Atlas-based image segmentation: A Survey

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***Abstract*—Image segmentation is often the first step in image analysis. Its goal is to simplify or change the representation of an image into something more meaningful or easier to analyze. Comparative advantage of the atlas-based segmentation with respect to the other segmentation methods is the ability to segment the image with no well defined relation between regions and pixels' intensities. This is usually the case when the objects of the same structure need to be segmented (i.e. have the same texture), and the information about difference between these object is incorporated in spatial relationship between them, other objects, or within their morphometric characteristics.**

While different surveys on image registration, image segmentation and even atlas construction do exist, in this work we aim to present the guide for classification and distinction of different methods that can be used for atlas-based segmentation. The idea of this work is to use as an aid for beginners in the field while giving an overview of knowledge needed for certain problem solving.

***Index Terms*—Atlas-based image segmentation, medical image registration, atlas construction, statistical model, unbiased atlas selection, transformation, mappings, similarity measure, optimization algorithm, survey.**

I. PURPOSE

Using the process of image segmentation the image can be divided into different region. From segmented image the desired objects can be separated from the background, measured, counted or in other means quantified. In the case of medical applications, the automatic interpretation of images can relieve clinicians from the labor intensive aspects of their work while increasing the accuracy, consistency, and reproducibility of the interpretations, in the meantime allowing them to focus more on other aspect of their work.

Just to show the clinicians' increasing amount of work in the field of cardiovascular disease we will point out some statistical details. At the beginning of the 20th century, cardiovascular disease was responsible for fewer than 10% of all deaths worldwide, while today that figure is about 30%, with 80% of the burden now occurring in developing countries [1]. In 2001, cardiovascular disease was the leading cause of death worldwide [1]. In United States, coronary heart disease caused 1 of every 5 deaths in 2004 [2]. Croatia is not an exception from this case, as it saw an increase of more than 60% in coronary heart disease death rates between 1988 and 1998 [1].

This shows that automatic image interpretation and analysis could have a large impact in this field. However, issues such as low spatial (or temporal) resolution, ill-defined boundary, poor contrast, acquisition artifact or other noise place additional demands on segmentation. Therefore it is illusory to believe that segmentation can be achieved using pixels' intensities information only. As a solution a prior knowledge is often used. One way to do this is to incorporate the knowledge within the segmentation process in the form of the model that will be used as a prototype for segmentation of desired object.

In the following section we will fist give an short introduction on what the image segmentation is, give few examples of different application in which the segmentation techniques are used and propose few sources for further research on this topic. Next we will take a short look on deformable model segmentation, which is an alternative with very similar idea but different implementation. In the rest of the paper, we will present the atlas-based segmentation with dedicated sections on atlas construction and image registration. There we will describe different methods for atlas construction and propose a classification for image registration methods with respect to the techniques used to achieve registration of the images.

II. IMAGE SEGMENTATION

Image segmentation, defined as the separation of the image into regions, is one of the first steps leading to image analysis and interpretation [3]. It is used in many practical applications in machine vision, biometric measurements, medical imaging etc. for the purpose of detecting, recognition or tracking of an object. In general, image segmentation approaches can be classified according to features or type of the technique used. This would lead to three mayor group of segmentation techniques: region based, edge-based or classification [4], which correspond to feature extracted from pixel intensities, gradient and texture. However, segmentation shows up in different fields, sometimes the image segmentation approaches are classified with respect to the object, sensor (modality) or application usage, where different surveys are given (see for example [5], [6] or [7]). In [8] the segmentation techniques are divided in low-level segmentation techniques (described in [3]) and high-level techniques, where as a mayor difference between them is the level of the *a priori* information used in the process of segmentation. In this work, we will focus on the techniques that do not relay on the gray-level information only but rather incorporate the available a prior information.

In the model-based segmentation the segmentation problem is moved away from the pixel intensity properties to more abstract formulation of the problem, where mathematical operation such as warping of underlying space of the image, or physical properties such as elasticity of the curve, play significant role for object segmentation. In general, these models can be either statistical or in-silico models, with different knowledge (properties) incorporated within them. It is general belief that the statistical models would be more objective, therefore they are the ones that interest us most. These models are often referred as atlases, and will be discussed in further sections.

