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Learning Active Contour Models for Medical Image Segmentation

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Abstract

Image segmentation is an important step in medical image processing and has been widely studied and developed for refinement of clinical analysis and applications. New models based on deep learning have improved results but are restricted to pixel-wise tting of the segmentation map. Our aim was to tackle this limitation by developing a new model based on deep learning which takes into account the area inside as well as outside the region of interest as well as the size of boundaries during learning. Specically, we propose a new loss function which incorporates area and size information and integrates this into a dense deep learning model. We evaluated our approach on a dataset of more than 2,000 cardiac MRI scans. Our results show that the proposed loss function outperforms other mainstream loss function Cross-entropy on two common segmentation networks. Our loss function is robust while using different hyperparameter λ .

1. Introduction

Image segmentation is a fundamental and challenging problem in computer vision, with the aim of partitioning an image in a meaningful way so that objects can be localized, distinguished and/or measured. In medical imaging, this is vital for further clinical analysis, diagnostics, treatment planning and measuring disease progression. High precision is typically required in bio-medical image segmentation [6, 24]. Recently, segmentation techniques based on deep convolutional neural networks (CNNs) have been developed for various medical imaging modalities, such as MRI, CT and X-ray, showing promising results and overcoming the limitations of conventional segmentation



Figure 1: Our proposed loss function

methods [17]. During the training process of a CNN model, its parameters are optimized through gradient descent approaches based on the errors measured by a loss function, which compares the prediction and ground truth images. Loss functions are critical for model optimization. In terms of classification problems, the L2 norm is also known as mean squared error (MSE) and cross-entropy (CE) are commonly used as loss functions [8, 33]. CE and the Dice coefficient (DC) have typically been used for segmentation problems [24, 12].

Despite the recent progress of using CNNs for biomedical image segmentation, the commonly used loss functions generally evaluate pixel-wise similarity. For instance, CE and DC focus on extracted features from specific regions [28]. While this can result in good classification and segmentation performance, low resultant loss function values may not necessarily correspond to a meaningful segmentation. For example, a noisy result can add many contours in the background representing incorrect segmentation, and object boundaries can be fuzzy due to the difficulty of classifying pixels near the boundary. We propose to address these issues by (i) building the length of the boundary segmentation contour into the loss function so that this is constrained and (ii) considering the fitting inside and outside of the estimated boundaries in order to preserve shape.

According to the WHO, cardiovascular disease (CVD) is the world's number one killer, taking 17.9 million lives per year. The segmentation of Cardiac Magnetic Resonance (CMR) images is important for the assisted diagnosis of CVD. However, there are a limited number of fully-automatic segmentation methods, which is essential for CVD diagnosis. Our segmentation work is part of the effort to address this global challenge by developing new solutions for the accurate and reliable analysis of CMR images for improved decision making.

1.1. Contributions

To the best of our knowledge, this is the first work which integrates length and region constraints into the loss function of CNN-based segmentation, as shown in Figure 1. The contributions of this work are:

- We develop a new loss function combining contour length and region information.
- Based on this, we develop a CNN model based on conventional Dense U-Net.
- We evaluate our model in a supervised bio-medical segmentation setting for CVD diagnosis.

2. Related Work

In this section, conventional and CNN-based segmentation methods and related to this work briefly reviewed in the following context.

2.1. Conventional Segmentation Methods

In the past few decades, various models have been proposed ranging from thresholding, edge detection, clustering, region-growing to more complex active contour models. Early models such as thresholding and region growing approaches are able to implement but the performance is limited due to its nature of using image intensity or texture information only [7]. Active contour models (ACMs) have shown more performance as represented by the active contour without edge (ACWE) model [4] and also Mumford-Shah' work [21]. In Chan and Vese's work, level set functions are introduced to formulate the segmentation model treated as an energy minimization problem solved through solving partial differential equations (PDEs). Later on, this model has been extended to multiphase problems and texture problems [31, 29]. Efficient solvers such as dual projection and graph cut methods have been introduced to improve the computational efficiency [20]. The common challenges for these models are time-consuming. On the other hand, supervised segmentation models based on feature extraction and neural networks or support vector machines also showed reasonable results. However, these models are based on hand-craft features for the segmentation thus dependent on the skills and experience of the researchers so it's limited applicability and result quality.

