A Level Set Bridging Force for the Segmentation of Dendritic Spines

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Abstract. The paper focusses on a group of segmentation problems dealing with 3D data sets showing thin objects that appear disconnected in the data due to partial volume effects or a large spacing between neighbouring slices. We propose a modification of the speed function for the well-known level set method to bridge these discontinuities. This allows for the segmentation of the object as a whole. In this paper we are concerned with treelike structures, particularly dendrites in microscopic data sets, whose shape is unknown prior to segmentation. Using the modified speed function, our algorithm segments dendrites and their spines, even if parts of the object appear to be disconnected due to artifacts.

1 Motivation

A number of problems arise when an object in a 3D data set should be segmented. Depending on the modality there may be certain artifacts, e.g. magnetic field inhomogeneities in MR-images or metal artifacts in CT-images.

An artifact common to almost all image acquisition techniques is the partial volume effect (PVE). In digital images the grey value of a pixel is the mean value of all the information that was measured in the area represented by this pixel. The result is a blurring of regions with large variances in grey values. This is especially evident at the borders of objects. It is amplified even more between neighbouring slices in data sets, as the slice thickness is often larger than the pixel spacing within a slice. Structures whose diameter is smaller than the width of a pixel will merge into the background and may even vanish entirely.

When segmenting objects with a known shape, one can simply devise a model describing this shape and its variation to detect and/or segment the object within the data set. The location of small parts not visible in the data can then be estimated based on the parts of the object that have been segmented. Examples of such models are the Active Shape Model[2], Snakes[7] or Mass Spring Models[4].

With objects whose shape is very complex or not known prior to segmentation, partial volume effects may pose a big problem. It is difficult to determine the exact location of the borders of the object. Furthermore, parts of the structures that appear disconnected within or, more likely, between slices are usually not segmented at all.

W.G. Kropatsch, M. Kampel, and A. Hanbury (Eds.): CAIP 2007, LNCS 4673, pp. 571–578, 2007.

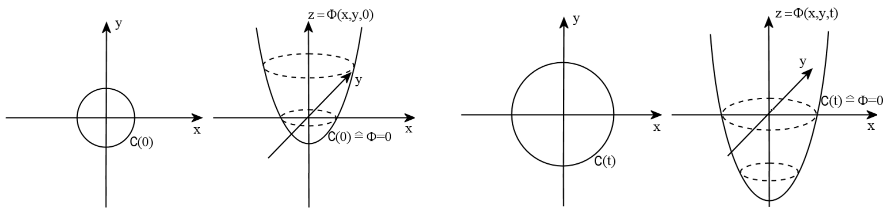


Fig. 1. Illustration of the front propagation process: The left image shows an initial curve C and the level set function Φ at time t=0. The right image shows both functions at a later time.

Due to its implicit definition, the level set method is an appropriate means to segment objects whose shape is not known a priori or whose shape varies significantly between data sets. Therefore, we device a solution to the problem mentioned above using a modification of the level set method. We propose a new force term for the level set speed function to bridge small gaps in the representation of objects, such as those resulting from PVE.

2 Level Sets Methods and Speed Functions

Level sets were introduced by Osher and Sethian [10] for the solution of surface motion problems. They are used to describe the propagation process of a closed curve $C \in \Re^n$. This curve C is represented as the zero level set of a higher dimensional function $\Phi \in \Re^{n+1}$, i.e.

$$C(t) = \{\mathbf{x}|\Phi(\mathbf{x}(t), t) = 0\}. \tag{1}$$

C is moving in its normal direction over time. The speed of each point on C is given by a speed function F that is dependent on various internal and external forces, such as local curvature or image gradients, respectively.

This leads to the level set equation

$$\Phi_t + F|\nabla\Phi| = 0, \tag{2}$$

where $|\nabla\Phi|$ denotes the normalised gradients of the level set function and F is the speed function.

The advantage of this representation is that Φ always remains a function even if C splits, merges or forms sharp corners. Also, this representation is independent of the number of dimensions of C. As Φ changes over time its zero level set $\Phi(\mathbf{x}, t) = 0$ always yields the propagating front, i.e. $C(\mathbf{x})$ at time t.

