity level in the lungs may be analyzed at different time points [2]. In this particular application, the user provides parts of the diseased lungs as positive segmentation and the rib cage and spine as negative segmentation. We first test the algorithm on controlled experiments to assess its robustness to missing data and its ability to exclude the negative segmentation from the final segmentation. We present lung segmentation results on μCT images of *M. tuberculosis* infected mice.

2. TEMPLATE REGISTRATION WITH USER INPUT

2.1. User Input: Positive and Negative Segmentation

We denote by $I : \mathbb{R}^3 \to \mathbb{R}$ an intensity image and by $I_0 : \mathbb{R}^3 \to \{0, 1\}$ a binary template that contains a template shape of the organ of interest. The *positive segmentation*, denoted $I_+ : \mathbb{R}^3 \to \{0, 1\}$, is a binary image containing parts of the target organ. We make the assumption that the positive segmentation contains only few errors, i.e. voxels that do not belong to the target organ are not included in the positive segmentation. However, we tolerate that parts of the diseased organ may be missing. In this work, we assume that the user provides the positive segmentation. While it is generally time

consuming and challenging to provide a complete segmentation, it is significantly easier to produce a partial segmentation of an organ of interest, even when lesions are present.

In addition, the user may provide a *negative segmentation*, denoted $I_- : \mathbb{R}^3 \to \{0, 1\}$. It is a binary image, defined on the target image domain, which contains some of the surrounding anatomical structures that should be excluded from the final segmentation. For instance it is frequent that parts of the rib cage and the spine are mistakenly included into the lung volume segmentation. By assigning the surrounding bones to the negative segmentation, the user ensures that those structures will be excluded from the final segmentation. Figure 1 presents an example of user input for the segmentation of mouse lungs from CT images.

2.2. Template Registration by Energy Minimization

Like many template registration algorithms, the proposed method is formulated as an energy minimization problem. The template, denoted by I_0, is deformed by ϕ, a smooth deformation from $\mathbb{R}^3$ to $\mathbb{R}^3$. The target is composed of two non-overlapping binary fields: I_+ , the positive segmentation, and I_-, the negative segmentation. The energy function is composed of two terms,

$$\mathcal{R}(\phi) + \gamma \mathcal{A}\left(\{I_+, I_-\}, I_0, \phi\right), \tag{1}$$

with $\gamma \in \mathbb{R}$, a weighting factor. The data term, $\mathcal{A}$, measures the similarity between the deformed template, $I_0 \circ \phi^{-1}$, and the target, $\{I_+, I_-\}$, while the regularization term, $\mathcal{R}$, penalizes for non-smooth deformations.

2.3. Deriving the Data Attachment Term

Rather than designing the registration data term arbitrarily, we design a simple generative model and use the negative log-likelihood of the observed target image as similarity measure, as proposed in [3].

2.3.1. Statistical Model

We model each voxel of each target field (I_+, I_-) as a random variable that follows a Bernoulli distribution, whose parameter depends on the voxel location and the value of the corresponding voxel in the template. For instance, assuming that ϕ is the deformation that brings the template and the target into correspondence, if a voxel of the template domain $y = \phi^{-1}(x)$ belongs to the template lung, i.e. $I_0(y) = 1$, the corresponding voxel x in the target image should belong to the positive segmentation, i.e. $I_+(x) = 1$, unless it belongs to a lesion that was not included in the positive segmentation, i.e. $I_+(x) = 0$. Hence:

$$P(I_+(x) = 1 | I_0(y) = 1) = 1 - \delta_+, \tag{2}$$

where $\delta_+ \in [0, 1]$ represents the proportion of lesions not included in the positive segmentation. If the template and the target are aligned, the probability that voxel x belongs to the negative segmentation is low. Denoting ϵ a small positive quantity:

$$P(I_-(x) = 1 | I_0(y) = 1) = \epsilon. \tag{3}$$

Similarly, if a voxel of the template image does not belong to the organ of interest, i.e. $I_0(x) = 0$, it is unlikely that the corresponding target voxel $x = \phi(y)$ belongs to the organ to be segmented, i.e. $I_+(x) = 1$, hence:

$$P(I_+(x) = 1 | I_0(y) = 0) = \epsilon. \tag{4}$$

However, voxel x may belong to the negative segmentation:

$$P(I_-(x) = 1 | I_0(y) = 0) = 1 - \delta_-, \tag{5}$$

with $1 - \delta_-$ the proportion of voxels of the target image that belong to the negative segmentation among all the voxels that do not belong to the positive segmentation.