2.2. CNN-based Methods for Segmentation

As a class of deep neural networks, CNNs show remarkable performance in many computer vision tasks, such as classification, segmentation and registration. One of the particular strength of CNN based models is that they work in an end-to-end fashion, which can extract hierarchical and multi-resolution features during the learning process. CNN architectures like Alex-Net [14], VGG-Net [25], Google-Net [26] and Dense-Net [9] have been developed and introduced into various image recognition tasks. Broadly speaking, CNN based segmentation models can be classified into pixel-based or images-based approaches. The pixel-based approaches will classify each pixel into different objects as a classification problem. A patch is often produced for each pixel (or super-pixel) and the patch is used as input to CNN models for classification with the label of the pixel used as the target to train the model [5]. The image-based approaches, such as U-Net [24], will make an image as input and output will be the segmentation of the input image (the size will be the same). U-Net like models have become popular because of its good performance and simplicity when compared to pixel-wise approaches [28, 15, 12](Please sort out these references). However, due to the lack of consideration on outside the target so that small segmented objects occur around the boundaries. In order to tackle this problem, a network based on Dense-Net called one hundred layers Tiramisu was proposed by Jégou et.al [12] making each layer to connect with others in a feed-forward fashion for encouraging extracted features to reuse and for strengthening feature propagation so that Dense-Net can reduce the influence from outside features of targets. Dense-Net overcomes this limitation of U-Net in various medical image applications [15][12]. However, some researchers prove that developing different loss functions is also able to improve the performance of U-Net during the training process [18, 27, 1]. Arif et.al [1] address the gap by introducing a shape-aware term in the segmentation loss function. Their approach significantly improved the performance of cervical X-ray images by 12%. Inspired by the recent progress in loss function, we present a novel loss function borrowed from the conventional model to further improve the segmentation performance.

2.3. Loss functions

To train a CNN model, the loss function (or cost function) plays a significant role. Loss function is a function to measure the error of prediction or segmentation which can be back propagated to previous layers in order to update/optimize the weights. Here, we briefly review the commonly used loss functions. In the following equations, ground truth image (or expert annotation) and the prediction (or segmentation) is denoted as $T, P \in [0, 1]^{m \times n}$ respectively; n indexes each pixel value in image spatial space N; the label of each class is written as l in C classes.

Cross-Entropy (CE) Loss: CE is a widely used pixel-wise measure [24] to evaluate the performance of classification or segmentation model. For two-class problems, CE loss function can be expressed as Binary-CE (BCE) loss function as follows:

$$Loss_{BCE}(T, P)$$

= $-\frac{1}{N} \sum_{n=1}^{N} \left[T_n \cdot \log(P_n) + (1 - T_n) \cdot \log(1 - P_n) \right]$

CE loss functions treat the output from softmax layer as a pixel classification problem to evaluate each pixel. *Ronneberger et al.* [24] pointed out that in order to improve the performance in cells' border segmentation from biomedical images, CE loss function with weighting scheme can be as one of the solutions to help U-Net model segments cells border as accurately as possible. Moreover, there are numerous studies on CE-based loss functions but merely a few functions consider the geometric detail of objects [16].

Dice Coefficient (DC) Loss: DC is traditionally used as a metric for the evaluation of the segmentation performance and now also demonstrated a good performance as a loss function [19]. DC measure the degree of overlapping between the reference and segmentation. This element-wise measure ranges from 0 to 1 where a DC of 1 denotes perfect and complete overlap. DC can be defined as:

$$DC(T, P) = 2 \cdot \frac{\sum_{n=1}^{N} (T_n \times P_n)}{\sum_{n=1}^{N} (T_n + P_n)}$$
(1)

DC loss is defined in Eq.(2) as it tends to the best segmentation.

$$Loss_{DC}(T, P) = 1 - DC(T, P)$$
⁽²⁾

Even though CE and DC loss functions have achieved a success in image segmentation, there are two main limitations: they are pixel-wised loss functions to measure the similarity between T and P, but the geometrical information are not taken into consideration.