The speed function F governs the way the front is propagating. Usually F consists of a number of different forces that are combined in a meaningful way. Using level set methods for image processing applications, one can differentiate between external force terms derived from the underlying image and internal force terms derived from the properties of the front itself. An example for a speed function of a level set function for an image processing task is given by

$$F = F_{\nabla I}(F_A + F_\kappa), \tag{3}$$

where F_A is an advection term for expanding the front, F_κ is a force based on local curvature, usually given by

$$F_\kappa = \nabla \frac{\nabla \Phi}{|\nabla \Phi|}, \tag{4}$$

and $F_{\nabla I}$ is an external force based on image gradients. One way to define such a force is given by

$$F_{\nabla I}(\mathbf{x}) = \frac{1}{1 + |\nabla G_\sigma * I(\mathbf{x})|}, \tag{5}$$

other approaches are described in [9] and [1]. In equation 5, $G_\sigma * I(x, y)$ denotes an image convolved with a Gaussian low pass filter with a standard deviation of σ.

If many force terms are used it is necessary to find meaningful weights for all forces to guarantee that the results of all forces have approximately the same order of magnitude.

The definition of image-based forces is by no means limited to simple image features. Van Bemmel et al.[12] devise a force term based on the size of cross section areas and the eigenvalues of the Hessian matrix at each pixel for the segmentation of blood vessels in MRA images. The resulting speed term gives high values inside of cylindrical objects and low values otherwise. Leventon et al. [8] proposed a method to use curvature and intensity profiles along the gradients of the propagating front to segment the corpus callosum and the femur in MR images.

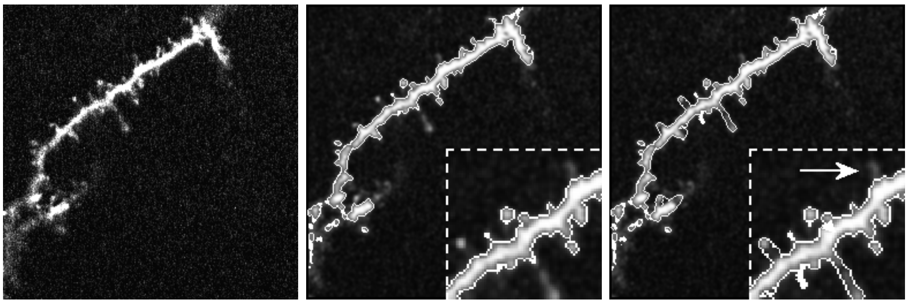
Such advanced speed terms containing model-based aspects often result in a more robust and reliable segmentation result. Unfortunately, they are also often limited to the specific application they were designed for. Also, the independence of the level set method to the number of dimensions of the data is lost.

A paper by Han et al. [5] introduces topology preserving level sets. This modification to the speed function prevents the propagating front from splitting or merging. In [5] this is used for the segmentation of grey matter in MR images of the human brain and the segmentation of bones in CT images.

Like the speed term proposed in this paper, the modification in [5] is somewhat weaker in its contribution to the speed function. But it is consistent with the definition of level sets and not limited to a single application.

3 Bridging Gaps in Data

The goal of this section is to define a speed term that allows the complete segmentation of objects, even if parts of those objects are not connected. As



(a) (b) (c)

Fig. 2. Image 2(a) is an example of one slice of a contrast enhanced 3D microscopic image depicting a dendrite with various spines (see section 4 for details). The original image is convolved with a small gaussian filter and segmented using the level set method. Image 2(b) depicts the result using a common speed function. While some spines have been segmented during this segmentation process, others have been missed. Image 2(c) shows the segmentation result using a modified speed function containing our new speed term. Almost all spines have been segmented. See the enlarged regions in the lower right corner for more details. The missing spines are barely visible (e.g. one spine marked by the white arrow in the enlarged section in image 2(c)) and cannot be segmented without either the incorporation of additional knowledge or an oversegmentation in other parts of the image.

described in section 1 such gaps may occur in medical imaging due to partial volume effects when thin objects are seemingly disconnected due to a large pixel spacing in the data set.

To solve this problem we define a new speed term that allows the propagating front to "look ahead" of its current positions. That is, we incorporate a term that for each pixel on the front decides if it should be moved even if the underlying image features in the data (grey values, gradients, etc.) suggest that it should be stopped.

In a prior paper [11] we used the pixels along the surface normal to decide if the front should continue to propagate. This method is very fast, as the surface normal is easily derived from the level set representation. While this works well with most objects, problems occurred unter certain circumstances. Because the surface normal is calculated from a discrete representation of the level set function, the approximation at places of high curvature tends to be very inexact. This is obviously a problem when dealing with thin objects. On the other hand, these objects are of special interest as partial volume effects tend to affect particularly the representation of thin objects within the data.