III. Deformable Model Segmentation

The knowledge that we want to incorporate into the model can be the knowledge about the shape, object orientation, continuity, elasticity or smoothness of the object needed to be segmented. This can be done both using an atlas or deformable model. The main difference between deformable model atlas registration is in the formulation of the problem. In the most broad sense the deformable models are implemented as the physical bodies with certain elasticity and force that tries to keep their form, while the image that we want to segment is represented as potential field with force that tries to stretch the model and adapt it. The best fit is found as the minimum energy solution, i.e. when both the forces are in balance. A survey on different techniques used for deformable modeling in computer graphics can be found in the work of Gibson et al. [9], while a good place for research of application of deformable model in medical image analysis can be found in [10] and [11].

Since the aim of this paper is not to provide the complete overview on deformable model segmentation, this topic will not be investigated further. Other ways to construct a model with incorporated a prior information of the object (that needs to be segmented) is using the expert knowledge or by extracting the statistical information from the available examples. The latter one is known as atlas-based segmentation where the a prior knowledge can be incorporated in both atlas construction (atlas size, orientation or shape) and atlas fitting procedure (energy function and optimization procedure).

IV. Atlas-based Segmentation

When compared to other methods for image segmentation, the atlas-based segmentation has an ability to segment the image with no well defined relation between regions and pixels' intensities. This can be due to lack of the border or excessive noise or in the case when the objects of the same texture need to be segmented. If the information about difference between these object is incorporated in spatial relationship between them, other objects, or within their morphometric characteristics, the atlas-based segmentation is expected to work well. Another important advantage of atlases is in their use in clinical practice, for computer aided diagnosis whereas they are often used to measure the shape of an object or detect morphological differences between patient groups.

On the other hand the disadvantage of an atlas-based can be in the time necessary for atlas construction wherever iterative procedure is incorporated in it (as in [12]), or a complex non-rigid registration. Since the atlas based segmentation is usually used when the information from the gray level intensities are not sufficient, it is difficult to produce objective validation. Whenever the manual or semi-manual segmentation is used as a golden standard one cannot observe this as objective validation since it is user dependent. As a solution for this problem, the unsupervised evaluation, which is user independent by definition, automatic and can, therefore, be considered (more) objective, should be discussed (as in [13]). While using the supervised rather than unsupervised methods can be observed as a flaw, it is also important to raise a question: *If we do have automatic (unsupervised) evaluation why not use it for further enhancement of the segmentation procedure?* However, after we have used this evaluation within a segmentation process we cannot (re-) use it to objectively evaluate the segmentation process, and by looking for the different evaluation method we again end up with (semi-) manual golden standard.

With proper selection of an atlas and enough plastic transformation the different segmentation properties may be achieved. If we want to use the atlas based segmentation for segmentation of an object within image, we have to have an atlas and also have to define the registration procedure. Therefore, in the next section we will discuss the atlas construction and methods used for construction of an atlas. Further, we will discuss image registration.

V. Atlas construction

When comparing experimental data obtained from different subjects, a standard approach is to display results on an atlas, as a common anatomical substrate. This is done to bring useful prior information to segmentation and registration tasks, so that variation within population can be described with fewer (transformation) parameters. Atlases have broad application in medical image segmentation and registration and are often used in computer aided diagnosis to measure the shape of an object or detect the morphological differences between patient groups. Various techniques for atlas construction are developed for different human organs, like the heart [14], [15], [16] and especially the brain [17], [18], [19], [20], [21], [22], [23], [24], [25], [26].

Some techniques for atlas construction were described by Rohlfing et al. [27] and expored in more details in [28] where the strategies for the atlas selection were discussed. They investigated four different selection of an atlas. First, one individual from the set was selected, second, the average shape atlas was constructed, third, the most similar instance from the set was selected as atlas and fourth, several individual images were used as atlases and multi-classifier approach was introduced before final segmentation. However, these are not the only possible options from which one can select an atlas, so we will list few more approaches for atlas construction.