2.4. Active Contour Models

In this section, we provide some background knowledge of the ACMs firstly proposed by *Kass et al.* [13]. ACM models treat segmentation as an energy minimization problem where the energy of an active spline/contour is minimized by PDEs-based methods toward the objects' boundaries. In classic ACMs, detecting objects' boundaries is by image gradients. However, this has one main limitation that it will be stuck at a local minimum. Therefore, it cannot get satisfactory segmentation results. In the past two decades, a number of ACMs have been proposed, such as active contour without edge (ACWE) model and fast global minimization-based active contour model (FGM-ACM) proposed by *Bresson et al.* [3].

The ACWE model can be formulated as the following energy minimization problem:

$$\min_{\Omega_c, c_1, c_2} \{ E_1^{ACWE}(\Omega_c, c_1, c_2, \lambda) \\
= \int_0^{Length(C)} ds \\
+\lambda \int_{\Omega} (c_1 - f(x))^2 dx \\
+\lambda \int_{\Omega/\Omega_c} (c_2 - f(x))^2 dx \},$$
(3)

where ds is the Euclidean element of length, the first term of Eq.(3) is the length of the curve C, and f is the image to be segmented, Ω_c is a closed subset of the image f domain Ω . The mean value of f outside and inside are denoted as c_1 and c_2 , respectively. λ is an arbitrary fixed parameter ($\lambda > 0$) to controls the balance between regularization process and c_1 , c_2 . The energy E_1^{ACWE} (3) can improve because it naturally adds more constraints including the contour length than DC and CE loss function. In order to solve the segmentation formulation, Heaviside function of level set method and PDEs were introduced to decrease the energy E_1^{ACWE} . E_1^{ACWE} can be rewritten as follows:

$$E_2^{ACWE}(\Omega_c, c_1, c_2, \lambda)$$

$$= \int_{\Omega} |\nabla H_{\epsilon}(\phi)| dx$$

$$+\lambda \int_{\Omega} H_{\epsilon}(\phi)(c_1 - f(x))^2 dx \bigg\}$$

$$+\lambda \int_{\Omega/\Omega_c} H_{\epsilon}(-\phi)(c_2 - f(x))^2 dx \bigg\}$$
(4)

where H_{ϵ} is a smooth approximation of the Heaviside function. And the gradient descent method minimizing of E_2^{ACWE} (4) is defined as:

$$\partial_t \phi = H'_{\epsilon}(\phi) \left\{ div \left(\frac{\nabla \phi}{|\nabla \phi|} \right) - \lambda r_1(x, c_1, c_2) \right\}$$
(5)

where $r_1(x, c_1, c_2) = (c_1 - f(x))^2 - (c_2 - f(x))^2$ shown in Eq.(5). However, PDEs-based solutions including ACWE need to be solved on each individual image, which is time-consuming. While they can give very good results, this makes ACWE less suitable for application in clinical settings where fast results, often as short as a few seconds, are needed. In order to achieve global minimization fast and stable, a E^{ACWE} based on total variation energy TV was proposed [3] which is defined as in Eq.(6):

$$E_4^{ACWE}(u,c_1,c_2,\lambda) = TV_g(u) + \lambda \int_{\Omega} r_1(x,c_1,c_2) u dx$$
(6)

where u is a characteristic function $\mathbf{1}_{\Omega_c}$. $TV_g(u)$ is total variation energy. Eq.(6) can also be written as:

$$E_4^{ACWE}(u, c_1, c_2, \lambda) = \underbrace{\int_0^{Length(C)} g|\nabla u|ds}_{\text{Length}} + \lambda \underbrace{\int_\Omega ((c_1 - f(x))^2 - (c_2 - f(x))^2)udx}_{\text{Region}}$$
(7)

where, u is a characteristic function valued between 0 and 1. $E_4^{ACWE}(7)$ provides a global minimum for ACWE model. Moreover, due to the limitation of the previous version of ACWE model based on Heaviside function and PDEsbased solutions, it provides a fast and non-stationary solution while u is restricted from 0 and 1. And also, this minimization problem of ACME to carry out segmentation task is able to apply into the deep learning field as it is constrained and some parameters can be fixed due to supervised learning and some parameters can be treated as trainable parameters to evaluate this minimization equation in an end-to-end learning fashion. In the §3 we will present more details of it.

3. Our Method

We propose a loss function inspired by the general idea of active contour model building in region and length terms for bio-medical image segmentation by U-Net-like based deep learning architectures. The work-flow is displayed in Figure 2. Our loss function denoted as AC, is in §3.1. Our main CNN Architecture in §3.2 is introduced.