The new definition of our "bridging force" doesn't rely on the surface normal anymore. Instead, for each pixel $\mathbf{x}$ on the front all pixels $\mathbf{y}$ in a given neighbourhood with $\Phi(\mathbf{y}) > 0$ are checked. The best pixel is selected using various, easily computed conditions:

- **y** fulfills the image-based conditions of the level set speed function (i.e. the pixel would be segmented if it was connected to the object)
- the angle γ between the surface normal of **x** and the vector **y-x** is smaller than 90 degrees
- the distance between **x** and **y** is smaller than the distance between **y** and the neighbours of **x** on the propagating front.

Note, that the image-based conditions (e.g. gradient length, grey values, etc.) need to be calculated only once before the start of the propagation process and are needed for the use of other image based forces anyway. Also, instead of actually calculating γ we simply compute the scalar product $(\mathbf{n} \cdot (\mathbf{y}\text{-}\mathbf{x}))$, where **n** is the surface normal of the front at the position of **x**.

Furthermore, we need only to calculate this force term if the speed of the front at position **x** is very small. Otherwise the front is currently still moving at this position, so there cannot be any gap that has to be bridged.

The speed function of the level set equation is now rewritten as

$$F(\mathbf{x}) = \begin{cases} \alpha F_I(\mathbf{x})(F_A + \beta F_\kappa(\mathbf{x})), & \text{if } F > \varepsilon, \\ \alpha F_I(\mathbf{y}) F_A, & \text{otherwise.} \end{cases} \tag{6}$$

F_I denotes the combination of all image-based speed terms, F_κ is the curvature-based speed term and $\alpha, \beta \in [0, 1]$ control the influence of image- and curvature-based forces, respectively.

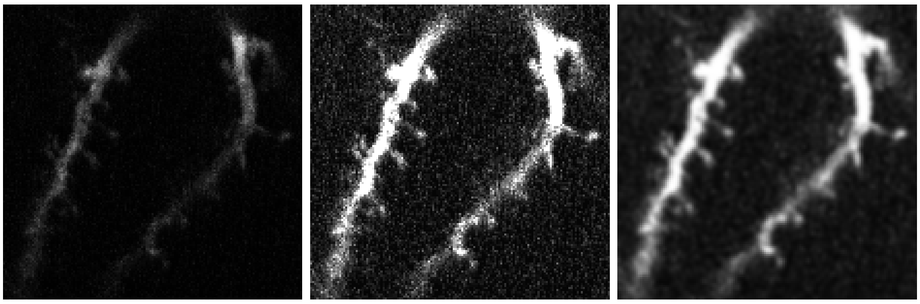
Using the speed function given in equation 6 the propagating front may cross areas of the image that would not be segmented using a common speed function such as given in equation 3. Still, the front will not leak into the background of the image if the speed function is defined appropriately because the image-based speed terms represented by F_I will prevent any propagation in these locations (see figure 4).

While disconnected parts of the desired object are segmented in almost all cases the chosen path of the front was not always the semantically correct way. If two different parts of the front may potentially be connected to a given part of the object, it cannot be decided which connection would be the correct one (see figures 5(b) and 5(c)). In order to guarantee a correct decision, more semantic knowledge of the desired object would be required, which in turn would restrict the general use of our "bridging force" for various applications. Nevertheless, corrections of these semantically wrong "bridges" could be realised in a postprocessing step.

Also, the size of the neighbourhood is important to consider. If the neighbourhood is too small, some parts of the desired object may not be found (see figure 5(a)). On the other hand, if the neighbourhood is too large, the number of unwanted bridges may increase, depending on the topology of the data.

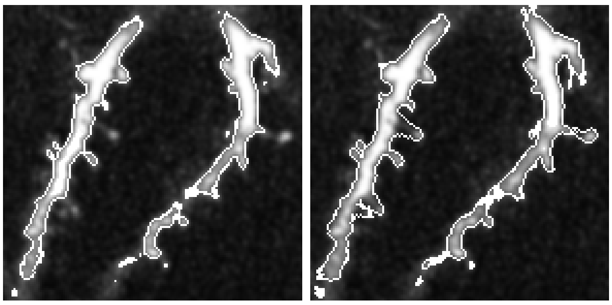
4 Experimental Results

The modified speed function was tested on images depicting branches of neurons, called dendrites, which have been injected with a luminescent dye. These



(a) (b) (c)