If we want to construct an atlas from several images, a common approach to build an atlas is to pick one individual from a sample (a target on which the atlas is going to be built) and transform other images onto that target, to have the same spatial frame for further processing [29], [30], [31]. The resulting atlas using this approach is biased towards the chosen reference image, which is especially visible if the reference is picked far from the population mean [32], [33], [34]. To overcome this problem different methods were used, which generally reduces to two approaches: ether to pick the sample (whereas is best to pick a sample closest to the mean), or to try to estimate (or converge to) the true mean of the population. Both approaches have their strength and weaknesses. The first approach is easier and gives the atlas with the smallest possible bias but nevertheless this atlas is still biased. The second approach reduce this bias but may give the result which in some case falls out from the space of possible samples (alike the mean value of the bits in computer, which is around 0.5, but it falls out from the sample of possible events which is $\{0,1\}$, since bit with value 0.5 is impossible event). In the case of medical atlas this could result with the atlas which is anatomically impossible. This can be solved with two separate atlases for each class (in the bit example above, this would be classes 1 and 0). With the assumption that instances used for atlas construction were carefully selected so that they at the end lead to anatomically valid atlas we'll make a short survey over the different methods that can be found in the literature.

In [35], Guimond et al. developed an iterative averaging algorithm to reduce the bias. Marsland et al. in [12] proposed a method for least biased selection of target image, using iterative algorithm that minimizes the distance and maximizes the mutual information. Park et al. in [30] proposed an alternative algorithm that estimate the target image based solely on distance and argues that the least biased atlas should be done in this way because it is more robust since it is less affected by inherent noise in the images, and, since it uses estimation technique instead of iterative algorithm, is faster. In [26] the iterative technique whereby the atlas converges to the unknown population mean is also described by Toga and Thompson. It is important to notice that they used an algorithm that independently averages shape and intensity. Bathia et al. in [19] proposed the similar approach where one arbitrary image is used just as an intensity reference, after which the similarity between images is maximized using non-rigid transformation. To assure that the image calculated in this fashion is actually the mean (with respect to the transformation) they put the constrain that the sum of all transformation is equal to zero. In [18], Joshi et al. proposed the method which is invariant to target image selection since after the construction of the atlas in the space frame of the target image, the target image is transformed to the space frame of the mean transformation. The mayor improvement of this work is that this was done for large deformations which was not the case with [19]. As the dissimilarity measure the squared error distance was used and it was shown that the optimal atlas (for the selected dissimilarity measure) is an average intensity atlas. A similar work using Kullback-Liebler divergence is described in [20] by Lorenzen et al..

VI. Image Registration

Due to the development of acquisition devices the diversity of applications for image registration have grown significantly. For example, Zitova et al. in [36] states that, according to the database of the Institute of Scientific Information (ISI), within the period 1993–2003 more than 1000 papers were published on the topic of image registration. More recent numbers, from the same database, shows that in just last two years (2007 and 2008) more than 1000 papers were published on the topic of image registration. Therefore, we will not aim to cover all the publications within this fields, but rather just survey the methods, with the accent on the publications within a field of medical imaging.

A comprehensive survey of image registration methods can be found in [37], and the studies [38] and [39] offer a classification of the methods in the field of medical imaging. More recent surveys on image registration are work of Mäkelä et al. [40], which covers the field of cardiac image registration, the work of Pluim et al. [41], which covers mutual information based studies in medical imaging and the work of Zitova and Flusser [36] which discuss various use of of image registration in computer vision. The intention of this section is to provide an insight into the field of image registration with special attention on methodology and classification of methods. Various disciplines in which image registration methods were used are computer aided diagnosis, atlas construction, computer vision, remote sensing, cartography etc. ([37], [36], [39], [42]), just to name a few.

Noticing the variety of use of image registration, and having in mind that just in last two years more than 1000 papers on topic of image registration were published, one can conclude that the definition that aims to cover all these disciplines can only state that image registration is the process of overlaying two or more images to achieve maximum correspondence. If we want to make the definition useful we have to specify the "overlaying", "correspondence" and how to "achieve [its] maximum". The interrelationship between these processes, and how they form the process of image registration is depicted in Figure 1.