3.1. AC Loss Function

The idea of proposed AC loss is behind the minimization problem of ACWE model (6) to efficiently find an active contour which is a global minimization of active contour energy for automated image segmentation. In the following equations, ground truth (reference segmentation) and the predicted value is denoted as $v, u \in [0, 1]^{m \times n}$ respectively. A 2-dimensional example of our AC loss function is defined as follows:

$$Loss_{AC} = Length + \lambda \cdot Region,$$
 (8)

in which.

$$Length = \int_{C} |\nabla u| ds \tag{9}$$

$$Region = \int_{\Omega} ((c_1 - v)^2 - (c_2 - v)^2) u dx$$
(10)

Therefore, *Length* and *Area* of Eq.(9) and Eq.(10) can be written into pixel-wised way respectively as follows:

$$Length = \sum_{\Omega}^{i=1,j=1} \sqrt{\left| (\nabla u_{x_{i,j}})^2 + (\nabla u_{y_{i,j}})^2 \right| + \epsilon} \quad (11)$$

where, x and y from $u_{x_{i,j}}$ and $u_{y_{i,j}}$ are horizontal and vertical directions respectively. ϵ ($\epsilon > 0$) is a parameter to avoid square root is zero in practice.

Region =
$$\left| \sum_{\Omega}^{i=1,j=1} u_{i,j} (c_1 - v_{i,j})^2 \right| + \left| \sum_{\Omega}^{i=1,j=1} (1 - u_{i,j}) (c_2 - v_{i,j})^2 \right|$$
 (12)

where, in the ACWE model 3, c_1 and c_2 are variable and defined as follows:

$$\begin{cases} c_1 = \int v \cdot u dx / \int u dx \\ c_2 = \int v \cdot (1-u) dx / \int (1-u) dx \end{cases}$$
(13)

due to supervised-learning framework, c_1 and c_2 are represented as the energy of inside (foreground) and outside (background) and can be simply defined as constants in advance as $c_1 = 1$ and $c_2 = 0$. u and v are represented as prediction and a given image respectively. In practice, we set $\epsilon = 10^{-6}$ as a small positive number to avoid the $\sqrt{0}$ issue in Tensorflow initialization. Therefore, we proposed a new loss function building on the length of the boundary segmentation contour and considering the region fitting for not only has the same nature of non-convex from Eq.(7) but also our new loss function is fit for shape preservation.

3.2. CNN Architecture

In this subsection, we detail and use U-Net [24] and dense U-Net [24] architectures as our base segmentation frameworks to evaluate our proposed loss function performance. Recently, U-Net is proposed and widely used which is an end-to-end and encoder-decoder neural network for semantic segmentation with high precise results. As one of the



Figure 2: Overview of our proposed method which takes the object's area and length of the boundaries into account during training.

essential building blocks is skipped connections which are designed for forwarding feature maps from down-sampling path to the up-sampling path in order to localize high resolution features to generate a segmentation output. In the down-sampling path, each layer consists of two 3×3 convolution layers, one rectified linear unit (ReLU) and one max pooling layer. In the up-sampling path, every step includes one 2×2 up-convolution layer, one concatenation operation with related feature map by skipped connections and two 3×3 convolution layers. Overall, U-net network has 23 layers.

As CNNs based segmentation network going deeper, a "gradient vanish" problem occurs. Therefore, to address this problem, Dense block based U-Net, namely Dense-Net [24], was proposed which allows each layer to connect directly other layers for preserving the feed-forward nature. And also, parameters and extracted features from the network are more efficient and are able to reuse. In Dense-Net framework, a dense block layer, transition down and transition up are introduced. A dense block layer consists of Batch Normalization (BN), ReLU and a 3×3 convolution, in which these layers connect densely. The output of a dense block is the concatenation of the outputs of the above 4 layers. In the down-sampling path, it consists of 38 layers. There are 15 and 38 layers in the bottleneck and up-sampling path. In total, Dense-net network has 103 layers.

4. Experiments

We used U-Net and dense U-net as our two-class segmentation CNN architectures and compare the final segmented performance when using commonly used loss functions CE and DC and our proposed AC loss function, respectively.