2.3.2. Likelihood Expression

We model the labels in the positive and negative segmentations given the registering deformation ϕ as conditionally independent random variables, $\{I_+(x), I_-(x)\}$, when x belongs to the domain of the target image. We denote $y = \phi^{-1}(x)$, the location in the template domain that corresponds to location x in the target domain. The different fields of the target image are assumed to be independent with no intersection. Therefore the contribution of each voxel to the log-likelihood is a sum of 8 terms corresponding to each possible event: $(I_+(x) = 1 | I_0(y) = 1)$, $(I_+(x) = 1 | I_0(y) = 0)$, $(I_-(x) = 1 | I_0(y) = 1)$, $(I_-(x) = 1 | I_0(y) = 0)$ and the 4 complementary events. Each term of the sum is weighted by the associated log-probability. Summing over all the voxels of the image and neglecting the terms that do not depend on ϕ, the log-likelihood can be written as:

$$\begin{aligned} &\ell(\{I_+, I_-\}; \phi) \qquad (6)\\ &= \sum_x I_0(y) I_+(x) \log \frac{1-\epsilon}{\epsilon} \frac{1-\delta_+}{\delta_+} + \sum_x I_0(y) \log \frac{\delta_+}{1-\epsilon} \\ &+ \sum_x I_0(y) I_-(x) \log \frac{\delta_-}{1-\delta_-} \frac{\epsilon}{1-\epsilon} + \sum_x I_0(y) \log \frac{1-\epsilon}{\delta_-}. \end{aligned}$$

Since I_0 and I_+ are binary, we use the fact that: $(I_0(y) - I_+(x))^2 = I_0(y) + I_+(x) - 2 I_0(y) I_+(x)$ and rewrite (6) so that the sum of squared difference is apparent:

$$\begin{aligned} -\ell(\{I_+, I_-\}; \phi) = &\frac{1}{2} \log \frac{1-\epsilon}{\epsilon} \frac{1-\delta_+}{\delta_+} \sum_x (I_0(y) - I_+(x))^2 \\ &- \frac{1}{2} \log \frac{1-\epsilon}{\epsilon} \frac{1-\delta_+}{\delta_-} \frac{\delta_+}{\delta_-} \sum_x I_0(y) \\ &+ \log \frac{1-\delta_-}{\delta_-} \frac{1-\epsilon}{\epsilon} \sum_x I_0(y) I_-(x). \end{aligned} \tag{7}$$

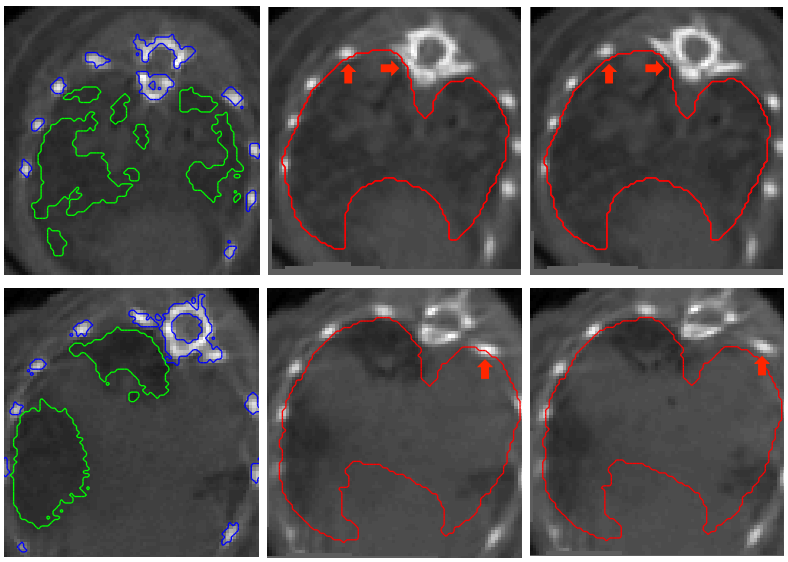

Fig. 1. **Left Column: User Input** - Axial view of the Positive Segmentation (Green) and Negative Segmentation (Blue) obtained by intensity thresholding and connected component on 2 examples of CT scans of TB infected mice. **Center and Right Columns: Segmentation Results** - Each image represents an axial slice of the CT image registered onto the template lungs using SSD+MP (center), the algorithm presented in [1] or SSD+UI (right) the proposed algorithm. The red contour delineates the segmentation volume. The red arrows point towards bones that are included in the lung segmentation after registration by SSD+MP but not after registration by SSD+UI. Note that in regions with fewer user annotations the segmentation is less precise.