Fig. 3. Preprocessing steps: A slice of the original 8 bit image (figure 3(a)) is contrast-enhanced (figure 3(b)) and convolved with a 5×5 gaussian filter (figure 3(c))



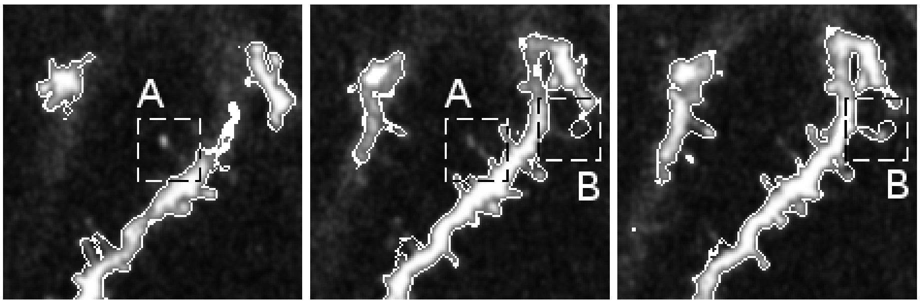
(a) (b)

Fig. 4. Advantages of the bridging force: Figure 4(a) depicts a slice of the 3D segmentation of the dendrite from figure 3(a) using a common level set function as given in equation 3. In contrast, the result in figure 4(b) uses the additional bridging force introduced in section 3.

dendrites have been scanned using a confocal laser scanning microscope. We used five data sets with a minimum resolution of 512x512x112 voxel. The voxel size in all images is $0.1\mu m^3$. A number of extensions are visible on the side of each dendrite. These dendritic spines are used for the transmission of signals between various neurons [6]. Figure 2(a) shows a slice from one of the data sets. It can be seen that there is often no visible connection between dendrites and their spines and a segmentation using the level set function does not find these disconnected spines (see figure 2(b)).

Prior to the segmentation, the original data has been contrast enhanced to allow for a more reliable calculation of the image based forces, and convolved with a 5×5 gaussian filter kernel to reduce the image noise (see figure 3).

As mentioned in section 3, the success of the segmentation depends on those image features that are used in the speed function and on the number of pixels that the bridging force is using to decide if a gap should be crossed.



(a) (b) (c)

Fig. 5. Drawbacks of the bridging force: Shown are three slices from the same data set. Region A is an example of a spine too similar to the background to be segmented. The bright part of the spine in figure 5(a) is too far from the dendrite to be detected. Region B shows a spine that has been detected. The level set function bridged over to the bright region from another spine, though, which is semantically not correct.

The algorithm was initialised with a single seed pixel within the dendrite. It did segment all spines with the specified image features that where either (visibly) connected to the dendrite or who were located within the neighbourhood specified by the bridging force. For the experiments shown in this paper we used a maximum look-ahead distance of six pixels. As shown in figure 5(a), a small number of spines were missed. Nevertheless this was a good tradeoff, since a larger neighbourhood increased the number of semantically incorrect connections.

In figure 2(c) we point out a number of hard to detect spines with image features similar to the background noise. Without the incorporation of additional semantic knowledge it is not possible to detect these spines.

Since no ground truth for a correct segmentation exists, we compared our result with various other segmentation techniques.

In figures 2(b) and 4(b) we depict results of a common level set segmentation. The results are comparable to other user guided segmentation techniques like region growing, fast marching, image foresting transform, etc. These techniques cannot segment disconnected parts of the specified objects without incorporating a modification similar to our bridging force.

As mentioned in section 1 model-based segmentation techniques are not applicable since there is no prior information on the shape of the object.

Simple pixel based techniques, e.g. thresholding methods, cannot connect disconnected spines to the dendrite, but we assume that it should be possible to achieve a correct segmentation using a markov random field [3] with an appropriate neighbourhood configuration.

5 Conclusions

We defined a new speed term to connect parts of an object that appear disconnected in the data due to partial volume effects. We aimed at a general definition applicable to various similar problems. This speed term was successfully applied to a number of microscopic images of neurons to segment dendrites and their dentritic spines. We found all spines given our specified image features, although not always the correct connection to the associated dendrite. We presented the advantages of our modified speed function to a common level set segmentation and also mentioned drawbacks due to the general definition of our new force term. To obtain a semantically correct segmentation the integration of further problem related knowledge will be necessary, although this will require a modification of our speed term adapted to the problem.

Acknowledgements

We like to thank Andreas Herzog for the fruitful discussion on the data sets.

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