4.1. Dataset

Therefore, we demonstrate our model on a publicly available large-scale and multi-centre study cardiac magnetic resonance (CMR) images dataset. This dataset was made available as which from a publicly available dataset: MICCAI 2017 Automated Cardiac Diagnosis Challenge $(ACDC 2017 Challenge)^1$. The primary reason for this is that it is always a challenging task to segment bio-medical images as there are huge variations between images and high reliability and accuracy are often required. The secondary reason for using CMR images is due to the publically availability which will allow reproducible research. Third, CMR images play an important role to help patients with heart disease in diagnosis as well as pre-/post-operative planning. However, due to labour-consuming and subjective biases suffered by human measurement, computerassisted diagnosis is demanded while there are only limited studies for the development of accurate approaches for the segmentation of cardiac CMR [28]. In total there are 150 volumetric MR image sequences of patients with cardiomyopathy acquired by two different MRI scanners. All the 1,891 Cine MR scans are re-sampled into 256×256 pixels. The corresponding ground truth label maps are annotated by a clinical expert team from the University Hospital of Dijon. In which, background, right ventricle, myocardium and left ventricle for each ground truth image are labelled, respectively. Example images and their corresponding ground truth are shown in the first left columns of Figure 5. In our experiment, the dataset is partitioned into three subsets: training (1193), validation (298) and testing (400).

4.2. Performance Metrics

For quantitative assessment of the segmentation, Hausdorff distance (HD) are used for segmentation accuracy assessment (smaller more better). HD is a symmetric measure

¹ACDC 2017 Challenge https://acdc.creatis.insa-lyon.fr/



Figure 3: Segmentation results of left ventricle (red), right ventricle (green) and myocardium (blue) of five examples images using 2D U-Net and 2D Dense-Net with CE and our AC loss functions. From left to right, the example-original MR image, ground truth, segmentation results by U-Net+CE, U-Net+AC, Dense-Net+CE and Dense-Net+AC are shown respectively.

of distance between two contours and is defined as [23]:

$$\mathbf{D}_{H}(T,P) = \max\left\{\sup_{t\in T} \inf_{p\in P} d(T,P), \sup_{p\in P} \inf_{t\in T} d(T,P)\right\}$$
(14)

where $T, P \in [0, 1]^{m \times n}$ are the ground truth contour and the predicted contour respectively, t and p represent pixels

of T and P, d(t, p) is Euclidean distance between t and p.

5. Results

We implemented our networks using Keras 1.1.0 with Tensorflow_gpu 1.10 as backend. We trained our models until convergence by using the ADAM optimizer with a learning rate of 10^{-4} . All the experiments were performed using an Intel CPU, and a NVIDIA TitanX GPU. Upon acceptance of the manuscript, our trained models will be made available online at *https://github.com/xuuuuuuchen/ACloss*. In Figure 3, segmentation results of left ventricle, right ventricle and myocardium of five examples images using 2D U-Net and 2D Dense-Net with CE and our AC loss functions are displayed respectively.

5.1. Performance

Table.1 showed the comparison results for the segmentation of left ventricle, right ventricle and myocardium between U-Net and Dense-Net when either CE or our AC loss function was used. The proposed approaches U-Net-AC has improved HD than U-Net-CE, so do Dense-Net+AC. As such we used the results of Dense-Net+AC for the comparative studies with previous studies. As shown in Table.1, our AC loss function based on Dense-Net (Dense-Net+AC) model achieves better results than others for all the segmentation tasks. The HD is 33.8%, 46.5% and 37.7% higher for the segmentation of left ventricle, right ventricle and myocardium respectively.

In Table.2, it presents that comparison with U-Net and Dense-Net with CE loss function and our AC loss function. In which, left ventricle, right ventricle and myocardium are listed at the top respectively. We use DC and HD for evaluating the performance. The proposed approaches U-Net-AC, as well as Dense-Net+AC, are compared against general segmentation frameworks: U-Net and Dense-Net with CE loss function. In Figure 4, the computing time per epoch for AC is 110s, shorter than CE at 121s, during training for DenseNet. For UNet, AC takes 15s while CE takes 17s. For testing, it takes almost the same time when the same network is used.