The log-likelihood is composed of 3 terms: the usual sum of squared differences and two corrective terms. The first corrective term measures the volume of the deformed template and penalizes for shrinking excessively the template. The second corrective term penalizes deformations that lead the deformed template to intersect with the negative segmentation. The log-likelihood is therefore maximized when the deformed template includes the positive segmentation without shrinking excessively, and avoids the negative segmentation.

2.4. Registration Algorithm

The deformation is modeled by the evolution of a smooth velocity vector field, such that the template shape is deformed into the target shape. The solution of the evolution equation, so-called EPDiff, is unique and generates a diffeomorphism uniquely characterized by the initial momentum, the velocity vector field at time 0. Plugging in the negative log-likelihood (7) in the energy function (1) we obtain:

$$\|w\|_V^2 + \lambda \int \left(I_0(\phi^{-1}(x)) - I(x)\right)^2 dx \tag{8}$$

$$+ \lambda_1 \int I_0(\phi^{-1}(x))dx + \lambda_2 \int I_0(\phi^{-1}(x))I_-(x)dx, \tag{9}$$

with

$$\lambda = \gamma \log \frac{(1-\epsilon)}{\epsilon}\frac{(1-\delta_+)}{\delta_+},$$

$$\lambda_1 = -\gamma \log \frac{\delta_+(1-\delta_+)}{\delta_-^2}\frac{1-\epsilon}{\epsilon}, \lambda_2 = 2\gamma \log \frac{1-\epsilon}{\epsilon}\frac{1-\delta_-}{\delta_-},$$

and $\|w\|_V$ the norm of the initial momentum in some adequate Hilbert space V. If there is no negative segmentation, i.e. $\delta_- = 1-\epsilon$, $\lambda_2 = 0$, the registration algorithm is equivalent to the method proposed in [1]. If in addition the positive segmentation includes the complete organ of interest, i.e. $\delta_+ = 1-\delta_- = \epsilon$, the data term boils down to the usual SSD. More details about the minimization algorithm can be found in [4] in the latter case. The general case comes as a straightforward modification.

2.5. Choice of the Model Parameters

The matching algorithm depends on the choice of 4 parameters: ϵ, δ_+, δ_-, and γ. ϵ is a small positive quantity that represents the probability of the unlikely events. It is set manually by the user, in the following experiments ϵ is set to 10^{-10}. ϵ indirectly controls the weight of the penalization terms in the registration algorithm. The smaller ϵ is, the larger the penalization for shrinking the template and for intersecting with the negative segmentation.

Both δ_+ and δ_- are related to the user input. Assuming that the organ of interest has the same volume as the template, δ_+ is estimated as the ratio of the volume of the positive segmentation over the volume of the template organ. As for $1-\delta_-$, it is estimated as the ratio of the volume of the negative segmentation over the volume of the target image minus the volume of the positive segmentation.

Finally, we determine the value of γ when $\delta_+ = 1-\delta_- = \epsilon$, i.e. when $\lambda_1 = \lambda_2 = 0$, which corresponds to the user providing a complete segmentation of the organ of interest and no negative segmentation. We determine that $\lambda = \lambda_0 = 6 \cdot 10^4$ produces satisfying segmentation of the complete lung volumes (c.f. 3.1.1), hence:

$$\gamma = \frac{\lambda_0}{2}\left(\log \frac{1-\epsilon}{\epsilon}\right)^{-1}, \tag{10}$$

from which λ, λ_1 and λ_2 can be computed.