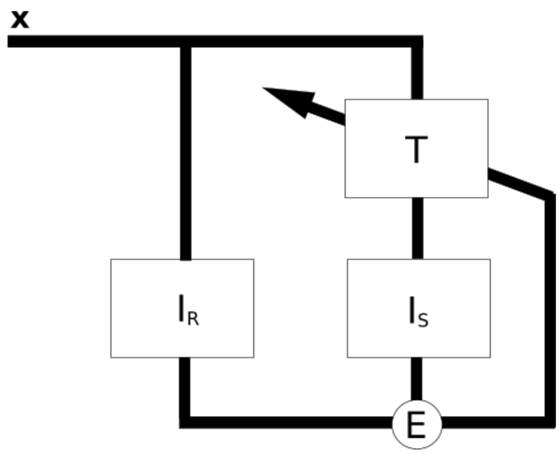

Fig. 1. The diagram shows the process of registering two images I_R and I_S. The correspondence between them is defined with energy function (denoted with E), whose output is used to control the transformation function (T). The transformation function warps the underlying space of images I_R and I_S (denoted with $\mathbf{x}$) until they reach the maximum correspondence. See text for details

In Figure 1 we can notice the three basic building blocks of image registration:

1) Transformation
2) Similarity measure
3) Optimization algorithm

The transformation is a class of geometric transformation (or parameters of freedom) which explains how do we actually overlay one image onto the other (denoted T in the Figure 1). The similarity measure is also known as alignment measure, registration function etc., or more general, energy function, cost function or score. It quantifies the similarity (correspondence) between two images. The optimization algorithm explains how to find the similarity measure maximum and in Figure 1 is shown as a feedback loop.

Unfortunately, all three registration's building blocks, varie across these disciplines and even across individual implementation, and universal registration method is impossible to propose. Since the medical image registration is of our main interest we will focus on classification criteria within this disciplines to ease the search for ideal transformation, energy function and optimization algorithm within problems of the same kin.

While different approaches for classification of image registration methods are proposed in different studies (such as [36], [37], [39] etc.), we determine to use one of our own since it seems to be the most appropriate for the introduction in the field, while giving an overview on details needed for implementation of certain methodology. The proposed classification although inspired by [36], [37], [38] and [39], it is based on three different criteria: technical requirements, nature of distortion and methodology. All three criteria are heavily coupled since nature of distortion (within images) narrows down the choice of methodology while technical requirements place additional restrictions (on methodology). We will take a look on this in the sequel of this section. The main accent will be on the methodology, while the problem specific classification such as classification according to object type will be consindered irrelevant.

Technical requirements are usually placed on the algorithm speed, dimensionality of the image and user's interaction. Therefore we differentiate online and offline algorithm, where online implies that heavy time requirements are placed on algorithm, which usually means that it is done in real time. On the other hand problem can be classified with respect to the dimensionality of the image, since even 3D volumes or 2D + time (sometimes referred as 2.5D to notify the difference) are sometimes considered as images. At last, restriction can be placed on the level of interaction with the registration algorithm, so the registration can be made automatic, semi-automatic, or interactive. Therefore, the different technical requirements that can be put on the image registration methodology, and according to which we may divide image registration techniques are:

1) Speed
2) Dimensionality
3) Interaction

The registration can be classified with respect to the nature of the distortion (sometimes referred as variation or degradation). Two mayor type of distortions can be observed as consequence of change on the observed subject or scene. First, let's observe the image distortion as the consequence of a variation of a subject. If the images that need to be registered belong to the same subject than we speak of intra-subject registration, if they belong to different subjects it is the inter-subject registration. Another type of the registration is when a subject's image is registered to a model (mathematical or an atlas). Other type of distortion are variations of the scene. If the distortion between the images that needs to be registered is caused by the change of type of sensors, than we are speaking of multimodality registration, if the scene is changed due to change in sensor position than we have multiview registration and if we have the same scene taken in different time than we speak of multitemporal registration. It is important to notice that registration of images acquired by scene changes usually makes sense only if the subject remains unchanged. This classification we can list as:

1) Subject
    a) Inter-subject [43]
    b) Intra-subject
    c) Model [14]
2) Scene
    a) Multimodality ([44], [45], [21])
    b) Multiview
    c) Multitemporal

Finally, we will classify the image registration techniques according to the methodologies used. We will sort these methodologies according to the transformation, similarity measure and optimization algorithm. Both transformation and similarity measure can be sub-divided on local and global subsection. None of this will be listed in the classification, since this is used in various different studies. Other reason for this is that this classification is coupled with similarity measure, but however does not define the similarity measure with enough accuracy. Therefore we propose the classification as follows:

1) Transformation
    a) Rigid
    b) Affine ([46])
    c) Curved ([16], [47], [48], [49])
2) Similarity measure
    a) Intensity based
        i) Pixel identity methods
        ii) Correlation like methods ([46], [47], [50])
        iii) Entropy like methods ([51], [45], [16], [52])
    b) Landmark based
        i) Extrinsic ([53], [54])
        ii) Intrinsic
            A) Anatomical ([46])
            B) Geometrical ([55], [56])
3) Optimization algorithm
    a) Deterministic
    b) Heuristic ([57])

or

a) Constrained ([19])
b) Unconstrained

The classification with respect to optimization algorithm is not extensively discussed since optimization is by itself topic broad enough, and as an in-depth and comprehensive survey the book of Fletcher can be used [58]. While various other and more detailed classification are also possible, this will not be pursued any further and for the same reason the optimization will not be discussed in the separate subsection.

Finally, let us mention the works of Christensen et al., Skrinjar et al. and Lorenzen et al. (see [21], [59], [60], [61]), where image registration process is observed through prism of inverse consistency and transitivity. These works are worth mentioning since the transitivity and inverse consistency are often preferable or even used as measure of quality of the registration, although they do not guarantee the accuracy of the registration [21], [59]. Insights from this works can be used to achieve more symmetric transformation or for an unsupervised registration evaluation.

Now, after proposed methodological classification we will describe the usual nomenclature and formulae used in the literature. This will be done for both the transformation function and the similarity measure.

A. *Transformation*

In this section we will start from the simplest of transformations and proceed towards more complicated transformations. The rigid transformation is defined as transformation that preserve all distances. This means that rigid transformation allows image only to rotate and translate. Using homogeneous coordinates this can be written in matrix notation as:

$$\mathbf{x}' = RT\mathbf{x} \tag{1}$$

where **x** represents column vector with the coordinates of the image with appended one in the last row (see Eq. 2), R stands for the rotation matrix, and T for translation matrix. In the case of 2D image, we write this as:

$$\begin{bmatrix} x \\ y \\ 1 \end{bmatrix} = \begin{bmatrix} \cos\theta_z & -\sin\theta_z & 0 \\ \sin\theta_z & \cos\theta_z & 0 \\ 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} 1 & 0 & t_x \\ 0 & 1 & t_y \\ 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} x \\ y \\ 1 \end{bmatrix} \tag{2}$$

In this equation x and y stand for coordinates of the image, θ_z for the angle of rotation around z-axis (the only rotation defined for 2D image) and t_x and t_y stand for translation in x and y direction, respectfully.

The homogeneous coordinates were introduced by August Ferdinand Möbius in his 1827 work *Der barycentrische Calcül*, to ease claculus by representing affine (and projective) transformation in matrix form. This is precisely the next transformation that we will observe. First notice that additional parameter that can be added to transformation function is scaling. Scaling can be defined as separate matrix as the one defined in equation 3 (again in homogeneous coordinates), where s_x stands for scaling along x-axis, same as s_y for scaling along y-axis.

$$S = \begin{bmatrix} s_x & 0 & 0 \\ 0 & s_y & 0 \\ 0 & 0 & 1 \end{bmatrix} \tag{3}$$

All these transformations of the form $S \cdot R \cdot T$ are special cases of more general affine transformation which preserves straightness of lines and parallelism, and can be written as matrix A:

$$A = \begin{bmatrix} a_{11} & a_{12} & t_x \\ a_{21} & a_{22} & t_y \\ 0 & 0 & 1 \end{bmatrix} \tag{4}$$

without any restrictions on the elements a_{ij}.