Figure 4: Running time per epoch for AC and CE loss functions within different models

5.2. Robustness Analysis

We evaluated the effect of the regularization weight λ in our AC loss function Eq.(8) by DC score. As shown in the Figure 5, our DenseNet-based model is robust to the choice of λ with different λ values. When λ is close to zero, the DC result tends to be worse because only boundary term contributes to our loss function. We aslo evaluated the DenseNet-based model with region terms only under the same conditions compared with Dense-CE model. The performance (Dice Score) for this is 0.9634, worse than AC (0.9708) but better than CE (0.9442).



Figure 5: Effect of varying the parameter λ on DC score

6. Discussion

Our proposed method AC loss function is able to take into account geometric information of the areas be segmented. We present two basic segmentation models U-Net and Dense-Net as a base to prove that our proposed loss function is robust in mainstream architectures. Our results also demonstrate that our model of loss function performs signicantly better than commonly used loss functions such as CE and DC when we test on a public MR ventricle dataset. Our results also demonstrate superior performance when compared to other start-of-art segmentation approaches. Compare to standard ACWE models which require iteration in solving PDEs, the use of CNNs have hugely reduced the computational time on new images although the training time will be longer.

We tested different values of the regularization weight λ to show this loss function is robust. In future work, we will investigate how to make λ can be learned during the training process. Similar to CE and DC that can be extended to multi-class segmentation problems [22], the proposed loss function can also be extended to solve multi-phase segmentation problems as the traditional ACM have demonstrated [32].

Table 1: Comparison with two different network: U-Net and Dense-Net on cardiac segmentation followed by CE loss function and our AC loss function. The three objects from cardiac MR scans (left ventricle, right ventricle and myocardium) are listed respectively. We use HD for evaluating the performance of segmentation. The proposed approaches U-Net-AC and Dense-Net+AC are compared against state-of-the-art segmentation U-Net and Dense-Net with CE loss function. Standard deviation is presented in the buckets respectively.

Objects	left ventricle	right ventricle	myocardium	
Methods	Hausdorff Dist.	Hausdorff Dist.	Hausdorff Dist.	
	(mm)	(mm)	(mm)	
U-Net-CE	18.29 (2.04)	23.76 (2.52)	18.04 (1.97)	
U-Net-AC	17.36 (2.76)	22.94 (2.48)	16.60 (2.05)	
DenseNet+CE	5.43 (1.81)	6.21 (1.05)	6.34 (1.56)	
DenseNet+AC	4.73 (1.35)	5.95 (0.99)	5.42 (1.10)	

Table 2: Comparison with previous approaches on cardiac segmentation. In the top of table, the three objects (left ventricle, right ventricle and myocardium) are listed respectively. The accuracy is evaluated in terms of mean Dice Coefficient (DC) score and Hausdorff distance (HD). The proposed approach (Dense-Net+AC) is compared against state-of-the-art cardiac segmentation models: Wolterink et al. [30], Baumgartner et al. [2], Yeonggul Janget al. [11] and Isensee et al. [10]. Standard deviation is presented in the buckets respectively.

Objects	left ventricle		right ventricle		myocardium	
Methods	Dice Score	Hausdorff Dist.	Dice Score	Hausdorff Dist.	Dice Score	Hausdorff Dist.
	(%)	(mm)	(%)	(mm)	(%)	(mm)
Wolterink et al.	0.930	8.68 (4.51)	0.880	14.21 (6.04)	0.870	11.31 (5.62)
Baumgartner et al.	0.950	N/A	0.893	N/A	0.899	N/A
Yeonggul Jang et al.	0.938	7.27 (4.83)	0.890	13.69 (4.83)	0.879	9.76 (0.04)
Isensee et al.	0.950	7.14 (N/A)	0.923	11.13 (N/A)	0.911	8.69 (N/A)
Dense-Net+AC	0.986	4.73 (1.35)	0.940	5.95 (0.99)	0.969	5.42 (1.10)

7. Conclusion

In this paper, we introduced a new AC loss function that was inspired by ACMs for the segmentation tasks. The advantage of this new loss function is that it can seamlessly combine the geometrical information (e.g. boundary length) with region similarity thus leading to more precise segmentation. After implementation, we applied it to a large-scale CMR dataset and the results showed that the proposed approach outperforms state-of-the-art approaches. It is believed that this new development will be readily applied to other challenging segmentation tasks posed by various real applications.

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