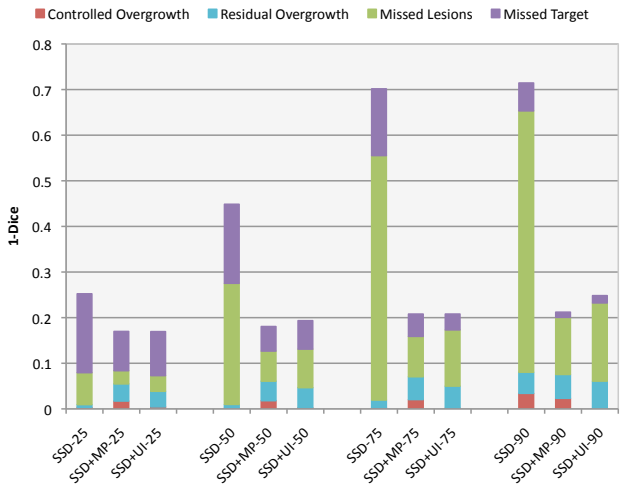

Fig. 2. **Segmentation error** for different amounts of lesions after registration using either the usual sum of squared differences (**SSD**), or the data attachment term dealing with missing data (**SSD+MP**), or the proposed algorithm that takes user input into account (**SSD+UI**). For instance **SSD+UI-25** stands for experiments with **25%** of missing data using **SSD+UI**.

3. EXPERIMENTS

3.1. Controlled Experiments

3.1.1. Image Data and Generation of Synthetic Data

A group of mice is infected and imaged by CT at a resolution of .2x.2x.2mm at different stages of infection. Uninfected mice are also imaged at each time point. We extract the lungs from the CT scans of two uninfected animals using intensity thresholding and connected components. In the following experiments, one of the lung volumes is used as a template, while the other volume is used as a target.

We randomly generate targets with missing data. Between 25 and 90% of the segmented volume is removed by sampling random spheres of 10 voxels of diameter. We segment by intensity thresholding the rib cage and spinal cord in the target image to be used as negative segmentation. We use the proposed algorithm (SSD+UI) to segment the target and compare the result to the results of other algorithms, see Figure 2.

3.1.2. Performance Assessment

The segmentation results are assessed using the Dice coefficient [5]. DT denotes the deformed template and T the complete target. T is partitioned into the lesions L and the positive segmentation PS. As for $\overline{\mathrm{T}}$, it is partitioned into the negative segmentation NS and the background B. The segmentation error, $1 - \mathrm{Dice}(\mathrm{DT}, \mathrm{T})$ is a sum of 4 terms:

$$\frac{|\mathrm{DT} \cap \mathrm{NS}|}{|\mathrm{DT}| + |\mathrm{T}|} + \frac{|\mathrm{DT} \cap \mathrm{B}|}{|\mathrm{DT}| + |\mathrm{T}|} + \frac{|\overline{\mathrm{DT}} \cap \mathrm{L}|}{|\mathrm{DT}| + |\mathrm{T}|} + \frac{|\overline{\mathrm{DT}} \cap \mathrm{PS}|}{|\mathrm{DT}| + |\mathrm{T}|} \quad (11)$$

The first 2 terms of (11) measure the set of voxels falsely included into the segmentation, which is partitioned into the controlled overgrowth $|\mathrm{DT} \cap \mathrm{NS}|$ and the residual overgrowth $|\mathrm{DT} \cap \mathrm{B}|$. SSD+UI is designed to limit the controlled overgrowth. The 3rd term, called missed lesions, accounts for the lesions that are not included in the final segmentation. The 4th term, called missed target, accounts for the voxels included in the positive segmentation but not in the final segmentation.

Figure 2 presents the 4 components of the error for different amounts of missing data and for different registration algorithms. Both SSD+UI and SSD+MP successfully control the segmentation error when the amount of missing data increases[1]. In addition we observe that in all cases SSD+UI eliminates the intersection between the deformed template and the negative segmentation. It shows that the SSD+UI is able to incorporate user input to modify the segmentation.

3.2. Segmentation of *M. Tuberculosis* Infected Lungs

Figure 1 shows preliminary results on the segmentation of infected lungs from CT scans (c.f. 3.1.1) using SSD+MP or SSD+UI. The positive and negative segmentations are obtained by intensity thresholding and connected components. We use the lungs of an uninfected animal as template.

4. CONCLUSION

We have shown that the proposed method allows the user to control template-based segmentation by providing a positive and negative segmentation. It is intuitive as well as applicable to other organs, species, pathologies, and imaging modalities.

5. REFERENCES

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[1] A larger study would be needed to assess the significance of difference of performance between SSD+MP and SSD+UI.