Finally, the curved transformations are the most flexible transformations and they even do not preserve the straightness of lines. The simplest functional form in which we can write this transformation is a polynomial in the components of **x**:

$$\mathbf{x}' = \sum_{ijk}^{IJK} \mathbf{c}_{ijk} x^i y^j z^k \tag{5}$$

B. *Similarity measure*

Among various different similarity measures, we well observe here just three different classes of similarity measure. All three will be observed through the prism of intensity-based similarity measures since landmark-based similarity measure can be reduced to simple distance measures once the landmark is chosen and according to Roche et al. [62] the intensity-based similarity measures are increasingly used in medical image registration. The intensity-based measures are divided with respect to (often implicit) assumption of relationship between two images that need to be registered. As an inspiration for this classification, the work of Roche et al. (primarily [62], [63]), which comprehensively and deeply discuss these assumptions and corresponding similarity measures was used, while other works which discuss the role of similarity measures in image registration were also consulted (see [64], [65] or [66]).

The two images that are mutually registered are usually denoted as the reference image (or model) and the source image (or input). These two images we shall denote $I_R(\overrightarrow{x})$ and $I_S(\overrightarrow{x})$, where $\overrightarrow{x}$ stands for the coordinates vector of the image.

If we assume identical images I_R and I_S (except for the misalignment) intuitive similarity measure is the sum of squares of intensity differences (SSD). In this case, if the correct alignment is achieved the SSD will be zero. Intuitively, if only a small fraction of the pixels being aligned, are likely to have changed between image acquisition the SSD is likely to work well (for example see [67], [68]). The certain image registration problems are reasonably close to this ideal case, while in the slightly more realistic scenario, where the images differ only by Gaussian noise it can be shown that SSD is the optimal measure. This distance measure can be given as:

$$D = \sum_{x}^{X} (I_R(\overrightarrow{x}) - I_S(\overrightarrow{x}))^2, \forall \overrightarrow{x} = (x, y) \in X \tag{6}$$

where X denotes the underlying space of the images. Various other modification of this measure are possible, such as sum of absolute intensity differences or cross-correlation, which leads us to second type of similarity measures.

If we assume affine relationship between images the correlation coefficient is the most appropriate selection for similarity measure:

$$\rho(I_R, I_S) = \frac{cov(I_R, I_S)}{\sqrt{\sigma}_R \sigma_S} \tag{7}$$

where σ_R and σ_S stand for standard deviation of the pixel intensity values of the images I_R and I_S, respectfully, while $cov(I_R, I_S)$ denotes correlation between images I_R and I_S, which can be written as $E((I_R - \mu_R)(I_S - \mu_S))$ if E is used to denote entropy and μ to denote mean intensity of the images.

Finally, the most loose assumption that can be made about intensity-based similarity between two images, is that they have just statistical dependencies. The most popular measures for this are entropy-based measures, such as normalized mutual information.

$$NMI(I_R, I_S) = \frac{H(I_R) + H(I_S)}{H(I_R, I_S)} \tag{8}$$

where $H(I)$ stands for the entropy of the image I, and $H(I_R, I_S)$ for joint entropy of the images I_R and I_S.

VII. Conclusion

For the topic of this paper an interesting detail from a broad field of image segmentation was selected. As a main focus the segmentation of an image using a model was selected. This was done since any model has the property that it incorporates the a prior knowledge about the problem. Mainly we have discussed the atlas construction (as a form of statistical model) as well as image registration process which was dissolved into it's building blocks according to which the classification of the different methodologies for the image registration was proposed. Main accent of this work was on the researches from the field of medical imaging with special attention to the ones from the cardiac imaging. Also we have tried to present different studies that discuss some of the significant questions from the field of atlas based segmentation, whether this belongs to model selection, atlas construction, image registration, or validation of the process. In this broad topic from the field of image analysis we hope that we have offered one hard stepping stone for further researches on atlas-based segmentation.

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